A decision framework for recommending the use of health technologies

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

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Executive summary

Health Technology Assessment 2012; Vol. 16: No. 46
DOI: 10.3310/hta16460

Health Technology Assessment
NIHR HTA programme
www.hta.ac.uk

Executive summary

The general issue of balancing the value of evidence about the performance of a technology and the value of access to a technology can be seen as central to a number of policy questions. Establishing the key principles of what assessments are needed, as well as how they should be made, will enable them to be addressed in an explicit and transparent manner. The aims of this research are to (1) establish the key principles of what assessments are needed to inform an 'only in research' (OIR) or 'approval with research' (AWR) recommendation, (2) evaluate previous National Institute for Health and Clinical Evidence (NICE) guidance in which OIR or AWR recommendations were made or considered and (3) evaluate a range of alternative options to establish criteria, additional information and/or analysis that could be made available to inform the assessments needed. A series of recommendations, or options for NICE to consider, were developed with the involvement of key stakeholders. These establish the key principles and associated criteria that might guide OIR and AWR recommendations and identify what, if any, additional information or analysis might be included in the technology appraisal process, including how such recommendations might be more likely to be implemented through publically funded and sponsored research.

The relevance of this work, primarily to the NICE Technology Appraisal Programme, has been evaluated through two workshops involving key stakeholders, including members of NICE and its Advisory Committees (including lay members and other NICE programmes), patient representatives, manufacturers, and research and NHS commissioners, as well as relevant academics. Summaries of the research findings and key issues were provided in the form of briefing documents. These documents, which formed the basis of the workshop presentations and related group discussions, as well as a summary of feedback and list of participants, are available at www.york.ac.uk/che/research/teehta/workshops/only-in-research-workshop/.

The following elements of research form the basis of this report: (1) a critical review of policy, practice and literature in this area, (2) the key principles and the sequence of assessments needed, (3) a review of NICE technology appraisal guidance and (4) a checklist of assessments needed and its application to the four case studies using a range of additional information. Some of the possible implications for policy, process and methods of appraisal, distinguishing those issues directly relevant to the NICE remit and those that might be most relevant to other public bodies and stakeholders, were drawn together based on feedback provided at both workshops.

Key principles and assessments needed

The National Institute for Health and Clinical Evidence is increasingly making decisions about health technologies close to licence through the single technology assessment process. Inevitably these decisions are being made when the evidence base to support these technologies is least mature and when there may be substantial uncertainty surrounding their cost-effectiveness, as well as their effectiveness and potential for harms. In these circumstances further evidence may be particularly valuable as it would lead to better decisions that improve patient outcome and/or reduce resource costs. However, a decision to approve a technology will often have an impact on the prospects of acquiring further evidence to support its use. This is because, once positive guidance has been issued, the incentives for manufacturers to conduct research are limited. Also, the clinical community is unlikely to regard further randomised controlled trials to be ethical once positive guidance provides access with a funding mandate. Therefore, the decision to approve a technology should account for both the potential benefits of access to a cost-effective

technology and the potential costs to future NHS patients in terms of the value of evidence that may be forgone by early adoption.

The key principles and assessments needed fall into four broad areas: (1) expected cost-effectiveness and population net health effects (NHEs) (including benefits, harms and NHS and Personal Social Services costs), (2) the need for evidence and whether or not the type of research required can be conducted once a technology is approved for widespread use, (3) whether or not there are sources of uncertainty that cannot be resolved by research but only over time and (4) whether or not there are significant (opportunity) costs, which will be committed and cannot be recovered once the technology is approved.

Guidance will depend on the combined effect of all of these assessments because they influence whether or not the benefits of research are likely to exceed the costs and whether any benefits of early approval are greater than withholding approval until additional research is conducted or other sources of uncertainty are resolved. The key principles, represented by a sequence of assessment and judgements, can be summarised as a simple 7-point checklist that could be considered by Assessment Groups (AGs), Appraisal Committees and manufacturers:

- Is it expected to be cost-effective?
- Are there significant irrecoverable costs?
- Does more research seem worthwhile?
- Is the research possible with approval?
- Will other sources of uncertainty resolve over time?
- Are the benefits of research greater than the costs?
- Are the benefits of approval greater than the costs?

