



Public Health  
England

Protecting and improving the nation's health

# Familial Hypercholesterolaemia

## Implementing a systems approach to detection and management

**NICE** National Institute for  
Health and Care Excellence

**NHS**  
England



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## Foreword

Over the past 40 years progress in both treatment and prevention of heart disease has resulted in a halving of death rates. Over this time we've also made huge strides in the field of genomics. Our understanding of inherited heart conditions and the genes that cause them has grown exponentially.

Translating a rapidly evolving science into practice, however, has its challenges and despite how far we've come there are still enormous gains to be made in identifying and treating those with genetic predispositions such as Familial Hypercholesterolaemia (FH).

More than 85% of people with FH in the UK are unaware that they have the condition and that they are at risk of premature heart disease. Untreated, people aged 20-39 with FH have a 100-fold increased risk of death from heart disease compared to those of a similar age without FH, and so early identification and treatment are absolutely crucial.

By searching GP records for those at risk and offering DNA testing to family members of people diagnosed with FH we can start to address this hidden burden. The purpose of this guide is to support local areas to develop services that identify and treat people with FH as early as possible to ensure they can enjoy a long and healthy life.

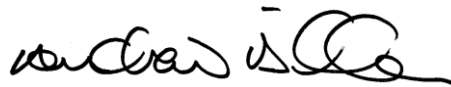
Written collaboratively by PHE, NICE, NHS England, HEART-UK and the British Heart Foundation, this resource highlights that improving care for those with Familial Hypercholesterolaemia will need a coordinated effort and a whole-system approach.



**Duncan Selbie**  
Chief Executive PHE



**Professor Huon Gray**  
National Clinical Director  
for Heart Disease for  
NHS England



**Sir Andrew Dillon**  
Chief Executive NICE

## Executive summary

The purpose of this guide is to support commissioners and service providers in implementing the recently updated NICE Guideline (CG71) Familial hypercholesterolaemia: identification and management.

Familial Hypercholesterolaemia (FH) is a common genetic condition that causes a high cholesterol concentration in the blood, leading to an increased risk of premature coronary heart disease. Management of FH with lipid-lowering therapy, eg statins, is highly effective; however, most people with FH are undiagnosed and are therefore untreated.

Early detection of FH is important as, if started early enough in life, treatment gives patients the same life expectancy as the general population. Systematic searching of GP records to find those at high risk of FH is an important way of identifying affected individuals, also key to early diagnosis is cascade testing. Cascade testing is the process of systematically offering DNA testing to the relatives of affected individuals. This allows people to be identified and treated at a young age.

Access to FH services across the country at present is patchy, with only around a third of the population in England covered by services offering diagnosis and management of FH. There is no standard service delivery model and approaches differ based on local circumstances. Case studies included as appendices illustrate these different approaches.

This implementation guide aims to provide practical support to organisations, helping them to identify the gaps in the provision of FH services in their local area, and helping them address these gaps in line with the recently updated NICE guidance.

## Acknowledgements

The Familial Hypercholesterolaemia Implementation Guide was developed in collaboration with Public Health England, NICE, NHS England, British Heart Foundation and HEART-UK. Partners all contributed both to the core content of the guide as well as to case studies and supporting materials presented in appendices. This work was also supported by the Familial Hypercholesterolaemia Steering Group whose membership includes representatives from a wider group of organisations including NHS providers.

## Purpose of the document

This implementation resource builds on the recently updated (2017) [NICE FH guideline \(CG71\)](#). It aims to set out measures that could be taken to improve the diagnosis and treatment of FH, based on the available evidence and expertise. It aims to:

- highlight and explain the new recommendations included in the updated NICE guideline
- outline key messages for professionals and the public
- outline relevant national and European policy documents
- support local commissioners to make the case for developing FH services
- support primary care to deliver the guidelines and local areas to organise and plan their services
- share best practice through service development examples and case studies
- provide information on, and links to, other key documents to support commissioners

## Who this document is for

This document is for local commissioners and service providers, including specialised commissioning, CCGs, STPs, ICSs, hospital trusts, primary care, lipid services and genetics services

## Checklist for action

Readers of this implementation guide should consider the following actions:

- **Review existing service delivery**  
Are there services in your area? (see [current service coverage](#)) Are services in your area following NICE Guidance on FH? (see [delivering FH services](#))
- **Make the case for implementation**  
Why are FH services a priority for implementation? (see [policy drivers](#) and evidence of [cost-effectiveness](#))
- **Consider service delivery models**  
What are the components of quality care in FH, and which service model would best deliver this in your area? (see [key messages](#) and [delivering FH services](#))
- **Consider commissioning models**  
Considering existing relationships and infrastructure, which commissioning arrangements would best support services? (see [commissioning models](#))
- **Consider monitoring and evaluation**  
How will FH services in your area be monitored and evaluated? (see [ongoing assessment and monitoring](#), and [FH registry](#))

# Key messages

## Facts and figures

In some people, a high cholesterol concentration in the blood is caused by an inherited genetic disorder known as familial hypercholesterolaemia (FH).

FH affects approximately between 1 in 250 to 1 in 500 people in the UK, which is about 130,000 - 260,000 people, including children<sup>1</sup>.

Most people with FH have inherited a defective gene from only one parent and are therefore heterozygous. Less frequently, a person will inherit a genetic defect from both parents and will have homozygous FH.

The disease is transmitted from generation to generation in such a way that siblings and children of a person with FH have a 50% risk of inheriting FH.

The elevated cholesterol concentration that characterises heterozygous FH leads to a greater than 50% risk of coronary heart disease in men by the age of 50 years and at least 30% in women by the age of 60 years.

Diagnosing and treating people with FH contributes to reducing the burden of cardiovascular disease (CVD) and reducing premature mortality due to CVD.

## Understanding risk

It is important for individuals to know their risk of developing CVD. Serum cholesterol levels contribute significantly to lifetime risk of CVD. Many people will have a raised cholesterol due to polygenic and lifestyle factors, but the chances of having monogenic FH increases above total cholesterol levels of 7.5mmol/L. For this reason NICE states that:

- An individual may be at risk of FH if they have:
  - total cholesterol greater than 7.5mmol/L **and/or**
  - a personal or family history of early coronary heart disease (a coronary event before 60 years for yourself or a first degree relative – parents, sibling, child)

NHS Health Checks (NHS HC), for those aged 40-74 years, presents an opportunity to identify people with FH through cholesterol testing. NHS HC Best Practice

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<sup>1</sup> Please note, current accepted evidence states the prevalence is likely to be 1 in 500, but recent research suggests this may be closer to 1 in 250 in the UK and some countries in Europe



Guidance states that people who have a total cholesterol level over 7.5mmol/L **and/or** have a personal or family history of premature coronary heart disease should be referred to their GP for consideration of FH.

NICE also recommends that coronary heart disease risk estimation tools, such as QRISK2 and those based on the Framingham algorithm, should not be used because people with FH are already at a high risk of premature coronary heart disease.

## Diagnosis

Most people with FH are undiagnosed and are therefore untreated.

Early detection of FH is important as treatment is likely to be more effective the sooner it is started.

To enable early detection NICE guidance recommends that primary care records should be systematically searched for people:

- younger than 30 years, with a total cholesterol concentration greater than 7.5 mmol/L **and**
- 30 years or older, with a total cholesterol concentration greater than 9.0 mmol/L as these are the people who are at highest risk of FH

Cascade testing allows children to be diagnosed at a young age, reducing their lifetime risk. NICE guidance says that children of parents with FH should be tested before they reach age 10 years, or at the earliest opportunity thereafter.

NICE recommends that people who meet clinical criteria for FH should be referred to a specialist service for DNA testing to confirm their diagnosis (index case testing).

NICE also recommends that cascade testing (using DNA testing) should be carried out to identify affected relatives of people with a diagnosis of FH.

All local areas should provide access to DNA testing for people with suspected FH, and cascade testing for family members of those with confirmed FH.

Cascade testing to identify and diagnose relatives of people with suspected FH is highly cost-effective.

## Treatment

NICE says that adults with FH should initially be offered a high-intensity statin at the lowest acquisition cost as treatment unless contraindicated or not tolerated.

NICE also says that children with FH should, with their parent(s), be offered specialist advice in a child-focused setting regarding starting a statin by the age of 10 years, or at the earliest opportunity thereafter. A statin licensed for use in the appropriate age group should be considered.



# Context

## Introduction

Raised cholesterol is now the 4th leading risk factor contributing to deaths in the UK, ranking higher than blood glucose or alcohol [1]. Approximately 6 in 10 adults in England have raised cholesterol levels (hypercholesterolaemia) sufficient to contribute to a risk of developing CVD [2] (2011).

Familial hypercholesterolaemia (FH) is an inherited cardiac condition resulting in high levels of cholesterol. A raised cholesterol concentration in the blood is present from birth and may lead to early development of coronary and other vascular disease, which can be reduced considerably with effective treatment.

FH is an autosomal dominant condition meaning that brothers and sisters, or children of someone with FH have a one in two (50%) chance of having the condition. It has been estimated that somewhere between 1 in 250 [3] and 1 in 500 of the UK population have heterozygous FH, which means that between approximately 130,000 and 260,000 people are affected, making it a relatively common disease. Based on these figures, up to 56,000 children in the UK may have FH but only 600 of these are known.

