Familial Hypercholesterolaemia: a Primary Care Perspective

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in collaboration with
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Cholesterol....

“Good news. Your cholesterol has stayed the same, but the research findings have changed.”

Harley Schwadron for Reader's Digest
Lambeth DataNet (LDN)

- Data source: Lambeth DataNet Primary Care EHRs from 44 practices (~400,000 patients), in SE London, inner city ethnically diverse population.

'Personal profile' data:
Ethnicity*, language*, religion, country of birth*

Clinical data: Clinical diagnoses, laboratory values, medication, measurements BMI, Blood pressure

Prescribing: Dose, frequency, amount

Longitudinal data: monitoring conditions, treatments, outcomes
Lambeth, London

Simon Broome criteria

Definite FH:
- TC > 6.7 mmol/l or LDL-C > 4.0 mmol/l (child < 16y)
  or TC > 7.5 mmol/l or LDL-C > 4.9 mmol/l (adult)
  (levels either pre-treatment or highest on treatment)
  plus
  - tendon xanthomas in patient, or in 1st relative (parent, sibling, child), or in 2nd relative (grandparent, uncle, aunt)
  or
  - DNA-based evidence of an LDL receptor mutation, familial defective apo B-100, or a PCSK9 mutation.

Possible FH is defined as above lipids plus one of:
- family history of myocardial infarction: below age of 50 years in 2nd relative or below age 60 years in 1st relative
  or
- family history of raised TC > 7.5 mmol/l in adult 1st or 2nd relative or > 8.7 mmol/l in child or sibling < 16y

- FH assessed according to modified Simon Broome Criteria
  cholesterol ≥ 7.5mmol/L and raised LDL ≥ 4.9mmol/L
- Explored by age strata and ethnic groups
2019 Lambeth population by ethnic group (all ages)
n = 399036
Age adjusted lipid distribution in adults ≥ 40 years

n=151, 140

Age adjusted percentage in Lambeth LSOAs for raised cholesterol ≥ 7.5mmol/L

Age adjusted percentage in Lambeth LSOAs for raised LDL ≥ 4.9mmol/L

Age adjusted percentage in Lambeth LSOAs for raised cholesterol ≥ 7.5mmol/L and raised LDL ≥ 4.9mmol/L

Lambeth DataNet Extract 05/2018
Screening for possible FH: cholesterol $\geq 7.5$mmol/L and raised LDL $\geq 4.9$mmol/L

**Methods:**

Generalised linear models (R) (GLM) is a flexible generalization of ordinary linear regression - allows for response variables that have error distribution models other than a normal distribution

Model of raised cholesterol by i) age-group and ii) ethnicity
Prevalence of cholesterol $\geq 7.5$mmol/L and raised LDL $\geq 4.9$mmol/L by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Prevalence modelled (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40s</td>
<td>0%</td>
</tr>
<tr>
<td>50s</td>
<td>1%</td>
</tr>
<tr>
<td>60s</td>
<td>2%</td>
</tr>
<tr>
<td>70s</td>
<td>3%</td>
</tr>
<tr>
<td>80s</td>
<td>4%</td>
</tr>
<tr>
<td>90+</td>
<td>5%</td>
</tr>
</tbody>
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Interpretation: For patient in 40’s there is a probability (fit) $\sim 1.2\%$ of raised cholesterol & LDL increases to around 6.3% in 70’s then decreases.
Prevalence of cholesterol ≥ 7.5mmol/L and raised LDL ≥ 4.9mmol/L by ethnic group in adults ≥ 40 years

![Bar chart showing prevalence of cholesterol and LDL by ethnic group.](chart.png)
FAMCAT FEASIBILITY PILOT: South London

Aim: To prospectively evaluate usability of the FAMCAT tool to identify familial hypercholesterolaemia in primary care.