These principles suggest that the categories of guidance available to NICE have wider application than is reflected in our review of previous guidance. Importantly, which category of guidance will be appropriate depends only partly on an assessment of expected cost-effectiveness and hence this assessment should be regarded only as an initial step in formulating guidance. In general, as well as AWR for technologies expected to be cost-effective and OIR for those not, there are other important circumstances when OIR should be considered. In particular, for technologies expected to be cost-effective, OIR rather than approve may be appropriate when research *is not possible* with approval and OIR or even reject rather than AWR or approve may be appropriate even if research *is possible* with approval when there are significant irrecoverable costs.

Implications for value-based pricing

Any change in the effective price of the technology, either through patient access schemes or through direct price changes (possibly negotiated though a value-based pricing scheme), will affect the key assessments, leading to different categories of guidance. The price at which the technology would just be expected to be cost-effective is commonly regarded as the value-based price for the technology. This describes the threshold price below which approve rather than reject would be appropriate if OIR or AWR are not available as policy options. However, if they are available, there are often a number of relevant price thresholds. Once uncertainty and the need for evidence, as well as the impact of irrecoverable costs, are recognised, the threshold price that would lead to approve rather than OIR will always be lower than a single value-based price based on expected cost-effectiveness alone.

Even if price negotiation becomes possible alongside NICE appraisal, it will be important to retain OIR and AWR as available categories of guidance for two reasons: (1) there is no guarantee

that manufacturers will always agree to the lower price below which approve rather than OIR or AWR would be appropriate and (2) there may be many circumstances when no effective price reduction would make approve appropriate, for example reject or OIR guidance may be appropriate even if the effective price of a technology is zero if there is substantial uncertainty about its effectiveness and/or potential for harms.

Incentives for evaluative research

It is important that policy provides appropriate incentives for manufacturers to conduct the type of research needed to support NICE guidance at launch. The use of OIR and AWR guidance, and its link to effective price, provides clear signals and an incentive to ensure that the type of evidence which would require research that cannot be conducted once a technology is approved for NHS use is sufficient at launch. Therefore, a predictable OIR and AWR policy signals what type of evidence is likely to be most important at an early stage. It offers manufacturers a choice: (1) accept OIR guidance at a higher price but restricted volume, (2) reduce the effective price to achieve approval, or AWR where that is possible or (3) conduct the evaluative research at an earlier stage so that additional evidence at launch is not required.

How the NHS and manufacturers are likely to share the value of evidence might inform whether manufacturers should be expected to conduct the research specified in AWR or OIR guidance or contribute to the costs of publically funded research that may ultimately benefit their product. Two issues need to be considered: (1) the resource constraints on publically funded research may mean that other research priorities (often without commercial interest) may be more valuable to the NHS and (2) the success of AWR recommendations when manufacturers are asked to conduct the research will depend on whether NICE and/or the Department of Health are able to establish contractual arrangements as part of an AWR recommendation, that is, arrangements that can be monitored and enforced with credible penalties to ensure that agreed research is conducted and in the way intended. At present, NICE does not have a credible mechanism because removing approval of a technology simply because recommended research has not been conducted is not considered ethically appropriate or a credible threat.

The assessments that need to be made can also be used to consider what would be the value of (1) being able to conduct research while a technology is approved, (2) making evidence that is needed by the NHS available at launch and (3) being able to acquire evidence more quickly. This might inform a range of policies, such as early advice, public investment in early transitional and evaluative research or better data collection or information systems, that might make AWR possible. Understanding the relationship between the time taken for research to report and the value of the evidence to future populations can also help to inform (1) investments that might make research findings more quickly available, (2) the trade-off implicit in the choice of alternative research designs and (3) identification of those areas where, if research is to be undertaken, there must be confidence that it can report quickly.

How should assessment be undertaken?

