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A guide to NICE

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This booklet is a simple guide to the work of the National Institute for Health and Clinical Excellence (NICE). We hope you find it useful – whatever your interest in the work of NICE. If you have any comments on this guide, please contact the communications department at NICE.

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General information about NICE

What is NICE?

The National Institute for Health and Clinical Excellence (NICE) is the independent organisation responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health.

What are the roles and responsibilities of NICE?

We produce guidance in three areas of health:

- public health – guidance on the promotion of good health and the prevention of ill health for those working in the NHS, local authorities and the wider public and voluntary sector
- health technologies – guidance on the use of new and existing medicines, treatments and procedures within the NHS
- clinical practice – guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS.

Does NICE cover the whole of the UK?

No. NICE produces guidance on health technologies and on clinical practice for the NHS in England and Wales. Our

guidance on interventional procedures, which states whether interventional procedures are safe and work well enough for use in the NHS, covers England, Wales and Scotland. NICE guidance on public health covers England.

Why was NICE set up?

NICE's role was set out in the 2004 White Paper 'Choosing health: making healthier choices easier'. In it the government set out key principles for helping people make healthier and more informed choices about their health. The government wants NICE to bring together knowledge and guidance on ways of promoting good health and treating ill health.

NICE was preceded by the National Institute for Clinical Excellence, which was set up in 1999 and also known as NICE. The functions of another NHS organisation, the Health Development Agency (HDA), were transferred to NICE on 1 April 2005.

How are topics for NICE guidance identified?

The Department of Health commissions NICE to develop clinical guidelines and guidance on public health and technology appraisals. Full details of the process they follow can be found at www.dh.gov.uk – search for 'topics for NICE'.

We provide guidance on public health, health technologies and clinical practice

The government wants NICE to bring together knowledge and guidance on promoting good health and treating ill health

Several different groups suggest topics on which NICE should develop guidance.

- Health professionals, patients, carers and the general public suggest topics on which they think a NICE public health intervention or programme (see page 11), technology appraisal (see page 14) or clinical guideline (see page 22) would be useful.
- The National Horizon Scanning Centre suggests emerging health technologies that might need to be assessed by NICE.
- The Department of Health's National Clinical Directors and policy teams suggest topics.

You can suggest a topic for NICE guidance on the NICE website (www.nice.org.uk): click on 'Suggest a topic' on the home page. Or you can email topicsuggestion@nice.nhs.uk or call 020 7067 5898 to ask for a copy of the topic suggestion form.

We will check suggested topics to make sure that it would be appropriate to refer them to NICE and whether they are already included in our work. The Department of Health will then decide whether they wish to refer the topic to NICE.

Topics for interventional procedures guidance are notified to NICE directly, usually by clinicians (see page 18).

You can suggest a topic on which you would like NICE guidance

The impact of NICE guidance

Once NICE publishes clinical guidance, health professionals and the organisations that employ them are expected to take it fully into account when deciding what treatments to give people. However, NICE guidance does not replace the knowledge and skills of individual health professionals who treat patients; it is still up to them to make decisions about a particular patient in consultation with the patient and/or their guardian or carer when appropriate.

Since January 2002, NHS organisations in England and Wales have been required to provide funding for medicines and treatments recommended by NICE in its technology appraisals guidance (see page 14). The NHS normally has 3 months from the date of publication of each technology appraisal guidance to provide funding and resources. Local NHS organisations are expected to meet the costs of medicines and treatments recommended by NICE out of their general annual budgets.

When NICE publishes clinical guidelines, local health organisations should review their management of clinical conditions against the NICE guidelines. This review should consider the resources required to implement the guidelines, the people and processes involved, and how long it will take to do all this. It is in the interests of patients that the NICE recommendations are acted on as quickly as possible.

If a drug or device is being appraised by NICE, NHS organisations should make decisions on its use locally, using their usual arrangements, until the NICE guidance is published.

