Appendix A
Guidelines scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

Guideline title

Familial hypercholesterolaemia: the identification and management of adults and children with familial hypercholesterolaemia

Short title

Familial hypercholesterolaemia

Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Primary Care to develop a clinical guideline on familial hypercholesterolaemia (FH) for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health and Welsh Assembly Government (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines will support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their

individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

Clinical need for the guideline

a) In some people, a high cholesterol level in the blood is caused by an inherited genetic defect known as familial hypercholesterolaemia (FH). Most people with FH have inherited a defective gene for FH from only one parent, and are therefore heterozygous, and are at increased risk of cardiovascular disease. Rarely, a person will inherit the gene from both parents. This group of people who are homozygous are at very high risk of early death.

b) The raised cholesterol level in the blood is present from birth and it leads to an early development of atherosclerosis and cardiovascular disease. The disease is transmitted from generation to generation in such a way that siblings and children of a person with FH have a 50 per cent risk of inheriting the genetic defect.

Burden of disease

c) The prevalence of heterozygous familial hypercholesterolaemia in the UK population is estimated to be 1 in 500, which means that approximately 110,000 people are affected. The elevated serum cholesterol concentrations that characterise heterozygous FH lead to a greater than 50% risk of coronary heart disease by the age of 50 in men and at least 30% in women aged 60.

d) Homozygous familial hypercholesterolaemia is rare, presents in children and is associated with early death from cardiovascular disease. Homozygous FH has an incidence of approximately one case per million.

Evidence of effective interventions

e) Early detection and treatment with hydroxy-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors (statins) has been shown to reduce morbidity and mortality in people with heterozygous FH. Low density lipoprotein (LDL) apheresis and liver transplantation are treatment options for people with homozygous FH, with LDL apheresis being occasionally used for people with heterozygous FH who are refractory to conventional lipid-lowering therapy.

f) There is evidence that screening can be effective in identifying people in the early stages of FH. Methods proposed include opportunistic screening and cascade screening of the relatives of people identified as having FH ('index cases').

g) Currently, diagnosis involves clinical assessment and biochemical tests (lipid profile). DNA-based testing may play a greater role in the identification and management of FH in future.

Evidence of variation in clinical practice

h) The current strategy of opportunistic case identification in the UK means that many people with FH are diagnosed only after developing established coronary heart disease. This could be addressed by the development and implementation of cascade screening strategies.

The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The

guidelines manual' provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health and Welsh Assembly Government (see appendix).

c) The areas that will be addressed by the guideline are described in the following sections.

Population

Groups that will be covered

a) Adults and children with heterozygous FH.

b) Adults and children with homozygous FH.

Groups that will not be covered

a) People with secondary hyperlipidaemia.

b) People with polygenic and combined hyperlipidaemia.

c) People with hypertriglyceridaemia and type III hyperlipoproteinaemia.

d) Children with other abnormalities of lipid metabolism, such as sitosterolaemia or physterolemia.

Healthcare setting

a) Primary, secondary or tertiary care settings dealing with case identification, diagnostic testing and the management of heterozygous FH in adults and children.

b) Tertiary care for the rare condition of homozygous FH in all age groups.

Clinical management

a) Methods for the identification of people with heterozygous or homozygous FH, specifically the role of:

- opportunistic identification
- cascade screening.

b) Methods of diagnostic testing for familial hypercholesterolaemia, used alone or in combination, including:

- positive family history
- clinical symptoms and signs
- biochemical tests made on serum/plasma samples
- DNA-based tests.

c) The management of adults and children with homozygous and heterozygous FH will address, as appropriate, lipid modification, cardiovascular risk reduction and assessment of the degree of atherosclerosis. The following specific interventions will be considered.

- Pharmacological interventions to modify blood lipids, used singly and, where appropriate, in combination. The following classes of drugs will be considered:
  - statins
  - anion-exchange resins
  - fibrates
  - nicotinic acid
  - ezetimibe (note that the guideline will incorporate the recommendations of the NICE technology appraisal on the use of ezetimibe in adults with heterozygous FH, currently in progress – see section 4.4.1)
  - fish oils.

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only where clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

- Other interventions:
  - apheresis for both adults and children with homozygous and heterozygous FH
  - liver transplantation for people with homozygous FH (up to the point of referral).

d) Advice on the following ongoing lifestyle modifications for people with FH, with cross reference and incorporation of other NICE guidelines as appropriate:

- diet (including use of plant stanols and sterols)
- exercise and regular physical activity
- smoking cessation.

e) In women of child-bearing age with FH, counselling regarding appropriate contraceptive choices will be considered due to the potential risk of adverse effects, including the use of hormonal contraception in women at high cardiovascular risk and the use of statins in pregnancy.

f) The need for continuing clinical assessment and review of people with FH. The key components of assessment and review will be considered.

g) Information and support for people with FH and their families before and after testing, including the timing and need for genetic counselling.

Areas that will not be covered

a) Techniques for liver transplantation.

b) Measurement and reporting of blood lipids (this is covered by the NICE clinical guideline on cardiovascular risk assessment, see section 4.1.1).

c) Population-based screening programmes for FH.

d) The guideline development group will consider making recommendations on the principal complementary and alternative interventions or approaches to care relevant to the guideline topic.

e) The guideline development groups will take reasonable steps to identify ineffective interventions and approaches to care. When robust and credible recommendations for re-positioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources, can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

Status

Scope

This is the final scope.

The guideline will incorporate the following NICE technology appraisals.

- Statins for the prevention of cardiovascular events in people at increased risk of developing cardiovascular disease or those with established cardiovascular disease. NICE technology appraisal 94 (2006). Available from www.nice.org.uk/TA094
- Ezetimibe for the treatment of hypercholesterolemia. Publication expected August 2007.

The following related NICE guidance will be referred to as appropriate:

- Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health intervention guidance 1 (2006). Available from www.nice.org.uk/PHI001
- Long acting reversible contraception: the effective and appropriate use of long-acting reversible contraception. NICE clinical guideline 30 (2005) Available from www.nice.org.uk/CG030.
- MI: secondary prevention in primary and secondary care for patients following a myocardial infarction. NICE clinical guideline. Publication expected March 2007.
- Cardiovascular risk assessment: the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline. Publication expected December 2007.

Guideline

The development of the guideline recommendations will begin in October 2006.

Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

Appendix: Referral from the Department of Health

The Department of Health and Welsh Assembly Government asked the Institute to develop a guideline:

'… for the NHS in England and Wales for the identification and management of patients suffering from familial hypercholesterolaemia to include advice regarding the optimal approach to case identification, cascade screening, medical management and the use of apheresis.'