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MRC-NICE Scoping Project: Identifying the National Institute for Health and Clinical Excellence's Methodological Research Priorities and an Initial Set of Priorities

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MRC-NICE Scoping Project: Identifying the National Institute For Health And Clinical Excellence's Methodological Research Priorities and an Initial Set of Priorities

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Background

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EXECUTIVE SUMMARY

Background

As part of the co-coordinated strategy for health research under the Office for Strategic Coordination of Health Research (OSCHR), the Medical Research Council (MRC) is the lead organisation for methodological research in the UK. The National Institute for Health and Clinical Excellence (NICE) is an important public stakeholder in this research area, and it has faced a range of challenges in the selection and specification of research methods employed in the production of its guidance for the NHS.

Objectives

The aim of this 6-month project was to undertake a scoping study to provide recommendations for identifying NICE's methodological research priorities and to establish an initial set of such priorities. Specifically the project had three main objectives:

(i)   To describe current processes by which methodological research topics are identified and prioritised at NICE.
(ii)   To suggest a range of additional and/or alternative approaches to identifying these priorities.
(iii)   To generate an initial short list of methodological research topics.

Methods

A focussed review of recent key policy reports and documents produced by NICE was conducted to obtain information on the process by which methodological research needs are currently identified and prioritised at NICE. The review also sought to identify suggestions for methodological research topics directly related to decision-making at NICE. These documents were supplemented by a focussed review of the literature for the purpose of identifying suggestions for methodological research topics.

A series of semi-structured interviews with individuals involved in various ways with NICE was undertaken by telephone and in face-to-face meetings. Those interviewed included employees of NICE, members of its advisory committees, individuals from industry and representatives of organisations closely linked to NICE, such as the Medical and Healthcare products Regulatory Agency (MHRA). The objectives of the interviews were to obtain information on the current processes of identifying and prioritising methods research needs at NICE, and elicit opinions on how these processes could be further developed. Interviewees were also asked about their suggestions for priority topics for future research. An email survey was administered to a broader range of NICE employees, the academic groups who conduct reviews of the evidence for NICE and representatives of a selection of similar organisations outside of the UK.

A list of potential research topics identified from the literature, interviews and the email survey was collated. A workshop was held to discuss the list of topics, to consider how these might add value to NICE's decision-making and whether the questions could be further defined. Participants were also encouraged to highlight potential priority topics missing from the list and to feedback on topics within and across areas of methodology. Following the workshop an amended list of topics was made available via a feedback form on the MRC website. The list was publicly available and people who had been invited to attend the workshop were specifically encouraged to complete the feedback form. Individuals were given the opportunity to score each topic on the list (using a categorical scale: very important, important, somewhat important and not important), to provide comments and to offer other potential topics. In addition respondents were asked to identify three topics they considered to be the most important for future research.

Results

A total of 18 interviews were undertaken and 13 (39%) of a possible 33 responses to the email survey were received. Seventy-six responses to the web feedback exercise were received.

Process

Little emerged from the review of literature and key policy documents regarding how NICE currently identifies and prioritises potential methodological research topics. Several formal and informal processes at NICE were, however, highlighted during interviews and the email survey. Formal processes include the regular reviews of the NICE methods guides, the activities of the NICE Research and Development Advisory Committee (RDAC) which advises NICE about its research and development work and a Technical Forum of NICE's technical staff. A range of informal processes for identifying methodological research topics was noted including identification of issues arising during the course of guidance production. Many interviewees commented on a lack of a formal Institute-wide process to collate and prioritise methodological research topics.

Specific suggestions for changes in the future included the creation of a 'Methodology Committee' with members from both within and outside of NICE, the identification of potential topics as a specific agenda item in existing (decision-making) committee meetings, greater collaboration between interested parties both within and outside of NICE and the creation of a formal process for following up recommendations for topics which have come from the various methods guides. Respondents felt that an explicit process for prioritisation would be useful. Most of the respondents felt that any criteria for prioritisation should be on the basis of the issues most important to NICE decision-making. The need to identify funding for methods work was also raised by many of the respondents, particularly those external to NICE.

Topic suggestions

Within each stage of the project a slightly different group of individuals, each with varying degrees of links to NICE, was canvassed for their views on priority topics. Those who were interviewed and included in the email survey had direct links with NICE, mostly as members of staff, advisory committees or designated providers of evidence. The workshop included those with direct links to NICE and a broader group, including methods experts. The web feedback exercise included responses from some of those who attended the workshop, but also people who stated that they had no direct involvement with NICE. The topics emerging as priorities from the different exercises are noted below.

Priorities emerging from the interviews and email survey:

- methodology for indirect and mixed treatment comparisons
- synthesis of qualitative evidence in the NICE decision-making process
- use of quality adjusted life years in decision-making (specifically establishing what benefits of treatment are not captured by the QALY and/or standardised measures of health-related quality of life)
- establishing the threshold for cost-effectiveness (including the appropriate methods for estimating this)
- determining how data on the uncertainty of effectiveness and cost-effectiveness data should be taken into account in the decision-making process

Priorities emerging from the workshop:

- methods for keeping research synthesis up to date (including developing repositories of 'approved' networks of evidence in key diseases)
- methods to assess what types of evidence from patients should be used at different stages of NICE's decision-making processes (e.g. when to undertake reviews of qualitative evidence? When should colloquial evidence be used?)
- extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty

- establishing what effects of interventions and programmes are/are not currently captured by the EQ-5D
- methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead
- methods for valuing health at different time points in a person's life (e.g. at the end of life)
- methods to determine whether public or patient valuations of health should be used in economic evaluation
- methods for establishing opportunity cost of NICE guidance (i.e. the threshold) and empirical data on interventions that are being displaced by NICE guidance

Priorities emerging from the web feedback exercise:

- optimal methods for analysing disease registers and other non-experimental data sources
- methods to adjust for bias in meta-analysis
- methods for conducting systematic reviews of complex interventions
- optimal methods for evaluating diagnostic and screening technologies
- methods for conducting efficient systematic reviews
- methods for the extrapolation of costs and benefits
- research to assess whether the predictions of economic models are borne out in practice
- methods to capture wider benefits not captured in the QALY
- methods to assess whether additional evidence is needed prior to the routine introduction of interventions (e.g. 'only in research' or 'coverage with evidence' decisions).

Conclusions

Methodological topics have been discussed with the MRC and, in a few cases, taken forward as vignettes and, in one case, active commissioning has taken place. This indicates that some form of process exists through which these topics were selected and progressed. However, there is clearly a need for a formal Institute-wide process to collate and prioritise topics. A range of ideas emerged on how this might be progressed. Issues to consider in any changes to the process include:

- How the full range of NICE's activities are to be covered, recognising the variety of methods issues that are likely to be seen as important across the centres and teams.
- Which team or as yet unspecified group of individuals within the Institute is to be the repository for topic suggestions over time? To what extent would this team/group be proactive in identifying topics or wait to be contacted by others?
- Whether specific discussion forums within NICE are organised at which methodological issues are discussed with a view to identifying potential research topics and feeding into the prioritisation process.
- What role would be played by those not formally employed by NICE, but closely related to its activities, in the identification process?
- What role would be specified for external methodologists in the process of identification and prioritisation?
- What role could external stakeholders and research funders play in the process of topic identification and prioritisation (e.g. technology manufacturers)?

Relatively few comments emerged on the process of prioritisation of a long-list of potential research topics. One feature of a more explicit process that may be of value (and has been part of the web-based prioritisation reported here) is to ask those individuals and groups forwarding topics to justify their suggestions by addressing some very key questions for each. These might include: To which area of NICE's activities does the research relate? What potential exists for methodological research to increase the value or efficiency of NICE's activities?

Little was discussed in the interview and survey about two particular issues. The first is how to translate an area of methodological uncertainty where it is felt that research might be potentially helpful into a researchable question. The second relates to the use of methodologists external to NICE who might contribute to the process of identifying and prioritising research topics, and then working them up into researchable questions. The advice of such externals is likely to be important in

the process, but the problem of their potential conflicts of interest are clear if they were subsequently to bid for research in a topic on which they have advised.

An alternative approach would be to work with the MRC to prepare quite general calls for methods research applications – that is, to take topics which are not much more specifically defined than those detailed here as coming out of the scoping project.

In terms of potential topics, a total of 125 topics were presented on the web survey, with a limited number of additional suggestions coming from that part of the process.   Across the five areas into which topics were arranged, there appears to be a broad relevance across the range of NICE's decision-making activities.

The issue of what constitutes methodological research was raised throughout the project. This needs to be addressed as research topics are considered further and attempts are made to link them with appropriate potential research funders.   A large proportion of suggested topics would probably be considered clearly methodological in that they relate to the further development and refinement of evaluative and analytical tools which have relevance beyond a single application.   Other topics may be considered less obviously methodological. It may be that research commissioners other than the MRC Methodology Research Programme, whose remit is specifically focussed on generalisable methods development research, should be approached about funding some of the topics suggested in this document.

1. Introduction

1.1 Introduction

The National Institute for Health and Clinical Excellence (NICE) has established a national and international reputation for its use of evidence and rigorous analytical methods to inform decisions about the effectiveness and the cost-effectiveness of medical and public health interventions and programmes. Few health care organisations globally have been so ambitious in their use of evidence-based decision-making. All aspects of NICE's activities have faced a range of challenges, in particular regarding the selection and specification of research methods. For example, in reviewing NICE's Technology Appraisal Programme, the House of Commons Health Select Committee drew attention to a number of issues with important methods implications.[1]

As part of the co-coordinated strategy for health research under the Office for Strategic Coordination of Health Research (OSCHR), the Medical Research Council (MRC) is the lead organisation for methodological research. NICE is an important public stakeholder in this research area, and improving methods for undertaking health technology assessments, appraisals and evidence synthesis was also highlighted as an area for further research in the Cooksey review.[2] Issues of appropriate research methods have also been raised by the Office of Fair Trading's report on pharmaceutical price regulation.[3]

To help identify priority methodological research topics to support NICE's decision-making, the MRC commissioned a group of researchers to undertake a short scoping project to provide recommendations for identifying NICE's methodological research priorities and to establish an initial set of such priorities.

1.2 Aims and objectives

The agreed aim of the project was to undertake a scoping study to provide recommendations for identifying NICE's methodological research priorities and to establish an initial set of such priorities. Specific objectives agreed with the MRC were:

1. To describe current processes by which methodological research topics are identified and prioritised at NICE.
2. To suggest a range of additional and/or alternative approaches to identifying these priorities.
3. To generate an initial shortlist of methodological research topics by:
    (a) Reviewing recent key literature relating to NICE's activities with a view to identifying issues with potential implications for methodological research.
    (b) Convening a workshop to develop a 'long list' of methodological research priorities.
    (c) Using a web-based interface, to engage the methodological research community in scoring topics from the 'long list'.

2. Methods

2.1 Literature review

Given the time and funding constraints, it was not possible to undertake an extensive literature review. A highly focussed literature review was undertaken to identify two types of information:

1. Details of the process by which methodological research needs are currently identified and prioritised at NICE.
2. Suggestions for methodological research topics.

A broad view of methodological research was taken. The review specifically focussed on recent publications relating to NICE which may have discussed the process of identifying and/or prioritising methods topics at NICE and/or raised issues with potential implications for methodological research.

A number of key policy documents and journal articles such as the Cooksey report on health research funding, the House of Commons Health Select Committee report on NICE and the NICE methods guidance documents were identified by the project team and its advisors, and included reports identified in the project specification. A full list of the policy documents considered is provided in Appendix A7. The documents were reviewed in their entirety and data extracted using a number of headings. Specifically these were:

1. Does the paper comment on the current process/system that NICE uses to prioritise methodological research?
2. Does the paper make suggestions for research into methodology that is relevant to decision-making at NICE?
3. Does the paper work these suggestions into researchable questions?
4. Does the paper comment on the type of research required to address these questions?
5. Does the paper make any other relevant comments?

In addition, focussed searches (see below for search strategies) were conducted by an information specialist. These included searches of recent conference abstracts (e.g. NICE conference) and reference lists of important identified articles. This was supplemented by use of recent literature searches that are routinely conducted by information specialists at NICE for the purpose of identifying articles of interest for NICE technical staff. In addition, reports from a series of workshops held as part of the 2008 review of the methods for NICE technology appraisals were reviewed. Suggestions for key articles were also canvassed from the wider project team.

2.1.1 Search strategies

An initial current awareness search on NHSEED (which searches MEDLINE and EMBASE) and the Cochrane Methodology register was conducted by colleagues at the Centre for Reviews and Dissemination (CRD) at the University of York. This focused on identifying methods papers in the period 2004-2008. Search terms were restricted to *methodology, method, methods*.

In addition, papers were identified by a NICE information specialist. These searches are restricted to Medline and Medline-in process. The search terms used are given in Appendix A1.

2.2 Interviews

Discussions with individuals involved with NICE's activities (hereafter referred to as 'stakeholders') were central to defining options for alternative approaches for identifying research needs. The list of individuals to interview was guided by the MRC and NICE.

A combination of face-to-face and telephone interviews was used with the various stakeholders. Stakeholders who were interviewed included: the chair (and other members) of the NICE Research and Development Committee; directors of the centres of Health Technology Evaluation, Clinical Practice and Public Health Excellence and the Clinical and Public Health Director; representatives of the Technology Appraisal Committees, Public Health Interventions Advisory Committee, Interventional Procedures Advisory Committee and guideline development groups; and

representatives from the pharmaceutical industry. The full list of interviewees can be found in Appendix A2 in the appendix, along with the methods employed for the interviews.

The interviews were semi-structured and their content was shaped, in part, by the review of key documents described above. The interview schedule for face-to-face and telephone interviews is presented in Appendix A3. The questions in the schedule were used as prompts where necessary and questions were not necessarily asked to all interviewees if they were not appropriate.

Interviewees were asked about the current processes at NICE for identifying and prioritising methodological research, and for their opinions regarding potential changes to those processes. During the interviews stakeholders were also asked to identify priority topics for methodological research. These were topics that could have a direct impact on the decision-making process at NICE.

2.3 Email survey

In addition to the face-to-face and telephone interviews, an email survey of other stakeholders was also conducted. This was to allow the views of a wide range of NICE stakeholders to be accounted for. The recipients of the email survey included:

- NICE employees (associate directors with responsibility for methodology in the clinical guideline and public health programmes, and technical advisers)
- NICE Technology Assessment Group (TAG)/Evidence Review Group representatives
- National Collaborating Centres (NCCs) Clinical Guideline representatives
- Healthcare Commission
- National Institute for Health Research
- Health Departments (England, Northern Island, Scotland, Wales)
- The Cochrane Collaboration
- The Campbell Collaboration
- The Society for Research Synthesis Methodology
- International Organisations (German Agency for HTA, European Network for HTA, Agency for Healthcare Research and Quality, International Society for Pharmacoeconomics and Outcomes Research).

The selected respondents were divided into four groups based on their relationship with NICE, their role within similar organisations, and their role within a research funding/providing organisation. Using these groupings, stakeholders were sent one of four versions of the survey (see Table 1 below). Copies of the four surveys can be found in Appendix A4, along with a list of responders.

Table 1: Content of email survey by respondent group

Group	Potential methodological research priority topics	Potential future processes for identifying methodological research priorities	Current NICE process for identifying methodological research priorities	Current process [in their own organisation] for identifying methodological research priorities
1. NICE secretariat	Y	Y	Y	
2. UK Healthcare/ Research organisations/ International HTA	Y	Y		Y
3. Evidence Collaboration Organisations	Y		Y	
4. UK HTA methodologists/ NCC and TAG representatives	Y			

2.4 Workshop

A 1-day workshop was organised with the objective of clarifying and refining the list of potential methodology research topics identified via the literature review and interviews.

The workshop involved 38 participants whose selection was agreed with the MRC and NICE. The participants included the project team, key staff from NICE, members of NICE decision-making committees, representatives from InterTASC (the collaborative group of academic technology assessment groups), national collaborating centres, public health assessment groups, industry, other stakeholders and methodologists. The full list of workshop participants can be seen in Appendix A5.

The agenda for the workshop is presented in Appendix A6. The workshop was structured around the potential methodological research topics identified from all the preceding stages of the project which were grouped into five broad methodological areas:

1. Analysis and design of effectiveness studies and their synthesis
2. Synthesis of evidence from patients, the public and stakeholders
3. Economic analysis and uncertainty
4. Measurement and valuation of benefits
5. Decision-making at NICE

Following presentations from key methodologists who gave an overview for each of the topic areas, delegates engaged in a series of small group discussions about the topics within each area. Each small group was assisted by a facilitator and a scribe. Participants were asked to review the list of topics and consider the following questions:

- Do they address challenges?
- How can they add value to NICE's role?
- Can questions be further defined?
- Are there additional topics?
- What should be the initial prioritisation?

The intended output from the workshop was the suggestion of other topics not identified via the literature review and interviews, dismissal of particular topics which the workshop attendees felt had been significantly well researched not to require further prioritisation and general feedback on the priority of topics within and across areas of methodology.

2.5 Web-based consultation

The list of topics generated from the literature review, interviews and email survey were updated following feedback from the workshop. This list of topics was then placed on the MRC website to which those invited to the workshop, and a wider group of individuals, were given access. Individuals were given the opportunity to score each topic on the list (with options of very important, important, somewhat important and not important), to provide comments and to offer other potential topics. In addition, they were asked to provide their top three topics across areas and themes. The aim of this aspect of the project was to identify topics to feed into NICE's future determination of methodological research priorities.

2.6 Analytical methods

2.6.1 Analytical methods relating to processes

Responses to the face-to-face and telephone interviews were collated with responses to the email survey. A thematic analytical approach was used to summarise the comments. This identifies themes emerging from the qualitative interviews.[4]

Comments relating to any current process for identification and prioritisation at NICE were largely based on responses from NICE staff. These were divided into comments relating to formal and informal processes employed at NICE. The wider network of respondents was used to summarise

comments relating to future processes. These distinguished issues relating to identification, prioritisation and funding of topics.

Comments relating to the process for identifying and prioritising topics at other organisations were summarised separately from the comments relating to NICE.

2.6.2 Analytical methods relating to topic suggestions

Topics identified in the literature review were added to those obtained from the interviews and email survey. Duplicate topics were removed and similar topics combined. A reasonably broad definition of methodological research was taken to ensure all relevant topics were captured, and that these related to all areas of NICE's decision-making activities. Topics were excluded that were considered not to relate to methodological research or that did not relate to decision-making at NICE. Following the workshop, some topic suggestions were rephrased for clarity and/or merged with other topic suggestions.

3. Process of identifying and prioritising topics

3.1 Process of identifying and prioritizing methodological topics at NICE

3.1.1 Literature review

Ten policy documents were reviewed.   With respect to journal articles, a total of 759 records were identified from the Centre for Reviews and Dissemination (CRD) current awareness searches along with 423 records from the NICE 'what's new' bulletin searches. Forty duplicate records were found which gave 1142 records in total. In addition six reports were included from workshops held as part of the 2008 review of the NICE Technology Appraisals Methods Guide.

The wider project team was consulted on the list of included papers. As a result two additional (in press) papers were identified. In total 1150 papers were screened for inclusion in the review. The titles and abstracts for all 1150 records were screened by two reviewers. No disagreements were found between the two reviewers.

After initial screening, only 19 papers were identified as considering methodological issues specific to NICE decision-making. These papers are listed in Appendix A7 and were reviewed in detail.

As described in the methods section, relevant information from these documents and articles was extracted using predefined questions. Three policy documents referred to processes used by NICE to develop or promote methodological research.[1, 5, 6] From the journal articles, no comments were made about the process that NICE uses, or could use, to identify and prioritise methodological research relevant to NICE's decision-making. The full extraction from these documents and articles can be found in Appendix A7, and a summary is provided below.

- The House of Commons Health Select Committee[1] praised the open nature of the development of the NICE methods guides, and comments that NICE's process and methodology should be continually developed and debated.

- The NICE Guide to the methods of technology appraisal[7] comments on the specific process by which the methods guide is updated, encouraging further development of methods, and describes how the Institute looks to regularly review its processes and methodology. It states that the Institute sponsors future research into HTA, and that it welcomes suggestions for research topics.

- The NICE R&D programme consists of a small team within the Clinical and Public Health Directorate and a Research and Development Advisory Committee (RDAC). One of their key objectives is to improve the research methods used by NICE. The programme also takes responsibility for the Citizens Council, a group of 30 members of the public which advises NICE on its social value judgements (www.nice.org.uk/aboutnice/howwework/researchanddevelopment/). The objectives, as stated in the most recent version of the R&D strategy, are detailed in full in Box 1. This document is in the process of being updated and some elements are no longer applicable (for example, the National Coordinating Centre for Research Methodology has ceased to operate). The 2004 R&D strategy document[5] highlights that NICE has limited capacity to act directly on resolving and producing research into methodological issues when they arrive. However, RDAC will consider topics of methodological uncertainty and, if it is agreed that these are of importance, relevance and benefit to NICE and other organisations, as well as being researchable, it will be directed to an external research funding body.

- NICE's 'End of Life' consultation document[6] was reviewed and, whilst no direct comments about the process that NICE uses to prioritise methodological research were made, this supplementary methods guidance is a formal change to NICE's decision-making criteria, and has not been developed through one of the formal reviews of NICE's methods, or the R&D process. It should be noted, however, that research commissioned by NICE and NHS R&D into weighting of QALYs had suggested that the public did not consider that the current NICE position that all QALYs should be considered equal was sustainable. The nature of this type of development does highlight a need for a responsive process of NICE methods research identification and mechanisms to ensure it can be undertaken within the necessary timeframe.

Box 1: Improving NICE methods (adapted from 2004 NICE Research and Development Strategy page 10 - http://www.nice.org.uk/niceMedia/pdf/R&D_strategy_2006.pdf)

NICE 2004 Research and Development Strategy - Objective 2 – Improving NICE methods

Background

The Institute's work programmes use a wide range of complex methods to develop questions, identify and critically appraise relevant evidence, involve stakeholders with a range of views, and generate guidance. NICE and its partners have taken great care to ensure that the methods used are robust and informed by up to date research and current best practice. Nonetheless, areas of uncertainty exist – for example, debate continues about the best approach to grading evidence and classifying clinical recommendations in NICE guidelines. These uncertainties present opportunities for improvement in the research base so that the methods underpinning the Institute's guidance continue to be of the highest quality.

Uncertainties can be uncovered in the process of work on a particular piece of guidance, but are more often highlighted as the processes and methods used by a programme are formally reviewed (as happens on a regular basis in all programmes). Some of these uncertainties are relatively intractable, and are likely to remain. Others can be resolved, or at least reduced, by the application of research findings. The Research and Development Programme will support the Institute in these areas.

Process
Uncertainties amenable to resolution within NICE
The Institute has access to some research capacity, including that of its own staff (e.g. Technical Forum) and staff employed in partner organisations (including the Review Body for Interventional Procedures, the National Collaborating Centres, the Technology Appraisals Review Groups and the Decision Support Unit). This capacity can be used to resolve some methodological uncertainties, which may constitute a good use of Institute resources, as well as developing internal capacity.

In such cases the R&D programme will have an important role in scrutinising and commenting on study protocols, providing support for ethical committee applications and advising on the approach taken. Additionally, the R&D programme will keep a record of such work. (For more details about the programme's approach to research in which it is involved, see section 7).

Larger questions
Some areas of methodological uncertainty are too large to be resolved using 'in-house' capacity. In such cases the following process will be followed.

• The programme proposing the research will submit a methods research recommendation to the Research and Development Advisory Committee.

• The Research and Development Advisory Committee will discuss the recommendation, reviewing its importance, clarity, relevance and benefit to NICE, relevance to other organisations and feasibility. The Advisory Committee will also wish to consider other ongoing methods research of relevance to the recommendation.

• If the Advisory Committee supports the recommendation it will be promoted to an external research funder, if it is of general importance to the NHS or others. Alternatively, if it is of particular interest to NICE, the R&D programme may fund the research, normally in partnership with the National Coordinating Centre for Research Methodology.

3.1.2 Interviews with stakeholders and email survey

The interviews with stakeholders were conducted by two of the project team members. In total 18 face-to-face and telephone interviews were completed (a list of the stakeholders that were interviewed is given in Appendix A2).

Response rates for the email survey were disappointing (see Table 2). Of thirty-three invited respondents, only thirteen (39%) completed surveys. Whilst the response rate is low, there was a reasonable response rate from NICE employees, UK HTA methodologists and NCC and TAG representatives. No responses were returned from evidence collaborations (group 3); however, two of the three invited recipients in this group responded that they did not feel sufficiently informed regarding NICE to respond.

Table 2: Response rates for the email survey

	Invited recipients	Respondents (proportion of invited recipients)
Group 1: NICE employees	5	3 (60%)
Group 2: UK Healthcare/ Research organisations/ International HTA	13	2 (15%)
Group 3: Evidence collaboration organisations	3	0 (0%)
Group 4: UK HTA methodologists/ NCC and TAG representatives	12	8 (75%)
Total	**33**	**13 (39%)**

The results of these interviews and responses to the email survey are summarised below. *Current* process for identifying and prioritising topics at NICE have been distinguished from *changes* to the process for identifying and prioritising topics.

3.1.2.1 *Current processes within NICE*

Formal processes. NICE staff described a number of formal processes within NICE, that contribute towards the identification and prioritisation of methods topics. These processes, however, have limited visibility to many people outside of NICE and many are unsure how these processes are connected, in particular to whom methods topics are fed for further consideration, and how they are taken forward. There was felt to be no overall strategic plan regarding the identification and prioritisation of methods topics. Areas that require methodological development tend to currently be identified at a team level rather than an Institute level, and these tend to be 'needs driven' rather than forming part of an overall strategic plan. Specifically NICE staff suggested that methods topics can be identified via the following avenues:

- We were told that the R&D team is very small and no longer has a formal budget for research funding. Perhaps because of this, the R&D team is used for what was described as *ad hoc* methodological issues. Not all of them are related to research (e.g. to help formulate and implement equalities plan).