NICE guidance helps to improve public health and make access to healthcare more equal across the country

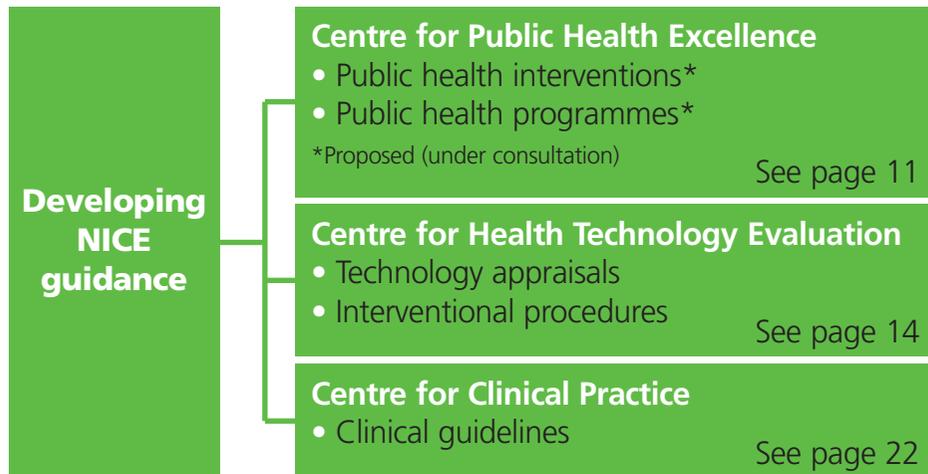
Local government and NHS organisations are expected to take account of NICE public health guidance in taking action to achieve the targets set out in the 'Choosing health' White Paper and in the development of local area agreements.

NICE's impact on patients and the public

NICE provides authoritative advice on the effectiveness of interventions to improve health and reduce health inequalities and on treatments and the best clinical practice. We make sure that this information reaches the wider public, the NHS and patients. By using effective public health interventions and programmes, the health of the population can be improved consistently and equal access to NHS care can be achieved.

The different parts of NICE

NICE's guidance work is divided across its three Centres (see diagram below).



Centre for Public Health Excellence

The Centre for Public Health Excellence at NICE develops guidance on the promotion of good health and the prevention of ill health. Its guidance is for those working in the NHS, local authorities and the wider public, private and voluntary sectors.

Initially, NICE will publish guidance that was commissioned by the Health Development Agency. From the end of 2005, our guidance will be in the form described below.

Guidance on public health – a new role for NICE

Topics for public health guidance

The Centre for Public Health Excellence will produce guidance in nine key areas. First, there are themes that the Government picked out in the 2004 White Paper 'Choosing health: making healthier choices easier':

- smoking and tobacco control
- obesity, diet and nutrition
- exercise and physical activity
- alcohol
- sexual health
- mental health.

The Centre is also looking at three other key areas central to government policy:

- drug misuse
- promoting the health of children and young people
- preventing accidental injury.

How NICE will develop guidance on public health

NICE will produce two types of guidance on public health.

- **Public health intervention guidance:** this will make recommendations on clear types of activity ('interventions') provided by local organisations with public health responsibilities. These interventions will help to promote or maintain a healthy lifestyle or reduce the risk of developing a disease or condition (for example, giving patients advice – at home, in GP practices or in clinics – to encourage them to take more exercise).
- **Public health programme guidance:** this will deal with broader activities for the promotion of good health and the prevention of ill health. This guidance may focus on a topic (such as strategies to help people give up smoking) or on a particular population (such as young people or pregnant women) or on a particular setting (for example, the workplace).

The processes for developing these two new forms of guidance are in development. You can find out the latest position by visiting our website (www.nice.org.uk).

Where you can get a copy of NICE guidance

You can order a copy of NICE guidance on public health by calling 0870 121 4194, or by downloading a copy from www.publichealth.nice.org.uk

We also produce a free monthly e-newsletter, which contains details of forthcoming public health guidance. To receive the e-newsletter, visit the NICE website and register your details.

NICE will produce two types of guidance on public health: public health intervention guidance and public health programme guidance

The processes for developing these two forms of guidance are in development

Centre for Health Technology Evaluation

The Centre for Health Technology Evaluation at NICE develops guidance on the use of new and existing medicines, treatments and procedures within the NHS.

Technology appraisals

What are technology appraisals?

What NICE calls technology appraisals are recommendations on the use of new and existing medicines and treatments within the NHS, such as:

- medicines
- medical devices (for example, hearing aids or inhalers)
- diagnostic techniques (tests used to identify diseases)
- surgical procedures (such as repairing hernias)
- health promotion activities (for example, ways of helping people with diabetes manage their condition).

We base our recommendations on a review of clinical and economic evidence. Clinical evidence measures how well the medicine or treatment works. NICE also takes account of economic evidence, that is how well the medicine or treatment works in relation to how much it costs the NHS – does it represent value for money? NICE acknowledges

that something can be both expensive and value for money.