Most people with FH have inherited a gene for FH from only one parent and are therefore heterozygous. Rarely, a person will inherit a genetic defect from both parents and will have homozygous FH.

Atherosclerosis is the build-up of plaque inside arteries, which can lead to the narrowing of arteries. It is slowly progressive from childhood, and adults with a clinical diagnosis of FH who carry an FH-causing mutation are at a very high risk of this developing into CVD. These individuals warrant intensive lipid lowering management and DNA testing of their at-risk relatives. Those with no identifiable mutation, while still needing lipid-lowering treatment, are at much lower CVD risk, and no DNA testing of their relatives is required.

Intervention with statins (and other lipid lowering treatment where statins are not tolerated) is highly effective and gives treated patients the same life expectancy as the general population if treatment is started early enough in life.

The large majority of people with FH (adults and children), however, are undiagnosed, and provision of FH services is patchy across England.

## Why tackle FH?

While the **NICE guideline** and **Quality Standard** on the identification and management of FH have been available and in use since 2008 and 2013, respectively, comprehensive development and implementation of FH services across England has not followed. It is estimated that only around one third of the population in England currently has access to an FH Service, and most of these services have only been established in the past 5 years.

Most cases of FH remain undiagnosed, and only an estimated 8-15% of cases are known (based on prevalence estimates of 1:250 and 1:500). Developing services to identify and manage FH may also support greater awareness of the risks of high cholesterol in general, and encourage more people to be tested and better understand and manage their CVD risk. Diagnosis of adults with FH enables children to be tested and diagnosed early, greatly increasing their chances of a healthy life expectancy, potentially matching that of the general population. Since the original NICE guideline was published many statins have come off patent and their costs markedly reduced. There have also been advances in DNA testing, reducing the costs of testing index cases and cascade testing of family members.

Cascade testing offers an opportunity, if implemented across all Sustainability and Transformation Partnerships (STPs) / Integrated Care Systems (ICSs) / Clinical Commissioning Groups (CCGs), to make great strides in diagnosing cases of FH and has been shown to be a highly cost-effective intervention [4, 5]. The success of cascade testing services in Wales and other European countries such as the Netherlands [6] provide helpful exemplars for how services could be developed in England.

## Policy and guidance to support delivery and implementation

A number of pieces of guidance and policy documents that aim to highlight and drive improvements in the diagnosis and management of FH have been published in recent years. They may support the development of committee/board papers and business cases for FH services.

### NICE guideline (CG71)

Overview: The NICE guideline on the identification and management of familial hypercholesterolaemia (CG71) was first published in 2008 and updated in November 2017.

Recommendations cover:

- case finding and diagnosis
- identifying people with FH using cascade testing
- management (includes drug treatment, lifestyle, specialist treatment and adults, young people and children)
- information needs and support
- ongoing assessment and monitoring

The full list of recommendations can be found [here](#).

The 2017 update reviewed the evidence for case finding and diagnosis, identification using cascade testing, and management using statins. Among the **new or updated recommendations**, the latest NICE guideline recommends:

Systematic searching of primary care records to identify: people younger than 30 years with a total cholesterol concentration greater than 7.5 mmol/L **and** people 30 years or older with a total cholesterol concentration greater than 9.0 mmol/L. These are the people who are at highest risk of FH

FH should be suspected in adults with total cholesterol 7.5mmol/L or above **and/or** personal or family history of premature CHD (a coronary event before 60 years for yourself or a first degree relative – parents, sibling, child)

Coronary heart disease risk estimation tools, such as QRISK2 and those based on the Framingham algorithm, should not be used because people with FH are already at a high risk of premature coronary heart disease.

Children with FH are offered statins by age 10 years or at the earliest opportunity thereafter.

## NICE Quality Standard on FH (QS41)

Overview: NICE quality standards set out the priority areas for quality improvement in health and social care. They cover areas where there is variation in care. Each standard includes a set of statements to help improve quality and information on how to measure progress.

The NICE FH quality standard (QS41) was published in 2013. It was amended in November 2017 to reflect the updated NICE guideline. It will be reviewed in 2018. Quality statements are as follows:

1. Adults with a baseline total cholesterol above 7.5mmol/L are assessed for a clinical diagnosis of FH
2. People with a clinical diagnosis of FH are referred for specialist assessment.
3. People with a clinical diagnosis of FH are offered DNA testing as part of a specialist assessment.
4. Children at risk of FH are offered diagnostic tests by the age of 10 years.
5. Relatives of people with a confirmed diagnosis of monogenic FH are offered DNA testing through a nationwide, systematic cascade process.
6. Adults with FH receive lipid-modifying drug treatment to reduce LDL-C concentration by more than 50% from baseline.
7. Children with 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.
8. People with FH are offered a structured review at least annually.

## Consensus statement of the European Atherosclerosis Society (EAS) 2013

Overview: The EAS released a consensus statement on FH in 2013 titled 'Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease'. It was developed for the whole of Europe, rather than the UK specifically, and was developed using a different methodology to the process used by NICE.

The consensus statement highlights the underdiagnoses of FH and suggests prevalence figures of 1 in 500 underestimate the scale of the condition. It recommends cascade testing of family members of known FH cases ideally using plasma lipid profiles and genetic testing. It recommends use of the Dutch Lipid Clinic Network Criteria in adults for clinical diagnosis, LDL cholesterol targets for FH patients, management of heterozygous FH cases in primary care, and treatment with maximal doses of statins.

## Annual Report of the Chief Medical Officer 2016, Generation Genome, July 2017

**Overview:** Part of the annual series of independent reports from Dame Sally Davies, Chief Medical Officer for the Department of Health, Generation Genome focusses on how the NHS currently uses genomic technologies and how its potential could be developed in the future to ensure that genomic services are available to patients, whilst being cost effective for the NHS. Topics covered include care and treatment of cancer, diagnosing rare diseases, the use of genomics in screening and 'personalised' prevention, precision medicine and genomics in the context of society and the ethical issues around genomics.

**Reference to FH:** The document includes a case study on FH demonstrating the potential for genomic medicine to improve the diagnosis of FH and offer enhanced opportunities for the prevention of heart disease (Chapter 8, Personalised Prevention, page 8).

## Department of Health, Cardiovascular Disease Outcomes Strategy, 2013

**Overview:** The Cardiovascular Disease Outcomes Strategy aimed to provide advice to local commissioners, local authorities and providers about the action that could be taken to improve mortality rates in cardiovascular disease and improve people's quality of life, experience of care and the safety of that care, whilst ensuring that care is delivered in a cost effective manner.

**Reference to FH:** The Strategy includes the following ambitions for FH:

- implementing cascade testing from index cases of FH, resulting in 35,000 diagnoses, bringing the total to 50% of people with FH diagnosed (based on 1:500 prevalence figure)

## NHS England, Improving outcomes through personalised medicine, September 2016

**Overview:** The document outlines NHS England's strategy to embedding personalised medicine into mainstream healthcare and how it will work with partners to fully embrace the future, whilst ensuring ethical, equality and economic implications are recognised and addressed. This strategy aims to build on the 100,000 Genomes Project that is enabling the NHS to collect and use whole genome sequencing, for patients and families with cancer and rare disease, alongside routine clinical and diagnostic data on a large scale. The strategy outlines the four P's of personalised medicine:

- prediction and prevention of disease – using genomic technologies and other diagnostics to identify people most at risk of disease, before the onset of symptoms
- more precise diagnosis – knowledge of an individual's complex molecular and cellular processes, informed by clinical and diagnostic information, to enable clinicians to fully understand abnormal function and determine the true cause of symptoms

- targeted and personalised treatments – moving away from ‘trial and error’ prescribing to using genomic technologies to identify the best therapy for a patient based on their pharmacogenomic profile
- more participatory role for patients – ability for a clinician to discuss information about genomic characteristics with patients

**Reference to FH:** The Strategy highlights FH as an exemplar of how genomic technologies can be embedded into routine patient care, ensuring that early diagnosis leads to effective treatment and direct clinical benefit to individual patients.

### NHS England Annual Report 2016/17

Overview: NHS England’s Annual Report reports on NHS England’s annual performance against corporate priorities in 2016/17 and details how NHS England will improve health and secure high quality healthcare for people in England. The priorities reflect the main themes of the NHS Mandate, and the agenda of the Five Year Forward View. A key priority for 2016/17 was for NHS England to develop a strategy for personalised medicine.

**Reference to FH:** As part of its personalised medicine programme NHS England worked with the Academy of Medical Sciences to develop clinical exemplar pathways to demonstrate how personalised medicine approaches could be built into the diagnosis and treatment for therapy areas, including FH.

The Report identifies the need to establish standardised and consistent genetic testing process to support the implementation of a systematic approach to identifying FH patients retrospectively and prospectively. More information can be found [here](#).

### NHS RightCare, Cardiovascular Disease (CVD) prevention pathway

Overview: NHS RightCare developed evidence based pathways to support local health economies to secure optimal value from services and best practice case studies for elements of the pathway demonstrating what to change, how to change and the scale of improvement. The CVD pathway covers blood pressure, atrial fibrillation, high cholesterol including FH, type 1 and type 2 diabetes and chronic kidney disease.

