NICE support for commissioning for familial hypercholesterolaemia

August 2013

1 Introduction

Implementing the recommendations from NICE guidance and other NICE-accredited guidance is the best way to support improvements in the quality of care or services, in line with the statements and measures that comprise the NICE quality standards. This report:

- highlights quality improvement areas that have potential implications for commissioners
- considers the cost of implementing the changes needed to achieve the quality standard at a local level
- identifies where potential costs may be incurred and where cost savings may be made
- directs commissioners and service providers to a package of support tools that can help them implement NICE guidance and redesign services.

NICE quality standards describe high-priority areas for quality improvement in a defined care or service area. Each standard consists of a prioritised set of specific, concise and measurable statements. They draw on existing guidance, which provides an underpinning, comprehensive set of recommendations, and are designed to support the measurement of improvement. For more information see NICE quality standards.

NHS England’s CCG outcomes indicator set is part of a systematic approach to promoting quality improvement. The outcomes indicator set provides clinical commissioning groups (CCGs) and health and wellbeing boards with comparative information on the quality of health services commissioned by
CCGs and the associated health outcomes. The set includes indicators derived from NICE quality standards.

Using the quality standard to commission high-quality care for people with familial hypercholesterolaemia (FH) will help deliver:

- improvements in domain 1: preventing people from dying prematurely, through a reduction in under 75 mortality from cardiovascular disease
- the action identified in the Cardiovascular Disease Outcomes Framework, to better identify very high-risk families and individuals including those with FH.

Commissioners can use the quality standards to improve services by including quality statements and measures in the service specification of the standard contract and establishing key performance indicators as part of tendering. They can also encourage improvements in provider performance by using quality standard measures in association with incentive payments such as using the Commissioning for quality and innovation (CQUIN) payment framework. NICE quality standards provide a baseline against which improvements can be measured and rewarded, enabling commissioners to address gaps in service provision, support best practice and encourage evidence-based and care.

This report on the FH quality standard should be read alongside:

- Familial hypercholesterolaemia. NICE clinical guideline 71 (2008).
- Integrated services for the prevention of cardiovascular disease. NICE support for commissioning (2012).

### 2 Overview of familial hypercholesterolaemia

The best way to limit the damage caused by coronary heart disease is to identify those at risk as early as possible. Diagnosing and treating people with
heterozygous familial hypercholesterolaemia (FH)\(^1\) and testing their families through a process of cascade testing provides one of the best opportunities for preventing cardiovascular disease\(^2\).

FH is an inherited condition caused by an alteration in a gene, which results in a high cholesterol concentration in the blood. Raised cholesterol concentrations are present from birth and lead to early development of atherosclerosis and coronary heart disease\(^3\). FH is diagnosed using a combination of family history of premature heart disease, clinical signs, and cholesterol concentration, or DNA-based evidence of a genetic mutation.

Improving awareness among healthcare professionals of the benefits of cascade testing and encouraging collaboration between CCGs and regional networks to implement cascade testing will improve the identification of people with FH\(^4\). Despite identification of FH being cost effective, it is estimated that only 15–20% of people with FH have been diagnosed.

Early treatment with lipid-lowering drugs can increase life expectancy to near normal. If 50% of the predicted relatives of people with FH were diagnosed and received treatment, the NHS could save £1.7 million per year on healthcare for heart disease. Implementing cascade testing would save the NHS £1.4 million per year\(^5\).

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\(^1\) The scope of the quality standard is people with heterozygous FH. Homozygous FH has been excluded from the quality standard because it has a low incidence and people with homozygous FH need specialist care.


\(^3\) FH is transmitted from generation to generation in such a way that siblings and children of a person with FH have a 1 in 2 chance (50:50 risk) of also having FH. For further information, please see the quality standard.

\(^4\) Heart UK (2012) Saving lives, saving families: the health, social and economic advantages of detecting and treating familial hypercholesterolaemia. London: Heart UK

\(^5\) Heart UK (2012) Saving lives, saving families: the health, social and economic advantages of detecting and treating familial hypercholesterolaemia. London: Heart UK
2.1 Epidemiology of familial hypercholesterolaemia

FH is not considered a rare disease, with an estimated prevalence in the UK of around 1 in 500, which means that approximately 120,000 people are affected; around 100,000 in England.

However, around 85% of these are currently undiagnosed\(^6\), around 86,000 in England. Left untreated, more than 50% of men with FH will develop coronary heart disease by the age of 50 years and more than 50% of women with FH will develop coronary heart disease by the age of 60 years\(^7\).

