Familial Hypercholesterolaemia Genetic Testing Pathway FAQs

The East Genomic Laboratory Hub (GLH) Familial Hypercholesterolaemia (FH) Genetic Testing Pathway provides guidance for healthcare professionals with patients with a high likelihood of monogenic inherited hypercholesterolemia.

To access the FH genetic testing pathway and the FH test order form please visit the East Genomics FH Information Zone webpages.

To support healthcare professionals to utilise and adopt the FH genetic testing pathway, please find below some FAQs. If your question is not answered in this document please contact the East Genomic Laboratory Hub.

Where can I find the FH Genetic Testing Pathway?

The FH genetic testing pathway can be found on the East Genomics FH Information Zone webpages.

Why is the FH Genetic Testing Pathway being introduced?

The NHS Long Term Plan aims to increase the number of individuals tested for FH to improve patient outcomes. To support these aims, genetic testing for FH is now centrally commissioned by NHS England and all healthcare professionals in the East of England and East Midlands can order FH genetic testing for their patients.

East Genomics, alongside the East of England FH steering group, has created new FH Information Zone webpages, an FH genetic testing pathway and an FH Genomic Test order form. These have been produced to support healthcare professionals in identifying patients with a high risk of FH and in ordering genetic testing when appropriate.

This new pathway increases access to genetic testing for health professional including those in primary and community care. This means that patient referral to secondary care lipid clinics for genetic testing is not required, avoiding long waiting lists and supporting timely cholesterol management.

Who is the FH Genetic Testing Pathway intended for?

Any health care professional working in primary, secondary or tertiary care, looking after patients with, or at high risk of developing, atherosclerotic cardiovascular disease. The pathway intends to provide the support needed to those individuals to feel confident and competent in ordering genetic testing for FH, obtaining informed consent for genetic testing for FH and in informing patients of the result of the genetic test.

Which patients can be assessed using the FH Genetic Testing Pathway?

The pathway can be used to assess a patient's eligibility for genetic testing either individually or systematically. In individuals it would include those who are requesting the test, or those whose cholesterol is sufficiently high that the diagnosis of FH should be considered, or who have a personal or family history of premature atherosclerotic cardiovascular disease. The pathway can also be used in reviewing digital patient records to identify those who might be eligible for testing and who could be invited to discuss this further. Finally the pathway can also be used to reassess the eligibility of an individual if additional information becomes available later.

Is there more information about using the Simon Broome criteria, FHWales or the Dutch Lipid Clinic Network Score?

NICE guidance CG71 refers to the following resources:

Simon Broome criteria

Dutch Lipid Clinic Network Score

FHWales

How to proceed with post-menopausal cholesterol levels?

Cholesterol levels rise significantly after the menopause. When estimating the likelihood of FH in post-menopausal females any pre-menopausal lipid levels should be used if they are available.

What is premature Atherosclerotic Cardiovascular Disease (ASCVD)?

Atherosclerotic cardiovascular disease refers to atherosclerosis of the coronary, cerebral and peripheral arteries and its complications. It includes those with previous myocardial infarction, coronary revascularisation, angiographically demonstrated coronary artery disease, ischaemic stroke, carotid endarterectomy, TIA, peripheral arterial revascularisation or symptomatic peripheral arterial disease. Premature is generally taken to mean with onset earlier than 60 in the individual: when applied to family history it usually means with an onset before 60 in first degree relatives, or before 50 in second degree relatives.

Why does the pathway include the option "unable to assess family history"?

The Simon Broome criteria, FHWales and the Dutch Lipid Clinic Network Score all use family history information to assess likelihood of FH in an individual. In the absence of this information a full score cannot be worked out. All reasonable efforts to obtain the relevant information should be pursued, but where it proves impossible to do so the clinician will have to make a judgement whether genetic testing should be carried out. As a minimum the LDL cholesterol should be at least 4.9 on two separate occasions 3 months apart with all secondary causes excluded or managed and lifestyle optimised. However, in a younger individual with no secondary causes, a good diet and exercise regime and an LDL cholesterol much greater than 4.9 then it would be reasonable to proceed to genetic testing, perhaps after a confirmatory lipid profile a couple of weeks later.

How can I arrange genetic testing for FH?

The East GLH FH Genetic Testing Pathway and East Genomics FH Information Zone aims to provide the resources required to support all healthcare professional to become competent in assessing an individual's risk for monogenic FH and to order genetic testing for FH.

If preferred, patients can be referred to your local Lipid Clinic for assessment.

Can I contact my local Lipid Clinic if I have any questions?

Yes. Lipid Clinic contact details in the East Midlands and East of England.

Where can I find resources for patients?

Useful resources for patients and family members can be found on the British Heart Foundation and Heart UK websites.

FH Genetic Testing FAQs

Is there a specific FH Genetic test order form that I need to use?

