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NICE: faster access to modern treatments? Analysis of guidance on health technologies

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Introduction

The National Institute for Clinical Excellence (NICE) was set up as a special health authority for England and Wales in 1999. Its role is to provide patients, health professionals, and the public with authoritative, robust, and reliable guidance on current "best practice." It has three main functions: to appraise new technologies, to produce or approve guidelines, and to encourage improvement in quality. NICE was first announced in the new Labour government's white paper *The New NHS*.[1] As a special health authority it is part of the Department of Health. NICE marks an innovation internationally in that while some other countries have bodies to provide advice on which new health technologies to use, NICE is the first national body with power to issue guidance covering the full range of health technologies.[2] Guidance from NICE applies to the NHS in the same way as guidance from other parts of the Department of Health; while health authorities are required by statute to take account of but not necessarily follow guidance, general practitioners have greater discretion.[3]

NICE is a relatively small organisation with just under 30 members of staff and a budget of around £10m which covers various "inherited projects" (mainly to do with audit). NICE relies heavily on unpaid input in the form of seven non-executive directors and 46 members of its appraisal committee, which is made up of doctors, NHS and commercial managers, academics, nurses, and patient representatives (full details on www.nice.org.uk). NICE is largely a "virtual" organisation relying on a small office and a large network, centred on electronic communication, and contracting out specific tasks.

Transparency

NICE aims to be transparent, not least by publishing all guidance and background appraisals on its web page (www.nice.org), the source of all the guidance discussed here. Minutes of board and appraisal committee meetings, along with membership, supporting documents, and appeal proceedings are published on the website. The only exceptions are submissions that industry deems "commercial-in-confidence." Because of advance leaks of three appraisals (all unfavourable to the technology), in early 2001 NICE decided to publish its provisional technology appraisals[4] as well as final appraisal documents.

The Department of Health selects health technologies for assessment by using four criteria: possible health benefit, links to health related policies, impact on NHS resources, and the added value of NICE guidance.[5] New health technologies are identified for the Department of Health by the National Horizon Scanning Centre in the University of Birmingham. The task of NICE is to make recommendations on use in the NHS of particular health technologies based on

Summary points

Of the 22 health technologies on which NICE had issued guidance by March 2001, it recommended against use in three (with a change of judgment on zanamivir)

The guidance recommending use of the 19 other health technologies cited clinical benefit in all instances but could cite cost per QALY in only around half

Restrictions on the recommended use of most health technologies (for instance, in most severely ill patients) helped keep the cost per QALY below around £30 000, with only one exception—riluzole for motor neurone disease, which had a cost per QALY of £34 000 to £44 000

NICE's provisional recommendation against the use of beta interferons or glatiramer acetate for multiple sclerosis cited its high cost per QALY in relation to technologies previously appraised

The net cost of implementing NICE's guidance was around £200m, or less than 0.5% of annual spending on the NHS

appraisal and assessment of their "clinical and cost effectiveness."

Companies who manufacture the relevant technologies ("sponsoring companies") and professional and patient groups are invited to submit evidence. NICE's appraisal committee (which was doubled in size in 2001) appraises technologies on the basis of submissions and commissioned independent assessments. The form of evidence is specified as clinical outcomes, cost per quality adjusted life year (QALY), and impact on the cost of NHS and social services.[5 6] Seven academic centres have been commissioned to provide independent assessments to NICE, after a public tendering process.

The appraisal committee appraises each health technology, using its commissioned assessments and industry submissions and taking into account the views of both professional and patient groups. These groups are invited to the relevant meetings of the committee. After coming to a conclusion in a closed session the committee drafts a provisional appraisal, which, when finalised after consultation, forms the basis of guidance which NICE issues in line with the secretary of state's directions.

Independence

NICE is independent in relation to its assessment of clinical and cost effectiveness, but the secretary of state for health, Alan Milburn, has emphasised that the Department of Health has responsibility for affordability and hence for the guidance.[7] Decisions by NICE can be subject to appeal by the sponsoring company or by other consultees (manufacturers or other sponsors, professional and patient groups, Department of Health).[8]

The British pharmaceutical industry was initially hostile to NICE, arguing that, once licensed, doctors should be free to prescribe. More recently, through the Association of the British Pharmaceutical Industry, the industry has been engaged with the government "in comprehensive discussions about how NICE operates, including its impact on uptake of new medicines."[9]

Review of NICE's guidance

I reviewed NICE's published guidance on 22 technologies with the three criteria originally outlined in its requirements for submissions of evidence: clinical benefits, cost per QALY, and impact of cost on NHS.[5] I used March 2001 as a cut-off point as NICE issued revised criteria in that month.[6] I downloaded each published guidance from the NICE webpage and checked it against these criteria.