- Within the R&D programme the Research and Development Advisory Committee (RDAC), was established in 2003, to advise NICE about its research and development work. We were told that this committee was originally a sub-Committee of the NICE board and, following NICE gaining responsibility for the confidential enquiries programme, had a specific budget associated with restructuring enquiries. However, the confidential enquiries programme is no longer part of NICE and the RDAC is now a strategic committee without a dedicated budget. The RDAC includes representatives from key partner organisations such the MHRA and MRC, as well as direct lay representation.   NICE staff suggested that the RDAC was originally intended to meet approximately three times per year, but had met infrequently at the time of writing. Many respondents felt that the role of this committee was unclear, in particular if research considered by the committee was clinical or methodological or a combination of both. Previously the RDAC has provided criteria for prioritising clinical research topics, and has also supported topic-specific initiatives, such as a joint workshop with AHRQ to discuss recommending interventions only in the context of research (OIR) initiative, a topic which was subsequently referred to the MRP and is currently in the process of being commissioned.

- The majority of respondents discussed the NICE's methods guides which are a highly visible output of NICE that contributes towards the promotion and development of methods work. Respondents indicated that each programme has a methods guide for stakeholders which is regularly updated. As part of the updating process, we were told that methodology areas that have caused concerns or uncertainties are highlighted. Some respondents considered that the topics that emerge from this process usually involve a tweak to existing methods rather than recommendations to commission major new research. It was noted that the methods issues listed in the guides are just the *current* recommendations and as such the process is repeated during each methods update. Despite the general optimistic view of the methods guides from NICE staff and respondents external to NICE, in terms of generating and promoting methods research, one respondent external to NICE felt that the methods guide had not impacted on methodological research.

- Respondents referred to the use of methods reviews (for all NICE programmes) to actively highlight areas where methods development is needed. For example, as part of the 2008 review of the methods guide for the Technology Appraisals programme, a series of workshops of specific methodological areas were held. A series of briefing papers produced by NICE's Decision Support Unit was commissioned to facilitate discussion at those workshops. The main aim of the workshops was to discuss possible changes to the Technology Appraisals methods guide; however, we were told that some methodological development needs were also identified as part of this process (i.e. without a workshop). A few of the respondents stated that the methods guide and supporting documentation helps to highlight the methods areas that are felt to need further work, which can be helpful for some researchers obtaining funding for research. It was felt that the downside of this is that subjects that are not mentioned as areas of uncertainty in the methods guide, but still actually are, may get overlooked (an example was given of the use of patient or public preferences for deriving Quality Adjusted Life Year (QALY) weights).

- The technical forum is a monthly meeting of technical staff within the Institute. It is an environment in which to discuss issues with a mix of internal and external speakers. It has a role in sharing experience across programmes. As well as the technical forum, we were told that other workshops organised by NICE provide opportunities to identify methodological development needs and to exchange views between internal and external people (e.g. the workshop on economic evaluation of public health interventions).

Informal processes

In addition to the more formal processes to identify methods topics, a number of informal processes for identifying methodological research needs were described by members of NICE staff. These take a number of forms:

- Respondents noted that members of NICE staff identify topics via a personal/professional interest. This is more a consequence of professional observations rather than an explicit process of identification. NICE staff use methods during the process of producing guidance and consequently assess whether they are appropriate; and, as such, a portfolio of themes constantly emerges. We were told that, during discussions amongst technical staff, topics often 'bubble up' over time and gradually priorities emerge. It is during these 'acute moments of learning' that work such as the 'End of Life'[6] can be initiated. It was suggested that often a fairly quick solution is needed to methodological issues and that the NICE programmes often have a clearer view than the academic world of the issues that are important to the work of NICE in producing guidance on appropriate patient care for the NHS.

- Respondents indicated that, when a problem is identified, work is often commissioned externally or, to a more limited extent, conducted internally. For internally conducted work, often no explicit funding is available for this work and, instead, it is funded by soft resources. An example of this is the use of student placements. For example, in 2007 the Technology Appraisals directorate looked at the selection and use of health state utility values in NICE Technology Appraisals. Explicit funding in these circumstances was seen by some respondents to be beneficial, although it is not clear where this funding would come from. It was generally agreed by respondents that, within NICE, it should be everyone's responsibility to identify topics, whichever area they are in and to communicate these appropriately.

- One respondent suggested that there were differences in research-culture amongst Institute teams. The reasons were not probed in-depth but it was suggested that there were different incentives and support, for example the background of individuals within the teams.

- One respondent felt that public health in particular has been challenged because limited methodology existed in the same way it did for HTA. It was considered that this programme has been very proactive in developing methodology.

- It was noted that the Patient and Public Involvement Programme (PPIP) has undertaken their own evaluation of patient expert experience, including a survey of lay members of appraisal committees, guidelines development groups (GDGs) and the citizens' council. We were told that, during this process, a whole raft of issues around assessing quality of life was identified. As well

as the team within NICE, the NCCs linked with NICE often identify methodological research and conduct it independently. However, it was noted that there is no formal route from an NCC to NICE for identifying methodological research development needs or communicating ongoing methodological work.

- We were informed that, to encourage discussion including issues of methodology, each of the analyst teams within NICE has an annual away day. For many of the teams, part of the day is focussed on identifying methodological questions of relevance.

- Some respondents stated that, although there is no formal process during committee meetings to feed methods topics forwards and to develop them, methodological issues often arise in these meetings. These are often context specific, but there are some topics that are over-arching such as which perspective to take, issues relating to QALYs and what cost-effectiveness threshold to use. It was noted that concerns are also expressed by stakeholder groups during the course of guidance development, for example how information from patients is incorporated into evidence used by NICE. Despite topics often arising during committee meetings, many respondents expressed the concern that there is no formal mechanism for taking these issues forward.

- Respondents indicated that, more generally, methods gaps are highlighted when applying the methods guides to the development of individual pieces of guidance. It was noted that a few pieces of guidance (for example, Public Health Guidance on Behaviour Change) contain methods research recommendations. In addition, issues arise during consultation with stakeholders or during the appeal process for technology appraisals. Issues that arise repeatedly during guidance development tend to be informally collated until they are considered sufficiently important to warrant further work. It was noted by respondents that issues that affect the process are often considered particularly important and take precedent.

- Respondents noted a number of other informal systems which can be used to identify methods gaps, in addition to core NICE activities. Gaps can be highlighted during *ad hoc* meetings of chairs, for example PHIAC's discussions on methodology in public health evaluation led to the recent workshop on economics in public health. The Centre for Clinical Practice (CCP) technical team also works closely with technical staff from collaborating centres to identify broad areas of need. The collaborating centres and NICE conducted a review of methods needs in 2005 to identify areas of challenging methods across the programme.

- Respondents suggested that the 'What's new' internal bulletin also serves to highlight issues that may be relevant for NICE decision-making to NICE staff. This is essentially a sift of methods papers from some key journals by an information specialist and two senior members of staff for internal circulation. The aim is not specifically to identify methods research needs but these are often highlighted as part of the searches.

- We were told that NICE also benefits from the relationships it has built with various academic groups, in particular relationships forged with those who conduct assessments of evidence for the Institute. There is an expectation that these centres will have the highest awareness of methodological developments in HTA. Academic groups who have worked with NICE and helped to produce the technical manuals have taken forward some issues in the past (e.g. value of information). Some NICE staff did express a concern about competing interests when allowing external collaborators to lead the focus of methods work. They considered that, for NICE, the focus should always be on identifying where methods development is needed to support NICE decision-making rather than pursuing academic interests of external collaborators.

In summary, several current formal processes for identifying topics were highlighted during interviews with staff at NICE, including the work of RDAC which advises NICE about its research and development work, the regular updating of the methods guides and the technical forum. In addition to the more formal processes to identify methods topics, a number of informal processes were described by members of NICE staff. These included identification of topics by NICE staff motivated by personal/professional interest, discussions during committee meetings, *ad hoc* meetings of NICE chairs, staff away days and the 'What's new' internal bulletins. These processes are intended to help identify and promote methods work with NICE; however, many respondents outside of NICE felt that

the mechanisms to identify methods topics had limited visibility and they were unsure how these various processes were co-ordinated.

All of the formal and informal processes described by the interview respondents and email survey focus on the identification of topics rather than their prioritisation or their development into specific researchable questions. There are no defined systems of prioritisation and no current criteria for prioritisation of methods research.

3.1.2.2 *Suggested improvements to the NICE process*

Identification of topics. Respondents external to NICE and members of NICE staff had some clear ideas about how the process for identifying methods topics should be changed. In particular, they advocated the idea of a more explicit and coherent plan for identifying topics; engaging the individual teams within NICE more formally, something perhaps along the lines of the existing topic selection panels. A number of specific suggestions were made. These suggestions were not intended as mutually exclusive options and could be used in combination, where appropriate. The suggestions were:

- A 'Methodology Committee' with members from both within and outside of NICE, including methodologists. The committee would meet regularly and be clearly visible within NICE and externally. Caution would have to be exercised to avoid duplication of effort with other bodies such as MRP. Suggestions for the types of people who should be involved were: NICE staff – technical advisors, associate directors, members of the R&D group; representatives from groups reviewing the evidence for NICE; key people from industry (e.g. access strategy group within ABPI); and representatives from research funding organisations. Key members of the appraisal committees, external methodologists and clinicians and other stakeholders such as NCCHTA might also be involved. In addition it was suggested that there should be an overarching group of methodologists, such as members of the MRP committee, NICE methods advisors and wider methods advisors. A more select group could also be used, for example the MRC or NICE could have quarterly debriefings with committee chairs, where methodological issues that have arisen/emerged as priority areas during previous period are discussed.

- RDAC could coordinate a methods identification process by developing a database of research recommendations generated by guidance-producing centres of the Institute. NICE currently has such a database for clinical and public health research topics, but this does not include methods research topics. Information generated by this process could then be fed back to the relevant guidance producing centres.

- The identification of topics could be included as a specific agenda item in existing committee meetings. This agenda item would need sufficient time dedicated to it, but would not necessarily have to be an agenda item at each meeting. Committee chairs and vice chairs should feed into the process of identifying areas where methodological research is needed. A mechanism for feeding back any topic suggestions would also have to be established.

- The creation of a formal process for following up recommendations for topics which have come from the various methods guides, involving a thorough exploration of the basis of the evidence provided from recommending topics for further research. This would help to provide a better grounding for the topic recommendations. In addition to the methods guides the outputs from relevant methods workshops could continue to highlight suggestions for further research.

- Greater collaboration between interested parties both within and outside of NICE was suggested (including industry, HTA, James Lind organisation and other international organisations). Many felt that opportunities for collaboration on methodological topics are not being fully exploited. Two respondents from industry felt that the need for industry involvement in generating methods topics is further highlighted during the single technology appraisal (STA) process. They noted that industry put together the submissions and thus address the methodological issues associated with specific appraisals. Lots of decisions are made by the companies themselves and more specific guidance on acceptable methods are

needed. They considered that collaboration on topic generation would also be good outside of the assessment process so that any competing objectives/tensions could be put aside.

- Related to the above point, one of the respondents felt that a key issue is capturing the views of expert advisors that support NICE and getting them to focus on methods rather than specific appraisals. NICE could set aside time with external advisors away from its day-to-day process with a focus on methods and identifying the big (top-level) questions. The experts contributing to this process should be from the NICE advisory committees and from the groups conducting the evidence reviews for NICE. There could be key methodologists facilitating the process e.g. statisticians, systematic reviewers. However, it was suggested that NICE does not want these experts to sway the discussion. It was argued that the topics that are raised must be things that are understood and valued by people actually using the methods for decision-making. This said, there were some stakeholders that felt that identification of topics should be done exclusively by people within NICE, and that there is sufficient expertise within NICE. They considered there to be a need for generating the mechanisms to bring this expertise together in some kind of forum.

- An additional way to identify topics would be to take a retrospective look at past appraisals, to identify areas that have caused problems in the past or where different methods could have made a difference to the decision. There should be a general process for audit of critical inputs that most influence cost-effectiveness and what makes a difference to the decision, as well as of methodological problems that have arisen.

- In relation to the future identification of topics, the role of the R&D programme was mentioned by a few respondents. A paper on the R&D strategy is planned for 2009, and this will involve revising the role and function of RDAC. There was a desire for individual centres in the Institute to contribute to the delivery of future strategy, with R&D as a coordinating and enabling function; for example, through the quarterly meetings that are held with each centre to discuss what needs doing and how it could be done. It was noted that there is a need for the individual centres to inform R&D of the issues that are important to the specific guidance producing programmes. It was also noted that RDAC could be transformed into a research forum rather than a committee, possibly with an annual forum plus other seminars.

- Many respondents felt that that NICE should be more proactive and strategic thinking rather than reactive to individual problems on an *ad hoc* basis. To operationalise this it was suggested that NICE needs to develop its expertise in identifying and conducting methodological work, collaboration on methodology could come in the form of external placements/interns. This could also be extended to opportunities for NICE staff to undertake some research, including in collaboration with other institutions. It was felt that the technical forum currently used at NICE could be more effective if internal staff were more actively involved in suggesting speakers and presenting themselves.

- Despite a general feeling that a more explicit formal process would be beneficial, one stakeholder did stress that any changes to the process should not impinge on the ability of individuals within the Institute to identify areas where methodology needs to be further developed. As well as formal processes, there is a need for informal discussion and iteration - letting things emerge as methods are applied. Across the Institute as the teams operationalise the methodology, different sets of topics and priorities will be emerging and this process should still be encouraged.

Prioritisation of topics. Again, the general consensus was that there should be an explicit process for prioritisation or at least a clearer pathway for feeding topics forward within NICE. One respondent felt that topics can get put on the 'back burner' or pushed forward ahead of other worthwhile topics, because of the political issues associated with them. If there was an explicit process for prioritisation this would be less likely to happen.

Most of the respondents (both from within and external to NICE) felt that prioritisation of topics should be on the basis of the issues most important to NICE; specifically, will the research make a difference to NICE? In determining this, it was proposed that the following questions need to be considered:

- Is the methods research needed to inform the NICE assessment and decision-making process?
- What are the consequences of not doing the research?
- Will the methods impact on patient care?
- Will the research impact on equity?
- Is the topic researchable and how long will it take to resolve?
- What is the scale of the topic contribution – is it a big issue in the assessment process, and does it cross themes and will it affect decisions? There is a need to consider things that are currently issues and things that will be issues in the future.
- Does the topic inform gaps in current methods evidence and/or does it inform issues of uncertainty and/or a lack of confidence?
- How is the issue perceived by stakeholders?
- Does the research improve the robustness and transparency of NICE's work?

In consolidating the information on each of these aspects, there were contradictory views on what mechanisms could be used. A few of the respondents advocated the use of scoring, possibly using some kind of Likert scale as suggested by one respondent external to NICE. This would have to include the issue of whether the topic is researchable (in terms of the area but also in terms of availability of skills). This might enable the generation of a profile of scores (it may not be necessary have to produce a single score).

Others felt that scoring research topics/questions had little value, especially if conducted in isolation. Instead priorities should be decided by round table discussion probably by a specific committee with a similar membership to the topics selection committees.

In terms of who should prioritise topics, many respondents felt this should be handled internally within NICE. External organisations that have relevant expertise may be able to offer advice and guidance but may be biased in terms of their research interests and may not fully appreciate NICE's priorities.

Funding of topics. Aside from the issues of identifying and prioritising methods topics, many of the respondents, particularly those external to NICE, felt that a clear link with funding sources for methods research would be useful. The current lack of funding specific to NICE methods research has meant that a lot of important work has been shelved. Likely funders for this type of work are the MRC and NHIR. In seeking external funding there is the potential for NICE staff to act as co-applicants for grant applications along with external researchers. Where there is a lack of capacity, interest or capability within NICE, external collaborators should lead on the application for funding.

It was suggested that at the very least external funders should be made aware of the priority topics. Such a system is currently in place for NICE to make the NHS HTA programme aware of clinical research priorities but these priorities cannot be enforced. In addition some methodological topics are referred to MRP by NICE e.g. a project was recently commissioned by the MRP entitled 'Informing a decision framework for when NICE should recommend the use of health technologies only in the context of an appropriately designed programme of evidence development ("only in research")'.

An alternative suggested was that NICE would have its own direct funding for methodological research. This would require a clear work programme at NICE and some felt this would be a significant step. NICE would not need to have its own methodologists in house as it could commission these from other organisations. One respondent suggested that the source for this in house funding was for the MRC to devolve some budgetary responsibility to NICE for methods work.

In summary the key suggestion for future change was the idea of a more explicit and coherent plan for identifying and prioritising methods topics. As part of this a number of specific suggestions relating to the identification of topics were made, including the creation of a 'Methodology Committee' with members from both within and outside of NICE, the identification of potential topics as a specific agenda item in existing (decision-making) committee meetings, greater collaboration between interested parties both within and outside of NICE and the creation of a formal process for following up recommendations for topics which have come from the various methods guides. In terms of prioritisation, most of the respondents felt that any criteria for prioritisation should be on the basis of the issues most important to NICE decision-making. The need to identify funding for methods work was also raised by many of the respondents, particularly those external to NICE.

3.2 Current processes by which methodological research topics are identified and prioritised in other organisations

Information on methods to identify and prioritise methodological research topics within other organisations was not forthcoming from the telephone and face-to-face interviews. However, a number of respondents to the email survey did provide some detail.

A spokesperson from the European Network for Health Technology Assessment (EUnetHTA) commented on the process that EUnetHTA uses to identify potential methodological research topics. It has no systematic process, but identifies topics through an *ad hoc* review of reports, and their multidisciplinary Scientific Advisory Board may also point to required methods research. A granting mechanism for external methodologically oriented projects ended in 2007, and the possibilities of initiating methods research are currently limited. The EUnetHTA handbook is available at: http://www.sst.dk/publ/Publ2008/MTV/Metode/HTA_Handbook_net_final.pdf.

A spokesperson from the Agency for Healthcare Research and Quality (AHRQ) stated that it has a fairly formal method for identifying new needs for methods research. It convenes its researchers and forms work groups to take a lead on systematically reviewing current methods and recommending new areas of methods research. It holds expert meetings where invited experts are able to present work on specific areas of methodology, and the AHRQ sets aside a portion of its budget to fund novel methods work, led by AHRQ staff.

The AHRQ is currently in the process of documenting their system for identifying methods topics. Identified areas for research are prioritised by critical review, identified limitations in existing methods research and their direct impact on the mission of AHRQ. Identified topics are funded by the AHRQ and competitively assigned after soliciting and peer reviewing proposals. The AHRQ hosts a symposium (http://effectivehealthcare.ahrq.gov/documents/2008_1209AHRQCallforAbstracts.htm) to examine new and emerging methods. The AHRQ's guide for HTA methods can be found at (http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60).

4. Methodological topics

4.1 Results from the literature review

Section 3.1 provides details of the documents reviewed in the project. The documents are listed and extracted in Appendix 7.

Suggestions for methodological research aimed directly at informing decision-making at NICE were reported in 11 of the papers. All of these papers referred to areas where methodological development was considered to be potentially useful, and did not report the suggestions as researchable questions.

4.2 Interviews

Details of the interviews and responses to the email survey are reported in Section 3.1.2. Topics for future methods development/research were added to those obtained from the literature.

During the interview phase of the project, the definition of what constitutes methodological research was raised. Some interviewees referred to potential research topics that were not aimed directly at developing new methods, but rather at reviewing or auditing the use of existing methods or developing repositories of evidence previously used to develop NICE guidance. The final list of topics included in the web-based feedback exercise was limited to topics that would develop new or existing methods, such that if the reviews or audits required methodological development they were included, but reviews or audits or particular parameter values were not included.

4.3 Topics

4.3.1 Overview

Over one hundred topics for potential methodological research were suggested through the interviews and email survey, and from the focussed review of the literature. The topics identified from the different sources were combined. All suggested topics were grouped into the following five areas of methodology. Each area relates to a different aspect of the assessment and appraisal process. Some of the topic suggestions related to more than one area of methodology; in which case they were categorised according to the most closely related area.

- Area 1: Analysis and design of effectiveness studies and their synthesis
- Area 2: Synthesis of evidence from patients, the public and stakeholders
- Area 3: Economic analysis and uncertainty
- Area 4: Measurement and valuation of benefits
- Area 5: Decision-making at NICE

Within each of the five areas, the topics were grouped into related themes. The themes under each of the five areas are presented in Box 2. Details of specific topic suggestions are detailed in Appendix A8 as presented at the workshop (see below).

Most of the topics suggested during the interviews and email survey were each raised by a single respondent. However, some suggestions were raised by several people. Those research topics raised independently by more than four interviewees included:

- Methodology for indirect and mixed treatment comparisons
- Synthesis of qualitative evidence in the NICE decision-making process
- Use of quality adjusted life years in decision-making (specifically establishing what benefits of treatment are not captured by the QALY and/or standardised measures of health-related quality of life)
- Establishing the threshold for cost-effectiveness (including the appropriate methods for estimating this)
- Determining how data on the uncertainty in estimates of effectiveness and cost-effectiveness should be taken into account in the decision-making process

Box 2: Areas and themes under which methodological research questions were grouped

Area 1: Analysis and design of effectiveness studies and their synthesis

    A. Systematic reviews
    B. Meta-analysis (including indirect and mixed treatment comparisons)
    C. Use of non-experimental data
    D. Interpretation and analysis of clinical trial data
    E. Clinical heterogeneity
    F. Diagnostics and medical devices
    G. Behavioural research

Area 2: Synthesis of evidence from patients, the public and stakeholders

    A. Evidence from patients
    B. Evidence from the general public
    C. Evidence from stakeholders

Area 3: Economic analysis and uncertainty

    A. Costing
    B. Perspective for analysis
    C. Time horizon for analysis
    D. Economic modelling
    E. Uncertainty
    F. Other

Area 4: Measurement and valuation of benefits

    A. Use of the QALY
    B. Standardised measurement tools
    C. Valuation of health
    D. Use of health state utility data in economic models

Area 5: Decision-making at NICE

    A. Threshold for cost-effectiveness
    B. Influences on NICE decision-making
    C. Handling uncertainty in decision-making
    D. Process of decision-making
    E. Developing the format/ type of NICE recommendations

4.3.2 Relationship of topics to NICE activities

Some topic suggestions were specific to the work of a single guidance-producing NICE centre, whilst others could potentially inform the work of multiple centres or NICE in general. In addition, the topic suggestions could inform one or more stages of NICE guidance production including formulating the scope of the guidance, aspects of evidence review and analysis, interaction with NICE stakeholders and the process of decision-making. Figures 1 to 5 show how each of the areas and specific topic

suggestions relate to each of the NICE programmes and specific activities undertaken when formulating NICE guidance.

The research theme is noted in the central column of each figure. The arrows to the left demonstrate the programme to which the topics in each research area relate. These include Interventional Procedures, Technology Appraisals, Public health, Clinical Guidelines. A separate box indicates topics that could be applicable to all programmes (All) and, given that many of the suggested topics relate to economic evaluation and that cost-effectiveness is not a consideration in the development of IP guidance; an additional box represents all the guidance producing programmes except interventional procedures. The numbers on the arrows relate to the specific topic suggestion within that theme and area. For example, from Figure 1 all of the topics grouped under Theme E (use of non-experimental data) could apply to all of the NICE programmes and all relate to the synthesis of evidence. The arrows to the right indicate the activity in the guidance production process that the suggested research area is aimed towards.

The majority of topics suggested were relevant to all of NICE's guidance producing programmes, with only a few being specific to individual programmes (e.g. methods to evaluate behaviour change in the context of public health).   Most of the methods related to the evidence gathering/analysis (assessment) phase of producing NICE guidance (areas 1, 3 and 4), although a small number of topics related to the engagement with different types of stakeholder (area 2) and the decision-making process (area 5).

