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What are the HTA processes in the UK?

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- **Health technology assessment (HTA)** has a long history in the UK. In recent years HTA has become synonymous with the activities of the **National Institute for Health and Clinical Excellence (NICE)** in England, although important entities also exist in Scotland **(Scottish Medicines Consortium [SMC])** and Wales **(All Wales Medicines Strategy Group [AWMSG]).**
- The NICE technology appraisals programme is coordinated by the institute's Centre for Health Technology Evaluation, which develops guidance on the use of new and existing medicines, treatments and procedures within the NHS.
- NICE commissions so-called technology assessment groups to prepare assessment reports for consideration by the **Technology Appraisal Committee,** which is the primary decision-making body in the production of guidance on new health technologies.
- Guidelines on the methods of technology appraisal, which have been issued by NICE, embody the concept of the **reference case.**
- The standard approach to technology appraisals is called **multiple technology appraisal (MTA).** MTAs take 54 weeks from initiation of the process to issuing of guidance.
- NICE has also developed the **single technology appraisal** process for the review of single technologies for a sole indication. This is similar to the assessment process in Scotland and is a little quicker than the MTA process.
- Advantages of NICE's approach to technology appraisals include its methodological rigour, the encouragement of extensive stakeholder involvement and the fact that its activities are fairly transparent.
- Issues of concern are a lack of independence of NICE from the government, the amount of time it takes to conduct an assessment, the use of a cost-effectiveness threshold, the use of the quality-adjusted life-year as a measure of health benefit, and the uneven implementation of NICE guidance across the NHS.
- The HTA procedures in Scotland and Wales are more timely, but the SMC and AWMSG face many of the other challenges also faced by NICE.

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Background to the use of health technology assessment

Health technology assessment (HTA) has been defined as 'a **multidisciplinary field of policy analysis** studying the medical, economic, social and ethical implications of the development, diffusion and use of health technologies.'[1]

HTA has a fairly long history in the UK, with prominent early studies being those on major programmes funded by the Department of Health such as the heart transplant and mammography screening for breast cancer programmes. However, the major shift in the conduct of HTA came in 1991, with the establishment of the NHS Research and Development (R&D) programme and a commitment to spend up to 1.5% of the NHS budget on research that is oriented towards efficacy and safety.

Although the greatest expenditure was on primary research – mainly clinical trials – HTA became an increasingly influential part of the NHS R&D programme. The National Coordinating Centre for Health Technology Assessment was established in 1996 to handle the processes of priority setting (for topics), commissioning of studies, assessment of results from studies and dissemination of the results.

Despite considerable attention being paid to the growing body of evidence produced by the R&D programme, it became clear, however, that HTA was still not having sufficient impact, especially regarding changes in clinical practice. In addition, the absence or lack of attention to evidence on the effectiveness and cost-effectiveness of health technologies was leading to so-called 'postcode rationing', whereby expensive new technologies, such as interferon beta therapy for multiple sclerosis, were available in some locations and not others. Therefore, in 1999, the Department of Health established the National Institute for Clinical Excellence (NICE; the institute changed its name to **National Institute for Health and Clinical Excellence** in 2005, when it assumed the responsibilities of the former Health Development Agency for providing guidance on the use of public health programmes, although it kept the acronym NICE).

In broad terms, NICE acts as an 'arm's-length' organisation that provides guidance on the use of treatments and procedures in the NHS. It produces four types of guidance: **technology appraisals, clinical guidelines, public health guidance** and **reports on interventional procedures**. In producing its guidance, NICE **considers both clinical and cost-effectiveness**.

NICE guidance applies in England and sometimes also in Wales (see below). In Scotland, assessments of the clinical and cost-effectiveness of all new drugs are conducted by the Scottish Medicines Consortium (SMC) and clinical guidelines are produced by the Scottish Intercollegiate Guidelines Network (SIGN). In Wales, the All Wales Medicines Strategy Group (AWMSG) undertakes assessment of new drugs, particularly in areas where there is no NICE guidance.