Design: Feasibility study 5 EMISWEB practices in S London (Lambeth & Southwark)

Intervention:
1. Use of a FAMCAT, in GP electronic health records, to identify patients with a high probability of FH
2. FAMCAT tool feedback

Outcomes: Ranked list high risk FH cases for further clinical assessment
**Familial Hypercholesterolaemia Case Ascertainment Tool (FAMCAT) & web based calculator**

**Risk score**

<table>
<thead>
<tr>
<th>ENTER/SELECT DETAILS BELOW:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Gender: Male</td>
<td></td>
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<tr>
<td>Age at the time cholesterol measured (years): 65</td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L): 7.5</td>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol (mmol/L): 4.9</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mmol/L): 2.12</td>
<td></td>
</tr>
<tr>
<td>On lipid lowering drug therapy when cholesterol measured: Atorvastatin 5 mg/day</td>
<td></td>
</tr>
<tr>
<td>Family history of familial hypercholesterolaemia: No</td>
<td></td>
</tr>
<tr>
<td>Family history of myocardial interction: Yes</td>
<td></td>
</tr>
<tr>
<td>Family history of raised cholesterol: No</td>
<td></td>
</tr>
<tr>
<td>Previously diagnosed with diabetes: No</td>
<td></td>
</tr>
<tr>
<td>Previously diagnosed with chronic kidney disease: No</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>FAMCAT Calculator</th>
<th>Probability (%)</th>
<th>Relative Population Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likelihood of having familial hypercholesterolaemia</td>
<td>0.01</td>
<td>3.13</td>
</tr>
</tbody>
</table>
Familial Hypercholesterolaemia Case Ascertainment Tool (FAMCAT)

Five key actions following use of the FH quality improvement tool

Review any patients at very high risk of developing FH who have not had recent screening

Click through the summary sheet to access this patient list. The inbuilt mail merge function can also assist with generating invitation letters.

Review any patients with FH who have not had recent screening

Patients with a coded diagnosis of FH who have not had screening in the last 12 months may also benefit from review to ensure they are on the best treatment.

Improve recording of important family history information through systematic collection

Patients classified as being at high risk of FH who do not have a family history recorded should be encouraged to collect systematic family history. High risk patients may well become very high risk once an accurate family history has been recorded (and this is positive). The mail merge function can assist with generating letters to send to these high risk patients about collecting their family history.

Assess current treatment regimes

Review the type and dosage of lipid lowering therapy for patients who are diagnosed with FH. If diagnosed patients are not currently being treated (and are not contraindicated), consider commencement of lipid lowering medication.

Review coding standards within the practice

Use the information provided with the report to assess the accuracy of coding, particularly in relation to confirming FH diagnoses, drug allergies and contraindications and important family history codes. Consider the reasons why any data items are missing and how to prevent recurrence for other patients.

FAMCATT Searches Lambeth: FH CHART Summary Report

Total very high risk FH (4 practices; 5th IP) n=234/37, 365 ~0.07%

Diagnosis and Screening

Family History Recording

Lipid lowering prescribing
Ranked list highest>lowest probability of FH

Several (< 50 years) with high FH risk

Risk stratification → these are the priority cases to be assessed

Sample patient data from a South London general practice
Why documenting cholesterol is important:
CPRD Matched cohort study of new users of AC/AP drugs
Comparator = non-use (within 365 days before index date)

Risk 1 (death, 10218 events)
Risk 2 (hospital admissions, 57678 events)
Risk 3 (ICB (stroke), 430 events)
Risk 4 (Gastrointestinal Bleed, 5385 events)
Bias: Informative missingness

Risk 1 (death): Longitudinal data suggest patients with missing cholesterol have poorer survival
Conclusions

Burden of undiagnosed and untreated cases - avoidable CVD and morbidity

Inequalities and unmet need: significant younger age groups

Feasible diagnostic and ascertainment pilot in S London
With thanks to Nadeem Qureshi, Stephen Weng, Ton Coolen, Mark Rowley, participating practices and patients and colleagues
Prevalence of cholesterol ≥ 7.5mmol/L and raised LDL ≥ 4.9mmol/L by ethnic group

Ethnicity

Prevalence (age adjusted %)