Figure 1: Schematic of topic suggestions for area 1 (analysis and design of effectiveness studies and their synthesis)

NICE PROGRAMME

THEME

ACTIVITY
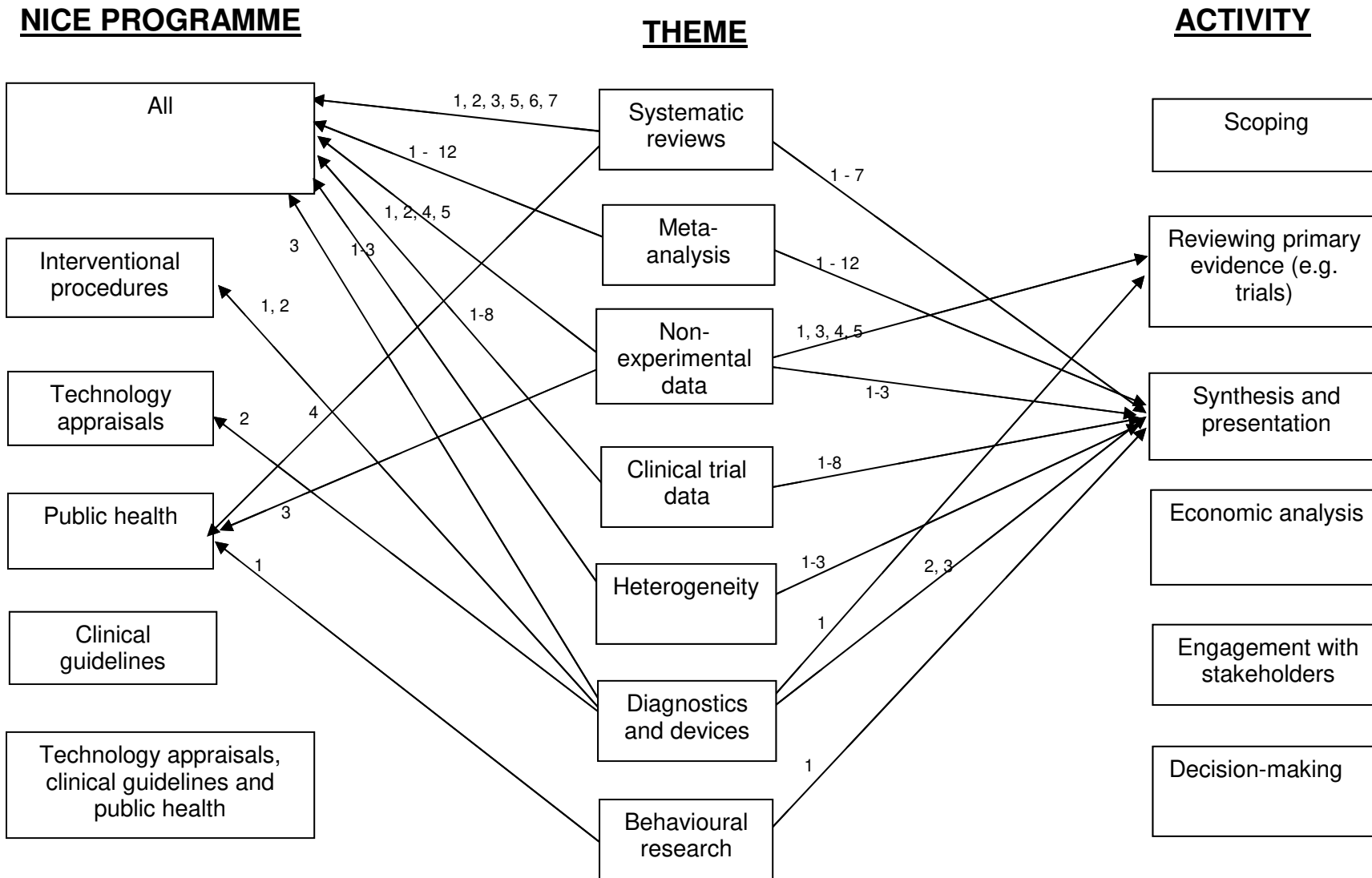
Figure 2 Schematic of topic suggestions for area 2 (Synthesis of evidence from patients, the public and other stakeholders)
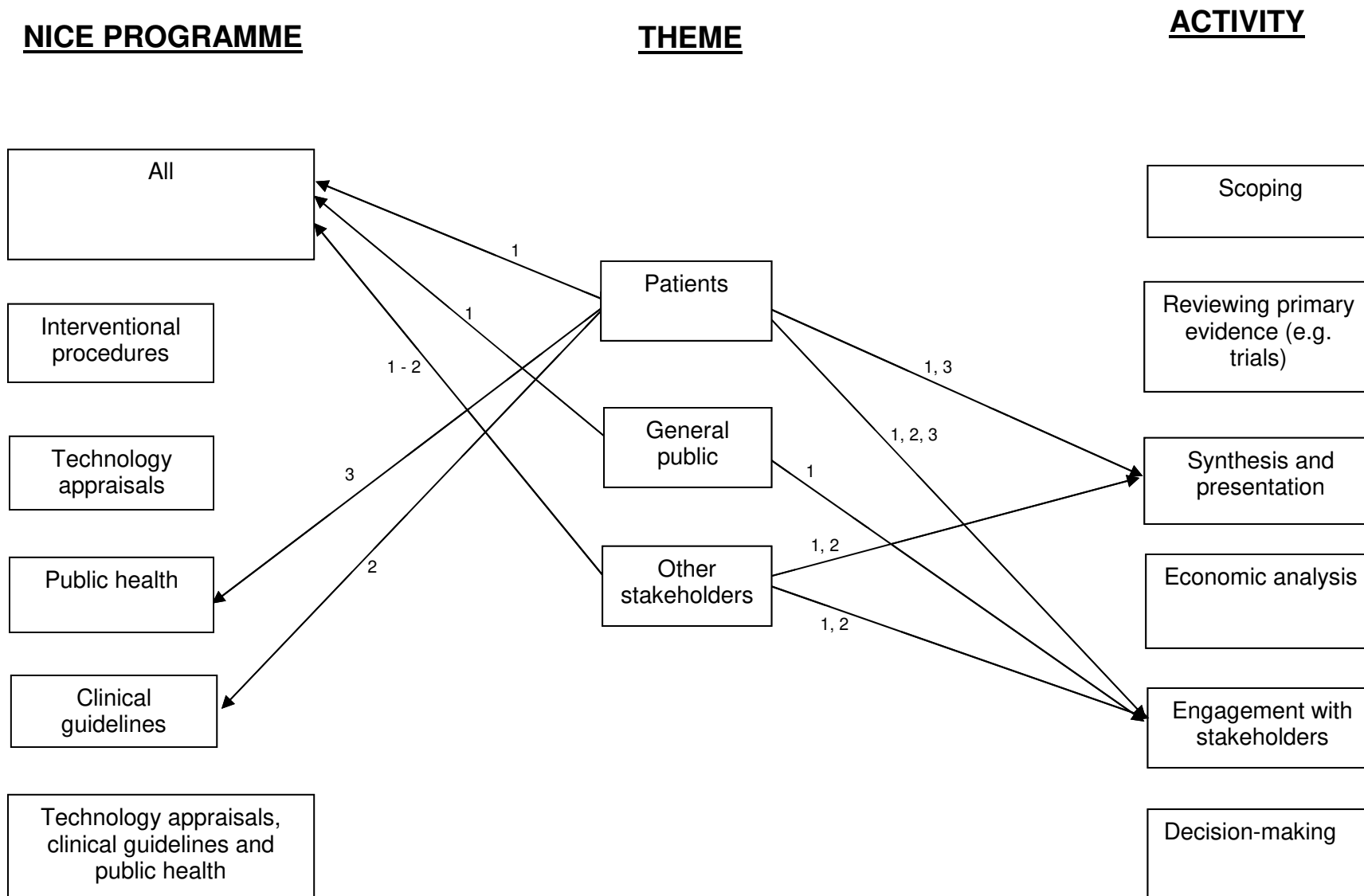
Figure 3: Schematic of topic suggestions for area 3 (Economic analysis and uncertainty)

NICE PROGRAMME   **THEME**   **ACTIVITY**

All

Interventional procedures

Technology appraisals

Public health

Clinical guidelines

Technology appraisals, clinical guidelines and public health

Costing

Perspective

Time horizon

Modelling

Uncertainty

Other

Scoping

Reviewing primary evidence (e.g. trials)

Synthesis and presentation

Economic analysis

Engagement with stakeholders

Decision-making

Figure 4: Schematic of topic suggestions for area 4 (Measurement and valuation of health benefits)
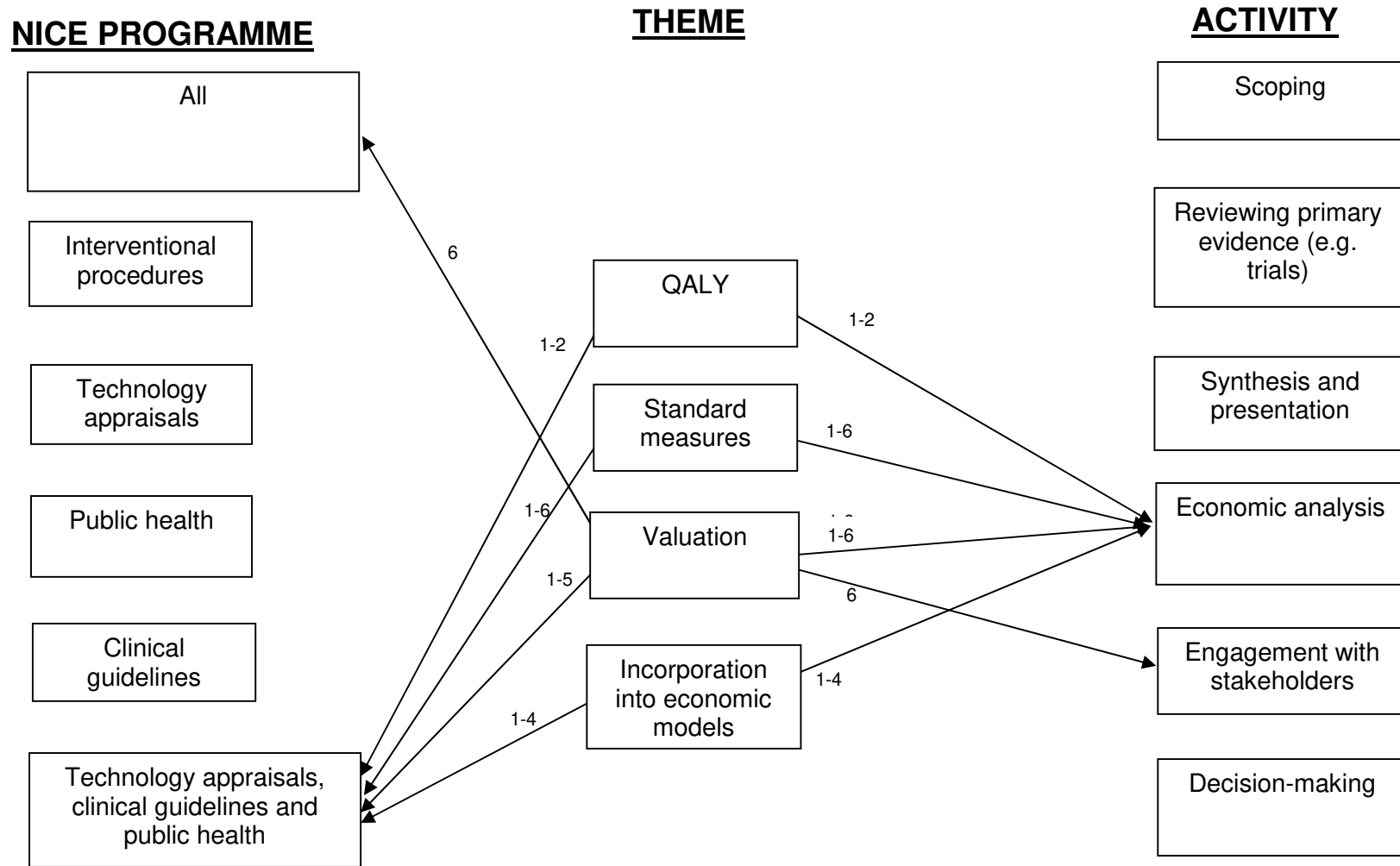
Figure 5: Schematic of topic suggestions for area 5 (Decision-making at NICE)
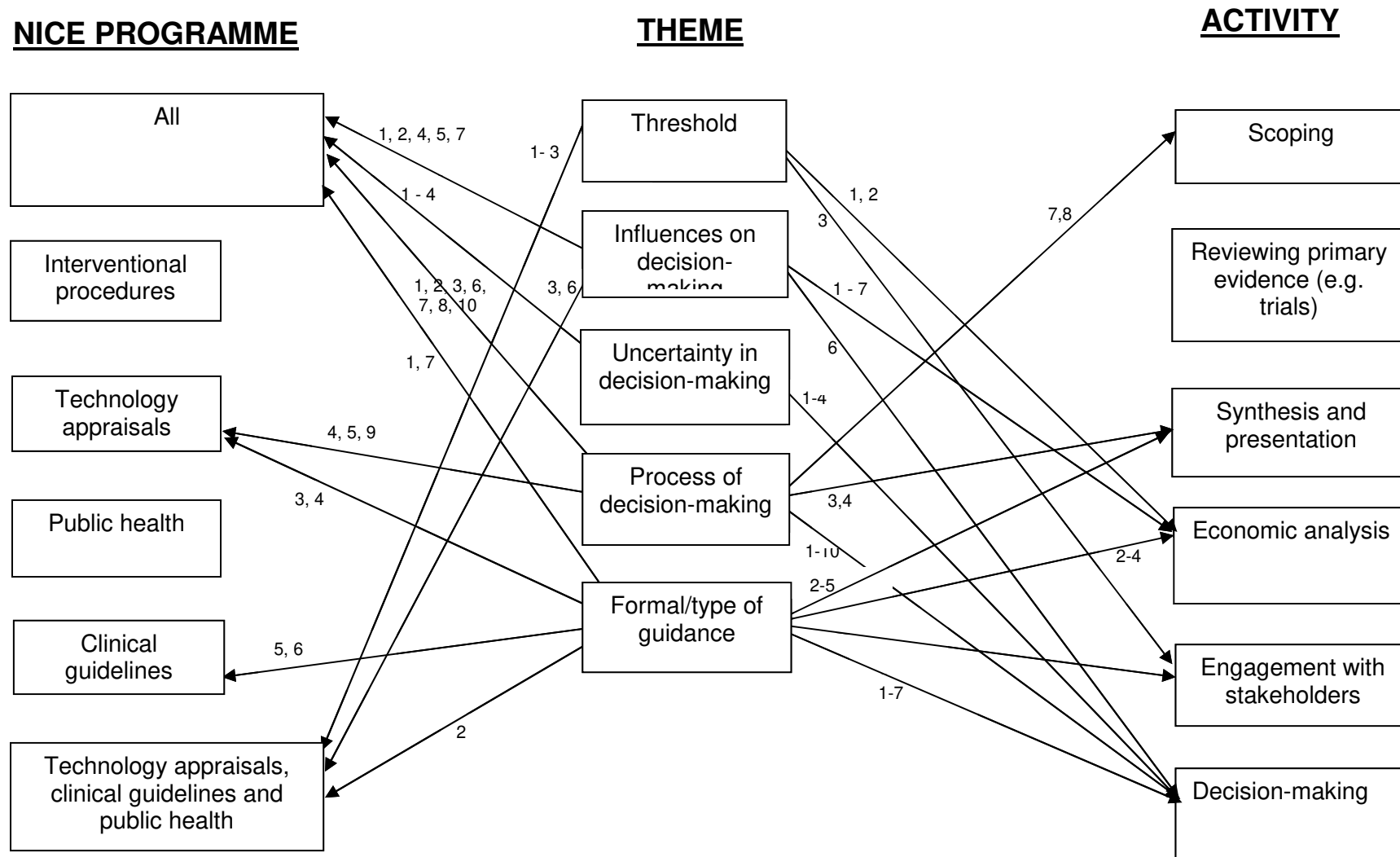
4.3.3 Workshop

During the workshop, participants discussed the topics identified during the preceding steps of the project. Topics that were highlighted by delegates within the small-group discussions to be priorities for methodological research that could benefit NICE decision-making are presented in Appendix A9. Some topics were highlighted as priorities by more than one group. These included the following:

- Topic 1.A.2: Methods for keeping research synthesis up to date; developing on-going and up to date repositories of 'approved' networks of evidence in key diseases using mixed treatment comparison
- Topic 2.A.1: Methods to assess what types of evidence from patients should be used at different stages of NICE's decision-making processes (e.g. when to undertake reviews of qualitative evidence? What types of reviews should be conducted? When should colloquial evidence be used?)
- Topic 3.C.2: Extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty
- Topic 4.B.3: Establishing what effects of interventions and programmes are/are not currently captured by the EQ-5D
- Topic 4.C.1: Methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead
- Topic 4.C.3: Methods for valuing health at different time points in a person's life (e.g. at the end of life)
- Topic 4.C.4: Methods to determine whether public or patient valuations of health should be used in economic evaluation
- Topic 5.A.1: What is the current incremental cost-effectiveness ratio (ICER) of things that are being displaced by NICE guidance (i.e. opportunity cost of NICE guidance)?
- Topic 5.A.2: Methods to estimate the opportunity cost of NICE guidance (i.e. the threshold) including changes over time

Following feedback during the workshop, some of the topics identified from the interviews, email survey and literature were rephrased and re-allocated into different areas and/or themes.

4.3.4 Web survey

The web survey can be seen in Appendix A10. Respondents were first given an overview of the project and link to MRP and were then asked questions on their professional background, whether they had attended the workshop and their involvement with NICE. The survey is then split into the 5 topic areas as described previously in 4.3.1 (Box 2).

Respondents were asked to rate each topic, within each area and theme, by their level of importance. At the end of each area respondents were asked to suggest any additional topics. When completing the questionnaire they were asked to provide their top three topics (across areas and themes) along with some further detail on why these are important topics for NICE decision-making. Finally, respondents were asked to suggest any areas and themes they thought had been omitted along with any feedback on the survey.

The web survey was made publicly available (for a period of four weeks) on the MRC website and linked to the NICE website. Invitations to complete the survey were sent to all workshop attendees, people who were invited to the workshop but could not attend, individuals interviewed as part of the project, people who were invited to be interviewed but could not participate, the wider project team and others suggested by NICE and the MRC.

The characteristics of respondents can be seen in Table 3. Seventy-six people completed the online questionnaire, the majority of who were based within academia (65%). A large number of respondents were health economists or health service researchers (56%). Clinicians and public health specialists were also well represented in the survey (13% and 9% respectively). The majority of respondents did not attend the workshop (68%) and were not interviewed as part of the project (89%). The large majority of respondents had worked with NICE (76%) with 13% directly employed by NICE.

Table 3: Characteristics of web respondents (n=76)

Organisation	
University	50
Private consultancy	1
Pharmaceutical company	7
NHS	5
NICE	10
Patient organisation	0
Other:	
Charity	1
James Lind Initiative	1
Government	1
Professional background	
Health Economist	20
Public health specialist	7
Clinician	10
Statistician	6
Health services researcher	23
NHS manager	2
Other:	
Health Psychologist	1
HTA manager	1
Information specialist	1
Multi-disciplinary team	1
Research psychologist	1
Social scientist	2
Academic research (systematic reviews)	1
Attendance at the workshop	
Attended	16
Invited but could not attend	8
Did not attend	52
Interviewed as part of scoping study	
Yes	8
No	68
Involvement with NICE	
Employed directly by NICE	10
Member of NICE committee/guidelines group	9
Academic reviewer/provider of evidence	21
Provider of submission on behalf of sponsor organisation	7
Other:	
Advised of NICE outputs	1
Advisory committee for NHS evidence	1
Former member of partner council	1
Involved in implementation of guidance	3
Decision support unit	1
NIHR	1
Previous NICE employee	1
Previous committee member	1
Involved in work co-funded by NICE	1
No involvement	18

As part of the web survey respondents were given the opportunity to suggest areas and topics additional to those listed in the survey. Additional topics suggested by respondents are given in Appendix A11. No additional areas were suggested.

4.4 Prioritisation

The results of prioritisation of topics can be seen below in Tables 4 and 5. In Table 4 the top five topics in each area are listed. These represent the topics most often rated as 'very important' or 'important'.

Table 4: Results from web survey prioritisation: top five topics within areas (percentage reporting 'very important' or 'important')

Rank	Topic	%
	Area a: analysis and design of effectiveness studies and their synthesis (n=75)*	
1	1_C_1: Establishing optimal methods for analysis of disease registers and other sources of non-experimental evidence (e.g. What methods to use? When should non-experimental data be used? How are non-experimental data currently used at NICE?)	77
2	1_B_1: Methods to adjust for potential bias in meta-analysis (for example, issues of multiple sources of bias and confounding)	76
3	1_A_7: Methods for conducting systematic reviews of complex interventions (e.g. in public health)	76
4	1_F_3: How best to evaluate diagnostic and screening technologies	75
5	1_A_1: Establishing methods and rules for efficient systematic reviews of effectiveness, diagnostic test accuracy and prognostic factors (i.e. tackling the trade off between efficiency and quality)	75
	Area b: synthesis of evidence from patients, the public and stakeholders (n=75)	
1	2_A_1: Methods to assess what types of patient evidence should be used at different stages of NICE's decision-making process (e.g. when to undertake reviews of qualitative evidence? What types of reviews should be conducted? When should colloquial evidence be used?)	66
2	2_B_1: Methods to understand how the public view characteristics of conditions and the technologies used to treat them	47
3	2_C_1: The appraisal and synthesis of 'colloquial evidence' (e.g. comments received from stakeholders during consultation)	44
4	2_C_2: Evaluation of the existing, and development of new methods for participation of different stakeholder groups at different stages of NICE's decision-making process (including representatives of the general public, patients and practitioners)	42
5	2_A_3: Methods for using colloquial evidence to determine the effect of complex interventions (e.g. in public health)	32
	Area c: economic analysis and uncertainty (n=74)	
1	3_C_2: Extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty	82
2	3_D_3: Research to assess whether the predictions of economic models used to inform NICE guidance are borne out in practice	75
3	3_F_5: Methods to assess the cost- effectiveness of interventions which have costs and (dis)benefits outside of the health care sector	74
4	3_D_9: Methods for determining the optimal complexity of economic models (i.e. how complex does a model need to be to be fit for purpose?)	70
5	3_D_4: Methods for the use of surrogate or intermediate measures in models	69
	Area d: measurement and valuation of benefits (n=73)	
1	4_A_1: Methods to capture a wider set of (dis)benefits that may not be included in the QALY	78
2	4_B_6: Methods for the measurement of changes in the health of children and people unable to report the status of their own health	71
3	4_A_2: Consolidating patient reported outcomes with other measures of benefit (e.g. QALYs)	70
4	4_C_1: Methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead	68
5	4_C_3: Methods for valuing health at different time points in a person's life (especially at the end of life) 4_C_4: Methods to determine whether public or patient valuations of health should be used	68
	Area e: decision-making at NICE (n=74)	
1	5_C_3: How should NICE assess whether additional evidence is needed, what type of evidence is required and the type of evidence for 'coverage with evidence' decisions 5_E_2: Development of methods to produce guidance to the NHS on the disinvestment of existing interventions	78
2	5_A_1: What is the current ICER of things that are being displaced by NICE guidance (opportunity cost of NICE guidance?)? 5_A_2: Methods to estimate the opportunity cost of NICE guidance (i.e. the threshold) including changes over time	74
5	5_B_4: Methods for taking factors other than cost-effectiveness (e.g. societal costs/effects) into account in NICE decision-making (e.g. using multi-criteria decision-making analysis)	66

*Number of respondents that completed any of this section

Respondents were asked to list three topics, across all areas and themes, that they considered most important. The topics most frequently listed are shown in Table 5. Unfortunately, due to a technical issue with the web survey, only 55 respondents listed three priority topics; others did not complete this section or listed more than three topics. Therefore, the results of this part of the survey should be viewed with caution.

Table 5: Results from web survey prioritisation: Most highly rated topics across areas (n= 55)

Rank overall	Topic	Number times ranked in top 3
1	1_G_1: Methods to evaluate interventions to change behaviour in the context of public health	13
2	1_A_7: Methods for conducting systematic reviews of complex interventions (e.g. in public health)	7
3	1_A_1: Establishing methods and rules for efficient systematic reviews of effectiveness, diagnostic test accuracy and prognostic factors (i.e. tackling the trade off between efficiency and quality)	6
	1_B_5: Establishing the reliability of mixed treatment comparisons and consistency with direct data	6
4	1_A_2: Methods for keeping research synthesis up to date; developing on-going and up to date repositories of 'approved' networks of evidence in key diseases using mixed treatment comparison	5
	1_D_8: Methods to attribute outcomes to specific components of care within complex interventions (e.g. public health interventions)	5
	5_A_2: Methods to estimate the opportunity cost of NICE guidance (i.e. the threshold) including changes over time	5
	5_B_4: Methods for taking factors other than cost-effectiveness (e.g. societal costs/effects) into account in NICE decision-making (e.g. using multi-criteria decision analysis)	5
	5_E_2: Development of methods to produce guidance to the NHS on the disinvestment of existing interventions	5
5	1_B_12: Methods for synthesising both qualitative and quantitative research	4
	1_C_1: Establishing optimal methods for analysis of disease registers and other sources of non-experimental evidence (e.g. What methods to use? When should non-experimental data be used? How are non-experimental data currently used at NICE?)	4
	2_A_1: Methods to assess what types of patient evidence should be used at different stages of NICE's decision-making process (e.g. when to undertake reviews of qualitative evidence? What types of reviews should be conducted? When should colloquial evidence be used?)	4
	3_C_2: Extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty	4
	3_D_1: Methods to develop 'standardised' and 'approved' models in a given disease area, including parameter inputs	4
	5_B_3: Should NICE decision-making be based on cost-effectiveness analysis (CEA) modified by social value judgements, or should a range of social values be used of which CEA is one?	4
	5_B_7: How to take inequalities into account at different stages of NICE guidance production?	4

Topic 1_G_1 on 'Methods to evaluate interventions to change behaviour in the context of public health' was ranked in the top 3 most important topics the greatest number of times. However, it was not in the list of topics within area A considered to be important or very important by the most respondents (65% of respondents rated it as very important or important). This may be due to fewer people completing the top 3 ranking section of the survey. Some of those respondents who prioritised this topic considered it to be important because of a challenge for NICE to assess the benefits from these public health interventions in an exchangeable way with the benefits from pharmaceutical interventions. It was noted that many public health interventions focus on changing behaviours, and then the change in behaviour must then be linked to changes in health outcomes.

The topic included in the top 3 priorities the second most frequently also related to public health (Methods for conducting systematic reviews of complex interventions). Information on how it would

inform NICE guidance was not provided but suggestions for research questions were proposed (see Appendix A12).

The third most frequently prioritised topic was methods and rules for the efficient systematic review of effectiveness and diagnostic test accuracy. One respondent stated that they prioritised this topic because of the importance of the trade-off between time pressures and quality of reviews. Another respondent stated that it was prioritised because more transparent decisions need to be based on reliable methods. Two people who prioritised this topic made specific reference to diagnostic tests. They stated that NICE will increasingly need to evaluate diagnostics and highlighted that research should include the integration of the evidence from systematic reviews within decision models. Another noted that diagnostic procedures are being used increasingly within the NHS, yet is unclear how their effectiveness should be measured and rated against other types of intervention. Comments provided in support of the most frequently prioritised topics are provided in Appendix A13.

4.5 Summary of suggestions for priority research topics

A long list of potential methods research topics relevant to NICE's decision-making activities was identified through a variety of exercises including a focussed review of the literature, interviews with representatives from NICE and its collaborators, an email survey, a workshop and a publicly available website. Within each stage of the project a slightly different group of individuals, each with varying degrees of links to NICE, was canvassed for their views on priority topics. Those who were interviewed and included in the email survey had direct links with NICE; mostly as members of staff, advisory committees or designated providers of evidence. The workshop included those with direct links to NICE and a broader group of people, including methods experts. The web feedback exercise included responses from some of those who attended the workshop, but also people who stated that they had no direct involvement with NICE. The topics emerging as priorities from the different exercises are noted below.

The following topics were noted by several people who were interviewed or responded to the email survey:
- methodology for indirect and mixed treatment comparisons
- synthesis of qualitative evidence in the NICE decision-making process
- use of quality adjusted life years in decision-making (specifically establishing what benefits of treatment are not captured by the QALY and/or standardised measures of health-related quality of life)
- establishing the threshold for cost-effectiveness (including the appropriate methods for estimating this)
- determining how data on the uncertainty of effectiveness and cost-effectiveness data should be taken into account in the decision-making process

The following topics emerged as priorities from the workshop:
- methods for keeping research synthesis up to date (including developing repositories of 'approved' networks of evidence in key diseases)
- methods to assess what types of evidence from patients should be used at different stages of NICE's decision-making processes (e.g. when to undertake reviews of qualitative evidence? When should colloquial evidence be used?)
- extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty
- establishing what effects of interventions and programmes are/are not currently captured by the EQ-5D
- methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead
- methods for valuing health at different time points in a person's life (e.g. at the end of life)
- methods to determine whether public or patient valuations of health should be used in economic evaluation
- methods for establishing opportunity costs of NICE guidance (i.e. the threshold) and empirical data on interventions that are being displaced by NICE guidance

The following topics were rated as important or very important by 75% or more of respondents to the web feedback exercise:

- optimal methods for analysing disease registers and other non-experimental data sources
- methods to adjust for bias in meta-analysis
- methods for conducting systematic reviews of complex interventions
- optimal methods for evaluating diagnostic and screening technologies
- methods for conducting efficient systematic reviews
- methods for the extrapolation of costs and benefits
- research to assess whether the predictions of economic models are borne out in practice
- methods to capture wider benefits not captured in the QALY
- methods to assess whether additional evidence is needed prior to the routine introduction of interventions (e.g. 'only in research' or 'coverage with evidence' decisions).