3 Commissioning and resource implications

In England, CCGs are responsible for commissioning for FH\(^8\). In order to improve outcomes for people with FH, CCGs should:

- Review their local commissioning arrangements for FH.
- Commit to improving the identification of people with FH as a priority within their integrated local plans for cardiovascular disease prevention.
- Collaborate with neighbouring CCGs and networks, such as the strategic clinical network for cardiovascular disease, to help develop a cost-effective regional approach to service development and clinical pathways for people with FH.

Figure 1 summarises the service components and quality improvements areas for people with FH. It demonstrates how improving quality can help deliver improved outcomes for people with FH.

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\(^6\) Seed M et al (2012) Current statin treatment, DNA testing and cascade testing of UK patients with familial hypercholesterolaemia. Primary Care Cardiovascular Journal, 5, 181-185


Figure 1 Commissioning service components for familial hypercholesterolaemia

Outcomes:
- Reduction in under 75 mortality from cardiovascular disease (NHS OF, CCG-OF)
- Identify very high risk families and individuals including those with FH (CVD outcomes framework)

Identification and assessment for clinical diagnosis of FH in adults:
- Assess adults with baseline cholesterol >7.5mmol/l
- Exclude secondary causes of hypercholesterolaemia
- Use 2 measurements of LDL-C concentration and Simon Broome criteria

Referral for specialist assessment and DNA testing:
- Protocol for referral for specialist assessment
- Confirmation of clinical diagnosis by a healthcare professional with expertise in FH
- Offer of DNA testing

Drug treatment in adults:
- Lipid-modifying drug treatment to reduce LDL-C concentration by more than 50% from baseline
- Drug treatment initiated by healthcare professional with expertise in FH

Diagnosis and drug treatment in children:
- Offer children at risk of FH diagnostic tests by the age of 10 years
- Assess children with FH for lipid-modifying treatment by the age of 10 years
- Deliver care in child-focused setting

Annual review:
- Offer structured review at least annually

Opportunistic, in primary and secondary care
- Healthcare professionals with expertise in FH, with access to a wider MDT

Healthcare professionals with expertise in FH, Primary care using shared-care arrangements

CCG: clinical commissioning group
CVD: cardiovascular disease
NHS OF: NHS Outcomes Framework
CCG-OF: Clinical commissioning group outcomes indicator set
FH: familial hypercholesterolaemia
MDT: multi-disciplinary team
The cost of improving outcomes for people with FH depends on current local and regional practice, and the progress organisations have made in implementing NICE and NICE-accredited guidance for FH. There is no fixed or nationally agreed price for an FH service so this should be negotiated locally.

Table 1 summarises the commissioning and resource implications for improving the quality of FH services.

**Table 1 Potential commissioning and resource implications of achieving the quality standard for familial hypercholesterolaemia**

<table>
<thead>
<tr>
<th>Quality improvement area</th>
<th>Commissioning implications</th>
<th>Estimated resource impact per 100,000 population</th>
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<tbody>
<tr>
<td>Identification and assessment for clinical diagnosis of FH in adults (quality statement 1)</td>
<td>Consider how to raise local awareness of FH among healthcare professionals, especially those working in GP surgeries, pharmacy and cardiology services. This should increase the number of people being assessed for a clinical diagnosis of FH.</td>
<td>Variable depending on clinical model used and timescale of implementation. Not considered significant cost if identification is opportunistic. Where case-finding takes place, a local cost assessment of cost should be made.</td>
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<tr>
<td>Specialist assessment including DNA testing (quality statements 2 and 3)</td>
<td>Develop pathways for the referral of people with FH to a healthcare professional with expertise in FH who can provide specialist assessment and offer DNA testing. Collaborate with neighbouring CCGs and networks, such as the strategic clinical network for cardiovascular disease, to help develop a cost-effective regional approach to service development and clinical pathways for people with FH.</td>
<td>Variable. If 10% (16) of undiagnosed cases are referred, cost impact may be around £3000. DNA testing costs are variable. If 10% of undiagnosed cases are tested, cost impact may be around £4800. A local assessment should be made of cost impact of providing counselling.</td>
</tr>
<tr>
<td>Cascade testing (quality statement 5)</td>
<td>Ensure there are protocols and systems for cascade genetic testing for people with monogenic FH. This should include appropriate arrangements for confidentiality and</td>
<td>If 10% (16) of undiagnosed cases are offered cascade testing, cost impact may be around £14,000.</td>
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<tr>
<td><strong>Drug treatment in adults (quality statement 6)</strong></td>
<td>Ensure that pathways identify who is responsible for initiating drug treatment and ongoing monitoring.</td>
<td>Variable depending on drug treatment and dose. If 10% (16) of undiagnosed cases are offered drug treatment, cost impact may be around £2700–£3900 per year. Savings from cardiovascular events avoided may be around £9200 per year if all undiagnosed people are identified and treated. Local assessment is encouraged.</td>
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<tr>
<td><strong>Diagnosis and treatment of children (quality statements 4 and 7)</strong></td>
<td>Ensure pathways identify a specialist with expertise in FH in children and young people to offer diagnostic tests and treatment for children and young people.</td>
<td>Variable depending on drug treatment and dose. If 10% of undiagnosed cases are offered drug treatment, cost impact may be less than £1000 per year to treat around 3 children. Cost impact of annual reviews is variable depending on service model. If 10% of undiagnosed cases are reviewed, cost impact may be less than £2000 in secondary care to treat around 3 children.</td>
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<tr>
<td><strong>Annual review of adults (quality statement 8)</strong></td>
<td>Ensure that pathways identify who is responsible for offering structured annual review, at least annually.</td>
<td>Cost impact of annual reviews is variable depending on service model. If 10% (16) of undiagnosed cases are reviewed, cost impact may be around £1800 in secondary care. If provided in primary care, no significant cost impact is anticipated.</td>
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FH Familial hypercholesterolaemia.

