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What is NICE?

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- The National Institute for Clinical Excellence (NICE) was established as a Special Health Authority in April 1999.
- As one of the key elements of the NHS in England and Wales, NICE aims, as its principal role, to provide patients and the healthcare industry with authoritative, robust and reliable guidance on best-practice procedures in healthcare.
- Appraisal of new and existing pharmaceutical interventions and medical technologies is a key function of NICE, with emphasis on the demonstration of the value that these products and devices can bring to the NHS based upon proven clinical and cost-effectiveness.
- NICE is also involved in the development and implementation of evidence-based guidelines for appropriate clinical practice, and in the production of tools that can be used for clinical audit within the NHS.
- Introduced as one of several interlinked initiatives aimed at promoting a strategy of high-quality patient care across the health service,[1] NICE marks an explicit move towards the practice of evidence-based medicine in England and Wales, offering positive guidance for products or technologies with proven clinical and cost-effectiveness.

Prescribing information is on page 8

What is NICE?

NICE was established with a view to reducing inequalities in healthcare provision brought about by the practice of postcode prescribing. Other important aims were to reduce inadequacies in the use of evidence in routine clinical practice and to provide faster access to modern therapies.

The following inadequacies were of particular concern.

- New technologies have often been adopted without there being adequate evidence of their clinical and cost-effectiveness.
- Uptake in the use of those technologies shown to be effective and to offer value for money has been slow and variable.
- Insufficiency of time and expertise has prevented individual practitioners from making judgements about the clinical value of each and every new technology.
- Guidelines for new technologies have too often been of inadequate or indeterminate quality, or have been indigestible or inaccessible to the user.[2]
- With the existence of numerous guidelines, it has often been difficult to determine which offers the most credible advice.

NICE has attempted to address these inadequacies by:

- 'Enabling evidence of clinical effectiveness and cost-effectiveness to be brought together to inform a judgement on the value of the treatment relative to alternative uses of NHS resources'[3]
- 'Issuing guidance on whether the treatment can be recommended for routine use in the NHS (and, if so, under what conditions or for which groups of patients), together with a summary of evidence on which the recommendation is based.'[3]

This remit has been assumed so far in Scotland by the Health Technology Board for Scotland (HTBS), which was established in April 2000 to provide a single Scottish source of advice on the clinical and cost-effectiveness of new and existing health technologies, and authoritative comment on NICE appraisal and guidance, developing it within a Scottish perspective where necessary.[4] However, the role of the HTBS is currently being redefined as part of a national review of the relationship between the various clinical effectiveness bodies in Scotland (including the Clinical Standards Board for Scotland and the Scottish Intercollegiate Guidelines Network, which also offer guidance on health technologies and services). The aim of this restructuring is to achieve better integration and co-ordination.[5]

Areas of NICE activity

The role of NICE extends to three clearly defined areas of activity: technology appraisal, guidelines for clinical practice, and clinical audit.

Technology appraisal

In terms of technology appraisal, the role of NICE is to assess the evidence base for the clinical and cost-effectiveness of new and existing health technologies, with a view to providing a single, authoritative source of advice on these treatment interventions and other medical procedures.

Clinical guidelines

To promote best practice in healthcare, NICE must develop evidence-based guidelines to help healthcare professionals and patients to make informed decisions about healthcare in specific clinical circumstances. Guidelines must take clinical and cost-effectiveness into account, and advise as to the appropriate management of specific conditions.

Clinical audit

The third explicitly stated function of NICE is to produce tools that can be used to monitor the use of particular interventions or the care received by patients within the NHS. Any identified departures from 'best practice' can then be addressed, with a view to helping clinicians meet the requirements of the clinical-governance initiative locally.[3]

NICE and the new NHS

NICE was established under the auspices of the new NHS, with a view to improving the quality of healthcare across England and Wales. As such, other key elements of the new NHS impact significantly on the work of the institute. National Service Frameworks (NSFs), for example, set clearly defined targets for best practice in specific disease areas or population groups, while clinical governance encourages dependable local delivery by making clinicians responsible for improving the quality and efficacy of their clinical practice, based on appropriate evidence.[6] Finally, the Commission for Health Improvement (CHI), the National Performance Framework, and the National Patient and User Survey have been introduced to the NHS to monitor the standards achieved in clinical practice.[6] (See Figure 1)

How the system works

The technology appraisals conducted by NICE aim to provide guidance on the clinical and cost-effectiveness of new and existing health technologies. Such technologies include drugs, diagnostic tests, clinical devices, surgical and clinical procedures, health promotion and other therapeutic interventions.