5. Discussion and conclusions

5.1 Project limitations

Given the time and resource constraints of the project, it was necessary for the literature review to be highly focused. Ideally the review would have extended to literature relating to processes and methods priorities for organizations similar to NICE internationally. Indeed, it could have been broader, looking at the extensive methods literature relating to the evaluation of health service and medical technology evaluations. More extensive reviews such as these would have extended the project markedly. Moreover, it is unclear whether the methods research topics that might have emerged from this additional work would have directly applied to NICE's activities.

The interviews and email survey focused on individuals who are employed by NICE or who have a close professional association with the Institute. Although methodologists were involved in this process, and in the February 2008 workshop, more extensive involvement of methodology specialists, working across the range of NICE's activities, would have been desirable if time and resources had permitted. The value of such an extension, however, would depend on whether potential methodological research topics are better generated by those who understand the demands of NICE's decision-making responsibilities, or by individuals who are familiar with the potential of research methodology to support decision-making.

The web-based survey to prioritize potential topics was also limited by time – it was available for completion for a month. It is likely that this time constraint, and the extensive length of the questionnaire which reflected the number of potential topics identified in earlier stages of the project, limited the number of responses for analysis. There were also some technical problems with the survey such as the possibility for respondents to choose more than three priority topics across areas and themes despite being asked to select only three. Despite these limitations, the web comment provides some indication of how important the suggested topics are judged by a broad group of individuals with an interest in NICE and/or evaluation methods.

5.2 Issues of process

Little emerged from the focussed review of literature and key policy documents regarding how NICE currently identifies and prioritises potential methodological research topics. Methodological topics have been discussed with the MRP and, in a few cases, taken forward as vignettes and, in one case, active commissioning has taken place (although the MRP Panel and its processes for taking forward needs-led research have only been operating since April 2008). This indicates that some form of process exists through which these topics were selected and progressed.
However, from the interviews and email survey, many commented on the lack of an Institute-wide process. RDAC was widely understood to have a key role in the existing process, but the specification of this role was thought to be poorly developed. Several commented on NICE's reactive approach to methodological issues, with the changes to the methods guidance relating to 'End of Life' technologies evidenced in this regard. There was a feeling that a more proactive approach would be advantageous.

Overall, then, there was a feeling that the process of topic identification, communication and prioritisation needs either changing or making more clear and explicit. A range of ideas emerged on how this might be progressed. Issues to consider in any changes to the process include:

- How the full range of NICE's activities are to be covered, recognising the variety of methods issues that are likely to be seen as important across the centres and teams. Key to this is to provide very clear communication about the aims, objectives and processes of identifying and prioritising topics.
- Which team or as yet unspecified group of individuals within the Institute is to be the repository for topic suggestions over time? It would seem sensible for RDAC to have overall responsibility for this, or a sub-group which effectively acts as a 'methodology committee'. The existing database for potential research topics needs to be extended to include methodological topics, or a similar database considered. There may be value in developing a web-based interface to that database, to which NICE staff will have access and can make topic suggestions.

- To what extent would this team/group be proactive in identifying topics or wait to be contacted by others? It is likely that the centres responsible for generating guidance will have to take a lead in identifying topics. Questions remain, however, about the extent to which a methodological research culture exists in some parts of NICE. Therefore, there is likely to be a need for the group responsible for methodology to reach out to all parts of the Institute and to understand their needs.
- Whether additional specific discussion forums within NICE are organised at which methodological issues are discussed with a view to identifying potential research topics. The Technical Forum already exists and could be extended to cover the discussion of methodological research priorities. There is a need to get methodology research routinely into the minds of decision-making committees – for example, through specific agenda items being included in existing meetings (e.g. centre or committee away days, committee meetings).
- What role would be played by those not formally employed by NICE, but closely related to its activities, in the identification process?   This would include assessment groups/evidence review groups, NCCs, public health evidence groups, decision-making committees, REBIP and the NICE Decision Support Unit. These groups include individuals who have expertise in methodology as well as understanding the needs of NICE. They are surely essential in helping NICE staff to identify issues where methodological research would be potentially beneficial.
- What role would be specified for external methodologists in the process? Would this group extend any further than methodologists involved in NICE's decision-making bodies and evidence groups?
- What role could other external stakeholders play in the process (e.g. technology manufacturers)?

Relatively few comments emerged on the process of prioritisation of a long list of potential research topics, although there was some discussion regarding whether an explicit scoring system would be a useful part of the process.   One feature of a more explicit process that may be of value (and has been part of the web-based prioritisation reported here) is to ask those individuals and groups forwarding topics to justify their suggestions by addressing some very key questions for each. These might include: To which area of NICE's activities does the research relate? What potential exists for methodological research to increase the value or efficiency of NICE's activities?

Little was discussed in the interview and survey about two particular issues. The first is how to translate an area of methodological uncertainty, where it is felt that research might be potentially helpful, into a researchable question. This is not a trivial stage in the process as it requires an understanding of the range of methods available for a particular task (not just those currently used by NICE), methodological research already undertaken and alternative approaches to methodological research. The current process of developing topics for the MRC MRP involves some initial specification of a question by NICE which is then further developed into a vignette, for consideration by the MRC MRP, by a contracted researcher. Although this process serves more stakeholders than just NICE, there is a need to consider whether these arrangements are appropriate for NICE's needs over the longer-term. It is likely that NICE will require considerably more capacity to be available to develop researchable questions (when they exist) out of potential topics.

A second process issue that would need to be considered relates to the use of methodologists external to NICE who might contribute to the process of identifying and prioritising research topics, and then working them up into researchable questions. The advice of such externals is likely to be important in the process, but the problem of their potential conflicts of interest are clear if they were subsequently to bid for research in a topic on which they have advised. One way to address this is for academic advisors to agree in advance that they will not apply for a grant relating to the specific topics on which they are advising.

An alternative approach would be to work with the MRC to prepare quite general calls for methods research applications – that is, to take topics which are not much more specifically defined than those detailed here as coming out of the scoping project.   This would put the onus on those seeking research funding to define their proposed project and to justify its value to NICE's decision-making processes. One potential disadvantage of this is that it would potentially put a good deal of pressure on the MRP Panel to assess the value of the proposals. NICE would also presumably need to be involved in this process to ensure that proposed research is likely to satisfy their needs.

5.3 Methodological research topics

A series of activities was undertaken to assemble a long list of methodological research topics of potential value to NICE decision-making. These included interviews with key stakeholders, an email survey with a broader set of stakeholders and methodologists, a workshop and a web-based survey. A total of 125 topics were presented on the web survey, with a limited number of additional suggestions coming from that part of the process.   Figures 1 to 5 above show that, across the 5 areas into which topics were arranged, there appears to be a broad relevance across the range of NICE's decision-making activities.

One issue that was raised throughout the process, that needs to be considered as these topics are developed further, is, what constitutes methodological research?   A large proportion of suggested topics would probably be considered clearly methodological in that they relate to the further development and refinement of evaluative and analytical tools which have relevance beyond a single application.   Other topics may be considered less obviously methodological. An example relates to the empirical estimation of NICE's cost-effectiveness threshold where it might be argued that the estimation *per se* may not be methodological, but that there are a number of methodological questions that need to be addressed before such empirical work is undertaken. It may be that research commissioners other than the MRP whose remit is specifically focussed on generalisable methods development research, should be approached about funding some of the topics suggested in this document.

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ABBREVIATIONS

ABPI	Association of the British Pharmaceutical Industry
AHRQ	Agency for Healthcare Research and Quality
CCP	NICE Centre for Clinical Practice
CEA	Cost-Effectiveness Analysis
CG	NICE Clinical Guideline
CRD	Centre for Reviews and Dissemination, University of York
CUA	Cost Utility Analysis
EUnetHTA	European Network for Health Technology Assessment
HTA	Health Technology Assessment
ICER	Incremental Cost-Effectiveness Ratio
InterTASC	Technology Assessment Services Collaboration
IP	NICE Interventional Procedures programme
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
MHRA	Medical and Healthcare products Regulatory Agency
MRC	Medical Research Council
MRP	MRC Methodology Research Programme
MTA	Multiple Technology Appraisal programme
NCC	National Collaborating Centre
NCCHTA	NIHR Coordinating Centre for Health Technology Assessment
NETSCC	NIHR Evaluation, Trials and Studies Coordinating Centre
NHS	National Health Service
NHSEED	National Health Service Economic Evaluation Database
NICE	National Institute for Health and Clinical Excellence
NIHR	National Institute for Health Research
OSCHR	Office for Strategic Coordination of Health Research
PHIAC	NICE Public Health Interventions Advisory Committee
QALY	Quality Adjusted Life Year
RDAC	The NICE Research and Development Advisory Committee
STA	Single Technology Appraisal programme
TA	NICE Technology Appraisal
TAG	NICE Technology Assessment Group

KEY TECHNICAL TERMS[1]

Aggregated data: Data presented as the sum of all the resources and costs involved.

Assessment group: An independent assessment group commissioned by the NHS Research and Development Health Technology Assessment (HTA) programme to produce an independent review of the evidence for technologies being appraised within the multiple technology appraisal (MTA) process.

Assessment report: A critical review of the clinical and cost-effectiveness of a health technology/technologies being appraised within the multiple technology appraisal (MTA) process. It is prepared by the Assessment Group. To prepare the report, the Assessment Group carries out a review of the published literature and the submissions from manufacturers and sponsors.

Bias systematic: (as opposed to random) deviation of the results of a study from the 'true' results.

Case–control study: Comparative observational study in which the investigator selects people who have experienced an event (for example, developed a disease) and others who have not (controls), and then collects data to determine previous exposure to a possible cause.

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[1] Taken from the Glossary in the NICE Guide to the Methods of Technology Appraisal - 2008

Clinical effectiveness: The extent to which an intervention produces an overall health benefit, taking into account beneficial and adverse effects, in routine clinical practice.

Cohort study: A retrospective or prospective follow-up study. People included in the study are grouped on the basis of whether or not they have been exposed to a suspected risk factor or intervention. A cohort study can be comparative, but the study investigator has no control over who is exposed or not.

Co-morbidity: Coexistence of a disease, or more than one disease, in a person in addition to the disease being studied or treated.

Comparator: The standard intervention against which the intervention under appraisal is compared. The comparator can be no intervention, for example, best supportive care.

Cost-effectiveness analysis: An economic study design in which consequences of different interventions are measured using a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided, or cases detected). Alternative interventions are then compared in terms of cost per unit of effectiveness.

Cost-effectiveness model: An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources to estimate costs and health outcomes.

Data synthesis: Combining evidence from different sources.

Decision problem: A clear description of the interventions, patient populations, outcome measures and perspective adopted in a health technology evaluation, which relates specifically to the decision(s) that the evaluation is designed to inform.

Efficacy: The extent to which an intervention is active when studied under controlled research conditions.

EQ-5D: An instrument for the measure and valuation of health developed by the EuroQol Group

Evidence: Information on which a decision or guidance is based. Evidence is obtained from a range of sources, including randomised controlled trials, observational studies and expert opinion (of clinical professionals and/or patients/carers).

Experimental study (analytic study): A study with an explicit control group that allows testing of a hypothesis.

Extrapolation: In data analysis, predicting the value of a parameter outside the range of observed values.

Health-related quality of life (HRQL): A combination of a person's physical, mental and social wellbeing; not merely the absence of disease.

Health technology: Any method used by those working in health services to promote health, prevent and treat disease, and improve rehabilitation and long-term care. Technologies in this context are not confined to new drugs or items of sophisticated equipment.

Heterogeneity: Used in meta-analyses and systematic reviews to describe when the results or estimates of effects of a treatment from separate studies seem to be very different (for example, the size of treatment effects may vary across studies, or some studies may indicate beneficial treatment effects whereas others suggest adverse treatment effects). Such difference in results may occur by chance, because of variation in study quality or because of variation in populations, interventions, or methods of outcome measurement in the included studies.

Homogeneity: Used to describe when the results of studies included in a systematic review or meta-analysis are similar and there is no more variation than would occur by chance alone. Results are

usually regarded as homogeneous when any differences observed between studies could reasonably be expected to occur by chance.

Incremental cost-effectiveness ratio (ICER): The ratio of the difference in the mean costs of a technology compared with the next best alternative to the differences in the mean outcomes.

Indirect comparison: An analysis comparing interventions that have not been compared directly within a head-to-head randomised trial.

Meta-analysis: A statistical technique for combining (pooling) the results of a number of studies that address the same question and report on the same outcomes to produce a more precise summary estimate of the effect on a particular outcome.

Mixed treatment comparison: An analysis that compares two or more interventions using a combination of direct evidence (from head-to-head trials of the interventions of interest) and indirect evidence (trials that do not compare the interventions of interest directly in head-to-head trials).

Multiple technology appraisal (MTA): The name given to the NICE process in which appraisals of more than one technology, or a single technology for more than one indication, are conducted.

Opportunity cost: The opportunity cost of investing in a healthcare intervention is the other healthcare programmes that are displaced by its introduction. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.

Outcome: The measure of the possible results that may stem from exposure to a preventive or therapeutic intervention. Outcome measures can be either intermediate or final endpoints.

Parameter uncertainty: Uncertainty about the population mean values of parameters (for example, health outcomes, utilities and resource use) included in the model.

Patient-level data: Information on the outcome and cost of treatment collected for individual patients.

Quality-adjusted life year (QALY): An index of survival that is adjusted to account for the patient's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social, and other factors) of life. Used to measure benefits in cost–utility analysis.

Quality of life: See 'Health-related quality of life'.

Randomisation: Allocation of participants in a research study to two or more alternative groups using a chance procedure, such as computer-generated random numbers. This approach is used to attempt to ensure there is an even distribution of participants with different characteristics between groups and thus reduces bias and confounding.

Randomised controlled trial (RCT): A comparative study in which people are randomly allocated to intervention and control groups and followed up to examine differences in outcomes between the groups.

Reference case: When estimating clinical and cost-effectiveness, the reference case specifies the methods considered by NICE to be the most appropriate for the Appraisal Committee's purpose and consistent with an NHS objective of maximising health gain from limited resources.

Single technology appraisal (STA): The name given to the NICE process in which appraisals of single technologies for one indication are conducted.

Structural uncertainty: Uncertainty relating to the range of assumptions and judgements necessary in constructing a model. This can include design features of the model (for example, the assumed standard pathway of care) as well judgements about the relevance of evidence, assumptions about appropriate distributions for parameters and alternative methods of estimation.

Synthesis of evidence: A generic term to describe methods used for summarising (comparing and contrasting) evidence into a clinically meaningful conclusion to answer a defined clinical question. This can include systematic review (with or without meta-analysis), and qualitative and narrative summaries.

Systematic review: Research that summarises the evidence on a clearly formulated question according to a predefined protocol. Systematic and explicit methods to identify, select and appraise relevant studies, and to extract, collate and report their findings are used. Statistical meta-analysis may or may not be used.

Technology assessment: The process of evaluating the clinical, economic and other evidence relating to use of a technology to formulate guidance on its most efficient use.

Time trade-off: A method used to measure utility (for example, health states). The utility value is measured by finding the point at which the respondent cannot choose between two scenarios. For chronic illness, the choice is between the illness for a period of time and perfect health for a shorter time, both followed by death. For short-term illness, the choice is between the illness for a period of time and a worse health state for a shorter time, both followed by the same specified outcome.

Utility: A measure of the strength of a person's preference for a specific health state in relation to alternative health states. The utility scale assigns numerical values on a scale from 0 (death) to 1 (optimal or 'perfect' health). Health states can be considered worse than death and thus have a negative value.

APPENDICES

Appendix A1: NICE 'What's new' literature search strategies

Database: Medline (Ovid)
1. Guidelines as Topic/
2. Practice Guidelines as Topic/
3. Guideline Adherence/
4. exp *Epidemiologic Research Design/
5. Evidence-Based Medicine/
6. Technology Assessment, Biomedical/
7. exp Epidemiologic Research Design/mt, sn, st [Methods, Statistics and Numerical Data, Standards]
8. Meta-Analysis as Topic/
9. exp Review Literature as Topic/
10. exp *Epidemiologic Study Characteristics as Topic/
11. exp Epidemiologic Study Characteristics as Topic/mt, sn, st [Methods, Statistics and Numerical Data, Standards]
12. exp Controlled Clinical Trials as Topic/
13. exp *Statistics as Topic/
14. exp Statistics as Topic/mt, st [Methods, Standards]
15. Publication Bias/
16. Consensus/
17. ((grade$ or grading$) adj3 (evidence or recommendation$)).tw.
18. (consensus adj3 (develop$ or method$ or build$)).tw.
19. (indirect adj3 comparison$).tw.
20. or/1-19
21. limit 20 to (abstracts and english language)
22. Animals/ not Humans/
21 not 22

Database: Medline In-Process (Ovid)
1. guideline$.ti.
2. (meta-analy$ or metaanaly$).ti.
3. (systematic$ adj3 review$).ti.
4. ((randomi?ed or clinical) adj2 trial$).ti.
5. (diagnostic adj3 accuracy).ti.
6. ((diagnos$ or prognos$ or observational or qualitative) adj2 (stud$ or research)).ti
7. (publication adj3 bias$).ti
8. ((grade$ or grading$) adj3 (evidence or recommendation$)).ti.
9. (consensus adj3 (develop$ or method$ or build$)).ti.
10. (indirect adj3 comparison$).ti.
11. or/1-10
limit 11 to (abstracts and english language)

In addition the following journals and websites were specifically tracked for relevant papers.
BMC Health Services Research (alerts received every 7 days)
BMC Medical Research Methodology (alerts received every 7 days)
BMJ (published weekly – alert set up)
Emerging Themes in Epidemiology (BMC) (alerts received every 7 days)
Epidemiologic Perspectives & Innovations (BMC) (alerts received every 7 days)
International Journal of Technology Assessment in Health Care (published 4 times/year – alert set up)
Journal of Clinical Epidemiology (published 12 times/year – alert set up)
Journal of Health Services Research & Policy (published 4 times/year – alert set up)
Medical Decision-making (published 6 times/year – alert set up)
Quality & Safety in Health Care (published 4 times/year – alert set up)
Trials (BMC) (alerts received every 7 days)
NIHR HTA programme – alert set up for methodological reviews

Appendix A2: List of face-to-face and telephone interviewees

Stakeholder	Organisation
Ken Stein	University of Exeter
Tony Whitehead	ABPI
Matt Bradley	GSK
Georgios Lyratzopoulos	NICE
Catherine Law	Public Health Interventions Advisory Committee
Kent Woods	MHRA
Tom Walley	HTA
Mike Kelly	NICE
Steve Pilling	National Collaborating Centre for Mental Health
Adrian Griffin	ABHI
Peter Littlejohns	NICE
David Barnett	NICE
Andrew Stevens	NICE
Fergus MacBeth	NICE
Marcia Kelson	NICE
Carol Longson	NICE
Sarah Garner	NICE
Tony Culyer	NICE

Appendix A3: Face-to-face and telephone interview schedule

Background

This semi-structured interview schedule is designed to act as a guide for the interviewer so that the issues identified in the questions are addressed. The specific framing of the questions will be tailored to the interviewee's role and organisation where appropriate.

The sets of questions that interviewees will be asked will depend on whether they have been selected to discuss one or more of the following issues (i) current processes for identifying and prioritising methodological research (ii) potential future processes for identifying and prioritising methodological research at NICE (iii) potential priority topics for method development.

Introduction

We have arranged this interview as part of a project designed to assist NICE and MRC in identifying methodological research priorities. The purpose of this interview is to elicit details of the processes currently employed by NICE to identify priority areas for methodological research, your views on possible future processes for identifying topics and provide a proposed list of current priority areas for methodological research [delete as appropriate].

The scope of the project is limited to methodological research relevant to NICE decision-making. Therefore we are focussing on the development of methods, rather than the application of existing methodologies to generate data for specific appraisals or diseases. In addition the focus is on priority areas for development of methods that could directly enhance decision-making at NICE, rather than other more general developments in HTA methods.

Current NICE process for identifying methodological research priorities

Audience: To be addressed to members of NICE secretariat and Committee Chairs.

Aim: to identify current formal and informal processes for how potentially important methods research topics are identified and progressed through the NICE system.

Questions:
What processes are currently in place to identify areas where methods could be further developed to facilitate the needs of decision-makers at NICE?

Are there specific individuals or teams within the institute who have the responsibility of identifying potential areas for methodological research or development?

Are regular meetings held to discuss methodological research needs? If yes, what kind of meeting? (Senior management team meetings? Meetings of directorates? Meetings of technical teams within directorates? Across institute meetings (e.g. technical forum meetings)? Meetings of Chairs?)

Internal/external/mixed meetings? (e.g. Decision Support Unit? Intertasc (appraisals)? Guideline Development Groups (guidelines)?

If no, are there ad hoc meetings, or ad hoc agenda items added to existing meetings as required?

Does anyone within your team or the Institute regularly review literature for developments in methodology that may be potentially important to your work? (Who does this? What is reviewed? How often? How is this fed back to the team and/or the Institute?)

Does the need for further methodological research (as opposed to specific application of existing research methods to topic under consideration) arise during the production of a specific appraisal/guideline/guidance/review?

How often? What type of methods research need? (Give examples) Who would usually identify this need? (Technical analyst/advisor? Committee /Group member? External review team/ Consultee?)

Would the need for further methodological research be discussed during the deliberations of the Appraisal Committee/Guideline Group/Advisory Committee? How is this fed back to the Institute? Provide examples where possible

Are there any ongoing or planned changes to the current process?

Have there been any reviews conducted to identify such methodological research needs within the Institute/your team?

Who was involved?

What was reviewed (e.g. topic area)?

How was the review conducted?

Are such reviews conducted on an ad hoc basis or part of a regular review?

Have these led to formal processes being adopted? What problems were encountered?

Once a potential area of methods research has been identified who would this be referred to internally?

How would you/the Institute prioritise a potential area for future methodological research alongside other potential topics?

Are there formal mechanisms for this?

What are the criteria used?

Who decides?

How would the identified need for methods development be developed into a researchable question? How would funding for the research be obtained?

Directly from NICE (centrally or via the directorate?)? Referral to another body (e.g. MRC)/ Conduct research internally?

How does having the Methods Guide impact on identifying methods research priorities? E.g. are methods research topics identified during the process of producing the guides? Does it negatively impact on research development?

Current process for identifying methodological research priorities in other organisations

Audience: To be addressed to members of other research/HTA organisations

Aim: to identify current formal and informal processes for prioritisation in other organisations.

Questions:
Does your organisation currently identify areas where further methods development is required or desired?

How does your organisation go about doing this?

Are there teams/individuals in the organisation who have a specific responsibility for identifying potential topics for methodological research?

How do they identify potential topics?

Are reviews of potential areas for methodological research conducted? If so, are they conducted regularly or on an ad hoc basis? How are the reviews conducted (e.g. by reviewing literature? Consultation with external collaborators/organisations?)

Does the need for further methodological research (as opposed to specific application of existing research methods to topic under consideration) arise during the production of a specific review?

Is the process for identifying such topics published or documented?

Please give examples of where a need for further methodological research has been identified?

How are proposed areas for research prioritised?

Who would be involved in prioritising the topic area?

What criteria would be used to assess the priority of each topic?

If examples provided, were they prioritised? If so, how?

Once a potential area of methods research has been identified, how would it be progressed to a potential study?

How would a researchable question be developed from the identified need for further research? Would funding for the study be provided internally or would external organisations be contacted? Which organisations?

Does your organisation have a documented Guide for HTA methods? If yes, has this impacted on the identification of methods research priorities? If so, how? e.g. are methods research topics identified during the process of producing the guides? Does it negatively impact on research

Potential future processes for identifying methodological research priorities

Audience: Members of NICE secretariat and Committee Chairs.

Aims: to elicit opinions from those internally at NICE about improved processes for identifying research priorities

Questions:
How do you think the process for identifying potential methodological research needs could be improved?

Who do you think should be involved in identifying such requirements (internally/externally)?

How do you think the process for prioritising methodological research topics could be improved?

Who should be responsible for this (internally/externally)?

Is there anyone else who should be involved?

What do you think should be the basis for prioritisation of proposed methodological research topics?

Potential methodological research priority topics

Audience: To be addressed to all interviewees involved in NICE.

Aim: to produce a list of potential methodological research topics relevant to decision-making at NICE

Questions:

What do you think are the most important methodological research questions that need to be addressed to enhance/facilitate the needs of decision-makers at NICE? [Up to five topic areas can be provided]

Why do you think this is an important issue for NICE?

How will this research improve the decision-making process at NICE?

Can you give any examples of NICE work where improvements in this methodological area would have been beneficial?

Does the research topic relate to any recent policy developments?

Are you aware of any ongoing or recent research addressing this issue?

Are you aware of any barriers to conducting this research/ why has it not been conducted in the past (new methodological devt? New policy devt? Lack of funding? Not seen as priority?)

Appendix A4: Email surveys

Figure A4a: Email survey version 1

Review of methodological research priorities for NICE/MRC

Introduction

We have contacted you as part of a short project, funded by the MRC, which is designed to assist NICE in identifying priorities for methodological research to support its decision-making. The purpose of this is to elicit details of the processes currently employed by NICE to identify priority areas for methodological research, your views on possible future processes for identifying topics and provide a proposed list of current priority areas for methodological research.

The scope of the project is limited to methodological research relevant to NICE decision-making. Therefore we are focussing on the development of methods, rather than the application of existing methodologies to generate data for specific appraisals or diseases. In addition, the focus is on priority areas for development of methods that could directly enhance decision-making at NICE, rather than other more general developments in HTA methods.

Please place your answers in the text boxes provided. If you have no response to a particular question, please leave that box blank.

If you need additional space for your answers please continue in the space provided at the end of the questionnaire.

