NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

QUALITY STANDARDS PROGRAMME

Quality standard topic: Familial hypercholesterolaemia

Output: Full briefing paper

Introduction

This briefing paper presents a structured evidence review to help determine the suitability of recommendations from the key development sources listed below, to be developed into a NICE quality standard. The draft quality statements and measures presented in this paper are based on published recommendations from these key development sources:

Identification and management of familial hypercholesterolaemia. NICE clinical guideline 71 (2008; NHS Evidence accredited).

Structure of the briefing paper

The body of the paper presents supporting evidence for the draft quality standard reviewed against the three dimensions of quality: clinical effectiveness, patient experience and safety. Information is also provided on available cost-effectiveness evidence and current clinical practice for the proposed standard. Where possible, evidence from the clinical guideline is presented. When this is not available, other evidence sources have been used.

1 DNA testing

1.1 NICE CG71 Recommendation 1.1.12

1.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.1.12 Healthcare professionals should offer people with a clinical diagnosis of FH a DNA test to increase the certainty of their diagnosis and to aid diagnosis among their relatives.
Proposed quality statement	People with a clinical diagnosis of familial hypercholesterolaemia (FH) are offered DNA/molecular testing.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with a clinical diagnosis of FH are offered DNA/molecular testing. **Process:** The proportion of people with a clinical diagnosis of FH who receive DNA/molecular testing. Numerator – The number of people in the denominator receiving DNA/molecular testing. Denominator – The number of people with a clinical diagnosis of FH.
Definitions	Need to define clinical diagnosis of FH.

1.1.2 Clinical and cost-effectiveness evidence

No single method of diagnostic testing provides sufficient accuracy to be used exclusively. One study looked at 158 families with clinical definitions of probably (120) or definite (38) FH. Mutations were identified in 52 (33%) of the families. However, eight clinically definite FH families had no identified mutations.

In UK studies, with individuals from different parts of the country, DNA tests demonstrated a mutation in approximately 20% of those with a clinical diagnosis of possible FH; and up to 80% of those with a clinical diagnosis of definite FH. DNA tests are carried out to find the specific cause of the disorder in an individual with a clinical diagnosis of FH. The absence of an identified DNA mutation does not exclude the possibility that they have FH since the molecular techniques are not 100% sensitive. Although DNA testing has a role in increasing the certainty of diagnosis, FH can be managed without the knowledge of DNA mutation.

Knowing the specific family mutation means that the individuals relatives can be offered a simple single DNA test, where the laboratory tests for just the family mutation. Where DNA testing has excluded FH in a member of a

family, the GDG considered that the incidence of de novo mutations was so rare, that screening for these mutations or incorporating this issue in a recommendation did not offer sufficient practical utility.

1.1.3 Patient experience

No patient experience information was identified.

1.1.4 Patient safety

No issues identified relating specifically to DNA testing (see full accompanying report from the NPSA for broader themes).

1.1.5 Current practice

The national audit of the management of familial hypercholesterolaemia 2010[1] reported data for 122 sites across England, Wales, Northern Ireland and Scotland.15% of sites had DNA mutation testing for FH commissioned/funded for patients in their trust/organisation and 12% had commissioning/funding arrangements in development.

The audit reported 12% of trusts had arrangements for DNA mutation testing for FH patients attending a clinical service funded whilst 18% had arrangements which were not funded. Around 43% of trusts did not have any arrangements to offer DNA mutation testing.

The audit also reviewed a number of patient notes and reported around 22% of adults and 34% of children had a DNA test with evidence of consent, 5% of adults and around18% of children had a DNA test with no evidence of consent and 59% of adults and 36% of children had not been offered a DNA test. Only 0.9% of adults and 0.7% of children refused a DNA test whilst 13% of adults and 12% of children had no record of an offer of a DNA test.

1.1.6 Current indicators

None identified.