### 4 Commissioning implications and cost impact

This section considers the commissioning implications and potential resource impact of implementing the recommendations to achieve the NICE quality standard for FH.
4.1 Identification and assessment for clinical diagnosis of FH in adults

Quality statement 1: Diagnosis
Adults with baseline total cholesterol above 7.5 mmol/l are assessed for a clinical diagnosis of familial hypercholesterolaemia (FH).

It is estimated that only 15–20% of people with FH are currently diagnosed (see section 2). This suggests that there may be around 150–160 people with undiagnosed FH per 100,000 population in England.

Clinical commissioners should consider how to raise awareness of FH among relevant healthcare professionals such as GPs, pharmacy and cardiology services. This should improve the opportunistic identification of people with very high cholesterol, for example following routine blood tests or an NHS health check, who are then assessed for a clinical diagnosis of FH.

Commissioners could work with GPs with a special interest (GPSI) in cardiovascular disease or genetics to establish a network to provide education, support and updated information for relevant healthcare professionals. This will help healthcare professionals to make appropriate assessment and referral to a healthcare professional with expertise in FH (see section 4.2).

Commissioners could ask their pathology service to add a note to lipid test results to alert healthcare professionals when an assessment for FH may be indicated.

It is anticipated that assessment for a clinical diagnosis of FH can be done opportunistically, using existing resources. The cost of assessment is not considered to be significant. If proactive case-finding is undertaken, there may be a cost impact. This should be assessed locally.
Commissioners may wish to refer to the NICE support for commissioning on Integrated commissioning for the prevention of cardiovascular disease, which includes advice on commissioning NHS health checks and on FH.

### 4.2 Specialist assessment including DNA testing

**Quality statement 2: Specialist referral**

People with a clinical diagnosis of familial hypercholesterolaemia (FH) are referred for specialist assessment.

**Quality statement 3: DNA testing**

People with a clinical diagnosis of familial hypercholesterolaemia (FH) are offered DNA testing as part of a specialist assessment.

Following initial clinical diagnosis and using documented referral criteria, healthcare professionals should refer people with a clinical diagnosis of FH to a healthcare professional with expertise in FH, who can make a specialist assessment, offer DNA testing and confirm the clinical diagnosis.

The cost of specialist assessment will depend on the local service model used. A first appointment in an outpatient clinic with a consultant cardiologist is £166 and a first appointment with a consultant endocrinologist is £190.

Commissioners should locally assess the anticipated number of people who will be identified each year and the cost impact of specialist referrals. If 10% (16) of the estimated 160 people per 100,000 population were referred for specialist assessment in 1 year, assuming an outpatient cost of £180, there would be a cost impact of around £3000.

Pathways for specialist assessment should be determined locally. Most people with FH in England have specialist assessment and clinical diagnosis by expert healthcare professionals in a lipid clinic. There is good coverage of lipid clinics nationally, although commissioners should review local
accessibility. Service models vary and healthcare professionals with expertise in FH may also be based in other cardiology or genetic services.