THANK YOU FOR YOUR RESPONSE

1.   Current NICE process for identifying methodological research priorities

This section aims to identify current formal and informal processes for how potentially important methods research topics are identified and progressed through the NICE system.

1.1   How are potential areas of methodological research relevant to NICE decision-making currently identified at NICE?

In your answer you may wish to consider the following:

- What formal processes are currently in place?
- Do specific individuals or teams within the Institute have the responsibility of identifying potential areas for methodological research or development?
- Does anyone within your team or the Institute regularly review literature for developments in methodology that may be potentially important to the work of NICE?
- Are regular meetings held to discuss methodological research needs?
- Are people external to the Institute involved in identifying methodological research needs for NICE?
- Does the need for further methodological research arise during the production of a specific appraisal/guideline/guidance/review?

1.2   Are there any ongoing or planned changes to the current process?

1.3   Have there been any reviews conducted to identify such methodological research needs within the Institute/your team?

In your response you may wish to consider the following:

- Who was involved?
- What was reviewed (e.g. topic area)?
- How was the review conducted?
- Are such reviews conducted regularly or on an ad hoc basis?

- Have these led to formal processes being adopted?

1.4   Once a potential area of methods research has been identified, how would it be prioritised and developed into a research project?

In your response you may wish to consider the following:

- Who would the need for methodological development be referred to internally?
- How would you/the Institute prioritise a potential area for future methodological research alongside other potential topics?
- Are there formal mechanisms for this?
- What are the criteria used to prioritise methodological research?
- How would the identified need for methods research be developed into a researchable question?
- How would funding for the research be obtained (e.g. directly from NICE or an external organisation?)?

How does having the Methods Guide impact on identifying methods research priorities?
E.g. are methods research topics identified during the process of producing the guides? Does it negatively impact on research development?

2. Potential future processes for identifying methodological research priorities

This section aims to elicit your opinion about improved processes for identifying research priorities at NICE.

2.1.   How do you think the process for identifying potential methodological research at NICE needs could be improved?

In your response you may wish to consider who should be involved in the process.

2.2.   How do you think the process for prioritising methodological research topics could be improved?

In your response you may wish to consider the following:

- Who should be responsible for this (internally/externally)?
- Is there anyone else who should be involved?
- What do you think should be the basis for prioritisation of proposed methodological research topics?

3. Potential methodological research priority topics

This sections aims to produce a list of potential methodological research topics relevant to decision-making at NICE.

3.1. What do you think are the four most important methodological research questions that need to be addressed to enhance/facilitate the needs of decision-makers at NICE?

3.2. Why do you think these are important issues for NICE?

3.3. How will this research improve the decision-making process at NICE?

3.4. Can you give any examples of NICE work where improvements in this methodological area would have been beneficial?

3.5. Does the research topic relate to any recent policy developments?

3.6. Are you aware of any ongoing or recent research addressing this issue?

3.7. Are you aware of any barriers to conducting this research/ why has it not been conducted in the past (new methodological development? New policy development? Lack of funding? Not seen as priority?)

If you have any additional comments then please use the space below.

Figure A4b: Email survey version 2

Review of methodological research priorities for NICE/MRC

Introduction

We have contacted you as part of a short project, funded by the MRC, which is designed to assist NICE in identifying priorities for methodological research to support its decision-making. The purpose of this is to elicit details of the processes currently employed by your organisation to identify priority areas for methodological research, your views on possible future processes for identifying topics at NICE and provide a proposed list of current priority areas for methodological research.

The scope of the project is limited to methodological research relevant to NICE decision-making. Therefore we are focussing on the development of methods, rather than the application of existing methodologies to generate data for specific appraisals or diseases. In addition, the focus is on priority areas for development of methods that could directly enhance decision-making at NICE, rather than other more general developments in HTA methods.

Please place your answers in the boxes provided. If you need additional space for your answers please continue in the space provided at the end of the questionnaire.

THANK YOU FOR YOUR RESPONSE

1. Current process for identifying methodological research priorities

This section aims to identify current formal and informal processes for prioritisation in your organisation.

1.1.   Does your organisation currently identify areas where further methods development is required or desired? (please 'X' yes or no – if no please go to Section 2)

Yes

No

1.2.   How does your organisation identify areas where further methods development is required or desired?

In your response you may wish to consider the following:

- Are there teams/individuals in the organisation who have a specific responsibility for identifying potential topics for methodological research?
- How do they identify potential topics?
- Are reviews of potential areas for methodological research conducted? If so, are they conducted regularly or on an ad hoc basis? How are the reviews conducted (e.g. by reviewing literature? Consultation with external collaborators/organisations?)
- Does the need for further methodological research (as opposed to specific application of existing research methods to topic under consideration) arise during the production of a specific review?
- If possible, please give examples of where methodological research needs have been identified.

Is the process for identifying such topics published or documented? (If yes, please provide details)

1.3.   How are proposed areas for research prioritised?

In your response you may wish to consider the following:

- Who would be involved in prioritising the topic area?
- What criteria would be used to assess the priority of each topic?
- If examples provided, were they prioritised? If so, how?

1.4.   Once a potential area of methods research has been identified, how would it be progressed to a potential study?

- How would a researchable question be developed from the identified need for further research?
- Would funding for the study be provided internally or would external organisations be contacted? Which organisations?

1.5.   Does your organisation have a documented Guide for HTA methods?

- How has this impacted on the identification of methods research priorities?
- Does it negatively impact on research?

2. Potential future processes for identifying methodological research priorities

This section aims to elicit your opinion about improved processes for identifying research priorities at NICE.

2.1   How do you think the process for identifying potential methodological research at NICE needs could be improved?

In your response you may wish to consider who should be involved in the process.

2.2   How do you think the process for prioritising methodological research topics could be improved?

In your response you may wish to consider the following:

- Who should be responsible for this (internally/externally)?
- Is there anyone else who should be involved?
- What do you think should be the basis for prioritisation of proposed methodological research topics?

3 Potential methodological research priority topics

This sections aims to produce a list of potential methodological research topics relevant to decision-making at NICE.

What do you think are the four most important methodological research questions that need to be addressed to enhance/facilitate the needs of decision-makers at NICE?

3.1   Why do you think these are important issues for NICE?

3.2   How will this research improve the decision-making process at NICE?

3.3   Can you give any examples of NICE work where improvements in this methodological area would have been beneficial?

3.4   Does the research topic relate to any recent policy developments?

3.5   Are you aware of any ongoing or recent research addressing this issue?

3.6   Are you aware of any barriers to conducting this research/ why has it not been conducted in the past (new methodological development? New policy development? Lack of funding? Not seen as priority?)

Space for additional comments

Figure A4c: Email survey version 3

Review of methodological research priorities for NICE/MRC

Introduction

We have contacted you as part of a short project, funded by the MRC, which is designed to assist NICE in identifying priorities for methodological research to support its decision-making. The purpose of this is to elicit your views on possible future processes for identifying topics at NICE and provide a proposed list of current priority areas for methodological research.

The scope of the project is limited to methodological research relevant to NICE decision-making. Therefore we are focussing on the development of methods, rather than the application of existing methodologies to generate data for specific appraisals or diseases. In addition, the focus is on priority areas for development of methods that could directly enhance decision-making at NICE, rather than other more general developments in HTA methods.

Please place your answers in the text boxes provided. If you have no response to a particular question, please leave that box blank.

If you need additional space for your answers please continue in the space provided at the end of the questionnaire.

THANK YOU FOR YOUR RESPONSE

1. Potential future processes for identifying methodological research priorities

This section aims to elicit your opinion about improved processes for identifying research priorities at NICE.

1.1 How do you think the process for identifying potential methodological research at NICE needs could be improved?

In your response you may wish to consider who should be involved in the process.

1.2 How do you think the process for prioritising methodological research topics could be improved?

In your response you may wish to consider the following:

- Who should be responsible for this (internally/externally)?
- Is there anyone else who should be involved?
- What do you think should be the basis for prioritisation of proposed methodological research topics?

2. Potential methodological research priority topics

This sections aims to produce a list of potential methodological research topics relevant to decision-making at NICE.

2.1 What do you think are the four most important methodological research questions that need to be addressed to enhance/facilitate the needs of decision-makers at NICE?

2.2 Why do you think these are important issues for NICE?

2.3 How will this research improve the decision-making process at NICE?

2.4 Can you give any examples of NICE work where improvements in this methodological area would have been beneficial?

2.5 Does the research topic relate to any recent policy developments?

2.6 Are you aware of any ongoing or recent research addressing this issue?

2.7 Are you aware of any barriers to conducting this research/ why has it not been conducted in the past (new methodological development? New policy development? Lack of funding? Not seen as priority?)

Space for additional comments

Figure A4d: Email survey version 4

Review of methodological research priorities for NICE/MRC

Introduction

We have contacted you as part of a short project, funded by the MRC, which is designed to assist NICE in identifying priorities for methodological research to support its decision-making. The purpose of this is to provide a proposed list of current priority areas for methodological research.

The scope of the project is limited to methodological research relevant to NICE decision-making. Therefore we are focussing on the development of methods, rather than the application of existing methodologies to generate data for specific appraisals or diseases. In addition, the focus is on priority areas for development of methods that could directly enhance decision-making at NICE, rather than other more general developments in HTA methods.

Please place your answers in the text boxes provided. If you have no response to a particular question, please leave that box blank.

If you need additional space for your answers please continue in the space provided at the end of the questionnaire.

THANK YOU FOR YOUR RESPONSE

1. Potential methodological research priority topics

This sections aims to produce a list of potential methodological research topics relevant to decision-making at NICE.

1.1 What do you think are the five most important methodological research questions that need to be addressed to enhance/facilitate the needs of decision-makers at NICE?

1.2 Why do you think these are important issues for NICE?

1.3 How will this research improve the decision-making process at NICE?

1.4 Can you give any examples of NICE work where improvements in this methodological area would have been beneficial?

1.5 Does the research topic relate to any recent policy developments?

1.6 Are you aware of any ongoing or recent research addressing this issue?

1.7 Are you aware of any barriers to conducting this research/ why has it not been conducted in the past (new methodological development? New policy development? Lack of funding? Not seen as priority?)

Space for additional comments

Table A4a. Email survey respondents

Name	Organisation	E-mail Survey type
Janet Robertson	NICE	1
Alex Sutton	Society for Research Synthesis Methodology	4
Finn Borlum Kristensen	European Network for Health Technology Assessment (EUnetHTA)	2
Jean Slutsky	Agency for Healthcare Research and Quality	2
Norman Waugh	University of Aberdeen	4
Adrian Bagust	University of Liverpool	4
Matt Stevenson	ScHARR - University of Sheffield	4
Maggie Westby	NCC	4
Craig Whittington	NCC	4
Beth Shaw	NICE	4
Angela Melder	NCC	4
Francis Ruiz	NICE	1

Appendix A5: List of workshop participants

	Name	Affiliation
Dr	Bhash Naidoo	NICE
Professor	Catherine Law	UCL Institute of Child Health
Dr	Celia Brown	University of Birmingham
Dr	Chris Hyde	University of Birmingham
Professor	David Barnett	University of Leicester
Professor	David Hughes	Swansea University
Professor	David Jones	University of Leicester
Dr	Allan Wailoo	University of Sheffield
Dr	Fergus MacBeth	NICE
	Francis Ruiz	NICE
Dr	Georgios Lyratzopoulos	NICE
Professor	James Raftery	University of Southampton
	Janet Robertson	NICE
	Jim Chilcott	University of Sheffield
Professor	John Brazier	University of Sheffield
Professor	Jon Nicholl	University of Sheffield
	Jon Tosh	University of Sheffield
Dr	Julia Earnshaw	GlaxoSmithKline
Professor	Karl Claxton	University of York
Professor	Keith Abrams	University of Leicester
Dr	Laura Bojke	University of York
Dr	Louise Longworth	University of Sheffield
Dr	Marcia Kelson	NICE
Professor	Mark Sculpher	University of York
	Meindert Boysen	NICE
Dr	Nerys Woolacott	University of York
Professor	Peter Littlejohns	NICE
Dr	Ruth Garside	University of Exeter
Dr	Sarah Garner	NICE
	Simon Ellis	NICE
Professor	Susan Michie	UCL
Professor	Tim Peters	University of Bristol
Professor	Tom Treasure	UCL
Professor	Tony Ades	University of Bristol
Dr	Tony Whitehead	sanofi-aventis
Professor	Trevor Sheldon	University of York
Dr	Nichole Taske	NICE
Professor	Adrian Towse	OHE

Appendix A6: Workshop agenda

NICE Methodology Scoping Study

Agenda for Workshop 6th February 2009

9.15 – 9.45	Coffee	
9.45 – 10.00	Welcome and introductions	Facilitator: Trevor Sheldon
	- Aims and objectives of the day	
	- The organisation of the day	
10.00 – 10.15	Overview of study	Mark Sculpher

Plenary: overviews of key methodology themes

10.15 – 10.45	Analysis and design of effectiveness studies and their synthesis	Keith Abrams
10.45 – 11.15	Synthesis of evidence from patients, the public and stakeholders	Ruth Garside
11.15 – 11.30	Coffee	
11.30 – 12.00	Measurement and valuation of benefits	John Brazier
12.00 – 12.30	Economic analysis and uncertainty	Karl Claxton
12.30 – 1.00	Decision-making and NICE	Peter Littlejohns
1.00 – 1.45	Lunch	

1.45 – 3.30 Small group discussion[*]

5 small groups. Three sessions lasting for 30 minutes each (i.e. each participant can joins three groups

3.30 – 4.00
The MRC Methodology Research Programme (Angela Cooper)
Next steps (Mark Sculpher)

Appendix A7: Policy documents and journal papers included in the literature review

Reference	Comment on the current processes?	Has the publication made any suggestions for methodological research that would be or could be used by NICE in making decisions?	What are these?	Have these been worked up into researchable questions?	Have the authors reported suggestions for the type of research needed to answer these questions?
JOURNAL PAPERS					
Claxton et al (2005)[8]	No	No	Not a direct suggestion for methodological research - A continued "need to quantify the implications of the imprecision in parameter estimates for decision uncertainty". This paper discusses the appropriateness and methods of PSA, which is a method now incorporated into NICE methods.	No. Paper is a research piece on PSA methods and its incorporation in the NICE TA process	No
Claxton et al (2002)[9]	No	No	The appropriateness of EVPI and its implications for NICE.	No, the paper is a research piece on EVPI, and proposes that it is used in NICEs decision-making framework.	No
Culyer et al (2007)[10]	No	Yes	Identifying the optimal threshold implied by the prevailing NHS budget	No	No
Mauskopf (2000)[11]	No	Yes	Extrapolation – how a new drug will impact on lifetime treatment patterns.	No	No
Sculpher et al (2005)[12]	No	Yes	Quality and exchangeability or relevant of evidence. Link between intermediate end points and health gain. Extrapolation – duration of treatment effect beyond that observed in trails	No	No

Report of Methods Review Working Party: Sub-groups	No	Yes	- Further research on the relationship between baseline event risks and treatment effect. - Methods to combine individual patient-level data and aggregate data and modelling baseline and treatment effects without them interfering. - Bayesian methods for subgroup analysis e.g. biological plausibility of a subgroup in terms of a prior probability. - Cost implications of not considering subgroups and methods to do this. - Equity issues of subgroups and impact on decision-making.	Some suggestions for particular focus within areas (see previous column) but a research question not proposed.	No
Report of Methods Review Working Party: Costs	No	No	No	No	No
Report of Methods Review Working Party: Evidence synthesis	No	Yes	- Studies applying indirect and mixed treatment frameworks from pre-defined protocols to empirical data. - The impact of extending networks of evidence on results. - Empirical research into the consistency of using mixed treatment comparisons with direct trial evidence for the analysis of relative treatment effects. - Feasibility of developing approved networks of evidence for difference diseases.	Some suggestions for particular focus within areas (see previous column) but a research question not proposed.	Empirical research for area 3 suggested. No suggestions for other areas.
Report of Methods Review Working Party: Diagnostic Technologies	No	No	No	No	No
Report of Methods Review Working Party: Uncertainty	No	Yes	Feasibility of recommending a common set of models relating to disease areas for which there are frequent referrals. - Methods of assessing the need for evidence and the consequences of an uncertain decision	Some suggestions for particular focus within areas (see previous column) but a research	No

				question not proposed.	
Report of Methods Review Working Party: Utility measurement	No	Yes	- Developing a repository for health state utilities. - Methods for synthesising health-state utilities.	Some suggestions for particular focus within areas (see previous column) but a research question not proposed.	No
Brazier	No	Yes	- Research into methods for the synthesis of health state utility values, including the use of meta-regression using published or patient-level data. - How to use and adapt health state utility values published in the literature for cost-effectiveness models (for example, accounting for co-morbidities or socio-demographic factors). - How uncertainty in health state utility values should be quantified and how that uncertainty should be incorporated into economic analyses. - Does the value of a QALY depend on when it arises and who receives it (e.g. age, severity, social class, responsibility)? Noted the following current areas of promising early research: - Use of ranking and discrete choice experiments to value health states. - Ways of measuring experience values (valuation of utility moment by moment) and incorporating values into cost-effectiveness analysis. - Deriving vignettes to describe health states using cluster analysis.	Some suggestions for particular focus within areas (see previous column) but a research question not proposed.	N
Chalkidou [13]	No	Yes	- Research to establish who should pay for the research when recommended through OIR recommendations? - How should NICE establish the value for money of conducting further research (do the costs outweigh the benefits?)	Some suggestions for particular focus within areas (see previous	N

Claxton, 2008[14]	No	Yes	- How can NICE assess whether publicly funded research will impact on current policy and practice? - Perceptions of Only in Research recommendations and ethical implications? (E.g. Are they coercive?). - Recent reforms to NICE processes and UK health research funding lead to the need for new ways of prioritising and effectively communicating the importance of additional evidence to those responsible for commissioning research. - For 'coverage with evidence' decisions, research needed into how NICE should assess whether (i) additional evidence is needed (ii) what type of evidence is required (iii) the type of evidence	column) but a research question not proposed. Some suggestions for particular focus within areas (see previous column) but a research question not proposed.	N
Claxton, 2005[8]	No	Yes	For model averaging: - Who should be responsible for choosing the weights - How can differing views be combined - Which methods can be used to elicit probabilities - How many scenarios can be used to represent the possibilities For elicitation: - Who should provide judgements - Which methods of elicitation should be used - How should the quality of judgements be calibrated and weighted - Should more than one expert be used? If so how should multiple judgements be combined - Develop criteria for selecting an appropriate structure for a decision model given available evidence on disease prognosis and the impact of alternative interventions	N	N
Koopmanschap	No	No	N0	No	No
Martelli[16]	No	No	No	No	No
Miller[17]	No	No	No	No	No
Noorani[18]	No	No	No	No	No
Sculpher[19]	No	Yes	- Which types of sub-groups should be considered in economic evaluation studies undertaken to inform the decisions of the Institute? In particular, are there other	Some suggestions for particular focus	No

			sources of heterogeneity that are not described in this paper? - Is there any role for looking at any forms of preference sub-groups which were not explcitly considered in the 2004 methods guidance.	within areas (see previous column) but a research question not proposed.	
Miners[20]	No	Yes	- How should costs be proportioned / attributed in cases where the NHS / PSS is only partially responsible for a cost, either for a specific individual or across different population groups? An example of the latter could be if the costs of residential care were dependent on individuals levels of wealth, with the health care purchaser covering a greater proportion of the costs of care for relatively less wealthier individuals.	Some suggestions for particular focus within areas (see previous column) but a research question not proposed.	No
Sutton[21]	No	Yes	- Methods to incorporate information on the validity of evidence into a synthesis model used in technology appraisal - Development of user friendly software to fit MTC models - When an intervention is a relevant comparator but not connected to an evidence network, what are the methods issues of linking that treatment in, for example using observational evidence? - Since the resources required for study identification and data extraction will also increase with the size of the network there may be a point after which it will not be cost-effective to expand a network, although no formal methods exist for indicating when this is. - Since MTC methods are presently in their infancy; do we know enough about the performance of such methods to recommend them for routine practice? - Slightly different model specifications exist in the literature for conducting MTC analysis; is more methodological research required before a specific modelling approach can be recommended? If so, what? - Development of more user-friendly software to fit MTC models.	No	No

Turner, 2008[22]	No	Yes	- Need for interactive elicitation software	No	No
Welton, 2008[23]	No	Yes	- Explore values assigned to bias variance parameters - Assumption that the mean bias in a new meta analysis is exchangeable with the mean biases in the meta-analyses included in previous empirical studies - Issue of multiple sources of bias and confounding - Using bias adjustment methods for observational studies	No	No
REPORTS/GUIDES					
The Pharmaceutical Price Regulation Scheme; An OFT Market Study. The Office of Fair Trading. 2007[3]	No	No	Comments about the wider view of therapeutic value should included others who are affected by a patients condition, such as carers	No	No
House of Commons Health Committee: National Institute for Health and Clinical Excellence. House of Commons 2007/08[1]	The department praises the open nature of the (re)development of NICE methods guides: [p 29] "The ongoing development of NICE's methods of working and its open discussion of them were praised by the Department: It [is] right that NICE's process and methodology is the subject of continued development and debate and [the Department] welcomes the open and consultative approach NICE takes to the development of its work"	Yes	Research is undertaken to follow up specific guidance to see whether the predictions of the cost-effectiveness analysis are borne out in practice Wider benefits and costs, such as costs borne by carers and social care services, be more fully incorporated into NICE's assessment. Recommend that more work similar to that undertaken by Professor Smith and colleagues at York University takes place on the thresholds used by NICE.	No	No

Cooksey, D. A Review of UK Health Research Funding. Treasury 2006[2]	No	Yes	- biostatistics - indirect comparisons between treatment options - economic evaluation of public health - appraisal of evidence derived from clinical trials - disinvestment methods - behavioural research - the assessment of the impact of NICE guidance pilot studies for new approaches by the NHS HTA programme and NICE, involving earlier engagement in assessing new drugs, perhaps involving those pharmaceutical companies who are more open to such an approach. This may well need to be backed by more underpinning research into HTA methodology and health economic models; Diagnostic Tests	"Investigate improvements in methodologies for use in both NICE appraisals and assessments of the impact of NICE guidance on the NHS"	Recommends the establishment of "Knowledge Transfer Champions – under the joint auspices of the NHS SDO programme and the NHS Connecting for Health 'National Knowledge Service', this small number of full-time 'KTCs' would disseminate the findings of health service research and facilitate the early adoption of those findings into routine practice in the NHS
Guide to the methods of technology appraisal. NICE. June 2008[7]	Yes: P4 – "The Institute regularly reviews its processes and methodology" "The Institute would like to encourage further development of the	No		No	No

	methods of technology appraisal." "The Institute sponsors research into the methods of technology appraisal and welcomes suggestions to the Director of the Centre for Health Technology Evaluation for both primary and secondary research that might lead to improvements in methods and make subsequent editions of this document more helpful."				
NICE Research and Development Strategy. May 2004[5]	Yes – Objective 2	No	No	No	No
Darzi (2008)[24]	No	Yes	An introduction of a National Quality Board which will offer advice on what priorities should be for clinical standard setting by NICE. Formal introduction of this input into the NICE decision-making process will obviously be required Faster appraisal process, within a few months of drug launch. Improvements to topic selection process. NICE will manage evidence synthesis and dissemination through NHS Evidence. Clearer standards from NICE on disinvesting superseded treatments	No	No
End of Life consultation[6]	Not directly. This supplementary piece of guidance is a formal change to the decision-making criteria used by NICE, and	No	Comments that "The advice will be subject to a methodological evaluation. The Institute will design and manage the methodological evaluation, which will be published and used to make modifications to the supplementary advice, if necessary."	No	No

	has not been developed through one of the formal reviews of NICE's methods, or the R&D process. The ad hoc nature of its development highlights the importance of a formal process of NICE Methods research identification.				
Guidelines Manual - 2009[25]	No	No	No	No	No
Interventional Procedures Programme – Methods Guide – June 2007[26]	No	No	No	No	No
Methods for the development of NICE public health guidance – Draft for consultation – October 2008[27]	No	No	No	No	No

Appendix A8: Draft list of topics discussed at workshop

Area 1: Analysis and design of effectiveness studies and their synthesis
Systematic reviews

Topic 1.A.1: Establishing methods and rules for efficient systematic reviews (trade-off between efficiency and quality)
Topic 1.A.2: Methods for keeping research synthesis up to date
Topic 1.A.3: Methods for identifying, appraising and synthesising 'grey literature'
Topic 1.A.4: Methods for best conducting reviews of effectiveness, diagnostic test accuracy and prognostic factors, and other observational studies that are of high quality, in a short timeframe

Meta-analysis (including indirect and mixed treatment comparisons)
Topic 1.B.1: Bias adjusted meta-analysis techniques (for example, values assigned to bias variance parameters and issues of multiple sources of bias and confounding)
Topic 1.B.2: Methods to combine individual patient and aggregate data
Topic 1.B.3: Assessing the effect of extending networks of evidence for NICE guidance on the reliability of results
Topic 1.B.4: Establishing the extent to which networks of evidence should be expanded for NICE guidance in terms of conducting cost-effective research
Topic 1.B.5: Methods for linking treatments into networks of evidence where there is no direct evidence link (for example using observational evidence)
Topic 1.B.6: Establishing the reliability of MTC results and consistency with direct trial data
Topic 1.B.7: Weighting of different comparators (for example, weighting of comparators less frequently used in clinical practice)
Topic 1.B.8: How to assess the comparability of control arms when included in meta-analyses/MTC
Topic 1.B.9: Feasibility of developing approved networks of evidence for different diseases
Topic 1.B.10: Application of indirect and mixed treatment frameworks from pre-defined protocols to empirical data
Topic 1.B.11: Methods to incorporate information on the validity of evidence into a synthesis
Topic 1.B.12: Software to carry out meta-analysis and MTC

Use of non-experimental data
Topic 1.C.1: Use of data from disease registers to estimate effectiveness
Topic 1.C.2: Establishing efficacy for an overall composite comparator
Topic 1.C.3: Research to produce better methods and solutions for accessing evidence from observational research streams (including interventional procedures registers) in a valid and timely fashion
Topic 1.C.4: The use of routine surveillance and monitoring data in developing NICE public health recommendations
Topic 1.C.5: Using bias adjustment methods for observational studies

Interpretation and analysis of clinical trial data
Topic 1.D.1: Translating trial data from adults to children
Topic 1.D.2: Translating phase II research
Topic 1.D.3: Research to produce better methods to handle evidence uncertainty and validation of these methods, particularly for rare events
Topic 1.D.4: Reflecting the quality and exchangeability of evidence in analyses
Topic 1.D.5: Appraisal of evidence derived from clinical trials
Topic 1.D.6: Use of surrogate or intermediate measures
Topic 1.D.7: The analysis of treatment sequences
Topic 1.D.8: How best to present data for NICE Committees
Topic 1.D.9: Development and validation of ways to synthesise evidence and illustrate 'risk' in the context of new interventional procedures.
Topic 1.D.10: Methods to incorporate information on the validity of evidence into a synthesis model used in technology appraisal

Clinical heterogeneity
Topic 1.E.1: Methods to assess the applicability of evidence to different populations

Topic 1.E.2: Bayesian methods for subgroup analysis e.g. biological plausibility of a subgroup in terms of a prior probability
Topic 1.E.3: Use of, and problems associated with, meta-regression based on summary data to consider the relationship between baseline event risks and treatment effects
Topic 1.E.4: Methods to combine IPD and aggregate data

Diagnostics and medical devices
Topic 1.F.1: Ethical and practical challenges in using 'sham' procedures (or control arms) in a surgical environment.
Topic 1.F.2: How should the product life-cycle and the procurement of devices in the NHS be factored into the appraisal process
Topic 1.F.3: How best to evaluate diagnostic technologies
Topic 1.F.4: How does NICE best produce reviews of effectiveness, diagnostic test accuracy and prognostic factors that are of high quality, but are carried out quickly?