NICE technology appraisal recommendations are prepared by an independent committee (the 'Appraisal Committee'). Members of the Committee include health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

How you can be involved

Organisations representing patients, carers and health professionals, manufacturers of the technology being appraised, and relevant NHS organisations have a chance to be involved throughout the appraisal process as 'consultees'.

NICE's technology appraisal guidance covers medicines, medical devices, tests to identify diseases, surgical procedures and health promotion activities

The Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, and its advice is independent of any vested interests

Consultees can:

- comment on the scope of the appraisal (the scope sets out what the appraisal will cover and the questions that need to be asked)
- submit evidence to the Appraisal Committee
- recommend other consultees whom they think should take part
- comment on the 'assessment report' (a review of the evidence prepared by an independent academic centre)
- comment on the Appraisal Committee's provisional recommendations which are set out in the 'appraisal consultation document'
- appeal against the Appraisal Committee's final decision, which is set out in a document called the 'final appraisal determination'.

Professionals' and patient/carers' organisations can nominate experts and patients to speak directly to the Appraisal Committee.

Members of the public and individual health professionals who are not consultees can send their own feedback directly to NICE after the appraisal consultation document has been published on the NICE website for 3 weeks' consultation.

To encourage patient involvement in the development of our guidance, we have set up a Patient Involvement Unit. The Unit advises us on patient and carer involvement, and supports and trains patients and carers who are involved in the development of appraisal guidance.

We value evidence from patients; we want to hear personal experience about the impact of a disease and the difference a 'technology' can make. And sometimes patients and carers can tell us about things that are important but that do not show up in formal research.

Further information

NICE has produced documents explaining its technology appraisal process. 'Guide to the technology appraisal process' (reference N0514) provides an overview, and the following documents focus on more specific aspects of the process:

- Guide to the methods of technology appraisal (reference N0515)
- Contributing to a technology appraisal: a guide for patient/carers groups (reference N0516)
- Contributing to a technology appraisal: a guide for healthcare professional groups (reference N0517)
- Contributing to a technology appraisal: a guide for manufacturers and sponsors (reference N0518)
- Contributing to a technology appraisal: a guide for NHS organisations (reference N0519)
- Appraisal process: guidance for appellants (reference N0520).

You can download these documents from the NICE website or order them from the NHS Response Line (telephone 0870 1555 455) – tell them the reference number for the booklet you want.

You can download copies of completed NICE technology appraisal guidance from the NICE website. Or, you can phone the NHS Response Line on 0870 1555 455 and ask for a printed copy

Where you can find out about forthcoming appraisals

For information on forthcoming appraisals, visit the NICE website at www.nice.org.uk/clinicalexcellence and click on 'Our guidance' and then 'Appraisals' and select 'Appraisals in development'.

We also produce a free monthly e-newsletter, which gives details of forthcoming technology appraisals. To receive the e-newsletter, visit the NICE website and register your details.

Interventional procedures

What is an interventional procedure?

An interventional procedure is a procedure used for diagnosis or for treatment, which involves the following:

- making a cut or a hole to gain access to the inside of a patient's body – for example, when carrying out an operation or inserting a tube into a blood vessel
or
- gaining access to a body cavity (such as the digestive system, lungs, womb or bladder) without cutting into the body – for example, examining or carrying out treatment on the inside of the stomach using an instrument inserted via the mouth
or
- using electromagnetic radiation (which includes X-rays, lasers, gamma-rays and ultraviolet light) – for example, using a laser to treat eye problems.

The aim of the guidance

NICE guidance tells you about the safety of interventional procedures used for diagnosis or treatment and says whether they work well enough for routine use (or whether special arrangements are needed for patient consent).

The aim of NICE's interventional procedures guidance is to protect patients' safety and to support people in the NHS in the process of introducing new procedures.

Many of the procedures that NICE investigates are new, but we also look at more established procedures if there is uncertainty about their safety or how well they work.

To develop NICE interventional procedures guidance, NICE reviews evidence and collects and analyses information. By providing guidance on how safe procedures are and how well they work, NICE makes it possible for new treatments and tests to be introduced into the NHS in a responsible way.

NICE interventional procedures recommendations are prepared by an independent committee (the 'Interventional Procedure Advisory Committee'). Members include health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. The Committee takes advice from specialist advisors, nominated by health professional bodies whose members are involved in the use of interventional procedures.