Table 1 lists the 22 topics and summarises my findings. Three technologies were not recommended:

Table 1 Topics on which NICE had issued guidance to March 2001 (in order of issue of guidance)

Topic	Finding
Zanamivir in managing influenza	Not recommended for 1999-2000. Recommended for 2000-1 for adults at risk when consultations for influenza rise above 50/week/100 000 population
Removal of wisdom teeth	"The routine practice of prophylactic removal of pathology free impacted molars should be discontinued in the NHS"
Coronary artery stents for ischaemic heart disease	Use routinely where percutaneous coronary intervention is appropriate for patients with either stable or unstable angina or acute myocardial infarction or . . .
Taxanes for ovarian cancer	Recommended as part of combination treatment for patients with ovarian cancer after surgery and patients with recurrent ovarian cancer (if not previously so treated)
Selection of hip prostheses for primary total hip replacement	Recommended prostheses likely to meet "benchmark of less than 10% revision rate at 10 years or more. Such evidence favours cemented prostheses"
Liquid based cytology for cervical screening	"Could provide significant and important benefits . . . insufficient evidence to justify nationwide introduction . . . pilot implementation projects should be undertaken"
Taxanes for breast cancer	"Should be available for treatment of advanced breast cancer where initial cytotoxic chemotherapy has failed or is inappropriate"
Proton pump inhibitors for dyspepsia	Healing and maintenance dose when appropriate (failure to eradicate *H pylori*, ulcers induced by non-steroidal anti-inflammatory drugs to heal severe gastro-oesophageal reflux disease. Not recommended for non-ulcer dyspepsia
Hearing aid technology	Insufficient evidence for digital hearing aids. Full range of analogue devices should be available
Rosiglitazone for type 2 diabetes mellitus	"Use for patients with inadequate blood glucose control on conventional agents"
Inhaler systems for under 5s with asthma	Recommended where specified good practice is not clinically effective
Implantable cardioverter defibrillators (ICDs) for arryhthmias	Recommended for primary and secondary prevention in specific patient groups
Glycoprotein IIb/IIIa inhibitors for acute coronary syndromes	Recommended for high risk patients with unstable angina or non-Q wave myocardial infarction and patients undergoing percutaneous coronary intervention
Methylphenidate for attention deficit hyperactivity disorder in childhood	Recommended as part of comprehensive programme for children with severe attention deficit hyperactivity disorder
Tribavirin and interferon alfa for hepatitis C	Recommended for patients with moderate to severe disease, depending on experience with other treatments, with monitoring of response (unless risky). Not recommended for injecting drug users
Laparoscopic surgery for colorectal cancer	Not recommended except in clinical trials
Autologous cartilage transplantation for defects in knee joints	Not recommended except in clinical trials
Donepezil, rivastigmine, and galantamine for Alzheimer's disease	Recommended as one component for managing mild and moderate Alzheimer's disease, if mini-mental state examination >12 points and ongoing improvement
Laparoscopic surgery for inguinal hernias	Recommended only for recurrent and bilateral inguinal hernia. Totally extraperitoneal procedure preferred. Restrict to appropriately trained teams
Riluzole for motor neurone disease	Recommended for treatment of patients with amyotrophic lateral sclerosis form of MND
Orlistat for obesity in adults	Recommended only for people who have lost at least 2.5 kg by dietary control and physical activity alone in previous month and who meet body mass index criteria. To be restricted to adults who show specified improvements, for up to three months
Pioglitazone for type 2 diabetes mellitus	Recommended as possible alternative to rosiglitazone (see above)

Source: www.nice.org/

Table 2 NICE guidance: cost per QALY and cost impact on NHS of various technologies