Behavioural research
Topic 1.G.1: Methods for changing behaviour in the context of public health
Topic 1.G.2: Methods for establishing incentives to change behaviour

Area 2: Synthesis of evidence from patients, the public and stakeholders
Evidence from patients
Topic 2.A.1: Incorporating patients' opinions into the decision-making process
Topic 2.A.2: Guidance on providing information to patients/carers on breaking bad news
Topic 2.A.3: How does NICE guidance address the needs of the 'real patient' (e.g. those with multiple co-morbidities)
Topic 2.A.4:   The appraisal and synthesis of 'colloquial evidence' (from policy, stakeholder comments, expert opinion, committee expertise)

Evidence from the general public
Topic 2.B.1: Understanding how the public view characteristics of conditions and technologies used to treat them
Topic 2.B.2: Evaluation of the existing, and development of new, methods for citizen participation into HTA for NICE

Qualitative research
Topic 2.C.1: Synthesising qualitative and quantitative research
Topic 2.C.2: Methods for quality assessing qualitative research
Topic 2.C.3: Methods for identifying qualitative research
Topic 2.C.4: The appraisal and synthesis of descriptive data/process evaluations

Area 3: Economic analysis and uncertainty
Costing
Topic 3.A.1: What is the most appropriate source of cost data for NICE decision-making?
Topic 3.A.2: How should costs be apportioned where the NHS/PSS is only partially responsible (either for a specific individual or across different population groups)?
Topic 3.A.3: Methods for estimating the opportunity cost of making recommendations for whole populations rather than subgroups

Perspective for analysis
Topic 3.B.1: What is the appropriate perspective for the analysis of public health interventions?
Topic 3.B.2: Should a societal perspective be adopted in technology appraisals? How should this best be done?

Time horizon for analysis
Topic 3.C.1: Including long-run effects of interventions in analyses (e.g. inclusion of treatment costs unrelated to initial disease by extending morbidity)
Topic 3.C.2: Extrapolation of duration of treatment effects beyond those observed in trials

Economic modelling
Topic 3.D.1: Establish standardised lists of parameter values that have been used in previous technology appraisals
Topic 3.D.2: Establish checklists for establishing quality of economic models and input parameters
Topic 3.D.3: Research to assess whether the predictions of the cost-effectiveness analysis used to inform specific pieces of guidance are borne out in practice
Topic 3.D.4: Methods related to the use of surrogate or intermediate measures
Topic 3.D.5: Assessment of the feasibility of recommending/producing a common set of models relating to disease areas for which there are frequent referrals
Topic 3.D.6: Development of criteria for selecting an appropriate structure for a decision model given available evidence on disease prognosis and the impact of alternative interventions
Topic 3.D.7: Better methods for estimating cost-effectiveness in subgroups
Topic 3.D.8: Assessing the cost-effectiveness of 'long' diagnostic/treatment pathways
Topic 3.D.9: The identification and use of prognostic data in economic models
Topic 3.D.10: The role of QALYs in NICE decision-making and establishing how best to go beyond QALYs
Topic 3.D.11: Methods for determining the optimal complexity of economic models

Uncertainty
Topic 3.E.1: Methods for conducting probabilistic sensitivity analysis for more complex models
Topic 3.E.2: Developing methods for eliciting priors from people
Topic 3.E.3: Alternatives to probabilistic sensitivity analysis for handling uncertainty
Topic 3.E.4: Bayesian and frequentist models for analysis – what are the differences between the approaches & which is most appropriate for NICE?
Topic 3.E.5: Methods of assessing the need for evidence and the consequences of an uncertain decision
Topic 3.E.6: Model averaging for representing structural uncertainty (e.g. whose weights to use, elicitation methods)
Topic 3.E.7: Quantifying the implications of imprecision in parameter estimates on decision uncertainty

Other
Topic 3.F.1: What is the appropriate discount rate for health?
Topic 3.F.2: Methods for the economic evaluation of public health interventions
Topic 3.F.3: Methods for consolidating the range of costs and outcomes that decision makers are presented with
Topic 3.F.4: Translation of research methods so that the process is understandable/transparent

Area 4: Measurement and valuation of benefits

Role of the QALY
Topic 4.A.1: Understanding the role of the QALY in the NICE decision-making process
Topic 4.A.2: Establishing what is/is not currently captured by the QALY
Topic 4.A.3: How to capture those things not included in the QALY
Topic 4.A.4: Consolidating patient reported outcomes with other measures of benefit (e.g. QALYs)
Topic 4.A.5: Establishing how much utility data drives the outcome of decision-making

Standardised measurement tools
Topic 4.B.1: Use of mapping techniques
Topic 4.B.2: Alternatives to the EQ-5D – deviations from the reference case
Topic 4.B.3: Appropriateness of EQ-5D (e.g. sensitivity of instrument)
Topic 4.B.4: Use of disease specific measures in decision-making
Topic 4.B.5: Evaluating health in less bounded ways (beyond questionnaires)
Topic 4.B.6: Measuring the impact of public health interventions
Topic 4.B.7: Methods for consolidating various measures of benefit

Valuation of health
Topic 4.C.1: Re-evaluation of the EQ-5D tariff
Topic 4.C.2: Comparison/re-evaluation of the methods of preference elicitation

Topic 4.C.3: Establishing the trade-off between quantity and quality of health at different time points in a person's life including at the end of life)
Topic 4.C.4: Public versus patient valuations: why do they differ and whose values should be used?
Topic 4.C.5: Weighting QALYs for disease severity – should we and how?
Topic 4.C.6: Weighting QALYs for socio-demographic characteristics – should we and how?
Topic 4.C.7: How do patients view the burden of a condition (possibly outside of the HRQL framework)?

Use of health state utility data in economic models
Topic 4.D.1: Developing a repository for health state utilities
Topic 4.D.2: Methods for synthesising health-state utilities (e.g. the use of meta-regression using published or patient-level data)
Topic 4.D.3: How to use and adapt health state utility values published in the literature for cost-effectiveness models (for example, accounting for co-morbidities or socio-demographic factors)
Topic 4.D.4: How uncertainty in health state utility values should be quantified and how that uncertainty should be incorporated into economic analyses

Area 5: Decision-making at NICE

Threshold for cost-effectiveness
Topic 5.A.1: What is the current ICER of things that are being displaced by NICE guidance (opportunity cost of NICE guidance?)?
Topic 5.A.2: Should the threshold change to reflect changes over time (e.g. inflation, changes to NHS funding)?
Topic 5.A.3: Methodological challenges in estimating the opportunity cost of NICE guidance (i.e. the threshold)

Influences on NICE decision-making
Topic 5.B.1: What other factors should be considered for decision-making for interventions for children, including the use of medicines 'off-license'?
Topic 5.B.2: How should equity and utility feed into NICE decision-making?
Topic 5.B.3: Should NICE decision-making be based on cost-effectiveness analysis (CEA) modified by social value judgements, or should a range of social values be used of which CEA is one?
Topic 5.B.4: Defining and using multi-criteria decision analysis for NICE decision-making
Topic 5.B.5: Establishing the societal and professional 'belief system' about judging what is 'safe' and what is 'efficacious', and the influence of contextual factors
Topic 5.B.6: Which types of sub-groups should be considered in economic evaluation studies undertaken to inform the decisions of the Institute (including consideration of equity issues)?

Handling uncertainty in decision-making
Topic 5.C.1: Establishing decision rules for incorporating estimates of uncertainty into decision-making?
Topic 5.C.2: How can NICE predict whether guidance may lead to 'only in research' or 'coverage with evidence development' recommendations
Topic 5.C.3: What criteria should be used for establishing only in research recommendations?
Topic 5.C.4: How should NICE establish the value for money of conducting further research (do the costs outweigh the benefits)?
Topic 5.C.5: How can NICE assess whether publicly funded research will impact on current policy and practice?
Topic 5.C.6: What are the ethical implications of 'only in research' recommendations?
Topic 5.C.7: How NICE should assess whether additional evidence is needed, what type of evidence is required and the type of evidence for 'coverage with evidence' decisions
Topic 5.C.8: The use of expected value of perfect information (EVPI) methods to make both appraisal recommendations and research recommendations

Process of decision-making
Topic 5.D.1: How do/should Committees and Guideline Development Groups operate?
Topic 5.D.2: Evaluation of the psychology of decision-making and the effect of contextual factors (such as public presence or media campaigns)
Topic 5.D.3: Review existing analytical methods to ensure they add value for decision-making

Topic 5.D.4: A comparison of the Appraisal Committee views on the two different processes for conducting technology appraisals

Topic 5.D.5: A review of the quality of assessment reports that inform decision-making at NICE

Topic 5.D.6: What changes should be made to the development of NICE guidance so that electronic decision support tools can be produced simultaneously?

Topic 5.D.7: What are the best methods for determining the most important clinical questions for a given topic?

Topic 5.D.8: Methods for earlier engagement in assessing new drugs

Topic 5.D.9: An evaluation of the short guideline program compared to the standard process, and possibilities for modification of the two processes

Topic 5.D.10: Methods for communicating to professionals and public (e.g. risk, results of economic analysis)

Topic 5.D.11: Methods for scoping decision problems

Topic 5.D.12: An evaluation of the current appraisal programme in the context of the original intention for the programme (e.g. focus on pharmaceuticals) and the reasons for differences (e.g. why other interventions are harder to evaluate)

Developing the format/ type of NICE recommendations

Topic 5.E.1: Methods to assess the impact of NICE guidance on changing health states (or the 'payback' from NICE) and/or changing clinical practice

Topic 5.E.2: Development of methods to produce guidance to the NHS on the disinvestment of existing interventions

Topic 5.E.3: Development of methods to consider value based pricing arrangements

Topic 5.E.4: Methodological issues in evaluation of patient access schemes

Topic 5.E.5: Evaluation of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process

Topic 5.E.6: How can NICE produce symptom-led guidance, rather than disease-based guidance?

Topic 5.E.7: Improved methods for the evaluation of diagnostic technologies

Topic 5.E.8: Improved methods for the evaluation of screening interventions/programmes

Appendix A9: Topics highlighted as priorities for research at the workshop (topics highlighted in bold were raised by multiple groups)

Area 1: Analysis and design of effectiveness studies and their synthesis

Topic 1.A.1: Establishing methods and rules for efficient systematic reviews of effectiveness, diagnostic test accuracy and prognostic factors (i.e. tackling the trade-off between efficiency and quality)

Topic 1.A.2: Methods for keeping research synthesis up to date; developing on-going and up to date repositories of 'approved' networks of evidence in key diseases using mixed treatment comparison

Topic 1.B.1: Methods to adjust for potential bias in meta-analysis (for example, issues of multiple sources of bias and confounding)

Topic 1.B.12: Methods for jointly synthesising qualitative and quantitative research

Topic 1.C.1: Establishing optimal methods for analysis of disease registers and other sources of non-experimental evidence (e.g. What methods to use? When should non-experimental data be used? How are non-experimental data currently used at NICE?)

Topic 1.C.4: Using bias adjustment methods for observational studies, including adjustments for indication bias in data from registers

Topic 1.D.4: Methods for the optimal use of surrogate or intermediate measures in assessing effectiveness

Topic 1.D.5: Methods for the assessment of the effectiveness of treatment sequences

Topic1.D.8: Methods to attribute outcomes to specific components of care within complex interventions (e.g. public health interventions)

Topic 1.E.1: Methods to assess the applicability of evidence from different countries to UK populations

Topic 1.F.3: How best to evaluate diagnostic and screening technologies

Area 2: Synthesis of evidence from patients, the public and stakeholders

Topic 2.A.1: Methods to assess what types of patient evidence should be used at different stages of NICE's decision-making processes (e.g. when to undertake reviews of qualitative evidence? What types of reviews should be conducted? When should colloquial evidence be used?)

Area 3: Economic analysis and uncertainty

Topic 3.A.4: Should potential reductions in pharmaceutical prices over time be reflected in economic analysis. If so, what methods should be used?

Topic 3.B.2: Methods to determine the appropriate costs and benefit perspective for the analysis of health technologies?

Topic 3.C.2: Extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty

Topic 3.D.1: Methods to develop 'standardised' and 'approved' models in a given disease area, including sets of parameter inputs

Topic 3.D.6: Better methods for estimating cost-effectiveness in subgroups

Topic 3.D.7: Assessing the cost-effectiveness of 'long' or complex diagnostic/treatment pathways

Topic 3.E.4: Methods of assessing the need for evidence and the consequences of uncertain decisions to the NHS (e.g. in terms of sunk costs)

Topic 3.E.5: Averaging of model results to representing structural uncertainty (e.g. When should averaging be used? What methods should be used?)

Topic 3.F.1: What is the appropriate discount rate for health and under what circumstances might it vary?

Topic 3.F.4: Translation of research methods so that the process is understandable/transparent to non-specialists

Area 4: Measurement and valuation of benefits

Topic 4.A.2: Consolidating patient reported outcomes with other measures of benefit (e.g. QALYs)
Topic 4.B.3: Establishing what effects of interventions and programmes are/are not currently captured by the EQ-5D
Topic 4.B.4.: Methods to establish when disease specific measures of health outcomes should be used instead of, or as supplementary to, the EQ-5D
Topic 4.B.6: Methods for the measurement of changes in the health of children and people unable to report the status of their own health
Topic 4.C.1: Methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead
Topic 4.C.3: Methods for valuing health at different time points in a person's life (e.g. at the end of life)
Topic 4.C.4: Methods to determine whether public or patient valuations of health should be used

Area 5: Decision-making at NICE

Topic 5.A.1: What is the current ICER of things that are being displaced by NICE guidance (i.e. opportunity cost of NICE guidance)?
Topic 5.A.2: Methods to estimate the opportunity cost of NICE guidance (i.e. the threshold) including changes over time
Topic 5.A.3: Methods to communicate concept of a threshold and related issues to non-specialists
Topic 5.B.2: Methods to feed equity into NICE decision-making?
Topic 5.B.4: Methods for taking factors other than cost-effectiveness (e.g. societal costs/effects) into account in NICE decision-making (e.g. using multi-criteria decision analysis)
Topic 5.B.7: How to take inequalities into account at different stages of NICE guidance production?
Topic 5.C.2: What criteria should be used for establishing Only in Research recommendations (including a consideration of the ethical implications and whether publicly funded research will impact on current policy and practice)?
Topic 5.D.1: How do/should Committees and Guideline Development Groups operate?
Topic 5.D.3: Methods to review existing analytical methods for systematic reviews and economic analyses to ensure they add value for decision-making
Topic 5.D.4: Methods to evaluate the different processes within the technology appraisals programme and within the clinical guidelines programme (including Appraisal Committee and stakeholder views and the impact on recommendations)
Topic 5.D.8: Methods for scoping decision problems, including the potential use of qualitative research
Topic 5.E.7: Methods for communicating guidance and supporting evidence to the general public

Appendix A10: Web survey

NICE/MRC scoping study: Identifying NICE's methodological research needs and priorities

Web feedback and opportunity to comment

Introduction

As part of the co-coordinated strategy for health research under OSCHR, MRC is the lead organisation for methodology research. NICE is an important public stakeholder in this research area and improving methods for undertaking health technology assessments, appraisals and evidence synthesis was also highlighted as an area for further research in the 2007 Cooksey review (http://www.hm-treasury.gov.uk/media/4/A/pbr06_cooksey_final_report_636.pdf).

To help identify priority methodology research topics to support NICE's decision-making, MRC commissioned a group of researchers at the Universities of York (Professor Mark Sculpher and Laura Bojke) and Sheffield (Dr Louise Longworth and Jonathan Tosh) in September 2008 to undertake a short scoping project. As part of the project the group has generated a list of possible future research topics. These topics were identified via consultation with stakeholders, literature review and a workshop involving people at NICE, the MRC and other representatives from academia and industry.

The final stage of this project is to rank the topics by level of importance. This web-based feedback offers the wider research community, as well as those who have already contributed to the scoping project, the opportunity to participate in this project by rating the level of importance of each topic.

Following this feedback survey, responses will be collated and the research team will provide a final project report which will then be considered by the MRC/NIHR Methodology Research Programme Panel, which oversees the MRC-led methodology work stream.

Details of how to complete the feedback survey are given below.

Completing the questionnaires

You are first asked to provide some information about yourself.

The questionnaire then splits into 5 broad areas, analysis and design of effectiveness studies and their synthesis, synthesis of evidence from patients, the public and stakeholders, economic analysis and uncertainty, measurement and valuation of benefits, decision-making at NICE.

Each area is divided into themes. Within each theme there are a number of specific topics. You are asked to rate each topic by their level of importance as research areas. At the end of each theme you are also asked to provide any suggestions for topics which you think may have been omitted. You can comment on as many of these themes as you wish.

At the end of the questionnaire you are asked to provide your top three topics (across areas and themes) along with some further detail on why these are important topics for NICE decision-making. You can also suggest any areas and topics which you think may have been omitted. There is a free text box at the end of the questionnaire for any additional comments. The questionnaire should take approximately 30-45 minutes to complete.

Personnel information

What type of organisation do you work in?

University ☐

Private consultancy ☐

Pharmaceutical company ☐

NHS ☐

NICE ☐

Patient organisation ☐

Other ☐

What is your professional background?

Health economist ☐

Public health specialist ☐

Clinician ☐

Statistician ☐

Health services researcher ☐

NHS manager ☐

Other ☐

Did you attend the workshop, held as part of this scoping study?

Attended ☐

Invited but could not attend ☐

Did not attend ☐

Were you interviewed as part of this scoping study?

Interviewed ☐

Not interviewed ☐

What is your involvement with NICE?

Employed directly by NICE ☐

Member of a NICE committee or guidelines development group ☐

Academic reviewer or provider of evidence ☐

Provider of submission on behalf of sponsor organisation ☐

Other DESCRIBE ☐

No involvement with NICE ☐

Area 1: Analysis and design of effectiveness studies and their synthesis

Theme A: Systematic reviews

Topic 1.A.1: Establishing methods and rules for efficient systematic reviews of effectiveness, diagnostic test accuracy and prognostic factors (i.e. tackling the trade-off between efficiency and quality)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.A.2: Methods for keeping research synthesis up to date; developing on-going and up to date repositories of 'approved' networks of evidence in key diseases using mixed treatment comparison

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.A.3: Methods for identifying, appraising and synthesising 'grey literature'

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.A.4: Development of a checklist or reporting rules for standardised reporting of public health reviews including undertaking sensitivity analysis

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.A.5: Methods for quality assessing qualitative research

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.A.6: Methods for the timely identification and synthesis of qualitative research within the context of NICE processes

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.A.7: Methods for conducting systematic reviews of complex interventions (e.g. in public health)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Theme B: Meta-analysis (including indirect and mixed treatment comparisons)

Topic 1.B.1: Methods to adjust for potential bias in meta-analysis (for example, issues of multiple sources of bias and confounding)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.2: Methods to combine individual patient and aggregate data in evidence synthesis

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.3: Assessing the implications of extending networks of evidence for NICE guidance on the reliability of results

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.4: Methods for linking treatments into networks of evidence where there is no direct evidence link on the basis of randomised trials (for example using observational evidence)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.5: Establishing the reliability of mixed treatment comparisons and consistency with direct trial data

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.6: Methods to deal with treatments not routinely used in practice within evidence synthesis

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.7: How to assess the comparability of control arms when included in evidence synthesis

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.8: What needs to be defined in a protocol for a mixed treatment comparison?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.9: Methods to assess the quality of randomised studies and to incorporate this into a formal quantitative synthesis

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.10: A review of software to carry out meta-analysis and mixed treatment comparison

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 1.B.11: Methods to assess the exchangeability of studies and to reflect the in evidence synthesis

Not important   **Somewhat important**   **Important**   **Very important**

Topic 1.B.12: Methods for synthesising both qualitative and quantitative research

Not important   **Somewhat important**   **Important**   **Very important**

Theme C: Use of non-experimental data

Topic 1.C.1: Establishing optimal methods for analysis of disease registers and other sources of non-experimental evidence (e.g. What methods to use? When should non-experimental data be used? How are non-experimental data currently used at NICE?)

Not important   **Somewhat important**   **Important**   **Very important**

Topic 1.C.2: Methods to establish the efficacy of a 'composite comparator' (e.g. current practice)

Not important   **Somewhat important**   **Important**   **Very important**

Topic 1.C.4:   The use of routine surveillance and monitoring data in developing NICE public health recommendations

Not important   **Somewhat important**   **Important**   **Very important**

Topic 1.C.5: Using bias adjustment methods for observational studies, including adjustments for indication bias in data from registers

Not important   **Somewhat important**   **Important**   **Very important**

Topic 1.C.6: Methods to assess the sensitivity of observational study results to study design

Not important   **Somewhat important**   **Important**   **Very important**

Theme D: Interpretation and analysis of clinical trial data

Topic 1.D.1: Methods for translating trial evidence from adults to children

Not important   **Somewhat important**   **Important**   **Very important**

Topic 1.D.2: Methods for translating phase II research for NICE decisions

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 1.D.3: Methods to quantify the incidence of rare events from interventions

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 1.D.4: Methods for the optimal use of surrogate or intermediate measures in assessing effectiveness

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 1.D.5: Methods for the assessment of the effectiveness of treatment sequences

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 1.D.6: How best to present effectiveness data for NICE Committees including the likelihood of anticipated and unanticipated events

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 1.D.7: Methods to assess the effect of practitioner experience (and other potentially relevant contextual factors) on effectiveness

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic1.D.8: Methods to attribute outcomes to specific components of care within complex interventions (e.g. public health interventions)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Theme E: Clinical heterogeneity

Topic 1.E.1: Methods to assess the applicability of evidence to different populations between countries

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 1.E.2: Bayesian methods for subgroup analysis (e.g. biological plausibility of a subgroup in terms of a prior probability)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 1.E.3: Use of, and problems associated with, meta-regression based on summary data to consider the relationship between baseline event risks and treatment effects

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Theme F: Diagnostics and medical devices

Topic 1.F.1: Ethical and practical challenges in using 'sham' procedures (or control arms) in a surgical environment

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 1.F.2: How should the product life-cycle and the procurement of devices in the NHS be factored into the appraisal process

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 1.F.3: How best to evaluate diagnostic and screening technologies

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Theme G: Behavioural research

Topic 1.G.1: Methods to evaluate interventions to change behaviour in the context of public health

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Are there any topics, within this area that you think have been omitted? Please provide detail in the box below.

Area 2: Synthesis of evidence from patients, the public and stakeholders

Theme A: Evidence from patients

Topic 2.A.1: Methods to assess what types of patient evidence should be used at different stages of NICE's decision-making processes (e.g. when to undertake reviews of qualitative evidence? What types of reviews should be conducted? When should colloquial evidence be used?)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 2.A.2: Guidance on providing information to patients/carers on breaking bad news

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 2.A.3: Methods for using colloquial evidence to determine the effect of complex interventions (e.g. in public health)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Theme B: Evidence from the general public

Topic 2.B.1: Methods to understand how the public view characteristics of conditions and the technologies used to treat them

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Theme C: Evidence from stakeholders

Topic 2.C.4:   The appraisal and synthesis of 'colloquial evidence' (e.g. comments received from stakeholders during consultation)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 2.C.2: Evaluation of the existing, and development of new, methods for participation of different stakeholder groups at different stages of NICE's decision-making processes (including representatives of the general public, patients and practitioners)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Are there any topics, within this area that you think have been omitted? Please provide detail in the box below.

| |
| |

Area 3: Economic analysis and uncertainty

Theme A: Costing

Topic 3.A.1: What are the most appropriate sources of cost data for NICE decision-making?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.A.2: Methods to establish the amount of costs of resources should be included in analysis where these fall only partially on the National Health Service/Personal Social Services (either for a specific individual or across different population groups)?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.A.3: Methods for estimating the opportunity cost of recommending treatments for aggregate populations rather than for subgroups

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.A.4: Should potential reductions in pharmaceutical prices over time be reflected in economic analysis. If so, what methods should be used?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Theme B: Perspective for analysis

Topic 3.B.1: Methods to determine the appropriate costs and benefit perspective for the analysis of public health interventions?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.B.2: Methods to determine the appropriate costs and benefit perspective for the analysis of health technologies?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.B.3: Methods for the evaluation of interventions from a societal perspective

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Theme C: Time horizon for analysis

Topic 3.C.1: Including long-run effects of interventions in analyses (e.g. inclusion of treatment costs unrelated to initial disease by extending morbidity)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.C.2: Extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Theme D: Economic modelling

Topic 3.D.1: Methods to develop 'standardised' and 'approved' models in a given disease area, including parameter inputs

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.2: Further develop checklists for establishing the quality of economic models including input parameters and reporting standards

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.3: Research to assess whether the predictions of economic models used to inform NICE guidance are borne out in practice

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.4: Methods for the use of surrogate or intermediate measures in models

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.5: Development of criteria for selecting an appropriate structure for a decision model given available evidence on disease prognosis and the impact of alternative interventions

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.6: Better methods for estimating cost-effectiveness in subgroups

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.7: Assessing the cost-effectiveness of 'long' or complex diagnostic/treatment pathways

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.8: The identification and use of prognostic data in economic models

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.9: Methods for determining the optimal complexity of economic models (i.e. how complex does a model need to be to be fit for purpose?)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.10: Methods for the incorporation of evidence on adherence in economic models

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.11: Methods to identify and inform appropriate structure of economic models

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.D.12: Methods for modelling complex social interventions

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Theme E: Uncertainty

Topic 3.E.1: Methods for quantifying the uncertainty in cost-effectiveness models, including for complex models, and for showing the implications of uncertainty for decisions

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.E.2: Developing methods for eliciting 'prior' parameter estimates from relevant experts

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.E.3: Bayesian and Frequentist models for analysis – what are the differences between the approaches & which is most appropriate for NICE?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.E.4: Methods of assessing the need for evidence and the consequences of uncertain decisions to the NHS (e.g. in terms of sunk costs)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 3.E.5: Averaging of model results to represent structural uncertainty (e.g. When should averaging be used? What methods should be used?)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 3.E.6: Quantifying the implications of imprecision in parameter estimates on decision uncertainty

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Theme F: Other

Topic 3.F.1: What is the appropriate discount rate for health and under what circumstances might it vary?