How you can get involved

Any individual or organisation can notify NICE about procedures that are being performed or are likely to be performed within the NHS. It is usually doctors who tell NICE about procedures;

By providing guidance on how safe procedures are and how well they work, NICE makes it possible for new treatments and tests to be introduced into the NHS in a responsible way

Any individual or organisation can tell NICE about procedures that are being performed or likely to be performed in the NHS

they are responsible for doing this when they are considering using a procedure for the first time in the NHS. (NICE does not need to be notified when a doctor is considering using a procedure that is considered to be standard practice and for which the benefits and risks are sufficiently well known, but that has not been performed previously by that particular doctor.)

You can notify a procedure, or check whether a procedure has already been notified; visit www.nice.org.uk/clinicalexcellence, then go to 'Our guidance' and click on 'Interventional procedures' and select 'Notifying an interventional procedure'.

You can comment on the draft guidance ('the interventional procedures consultation document') when it is posted on the website for a 4-week consultation period.

Professionals, patients and any other interested person or group can 'register an interest' in a procedure via the NICE website. Everyone who registers an interest is informed (by email only) when consultation begins and is able to submit comments via the NICE website or by post. To register an interest visit www.nice.org.uk/clinicalexcellence, then go to 'Our guidance' and click on 'Interventional procedures' and select 'List of all interventional procedures'.

The Patient Involvement Unit prepares a list of patient organisations that may wish to take part in consultation on each procedure, and invites each of them to participate. If an

organisation wishes to respond, NICE sends it information about interventional procedures guidance and the consultation process, as well as the consultation document when it is issued. The Patient Involvement Unit is available to support patient organisations during the consultation.

Where you can find out more

For further information on interventional procedures, please visit the NICE website at www.nice.org.uk/clinicalexcellence and click on 'Our guidance' and then 'Interventional procedures'.

NICE has produced a manual explaining its process for developing guidance on interventional procedures:

- The interventional procedures programme – programme manual.

You can download the manual from the NICE website or order it from the NHS Response Line (telephone 0870 1555 455 and quote reference number N0712).

Decision support systems

A new programme to evaluate the safety of decision support systems (software used by health professionals to help them make diagnoses and treatment decisions) and how well they work is being set up within the Centre for Health Technology Evaluation.

We will be consulting on proposals for establishing this programme during the second half of 2005.

You can download copies of completed NICE interventional procedures guidance from the NICE website. Or, you can phone the NHS Response Line on 0870 1555 455 and ask for a printed copy

Centre for Clinical Practice

The Centre for Clinical Practice at NICE develops clinical guidelines.

What are NICE clinical guidelines?

Clinical guidelines are recommendations by NICE on the appropriate treatment and care of people with specific diseases and conditions within the NHS. They are based on the best available evidence.

Guidelines help health professionals in their work, but they do not replace their knowledge and skills.

Clinical guidelines aim to improve the quality of healthcare

The aim of clinical guidelines

Good clinical guidelines aim to improve the quality of healthcare. They can change the process of healthcare and improve people's chances of getting as well as possible. For example, well-constructed and up-to-date clinical guidelines:

- provide recommendations for the treatment and care of people by health professionals
- can be used to develop standards to assess the clinical practice of individual health professionals

- can be used in the education and training of health professionals
- can help patients to make informed decisions, and improve communication between the patient and health professional.

The National Collaborating Centres

NICE has established several National Collaborating Centres (NCCs) to help develop the clinical guidelines by harnessing the expertise of the royal medical colleges, professional bodies and patient/carer organisations. Each NCC is a professionally led group. The NCCs are:

- NCC for Acute Care
- NCC for Cancer
- NCC for Chronic Conditions
- NCC for Mental Health
- NCC for Nursing and Supportive Care
- NCC for Primary Care
- NCC for Mental Health
- NCC for Women's and Children's Health.

For details of the member organisations of the NCCs, visit the NICE website at www.nice.org.uk/clinicalexcellence. Click on 'Our guidance' and then 'Clinical guidelines' and select 'About clinical guidelines'.

An NCC sets up an independent Guideline Development Group to develop each guideline. The members have relevant experience and expertise. They include health professionals and patient/carer representatives. Stakeholder groups that have registered an interest are invited to nominate people to join the Guideline Development Group.

NICE harnesses a wide range of expertise to help develop good clinical guidelines

The Guideline Development Group looks at the evidence available and considers comments made on two draft versions of the guideline issued for consultation before making final recommendations.

The Guideline Review Panels

NICE has established a number of Guideline Review Panels, each consisting of four or five members, including a chair and a deputy. Each Guideline Review Panel is linked to one of the NCCs which manages the development of clinical guidelines for NICE.