[1] The National audit of the management of familial hypercholesterolaemia (2010)

2 Diagnosis in children

2.1 NICE CG71 Recommendation 1.1.15 [KPI]

2.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.1.15 (KPI) In children at risk of FH because of one affected parent, the following diagnostic tests should be carried out by the age of 10 years or at the earliest opportunity thereafter: • A DNA test if the family mutation is known. • LDL-C concentration measurement if the family mutation is not known. When excluding a diagnosis of FH a further LDL-C measurement should be repeated after puberty because LDL-C concentrations change during puberty.
Proposed quality statement	Children at risk of familial hypercholesterolaemia (FH) are offered diagnostic tests by the age of 10 years.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure children at risk of FH are offered diagnostic tests by the age of 10 years. **Process:** a) The proportion of children at risk of FH who receive a DNA test by the age of 10 years if the family mutation is known. Numerator – The number of people in the denominator receiving a DNA test by the age of 10 years. Denominator – The number of children at risk of FH where the family mutation is known. b) The proportion of children at risk of FH who receive LDL-C concentration measurement by the age of 10 years if the family mutation is not known. Numerator – The number of people in the denominator receiving a LDL-C concentration measurement by the age of 10 years. Denominator – The number of children at risk of FH where the family mutation is not known.
Definitions	Children at risk of familial hypercholesterolaemia have one affected parent. Need to define age range for children.
Discussion point for TEG	What happens to children whose parents are identified after they reach 10 years old?

2.1.2 Clinical and cost-effectiveness evidence

The Simon Broome criteria can be used to diagnose FH in children under 16 years of age. However studies show clinical signs are rarely present in affected children. In a single study of 88 children with molecularly defined FH only two children displayed arcus and none had xanthomata on clinical examination. A further study showed thickening of the Achilles tendon was abnormal in 8 out of 21 individuals.

Total and LDL cholesterol concentrations increase with age and affected children can have concentrations below those expected in adults with FH. In one study of 25 babies at risk of FH because of an affected parent there was significant overlap in LDL-C concentration within mutation positive and mutation negative groups at birth. The ranges were non-overlapping at one year of age. There are issues using LDL-C concentration and DNA testing for diagnosis in children. For example, although it is expected that cholesterol will be greater than the 95th centile (taken from age- and sex-specific charts) in an affected child, in reality, concentrations are often much higher than this. LDL-C concentration within a normal range for childhood does not necessarily exclude FH in children therefore DNA diagnosis is extremely helpful in children aged under 16 years.

2.1.3 Patient experience

No patient experience information was identified.

2.1.4 Patient safety

No issues identified relating specifically to diagnosis in children (see full accompanying report from the NPSA for broader themes).

2.1.5 Current practice

The National audit of the management of familial hypercholesterolaemia 2010[2] reviewed a number of patient notes and reported that if the family mutation was known 94% of children were offered a DNA test.

2.1.6 Current indicators

None identified.

[2] The National audit of the management of familial hypercholesterolaemia (2010)

3 Specialist referral

3.1 NICE CG71 Recommendation 1.2.2 [KPI] and 1.3.1.19 [KPI]

3.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.2.2 (KPI) Healthcare professionals should offer all people with FH a referral to a specialist with expertise in FH for confirmation of diagnosis and initiation of cascade testing. 1.3.1.19 (KPI) Healthcare professionals should offer all children and young people diagnosed with, or being investigated for, a diagnosis of FH a referral to a specialist with expertise in FH In children and young people. This should be in an appropriate child/young person-focussed setting that meets the standards with the 'National service framework for children, young people and maternity services'.
Proposed quality statement	People with familial hypercholesterolaemia (FH) are referred to a specialist with expertise in FH.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with FH are referred to a specialist with expertise in FH. **Process:** a) The proportion of adults with FH referred to a specialist with expertise in FH. Numerator – The number of people in the denominator referred to a specialist with expertise in FH. Denominator – The number of adults with FH. b) The proportion of children and young people with FH referred to a specialist with expertise in FH in children and young people. Numerator – The number of people in the denominator referred to a specialist with expertise in FH in children and young people. Denominator – The number of children and young people with FH.
Definitions	Need to define the age groups for adults, children and young people. Need to define people with FH. Need a definition of a specialist.
Discussion points for TEG	Does the statement capture people with suspected FH for whom the diagnosis will be confirmed by the specialist?