The NICE technology appraisals programme

Although several organisations are involved in HTA in the UK, NICE has become by far the most influential, and its activities will, therefore, be discussed in more detail. The **NICE technology appraisals programme**, coordinated by the institute's Centre for Health Technology Evaluation (CHTE), has attracted the most interest and debate. The centre develops guidance on the use of new and existing medicines, treatments and procedures within the NHS. Only a few technologies are selected for appraisal. Specifically, the stated criteria for selection include:[2]

- Burden of disease (population affected, morbidity, mortality)

- Resource impact (cost impact on the NHS or the public sector)
- Clinical and policy importance (whether the topic falls within a government priority area)
- Presence of inappropriate variation in practice
- Potential factors affecting the timeliness for the guidance to be produced (degree of urgency, relevancy of guideline at the expected date of delivery)
- Likelihood of guidance having an impact on public health and quality of life, the reduction in health inequalities, or the delivery of quality programs or interventions.

NICE usually commissions an independent academic centre or centres, called **technology assessment groups,** to prepare assessment reports for consideration by the **Technology Appraisal Committee (TAC).** The TAC is an independent entity with membership drawn from the NHS, patient organisations, academia and industry, and is the primary decision-making body in the production of guidance on new health technologies. While the TAC represents the views of its varied membership, its advice is intended to be separate from any vested interests.

In addition to the aforementioned, the CHTE confers with various 'consultee organisations', or stakeholders, which include national patient groups, health professional bodies, and manufacturers of the technology under review. Such entities are able to submit evidence during the evaluation process, comment on the appraisal documents and appeal against the TAC's final recommendations.

NICE has issued methods guidelines for technology appraisals,[3] which form the template for manufacturer submissions and the review by the independent assessment groups. The guidelines embody the concept of the **'reference case',** whereby preferred methods are outlined but manufacturers can also submit alternative analyses, if they think these are superior. The objective is to achieve some degree of standardisation of submissions without stifling methodological development. The NICE reference case is shown in Table 1.[3]

Table 1. The NICE reference case[3]

Element of health assessment	Reference case
Defining the decision problem	The scope developed by the institute
Comparator	Alternative therapies routinely used in the NHS
Perspective on costs	NHS and PSS for CCP and CHTE; public sector for CPHE
Perspective on outcomes	All health effects on individuals
Type of economic evaluation	Cost-effectiveness analysis
Synthesis of evidence on outcomes	Based on systematic review
Measure of health benefits	QALYs
Description of health states for calculation of QALYs	Health states reported directly by patients or carers and described using a standardised and validated generic instrument
Method of preference elicitation for health state valuation	Choice-based method, preferably the EQ-5D
Source of preference data	Representative sample of the public
Discount rate	An annual rate of 3.5% on both costs and health effects
Equity position	An additional QALY has the same weight regardless of the other characteristics of the individuals receiving the health benefit: 'a QALY is a QALY is a QALY'

CCP: Centre for Clinical Practice; CHTE: Centre for Health Technology Evaluation; CPHE: Centre for Public Health Excellence; NICE: National Institute for Health and Clinical Excellence; PSS: personal social services; QALY: quality-adjusted life-year

NICE's standard approach to technology appraisals, now called **multiple technology appraisal (MTA),** takes 54 weeks from initiation of the process to issuing of guidance. Key features of the process are **scoping of the topic,** which now includes a scoping workshop involving the manufacturers and other key consultees, a **company submission,** and an **independent technology assessment report (TAR)** by one of the assessment groups mentioned above. The TAR normally includes a systematic review of the clinical literature and an economic model, and can be quite extensive, especially since more than one technology is being assessed. The report and any other relevant evidence are considered by the TAC and an **appraisal consultation document** is issued. Consultees are then given an opportunity to comment before the **final appraisal determination** is issued, following a second discussion by the TAC. Consultees then have the opportunity to appeal, in which case an appeal hearing takes place. If no appeal is launched, the guidance is issued to the NHS within six weeks.

