

» Briefing

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NICE technology appraisals

Introduction

The National Institute for Health and Clinical Excellence (NICE) was set up to secure greater cost-effectiveness and consistency in the provision of publicly funded health services within a budget-constrained National Health Service (NHS). Its independent, evidence-based appraisals of health technologies aim to standardise access for NHS patients to cost-effective licensed drugs and treatments.

Yet the prevailing media image of NICE is as a controversial mechanism for denying patients expensive new drugs. Recent high-profile events have included protests from patient groups and cancer specialists (Sikora *et al* 2008) against draft guidance on kidney drugs, and an apology from NICE for taking more than two years to issue final guidance approving the macular degeneration drug Lucentis (BBC 2008a). The government's decision in November 2008 to permit patients to 'top up' their NHS care with privately purchased drugs further highlighted the issues that arise when a clinician wants to prescribe a drug that NICE has not recommended (Hansard 2008b).

This briefing looks at the role of NICE in the NHS in England, focusing on technology appraisals of drugs and treatments. It describes the appraisal process; outlines the impact of NICE appraisals, including on the availability of drugs when there is no guidance; and assesses recent policy proposals to address the system's perceived shortcomings.

Why was NICE established?

NICE was established on 1 April 1999 as the National Institute for Clinical Excellence, as part of the government's wider strategy to address 'unacceptable variations in performance and practice' in the NHS and to remove a 'lottery in care with patients being denied treatment available in neighbouring areas' (Department of Health 1998).

Previously there was 'no coherent approach' as to which treatments should be provided by the NHS. Guidance was issued 'by numerous bodies, at national, regional and local levels, each of which [had] different ways of appraising the evidence and developing recommendations'. This had led to NHS staff facing either a lack of evidence

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or ‘apparently contradictory advice’ about what services to provide (Department of Health 1998).

National Service Frameworks were introduced to set out what patients could expect to receive in major care areas or disease groups. NICE’s key task was to impose a rigorous value-for-money test and provide, for the first time, evidence-based guidance on which drugs and treatments were clinically effective and cost effective, in order to ensure the best use of NHS resources. NICE’s role was, and remains, distinct from the process of licensing drugs and devices; this is the responsibility of the Medicines and Healthcare products Regulatory Agency (and other bodies), which does not look at cost effectiveness.

In 2005, NICE took over the functions of the Health Development Agency, and its name changed to the National Institute for Health and Clinical Excellence to reflect the additional role of providing guidance on public health.

NICE is an independent special health authority, and is required to submit an annual report on its activities and finances to the Secretary of State for Health and the Welsh Assembly government. Almost all NICE’s funding comes from the Department of Health in England; its 2007/8 budget was £34.4m (NICE 2008j).

Guidance areas

NICE’s guidance falls into three main areas.

Health technology evaluation

- Technology appraisals – recommendations, based on clinical and economic evidence, on the use and cost-effectiveness of new and existing licensed technologies within the NHS. These include drugs/medicines, medical devices, diagnostic techniques, and surgical procedures. The guidance is mandatory, and the NHS in England and Wales is legally obliged to fund medicines and treatments recommended by NICE’s technology appraisals, usually within three months (NICE 2008d). There are two types of appraisals (Dillon 2008):
 - single technology appraisals, which assess new pharmaceutical products or new uses of existing products;
 - multiple technology appraisals, which compare groups of drugs already on the market.
- Interventional procedure guidance – evaluates the safety and efficacy of procedures that access the inside of a patient’s body or use electromagnetic radiation (NICE 2008b).

Clinical guidelines

Recommendations on the appropriate NHS treatment and care of people with specific diseases and conditions (NICE 2008a). These guidelines are advisory.

Public health guidance

Recommendations for NHS and local government professionals on promoting a healthy lifestyle and reducing the risk of developing a disease (NICE 2008c). These guidelines are advisory.

NICE’s guidance applies primarily to the NHS in England and Wales (Dillon 2008) (Table 1).