Yes, please use the East GLH FH Test Order Form on the East Genomics FH Information Zone webpages.

What sample is needed for Genetic Testing?

For FH Genetic testing a 5ml EDTA peripheral blood sample is required. Further details are available on the East Genomics Sample Requirements webpage.

What is Genetic Testing for FH?

Genetic variation in five genes is known to cause monogenic FH. The East GLH FH team sequence the DNA of patients and look for genetic variants in these five genes. No other genes are analysed as part of the FH test. If a genetic variant is identified then a Clinical Scientist will assess if the variant is likely to cause FH. A clinical report is then issued that indicates if a genetic variant has been identified that confirms a diagnosis of FH.

How do I consent a patient for FH Genetic Testing

An appropriate discussion of genetic testing and the possible implications for a patient and their family members should take place prior to genetic testing. The East GLH FH Test Order form includes four discussion points that can help guide the consent discussion. Further information can be found on the East Genomics FH Information Zone webpages.

How long does it take to get a genetic test result back?

The NHS Genomic Medicine Service turnaround times for FH testing are 42 days for both diagnostic and cascade testing.

Current turnaround times for genomic testing are on the East Genomics Service Turnaround times webpage.

I am a healthcare professional/clinician in primary or community care, do I need to inform anybody e.g. secondary care lipid clinics, if I make a referral for genetic testing?

You do not need to notify anyone that you have made a referral for genetic testing.

Please contact your local Lipid Clinic or the East GLH if you have a query or require assistance.

What is Cascade Testing?

Cascade testing aims to identify and provide appropriate screening and treatment to family members of FH patients. FH cascade testing is recommended for all first degree relatives of FH patients with a known FH genetic variant.

How is Cascade Genetic Testing performed for FH?

For cascade testing, the DNA of a family member is tested for the presence or absence of the genetic variant known to cause FH in that particular family.

If the FH family variant is not known then cascade testing cannot be performed.

Why is cascade referral at the top of the FH Genetic Testing Pathway and not LDL levels?

First degree relatives are eligible for cascade genetic testing regardless of LDL-Cholesterol levels. Early diagnosis and treatment of FH reduces the risk of cardiovascular events.

What is an index patient?

The term “Index Patient” refers to the first individual within a family where a FH genetic variant was identified.

What is a first degree relative?

First-degree relatives (parents, children, brothers and sisters) of someone with FH should be tested regardless of LDL Cholesterol level.

Should cascade testing be performed in children and young adults?

National guidelines suggest that, where possible, the offspring of anyone with a known FH genetic variant should be tested by the age of 10. If possible it would be helpful to check the child's lipid profile at the same time as arranging a genetic test. It is worth noting that LDL cholesterol levels decrease during puberty.

Can cascade testing be performed if the FH family genetic variant is not known?

No. Cascade testing cannot be performed if the FH family genetic variant is unknown. If a patient meets the eligibility criteria for diagnostic testing then a diagnostic genetic FH test can be ordered.

What do I do if a patient declines an FH genetic test?

Any individual has the right to decline genetic testing, but it would be good practice to explore the reasons for that decision and to document it in their notes, as well as offering that the decision can be revisited at any time the individual wishes.

What do I do if a patient is not eligible for an FH genetic test?

You should explain to the patient why they do not meet the eligibility criteria and document this in their notes. Most understand that this is a test that requires much more resource to process that most other blood tests.

You should tell the patient that if a first degree relative is subsequently found to have an FH causing variant then they will become eligible for cascade testing.

You should manage their overall cardiovascular risk, following guidelines for the particular context of the patient.

I am a GP. What codes should I use for documenting FH genetic testing?

SNOMED codes have been designated for documenting FH genetic testing in your patients.

SNOMED codes for FH from October 2022

Procedures:

925221000000106 | Familial hypercholesterolaemia comprehensive genetic test (procedure)

925211000000100 | Familial hypercholesterolaemia targeted genetic test (procedure)*

Oobservable entities:

163841000237109 | Familial hypercholesterolaemia comprehensive genetic test result (Observable entity)

163851000237107 | Familial hypercholesterolaemia targeted genetic test result (Observable entity)*

Findings:

204871000237101 | Apolipoprotein B gene mutation positive (finding)

204901000237101 | Apolipoprotein E gene mutation positive (finding)

204881000237104 | Proprotein convertase subtilisin/kexin type 9 gene mutation positive (finding)

204891000237102 |Low density lipoprotein receptor gene mutation positive (finding)

204931000237105 | Genetic variant causing familial hypercholesterolaemia not detected (finding)

204921000237108 | Genetic variant of uncertain significance detected (finding)

*This is the code for a "Cascade test" in a relative where only the family variant is tested for

Image reference: https://www.heartuk.org.uk/news/latest/post/184-new-snomed-codes-for-fh-dna-test-results