3.1.2 Clinical and cost-effectiveness evidence

The recommendations on specialist referral were based on GDG consensus, no studies on referral to a specialist were identified.

The GDG noted that initiation of second line therapies with respect to healthcare setting or referral was based on their experience or knowledge of the known efficacy of statins, likelihood of high baseline LDL-concentrations, experience of use of second line drug treatments in primary care, safety and tolerability. Due to variations in individual patient characteristics, dose titrations, timing of access and additional treatment options, the GDG felt it was not possible to specify an arbitrary time point after initiation of treatment when patients should be referred.

The GDG discussed the management of children and young people with FH. It was agreed that they should be referred to a healthcare professional with expertise in providing both holistic, integrated care (in accordance with the National Service Framework for Children, Young People and Maternity Services) and managing the specific condition (FH).

3.1.3 Patient experience

No patient experience information was identified.

3.1.4 Patient safety

No issues identified relating specifically to specialist referral (see full accompanying report from the NPSA for broader themes).

3.1.5 Current practice

The national audit of the management of familial hypercholesterolaemia 2010[3] reported 94% of trusts provided outpatient services for adults with FH and 59% for children. The audit showed the service fell within the diabetes and endocrinology or chemical pathology directorate.

Around 71% of sites had a lead clinician responsible for FH care. 26% of sites had a specialist service for the management of young people with FH.

On average sites reported 1 consultant PA per week for lipid management of which on average 35% is spent on management of FH patients. 86% of sites had no lipid specialist nurses. Although all sites report some clinician and nurse time for FH patient management, it appears that this is unlikely to be adequate if GP referral numbers increase markedly.

[3] The National audit of the management of familial hypercholesterolaemia (2010)

The report 'Savings lives, savings families'[4] by Heart UK reported 41.5% of PCTs indicated there was no appropriate services in their area for children and young people and a further 26% did not know whether there were any appropriate services.

3.1.6 Current indicators

None identified.

[4] Heart UK (2012) Saving lives, saving families

4 Cascade testing

4.1 NICE CG71 Recommendation 1.2.4 [KPI] and 1.2.1

4.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.2.4 (KPI) Cascade testing using a combination of DNA testing and LDL-C concentration measurement is recommended to identify affected relatives of those index individuals with a clinical diagnosis of FH. This should include at least the first- and second- and, when possible, third-degree biological relatives. 1.2.1 Healthcare professionals should use systematic methods (that is, cascade testing) for the identification of people with FH.
Proposed quality statement	Relatives of people with a clinical diagnosis of familial hypercholesterolaemia (FH) are offered cascade testing.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure relatives of people with a clinical diagnosis of FH are offered cascade testing. **Process:** a) The proportion of first-degree relatives of people with a clinical diagnosis of FH who receive cascade testing. Numerator – The number of people in the denominator receiving cascade testing. Denominator – The number of first-degree relatives of people with a clinical diagnosis of FH. b) The proportion of second-degree relatives of people with a clinical diagnosis of FH who receive cascade testing. Numerator – The number of people in the denominator receiving cascade testing. Denominator – The number of second-degree relatives of people with a clinical diagnosis of FH. c) The proportion of third-degree relatives of people with a clinical diagnosis of FH who receive cascade testing. Numerator – The number of people in the denominator receiving cascade testing. Denominator – The number of third-degree relatives of people with a clinical diagnosis of FH. **Outcome:** Number of people with FH.
Definitions	Need to define clinical diagnosis. Relatives should include at least the first- and second- and, where possible, third-degree biological relatives.

	Method of cascade testing: In families in which a mutation has been identified, the mutation and not the LDL-C concentration should be used to identify affected relatives. In the absence of a DNA diagnosis, cascade testing using LDL-C concentration measurements should be undertaken.

4.1.2 Clinical and cost-effectiveness evidence

Several studies showed the feasibility of cascade testing in the UK, and also showed the value of approaching relatives directly. The average age of diagnosis is reduced using this strategy. In one study 200 relatives were tested of whom 121 (60%) were found to have FH demonstrating the feasibility of cascade testing using direct contact by a clinic nurse. In the second study 23% of first-degree relatives were tested of whom 29% had lipid concentrations indicative of FH. 97% of children/young people under 18 years, where the parents were directly approached were tested, of whom 32% had lipid concentrations indicative of FH. A further study from the Netherlands found 37% of first and second degree relatives tested for the genetic mutation had a diagnosis of FH confirmed.