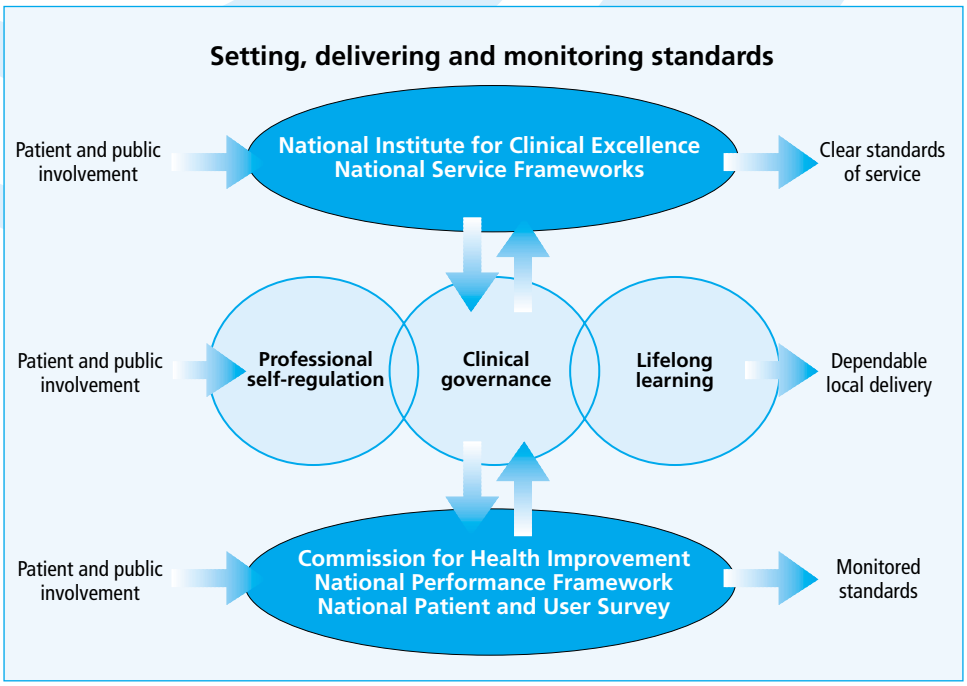
Prioritisation and topic selection

It would not be feasible for the institute to evaluate all technologies; instead, it aims to appraise at least 30 each year.

Topic selection for the NICE appraisal programme is undertaken by the Department of Health (DoH) and the National Assembly for Wales (NAW), who decide when guidance is required for a particular health technology and then refer it to the institute to be evaluated. The DoH is alerted by the National Horizon Scanning Centre to new technologies that might require evaluation. This specialist centre was set up with the remit of providing the DoH with early warning of emerging healthcare technologies, giving specific consideration to their potential impact on the NHS in terms of both cost and clinical practice.[7] Through horizon scanning, the impact of new drugs or other medical interventions, due to either expense or demand, can be predicted before they are introduced to the market, thus identifying those developments that will be of potential value to the NHS (Figure 2, overleaf).

Topics are chosen according to the value that NICE can give to the NHS by offering national guidance in that area. For example, technologies for use in therapeutic areas of major impact are particularly likely to be recommended for appraisal, especially in

Figure 1. The environment of NICE



cases where management guidelines are not already available or widely used.

The following criteria are used by the DoH and the NAW in the selection of technologies for NICE appraisal:

- The likely health benefits of the technology across the NHS as a whole, if given to patients for whom it is indicated
- The likely impact of the technology on the government's other health-related policies (for example, NSFs)
- The likely impact of the technology on NHS resources, if given to patients for whom it is indicated.[8]

