Suspected inherited lipid disorders (including Familial Hypercholesterolaemia)

Please see condition-specific referral criteria below for the 3 most common conditions:

A. Familial hypercholesterolaemia (FH)

FH affects up to 1 in 250 people in Scotland, confers a high-risk of early-onset cardiovascular disease (over half of untreated men will suffer an MI before the age of 50) and is under-diagnosed. FH is autosomal dominant and can be confirmed via a sensitive genetic screen. Upon identification of a case, genetic testing for close relatives is offered throughout Scotland. Referral to the lipid clinic (or clinical genetics) depends on whether a genetically confirmed diagnosis has been established:

- **Genetically-confirmed FH, but lost to lipid clinic follow-up** – refer to Lipid Clinic (unless patient has indicated that they do not wish to attend)
- **Suspected FH**
    - If your patient **has a close relative with genetically confirmed** FH, then they should be referred to Clinical Genetics. The referral should include name and DOB of relative diagnosed with FH, and the area of the UK in which they underwent genetic testing. (If the relative's name/DOB are unavailable then please request a full lipid profile and refer to the lipid clinic.)
    - **FH is suspected based on cholesterol levels and family history** (i.e. there is no known genetic FH diagnosis in the family), see following section to determine if a lipid clinic referral is required. **Suspected FH in adults (>16 years-old)**

Please refer individuals with raised LDL cholesterol* and a suggestive family history:

** exclude non-inherited causes such as alcohol excess, uncontrolled diabetes, untreated hypothyroidism etc*

Family history

1st/2nd degree relative(s) with:

- ASCVD <60 yrs

OR

- LDL-C ≥5.0 (or total chol ≥7.5)

***AND** any of:*

LDL-C above age-specific threshold:

Age (years)	**untreated LDL-C (mmol/L)**
16 – 29	≥5.0
30 – 39	≥5.5
40 – 54	≥6.0
≥ 55	≥6.5

OR

Personal history of ASCVD < 60 yrs AND untreated LDL-C ≥5.0

OR

Tendon xanthoma, or corneal arcus (<45 yrs) AND untreated LDL-C ≥5.0

ASCVD = atherosclerotic cardiovascular disease

It would also be reasonable to refer any adult with LDL-C ≥5.0 mmol/L, and a 1st/2nd degree relative with history of **very early-onset coronary artery disease** (under age of 45 years).

Additional information

FH patients have very elevated *LDL cholesterol*, and typically *normal triglycerides*

- elevated *total cholesterol* associated with triglycerides >3.0 mmol/L is **not** suggestive of FH
- FH is a life-long condition. FH is unlikely if a previous untreated LDL cholesterol was less than 4.5 mmol/L (since age of 25 years). This is particularly true if lifestyle factors (e.g. obesity, alcohol excess, medications) are likely to account for a more recent rise in cholesterol.

Contact us by email (Lipid Clinic Advice) if you are uncertain about whether to refer.

Children with suspected FH (<16 years-old):

- Consider FH where LDL-C ≥4.0 mmol/L, and 1st/2nd degree relative known to have ASCVD <60 yr, or hypercholesterolaemia
- Refer children with known or suspected inherited hyperlipidaemia to the paediatric inherited metabolic disorders service (Dr Alison Cozens, Consultant Paediatrician, RHCYP).

B. Suspected inherited mixed hyperlipidaemia: total chol >7.0 AND trigs >3.0 (in the absence of a secondary cause)

The two most common forms of inherited mixed hyperlipidaemia are:

- **Familial Combined Hyperlipidaemia (FCH)** – does **not** usually require referral to the lipid clinic and,
- **Type III hyperlipoproteinaemia** (also known as Remnant Hyperlipidaemia) which does require referral to the lipid clinic.

Familial combined hyperlipidaemia (FCH)

Consider diagnosis where total chol >7.0 AND trigs >3.0 mmol/L, AND family history of early-onset coronary heart disease (1st deg relative with ASCVD-onset before 60 years old). FCH is common and caused by a combination of non-inherited and polygenic factors. It is not amenable to genetic or other specialist diagnostic testing, and does not generally require referral to the lipid clinic.
Approach is guided by ASSIGN scoring:

- ASSIGNv2.0 score >10%*: recommend statin primary prevention
- ASSIGNv2.0 score <10%*: recommend 6 months of lifestyle measures. If hyperlipidaemia unresponsive to lifestyle measures, consider statin primary prevention – particularly where hyperlipidaemia is severe e.g. non-HDL-C >6.0 mmol/L or very strong family history or other major risk factors are proving refractory to improvement (e.g. heavy smoking, hypertension).

**threshold is 20% for older ASSIGNv1.5*

Type III hyperlipoproteinaemia (or Remnant hyperlipidaemia)

Consider where total chol >7.0 AND *fasting* trigs >4.5 mmol/L in the absence of a secondary cause. It is most commonly autosomal recessive i.e. siblings may be similarly affected. And confers high-risk of early-onset coronary heart disease and peripheral vascular disease. It may present with

eruptive xanthomata over extensor surfaces or trunk. The combination of palmar xanthoma (yellow-orange accentuation of palmar creases) and mixed hyperlipidaemia is pathognomic.

If Type III is suspected then please refer to lipid clinic for consideration of genetic screening, and statin or fibrate therapy.

C. Raised lipoprotein(a), or Lp(a)

Lipoprotein(a) or Lp(a) is a cholesterol-carrying particle similar to low-density lipoprotein (LDL). Most of the population have low levels of Lp(a) - under 30 mg/dL (or approx 75 nmol/L). When present at very high levels, Lp(a) confers a significant cardiovascular risk (independent to other CV risk factors) and is associated with early-onset CVD and aortic stenosis. Lp(a) is largely genetically determined although may also be elevated in nephrotic syndrome, CKD and hypothyroidism.

Referral criteria

- Individuals with a first-degree relative with very raised Lp(a) >180 mg/dL, or >400 nmol/L - consider Lp(a) measurement. This can be done by collecting blood into a pink-topped (EDTA) specimen tube and sending to the lab with a handwritten request form for "Lipoprotein (a)". The result should be available within 4 weeks. Please refer patients with Lipoprotein (a) >30 mg/dL to the lipid clinic for further advice or assessment.
- Patients with known raised Lp(a) - consider referral for advice or assessment if no previously agreed plan for management of cardiovascular risk. A raised Lp(a) is usually considered to be >30 mg/dL or >75 nmol/L. (The vast majority of patients with raised Lp(a) do NOT require long-term lipid clinic follow-up.)
- Please include the following information with your referral:
    - Lipoprotein (a) result – including units (mg/dL or nmol/L). Or if possible, attach a copy of the original laboratory report.
    - Family history of ASCVD or aortic stenosis (including age of onset)
    - ASSIGN (please specify if v1.5 or v2.0) or QRISK score
    - Recent full lipid profile, BP
    - Smoking status
    - Other relevant risk factors: diabetes, obesity, MASLD / fatty liver