There are specific issues associated with the diagnosis of FH in relatives of people with FH using LDL-C concentration or DNA testing. In the absence of information about the family mutation, the diagnosis of FH in a relative is made based on the elevation of fasting LDL-C concentration.

Two cost-effectiveness studies and a health technology assessment report concluded that family tracing is cost-effective compared to no tracing or universal screening. An economic analysis done for the guideline also found that the most cost-effective method for cascade testing is using DNA testing plus cascading compared to the Cholesterol method. Two cost-effectiveness studies also found that genetic based method (DNA) is cost-effective compared to no screening.

Overall, the evidence supported the use of a nationwide strategy of cascade testing as this would not then be limited by geographical boundaries. The evidence supported a direct approach to relatives.

4.1.3 Patient experience

No patient experience information was identified.

4.1.4 Patient safety

No issues identified relating specifically to cascade testing (see full accompanying report from the NPSA for broader themes) however some of the problems highlighted in tracing relatives with genetic susceptibility to

breast cancer may be relevant (especially family breakdown affecting patients' motivation and ability to contact relatives).

4.1.5 Current practice

The national audit of the management of familial hypercholesterolaemia 2010[5] reported 7% of sites had a designated clinic to test for FH by cascade testing and 19% were developing one. The report also showed around 12% of sites had a service for cascade testing commissioned/funded for the trust/organisation and another 14% were in development. 21% of sites had access to a family cascade testing system for FH in the trust and another 14% reported this was in development.

The audit also reviewed a number of patient notes and showed cascade testing had been discussed with 85% of adults with FH. For 72% of adults cascade testing had been initiated and 54% for children.

4.1.6 Current indicators

None identified.

[5] The National audit of the management of familial hypercholesterolaemia (2010)

5 Drug treatment

5.1 NICE CG71 Recommendation 1.3.1.3 [KPI]

5.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.3.1.3 (KPI) Healthcare professionals should consider prescribing a high-intensity statin to achieve a recommended reduction in LDL-C concentration of greater than 50% from baseline (that is, LDL-C concentration before treatment)
Proposed quality statement	People with familial hypercholesterolaemia (FH) receive care/treatment to achieve a reduction in LDL-C concentration of greater than 50% from baseline.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with FH receive care/treatment to achieve a reduction in LDL-C concentration of greater than 50% from baseline. **Process:** The proportion of people with FH who receive a high-intensity statin to achieve the reduction in LDL-C concentration of greater than 50% from baseline. Numerator – The number of people in the denominator achieving the reduction in LDL-C concentration of greater than 50% from baseline. Denominator – The number of people with FH. (It is not expected that the target for this process measure would be 100%) **Outcome:** Number of people with FH receiving statins who achieve the LDL-C concentration target.
Definitions	Baseline is the LDL-C concentration before treatment. Need to define people with FH. Should the statement be for adults only?

5.1.2 Clinical and cost-effectiveness evidence

FH is a condition that is characterised by elevated LDL-C concentrations which was agreed as the primary target of drug therapy. It was noted that people with FH may be prescribed drugs for lipid lowering at much earlier ages and therefore, although the side effects may be rare, the duration of drug treatment may be much longer that in the general population. The evidence showed that statins reduce both TC and LDL-C in adults with FH and adverse events are rare in the general population. Although the Simon Broome data shows a non significant decrease in CHD mortality following the advent of statins, statins are associated with a lowering of total and coronary mortality in

post MI patients, the only class of lipid lowering drug therapy to do so. Based on this evidence of safety, tolerability and efficacy, the GDG agreed that adults with FH should be treated with statins as initial therapy.

Recommendations on other drug therapy was taken from evidence which showed that nicotinic acid and fibrates affect outcomes other than LDL-C, including TG and HDL-C, so these may be additional factors in the clinical decision making around drug choice.