This briefing focuses on three areas: how NICE makes decisions on whether the NHS should fund health technologies; the impact of technology appraisal guidance; and how the appraisal system may develop in future.

Table 1: Applicability of NICE guidance in the United Kingdom

Country	Technology appraisals		Interventional procedures	Clinical guidelines	Public health guidance
	Single	Multiple			
England	Yes	Yes	Yes	Yes	Yes
Wales	Yes	Yes	Yes	Yes	No
Scotland	No	Yes ^a	Yes	No	No
Northern Ireland	Yes ^b	Yes ^b	Yes	Yes ^b	No

^a With advice on implementation in Scotland from NHS Quality Improvement Scotland; and

^b in Northern Ireland, from the Department of Health, Social Services and Public Safety.

Source: Dillon (2008)

How are NICE technology appraisal decisions made?

Topic selection

Potential topics for technology appraisals come from the National Horizon Scanning Centre at the University of Birmingham, the Department of Health's national clinical directors and policy teams, health care professionals, and the general public. NICE filters the suggestions using the Department of Health's selection criteria: burden of disease, resource impact, policy importance, inappropriate variation in practice across the country, and factors affecting the urgency for guidance (NICE 2008g).

The remaining list of potential topics are prioritised by one of NICE's seven expert consideration panels, whose members include health, social care and public health professionals, academics and researchers, and patient/carer representatives. Department of Health ministers take the final decisions on proposed appraisal topics (NICE 2008g).

NICE carries out appraisals on only a minority of new and existing licensed health technologies. There has been debate over whether all new licensed drugs should be assessed by NICE, as is the case in Scotland with the Scottish Medicines Consortium, and whether NICE should subject all existing drugs to the same level of appraisal as new technologies (House of Commons Health Committee 2008). The Office of Fair Trading (2007) pointed to two negative effects of NICE not appraising all drugs: prescribed drugs that have not been assessed by NICE may not be cost effective; and prescribers can be reluctant to use a drug that has not yet been assessed by NICE, even though it may well be cost effective – so-called 'NICE blight'.

The Cancer Reform Strategy now states that 'as a default position' all new cancer drugs and significant new licensed indications will normally be referred to NICE for appraisal (Department of Health 2007).

The appraisal process

The three phases of a technology appraisal are scoping, assessment and appraisal (NICE 2008g; NICE 2008f).

- In the **scoping** phase, NICE determines the questions to be addressed by the appraisal when considering the clinical effectiveness and cost-effectiveness of the technology.
- The **assessment** process normally has two components: a systematic review of the relevant evidence available on a technology and an economic evaluation of its cost-effectiveness for a specific indication. The assessment is undertaken by an independent academic centre. For multiple technology appraisals, this 'assessment group' carries out an independent systematic evidence review (including submissions from manufacturers) and usually prepares a new assessment of the costs and effects. For

single technology appraisals, an 'evidence review group' produces a critical assessment of a submission provided by the manufacturer or sponsor of a technology, and may request, or carry out, additional analysis. In all cases, confidential evidence is only accepted 'under exceptional circumstances'.

- The **appraisal** process is carried out by an independent 'technology appraisal committee' whose members are appointed by NICE for a three-year term and are drawn from the NHS, academia, patient and carer organisations, and pharmaceutical and medical devices industries. This committee considers the assessment report and additional information before making its first recommendations in an appraisal consultation document, which is put out for consultation. A 'final appraisal determination' is then produced, and submitted to NICE's Guidance Executive for approval. Subject to any appeal, the final recommendations are issued as NICE guidance.

The guidance for a technology can be positive (with or without restrictions), negative, or 'only in research' (whereby the technology is restricted to research programmes that will provide more information about effectiveness, safety or cost) (NICE 2008p). Reports relating to each stage of an appraisal are published on the NICE website as a public resource.