Although the NICE appraisal process may be well suited to identifying the *need for evidence* when assessing cost-effectiveness, these other critical assessments (*the type of research and its priority*) are not necessarily ones for which NICE and its Advisory Committees, as currently constituted, have particular expertise, not least because they reflect the decisions of those responsible for research design, prioritisation and commissioning. Therefore, more informed judgements and better decisions might be possible through greater involvement of the research community. A

Research Advisory Committee could be constituted that could consider provisional OIR or AWR guidance, translating the need for particular types of evidence into particular types of research, costs, ethics, relative priority, likelihood of success and when the research is likely to report. The committee might also make recommendations about whether research should be publically funded or undertaken by the manufacturer with appropriate contractual arrangements (which may require the involvement of the Department of Health at some stage).

The order of considerations in the checklist and algorithm means that all seven assessments do not necessarily need to be made. Therefore, one model for an efficient process of assessment would be to consider points 1–5 routinely. The Appraisal Committee would then be in a position to either rule out OIR or AWR and issue guidance in the usual way or indicate in the Appraisal Consultation Documents that OIR or AWR was provisionally recommended subject to advice from a Research Advisory Committee and subsequent analysis to support an assessment of points 6 and 7 of the checklist before Final Appraisal Determination. This model would avoid unnecessary analysis and incorporate the judgements of the research community without necessarily delaying appraisal.

What additional information and analysis might be required?

Cost-effectiveness was presented in terms of NHEs per patient treated and for the population of patients over time. This provides information in a way that is directly relevant to the assessments that need to be made. All of the information required to express expected cost-effectiveness in this way is commonly available from the type of analysis already conducted during appraisal.

An early indication of the potential importance of irrecoverable costs can be based on their scale relative to expected NHEs; the point at which any initial losses are expected to be compensated by later gains; whether treatment decisions are reversible; and what opportunities to improve health might be forgone by a delay to initiating treatment.

The question of whether or not further research might be worthwhile (point 3 of the checklist) requires some assessment of (1) how uncertain a decision based on expected cost-effectiveness might be and (2) what the consequences, in terms of population NHEs, are likely to be if an incorrect decision is made. The methods of analysis decompose this into a series of steps, presenting what is available within current appraisal but in ways that can more directly inform the assessment required. Commonly, there is also uncertainty about alternative assumptions or judgements that might be made, often represented by alternative scenarios.

An assessment of the type of evidence needed (point 4 of the checklist) requires judgements about (1) how important particular types of parameters (inputs to the economic model) are to estimates of costs and quality-adjusted life-years, (2) what values these parameters would have to take to change a decision based on expected cost-effectiveness, (3) how likely is it that parameters might take such values and (4) what would be the consequences if they did, that is, what might be gained in terms of population NHEs if the uncertainty in the values of these parameters could be immediately resolved. The methods of analysis take these steps in turn, presenting what is available within current appraisal but in ways that more directly inform the assessment required. It is only when assessing the consequences of uncertainty associated with particular parameters that additional analysis is required to provide quantitative estimates.

The information required to assess whether other sources of uncertainty will resolve over time (point 5 on the checklist) requires information that is not commonly sought as part of NICE appraisal. It requires information about (1) likely changes in prices of the technology and its

comparators, (2) the emergence of new technologies that might make existing ones obsolete or change their cost-effectiveness and (3) other relevant research reporting. A number of potential sources of information and evidence were examined; however, many sources were either proprietary or public access was restricted, making it difficult to inform these assessments. When information and estimates were available they were often not complete or directly relevant to a UK context. NICE many need to consider how AGs and manufacturers can be provided with access to this type of information.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Publication

Claxton K, Palmer S, Longworth L, Bojke L, Griffin S, McKenna C, *et al*. 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. *Health Technol Assess* 2012;**16**(46).

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ISSN 1366-5278 (Print)
ISSN 2046-4924 (Online)
ISSN 2046-4932 (DVD)

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.

Printed on acid-free paper in the UK by Charlesworth Press.

MRP