The GDG agreed that pre-treatment LDL-C concentration should be used as the baseline when considering offering treatment with a statin. The GDG believed that confirmation of the cholesterol concentration at diagnosis should be undertaken before considering patients for further lifelong management and investigation for FH.

Recommendations on the sequencing of different drugs were based on the consideration of indirect evidence and clinical experience, as no head-to-head trials were identified. Efficacy, safety, and tolerability were key factors considered and consideration to drug selection should be based on these factors in addition to informed patient preferences. Due to these considerations and the lack of trial evidence of significant improvement in clinical outcomes such as total mortality in either the FH or non FH populations, no sequencing of second line drugs was specified.

An economic model showed that high intensity statins are cost effective in the management of FH patients who are aged below 60 years when compared with low intensity statins.

5.1.3 Patient experience

No patient experience information was identified.

5.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the NPSA) identifies the main issues are in accurate prescribing of the associated medication and omission and delay in treatment. There is an issue that the dose used is at the upper-range. Confusion exists because this is out with ‘normal’ prescribing/dispensing and patient use.

The following incidents relating to hypercholesterolaemia (that may or may not have been familial):

- Potential inaccuracies in point-of-care testing for cholesterol levels

- Potential inaccuracies in laboratory testing of cholesterol levels related to triglyceride methodology

- Failure to act on test results through confusion between acceptable levels for LDL reading and cholesterol reading.

5.1.5 Current practice

The National audit of the management of familial hypercholesterolaemia 2010[6] reviewed patient notes and reported 44% of adults had achieved the 50% target. In adults the treated LDL-C levels showed a significant reduction from the untreated levels, down to 3.5mmol/l from a median of 6.1mmol/l which falls short of the NICE recommendation however this was only the third clinic visit for some people. Only 14% of adults were not receiving statins with the reasons clearly stated in the notes for all but 4%. The reasons stated included intolerance to statin, declining and pregnancy/breastfeeding.

In children the audit showed a reduction from 5.4mmol/l to 4.4mmol/l, a mean reduction of 20%. 44% of children were shown to not be receiving statins with 29% not stating a reason.

5.1.6 Current indicators

None identified.

[6] The National audit of the management of familial hypercholesterolaemia (2010)

6 Drug treatment in children

6.1 NICE CG71 Recommendation 1.3.1.20

6.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.3.1.20 Lipid-modifying drug therapy for a child or young person with FH should usually be considered by the age of 10 years. The decision to defer or offer lipid-modifying drug therapy for a child or young person should take into account: • their age • the age of onset of coronary heart disease within the family, and • the presence of other cardiovascular risk factors, including their LDL-C concentration.
Proposed quality statement	Children with familial hypercholesterolaemia (FH) are offered lipid-modifying drug treatment by the age of 10 years.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure children with FH are offered lipid-modifying drug treatment by the age of 10 years. **Process:** The proportion of children with FH who receive lipid-modifying drug treatment by the age of 10 years. Numerator – The number of people in the denominator receiving lipid-modifying drug treatment by the age of 10 years. Denominator – The number of children with FH. **Outcome:** Level of lipid modification achieved.
Definitions	Need to define age range for children. Need to define children with FH.

6.1.2 Clinical and cost-effectiveness evidence

The GDG agreed the treatment for children with heterozygous FH should be started early, with general agreement that this should usually be by aged 10 years (based on the median age of the included study populations, and very limited data on the use of drugs in younger children). Short term studies of statin use in children did not identify any adverse effects however longer term studies were not available.

Evidence from post-mortem studies (not individually reviewed in this guideline) showed that atherosclerosis is not evident in children younger than 10 years, but is evident in older children so treatment should be initiated before significant atherosclerosis has developed.

Evidence on drug therapy for children was more limited than for adults, so the recommendations were drafted to allow for the possible use of different drugs as first line treatment, based on clinical judgment and patient and parent/carer preference. The age of onset of cardiovascular disease within the family and presence of other cardiovascular risk factors including LDL-C concentrations in the child/young person should also be taken into account. 'Target LDL-C' levels were not specified in this guideline for children as there was an absence of evidence and values change with growth.

6.1.3 Patient experience

No patient experience information was identified.