Commissioners should ensure that their designated provider of specialist assessment complies with the definition in quality statement 2:

- A specialist assessment should be performed by a healthcare professional with expertise in FH who has access to the wider skills of a multidisciplinary team. This team should include a dietitian, cardiologist and paediatrician, and a clinical genetic specialist to take a family history and obtain informed consent for a DNA test. For children and young people, this should be a specialist with expertise in FH in children and young people.

Commissioners should ensure that the healthcare professional with expertise in FH can offer and explain the benefits of DNA testing to improve the certainty of diagnosis and enable cascade testing for people with monogenic FH (see section 4.3). The clinical genetic specialist who takes a family history and obtains informed consent for a DNA test could be a nurse specialist.

In 2010, it was estimated that only 15% of specialist services had access to funded DNA testing\(^9\). It is estimated that DNA testing costs between £100 and 500 per person, depending on whether the latest technology is used\(^10\). Commissioners should explore options that may reduce the cost of genetic tests, such as procuring next-generation sequencing technologies or using cost–volume agreements. They should note that after the confirmation of monogenic FH in one family member by DNA testing, genetic tests for other family members should be cheaper because they will focus on only one genetic mutation.

If 10% (16) of the estimated 160 undiagnosed people with FH per 100,000 population were referred for a DNA test in 1 year, assuming a midpoint cost of

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\(^9\) The National audit of the management of familial hypercholesterolaemia (2010).

\(^10\) £100 (the lower estimate) is derived from expert opinion. The higher estimate of £500 taken from [http://www.pcc-cic.org.uk/sites/default/files/articles/attachments/primary_care_service_framework_familial_hypercholesterolaemia.pdf](http://www.pcc-cic.org.uk/sites/default/files/articles/attachments/primary_care_service_framework_familial_hypercholesterolaemia.pdf)
£300, there would be a cost impact of around £4800. Counselling from a
trained professional, such as a nurse specialist, should be available. There
may be a cost impact locally if there is not enough capacity to offer
counselling or if genetic testing is not currently offered. If proactive
case-finding is undertaken, there may be a cost impact and this should be
assessed locally.

4.3 Cascade testing

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<th>Quality statement 5: Cascade testing</th>
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<tr>
<td>Relatives of people with a confirmed diagnosis of monogenic familial hypercholesterolaemia (FH) are offered DNA testing through a nationwide, systematic cascade process.</td>
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Networks need to collaborate to facilitate a nationwide, systematic cascade process for people with monogenic FH (see section 3). Working with networks, commissioners should ensure:

- There are protocols and systems for cascade genetic testing, including appropriate arrangements for confidentiality and information-sharing with other family members who may live in a different network or CCG area.
- There are healthcare professionals with an expertise in FH and genetics, such as nurse specialists, who can offer information about the benefits of DNA and cascade testing for FH and develop family pedigrees/trees.
- Healthcare professionals with expertise in FH have access to software for recording family pedigrees and the results of DNA and cascade tests. There is a database called PASS that can support this and CCGs should ensure that the service coordinating genetic and cascade testing has access to this.

Based on the costing template for NICE clinical guideline 71, if 10% (16) of the estimated 160 undiagnosed people with FH per 100,000 population were cascade tested in 1 year, using a midpoint DNA test cost of £300, it is
estimated that there would be an incremental cost of around £14,000. However, the time taken to identify people and conduct cascade testing and the way the service is commissioned varies, so the cost impact may be spread across several years. In areas where next-generation sequencing technology DNA testing is available at a lower cost, the cost impact will be lower.

Commissioners may wish to refer to the implementation advice for NICE clinical guideline 71, which considers implementation issues specific to cascade testing recommended in NICE guidance.

The Primary care services framework for familial hypercholesterolaemia and the Heart UK familial hypercholesterolaemia commissioning toolkit both contain service models that could be adapted locally when developing services for referral and genetic testing.

Commissioners may wish to refer to the NICE shared learning examples of implementing services for people with FH.

4.4 Drug treatment in adults

**Quality statement 6: Drug treatment in adults**

Adults with familial hypercholesterolaemia (FH) receive lipid-modifying drug treatment to reduce LDL-C concentration by more than 50% from baseline.

Commissioners should ensure that their pathway identifies who is responsible for initiating drug treatment in adults (16 years and over) who have been diagnosed with FH.