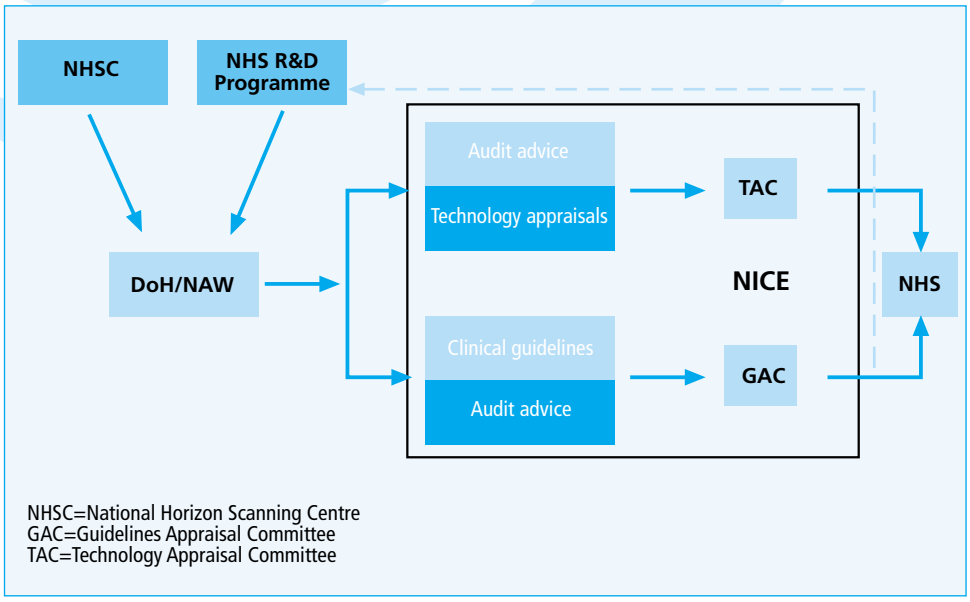
Process of appraisal

Once health technologies have been referred to NICE by the DoH and the NAW, NICE will undertake a detailed process of appraisal, over a period of approximately 12 months, before issuing guidance to the NHS on use of the selected technology. As part of the appraisal process, NICE invites contributions (submissions) from relevant stakeholders, who include manufacturers and national organisations representing either healthcare professionals (for example, the Royal Colleges) or patients and their carers. From the perspective of individual stakeholders, registration early in the process is important to allow time for preparation of the submission. Though the various contributors are asked to concentrate on their unique perspective in compiling their evidence, the submission should pertain to five clearly defined areas:

- Disease background (epidemiology, aetiology, pathology and prognosis of the disease; known subgroups)
- Description of the technology (mode of action; current indications or promoted uses; role in managing the disease; and the projected cost of treating the target population group)
- Clinical effectiveness (evidence of the technology's quality; its significant benefits over competitors; and potential disadvantages, such as adverse effects)
- Cost-effectiveness (likely costs of implementing the technology from the perspective of the NHS; including the estimated cost per quality-adjusted life-year {QALY})
- Wider implications to the NHS (health gain expected from use of the intervention; any changes in work patterns or reconfiguration of services required; personnel, education and training issues; and additional costs relative to cost savings associated with use of the technology).

The work of NICE in relation to its technology appraisals is supported by the Health Technology Assessment (HTA) programme, whose role is to ensure that the NICE Appraisal Committee has the knowledge and evidence it requires to produce appropriate advice to the NHS.

Figure 2. The process of NICE guidance generation



Once NICE has identified technologies for appraisal, the HTA programme identifies and commissions an appropriate academic team from a UK university to undertake an HTA report. Currently, the review groups are:

- Department of Public Health & Epidemiology, University of Birmingham
- NHS Centre for Reviews and Dissemination (CRD)
- School of Health Related Research, University of Sheffield
- Wessex Institute for Health Research and Development
- Health Economics Research Unit and Health Services Research Unit, University of Aberdeen
- Department of Pharmacology & Therapeutics, University of Liverpool.

The HTA report will include a systematic review of the evidence for the technology's clinical and cost-effectiveness (incorporating relevant evidence from stakeholder submissions). More information about the role of the HTA programme is available online (www.hta.nhsweb.nhs.uk).

An initial appraisal of stakeholder submissions and the HTA report is conducted by the NICE Appraisal Committee (which is comprised of independent experts from the organisations of healthcare professionals and patient representatives; experts in health economics and medical statistics; and NHS managers). The NICE Appraisal Committee then produces provisional advice on the technology and a consultation of this advice takes place between NICE, the stakeholders, and the DoH and the NAW. This stage of the appraisal process is referred to as provisional appraisal determination (PAD).

Final appraisal determination (FAD) follows with a second meeting of the Committee. The NICE Board then adopts and issues its final guidance to the NHS. This is subject to appeal by stakeholders before final release.

Box 1. NICE technology appraisal guidance: taxanes for breast cancer

Evidence assessed

Docetaxel

Four randomised controlled trials (RCTs) in ~1,000 women have shown a five to 16-week gain in progression-free survival compared with control therapy.

Paclitaxel

Two RCTs in ~500 women have shown approximately a nine-week gain in progression-free survival compared with control therapy.

(The cost in each case was between £7,000 and £23,500 per life-year gained)

Guidance offered *(issued June 2000, updated September 2001)*

Both docetaxel and paclitaxel should be available for the treatment of advanced breast cancer where initial cytotoxic chemotherapy (including anthracycline) has failed or is inappropriate.