6.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the NPSA) identified one case where the age was under 10. This was an example of omission and delay in treatment.

6.1.5 Current practice

The national audit of the management of familial hypercholesterolaemia 2010[7] reported 44% of children were not receiving a statin, of these 1% were intolerant, 8% declined, 7% were children aged 10 years and over but with low risk and for 29% the reason was not recorded.

6.1.6 Current indicators

None identified.

[7] The National audit of the management of familial hypercholesterolaemia (2010)

7 Smoking

7.1 NICE CG71 Recommendation 1.3.2.14 and 1.3.2.15

7.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.3.2.14 People with FH, especially children, who do not smoke should be strongly discouraged from starting because of their already greatly increased risk of coronary heart disease. 1.3.2.15 People with FH who smoke should be advised that, because of their already greatly increased risk of coronary heart disease, they should stop.
Proposed quality statement	People with familial hypercholesterolaemia (FH) are offered advice on the risks of smoking and, if appropriate, information on smoking cessation services.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with FH are offered advice on the risks of smoking and, if appropriate information on smoking cessation services. **Process:** a) The proportion of people with FH who receive advice on the risks of smoking. Numerator – The number of people in the denominator receiving advice on the risks of smoking. Denominator – The number of people with FH. b) The proportion of people with FH who smoke who receive information on smoking cessation services. Numerator – The number of people in the denominator receiving information on smoking cessation services. Denominator – The number of people with FH who smoke. **Outcome:** a) Number of non-smokers who start. b) Number of smokers who stop.
Definitions	Need to define people with FH.
Discussion points for TEG	Is this an FH specific issue? Is this not already being done in practice? Could this be included as part of the annual review? Smoking cessation QS is currently in development which picks up everyone who is smoking. Could this statement focus on promoting not smoking before people start?

7.1.2 Clinical and cost-effectiveness evidence

Recommendations on smoking advice were based on GDG consensus as no studies on smoking cessation in people with FH were identified.

General recommendations on lifestyle from other NICE guidance for example 'Brief interventions and referral for smoking cessation in primary care and other settings' (NICE public health intervention guidance 1) were referenced and specific factors stressed as appropriate for individuals with FH.

7.1.3 Patient experience

No patient experience information was identified.

7.1.4 Patient safety

No issues identified relating specifically to smoking (see full accompanying report from the NPSA for broader themes).

7.1.5 Current practice

The national audit of the management of familial hypercholesterolaemia 2010[8] reported 82% of sites had smoking cessation support services that FH patients could be referred to. These services included hospital/PCT/LHB or NHS stop smoking services. The audit also showed around 90% of trusts provided information leaflets containing information on smoking.

The audit also reviewed a number of patient notes and reported 96% of adults and 33% of children had their smoking status reported. 38% of adults were offered a referral to a smoking cessation service, 28% were given written advice and 34% received no referral or advice. The audit also showed that around 72% of adults and 43% of children were given advice about smoking.

7.1.6 Current indicators

None identified.

[8] The National audit of the management of familial hypercholesterolaemia (2010)

8 Annual review

8.1 NICE CG71 Recommendation 1.5.1.1 [KPI]

8.1.1 Relevant NICE clinical guideline recommendations and proposed quality statement

Guideline recommendations	1.5.1.1 (KPI) All people with FH should be offered a regular structured review that is carried out at least annually.
Proposed quality statement	People with familial hypercholesterolaemia (FH) are offered a structured review at least annually.
Draft quality measure	**Structure:** Evidence of local arrangements to ensure people with FH are offered a structured review at least annually. **Process:** The proportion of people with FH who receive a structured review at least annually. Numerator – The number of people in the denominator whose most recent structured review is no later than 12 months after the last previous review or diagnosis. Denominator – The number of people with FH.
Definitions	A structured review should include: • Recording progress of cascade testing among relatives • Update of family pedigree and note changes in the coronary heart disease status of relatives • Assessment of any symptoms of coronary heart disease and smoking status • Measurement of fasting lipid profile • Discussion of concordance with medication, possible side effects of treatment the patient may be experiencing • Discussion of any changes in lifestyle or lipid-modifying drug therapy that may be required to achieve the recommended LDL-C concentration.
Definitions	Need to define people with FH.
Discussion points for TEG	Should the review for children include monitoring of growth and pubertal development? Which aspects of the review are most important?

