Appendix

Box 1. Diagnostic criteria using Simon Broome register.

Definite familial hypercholesterolaemia is defined as

a) Total cholesterol > 6.7 mmol/l or LDL cholesterol above 4.0 mmol/l in a child < 16 years or Total cholesterol >7.5 mmol/l or LDL cholesterol above 4.9 mmol/l in an adult.
PLUS
b) b) Tendon xanthomas in patient, or in 1st degree relative (parent, sibling, child), or in 2nd degree relative (grandparent, uncle, aunt)
OR
c) DNA-based evidence of an LDL receptor mutation or familial defective apo B-100 or PCSK9 mutation

Possible familial hypercholesterolaemia is defined as

a) PLUS d) or e)
d) Family history of myocardial infarction: below age of 50 in 2nd degree relative or below age 60 in 1st degree relative
e) Family history of raised cholesterol:
>7.5 mmol/l in adult 1st or 2nd degree relative or
>6.7 mmol/l in child or sibling under 16

Box 2. Dutch Lipid Clinic Network diagnostic criteria for FH.

Group 1: family history		Points
(i)	First-degree relative with known premature (<55 years, men; <60 years, women) coronary heart disease(CHD)	1
	OR	
(ii)	First-degree relative with known LDL cholesterol > 95th percentile by age and gender for country	1
(iii)	First-degree relative with tendon xanthoma and/or corneal Arcus	2
	OR	
(iv)	Child(ren) <18 years with LDL cholesterol > 95th percentile by age and gender for country	2
Group 2: clinical history		
(i)	Subject has premature (<55 years, men; <60 years, women) CHD	2
(ii)	Subject has premature (<55 years, men; <60 years, women) cerebral or peripheral vascular disease	1
Group 3: physical examination		
(i)	Tendon xanthoma	6
(ii)	Corneal arcus in a person <45 years	4
Group 4: biochemical results (LDL cholesterol)		
>8.5 mmol/L(>325 mg/dL)		8
6.5–8.4 mmol/L (251–325 mg/dL)		5
5.0–6.4 mmol/L (191–250 mg/dL)		3
4.0–4.9 mmol/L (155–190 mg/dL)		1
Group 5: molecular genetic testing (DNA analysis)		
(i) Causative mutation shown in the LDLR, APOB, orPCSK9 genes		8

A ‘definite FH’ diagnosis can be made if the subject scores >8 points. A ‘probable FH’ diagnosis can be made if the subject scores 6 to 8 points. A ‘possible FH’ diagnosis can be made if the subject scores 3 to5 points. An ‘unlikely FH’ diagnosis can be made if the subject scores 0 to 2 points.

Familial Hypercholesterolaemia Primary Care Survey Questions

Q1: On a scale of 1 to 7; how familiar are you with familial hypercholesterolaemia?
Q2: Are you aware of guidelines on the detetion and management of familiar hypercholesterolaemia?

- Yes
- No

Q3: Which one description below best describes familial hypercholesterolaemia?

- The presence of family members with diagnosed high cholesterol
- A genetic disorder that is characterized by very high cholesterol and a family history of premature heart disease
- The presence of multiple lipid abnormalities that may be genetic in nature
- An ultra-rare, potentially fatal condition caused by cholesterol of levels that can be up to six times the normal level
- Don't know

Q4: Which one of the following lipid profiles is most consistent with the diagnosis of familiar hypercholesterolaemia? (Reference intervals: Total cholesterol <5.5mmol/L; Triglyceride <1.7mmol/L; HDL-cholesterol >1.0mmol/L; LDL-cholesterol <3.5mmol/L)

- Total cholesterol 6.0mmol/L; Triglyceride 3.4mmol/L; HDL-cholesterol 0.8mmol/L; LDL-cholesterol 3.8mmol/L
- Total cholesterol 6.3mmol/L; Triglyceride 12.2mmol/L; HDL-cholesterol 1.0mmol/L; LDL-cholesterol -mmol/L
- Total cholesterol 8mmol/L; Triglyceride 1.1mmol/L; HDL-cholesterol 1.0mmol/L; LDL-cholesterol 6.5mmol/L
- Total cholesterol 5.4mmol/L; Triglyceride 1.3mmol/L; HDL-cholesterol 1.7mmol/L; LDL-cholesterol 3.1mmol/L
- Total cholesterol 7.1mmol/L; Triglyceride 1.0mmol/L; HDL-cholesterol 3.5mmol/L, LDL-cholesterol 3.2mmo/L

Q5: Which one of the following options could usefully assist you in detection of familial hypercholesterolaemia in your practice?