**Reference to FH:** For FH the CVD prevention pathway recommends:

- maintain and improve systematic collection and audit of data on cholesterol levels, high CVD risk and possible FH in practices to support detection and management
- achieve local clinical consensus and establish an integrated pathway for detection and management of raised cholesterol and CVD risk
- commission local service for FH investigation and cascade testing



## NHS Health Checks Best Practice Guidance

**Overview:** The NHS Health Check programme aims to prevent heart disease, stroke, type 2 diabetes and kidney disease, and raise awareness of dementia both across the population and within high risk and vulnerable groups. NHS Health Checks Best Practice Guidance is updated annually and helps local commissioners and providers to understand the legal requirements underpinning the programme's delivery. It identifies where there is scope for local flexibility and innovation in delivery. It also signposts to a wide range of tools and resources that will support the delivery of a high quality local NHS Health Check programme.

**Reference to FH:** The December 2017 edition included updated advice on identifying and managing people with familial hypercholesterolaemia following an NHS Health Check. It states that all individuals whose total cholesterol level is found to be above 7.5mmol/L and/or have a personal or family history of premature coronary heart disease (an event before 60 years in an or first-degree relative) should be referred to their GP for consideration of FH and for cascade testing of family members if a FH diagnosis is confirmed.

## Paediatric FH Register

Children with FH should be identified before the age of 10 years, or at the earliest opportunity thereafter, in order that lifestyle, and where necessary statin treatment, should be initiated to reduce their subsequent risk. These children will be primarily found through 'cascade testing' by tracing the relatives of the 15,000 or so known index cases with FH currently being treated in lipid clinics throughout the UK.

In 2010 it was estimated that fewer than 400 children with FH had been identified in the UK, but over the next few years, in part driven by the funding from the BHF of FH Nurses, it is anticipated that a large number of children with FH will be identified. An electronic record of these children has been established in the Paediatric FH Register so that their management can be audited, but also so that several important questions about the long term safety and efficacy of statin treatment can be addressed.

The unique aspect of the registry is that, on an annual basis, the registering clinicians are prompted to update information from the latest outpatient visit with additional information collected about lipid profile, height and weight, progression through puberty, treatment, side effects and information about development of symptoms.

As of January 2018, over 460 children have been registered from over 60 centres UK wide, with more than 600 follow-up data points. Two papers [7, 8] have been published to date with key findings in Appendix Five.

# Delivering familial hypercholesterolaemia services

## Delivery of FH services

FH services are delivered through primary and secondary care services. There is no standard service delivery model and approaches differ based on local circumstances. Service development should involve CCGs, primary care, hospital trusts, genetics services, and local authority public health teams, as well as patient and public participation.

There are currently approximately 23 FH services in England; however there is still a need for clear and consistent clinical pathways that cover the whole patient pathway from pre-diagnosis to ongoing management and treatment. Wales provides an example of how a coordinated service for the diagnosis and treatment of FH for patients and families could be implemented.

A recent evaluation [9] of FH services by the British Heart Foundation found that services can be largely categorised into specialist-led, primary care-led or dual care models of delivery, with varying lead organisations. For example, the Wessex FH Service is hosted by Wessex Clinical Genetics Service, while the West Midlands Service is a CCG collaborative based in primary care and hosted by University Hospitals Birmingham NHS Foundation Trust; The Yorkshire and Humber Service is based at Hull and East Yorkshire Hospitals NHS Trust and the North East and Cumbria Service is hosted by City Hospitals Sunderland (CHS) NHS Foundation Trust, and delivered by a regional network of lipid clinics.

Many services include the provision of FH specialist nurses who often lead on case finding, assessment, diagnosis, and organising cascade testing of people with FH. Some are based in primary care and others in specialist clinics. The British Heart Foundation has funded 27 FH nurses across 12 UK sites since 2014, following the success of the co-funded cascade testing service in Wales. See Appendix One for case studies, and for further examples see [NICE's Shared Learning Database](#).

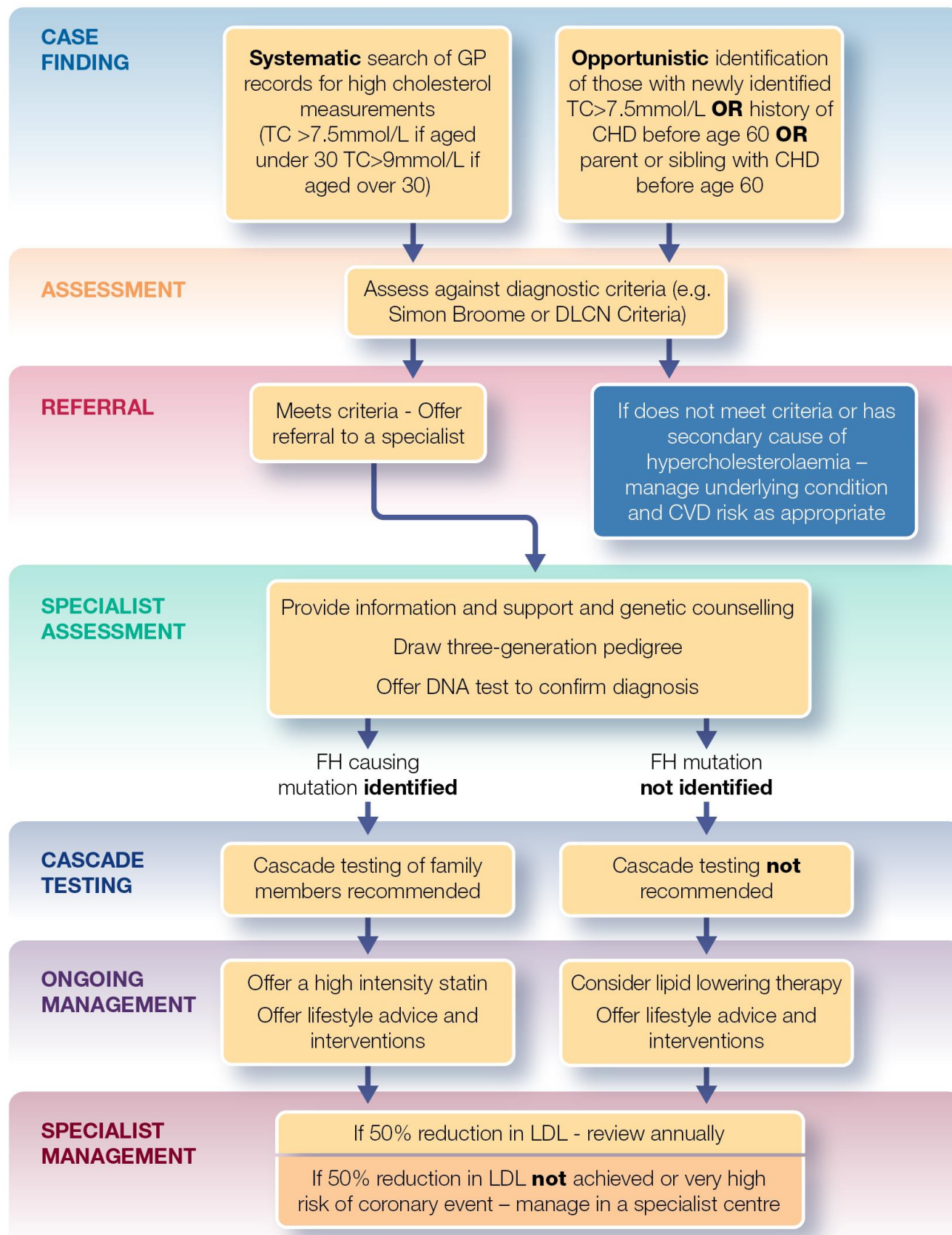
## FH patient pathway

Essential FH patient pathway components based on the updated NICE FH guideline should include:

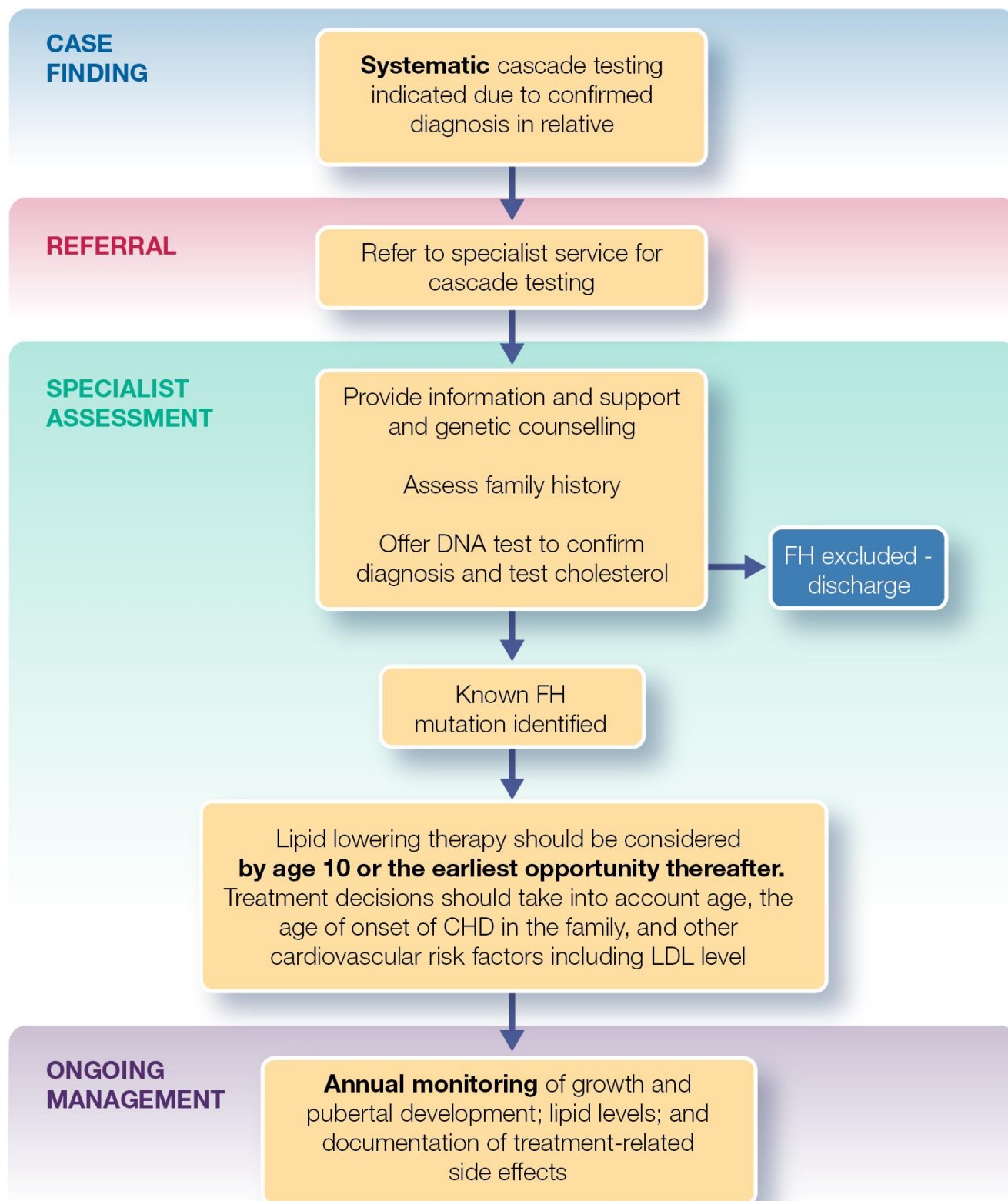
- systematic searching of primary care records to identify individuals that may have FH.
- assessment using Simon Broome or Dutch Lipid Clinic Network criteria to make a clinical diagnosis of FH by a health professional competent in the use of these tools
- referral to a specialist FH or genetic service for DNA testing
- genetic counselling
- cascade testing using DNA of all first degree relatives of people with a genetic diagnosis of FH
- treatment with lipid lowering therapy
- provision of lifestyle and dietary information and support
- ongoing assessment and monitoring
- referral to specialist care for people diagnosed with FH with symptoms or signs of CHD

The NICE Pathway on FH can be accessed [here](#). It contains everything NICE says on FH in an interactive flowchart.

## FH Adult Patient Pathway



## FH Child Patient Pathway



## Case-finding and diagnosis

People with FH should be identified using a combination of opportunistic and proactive approaches. NICE recommends:

- systematically search primary care records for people:
  - younger than 30 years, with a total cholesterol concentration greater than 7.5 mmol/L **and**
  - 30 years or older, with a total cholesterol concentration greater than 9.0 mmol/Las these are the people who are at highest risk of FH.
- suspect familial hypercholesterolaemia (FH) as a possible diagnosis in adults with:
  - a total cholesterol level greater than 7.5 mmol/L **and/or**
  - a personal or family history of premature coronary heart disease (an event before 60 years in an index individual or first-degree relative).
- for people with a personal or family history of premature coronary heart disease (an event before 60 years in an index individual or first-degree relative), but whose total cholesterol is unknown, offer to measure their total cholesterol.

For further information on case finding and diagnosis see [section 1.1](#) in the NICE guideline.

NHS Health Checks are an additional opportunity to identify and diagnose people with FH. People aged 40-74 years are offered an NHS Health Check every 5 years. This includes cholesterol testing. Best Practice Guidance for NHS Health Checks recommends referring anyone with suspected FH to their GP for further assessment. As local authority public health teams are responsible for commissioning NHS Health Checks locally, they should be involved in FH service development and monitoring.

Once those with suspected FH are identified they should be assessed by a healthcare professional competent in using [Simon Broome](#) or [Dutch Lipid Clinic Network \(DLCN\)](#) criteria, which should be used to make a clinical diagnosis of FH.

Once assessed, if a person meets Simon Broome criteria for possible or definite FH, or has a DLCN score of greater than 5, they should be referred to a specialist FH service for DNA testing. If details for an FH service are not known or there is no service available, then a GP should refer the person to their local specialist service that leads diagnosis of FH and where available, cascade testing.

Children should be assessed and managed in a child-focussed setting by clinicians with expertise in management of lipid disorders. Pathways for children need to be established by the metabolic clinical reference group (CRG) and paediatric lipid clinics. FH training should be considered for staff working with children.



Electronic tools have been developed to support primary care to undertake case finding and diagnosis of FH. These tools involve searching primary care electronic health records for individuals at high risk of FH. Four examples:

- FH quality improvement tool based on FAMCAT algorithm for predicting FH has been developed by the Primary Care Stratified Medicine group at the University of Nottingham and ranks patients from high to low probability of FH. This is currently distributed by PRIMIS.
- FH clinical decision support tool to identify patients in electronic health records that may fulfil DLCN or Simon Broome criteria. This tool was developed and evaluated by Medway Clinical Commissioning Group (FH prevalence increasing from one in 750 to one in 357 within the Medway population over the 3-year period) and used alongside nurse-led support clinics. This is currently distributed by Informatica. See [NICE shared learning examples](#) and [HEART UK report](#) for further information.
- HEART UK has developed a simple audit tool.
- a CVD Prevention Audit and Decision Support Tool is in development.

Even where there is no commissioned FH service in place, primary care has a role in ensuring those at risk of FH are properly assessed and diagnosed, and that CVD risk due to high cholesterol (at any level) is appropriately followed up and managed. Where there is a high cholesterol concentration but an FH diagnosis has been excluded, CVD risk should be managed as in the general population. See the NICE guideline, [Cardiovascular disease: risk assessment and reduction, including lipid modification \(CG181\)](#).

## DNA testing<sup>2</sup>

Where an identified mutation diagnostic of FH can be identified by a DNA test, this result can be used to confirm a patient's diagnosis and to offer their relatives cascade testing.

DNA testing or genetic testing for FH has been available in the NHS for some time and is an exemplar of how genomic technologies are being embedded into routine care in the NHS to drive earlier detection and personalised risk assessment, treatments and interventions. However, it has yet to be systematically adopted across England.

Genetic testing services in England are currently delivered through 17 Regional Genetic Centres. However, to create a more sustainable infrastructure that delivers high quality and equitable services, NHS England is procuring up to seven Genomic Laboratory Hubs (GLHs)

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<sup>2</sup> In addition to targeted genetic testing of the known FH genes in individuals meeting clinical criteria, the FH genes can also be examined in patients having a genomic test for an unrelated medical condition. This approach has been piloted in rare disease and cancer patients recruited into the 100,000 Genomes Project, who in most cases have opted in to receive additional findings, including testing for FH-causing mutations. The penetrance of mutations identified by this route has yet to be established; this information will be of use in planning the future approach to additional findings in diagnostic genomic testing.

that will be operational from October 2018. Each GLH will work as part of a national network to deliver a national genomic testing service, providing tests as set out in the National Genomic Test Directory, for a defined geography to a set of national standards and requirements. This means that from October 2018, only genetic testing for FH performed by one of the GLHs will be funded by NHS England.

### Identifying people with FH using cascade testing

Family members of those diagnosed with FH are at risk of FH. As FH is an autosomal dominant condition, children who have one parent with FH have a 50% chance of inheriting the condition.

Cascade testing is a mechanism for tracing the family of those diagnosed with a genetic condition. For FH, DNA testing is used to determine whether family members have inherited the identified mutation. Cascade testing has been shown to be highly cost-effective for identifying people with FH [4, 5]. Cascade testing ensures that children are diagnosed as early as possible, ideally soon after a parent is diagnosed. NICE recommends carrying out cascade testing using DNA testing to first (children, parents and siblings), second and where possible, third degree biological relatives of people with a genetic diagnosis of FH.

Healthcare professionals should offer all people with FH a referral to a specialist FH service or specialist with expertise in FH for confirmation of diagnosis and initiation of cascade testing. Cascade testing pathways should be set up locally in collaboration with lipid services and genetic laboratories with clear mechanisms for communication with patients, and back to primary care for ongoing monitoring and management of diagnosed cases of FH.

In developing cascade testing pathways, the method of contacting at-risk relatives to inform them of their risk and offer cascade testing, should be carefully considered. Minimum criteria for labs accepting referrals for DNA testing should also be clearly understood and available.

For further information on identifying people with FH using cascade testing see [section 1.2](#) in the NICE guideline.