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 3.F.2: Methods for the economic evaluation of public health interventions

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 3.F.3: Methods for consolidating the range of costs and outcomes that decision makers are presented

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 3.F.4: Translation of research methods so that the process is understandable/transparent to non-specialists

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 3.F.5: Methods to assess the cost-effectiveness of interventions which have costs and (dis)benefits outside of the health care sector

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 3.F.6: Methods to establish the type of economic model and appraisal process that should be used to formulate guidance (When is it necessary to commission development of a new economic model?)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.F.7: Methods to implement cost-effectiveness analysis (and evidence synthesis) early into the development of new technologies to inform future research and development decisions

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.F.8: Methods to reflect the objective of reducing inequalities in cost-effectiveness analysis

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 3.F.9: How should NICE establish the value for money of conducting further research (do the costs outweigh the benefits)?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Are there any topics, within this area that you think have been omitted? Please provide detail in the box below.

Area 4: Measurement and valuation of benefits

Theme A: Use of the QALY

Topic 4.A.1: Methods to capture a wider set of (dis)benefits that may not be included in the QALY

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.A.2: Consolidating patient reported outcomes with other measures of benefit (e.g. QALYs)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Theme B: Standardised measurement tools

Topic 4.B.1: Use of mapping techniques between clinical and patient-reported outcomes, and preference-based instruments for use in QALYs

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.B.2: Methods to derive quality of life weights (utilities) when no EQ-5D data are available or the EQ-5D is inappropriate

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.B.3: Methods to establish what effects of interventions and programmes are/are not currently captured by the EQ-5D

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.B.4.: Methods to establish when disease specific measures of health outcomes should be used instead of, or as supplementary to, the EQ-5D

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.B.5: Evaluating health in less bounded ways (beyond questionnaires)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.B.6: Methods for the measurement of changes in the health of children and people unable to report the status of their own health

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Theme C: Valuation of health

Topic 4.C.1: Methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.C.2: Comparison/re-evaluation of the methods of preference elicitation for QALYs

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.C.3: Methods for valuing health at different time points in a person's life (especially at the end of life)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.C.4: Methods to determine whether public or patient valuations of health should be used

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.C.5: Methods for weighting QALYs for characteristics of individuals (e.g. disease severity, social demographic characteristics)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.C.6: Methods to determine how patients view the burden of a condition (possibly outside of the HRQL framework)?

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Theme D: Use of health state utility data in economic models

Topic 4.D.1: Methods for synthesising health-state utilities (e.g. the use of meta-regression using published or patient-level data)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.D.2: How to use and adapt health state utility values published in the literature for cost-effectiveness models (for example, accounting for co-morbidities or socio-demographic factors)

Not important	Somewhat important	Important	Very important
☐	☐	☐	☐

Topic 4.D.3: How uncertainty in health state utility values should be quantified and how that uncertainty should be incorporated into economic analyses

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Are there any topics, within this area that you think have been omitted? Please provide detail in the box below.

Area 5: Decision-making at NICE

Theme A: Threshold for cost-effectiveness

Topic 5.A.1: What is the current ICER of things that are being displaced by NICE guidance (opportunity cost of NICE guidance?)?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.A.2: Methods to estimate the opportunity cost of NICE guidance (i.e. the threshold) including changes over time

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.A.3: Methods to communicate concept of a threshold and related issues to non-specialists

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Theme B: Influences on NICE decision-making

Topic 5.B.1: What other factors should be considered for decision-making for interventions for children, including the use of medicines 'off-license'?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.B.2: Methods to feed equity and utility into NICE decision-making?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.B.3: Should NICE decision-making be based on cost-effectiveness analysis (CEA) modified by social value judgements, or should a range of social values be used of which CEA is one?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.B.4: Methods for taking factors other than cost-effectiveness (e.g. societal costs/effects) into account in NICE decision-making (e.g. using multi-criteria decision analysis)

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.B.5: Methods for establishing how contextual affect decisions about the safety and efficacy of interventions (e.g. availability of alternatives, stage of life)

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.B.6: Which types of sub-groups should be considered in economic evaluation studies undertaken to inform the decisions of the Institute (including consideration of equity issues)?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.B.7: How to take inequalities into account at different stages of NICE guidance production?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Theme C: Handling uncertainty in decision-making

Topic 5.C.1: Establishing decision rules for incorporating estimates of uncertainty into decision-making

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.C.2: What criteria should be used for establishing only in research recommendations (including a consideration of the ethical implications and whether publicly funded research will impact on current policy and practice)?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.C.3: How should NICE assess whether additional evidence is needed, what type of evidence is required and the type of evidence for 'coverage with evidence' decisions

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.C.4: The use of expected value of perfect information (EVPI) methods to make both appraisal recommendations and research recommendations

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Theme D: Process of decision-making

Topic 5.D.1: How do/should Committees and Guideline Development Groups operate?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.2: Evaluation of the psychology of decision-making and the effect of contextual factors (such as public presence or media campaigns)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.3: Methods to review existing analytical methods for systematic reviews and economic analyses to ensure they add value for decision-making

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.4: Methods to evaluate the different processes within the technology appraisals programme and within the clinical guidelines programme (including Appraisal Committee and stakeholder views and the impact on recommendations)

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.5: Methods to review the quality of assessment reports that inform decision-making at NICE

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.6: What changes should be made to the development of NICE guidance so that electronic decision support tools can be produced simultaneously?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.7: What are the best methods for determining the most important clinical questions for a given topic?

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.8: Methods for scoping decision problems, including the potential use of qualitative research

Not important	**Somewhat important**	**Important**	**Very important**
☐	☐	☐	☐

Topic 5.D.9: An evaluation of the current appraisal programme in the context of the original intention for the programme (e.g. focus on pharmaceuticals) and the reasons for differences (e.g. why other interventions are harder to evaluate)

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.D.10: How should potential future changes in health care be taken into account in decision-making?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Theme E: Developing the format/ type of NICE recommendations

Topic 5.E.1: Methods to assess the impact of NICE guidance on changing health states (or the 'payback' from NICE) and/or changing clinical practice

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.E.2: Development of methods to produce guidance to the NHS on the disinvestment of existing interventions

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.E.3: Development of methods to consider value based pricing arrangements

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.E.4: Methodological issues in evaluation of patient access schemes

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.E.5: Evaluation of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.E.6: How can NICE produce symptom-led guidance, rather than disease-based guidance?

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Topic 5.E.7: Methods for communicating guidance and supporting evidence to the general public

Not important   **Somewhat important**   **Important**   **Very important**

☐   ☐   ☐   ☐

Are there any topics, within this area that you think have been omitted? Please provide detail in the box below.

| |
| |

Rating topics across areas

Please can you indicate what you consider to be the three most important topics across areas and themes. These should be on the basis of their importance as methodological research questions.

Please select three topics from the list below

Area 1: Theme A
Topic 1.A.1: Establishing methods and rules for efficient systematic reviews of effectiveness, diagnostic test accuracy and prognostic factors (i.e. tackling the trade-off between efficiency and quality)
Topic 1.A.2: Methods for keeping research synthesis up to date; developing on-going and up to date repositories of 'approved' networks of evidence in key diseases using mixed treatment comparison
Topic 1.A.3: Methods for identifying, appraising and synthesising 'grey literature'
Topic 1.A.4: Development of a checklist or reporting rules for standardised reporting of public health reviews including undertaking sensitivity analysis
Topic 1.A.5: Methods for quality assessing qualitative research
Topic 1.A.6: Methods for the timely identification and synthesis of qualitative research within the context of NICE processes
Topic 1.A.7: Methods for conducting systematic reviews of complex interventions (e.g. in public health)

Area 1: Theme B
Topic 1.B.1: Methods to adjust for potential bias in meta-analysis (for example, issues of multiple sources of bias and confounding)
Topic 1.B.2: Methods to combine individual patient and aggregate data in evidence synthesis
Topic 1.B.3: Assessing the implications of extending networks of evidence for NICE guidance on the reliability of results
Topic 1.B.4: Methods for linking treatments into networks of evidence where there is no direct evidence link on the basis of randomised trials (for example using observational evidence)
Topic 1.B.5: Establishing the reliability of mixed treatment comparisons and consistency with direct trial data
Topic 1.B.6: Methods to deal with treatments not routinely used in practice within evidence synthesis
Topic 1.B.7: How to assess the comparability of control arms when included in evidence synthesis
Topic 1.B.8: What needs to be defined in a protocol for a mixed treatment comparison?
Topic 1.B.9: Methods to assess the quality of randomised studies and to incorporate this into a formal quantitative synthesis
Topic 1.B.10: A review of software to carry out meta-analysis and mixed treatment comparison
Topic 1.B.11: Methods to assess the exchangeability of studies and to reflect this in evidence synthesis
Topic 1.B.12: Methods for jointly synthesising qualitative and quantitative research

Area 1: Theme C
Topic 1.C.1: Establishing optimal methods for analysis of disease registers and other sources of non-experimental evidence (e.g. What methods to use? When should non-experimental data be used? How are non-experimental data currently used at NICE?)
Topic 1.C.2: Methods to establish the efficacy of a 'composite comparator' (e.g. current practice)
Topic 1.C.3: The use of routine surveillance and monitoring data in developing NICE public health recommendations
Topic 1.C.4: Using bias adjustment methods for observational studies, including adjustments for indication bias in data from registers
Topic 1.C.5: Methods to assess the sensitivity of observational study results to study design

Area 1: Theme D
Topic 1.D.1: Methods for translating trial evidence from adults to children
Topic 1.D.2: Methods for translating phase II research for NICE decisions
Topic 1.D.3: Methods to quantify the incidence of rare events from interventions
Topic 1.D.4: Methods for the optimal use of surrogate or intermediate measures in assessing effectiveness
Topic 1.D.5: Methods for the assessment of the effectiveness of treatment sequences

Topic 1.D.6: How best to present effectiveness data for NICE Committees including the likelihood of anticipated and unanticipated events

Topic 1.D.7: Methods to assess the effect of practitioner experience (and other potentially relevant contextual factors) on effectiveness

Topic 1.D.8: Methods to attribute outcomes to specific components of care within complex interventions (e.g. public health interventions)

Area 1: Theme E

Topic 1.E.1: Methods to assess the applicability of evidence from different countries to UK populations

Topic 1.E.2: Bayesian methods for subgroup analysis (e.g. biological plausibility of a subgroup in terms of a prior probability)

Topic 1.E.3: Use of, and problems associated with, meta-regression based on summary data (e.g. to consider the relationship between baseline event risks and treatment effects

Area 1: Theme F

Topic 1.F.1: Ethical and practical challenges in using 'sham' procedures (or control arms) in a surgical environment

Topic 1.F.2: How should the product life-cycle and the procurement of devices in the NHS be factored into the appraisal process

Topic 1.F.3: How best to evaluate diagnostic and screening technologies

Area 1: Theme G

Topic 1.G.1: Methods to evaluate interventions to change behaviour in the context of public health

Area 2: Theme A

Topic 2.A.1: Methods to assess what types of patient evidence should be used at different stages of NICE's decision-making processes (e.g. when to undertake reviews of qualitative evidence? What types of reviews should be conducted? When should colloquial evidence be used?)

Topic 2.A.2: Guidance on providing information to patients/carers on breaking bad news Topic 2.A.3: Methods for using colloquial evidence to determine the effect of complex interventions (e.g. in public health)

Area 2: Theme B

Topic 2.B.1: Methods to understand how the public view characteristics of conditions and the technologies used to treat them

Area 2: Theme C

Topic 2.C.1: The appraisal and synthesis of 'colloquial evidence' (e.g. comments received from stakeholders during consultation)

Topic 2.C.2: Evaluation of the existing, and development of new, methods for participation of different stakeholder groups at different stages of NICE's decision-making processes (including representatives of the general public, patients and practitioners)

Area 3: Theme A

Topic 3.A.1: What are the most appropriate sources of cost data for NICE decision-making? Topic 3.A.2: Methods to determine the proportion of costs that should be included in analyses where there is variability in the amount paid by the National Health Service/Personal Social Services and by the individual patient?

Topic 3.A.3: Methods for estimating the opportunity cost of recommending treatments for aggregate populations rather than for subgroups

Topic 3.A.4: Should potential reductions in pharmaceutical prices over time be reflected in economic analysis. If so, what methods should be used?

Area 3: Theme B

Topic 3.B.1: Methods to determine the appropriate costs and benefit perspective for the analysis of public health interventions?

Topic 3.B.2: Methods to determine the appropriate costs and benefit perspective for the analysis of health technologies?

Topic 3.B.3: Methods for the evaluation of interventions from a societal perspective

Area 3: Theme C
Topic 3.C.1: Including long-run effects of interventions in analyses (e.g. inclusion of treatment costs unrelated to initial disease by extending life)
Topic 3.C.2: Extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty

Area 3: Theme D
Topic 3.D.1: Methods to develop 'standardised' and 'approved' models in a given disease area, including sets of parameter inputs
Topic 3.D.2: Further development of checklists for establishing the quality of economic models including input parameters and reporting standards
Topic 3.D.3: Research to assess whether the predictions of economic models used to inform NICE guidance are borne out in practice
Topic 3.D.4: Methods for the use of surrogate or intermediate measures in models
Topic 3.D.5: Development of criteria for selecting an appropriate structure for a decision model given available evidence on disease prognosis and the impact of alternative interventions
Topic 3.D.6: Better methods for estimating cost-effectiveness in subgroups
Topic 3.D.7: Assessing the cost-effectiveness of 'long' or complex diagnostic/treatment pathways
Topic 3.D.8: The identification and use of prognostic data in economic models
Topic 3.D.9: Methods for determining the optimal complexity of economic models (i.e. how complex does a model need to be to be fit for purpose?)
Topic 3.D.10: Methods for the incorporation of evidence on adherence in economic models
Topic 3.D.11: Methods for modelling complex social interventions

Area 3: Theme E
Topic 3.E.1: Methods for quantifying the uncertainty in cost-effectiveness models, including for complex models, and for showing the implications of uncertainty for decisions
Topic 3.E.2: Developing methods for eliciting 'prior' parameter estimates from relevant experts
Topic 3.E.3: Bayesian and Frequentist models for analysis – what are the differences between the approaches and which is most appropriate for NICE?
Topic 3.E.4: Methods of assessing the need for evidence and the consequences of uncertain decisions to the NHS (e.g. in terms of sunk costs)
Topic 3.E.5: Averaging of model results to representing structural uncertainty (e.g. When should averaging be used? What methods should be used?)
Topic 3.E.6: Quantifying the implications of imprecision in parameter estimates on decision uncertainty

Area 3: Theme F
Topic 3.F.1: What is the appropriate discount rate for health and under what circumstances might it vary?
Topic 3.F.2: Methods for the economic evaluation of public health interventions
Topic 3.F.3: Methods for consolidating the range of costs and outcomes that decision makers are presented
Topic 3.F.4: Translation of research methods so that the process is understandable/transparent to non-specialists
Topic 3.F.5: Methods to assess the cost-effectiveness of interventions which have costs and (dis)benefits outside of the health care sector
Topic 3.F.6: Methods to establish the type of economic model and appraisal process that should be used to formulate guidance (When is it necessary to commission development of a new economic model?)
Topic 3.F.7: Methods to implement cost-effectiveness analysis (and evidence synthesis) early into the development of new technologies to inform future research and development decisions
Topic 3.F.8: Methods to reflect the objective of reducing inequalities in cost-effectiveness analysis
Topic 3.F.9: How should NICE establish the value for money of conducting further research (do the costs outweigh the benefits)?

Area 4: Theme A
Topic 4.A.1: Methods to capture a wider set of (dis)benefits that may not be included in the QALY
Topic 4.A.2: Consolidating patient reported outcomes with other measures of benefit (e.g. QALYs)

Area 4: Theme B
Topic 4.B.1: Use of mapping techniques between clinical and patient-reported outcomes, and preference-based instruments for use in QALYs
Topic 4.B.2: Methods to derive quality of life weights (utilities) when no EQ-5D data are available or the EQ-5D is inappropriate (e.g. the use of condition-specific preference based measures or direct valuation of health state descriptions)
Topic 4.B.3: Establishing what effects of interventions and programmes are/are not currently captured by the EQ-5D
Topic 4.B.4: Methods to establish when disease specific measures of health outcomes should be used instead of, or as supplementary to, the EQ-5D
Topic 4.B.5: Evaluating health in less bounded ways (beyond questionnaires)
Topic 4.B.6: Methods for the measurement of changes in the health of children and people unable to report the status of their own health

Area 4: Theme C
Topic 4.C.1: Methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead
Topic 4.C.2: Comparison/re-evaluation of the methods of preference elicitation for QALYs
Topic 4.C.3: Methods for valuing health at different time points in a person's life (e.g. at the end of life)
Topic 4.C.4: Methods to determine whether public or patient valuations of health should be used
Topic 4.C.5: Methods for weighting QALYs according to the characteristics of individuals (e.g. disease severity, social demographic characteristics)
Topic 4.C.6: Methods to determine how patients view the burden of a condition (possibly outside of the HRQL framework)?

Area 4: Theme D
Topic 4.D.1: Methods for synthesising health-state utilities (e.g. the use of meta-regression using published or patient-level data)
Topic 4.D.2: How to use and adapt health state utility values published in the literature for cost-effectiveness models (for example, accounting for co-morbidities or socio-demographic factors)
Topic 4.D.3: How uncertainty in health state utility values should be quantified and how that uncertainty should be incorporated into economic analyses
Topic 4.D.4: Using EQ5D data routinely collected in Patient Reported Outcome Measures (PROMS) in the NHS to provide standardised quality of life weights (utilities) for economic models for NICE

Area 5: Theme A
Topic 5.A.1: What is the current ICER of things that are being displaced by NICE guidance (i.e. opportunity cost of NICE guidance)?
Topic 5.A.2: Methods to estimate the opportunity cost of NICE guidance (i.e. the threshold) including changes over time
Topic 5.A.3: Methods to communicate concept of a threshold and related issues to non-specialists

Area 5: Theme B
Topic 5.B.1: What other factors should be considered for decision-making for interventions for children, including the use of medicines 'off-license'?
Topic 5.B.2: Methods to feed equity into NICE decision-making?
Topic 5.B.3: Should NICE decision-making be based on cost-effectiveness analysis (CEA) modified by social value judgements, or should a range of social values be used of which CEA is one?
Topic 5.B.4: Methods for taking factors other than cost-effectiveness (e.g. societal costs/effects) into account in NICE decision-making (e.g. using multi-criteria decision analysis)
Topic 5.B.5: Methods for establishing how contextual details affect decisions about the safety and efficacy of interventions (e.g. availability of alternatives, stage of life
Topic 5.B.6: Which types of sub-groups should be considered in economic evaluation studies undertaken to inform the decisions of the Institute (including consideration of equity issues)?
Topic 5.B.7: How to take inequalities into account at different stages of NICE guidance production?

Area 5: Theme C
Topic 5.C.1: Establishing decision rules for incorporating estimates of uncertainty into decision-making

Topic 5.C.2: What criteria should be used for establishing Only in Research recommendations (including a consideration of the ethical implications and whether publicly funded research will impact on current policy and practice)?

Topic 5.C.3: How should NICE assess whether additional evidence is needed, what type of evidence is required and the type of evidence necessary for 'coverage with evidence' decisions

Topic 5.C.4: The use of expected value of perfect information (EVPI) methods to make both appraisal recommendations and research recommendations

Area 5: Theme D

Topic 5.D.1: How do/should Committees and Guideline Development Groups operate?

Topic 5.D.2: Evaluation of the psychology of decision-making and the effect of contextual factors (such as public presence or media campaigns)

Topic 5.D.3: Methods to review existing analytical methods for systematic reviews and economic analyses to ensure they add value for decision-making

Topic 5.D.4: Methods to evaluate the different processes within the technology appraisals programme and within the clinical guidelines programme (including Appraisal Committee and stakeholder views and the impact on recommendations)

Topic 5.D.5: Methods to review the quality of assessment reports that inform decision-making at NICE

Topic 5.D.6: What changes should be made to the development of NICE guidance so that electronic decision support tools can be produced simultaneously?

Topic 5.D.7: What are the best methods for determining the most important clinical questions for a given topic?

Topic 5.D.8: Methods for scoping decision problems, including the potential use of qualitative research

Topic 5.D.9: An evaluation of the current appraisal programme in the context of the original intention for the programme (e.g. focus on pharmaceuticals) and the reasons for differences (e.g. why other interventions are harder to evaluate)

Topic 5.D.10: How should potential future changes in health care be taken into account in decision-making?

Area 5: Theme E

Topic 5.E.1: Methods to assess the impact of NICE guidance on changing health (or the 'payback' from NICE) and/or changing clinical practice

Topic 5.E.2: Development of methods to produce guidance to the NHS on disinvestment from existing interventions

Topic 5.E.3: Development of methods to consider value-based pricing arrangements

Topic 5.E.4: Methodological issues in evaluation of patient access schemes

Topic 5.E.5: Evaluation of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process

Topic 5.E.6: How can NICE produce symptom-led guidance, rather than disease-based guidance?

Topic 5.E.7: Methods for communicating guidance and supporting evidence to the general public

Further detail on chosen topics

Topic 1

To which area of NICEs work does it relate?

How will it inform the challenges faced by NICE?

Ideas for specific research questions

Ongoing and previous research

Possible characteristics of research

Topic 2

To which area of NICEs work does it relate?

How will it inform the challenges faced by NICE?

Ideas for specific research questions

Ongoing and previous research

Possible characteristics of research

Topic 3

To which area of NICEs work does it relate?

How will it inform the challenges faced by NICE?

Ideas for specific research questions

Ongoing and previous research

Possible characteristics of research

Omitted areas

If you feel we have omitted any areas in this questionnaire please can you provide details along with suggested topics within the omitted area.

Any other feedback or suggestions

This space is for any additional feedback or suggests you may have.

Thank you for completing the questionnaire

Appendix A11: Additional topics suggested through the web survey

Area 1
Acceptability and feasibility of interventions for different groups. Identification and prioritisation of treatment outcomes by patients. Identifying and exploring why some interventions work, and others don't - i.e. the mechanisms (guilt, for example)
Econometric based analysis
Measurement and reliability of self-reported data on alcohol, diet and exercise; assessment effects and their potential for bias; direct effects of screening on risk behaviours; effectiveness of simple low-cost interventions with high potential for wide dissemination
Prevention Science is characterised by the use of complex statistical models, e.g. multi-level growth mixture models and more work is required to examine the rigour of these models and to understand the best way to communicate complex results to policy makers and public health specialists
How to develop a reliable method of defining intervention components and use of meta-regression in conjunction with such a method to identify effective components.
Problems of effectively diffusing 'good 'practice interventions that change professional practice
Similar issues surrounding evaluation of interventions to change behaviour in the context of chronic disease self-management (i.e. not just in a preventative context) Development and testing of measures of behaviour/behaviour change and associated factors, particularly in the context of chronic disease self-management
Methods to evaluate inequalities in outcome of behavioural interventions (e.g. across socio-economic groups, age groups, ethnic groups, sexes)
Methods to incorporate equity considerations or differential weighting of health benefits dependent on the characteristics of the patient to whom they accrue.
Increasing numbers of behaviour change interventions are being delivered online - these offer specific methodological challenges for evaluation, including the challenges of undertaking online trials. Methodological work on maximising the internal validity of online trials (esp re recruitment, retention, randomisation (and avoidance of re-registration by individual participants), fidelity of the intervention and data quality.
Role of regulation and environment on behaviour relative to individual behavioural interventions
My main observation is to question why there are no health psychologists on this panel, given that this is a/ the central discipline in developing health behaviour interventions, whereas there are 3 sociologists
Methods to assess behavioural components of complex interventions
Structural uncertainty of decision analytic models; Extrapolation of evidence and validation of results beyond the duration of trials
Ethical issues related to the use of interventions to change behaviour in the context of public health
These topics are focused. What is needed is a coherent policy for synthesis across these topics. I.e. when to use network meta-analysis, when to consider obs evidence, when to consider qualitative + quant evidence & how such data should inform the decision models. This is to ensure consistency in overall approach and thus fairness across all appraisals.
Area 2
NICE's new-found willingness to place differential values on health might be justified in terms of stakeholder's interests (general public). Methods to determine conditions under which NICE will weaken its own (rational) procedures should be made clearer.
Transparency over how stakeholders are recruited, and their interests. Lack of academic or specialist methodological expertise within review groups. No consistent peer review of the systematic reviews making up the guidelines.
2.C.2 needs to include specific reference to NHS commissioning organisations
I think that the questions in this section focus somewhat unhelpfully on process when the key issues is what information about patient views and experiences does NICE need - the methods for collecting it should then follow. So should be asking this question rather than evaluating current methods for collecting information when we still arent clear what information is needed.