Stakeholders

Aventis Pharma

Bristol-Myers Squibb

Breakthrough Breast Cancer

CancerBACUP

Imperial Cancer Research Fund

Macmillan Cancer Relief

Royal College of Obstetricians and Gynaecologists

Outcomes of appraisal

The guidance that NICE offers for new technologies falls generally into three broad categories. In the first category (a), the technology is recommended for routine use in the NHS for all licensed indications, for specific indications, or for specified patient subgroups only. The second category of guidance (b) recommends the technology for use in the NHS but only within the context of appropriate clinical trials. The third outcome (c) does not recommend the evaluated technology for use in the NHS for any group of patients (for specified reasons relating to lack of clinical or cost-effectiveness).[2]

Boxes 1 and 2 contain examples of recent NICE technology appraisals and the guidance issued as a result.

Guideline development

Guidance on the use of individual technologies has been NICE's most visible and highly publicised contribution to the NHS to date. However, clinical guidelines for the management of individual conditions are now being increasingly produced by NICE. NICE's

earliest clinical guidelines are based on an inherited work programme of guidelines that had already been developed by others (see Box 3). While NICE will continue to adopt existing guidelines as the basis for new clinical guidance (providing that they meet specific criteria relating to quality and content), the institute is expected to also commission guideline developers to draw up new guidance.

The process that NICE has put in place for the development of clinical guidelines has much in common with its process of appraisal and the subsequent development of related guidance. Clinical guidelines are based on a consideration of both clinical and cost-effectiveness. An independent Clinical Guidelines Committee is responsible for assessing the quality and content of the guidelines. A consultation of the content also takes place between NICE and stakeholders, who include healthcare professionals, patients and the healthcare industry as a whole.

Audit advice

To ensure that maintenance of best practice is monitored throughout the NHS, NICE has issued simple audit advice with each of the technology appraisals and clinical guidelines it has published to date (see Figure 2).

In comparison with the Royal Colleges and individual organisations, such as NHS trusts, NICE has broader responsibilities for clinical audit within the NHS. It has incorporated the National Centre for Clinical Audit and has assumed responsibility for the National Confidential Enquiries and the core audit funding of the Royal College Audit and Effectiveness Units and other national professional bodies in England and Wales. NICE has recently completed reviews of its inherited programme of ten sentinel national audits and four confidential enquiries. The resulting reports will determine NICE's future strategy in these areas.[9,10]

Dissemination of guidance

NICE guidance is disseminated through a variety of media. Copies of all published appraisals and guidelines can be downloaded from the NICE website (www.nice.org.uk). Information is also available from the National Electronic Library for Health, and on PRODIGY, an electronic system of guidelines aimed at prescribers. The DoH's routine mailing system will also send relevant information to the chief executive officers of all health authorities, trusts, primary care groups (PCGs) and other key organisations related to the NHS in England and Wales. A handbook offering practical information and support for the implementation of NICE guidance is also available from the National Prescribing Centre (www.npc.co.uk).

Box 2. NICE technology appraisal guidance: implantable cardioverter defibrillators (ICDs) for arrhythmias

Evidence assessed

Primary prevention

Three randomised, controlled trials (RCTs), two of which show clinical benefit over medical therapy

Secondary prevention

One RCT, demonstrating a cost per life-year gained of £26,000–£31,000 relative to controls over a five-year period

Guidance offered *(September 2000)**

ICDs should be routinely considered for:

- *Secondary prevention* – in patients with previous myocardial infarction (MI) due to ventricular tachycardia (VT) or ventricular fibrillation, or patients with spontaneous, sustained, serious VT
- *Primary prevention* – in patients with a history of MI plus VT, a left-ventricular ejection fraction of less than 35%, and an inherited heart problem that has a high risk of sudden death.

ICDs should not be routinely considered for spontaneous, sustained VT with good function, or syncope of unknown cause.

Stakeholders

Association of British Healthcare Industries

BIOTRONIK

British Pacing and Electrophysiological Group

ELA UK

EUCOMED

Guidant

Medtronic

St Jude Medical

*Guidance summarised – see full guidance for details

Box 3. NICE clinical guideline – prophylaxis for patients who have experienced a myocardial infarction (MI)*

Evidence assessed

A: directly based on category I evidence (meta-analysis of at least one RCT)

B: directly based on category II evidence (at least one controlled study without randomisation or one other type of quasi-experimental study) or extrapolated recommendation from category I evidence

C: directly based on category III evidence (non-experimental descriptive studies) or extrapolated recommendation from category I or II evidence

D: directly based on category IV evidence (expert committee reports or opinions and/or clinical experience of respected authorities) or extrapolated recommendation from category I, II or III evidence

Guidance offered *(issued April 2001)***

Prior MI, no heart failure

(1) Drug treatment

– Early initiation is required of beta-blocker + antiplatelet drug (aspirin) + ACE inhibitor (A) – if not in hospital, then as soon as possible in primary care (A).