### FH screening

There is no national population screening programme for FH in England. The UK National Screening Committee (UK NSC) reviewed the case for adult FH screening in 2011. The review concluded that population screening for FH in adults does not fulfil the criteria for a screening programme. The UK NSC last reviewed the evidence to screen children for FH at its February 2016 meeting, and recommended that population screening should not be introduced. The review found that the evidence is currently insufficient to answer the key questions around screening all children. This included:



- a suitable and feasible strategy for general population screening has not yet been identified.
- no studies have been identified that assessed whether child screening reduces illness or death from FH.
- there remain many unanswered questions about the ethics and acceptability of universal screening of children aged 1-2 years, relating to the management of screen-detected cases
- no cost-effectiveness studies have been published on screening all children between 1 and 2 years old [10].

A recent study [11] assessed the efficacy and feasibility of child–parent screening in primary care during routine immunisation visits for children aged 1-2 years (reverse cascade screening). The prevalence of children found to have an FH mutation was around 1 in 270, and the parent with a higher cholesterol level was found to have the same FH mutation in 5 out of 6 cases.

The UK NSC will review the evidence for FH (for both adults and children) screening again in 2018/19 as part of its 3-yearly cycle.

## Management

Once FH has been confirmed using DNA testing the individual should be referred back to primary care or a specialist (depending on local pathway) for ongoing treatment and management.

Individuals with a clinical diagnosis of homozygous FH should be referred back to a specialist for management and prescribing. Healthcare professionals should consider a clinical diagnosis of homozygous FH in adults with a low-density lipoprotein cholesterol (LDL-C) concentration greater than 13 mmol/L and in children/young people with an LDL-C concentration greater than 11 mmol/L. Upon diagnosis, healthcare professionals should offer all adults and children/young people with homozygous FH a referral for an evaluation of coronary heart disease.

Lipid-modifying drug therapy, which will be life-long, is the first line of treatment for FH. NICE recommends that people diagnosed with FH should be offered a high-intensity statin with the lowest acquisition cost as the initial treatment for all adults with FH and aim for a 50% reduction in LDL cholesterol concentration from baseline measurement as a treatment target. Statin therapy is highly effective in preventing CHD in people with FH. Children with FH should be offered a statin by the age of 10 or at the earliest opportunity thereafter – a statin licensed for use in the appropriate age group should be considered. Children and young people should usually be prescribed statins at doses outlined in the British National Formulary (BNF) for children.

Ezetimibe monotherapy is recommended as an option for heterozygous adults where statins are contraindicated or cannot be tolerated; see TA385 Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia.

Most FH patients can be managed in primary care. However, there are exceptions. NICE recommends that healthcare professionals should offer adults with FH a referral to a specialist with expertise in FH for consideration for further treatment:

- if treatment with the maximum tolerated dose of a high-intensity statin and ezetimibe does not achieve a recommended reduction in LDL-C concentration of greater than 50% from baseline (that is, LDL-C concentration before treatment)
- if they have been diagnosed with homozygous FH.
- if they are assessed to be at very high risk of a coronary event, that is, if they have any of the following.
  - Established coronary heart disease.
  - A family history of premature coronary heart disease.
  - Two or more other cardiovascular risk factors (for example, they are male, they smoke, or they have hypertension or diabetes)
- for individuals with intolerance or contraindications to statins or ezetimibe
- for individuals who are experiencing side effects that compromise concordance with lipid-modifying drug therapy

Children and young people should be offered referral to a specialist with expertise in FH in children and young people, in an appropriate child-focused setting.

For further information on drug treatment for FH, see [section 1.3.1](#) of the NICE guideline.

Specialist treatment such as LDL-lowering apheresis may be indicated for people with homozygous FH. For further information on specialist treatment, see [section 1.3.3](#) in the NICE guideline.

Lifestyle interventions are also an important component of management of FH (and anyone with hypercholesterolaemia). Specific and easy to understand information and advice on diet, physical activity, smoking advice, weight management and alcohol consumption should be provided to individuals and families diagnosed with FH - see [section 1.3.2](#) of the NICE guideline. It should be noted that NICE recommends that healthcare professionals should regard lifestyle advice as a component of medical management, and not as a substitute for lipid-modifying drug therapy. FH services can provide access to resources and tools to support people to make healthy lifestyle changes. FH services and primary care providers should have knowledge of local weight management, smoking cessation and exercise or referral services and referral criteria. Local authority public health teams can support primary care and FH services to maintain this information.

## Information needs and support

Individuals and families need clear and appropriate information (both verbal and written) throughout the journey from diagnosis, through testing and ongoing management.

This is particularly important in relation to genetic counselling and education and information provided to children and young people. FH services may need to consider the value and appropriateness of resources, training, and education needs of staff dealing with families and children.

Since there is some evidence that statins may slightly increase the risk of congenital birth defects, they are not prescribed for women trying to conceive or during pregnancy. Further information on information and counselling on contraception for women with FH and information for pregnant women with FH can be found in the NICE FH guideline, in sections [1.4.2](#) and [1.4.3](#)

Charities such as HEART UK and the British Heart Foundation have produced a number of useful resources and guides for health professionals and patients, including children. Appendix two includes links to a number of useful information and education resources.

## Ongoing assessment and monitoring

NICE recommends that individuals with FH should be offered a structured annual review that includes an assessment of any symptoms of coronary heart disease and smoking status, a fasting lipid profile, and discussion about medication, possible side effects of treatment the patient may be experiencing, and any changes in lifestyle or lipid-modifying drug therapy that may be required to achieve the recommended LDL-C concentration.

Data collection and monitoring of diagnoses, referrals and outcomes of DNA and cascade testing should be done locally. There is currently no mechanism or framework for collecting this data nationally. Currently, there are no indicators on FH in the NICE indicator menu. The NICE Indicator Advisory Committee have recommended that five new indicators are developed to support the implementation of the updated guideline. These will cover:

- assessment for a clinical diagnosis of FH
- referral of people for specialist assessment
- DNA testing
- cascade testing
- ratio of observed to estimated numbers of people with FH

NICE is also in the process of developing a business rule set for FH. It is recognised that there are a range of codes in both Read and SNOMED relating to FH, and that a defined set of codes will need to be agreed to facilitate systematic searching of records, service delivery and monitoring. It also recognised that new codes will need to be developed for primary care to ensure GPs are able to refer and code patients for DNA testing. This work is expected to be complete by the end of 2018.

## FH registry

An FH registry is available with PASS Clinical Genetics software and it is used by most FH services in England, Wales and Northern Ireland. This IT system is a register for patients and families that aids the coordination of national cascade testing and reporting of FH. The single, central database is hosted on the N3 network and used by lipid clinics and genetic laboratories. HEART UK have led the development of the registry with a limited number of funded licences, BHF also fund a PASS co-ordinator.

Information governance and data sharing should be considered carefully when setting up any local register or reporting system.

# Commissioning familial hypercholesterolaemia services

## Costs

Since the NICE guideline on FH was first published in 2008, patents have expired on some of the widely prescribed statins used to treat FH (reducing treatment costs), and the cost of genetic testing has also reduced due to advancements in DNA sequencing [12].

NICE has prepared a [resource impact tool and report](#) to support local areas to understand the costs and savings involved in delivering FH services. The costing is based on the following recommendations:

- systematically search primary care records for people who are at high risk of FH
- refer people to an FH specialist service for DNA testing if they meet the Simon Broome or Dutch Lipid Clinic Network (DLCN) criteria for possible or definite FH
- carry out cascade testing using DNA testing to identify relatives of people with a genetic diagnosis of FH

The cost of implementing the recommendations in guideline (CG71) in year 1 per 100,000 population is around £2,400, increasing in year 2 to around £7,500. NICE estimates that after 5 years the only recurring costs should be those associated with lipid lowering therapy prescribing for diagnosed cases, and costs associated with diagnosing and managing any opportunistic cases (assuming most have been identified through systematic searching of GP records).

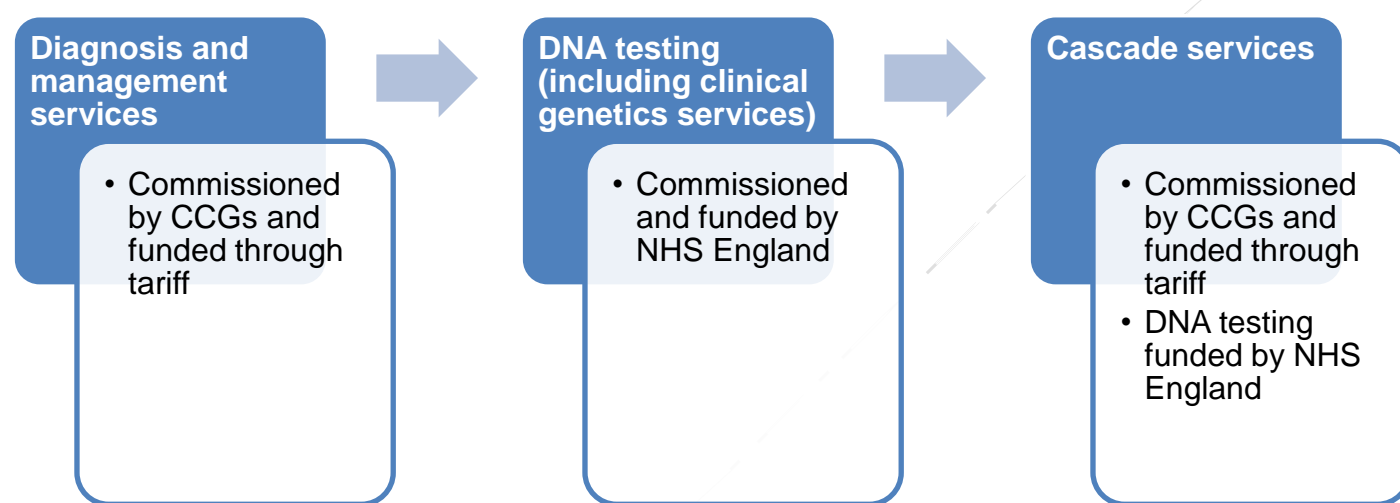
Cascade testing has been shown to be highly cost-effective for FH. A recent study [4] using data from UK cascade services estimated the incremental cost effectiveness ratio (ICER), or cost per QALY, to be £5806 and the net marginal lifetime cost per test to be £2781. NICE generally considers that interventions costing the NHS less than £20,000 per QALY gained are cost effective. Cascade testing for FH comes in well below this threshold.