In addition to the aforementioned appraisal procedure, NICE developed a **single technology appraisal (STA) process** in 2005 for the review of single technologies for a sole indication. This was introduced in response to criticisms surrounding the length of time taken by the MTA process. The STA process is similar to that of the full MTA appraisal process, as previously described, but in the former only evidence submitted by the manufacturer is formally considered in the independent review. Moreover, formal consultation procedures take place only if the TAC's preliminary recommendations are substantially more restrictive than the terms of the licensed indication of the product under appraisal.[4] The timelines for the STA process also differ from the MTA process.[4] Specifically, STAs require less time to produce the guidance; approximately 39 weeks from initiation of the appraisal to publication. The timeline for STAs is, however, not substantially compressed and with any delays in the appraisal or appeals, it could approach the duration required for an MTA. To date, the STA process has been applied only to drugs – mainly cancer drugs – although it is increasingly being employed in other disease areas. The processes for MTAs and STAs are outlined in Table 2.[4,5]

The new STA process developed by NICE is similar to the process that has been in operation in Scotland for several years, where, if a company wishes guidance on the use of its drug to be issued, it submits a dossier to the SMC. The dossier is then evaluated by the consortium's assessors before guidance is issued. There has been some interest in comparing and contrasting the costs and outcomes (in terms of decisions) of the English and Scottish approaches. It is clear that the SMC's approach is quicker and less costly. The outcomes of the assessments are quite similar, although it appears that NICE sometimes makes more detailed recommendations relating to specific patient subgroups.

Main issues arising from NICE HTA activities

There are many things to admire in NICE's approach to technology appraisals. First, there is considerable methodological rigour, especially in the conduct of MTAs. Second, compared with other comparable organisations, NICE encourages extensive stakeholder involvement in the scoping of appraisals, commenting on draft reports and appealing against decisions. Third, NICE's activities are fairly transparent, which is one of the reasons so much has been written about the institute. Nevertheless, several issues remain unresolved, or of concern to some parties.[6]

Lack of independence

Although NICE is classed as an 'arm's-length' organisation, there are accusations that the institute is essentially following a government, or payer's, agenda. Indeed, to a large extent this is true, since NICE's remit is to ensure that the use of NHS resources is consistent with the principles of clinical and cost-effectiveness. On occasions it is, therefore, bound to issue negative guidance if a given technology, or its use in certain indications, does not meet the criteria.

Whether this constitutes more rationing of

Table 2. NICE procedures for technology appraisals[4,5]

Week	MTAs	STAs
0	Organisations invited to participate as consultees and commentators; consultees invited to make submissions; professional and patient consultees invited to nominate clinical specialists and patient experts	Manufacturer/sponsor submission requested; consultee statements invited
2		Manufacturer/sponsor submission of decision problem received; nominations of experts requested from all non-manufacturer/sponsor consultee and commentators
9		Evidence submissions and consultee comments received; start of report preparation by the TAG
11		Request for clarification sent to manufacturer/sponsor
14	Submissions received by consultees	
15	Submissions from manufacturers and sponsors sent to TAG	
16	Selected clinical specialists and patient experts invited to attend Appraisal Committee meeting and asked to submit a written personal perspective	
17		TAG report received
19		Committee papers compiled and sent to Appraisal Committee
21		Positive opinion required at this point for STA to proceed; Appraisal Committee meeting to develop ACD
23		ACD consultation begins; marketing authorisation or regulatory approval issued
24		ACD placed on NICE website for public comment
26		ACD distributed to consultees and commentators for 15 working days during which consultee can appeal
27		ACD consultation ends
28	TAR received by NICE	
29		Appraisal Committee meets to develop FAD
30	TAR sent to consultees and commentators for comment	
32	Selected clinical specialists and patient experts submit personal perspectives	
34	Comments on TAR from consultees and commentators received by the Institute	FAD distributed to consultees and commentators for 15 working days during which consultee can appeal
36	Evaluation report compiled and sent to Appraisal Committee	
37	Appraisal Committee meeting to develop ACD	
39		Anticipated publication (if no appeal)
40	ACD distributed to consultees and commentators for four weeks' consultation	
41	ACD posted on NICE website for three weeks' public comment	
45	Appraisal Committee meeting to develop FAD	
51	FAD distributed to consultees and commentators	
52	FAD posted on NICE website	
54	Close of appeal period (if no appeal, guidance published within six weeks)	

ACD: appraisal consultation document; FAD: final appraisal determination; MTA: multiple technology appraisal; NICE: National Institute for Health and Clinical Excellence; STA: single technology appraisal; TAG: technology assessment group; TAR: technology assessment report

care than would have occurred in the absence of NICE is open to debate. Because the determination of the NHS budget is made by the Department of Health (DH) largely independent of NICE, it is likely that NICE has led to different rationing, as opposed to more rationing.