The costs of drugs to reduce LDL-C concentration vary depending on the choice of drug and the dose, as determined during the specialist assessment. Based on the costing template for NICE clinical guideline 71 with updated costs applied, an average cost of statins or other lipid-modifying drug
treatment is around £255–£375 per person per year. Applying the principles of the costing template for NICE clinical guideline 71, if 10% (16) of the estimated 160 undiagnosed people with FH per 100,000 population are offered drug treatments, the incremental cost per year is estimated to be around £2700–£3900.

Early treatment will help prevent cardiovascular events. Applying the principles of the costing template for NICE clinical guideline 71 to the number of people choosing drug treatment, there may be around two cardiovascular events avoided per 100,000 population. The commissioning and benchmarking tool for the prevention of cardiovascular disease estimated that an average weighted cost for a cardiovascular event is around £4600. It is expected that savings from cardiovascular events avoided may be around £9200 and would occur annually. There would be wider societal savings, including social care costs avoided.

For ongoing monitoring and prescribing, commissioners may wish to consider shared-care agreements with GPs. The agreement should clearly specify the dose of high-intensity treatment needed and monitoring criteria.

4.5 Diagnosis and treatment of children

Quality statement 4: Diagnosis in children
Children at risk of familial hypercholesterolaemia (FH) are offered diagnostic tests by the age of 10 years.

Quality statement 7: Drug treatment in children
Children with familial hypercholesterolaemia (FH) are assessed for lipid-modifying drug treatment by a specialist with expertise in FH in a child-focused setting by the age of 10 years.

Clinical commissioners should identify a specialist with expertise in FH in children and young people to offer diagnostic tests and treatment for children and young people (aged 15 years and younger). They may need to work
closely with specialised commissioners of children’s cardiology or genetic services.

Commissioners should ensure that children being offered diagnostic tests and receiving treatment are seen in a child-focused setting. The specialist should work closely with other healthcare professionals with expertise in FH (see section 4.2) to ensure there is an integrated FH pathway for families.

Costs of diagnosis for children will vary depending on the specialty that the specialist service is in, but may be around £220 for an outpatient appointment with a consultant paediatric cardiologist. Using assumptions in the costing template for NICE clinical guideline 71, if 10% of the estimated 160 undiagnosed people with FH per 100,000 population are identified, around 3 may be children or young people aged 15 years and younger. Using children and young people aged 15 years and younger as a proxy for children under 10 years, the cost of diagnosis by specialist assessment including DNA testing is anticipated to be less than £2000.

The costs of drugs will vary depending on the choice of drug and the dose, as determined during the specialist assessment. Based on the costing template for NICE clinical guideline 71 with updated costs applied, an average cost of statins or other lipid-modifying drug treatment is around £210–£260 per child per year. Applying the principles of the costing template for NICE clinical guideline 71, if 10% of the estimated 160 people with undiagnosed FH per 100,000 population are offered drug treatments, using those aged 15 years and younger as a proxy for children under 10 years, the incremental cost per year for children is estimated to be less than £1000.

4.6 Annual review

Quality statement 8: Annual review
People with familial hypercholesterolaemia (FH) are offered a structured review at least annually.
Commissioners should ensure that their pathway identifies who is responsible for offering a structured review of people with FH, at least annually. Structured annual review can be offered by a range of providers such as lipid clinics or GPSIs who are qualified to offer all of the components listed in the definition of structured review in quality statement 8.

The cost impact would vary depending on the model of delivery. If 10% (16) of the 160 undiagnosed people with FH per 100,000 population receive a review, if it takes place in secondary care, there may be an incremental cost of around £1800 for specialist outpatient follow-up appointments. If the annual review is performed by GPs in primary care, it is anticipated that costs will be covered by existing resources. The cost will vary according to the structure and staffing of the service, reflecting a mixed model of provision across the locality. A local assessment of the potential cost impact should be made.

5 Other useful resources

5.1 Policy documents

- Department of Health (2013) Cardiovascular disease outcomes strategy: improving outcomes for people with or at risk of cardiovascular disease

5.2 Useful resources

- Primary Care Commissioning (2010) Primary care service framework: familial hypercholesterolaemia
- Heart UK (2012) Familial hypercholesterolaemia toolkit

5.3 NICE implementation support

- Familial hypercholesterolaemia. NICE implementation advice (2012).
- Familial hypercholesterolaemia. NICE audit support (2008).
- Familial hypercholesterolaemia. NICE costing report (2009).
- Familial hypercholesterolaemia. NICE slide set (2012).
• **Integrated commissioning for the prevention of cardiovascular disease.**
  NICE support for commissioning (2012).

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