Systematic case-finding using GP electronic records has also been found to be cost-effective. The evidence review conducted for the update of the NICE FH guideline confirmed that cascade testing is cost-effective and that the addition of primary care case identification strategies is highly cost-effective at an ICER of £1,572/QALY gained. Secondary care case identification strategies in people with early myocardial infarction (MI) were not found to be cost effective with ICERs in the region of £70,000/QALY.

## Commissioning models

The commissioning of FH services is complex as FH services are delivered across different services in the health system. Funding flows should be set out locally, so that primary care and specialists can confidently make referrals for testing. Local estimates can be calculated using demographic data and resource impact figures in the NICE resource impact tool.

An indicative flow of the commissioning of FH services has been outlined below (although this may not be the most appropriate approach for all patient pathway models):



Key questions to consider when developing a local commissioning model include:

- will the commissioning model ensure consistent and equitable access to services across the FH pathway?
- are there future cost savings that can be realised through economies of scale?
- will there be requirements for co-ordination across traditional boundaries?
- what is the expected growth in the number of FH patients that will require access to the service, including children and paediatric services, and how will this impact on the commissioning?
- how will commissioning arrangements be reviewed?

Examples of services that are currently commissioned in England are included in Appendix One.

## Current service coverage

It is estimated that FH services currently cover around a third of the population in England.

The following maps provide information on coverage of FH services, lipid clinics, and areas where the paediatric FH register is in use.

- FH Services: View the [BHF's interactive map of FH services](#), including contact details and the areas covered by the services
- Lipid Clinics: View [HEART UK's interactive map of lipid clinics across the UK](#) including paediatric lipid clinics
- Paediatric FH register: View the [RCP's interactive map of hospitals participating in the Paediatric FH Register](#)

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# Glossary

## **Cardiovascular Disease**

Cardiovascular disease (CVD) is a general term that encompasses coronary heart disease as well as other diseases of the heart and circulation.

## **Cascade testing**

Cascade testing is a mechanism for identifying people at risk of a genetic condition by a process of family tracing. For FH the test employed is a DNA test where a disease-causing mutation has been identified in the index individual.

## **CCGs**

Clinical Commissioning Groups

## **Coronary Heart Disease**

Coronary heart disease is defined as the presence of angina, acute coronary syndrome, myocardial infarction, need for coronary artery bypass grafting, need for percutaneous coronary intervention or definite coronary artery disease on coronary angiography.

## **First-degree relative**

A person's biological parents, brothers and sisters, and children.

## **Heterozygous FH**

High levels of LDL cholesterol in the blood caused by an inherited mutation from one parent only. People with FH are at increased risk of cardiovascular disease.

## **Homozygous FH**

Very high levels of LDL cholesterol in the blood caused by an inherited mutation from both parents. When a person inherits exactly the same affected gene from both parents this is called truly 'homozygous' FH. When the mutations in the genes are different, this state is called 'compound heterozygous'. In general, the overall effect in both states is similar. Both groups of patients have the same clinical pattern and high risk of cardiovascular disease.

## **ICSs**

Integrated Care Systems

## **Index individual/Index Case**

The original patient who is the starting point for follow-up of other members of a family when investigating for possible causative genetic factors of the presenting condition.

## **Lipid profile**

These terms refer to the measurement of total cholesterol (TC), triglycerides (TGs), high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol.

## **Monogenic FH**

High levels of LDL cholesterol in the blood due to a single disease-causing gene mutation.

## **Mutation**

An identified change in the DNA sequence of a gene that is predicted to damage the normal function of the gene and so cause disease.

## **NICE**

National Institute for Health and Care Excellence

## **Pedigree**

A method of characterising the relatives of an index individual/case and their family relationship as well as problems or illnesses within the family. This information, often represented graphically as a family tree, facilitates analysis of inheritance patterns.

## **Polygenic Hypercholesterolaemia**

High levels of LDL cholesterol in the blood due to an accumulation of effects exerted by many different cholesterol-raising gene mutations.

## **Premature Coronary Heart Disease**

For the purpose of the NICE guideline, this refers to a coronary event that has occurred before 60 years of age in an index individual or first-degree relative.

## **Second-degree relative**

A person's biological grandparent, grandchild, uncle, aunt, niece, nephew, half-sister or half-brother.

## **STPs**

Sustainability and Transformation Partnerships

## **Third-degree relative**

A person's biological great grandparent, great grandchild, great aunt, great uncle, first cousin, grand-nephew or grand-niece.

## Appendix one: History of FH

### History

Through the 1980s and 90s, British Heart Foundation Professor Steve Humphries collected DNA samples from hundreds of FH patients and discovered the genetic mutations that cause FH. His research has shown that DNA testing can find which members of affected families also have the condition.

FH is caused by mutations in the low density lipoprotein receptor gene (*LDLR*), the apolipoprotein B-100 gene (*APOB*) or the proprotein convertase subtilisin/kexin type 9 (*PCSK9*) gene [13]. The most common class of genetic defect is a mutation in the *LDLR* gene.

The UK Simon Broome Familial Hypercholesterolaemia Register is a database that holds information about 3,400 registered patients with familial hyperlipidaemias, providing a resource for research with the aim of furthering more effective diagnosis and treatment and preventing early heart disease. In 1991 this showed that the cumulative incidence of coronary heart disease without treatment is about 50% by the age of 50 years in men and about 30% by the age of 60 years in women [14, 15, 16]. A follow up of this finding in 1999 [17], after the introduction of statin lowering therapy, showed that statins can significantly reduce coronary atherosclerosis and improve life expectancy.

## Appendix two: Service development case studies

### Case studies of FH cascade testing service models co-funded by the BHF

BHF Professor Steve Humphries first demonstrated in the 1990s that DNA testing could identify which members of affected families also have FH. Since then, the BHF has strongly advocated cascade testing of relatives and has so far invested over £7 million into FH research and implementation.

This sum includes implementation of the research into clinical practice. The BHF has funded 27 FH nurses across 12 UK sites since 2014, following a successful co-funded cascade testing service in Wales. By January 2018, these programmes had diagnosed over 2,000 new cases in England and Scotland and more than 900 in Wales.

These programmes are a clear demonstration of how an evidence-led approach can benefit local populations in today's NHS. We encourage NHS commissioners to read a BHF-commissioned [economic analysis](#) of the cost effectiveness of cascade testing for relatives of people with FH, and an independently commissioned [programme evaluation \[PDF\]](#) of our FH work.

To help explain the benefits of FH services, we present two examples of models that the BHF has pump-primed that are operating in the NHS today. Each site takes a slightly different approach to the challenge of identifying and managing FH.

#### Example 1: Wessex FH Cascade Testing Service

This successful FH cascade testing service established in Wessex is commissioned by 12 CCGs covering a population of 2.5 million people across Southampton, Hampshire, the Isle of Wight, Portsmouth and West Berkshire<sup>3</sup>. As of October 2017, the service has assessed or tested 966 patients and identified 365 positive cases, including 50 children<sup>4</sup>.

The service was among the first to be commissioned by CCGs in England and was pump-primed with funding from the BHF and the South Central Cardiovascular Network. It is hosted by the Wessex Clinical Genetics Service based at University Hospital Southampton NHS Foundation Trust.

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<sup>3</sup> From NICE Guidance to Clinical Practice: The challenge of Setting up a Service for Familial Hypercholesterolaemia (FH) Poster by Subhashini Balasingham, Angela Cazeaux and Melanie Watson, Wessex Clinical Genetics Service, Southampton, UK.

<sup>4</sup> BHF-funded FH nurse update for central SGM, October 2017

Patients are identified and referred along dual care pathways in primary and secondary. For instance, in West Berkshire patients are referred by their GP following a virtual lipid clinic, while in Southampton, Portsmouth and North Hampshire this operates via a combination of primary and secondary care referrals.

Once referred into the Wessex FH Cascade Testing Service, patients are triaged and those who meet the referral criteria are assessed by an FH Nurse in a clinical appointment. FH nurses provide patients with information about FH and DNA and cascade testing, as well as a lifestyle assessment and advice. A family pedigree is drawn up to identify affected individuals and relatives at risk; consent for genetic testing is obtained and blood samples are sent to Bristol for analysis. They are also entered into the National FH PASS database.