Since NICE's early days there has been criticism of the time the appraisal process takes, with pressure for guidance to appear sooner after a drug's licensing. A multiple technology appraisal compares different treatments for the same condition and takes around two years. In 2005 the single technology appraisal was introduced to provide a fast-track route for assessing a single new product for a particular condition. The move followed publicity about a primary care trust (PCT)'s refusal to fund Herceptin (trastuzumab) for a patient with early-stage breast cancer. At the time, the drug was not licensed for this condition. The Department of Health told NICE to look at the drug in parallel to the licensing process (House of Commons Health Committee 2008) and NICE approval came through just two weeks after licensing (Department of Health 2007).

Currently, a single technology appraisal normally takes 9–12 months from the time of referral. NICE 'would expect to be able to advise on use in the NHS (in the form of draft or final advice) within 3 months of licensing', provided the appraisal process starts when the manufacturer applies for regulatory approval and subject to consultation and appeal (House of Commons Health Committee 2008).

In practice, however, appraisal guidance has often not been available for two years or more after a new drug has been licensed (Hansard 2008b). Under the Cancer Reform Strategy, 'where possible' appraisal of new cancer drugs should now be carried out in parallel with licensing (Department of Health 2007).

Cost-effectiveness and the QALY

The cost-effectiveness analysis uses the QALY (quality-adjusted life years) measure, which is specified by NICE as 'most appropriate' for comparing the clinical effectiveness of different technologies. Alternative measures exist (for example, the 'healthy-year equivalent'), but NICE considers that the strengths and weaknesses of these measures are not fully established (NICE 2008g).

The QALY measures the impact of a health technology on how long a patient will live and on the quality of life (in terms of their health) during that period. Quality-of-life factors include the level of pain, degree of mobility, and sense of well-being; the overall rating ranges from negative values below 0 (zero accords with death; some health states may be considered worse than death and so have a negative score) to 1 (best possible health) (NICE 2008i). For example, if a treatment produces an expected two years of life with a

quality-of-life rating of 0.4, then this is measured as 0.8 QALYs. An additional QALY has the same weight regardless of a patient's socio-demographic profile or their pre-treatment level of health (NICE 2008g).

The cost-effectiveness analysis of a new drug looks at whether the difference in cost can be justified in terms of how much someone's life can be extended and improved by the new drug, when compared against the existing routine NHS treatment. This is done by calculating how much the drug or treatment costs per QALY gained – the incremental cost-effectiveness ratio (ICER). For instance, if the standard treatment produces 0.6 QALYs and the new treatment produces 0.8 QALYs, and the new treatment is £5,000 more expensive, then the ICER is £5,000 divided by the number of QALYs gained (in this case 0.2) ie, £25,000 per QALY gained (adapted from NICE 2008i).

Cost-effectiveness of a technology 'is not the sole basis for decision-making'. NICE does not set a precise ICER threshold to determine whether a drug or treatment can be approved but uses a range (NICE 2008g).

- Below £20,000 per QALY gained, a positive recommendation is normally based on the cost-effectiveness estimate.
- Between £20,000 and £30,000 per QALY gained, judgements about the acceptability of the technology will increasingly need to take account of the following factors: the degree of certainty around the economic analysis, possible under-representations of the quality-of-life gains, and whether benefits from the innovative nature of the technology have not been captured in the QALY measure.
- Above £30,000 per QALY gained, the appraisal committee needs to identify 'an increasingly stronger case' for supporting the technology, with regard to the factors mentioned.

The appraisal process involves judgements that place NICE's work in the context of the broader views of society. NICE's board regularly consults a Citizens Council – a group of 30 people, drawn from across the population – in order to define the principles that should underpin 'social value judgements' (NICE 2008p). Two of the principles specify that: appraisal decisions must consider the need to distribute health resources 'in the fairest way'; and that NICE can recommend restricting an intervention to a particular group of people (for example, by age or gender) only on the basis of clear evidence, 'fairness for society', or a legal requirement.