Topic	Incremental cost per QALY (or life year)	Funding implications for NHS
Zanamivir in managing influenza	£9 300-31 500 incremental £/QALY	£2.3m-11.7m drug cost only
Removal of wisdom teeth	No quality of life data	Save up to £5m
Coronary artery stents for ischaemic heart disease	Risks "very difficult to estimate"	"Net impact difficult and potentially misleading"
Taxanes for ovarian cancer	£6 500-10 000 per life year	£28m gross (4000 patients at £7000 each); £7m net
Selection of hip prostheses for primary total hip replacement	No data	Potential savings up to £8m
Liquid based cytology for cervical screening	"No direct evidence"	Possibly cost neutral because of improved productivity and improved detection rates
Taxanes for breast cancer	£7 000-24 000 per life year	£20m gross (5000 patients at £4000); £16m net
Proton pump inhibitors (PPIs) in treating dyspepsia	"Cost effectiveness evidence equivocal" and varied	Reduced PPI use by at least 15% could save £40m-50m in drug costs
Hearing aid technology	"Impossible to estimate"	Cost neutral
Rosiglitazone for type 2 diabetes mellitus	No quality of life data	Gross £14.5m
Inhaler systems for under 5s with asthma	No direct comparisons between devices	Cost neutral if British Thoracic Society guidelines followed
Implantable cardioverter defibrillators (ICDs) for arryhthmias	£26 000-31 000 per life year	£45m gross, £25m-30m net
Glycoprotein IIb/IIIa inhibitors for acute coronary syndromes	£7 000-12 000 per life year as part of percutaneous coronary intervention. No data for use in unstable angina or non-Q wave myocardial infarction	£34m gross, £30m-31m net
Methylphenidate for attention deficit hyperactivity disorder in childhood	£10 000-15 000 per QALY	£7m upper limit
Tribavirin and interferon alfa for hepatitis C	£3 000-7 000 per QALY for first 6 months' treatment, £5 000-36 000 for second 6 months	£55m spread over three years
Laparoscopic surgery for colorectal cancer	No cost effectiveness data	Possible unquantified cost savings
Autologous cartilage transplantation for defects in knee joints	"Not meaningful to make any estimate of cost effectiveness"	£3.6m-6.9m per year as second line treatment
Donepezil, rivastigmine, and galantamine for treating Alzheimer's disease	"Main benefits . . . can (not) . . . be reliably or easily estimated from existing trial evidence." Cost per QALY zero to somewhere over £30 000	£42m per year, assuming 50% are still taking drugs after 6 months
Laparoscopic surgery for inguinal hernias	£50 000 per QALY if used generally. Considerably less than if restricted to bilateral and recurrent hernia repair	"Budget impact . . . uncertain"
Riluzole for motor neurone disease	£34 000-43 000 per QALY	£7.5m gross, £5m net
Orlistat for obesity in adults	£20 000-30 000 if weight lost as specified	£16m gross, £10m net
Pioglitazone for type 2 diabetes mellitus	No published economic evaluations. May be more cost effective than alternatives	Eventual cost savings of £12m per year

Source: NICE web page (www.nice.org/)

prophylactic removal of wisdom teeth, laparoscopic surgery for colorectal cancer, and autologous cartilage transplantation for defects in knee joints. One other, the anti-influenza drug zanamivir, was not recommended in March 2000, but on the basis of new evidence NICE recommended it in December 2000 for adults at high risk at times when consultations for influenza exceeded a certain level.

Decision making

Given the decision making process described above, I could not conclusively establish how the balance between clinical benefit and economics (cost per QALY) influences NICE recommendations. An indication of the factors that influence decisions can be obtained from examination of the reasons outlined in the guidance. Each of the 19 guidance publications that recommended technologies cited evidence of clinical benefit. No such evidence was cited in the four publications that did not recommend a technology. Conditions generally applied to the use of the health technologies recommended, such as restricting use to patients at high risk or as second line treatment. For some technologies, however, more general use was approved, such as stents in coronary angioplasty and implantable defibrillators for cardiac arrhythmias.

For pharmaceuticals, the evidence for clinical benefits reflected those benefits required for drug licensing, but NICE's conditions were sometimes more restrictive than the licensed indications, which led to some appeals (taxanes for breast cancer and ovarian cancer, zanamivir, proton pump inhibitors, inhalers for children with asthma). As non-drug technologies do not require licensing, less information tends to be available on their efficacy. NICE guidance attempted to deal with this by setting standards for the clinical effectiveness of hip prostheses and by recommending pilot implementation of liquid based cytology in screening for cervical cancer. As a result, the Department of Health put the specifications for a national joint register out to public consultation and set up pilot schemes for liquid based cytology.