- Laboratory report on a lipid profile alerting possible familial hypercholesterolaemia
- Alert by the clinical software system in your practice
- Direct telephone call from the laboratory
- All of the above
- None of the above
- Don't know

Q6: What is the prevalence of familial hypercholesterolaemia in the UK?

- 1 in 100 persons
- 1 in 500 persons
- 1 in 1,000 persons
- 1 in 2,000 persons
- 1 in 5,000 persons
- Don't know

Q7: What is the likelihood that first degree relatives (i.e. parents, siblings and children) of someone who has familial hypercholesterolaemia will also have the condition themselves?

- 0%
- 25%
- 50%
- 75%
- 100%
- Don’t know

Q8: How much greater is the risk of premature coronary heart disease (CHD) in untreated familial hypercholesterolaemia patients compared to the general population?

- 2 times greater
- 5 times greater
- 10 times greater
- 20 times greater
- 50 times greater
- Don’t know

Q9: When you are assessing a patient’s family history, at what age for males and females do you consider heart disease to be ‘premature’? Leave blank if you wish to answer ‘Don’t know’.

Q10: In patients with documented premature coronary artery disease which of the following do you routinely carry out? (Please tick all that apply)

- Look for arcus cornealis
- Look for tendon xanthomata
- Take a detailed family history of coronary artery disease
- Screen close relatives for hypercholesterolaemia
- All of the above
- None of the above

Q11: Is the following statement true or false? An accurate diagnosis of familial hypercholesterolaemia can only be made via genetic test.

- True
- False
- Don’t know

Q12: How many patients currently under your care, if any, have been formally diagnosed with familial hypercholesterolaemia?

Q13: If you have patients with familial hypercholesterolaemia under your care do you routinely screen close relatives for this condition with a lipid profile?

- Yes patient’s children only
- Yes patient’s children and other close relatives
- No
- Not applicable

Q14: In your view, which healthcare providers would be most effective at early detection of familial hypercholesterolaemia and screening first degree relatives? (Please tick up to two)

- Lipid specialists
- General practitioners
- Cardiologists
- Nurses with experience in cardiac risk prevention
- Pediatricians
- Obstetricians/Gynecologists

- Endocrinologists

Q15: At what age would you test young individuals for hypercholesterolaemia in a family with premature coronary heart disease?

- 0 – 6 years
- 7 – 12 years
- 13 – 18 years
- None of the above
- Don't know

Q16: Are you aware of any specialist-clinical services for lipid disorders to whom you can refer patients?

- Yes
- No (Go to question 18)

Q17: If yes to question 16, have you referred patients with familial hypercholesterolaemia to this service?

- Yes
- No
- Don't know

Q18: Which drugs do you use to treat hypercholesterolaemia? (Please select all that apply)

- Exchange resins/bile acid sequestrants
- Ezetimibe
- Statins
- Fibrates
- Nicotinic acid
- None of the above

Q19: Which drug combinations do you use to treat severe hypercholesterolaemia? (Please select all that apply)

- Statin + Exchange resins/bile acid sequestrants
- Statin + nicotinic acid
- Statin + ezetimibe
- Statin + ezetimibe + nicotinic acid
- Statin + ezetimibe + Exchange resins/bile acid sequestrants
- None of the above

Q20: What is your gender?

- Female
- Male
- Prefer not to say

Q21: How would you describe the area of your practice?

- GP – Metropolitan
- GP – Outer metropolitan
- GP – rural
- Specialist physician – Cardiologist
- Specialist physician – Other

Q22: How many years have you been in practice since completing your medical degree?

Q23: Approximately how many patients do you see for any condition in an average month?

Q24: Have you previously completed this questionnaire?

- Yes
- No
- Not sure