The technology appraisal committee can choose to take into account a range of other considerations in reaching recommendations, including imminence of death, severity of condition, and lack of alternative treatments (NICE 2007a). Factors such as burden of disease (number of people affected by the condition) have been shown to influence NICE decisions (Devlin and Parkin 2004). When considering imatinib for the treatment of myeloid leukaemia, the Appraisal Committee accepted a cost per QALY of £48,000 (NICE 2008o).

Up to 1 November 2008, NICE had published final guidance from 160 technology appraisals covering 206 drugs (a single guidance may assess more than one drug, and a single drug may be appraised separately for use in different conditions). Of these, just 15 drugs were not recommended for use by the NHS or received an 'only in research' recommendation (Hansard 2008a; NICE personal communication 2008). That said, many positive recommendations include significant restrictions on which groups of patients should receive a drug or treatment, and at what stage of disease progression.

There has been much debate about the level of the threshold range, which has not changed since 1999 despite inflation and the increase in the NHS budget. NICE says that the range is 'based on the collective judgment of the health economists we have

approached across the country. There is no known piece of work which tells you what the threshold should be' (House of Commons Health Committee 2008).

If the NICE threshold range is too high, NHS resources may be diverted from other health care services that are better value for money and the efficiency of the NHS (in terms of total gains in the number of QALYs produced by the NHS budget) will be reduced (Appleby *et al* 2007).

Challenging NICE

Appeals against NICE technology appraisal guidance can be made on the grounds that NICE 'has failed to act fairly, has exceeded its powers or has formulated guidance which cannot reasonably be justified' (Department of Health 2005). New evidence or disagreement with an appraisal will 'almost certainly' not be accepted (Schlander 2008).

Appeals have been lodged against a significant proportion of technology appraisals. Of the 160 technology appraisals published by 1 November 2008, 58 had been appealed, with 23 appeals upheld on at least one point (NICE, personal communication 2008). Appeals can be made against a negative recommendation or against restrictions to a positive recommendation. The results of a successful appeal can range from minor rewriting to referral back to the appraisal committee.

There has been one High Court judicial review of NICE guidance. In 2007, the drug manufacturer Eisai challenged the recommendation that the drugs donepezil, rivastigmine and galantamine were not cost effective for mild Alzheimer's disease. In August 2007, the judge ruled in NICE's favour (NICE 2008k) on all but one point, but in May 2008 the Court of Appeal backed Eisai in saying NICE must make available fully executable versions of its economic models.

What is the impact of NICE technology appraisals?

Implementing NICE guidance

Since 2002, the NHS has been legally obliged to provide funding and resources in England and Wales for medicines and treatments recommended by NICE's technology appraisal guidance (both single and multiple), normally within three months of the final guidance (Healthcare Commission and NICE 2008). The draft NHS Constitution confirms 'the right to drugs and treatments that have been recommended by NICE for use in the NHS, if your doctor says they are clinically appropriate for you' (Department of Health 2008d).

Compliance has nevertheless been an issue. In a review of NICE guidance between 1999 and 2004, the Audit Commission found that implementation was not reliable, particularly where there were high capital costs or expensive drugs. Only 25 per cent of the sites visited could verify that appraisals were implemented within the three-month deadline, and 85 per cent of all respondents (chief executives of PCTs and NHS trusts) said that the funds available to implement technology appraisals were insufficient, particularly in relation to high-cost appraisals. The review found that NHS bodies did not routinely assess the likely financial impact of forthcoming NICE guidance (Audit Commission 2005).

There have been three reviews by the National Cancer Director of the usage of positively appraised cancer drugs. The 2004 review found usage of cancer drugs generally increased following a positive NICE appraisal but there was a 'considerable' variation geographically, apparently due to constraints in service capacity and differences in clinical practice. The 2006 review showed a reduced variation in usage and concluded there was no evidence that patients were being denied access to NICE-approved cancer drugs (Department of Health 2006b). The 2008 analysis found a further reduction in the variation in

usage for a majority of the NICE-approved drugs that were considered (Department of Health 2008b).