Cost per QALY

In only half the topics did the NICE guidance cite cost per QALY (table 2), suggesting that economics had a lesser role than evidence of clinical benefits. For the other half, NICE guidance stated that this measure of cost effectiveness was "very difficult" or "impossible" to estimate, mainly because of lack of data on the effects of the technology on patients' quality of life. Estimates of cost per QALY may have been available to NICE either in industry submissions (unpublished) or in independent appraisals (published), but the decision by NICE not to cite these estimates suggests it did not find them convincing. NICE's revised protocol for industry submissions reflects the difficulties in establishing estimates of cost per QALY by accepting disease specific measures of cost effectiveness for specific diseases.[6]

For those technologies for which cost per QALY or per life year was cited, all received positive recommendations, and all but one (riluzole) had cost per QALY below £30 000. The imposition of restrictions on recommended use generally reduced the cost per QALY. Patients' values were cited as the reason for recommending riluzole for motor neurone disease (amyotrophic lateral sclerosis form only), despite its relatively high cost per QALY of £34 000-44 000. NICE cited "the severity and relatively short life span of people with ALS and in particular … the values which patients place on the extension of tracheotomy free survival time."[10]

The provisional guidance that recommended against the use of beta interferons and glatiramer for multiple sclerosis cited their relatively high cost per QALY (£40 000 to £90 000 on the most optimistic estimates) and stated that NICE had in mind the cost effectiveness ratio of technologies it had previously recommended.[11]

The final element of each NICE guidance concerns the costs to the NHS of implementing the guidance (cost impact). Estimates of gross and net costs are provided, the latter taking into account any substitution of old technologies by new ones. The items that led to major increases in net costs were tribavirin and interferon alfa, both prescribed for hepatitis C (£55m in total, possibly spread over several years, and due mainly to a backlog of untreated cases) and glycoprotein IIb/IIIa inhibitors for acute coronary syndromes (net £30m-31m), with none of the others costing more than £20m. The impact on total net cost was reduced by projected savings for some technologies—notably, restricted use of proton pump inhibitors (projected saving £40m-50m annually). The combined net cost of the 22 judgments was £200m-214m or around 0.5% of annual NHS spending in England and Wales. This provides some indication, on the basis of individual technologies, of the extent to which new health technologies may change net healthcare spending. Increases of this magnitude should be readily achieved within the real increases in NHS spending of around 6% per year over the three years to 2004, although some local bottlenecks may become apparent.

Discussion

While NICE has been caricatured under the heading "it's easier to say yes than no,"[12] it would be more accurate to characterise it as saying "yes, but …" Its recommendations have all cited evidence of clinical benefits, while only around half have cited cost per QALY. Many of its recommendations have specified conditions for use, such as subgroups of patients most likely to benefit. This in turn requires guidelines covering the full range of treatment options for the different groups of patients. This second, guideline, function of NICE may prove more important and challenging over the longer term, given the magnitude of the task and the paucity of evidence. By October 2000 NICE had published four guidelines and was working on a further 31, often for the same diseases as those for which guidance on technologies has been issued.

The specification by NICE of conditions for use, which has generally enabled it to keep the cost per QALY below £30 000, could be seen as requiring rationing at a more detailed level, perhaps within some overall guidelines for use. Overall, however, NICE's guidance recommending use of most technologies appraised will arguably lead to "faster and more uniform access" to these technologies rather than to denial access.

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Corrections and clarifications

Prescriptions with potential drug interactions dispensed at Swedish pharmacies in January 1999: cross sectional study

In this paper by Juan Merlo and colleagues (25 August, pp 427-8) we mistakenly omitted from the figure legend the number of possible drug interaction pairs. The legend should have read: "Prevalence of potential drug interaction subtypes[3 4] among the 191 899 possible drug interaction pairs found in the 962 013 prescriptions containing two or more drugs dispensed to patients aged 15-95 from Swedish pharmacies in January 1999."

Revisiting the Cochrane Collaboration

Geographical gremlins muddled the authors' addresses at the end of this article by Mike Clarke and Peter Langhorne (13 October, p 821). Dr Clarke is associate director at the Cochrane Centre, Oxford OX2 7LG, and Professor Langhorne is professor in the academic section of geriatric medicine at the Royal Infirmary, Glasgow G4 0SF.

Prospective health impact assessment: pitfalls, problems, and possible ways forward

We have electronic gremlins too at the *BMJ*. This time they pushed off a note that should have appeared in the margin of this article by Jayne Parry and Andrew Stevens (17 November, pp 1177-82). The note would have alerted readers to the fact that additional references appear on bmj.com (these are cited in the main text as w1 to w17).