– Patients not taking a statin should be assessed and have treatment initiated 12 weeks after index MI (A).

(2) Non-drug treatment

– Patients should be offered enrolment in a rehabilitation programme that has a prominent exercise component within it (A). Although many of the trials imposed upper-age limits for recruitment, the guideline development group felt that it was more appropriate, in a service setting, to be guided by functional ability and patient preference (D).

Stakeholders

Not listed

*Guideline developers: Centre for Health Services Research, Unversity of Newcastle-upon-Tyne Evaluation Group, Centre for Health Economics, University of York

**Guidance summarised for one patient category only. For other categories of MI, see full NICE guidelines

As guidance for the NHS, NICE's technology appraisals and clinical guidelines are purely advisory. However, within the context of clinical governance, which makes individual organisations accountable for improving the quality and effectiveness of their own services, it is expected that NHS trusts, PCGs and other health professionals will be keen to implement the institute's guidance. The response of the health service to NICE guidance will be monitored, in part, by the CHI.

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What is NICE?

Abbreviated prescribing information: Taxotere® (docetaxel)

Presentation: Vials of concentrate for infusion containing 20mg docetaxel or 80mg docetaxel with accompanying vials of solvent. **Indications:** Locally advanced or metastatic breast cancer in combination with doxorubicin for patients who have not received prior cytotoxic therapy for this condition. Locally advanced or metastatic breast cancer after failure of cytotoxic therapy which should have included an anthracycline or alkylating agent. Locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of prior chemotherapy. **Dosage and Administration:** Taxotere is administered as a one-hour iv infusion every three weeks. The recommended dosage in breast cancer is 100 mg/m2, or 75 mg/m2 in combination with doxorubicin (50mg/m2). The recommended dosage in NSCLC is 75 mg/m2. Premedication with an oral corticosteroid is recommended for 3 days, starting one day prior to docetaxel administration. Elderly: No special instructions. Children: Safety and efficacy not established. Hepatic impairment: Reduce dosage; discontinue in severe cases. **Contraindications:** Hypersensitivity to the active substance or excipients, baseline neutrophil count of <1,500 cells/mm3, pregnancy or breast feeding, severe liver impairment. **Precautions and Warnings:** Reduce dosage with febrile neutropenia, neutrophils <500 cells/mm3 for more than one week, severe or cumulative cutaneous reactions, severe peripheral neuropathy, or moderately raised LFTs, ALT and/or AST >1.5 times the ULN concurrent with serum alkaline phosphatase >2.5 times the ULN. Severe hypersensitivity reactions require immediate discontinuation. Severe cutaneous skin reactions, such as eruptions followed by desquamation, may require interruption or treatment discontinuation. Severe fluid retention such as pleural effusion, pericardial effusion or ascites should be monitored closely. With serum bilirubin levels > ULN and/or ALT and AST >3.5 times the ULN concurrent with alkaline phosphatase levels > 6 times the ULN, no dose-reduction can be recommended and docetaxel should not be used unless strictly indicated. **Interactions:** Caution with compounds which induce, inhibit or are metabolised by cytochrome P450-3A, which may alter docetaxel metabolism. **Pregnancy and Lactation:** Contraindicated. **Adverse Reactions:** Neutropenia, thrombocytopenia, anaemia, hypersensitivity reactions, fluid retention, cutaneous reactions, peripheral neuropathy, infectious episodes, increased liver enzyme levels, alopecia, asthenia, mucositis, injection site reactions, gastrointestinal events, cardiovascular events (including hypotension and dysrhythmia), arthralgia, and myalgia. Pharmaceutical Precautions: Store vials between +2°C and +25°C; protect from bright light. Reconstitute concentrate with accompanying solvent and dilute with infusion solution (0.9% sodium chloride for intravenous injection or 5% dextrose for intravenous injection) before use. Apply usual cytotoxic precautions. **Package Quantities and Basic NHS Price:** Blister cartons containing one vial of TAXOTERE® concentrate and one vial of solvent: TAXOTERE® 20mg £175.00; TAXOTERE® 80mg £575.00. Legal Category: POM. Marketing Authorisation Numbers: TAXOTERE® 20mg EU/1/95/002/001; TAXOTERE® 80mg EU/1/95/002/002.
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