Overall compliance with NICE technology appraisals is monitored in England by the Healthcare Commission and is included in one of the 44 core standards used to assess NHS trusts. In 2007/8, 95 per cent of trusts were judged to be compliant, up from 89 per cent in 2006/7 (Healthcare Commission 2008).

Local decision-making and 'postcode prescribing'

Under the current system, many funding decisions about drug treatments must still be made by the NHS at a local level. This can occur when:

- NICE has not been asked to appraise a (new or existing) health technology
- appraisal of a (new or existing) technology by NICE is under way but no final guidance has been issued
- NICE has said a technology is not cost effective, but there may be grounds for a PCT to fund a special case.

There are significant geographical disparities in the availability of individual drugs not covered by NICE guidance (BBC 2008b), and in a number of high-profile legal cases patients have challenged the apparent 'postcode prescribing' of drugs.

The Department of Health says 'it is not acceptable to cite a lack of NICE guidance as a reason for not providing a treatment' (Department of Health 2006a). A PCT usually has general rules on funding drugs or treatments not covered by NICE guidance and an 'exception committee' makes decisions on cases where it is argued that circumstances (either clinical or social) justify a departure from normal practice.

Around 15,000 requests a year for exceptional funding of drugs are currently being made to PCTs in England; around one-quarter of these requests relate to cancer and three-quarters to other conditions. A recent survey of PCTs confirmed big variations in relation to drug approval practices and exceptional circumstances procedures (Richards 2008).

An audit by the Rarer Cancers Forum (2008) found that around 17 per cent of overall requests for exceptional funding of cancer drugs were rejected, but there was a big difference in request and success rates. One PCT received 180 requests while another reported only one; of 62 PCTs providing comparable information, 11 approved all requests, while 2 approved none (Rarer Cancers Forum 2008).

What happens next?

NICE is acknowledged as a world leader in its field, and a number of other countries have emulated its technology appraisals approach (Richards 2008). The website attracts a growing number of visitors from overseas; during September–October 2008 it received visitors from 209 countries/territories. In the first 10 months of 2008 there were 261,132 visitors from the United States, accounting for 5.34 per cent of the total number of visitors to the website in this period (NICE, personal communication 2008).

Coverage and speed of process

The House of Commons Health Committee (2008) recommended that all new drugs be assessed by NICE between the time of licensing and launch using a quicker, less thorough, process and a lower cost-effectiveness threshold. This initial appraisal would be followed by a full appraisal using the normal threshold range. The aim would be 'to

ensure that treatments which are obviously cost effective are available at an earlier stage than at present'. NICE rejected this twin-track approach on the grounds that the proposed initial timescale would not allow for effective scrutiny of the evidence, or for meaningful consultation (NICE 2008l).

The government has accepted the need for action on the speed and timing of appraisals. The Darzi NHS Next Stage Review proposed that the appraisal processes 'will be speeded up' so that NICE can issue the majority of its guidance 'within a few months' of a significant new drug's launch (Department of Health 2008a). The government's response to Mike Richards' review of top-ups included a new timetable for appraisals: 'In 2009, draft or final guidance will be available within six months of licensing for about half of the drugs that are being appraised through the fast-track single technology appraisal programme. In 2010, draft or final guidance for all new cancer drugs will be available within six months, on average, of a drug being licensed' (Hansard 2008b). The new commitment contrasts with NICE's own stated view that it is possible to issue single technology assessment guidance within three months of a drug's launch, subject to the timing of referral and consultation/appeals (House of Commons Health Committee 2008).

The Department of Health will report in early 2009 on further ways to speed up appraisals. According to NICE, past delays were sometimes due to it not being asked early enough to evaluate a new treatment or to a lack of capacity to do so immediately (NICE 2008l), and thus some improvement could be achieved by earlier commencement of appraisals. Speeding up the actual appraisal process would raise issues about the quality of evidence, and could result in the need for post-approval monitoring and earlier review.