The job of the panels is to validate the final guideline, paying particular attention to how the Guideline Development Group has responded to any comments received during consultation.

How you can get involved

NICE lists the guideline topics in its work programme on its website. Visit the website: go to www.nice.org.uk/clinicalexcellence, click on 'Our guidance' and then 'Clinical guidelines' and then select 'Published guidelines' or 'Guidelines in development'. National organisations representing patients and carers and also health professionals involved in their care are then able to register their interest as 'stakeholders' in particular topics.

These groups, together with representative NHS organisations, are consulted throughout the guideline development process. They are involved at the beginning of the process when the scope of the guideline is being established and in commenting on the draft versions of the guideline.

To encourage patient involvement in the development of our guidelines, we have set up a Patient Involvement Unit. The Unit advises us – and the NCCs – on patient and carer involvement, and supports and trains patients and carers who are involved in Guideline Development Groups.

Further information

NICE has produced two documents describing its guideline development process. The first is an overview of the process, which explains what happens and how stakeholder organisations can become involved. It is called 'The guideline development process: an overview for stakeholders, the public and the NHS'. You can download it from the NICE website: go to www.nice.org.uk/clinicalexcellence, click on 'Our guidance' and then 'Clinical guidelines' and select 'About clinical guidelines'. For a printed copy, call the NHS Response Line (telephone 0870 1555 455) – the reference number for the booklet is N0472.

The second document explains the methods used to develop NICE guidelines. It is chiefly to be used as a resource for the NCCs and guideline developers. The chapters are updated at regular intervals so that they continue to reflect current practice. This document may be of interest to anyone who wants more detail on NICE processes or the development of health guidance in general. 'Guideline development methods: information for national collaborating centres and guideline developers' is available from the NICE website only: go to www.nice.org.uk/clinicalexcellence, click on 'Our guidance' and then 'Clinical guidelines' and select 'About clinical guidelines'.

Where you can find information about forthcoming guidelines

For further information on forthcoming guidelines, please visit the NICE website at www.nice.org.uk/clinicalexcellence and click on 'Our guidance' and then 'Guidelines in development'.

NICE also produces a free monthly e-newsletter, which gives details of forthcoming clinical guidelines. To receive the free e-newsletter, please visit the NICE website and register your details.

You can download copies of completed NICE clinical guidelines from the NICE website. Or, you can phone the NHS Response Line on 0870 1555 455 and ask for a printed copy

Research and development

The NICE Research and Development (R&D) programme promotes and commissions research, with the aim of raising healthcare standards to the highest possible levels within the NHS. The programme focuses on:

- working with research organisations, patients and other partners to explain NICE's research needs
- using research to improve the methods that NICE uses to develop guidance
- using research to find out how NICE can help the NHS implement and apply NICE guidance better.

To find out more about the NICE R&D programme please visit the NICE website at www.nice.org.uk/clinicalexcellence and click on 'How we work' and then 'Research and Development'.

The NICE Research and Development (R&D) programme promotes and commissions research, with the aim of raising healthcare standards to the highest possible levels within the NHS

Implementing NICE guidance

Implementing guidance on public health

The objective of NICE's public health guidance is to bring about multi-level (social, economic, organisational, community and individual) change to improve health and reduce inequalities in health.

To achieve this objective, NICE will put mechanisms in place to support implementation. We recognise that for our public health guidance to be accepted by policy makers it will need to have the same weight and force as the NICE clinical practice guidance. This will be vital to ensure that the guidance is at the top of the agenda inside and beyond the NHS. NICE will work with Ministers to achieve this and seek, particularly, to ensure that the public health guidance is incorporated into national NHS standards.

Implementing clinical guidance

Putting NICE's clinical guidance into practice can be a big challenge. Many local NHS organisations have worked out specific plans to allocate resources and to support staff providing clinical care in putting NICE guidance into practice.

However, surveys undertaken over the past 2 years have shown not only that implementation happens more quickly in some places than in others but also that NHS organisations would like more help with putting guidance into practice.

A range of organisations have taken steps which, in their different ways, are calculated to encourage the take-up of NICE guidance. For example, in 2004 the Department of Health published 'Standards for better health', which sets out how NHS organisations should respond to NICE guidance. Technology appraisals and interventional procedures guidance are 'core' standards (the minimum level of service patients can expect); the clinical guidelines are 'developmental' standards (frameworks for planning improvements in services). The Healthcare Commission is responsible for monitoring progress, and more information can be found on the Commission's website (www.healthcarecommission.org.uk).