8.1.2 Clinical and cost-effectiveness evidence

The recommendations on annual review were based on GDG consensus. Due to the lack of evidence to support the recommendations the GDG referred to

the National Service Framework (NSF) for Coronary Heart Disease (2000)[9] and specifically the recommendations on effective policies for both primary and secondary prevention of CHD. People with FH clearly meet the NSF criteria for 'high risk' which includes those with multiple risk factors for heart disease.

Evidence was available for some aspects of the annual review:

Recommendations for monitoring cholesterol were as for people with FH (inclusive of children), again due to an absence of evidence specific for children.

Routine monitoring of growth and pubertal monitoring was recommended, although the limited evidence does not show any disturbances in growth or pubertal development. This is standard paediatric care, as is monitoring of BMI/weight in adults, but the reasons for monitoring of growth/weight are different in children and adults (the effect on growth compared with overweight/obesity respectively). Parents may be concerned that the drugs will affect the child's growth, so any drug should be initiated in children only after a full, informed discussion.

8.1.3 Patient experience

No patient experience information was identified.

8.1.4 Patient safety

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS care (see Appendix A). A comprehensive analysis of recent reported incidents (please see full accompanying report from the NPSA) identified a small number of incidents related to hypercholesterolaemia (that may or may not have been familial) suggesting:

- Failure to monitor treatment as planned, including patients unintentionally lost to follow up, and follow-up test results not reviewed or acted on.

8.1.5 Current practice

The national audit of the management of familial hypercholesterolaemia 2010[10] reported 67% of trusts routinely offered FH patients an annual review.

The audit also reviewed a number of patient notes and reported 90% of adults and 92% of children had their weight recorded at their most recent clinic

[9] National Service Framework (NSF) for Coronary Heart Disease (2000)
[10] The National audit of the management of familial hypercholesterolaemia (2010)

appointment. The audit also reported 96% of adults and 33% of children had their smoking status reported.

The audit reported 82% of adults and 88% of children had a review carried out at least annually since the initial diagnosis in secondary care. 1.4% of adults had a review in primary care. Of those who had a review in secondary care, around 95% of adults and 64% of children had evidence in their notes that the annual review covered response to drug treatment, 85% of adults and 61% of children covered side effects, 68% of adults and 37% of children covered CVD status, 72% of adults and 78% of children covered lifestyle and 47% of adults and 30% of children covered progress with cascade testing.

8.1.6 Current indicators

None identified.

Appendix A: Definition of patient safety

The National Patient Safety Agency (NPSA) defines patient safety in the following terms:

Every day more than a million people are treated safely and successfully in the NHS, but the evidence tells us that in complex healthcare systems things will and do go wrong, no matter how dedicated and professional the staff. When things go wrong, patients are at risk of harm, and the effects are widespread and often devastating for patients, their families and the staff involved. Safety incidents also incur costs through litigation and extra treatment, and in 2009/10 the NHSLA paid out approximately £827, 000,000 in litigation costs and damages. These incidents are often caused by poor system design rather than the error of individuals i.e. 'they are an accident waiting to happen'.

In short patient safety could be summarised as 'The identification and reduction of risk and harm associated with the care provided to patients 'or 'Preventing patients from being harmed by their treatment'. Examples of this might be 'operating on or removing the wrong organ, ten times the dose of an opioid, giving a colonoscopy to the wrong patient with the same name as someone else in the waiting room etc.' These risks are unlikely to be identified through clinical trials or traditional evidence bases and so other evidence sources, such as the National Reporting and Learning System, need to be analysed to highlight the risks and improve system development. This does not however give an accurate picture of prevalence in that way that methods such as casenote review may do.

On 1 June 2012 the key functions and expertise for patient safety developed by the National Patient Safety Agency (NPSA) transferred to the NHS Commissioning Board Special Health Authority. For more information, please see www.commissioningboard.nhs.uk and www.nrls.npsa.nhs.uk.