Setting the threshold

The question of what threshold to use when judging cost-effectiveness is also under debate. NICE has commissioned research to assess whether the current £20,000 to £30,000 range 'is reasonable or whether it should be altered' and the findings are due to be discussed at a workshop on cost-effectiveness in February 2009 (Smith 2008). NICE is interested in methods to determine what monetary value the public thinks should be attributed to different health gains, and whether such gains are valued differently for different beneficiaries (Department of Health 2008c). The issues include whether the public puts a higher value on a gain of one QALY for different types of recipients, for instance for a child compared with an adult with the same condition.

As part of the government's response permitting top-ups, NICE announced a new, more flexible approach to take into account 'the premium that society places on helping those with terminal illnesses' (Hansard 2008b). NICE has told Appraisal Committees to consider recommending drugs with ICERs above £30,000 when the expected number of new patients for the drug is fewer than 7,000 a year, such patients are not expected on average to live for more than two years, and there is evidence that the medicine 'offers a substantial extension to life' (NICE 2008e).

There is also the question of who should set the threshold range. It has been suggested that the cost-effectiveness threshold could be set by a new body including representatives from NICE, the Department of Health and PCTs (House of Commons Health Committee 2008) or by an independent panel modelled on the Bank of England's Monetary Policy Committee (Appleby et al 2007). NICE has said that it would need to retain flexibility in applying a threshold set by an outside body (NICE 2008l).

Looking ahead, the pharmaceutical companies, NICE and the government (Hansard 2008b) appear increasingly willing to use 'risk-sharing' schemes to enable a drug to pass the cost-effectiveness test, an approach first adopted in 2002 with beta interferon.

NICE's approval this year of Lucentis was based on the manufacturer Novartis paying for further treatment if more than 14 injections were needed (NICE 2008m). Other schemes include refunding drug costs to the NHS if patients do not respond (NICE 2007b), and a manufacturer offering to pay for the first cycle of a drug (NICE 2008n). However, the attractions of risk-sharing need to be balanced against any costs to the NHS, for example in terms of regular health monitoring of individuals on a drug.

One broader issue relating to cost-effectiveness appraisals gained prominence during protests over NICE's appraisal of drugs for treatment of Alzheimer's disease. It concerned whether the economic assessment should take account of wider benefits and costs to society, such as costs borne by carers, a suggestion supported by the House of Commons Health Committee (2008). The government has pointed to the potential for 'perverse effects' – such as prioritising interventions for working age if broader economic impacts are included – but will 'explore the issue in more detail' (Department of Health 2008c). Among various proposals for reforming NICE, the Conservative Party proposes allowing NICE to take into account 'the wider social cost of denying a drug to patients' when assessing its value or benefit (Conservative Party 2008).

Postcode prescribing

Under the current system, improved topic selection and faster appraisals would reduce the time between a drug's launch and NICE guidance, but this will not remove the issue of 'postcode prescribing'. The go-ahead for top-up payments will, for instance, mean that patients in some areas will be able to access some drugs only through top-up payments, while in other areas they are funded by the NHS.

The draft NHS Constitution (Department of Health 2008d), states that patients 'have the right to expect local decisions on funding of other drugs and treatments to be made rationally following a proper consideration of the evidence' and will receive an explanation from the local NHS if funding is withheld.

The top-ups review called for action on this commitment and said that PCTs should do more to pool expertise when making decisions about funding drugs (Richards 2008). The government now plans to publish a set of 'core principles' and guidance for PCTs on taking such decisions and on handling exceptional cases (Hansard 2008b).

Conclusion

If, as expected, health budgets tighten in the future, NICE will continue to have to take difficult and often unpopular decisions on whether or not treatments should be available on the NHS. If it is to maintain the broad support it has experienced in its first decade, it will have to respond effectively to the challenges outlined above.

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