Positive cases are offered a follow-up appointment for test results and to initiate cascade testing of other family members. Patients with diagnosed FH are managed via a shared care approach between primary and secondary care. If negative, patients are offered lifestyle advice and referral to support services. A paediatric service has been established: designated FH paediatric clinics in Southampton and Reading provide assessment and clinical management for children. These clinics take a family approach providing information and support for the whole family and further cascade testing as appropriate. This dual care model offers reduced costs to the NHS while improving identification of FH cases and access to genetic testing for first-degree relatives.

The BHF's pump-priming funding ended in June 2016 and the service has since been sustained by local CCGs.

## Example 2: West Midlands

With a population of around 5.6 million, the West Midlands has potentially around 22,000 FH cases yet only around 7.5% are identified to date. The BHF is pump-priming, through a two-year grant agreement with a CCG collaborative, five FH specialist nurses to operate a primary care-based model to detect, test and treat those at risk of FH, and their families. This large-scale project, covering all six STP footprints of Birmingham and Solihull, the Black Country, Staffordshire and Shropshire, Hereford and Worcestershire and Warwickshire, went live in early November 2017. The project has been led by the West Midlands CVD network (NHS England).

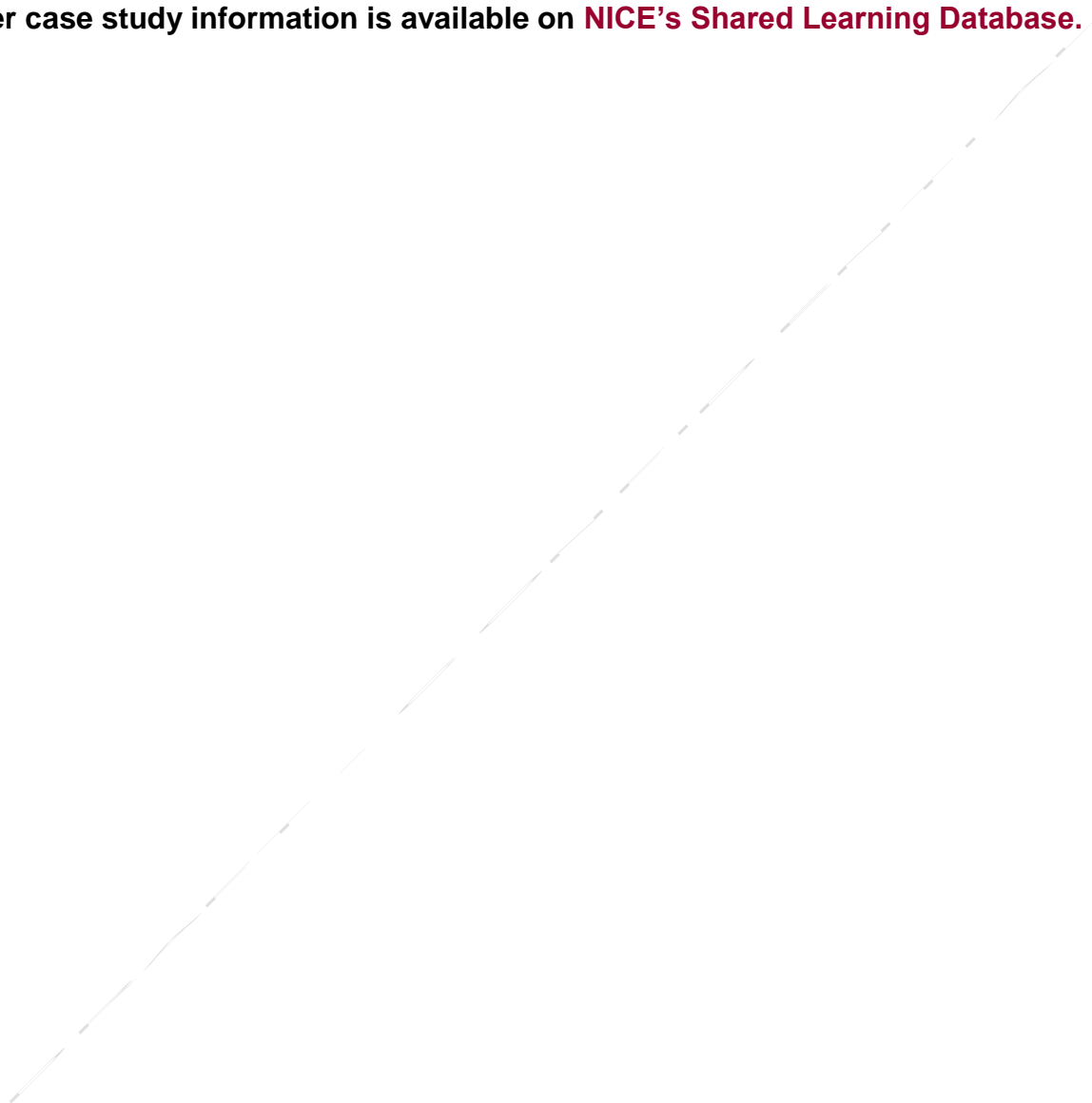
In the delivery model, the service is hosted by University Hospitals Birmingham NHS Foundation Trust but is based in primary care. FH nurses interrogate primary care records to proactively case-find individuals at risk. If FH is still indicated following assessment by the FH nurse, genetic testing via labs in Bristol is undertaken with patient consent. At present, a locally developed West Midlands database is being used to record information and contact trace relatives, before the team moves to using the PASS database. Patients are treated according to their results – for positive cases, cascade screening is initiated and patients are referred to a lipid clinic for cardiac risk assessment, and then managed in general practice. If negative,

patients are offered lifestyle advice and referral to support services. A parallel paediatric service is also in development in collaboration with Birmingham Children's Hospital.

Funding was initiated in November 2017 and will run for at least two years; thereafter, all 22 West Midlands CCGs will aim to commission the service going forward.

**For more information about the BHF's service innovation work on FH, visit [bhf.org.uk/fh-hub](https://bhf.org.uk/fh-hub)**

**Further case study information is available on [NICE's Shared Learning Database](#).**



## Appendix two: Personal case study

Katherine, age 32

I went to get a cholesterol test on the recommendation of my dad's GP, due to his high cholesterol and because he had a heart attack in his mid-40s. The result was an overall level of 10.1. Although I have not been offered genetic testing, my GP and my hospital consultant(s) have diagnosed me with FH and I have been being treated since then.

Despite my dad's history, I never expected to be told that I had this condition. It was very much a shock: I was in my 20s and found it ridiculous that I could have FH and need to go on statins. I thought it was just something that generally older, unhealthy people needed to take- I was certainly quite ignorant to the fact that young people (and children) could be at risk from high cholesterol.

After the initial shock, I realised I need to change some things. I attended a weight loss class to help me lose some weight and continue to lower my risk, as well as doing more exercise, and being much better with my eating habits. Generally, I have stuck to this over the years, but at times it is hard to say no to things that I want but shouldn't have.

I think it was difficult for my dad at first, as I think he felt some kind of guilt because it is a hereditary condition. He had been so supportive and it so pleased to see me involved with Heart UK.

There was obviously an impact on my husband with me needing to watch my diet more; but this was only a positive thing as he very much got involved and supported me- and so he has been getting fitter and healthier too.

Having FH and being on statins had a certain impact on our plans to start a family. My husband and I were very conscious that I would need to be off statins at least 3 months before hopefully conceiving, and then I would still be off them for as long as I breast fed. Knowing I'd be off medication for an unknown amount of time was worrying, but my GP and consultant were both very reassuring.

I am back on my medication and my cholesterol is coming back down, and I'm still working on my weight and fitness post-baby but I worry more about my little girl having FH.



## Appendix three: List of useful resource and tools

### NICE

- NICE FH guideline (CG71)
- NICE Quality Standard (QS41)
- NICE FH resource impact tool
- NICE Shared learning database case studies
- NICE Familial Hypercholesterolaemia: identification and management. Evidence reviews for case-finding, diagnosis and statin monotherapy
- NICE TA Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia (TA385)
- NICE TA Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia
- NICE TA Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia
- NICE Baseline assessment tool
- NICE into practice guide
- NICE Cardiovascular disease: risk assessment and reduction, including lipid modification guideline cg181
- NICE QS on Cardiovascular risk assessment and lipid modification QS100

### British Heart Foundation

- Delivery of FH Services: Identifying Enablers and Barriers, British Heart Foundation, 2016
- British Heart Foundation FH Hub
- Genetics webpage

### HEART UK

- FindFH.org.uk - A summary of the recommendations and helpful resources to find and treat FH
- HEART UK FH Toolkit
- HEART UK statement on the management of homozygous Familial Hypercholesterolaemia in the United Kingdom

### Paediatric FH

- Paediatric FH register
- Paediatric register info sheet for parents on statin use
- Paediatric FH service map – use of paediatric FH register

- HEART UK Children's FH resources

### NHS England

- NHS England Factsheet on FH
- NHS England Annual Report 2016/17
- STP aide memoire: Prevention

### PHE

- NHS Health Checks website
- Local health and care planning - menu of preventative interventions