Although NICE views the DH as its major stakeholder, there are very few examples of government actions that impinge on NICE's work. When NICE made the decision not to issue positive guidance on the use of interferon beta for multiple sclerosis, the DH, perhaps fearing a negative political backlash, brokered a risk-sharing scheme with the manufacturers. This allowed certain categories of patients to obtain, or to continue with, therapy, while limiting the financial risk to the NHS. More specifically, under the scheme, the government is entitled to a refund of part of the expenditure on interferon beta if the long-term benefits from treatment are not as favourable as the manufacturers claim. The DH also intervened to make trastuzumab available for the treatment of breast cancer, ahead of NICE's appraisal of the drug.

Timeliness

The concern has been raised that a period of 54 weeks (minimum) to conduct assessments is much too long. As mentioned previously, STAs were introduced to deal with this issue. However, STAs only reduce the core assessment time from 54 to 39 weeks and there are worrying signs that, with a higher proportion of appraisals going to appeal, the average time to issue guidance may increase.

These concerns are compounded by the fact that, once a technology is selected for appraisal by NICE, the NHS is less likely to introduce it, pending NICE's decision. The extent of so-called 'NICE blight' has not been formally studied, but does exist. Of course, the technology manufacturers feel (in the case of drugs) that all licensed products should be used until NICE issues guidance to the contrary. On the other hand, the NHS is cautious about introducing new technologies, which will be hard to remove or restrict if they are subsequently shown to be poor value for money.

Quality-adjusted life-years and social values

From the outset, NICE has been quite clear that the measure of health benefit to use in technology appraisals is the quality-adjusted life-year (QALY; Table 1).[3] The theoretical and methodological weaknesses of the QALY approach have been well discussed elsewhere and will not be reiterated here (see 'Further reading' section). An additional issue has arisen, however, in discussions about the decisions taken by NICE; namely, does the QALY capture all the elements of social value that are relevant to decisions about the allocation of healthcare resources?

NICE uses QALYs in a 'standard' fashion in its technology appraisals; namely, a QALY is considered of equal value regardless of who receives it. Some argue, however, that society, if consulted, would not apply this principle. For example, some research studies indicate that members of the public may value a QALY given to someone in a very poor health state higher than if it was given to someone in good health (a more detailed explanation of QALYs can be found in *What is a QALY?*).[7]

The cost-effectiveness threshold

The use, or non-use, by NICE of a threshold has been a continuing topic for debate, since it would be clear evidence that NICE rations care. Three criticisms have been raised: (1) there should not be a threshold, (2) the threshold has been set at the wrong level or is arbitrary and (3) different thresholds should apply, depending on the nature of the treatments or patient populations being studied.

Of course, the first criticism is rather meaningless, in that whenever decisions are made on whether or not to reimburse a particular technology, some assessment of value for money is being made. Perhaps a more relevant question is whether the cost-effectiveness threshold (or thresholds) should be explicitly stated. In its early days, NICE denied that it was applying a threshold. However, as the information on the decisions made by NICE accumulated, it became possible to infer what the threshold might be.

Rather than continue the speculation, the director and deputy director of NICE

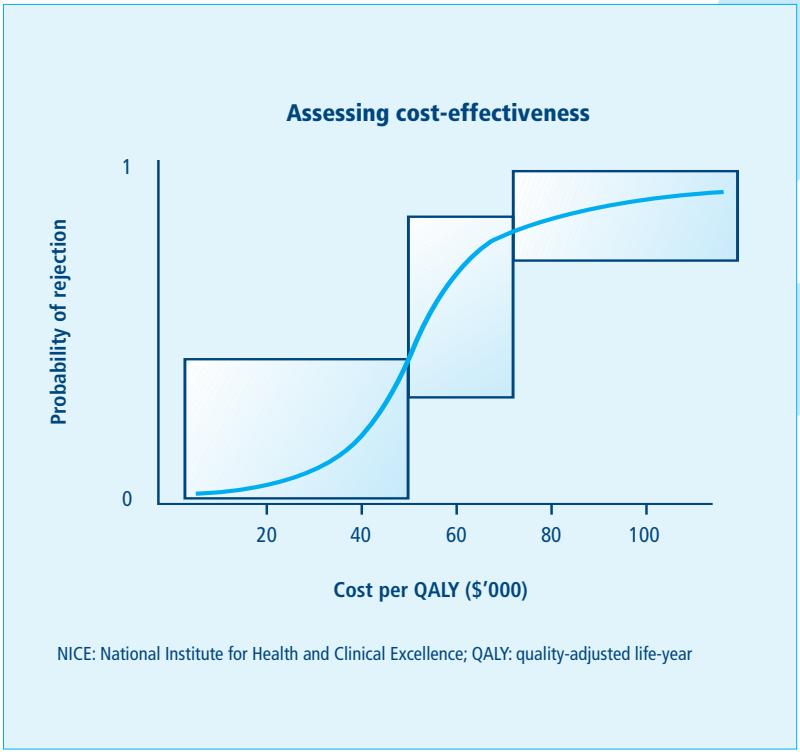
discussed the issues surrounding the use of cost-effectiveness thresholds and stated that NICE applied a threshold range; namely, interventions with an incremental cost per QALY ratio of less than £20,000 have a high probability of being funded, whereas those with a ratio exceeding £30,000 have a low probability of being funded (Figure 1).[8] Rawlins and Culyer also discuss possible situations where the upper bound of £30,000 might be exceeded; for example, on grounds of equity.