Manufacturers and patient organisations have used support groups and educational materials to draw attention to individual topics. Professional organisations use their journals and meetings to promote topics that are relevant to their particular disciplines.

How NICE is supporting implementation

NICE has set up an implementation support programme. We work sometimes directly, where we have the skills and the authority to do so, and sometimes in partnership with other organisations, either on joint initiatives or in support of their own activities.

NICE's implementation support strategy is based on the following principles:

- active engagement with the NHS, local government and the wider community (for example, by encouraging people to suggest topics for NICE guidance and to work with us as we develop guidance)
- directly spreading the word (such as sending quick reference guides for new clinical guidelines directly to the people who put the guidance into practice)
- creating tools to help put guidance into practice (for example, local costing templates for guidelines – available on the NICE website)
- education (for example, engaging with those responsible for undergraduate training programmes)
- monitoring and inspection (such as working with the Healthcare Commission and the Audit Commission to develop methods of monitoring how NICE guidance is put into effect)
- spreading good practice (telling people all over the country about good local work, so that other organisations can copy it).

How you can support implementation of NICE guidance

There are several things you can do, which include the following.

- Becoming a member of the external reference group which is being set up to provide overall advice on implementing NICE guidance within the NHS. The group will include representatives of professional groups which are engaged in the implementation of NICE guidance. There will be staff who give clinical care to patients in primary and secondary care, prescribing advisors, public health consultants, finance staff, chief executives and people whose job is 'clinical governance' (which makes NHS organisations accountable for continuously improving the quality of their services).
- Emailing NICE with examples of successfully developed implementation processes, and examples of implementation relating to specific NICE guidance. Many of these examples get published on the NICE website to spread good practice.
- Becoming involved with consultation stages during the guidance development process.

To find out more about how we support implementation, visit the NICE website at www.nice.org.uk/clinicalexcellence and click on 'Implementation'.

How NICE makes its information available

On the fourth Wednesday of each month NICE sends all clinical and public health guidance completed in that month to a core list of people (for example, chief executives of NHS and local government organisations).

Also at that time NICE sends copies of clinical guidance to health professionals working in the area covered by the guidance and NHS staff responsible for clinical governance (a framework within which NHS organisations are accountable for continually improving standards of care).

NICE sends copies of public health guidance completed that month to key audiences for a particular piece of guidance. This could include public health doctors, GPs and dentists, district nurses and others working in the community – such as health visitors. The guidance also goes to people working for local authorities and the public utilities – such as gas and water companies – and others working in services that contribute to the health of the public.

NICE keeps the broadcast and print media informed about the guidance it issues so that decisions can be publicised.

Who's who at NICE

Non-Executive Directors

Sir Michael Rawlins

Chairman

Dr Susanna Lawrence OBE

Vice Chair

Professor Leon Fine

Frederick George

Mercy Jeyasingham

Roy Luff OBE

Mary McClarey

Professor Helen Roberts

Mark Taylor

Executive Directors

Andrew Dillon

Chief Executive

Professor Peter Littlejohns

Clinical and Public Health Director

Andrea Sutcliffe

Planning and Resources Director

Dr Gillian Leng

Implementation Systems Director

Centre Directors

Professor Mike Kelly

Director of the Centre for Public

Health Excellence

Dr Carole Longson

Director of the Centre for Health

Technology Evaluation

Dr Mercia Page

Director of the Centre for

Clinical Practice

Louise Fish

Communications Director

Committee Chairs

Professor David Barnett

Chair of Appraisal Committee

Professor Andrew Stevens

Chair of Appraisal Committee

Professor Bruce Campbell

Chair of Interventional Procedures

Advisory Committee

Professor Sir Michael Marmot

Chair of Research and

Development Committee

Partners Council

The Partners Council is appointed by the Secretary of State. It has a statutory duty to meet annually to review the Institute's Annual Report. The Partners Council also provides a forum for the exchange of ideas, concepts and future plans. Members include patients and representatives of patient-focused organisations, professional organisations and relevant healthcare industries.

Citizens Council

The Citizens Council brings the views of the public to NICE decision-making about guidance on the promotion of good health and the prevention and treatment of ill health. A group of 30 people drawn from all walks of life, the Citizens Council tackles challenging questions about values – such as fairness and need.

Contacting NICE

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