### Primary care

- FAMCAT Tool – PRIMIS
- Systematically identifying familial hypercholesterolaemia in primary care – An audit within the Medway Clinical Commissioning Group, HEART UK 2015

### Royal Colleges

- National Clinical Audit of the Management of Familial Hypercholesterolaemia FULL REPORT

### Chief Medical Officer

- Annual Report of the Chief Medical Officer 2016, Generation Genome, 2017

### Genetics

- NHS UK Genetic Testing Network (UKGTN)
- PASS Software for FH

## Appendix four: Key contacts

### HEART UK:

Literature orders and general enquiries: 01628 777046

HEART UK Cholesterol Helpline: 0345 450 5988

Email: [ask@heartuk.org.uk](mailto:ask@heartuk.org.uk)

### British Heart Foundation:

Genetic helpline: 0300 456 8383

Health Services Engagement Team: [HSEteam@bhf.org.uk](mailto:HSEteam@bhf.org.uk)

### PASS Software:

Kate Haralambos

Email: [HaralambosK1@cardiff.ac.uk](mailto:HaralambosK1@cardiff.ac.uk)

Phone: 02920 743864

### Paediatric FH Register:

Maggie Heinrich

Email: [fh@rcplondon.ac.uk](mailto:fh@rcplondon.ac.uk)

Phone: 020 3075 1247

Professor Steve Humphries

Email: [s.humphries@ucl.ac.uk](mailto:s.humphries@ucl.ac.uk)

Dr Uma Ramaswami

Email: [Uma.Ramaswami@nhs.net](mailto:Uma.Ramaswami@nhs.net)

### Simon Broome FH Register:

Professor Steve Humphries

Email: [s.humphries@ucl.ac.uk](mailto:s.humphries@ucl.ac.uk)

### HEART UK's FH Intelligence Network:

HEART UK's FH Intelligence Network is a free monthly teleconference and open to health care professionals and commissioners of FH services.

Simon Williams

Email: [sw@heartuk.org.uk](mailto:sw@heartuk.org.uk)

Phone: 01628 777046

## Appendix five: Data from paediatric register



### Statin treatment in the Register children

Analysis of the baseline registration data [7] showed that overall 52.5% of the children were on statins. This varied significantly by age group, being 0% in those under 5 years, 16.7% in those between 5 and 10 years, 57.1% in those between 10 and 15 years and 73.2% in those over 15 years. Overall, statin treatment reduced LDL-C level by 31% (1.84mmol/L), but with 5.6% still having levels over the suggested target of 3.5mmol/L. In children over 10 years, of those not on statin treatment, 36% had evidence of a family history of early coronary heart disease (CHD), and 89.9% had LDL-C over 3.5mmol/L. Although these results are encouraging they suggest that there are still a significant proportion of children over the age of 10 years who are at high future risk of early CHD and where initiation of statin therapy should be actively considered.

### Analysis of Follow-up Register Data

We recently completed analysis of the follow-up data now accruing on the Register children, in particular looking at the changes in height and weight in children not being treated and those being treated with a statin. Our hypothesis was that there would be no difference in growth rate in statin treated vs non treated children, as statin treatment would not be associated with any such growth issues. This hypothesis was found to be correct. After adjustment for age and gender, there was no statistically significant difference in the increase in height or weight in the two groups. In addition, no statin-treated child showed elevated levels of markers of liver toxicity or muscle damage. This confirms many other reports of the short term safety of statin treatment with respect to growth of treated children.

### Are children on the register overweight?

As we are all aware, there is much current concern about the development of obesity in children in the UK, with the subsequent influence on morbidity. A recent study of >14,000 UK "Millennium" children reported that between 11.8-14.6% of 5-11 year old UK children are overweight (BMI > 85<sup>th</sup>ile) with 11.9-21.2% being obese [18]. We were unaware of any comparable data in UK FH children. For children, the appropriate measures of obesity are determined using age and gender specific percentiles, with a BMI at or above the 85<sup>th</sup> percentile being designated as overweight, and at or above the 95<sup>th</sup> percentile as obese. For the FH Register children, 16.9% were overweight and 11.1% were obese [8]. Compared to data from the Millennium children, the prevalence of overweight was similar (14.6% vs 16.9%  $p = 0.33$ ) but the prevalence of obesity was significantly lower (22.1% vs 11.1%  $p = 0.0002$ ). This encouraging result suggests that FH management guidelines are being followed, with children being successfully supported to adopt healthy eating habits, be physically active and make sensible life-style choices, to maintain an ideal body weight.

## Hyperlinks

NICE Guideline (CG71) Familial hypercholesterolaemia: identification and management

<https://www.nice.org.uk/guidance/cg71>

- recommendations section  
<https://www.nice.org.uk/guidance/cg71/chapter/Recommendations>
- subsection on case finding and diagnosis  
<https://www.nice.org.uk/guidance/cg71/chapter/Recommendations#case-finding-and-diagnosis>
- subsection on cascade testing  
<https://www.nice.org.uk/guidance/cg71/chapter/Recommendations#identifying-people-with-fh-using-cascade-testing>
- subsection on management  
<https://www.nice.org.uk/guidance/cg71/chapter/Recommendations#management>
- subsection on information needs and support  
<https://www.nice.org.uk/guidance/cg71/chapter/recommendations#information-needs-and-support>
- update section  
<https://www.nice.org.uk/guidance/cg71/chapter/Update-information>

NICE Quality Standard (QS41) Familial hypercholesterolaemia

<https://www.nice.org.uk/guidance/qs41>

NICE's Shared Learning Database.

<https://www.nice.org.uk/guidance/cg71/resources/shared-learning>

- Shared Learning - case study from Medway CCG  
<https://www.nice.org.uk/sharedlearning/improved-identification-of-familial-hypercholesterolaemia-fh-in-primary-care>

NICE Pathway – Interactive Flowchart

<https://pathways.nice.org.uk/pathways/familial-hypercholesterolaemia>

NICE resource impact tool and report

<https://www.nice.org.uk/guidance/cg71/resources/resource-impact-report-pdf-4660987501>

Consensus statement of the European Atherosclerosis Society (EAS) 2013

[https://www.eas-society.org/?page=fh\\_consensus](https://www.eas-society.org/?page=fh_consensus)

Annual Report of the Chief Medical Officer 2016, Generation Genome, July 2017

<https://www.gov.uk/government/publications/chief-medical-officer-annual-report-2016-generation-genome>

Department of Health, Cardiovascular Disease Outcomes Strategy, 2013

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/214895/9387-2900853-CVD-Outcomes\\_web1.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214895/9387-2900853-CVD-Outcomes_web1.pdf)

NHS England, Improving outcomes through personalised medicine, September 2016

<https://www.england.nhs.uk/wp-content/uploads/2016/09/improving-outcomes-personalised-medicine.pdf>

NHS England Annual Report 2016/17

[https://www.england.nhs.uk/wp-content/uploads/2017/07/Annual-Report-Full\\_201617.pdf](https://www.england.nhs.uk/wp-content/uploads/2017/07/Annual-Report-Full_201617.pdf)

NHS RightCare, Cardiovascular Disease (CVD) prevention pathway

<https://www.england.nhs.uk/rightcare/products/pathways/cvd-pathway/>

NHS Health Checks Best Practice Guidance

[https://www.healthcheck.nhs.uk/commissioners\\_and\\_providers/guidance/national\\_guidance1/](https://www.healthcheck.nhs.uk/commissioners_and_providers/guidance/national_guidance1/)

Paediatric FH Register

<https://audit.rcplondon.ac.uk/PaedFH/page.aspx?pc=homepage>

HEART UK Report Systematically Identifying Familial Hypercholesterolaemia In Primary Care: An audit within the Medway CCG

[https://heartuk.org.uk/files/uploads/documents/HEART\\_UK\\_Medway\\_report\\_WEB\\_2015.PDF](https://heartuk.org.uk/files/uploads/documents/HEART_UK_Medway_report_WEB_2015.PDF)

Simon Broome Register Criteria

[https://heartuk.org.uk/files/uploads/documents/HUK\\_AS04\\_Diagnostic.pdf](https://heartuk.org.uk/files/uploads/documents/HUK_AS04_Diagnostic.pdf)

Dutch Lipid Clinic Network Criteria

<https://www.nice.org.uk/guidance/cg71/chapter/recommendations#dutch-lipid-clinic-network-dlcn-criteriascore>

Cardiovascular disease: risk assessment and reduction, including lipid modification (CG181).

<https://www.nice.org.uk/guidance/cg181>

BHF's interactive map of FH services

<https://www.bhf.org.uk/fh servicemap>

HEART UK's interactive map of lipid clinics across the UK

<https://heartuk.org.uk/lipid-clinics/uk-map>

RCP's interactive map of hospitals participating in the Paediatric FH Register.

<https://audit.rcplondon.ac.uk/PaedFH/Page.aspx?pc=map>

BHF economic analysis of the cost-effectiveness of cascade testing

<http://dx.doi.org/10.1093/eurheartj/ehx111>

BHF report Delivery Of Familial Hypercholesterolaemia Services:

Identifying Enablers and Barriers

<https://www.bhf.org.uk/-/media/files/hcps/fh-evaluation-report2016final-vers-12122016.pdf?la=en>