Impact of stakeholder participation in appraisal committee meetings
Optimal nature and timing of stakeholder input to NICE processes
Area 3
Methods to openly peer-review the systematic reviews produced by collaborating centres. methods to assess the way recommendations were reached from the conclusions of the reviews.
Methods examining the validity of the cost-effectiveness threshold. The use of mathematical programming approaches for examining the optimal allocation of resources for different budgets over time
Methods to assess the trade offs between equity and efficiency in the delivery of interventions (including clinical and public health, simple and complex) which are unequally successful across population subgroups (e.g. socio-economic groups, ethnic groups, age groups, sexes)
Societal value of a QALY.
When should NICE withhold positive guidance due to uncertainty (OIR) and what methods would help the assessment of the importance of sunk costs and value of evidence forgone
Area 4
Assumptions of the standard QALY model
In relation to 4.C.1 the biggest problem with the existing EQ5D is the statistical method used to derive the weights, not the fact it comes from the general public. Work around comparisons between alternative utility based measures e.g SF6D and HUI3 and EQ5D-5L How to collect utility values for children
Investigation of the relative value of alternative utility based measures eg SF-6D or HUI3
Re-estimating the EQ5D tarrif using existing data but better methods to account for states worse than death. Establishing whether the assumptions of additivity and constant proportional time trade off matter, if so when they matter most and what alternative practical methods/adjustments would be most appropriate
Area 5
It seems odd that the public's view of the threshold has not been included as an option to 'vote' on. This would seem to be as important as trying to find a threshold through examination of NHS commissioners' decisions.
Methods for ensuring quality in development of guidelines, assessing staff support of guideline producers (e.g. research fellows)
The added value of developing a conceptual map (causal model) of the problem area in order to focus and guide literature reviewing
Evaluation of the impact of the differences in decision-making criteria between NICE and local level NHS Assessment of how to include an assessment/measure of innovation within appraisals/guidelines
for 5.a.1 Rather than look at the ICER of things displaced by NICE, the ICERs of the >80% of health care not currently being assessed should be considered

Appendix A12: Web Survey Prioritisation Results

	Very Important	Important	Somewhat Important	Not Important
Area 1: Analysis and design of effectiveness studies and their synthesis				
Theme A. Systematic reviews				
Topic 1_A_1: Establishing methods and rules for efficient systematic reviews of effectiveness, diagnostic test accuracy and prognostic factors (i.e. tackling the trade-off between efficiency and quality)	34.7%	40.0%	21.3%	4.0%
Topic 1_A_2: Methods for keeping research synthesis up to date; developing on-going and up to date repositories of 'approved' networks of evidence in key diseases using mixed treatment comparison	26.7%	40.0%	28.0%	5.3%
Topic 1_A_3: Methods for identifying, appraising and synthesising 'grey literature'	8.0%	30.7%	49.3%	12.0%
Topic 1_A_4: Development of a checklist or reporting rules for standardised reporting of public health reviews including undertaking sensitivity analysis	10.7%	32.0%	42.7%	14.7%
Topic 1_A_5: Methods for quality assessing qualitative research	17.3%	28.0%	37.3%	17.3%
Topic 1_A_6: Methods for the timely identification and synthesis of qualitative research within the context of NICE processes	24.0%	37.3%	29.3%	9.3%
Topic 1_A_7: Methods for conducting systematic reviews of complex interventions (e.g. in public health)	50.7%	25.3%	21.3%	2.7%
Theme B. Meta-analysis (including indirect and mixed treatment comparisons)				
Topic 1_B_1: Methods to adjust for potential bias in meta-analysis (for example, issues of multiple sources of bias and confounding)	30.6%	45.8%	20.8%	2.8%
Topic 1_B_2: Methods to combine individual patient and aggregate data in evidence synthesis	29.7%	41.9%	25.7%	2.7%
Topic 1_B_3: Assessing the implications of extending networks of evidence for NICE guidance on the reliability of results	21.4%	34.3%	38.6%	5.7%
Topic 1_B_4: Methods for linking treatments into networks of evidence where there is no direct evidence link on the basis of randomised trials (for example using observational evidence)	27.4%	41.1%	28.8%	2.7%
Topic 1_B_5: Establishing the reliability of mixed treatment comparisons and consistency with direct trial data	38.4%	34.2%	24.7%	2.7%
Topic 1_B_6: Methods to deal with treatments not routinely used in practice within evidence synthesis	6.8%	37.0%	41.1%	15.1%
Topic 1_B_7: How to assess the comparability of control arms when included in evidence synthesis	17.8%	45.2%	34.2%	2.7%
Topic 1_B_8: What needs to be defined in a protocol for a mixed treatment comparison?	20.5%	45.2%	26.0%	8.2%
Topic 1_B_9: Methods to assess the quality of randomised studies and to incorporate this into a formal quantitative synthesis.	24.7%	20.5%	38.4%	16.4%

Topic 1_B_10: A review of software to carry out meta-analysis and mixed treatment comparison	11.1%	19.4%	47.2%	22.2%
Topic 1_B_11: Methods to assess the exchangeability of studies and to reflect the in evidence synthesis.	9.7%	34.7%	45.8%	9.7%
Topic 1_B_12: Methods for synthesising both qualitative and quantitative research	16.4%	32.9%	34.2%	16.4%
Theme C. Use of non-experimental data				
Topic 1_C_1: Establishing optimal methods for analysis of disease registers and other sources of non-experimental evidence (e.g. What methods to use? When should non-experimental data be used? How are non-experimental data currently used at NICE?)	29.7%	47.3%	21.6%	1.4%
Topic 1_C_2: Methods to establish the efficacy of a 'composite comparator' (e.g. current practice).	12.2%	50.0%	31.1%	6.8%
Topic 1_C_3: The use of routine surveillance and monitoring data in developing NICE public health recommendations	15.3%	38.9%	41.7%	4.2%
Topic 1_C_4: Using bias adjustment methods for observational studies, including adjustments for indication bias in data from registers	21.9%	43.8%	28.8%	5.5%
Topic 1_C_5: Methods to assess the sensitivity of observational study results to study design	13.5%	44.6%	39.2%	2.7%
Theme D. Interpretation and analysis of clinical trial data				
Topic 1_D_1: Methods for translating trial evidence from adults to children	19.4%	27.8%	41.7%	11.1%
Topic 1_D_2: Methods for translating phase II research for NICE decisions	11.3%	29.6%	43.7%	15.5%
Topic 1_D_3: Methods to quantify the incidence of rare events from interventions	13.9%	30.6%	43.1%	12.5%
Topic 1_D_4: Methods for the optimal use of surrogate or intermediate measures in assessing effectiveness	26.4%	38.9%	30.6%	4.2%
Topic 1_D_5: Methods for the assessment of the effectiveness of treatment sequences	25.4%	47.9%	22.5%	4.2%
Topic 1_D_6: How best to present effectiveness data for NICE Committees including the likelihood of anticipated and unanticipated events.	17.8%	34.2%	32.9%	15.1%
Topic 1_D_7: Methods to assess the effect of practitioner experience (and other potentially relevant contextual factors) on effectiveness	23.3%	23.3%	43.8%	9.6%
Topic1_D_8: Methods to attribute outcomes to specific components of care within complex interventions (e.g. public health interventions)	27.0%	36.5%	31.1%	5.4%
Theme E. Clinical heterogeneity				
Topic 1_E_1: Methods to assess the applicability of evidence to different populations between countries	12.7%	35.2%	39.4%	12.7%
Topic 1_E_2: Bayesian methods for subgroup analysis (e.g. biological plausibility of a subgroup in terms of a prior probability)	17.1%	37.1%	37.1%	8.6%
Topic 1_E_3: Use of, and problems associated with, meta-regression based on summary data to consider the relationship between baseline event risks and treatment effects	14.7%	45.6%	30.9%	8.8%

Theme F. Diagnostics and medical devices				
Topic 1_F_1: Ethical and practical challenges in using 'sham' procedures (or control arms) in a surgical environment.	11.3%	29.6%	43.7%	15.5%
Topic 1_F_2: How should the product life-cycle and the procurement of devices in the NHS be factored into the appraisal process	12.9%	27.1%	40.0%	20.0%
Topic 1_F_3: How best to evaluate diagnostic and screening technologies	37.5%	37.5%	18.1%	6.9%
Theme G. Behavioural research				
Topic 1e.g.1: Methods to evaluate interventions to change behaviour in the context of public health	37.8%	27.0%	27.0%	8.1%
Area 2: Synthesis of evidence from patients, the public and stakeholders				
Theme A. Evidence from patients				
Topic 2_A_1: Methods to assess what types of patient evidence should be used at different stages of NICE's decision-making processes (e.g. when to undertake reviews of qualitative evidence? What types of reviews should be conducted? When should colloquial evidence be used?)	24.3%	41.9%	23.0%	10.8%
Topic 2_A_2: Guidance on providing information to patients/carers on breaking bad news	8.1%	8.1%	44.6%	39.2%
Topic 2_A_3: Methods for using colloquial evidence to determine the effect of complex interventions (e.g. in public health)	11.0%	20.5%	41.1%	27.4%
Theme B. Evidence from the general public				
Topic 2_B_1: Methods to understand how the public view characteristics of conditions and the technologies used to treat them	17.3%	29.3%	38.7%	14.7%
Theme C. Evidence from stakeholders				
Topic 2_C_1: The appraisal and synthesis of 'colloquial evidence' (e.g. comments received from stakeholders during consultation)	13.7%	30.1%	37.0%	19.2%
Topic 2_C_2: Evaluation of the existing, and development of new, methods for participation of different stakeholder groups at different stages of NICE's decision-making processes (including representatives of the general public, patients and practitioners).	19.4%	22.2%	44.4%	13.9%
Area 3: Economic analysis and uncertainty				
Theme A. Costing				
Topic 3_A_1: What are the most appropriate sources of cost data for NICE decision-making?	20.0%	45.7%	28.6%	5.7%
Topic 3_A_2: Methods to establish the amount of costs of resources should be included in analysis where these fall only partially on the National Health Service/Personal Social Services (either for a specific individual or across different population groups)?	14.3%	40.0%	31.4%	14.3%
Topic 3_A_3: Methods for estimating the opportunity cost of recommending treatments for aggregate populations rather than for subgroups	19.7%	40.8%	29.6%	9.9%

Topic 3_A_4: Should potential reductions in pharmaceutical prices over time be reflected in economic analysis. If so, what methods should be used?	24.6%	30.4%	33.3%	11.6%
Theme B. Perspective for analysis				
Topic 3_B_1: Methods to determine the appropriate costs and benefit perspective for the analysis of public health interventions?	28.8%	38.4%	24.7%	8.2%
Topic 3_B_2: Methods to determine the appropriate costs and benefit perspective for the analysis of health technologies?	22.2%	40.3%	29.2%	8.3%
Topic 3_B_3: Methods for the evaluation of interventions from a societal perspective	33.8%	31.1%	25.7%	9.5%
Theme C. Time horizon for analysis				
Topic 3_C_1: Including long-run effects of interventions in analyses (e.g. inclusion of treatment costs unrelated to initial disease by extending morbidity)	17.1%	41.4%	31.4%	10.0%
Topic 3_C_2: Extrapolation of the duration of the costs and benefits of interventions beyond those observed in trials, including the quantification of uncertainty	47.9%	33.8%	16.9%	1.4%
Theme D. Economic modelling				
Topic 3_D_1: Methods to develop 'standardised' and 'approved' models in a given disease area, including parameter inputs	20.3%	39.1%	29.7%	10.9%
Topic 3_D_2: Further develop checklists for establishing the quality of economic models including input parameters and reporting standards	10.6%	36.4%	28.8%	24.2%
Topic 3_D_3: Research to assess whether the predictions of economic models used to inform NICE guidance are borne out in practice	41.8%	32.8%	20.9%	4.5%
Topic 3_D_4: Methods for the use of surrogate or intermediate measures in models	20.0%	49.2%	24.6%	6.2%
Topic 3_D_5: Development of criteria for selecting an appropriate structure for a decision model given available evidence on disease prognosis and the impact of alternative interventions	14.3%	49.2%	31.7%	4.8%
Topic 3_D_6: Better methods for estimating cost-effectiveness in subgroups	15.2%	34.8%	43.9%	6.1%
Topic 3_D_7: Assessing the cost-effectiveness of 'long' or complex diagnostic/treatment pathways	24.2%	39.4%	30.3%	6.1%
Topic 3_D_8: The identification and use of prognostic data in economic models	12.3%	44.6%	38.5%	4.6%
Topic 3_D_9: Methods for determining the optimal complexity of economic models (i.e. how complex does a model need to be to be fit for purpose?)	22.4%	47.8%	23.9%	6.0%
Topic 3_D_10: Methods for the incorporation of evidence on adherence in economic models	16.7%	37.9%	40.9%	4.5%
Topic 3_D_11: Methods to identify and inform appropriate structure of economic models	26.9%	34.3%	28.4%	10.4%
Theme E. Uncertainty				
Topic 3_E_1: Methods for quantifying the uncertainty in cost-effectiveness models, including for complex models, and for showing the implications of uncertainty for decisions	25.4%	38.8%	28.4%	7.5%
Topic 3_E_2: Developing methods for eliciting 'prior' parameter estimates from relevant experts	13.6%	33.3%	37.9%	15.2%

Topic 3_E_3: Bayesian and Frequentist models for analysis – what are the differences between the approaches & which is most appropriate for NICE?	15.2%	33.3%	36.4%	15.2%
Topic 3_E_4: Methods of assessing the need for evidence and the consequences of uncertain decisions to the NHS (e.g. in terms of sunk costs)	22.7%	28.8%	36.4%	12.1%
Topic 3_E_5: Averaging of model results to representing structural uncertainty (e.g. When should averaging be used? What methods should be used?)	12.1%	39.4%	34.8%	13.6%
Topic 3_E_6: Quantifying the implications of imprecision in parameter estimates on decision uncertainty	13.6%	42.4%	33.3%	10.6%
Theme F. Other	11.6%	29.0%	40.6%	18.8%
Topic 3_F_1: What is the appropriate discount rate for health and under what circumstances might it vary?				
Topic 3_F_2: Methods for the economic evaluation of public health interventions	38.6%	30.0%	20.0%	11.4%
Topic 3_F_3: Methods for consolidating the range of costs and outcomes that decision makers are presented	10.6%	36.4%	42.4%	10.6%
Topic 3_F_4: Translation of research methods so that the process is understandable/transparent to non-specialists	43.7%	23.9%	21.1%	11.3%
Topic 3_F_5: Methods to assess the cost-effectiveness of interventions which have costs and (dis)benefits outside of the health care sector	30.4%	43.5%	21.7%	4.3%
Topic 3_F_6: Methods to establish the type of economic model and appraisal process that should be used to formulate guidance (When is it necessary to commission development of a new economic model?)	13.2%	52.9%	22.1%	11.8%
Topic 3_F_7: Methods to implement cost-effectiveness analysis (and evidence synthesis) early into the development of new technologies to inform future research and development decisions	26.9%	37.3%	23.9%	11.9%
Topic 3_F_8: Methods to reflect the objective of reducing inequalities in cost-effectiveness analysis	24.6%	30.4%	36.2%	8.7%
Topic 3_F_9: How should NICE establish the value for money of conducting further research (do the costs outweigh the benefits)?	22.5%	45.1%	21.1%	11.3%
Area 4: Measurement and valuation of benefits				
Theme A. Use of the QALY				
Topic 4_A_1: Methods to capture a wider set of (dis)benefits that may not be included in the QALY	41.7%	36.1%	18.1%	4.2%
Topic 4_A_2: Consolidating patient reported outcomes with other measures of benefit (e.g. QALYs)	40.0%	30.0%	21.4%	8.6%
Theme B. Standardised measurement tools				
Topic 4_B_1: Use of mapping techniques between clinical and patient-reported outcomes, and preference-based instruments for use in QALYs	16.4%	46.3%	26.9%	10.4%
Topic 4_B_2: Methods to derive quality of life weights (utilities) when no EQ-5D data are available or the EQ-5D is inappropriate.	27.9%	33.8%	30.9%	7.4%

Topic 4_B_3: Methods to establish what effects of interventions and programmes are/are not currently captured by the EQ-5D	35.8%	31.3%	26.9%	6.0%
Topic 4_B_4.: Methods to establish when disease specific measures of health outcomes should be used instead of, or as supplementary to, the EQ-5D	33.8%	29.4%	25.0%	11.8%
Topic 4_B_5: Evaluating health in less bounded ways (beyond questionnaires)	15.7%	27.1%	28.6%	28.6%
Topic 4_B_6: Methods for the measurement of changes in the health of children and people unable to report the status of their own health	24.6%	46.4%	24.6%	4.3%
Theme C. Valuation of health				
Topic 4_C_1: Methods for the re-evaluation of the EQ-5D preference set for the UK population with consideration to (i) the use of patient valuations of health and/or more informed public valuations and (ii) the appropriate valuation of health states considered to be worse than dead	22.1%	45.6%	20.6%	11.8%
Topic 4_C_2: Comparison/re-evaluation of the methods of preference elicitation for QALYs	14.7%	36.8%	27.9%	20.6%
Topic 4_C_3: Methods for valuing health at different time points in a person's life (especially at the end of life)	33.8%	33.8%	21.1%	11.3%
Topic 4_C_4: Methods to determine whether public or patient valuations of health should be used	33.8%	33.8%	23.9%	8.5%
Topic 4_C_5: Methods for weighting QALYs for characteristics of individuals (e.g. disease severity, social demographic characteristics)	14.3%	42.9%	25.7%	17.1%
Topic 4_C_6: Methods to determine how patients view the burden of a condition (possibly outside of the HRQL framework)?	20.0%	40.0%	18.6%	21.4%
Theme D. Use of health state utility data in economic models				
Topic 4_D_1: Methods for synthesising health-state utilities (e.g. the use of meta-regression using published or patient-level data)	10.9%	32.8%	42.2%	14.1%
Topic 4_D_2: How to use and adapt health state utility values published in the literature for cost-effectiveness models (for example, accounting for co-morbidities or socio-demographic factors).	7.6%	43.9%	37.9%	10.6%
Topic 4_D_3: How uncertainty in health state utility values should be quantified and how that uncertainty should be incorporated into economic analyses.	13.8%	36.9%	41.5%	7.7%
Topic 4_D_4: Using EQ5D data routinely collected in Patient Reported Outcome Measures (PROMS) in the NHS to provide standardised quality of life weights (utilities) for economic models for NICE	9.1%	34.8%	42.4%	13.6%
Area 5: Decision-making at NICE				
Theme A. Threshold for Cost-effectiveness				
Topic 5_A_1: What is the current ICER of things that are being displaced by NICE guidance (opportunity cost of NICE guidance?)?	41.2%	32.4%	20.6%	5.9%
Topic 5_A_2: Methods to estimate the opportunity cost of NICE guidance (i.e. the threshold) including changes over time	41.2%	32.4%	20.6%	5.9%

Topic 5_A_3: Methods to communicate concept of a threshold and related issues to non-specialists	27.9%	27.9%	26.5%	17.6%
Theme B. Influences on NICE decision-making				
Topic 5_B_1: What other factors should be considered for decision-making for interventions for children, including the use of medicines 'off-license'?	16.4%	31.3%	38.8%	13.4%
Topic 5_B_2: Methods to feed equity and utility into NICE decision-making?	26.1%	29.0%	31.9%	13.0%
Topic 5_B_3: Should NICE decision-making be based on cost-effectiveness analysis (CEA) modified by social value judgements, or should a range of social values be used of which CEA is one?	21.4%	37.1%	24.3%	17.1%
Topic 5_B_4: Methods for taking factors other than cost-effectiveness (e.g. societal costs/effects) into account in NICE decision-making (e.g. using multi-criteria decision analysis)	27.9%	38.2%	25.0%	8.8%
Topic 5_B_5: Methods for establishing how contextual affect decisions about the safety and efficacy of interventions (e.g. availability of alternatives, stage of life)	17.9%	34.3%	31.3%	16.4%
Topic 5_B_6: Which types of sub-groups should be considered in economic evaluation studies undertaken to inform the decisions of the Institute (including consideration of equity issues)?	16.2%	39.7%	29.4%	14.7%
Topic 5_B_7: How to take inequalities into account at different stages of NICE guidance production?	18.6%	27.1%	37.1%	17.1%
Theme C. Handling uncertainty in decision-making				
Topic 5_C_1: Establishing decision rules for incorporating estimates of uncertainty into decision-making	25.0%	32.8%	28.1%	14.1%
Topic 5_C_2: What criteria should be used for establishing only in research recommendations (including a consideration of the ethical implications and whether publicly funded research will impact on current policy and practice)?	29.9%	32.8%	29.9%	7.5%
Topic 5_C_3: How should NICE assess whether additional evidence is needed, what type of evidence is required and the type of evidence for 'coverage with evidence' decisions.	38.2%	39.7%	14.7%	7.4%
Topic 5_C_4: The use of expected value of perfect information (EVPI) methods to make both appraisal recommendations and research recommendations.	20.3%	20.3%	35.9%	23.4%
Theme D. Process of decision-making				
Topic 5_D_1: How do/should Committees and Guideline Development Groups operate?	23.6%	22.2%	36.1%	18.1%
Topic 5_D_2: Evaluation of the psychology of decision-making and the effect of contextual factors (such as public presence or media campaigns).	25.0%	25.0%	30.6%	19.4%
Topic 5_D_3: Methods to review existing analytical methods for systematic reviews and economic analyses to ensure they add value for decision-making	15.9%	33.3%	29.0%	21.7%
Topic 5_D_4: Methods to evaluate the different processes within the technology appraisals programme and within the clinical guidelines programme (including Appraisal Committee and stakeholder views and the impact on recommendations)	10.6%	34.8%	30.3%	24.2%
Topic 5_D_5: Methods to review the quality of assessment reports that inform decision-making at	18.3%	33.8%	36.6%	11.3%

NICE				
Topic 5_D_6: What changes should be made to the development of NICE guidance so that electronic decision support tools can be produced simultaneously?	7.5%	22.4%	40.3%	29.9%
Topic 5_D_7: What are the best methods for determining the most important clinical questions for a given topic?	24.2%	25.8%	34.8%	15.2%
Topic 5_D_8: Methods for scoping decision problems, including the potential use of qualitative research	17.6%	27.9%	33.8%	20.6%
Topic 5_D_9: An evaluation of the current appraisal programme in the context of the original intention for the programme (e.g. focus on pharmaceuticals) and the reasons for differences (e.g. why other interventions are harder to evaluate)	17.9%	28.4%	29.9%	23.9%
Topic 5_D_10: How should potential future changes in health care be taken into account in decision-making?	7.4%	33.8%	38.2%	20.6%
Theme E. Developing the format/ type of NICE recommendations				
Topic 5_E_1: Methods to assess the impact of NICE guidance on changing health states (or the 'payback' from NICE) and/or changing clinical practice	25.0%	39.7%	29.4%	5.9%
Topic 5_E_2: Development of methods to produce guidance to the NHS on the disinvestment of existing interventions	44.1%	33.8%	17.6%	4.4%
Topic 5_E_3: Development of methods to consider value based pricing arrangements	20.9%	35.8%	32.8%	10.4%
Topic 5_E_4: Methodological issues in evaluation of patient access schemes	19.7%	37.9%	27.3%	15.2%
Topic 5_E_5: Evaluation of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process	10.9%	18.8%	42.2%	28.1%
Topic 5_E_6: How can NICE produce symptom-led guidance, rather than disease-based guidance?	7.5%	22.4%	38.8%	31.3%
Topic 5_E_7: Methods for communicating guidance and supporting evidence to the general public	25.4%	29.9%	29.9%	14.9%

Comments on the most highly rated topics (n=55)

Topic	To which area of NICE's work does it relate?	How will it inform the challenges faced by NICE?	Ideas for specific research questions	Ongoing and previous research	Possible characteristics of research
1_G_1: Methods to evaluate interventions to change behaviour in the context of public health		NICE faces more and more complexity in the interventions being considered.			
	Appraisal of public health interventions	Many public health interventions focus on changing behaviours, and then the change in behaviour must then be linked to changes in health outcomes. The challenge for NICE is assessing the benefits from these interventions in an exchangeable way with the benefits from pharmaceutical interventions.			How to gather evidence to link change in behaviour with change in outcome. Evidence on the long-term behaviour change induced by such interventions.
1_A_7: Methods for conducting systematic reviews of complex interventions (e.g. in public health)	CPHE		How should searches for complex interventions progress? e.g. methods for iterative searching/ methods of intervention led searching. How should non RCT evidence be treated? How to synthesis evidence from multiple study designs. How might theory led review approaches help in CPHE reviews? (What does "systematic" mean in the context of reviews of complex interventions)	Realist review (Pawson et al) but not in this policy context.	Case studies to assess the merit and utility of different approaches. Empirical comparisons of the costs and benefits of different types of search strategy.

1_A_1	Technology appraisal	increasing diagnostics will need to be evaluated	not just the systematic review of diagnostics but also the integration of this evidence within a decision model	work at Birmingham & Leicester	review of methods used to date; implications of using different methods to case studies
	Appraisal and guidelines	Michael Rawlins' Harveian Oration suggested that evidence from studies in which selection bias had been addressed using random allocation was often insufficient for NICE's purposes, and that other kinds of evidence should used. However, he was not explicit about the circumstances in which non-randomised evidence should be used, or what empirical evidence should be used to guide such judgements.	In which circumstances does evidence from non-randomised studies provide a sufficiently robust basis for guiding practice?	Vist GE, Hagen KB, Devereaux PJ, Bryant D, Kristoffersen DT, Oxman AD (2007). Outcomes of patients who participate in randomised controlled trials compared to similar patients receiving similar interventions who do not participate. Cochrane Database of Methodology Reviews 2004, Issue 4. Art. No.: MR000009. DOI: 10.1002/14651858.MR000009.pub3. Glasziou P, Chalmers I, Rawlins M, McCulloch P. When are randomised trials unnecessary? Picking signal from noise. BMJ 2007;334: 349-351.	Replications of the above two studies, addressing Rawlins' concerns.
	Guidelines production	the trade-off between time pressures and quality is an important one. The bar needs to be set high. Staff are being squeezed and quality is at risk.	Document current staffing and change staffing (e.g. put 2-3 Rfs on a guideline not one) and conduct interviews		
	All	NICE has to use the best evidence, but collecting that evidence is very resource intensive. It needs to be done efficiently, but also consistently across all NICE	All aspects of systematic reviewing across all types of technologies, questions, is required	Significant amount already on efficient searching of literature.	

	stream: this is not the situation currently			
All	More transparent decisions based on reliable methods			
technology appraisal	Diagnostic procedures are being used increasingly within the NHS, yet it is unclear how their effectiveness should be measured and rated against other types of treatment	Can a standardised methodology be developed for the allow appraisal of this type of procedure?	I am aware that Jon Deek's group in Birmingham are researching some of the issues	Comparison of different approaches and investigation of the impact of these approaches on decision-making