To apply an explicit threshold, the decision-maker needs to know what the right level would be. NICE has never claimed to know the answer to this question and, in answering the concerns of the Health Select Committee, the institute described its decision-making process as a deliberative one, which, in essence, is searching for a threshold.[6]

The third concern is that the cost-effectiveness threshold, if one can be determined, may differ depending on the treatments being evaluated or the patient populations being studied. In part, this links back to the discussion above; if the QALY does not fully capture all the relevant elements of social value, it may not make sense to apply a single threshold. This issue has been raised in the context of drugs for rare diseases (so-called orphan drugs). Even if these treatments do not appear very cost-effective (that is, if they have a very high cost-effectiveness ratio), society may still prefer to make them available, because many of the diseases treated with orphan drugs are life-threatening and because it would be unfair for someone not to be offered treatment just because their disease is rare.[9]

Recently, NICE initiated a consultation on whether there should be a different threshold in the appraisal of 'end-of-life' treatments. The outcome has been a document which sets out supplementary advice to the appraisal committees.[10] The document notes that the current appraisal methodology guidelines recognise that there may be occasions where NICE approves therapies with an incremental cost-effectiveness ratio (ICER) above £30,000 per QALY. It also states that NICE 'considers it appropriate for its Appraisal Committees to have regard to the importance of supporting the development of innovative treatments that are anticipated to be licensed for small groups of patients who have an incurable illness'.

The supplementary advice should, therefore, be applied when a treatment offers an extension of life of at least three months in small patient populations with a life expectancy of less than 24 months and when no other treatments offering comparable benefits are available on the NHS. When these conditions are met, the following criteria will be considered: (1) the gain in life expectancy should be assumed to be experienced at a level equivalent to the full quality of life for a healthy individual of the same age, and (2) the magnitude of the extra weight assigned to the QALY benefits in this patient group would need to be sufficient for the ICER to fall within NICE's current threshold range. For example, if the ICER for the 'end-of-life' treatment is £60,000 per QALY, with QALYs being valued in the conventional way, the appraisal committee would need to agree that the QALYs experienced by the patients concerned are worth twice the norm to recommend use of the therapy.



NICE: National Institute for Health and Clinical Excellence; QALY: quality-adjusted life-year

Figure 1. NICE's cost-effectiveness threshold[8]

Implementation of NICE guidance

Several studies have shown that the implementation of NICE guidance is uneven across the NHS.[11] This is despite the fact that guidance resulting from technology appraisals is mandatory on the NHS and should be implemented within three months. This is particularly worrying since NICE was set up to reduce geographical variations in the adoption of new technologies (so-called 'postcode rationing'). NICE has established an implementation group to facilitate the implementation of its guidance, but full implementation remains difficult to achieve.

Conclusions

HTA has a long tradition in the UK. In recent years, the practice of HTA has become synonymous with the activities of NICE in England, although other important HTA entities exist in Scotland and Wales. Since its inception in 1999, NICE has been widely debated and often criticised. It can, however, claim several major achievements and it still represents one of the more sophisticated attempts to integrate HTA into the decision-making process. Nevertheless, many important issues remain unresolved and NICE, the SMC and the AWMSG definitely remain a 'work in progress'.

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Further reading

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