

# **Appendix F**

## **Simon Broome Diagnostic criteria for index individuals and relatives**

|            |   |          |
|------------|---|----------|
| <b>1</b>   | <b>SIMON BROOME DIAGNOSTIC CRITERIA FOR INDEX INDIVIDUALS (PROBANDS)</b>                                | <b>2</b> |
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## Diagnostic criteria

### 1 Simon Broome diagnostic criteria for index individuals (probands)<sup>1</sup>

Diagnose a person with **definite** familial hypercholesterolaemia (FH) if they have:

- cholesterol concentrations as defined in table 1 and tendon xanthomas, or evidence of these signs in first- or second-degree relative
- or
- DNA-based evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.

Diagnose a person with **possible** FH if they have cholesterol concentrations as defined in table 1 **and** at least one of the following.

- Family history of myocardial infarction: aged younger than 50 years in second-degree relative or aged younger than 60 years in first-degree relative.
- Family history of raised total cholesterol: greater than 7.5 mmol/l in adult first- or second-degree relative or greater than 6.7 mmol/l in child, brother or sister aged younger than 16 years.

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<sup>1</sup> From Marks D, Thorogood M, Neil HA, Humphries SE. A review on the diagnosis, natural history, and treatment of familial hypercholesterolaemia. *Atherosclerosis* 2003; 168(1):1-14.

**Table 1 Cholesterol levels to be used as diagnostic criteria for the index individual<sup>1</sup>**


|                    | Total cholesterol | LDL-C        |
|--------------------|-------------------|--------------|
| Child/young person | > 6.7 mmol/l      | > 4.0 mmol/l |
| Adults             | > 7.5 mmol/l      | > 4.9 mmol/l |


<sup>1</sup> levels either pre-treatment or highest on treatment.


LDL-C, low-density lipoprotein cholesterol.

## **2 Gender- and age-specific LDL-C criteria for the diagnosis of FH in relatives of a person with FH<sup>2</sup>**

These gender- and age-specific LDL-C criteria are to be used for the diagnosis of FH in the relatives of an index case with FH where the family mutation has not been identified. These are intended for use by healthcare professionals with expertise in FH.

 Relatives with LDL-C levels in the green zone are unlikely to have FH. In these instances, manage the person's coronary heart disease risk as in the general population (see 'Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease', NICE clinical guideline 67).

 Relatives with LDL-C levels in the red zone are likely to have a clinical diagnosis of FH.

 The diagnosis of FH for relatives in the grey zone is uncertain. A further measurement of LDL-C concentration should be carried out, and if the level is still in the grey zone this should be repeated annually. If the person's LDL-C concentration remains in the grey zone then coronary heart disease risk should be assessed and managed as in the general population (see 'Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease', NICE clinical guideline 67).

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<sup>2</sup> From Starr B, Hadfield SG, Hutten BA, Landsberg P, Leren TP, Damgaard D, Neil HAW and Humphries SE (2008) Development of sensitive and specific age- and gender-specific low density lipoprotein cholesterol cutoffs for diagnosis of first-degree relatives with familial hypercholesterolaemia in cascade testing. *Clinical Chemistry and Laboratory Medicine* 46 (6): 791–803.

**2.1 LDL-C females\***

| LDL-C females |          |          |          |          |              |
|---------------|----------|----------|----------|----------|--------------|
| Age (years)   |          |          |          |          |              |
| 0 to 14       | 15 to 24 | 25 to 34 | 35 to 44 | 45 to 54 | 55 and older |
| 5.3           | 5.3      | 5.3      | 5.3      | 5.3      | 5.3          |
| 5.2           | 5.2      | 5.2      | 5.2      | 5.2      | 5.2          |
| 5.1           | 5.1      | 5.1      | 5.1      | 5.1      | 5.1          |
| 5.0           | 5.0      | 5.0      | 5.0      | 5.0      | 5.0          |
| 4.9           | 4.9      | 4.9      | 4.9      | 4.9      | 4.9          |
| 4.8           | 4.8      | 4.8      | 4.8      | 4.8      | 4.8          |
| 4.7           | 4.7      | 4.7      | 4.7      | 4.7      | 4.7          |
| 4.6           | 4.6      | 4.6      | 4.6      | 4.6      | 4.6          |
| 4.5           | 4.5      | 4.5      | 4.5      | 4.5      | 4.5          |
| 4.4           | 4.4      | 4.4      | 4.4      | 4.4      | 4.4          |
| 4.3           | 4.3      | 4.3      | 4.3      | 4.3      | 4.3          |
| 4.2           | 4.2      | 4.2      | 4.2      | 4.2      | 4.2          |
| 4.1           | 4.1      | 4.1      | 4.1      | 4.1      | 4.1          |
| 4.0           | 4.0      | 4.0      | 4.0      | 4.0      | 4.0          |
| 3.9           | 3.9      | 3.9      | 3.9      | 3.9      | 3.9          |
| 3.8           | 3.8      | 3.8      | 3.8      | 3.8      | 3.8          |
| 3.7           | 3.7      | 3.7      | 3.7      | 3.7      | 3.7          |
| 3.6           | 3.6      | 3.6      | 3.6      | 3.6      | 3.6          |
| 3.5           | 3.5      | 3.5      | 3.5      | 3.5      | 3.5          |
| 3.4           | 3.4      | 3.4      | 3.4      | 3.4      | 3.4          |
| 3.3           | 3.3      | 3.3      | 3.3      | 3.3      | 3.3          |
| 3.2           | 3.2      | 3.2      | 3.2      | 3.2      | 3.2          |

**2.2 LDL-C males\***

| LDL-C males |          |          |          |          |              |
|-------------|----------|----------|----------|----------|--------------|
| Age (years) |          |          |          |          |              |
| 0 to 14     | 15 to 24 | 25 to 34 | 35 to 44 | 45 to 54 | 55 and older |
| 5.3         | 5.3      | 5.3      | 5.3      | 5.3      | 5.3          |
| 5.2         | 5.2      | 5.2      | 5.2      | 5.2      | 5.2          |
| 5.1         | 5.1      | 5.1      | 5.1      | 5.1      | 5.1          |
| 5.0         | 5.0      | 5.0      | 5.0      | 5.0      | 5.0          |
| 4.9         | 4.9      | 4.9      | 4.9      | 4.9      | 4.9          |
| 4.8         | 4.8      | 4.8      | 4.8      | 4.8      | 4.8          |
| 4.7         | 4.7      | 4.7      | 4.7      | 4.7      | 4.7          |
| 4.6         | 4.6      | 4.6      | 4.6      | 4.6      | 4.6          |
| 4.5         | 4.5      | 4.5      | 4.5      | 4.5      | 4.5          |
| 4.4         | 4.4      | 4.4      | 4.4      | 4.4      | 4.4          |
| 4.3         | 4.3      | 4.3      | 4.3      | 4.3      | 4.3          |
| 4.2         | 4.2      | 4.2      | 4.2      | 4.2      | 4.2          |
| 4.1         | 4.1      | 4.1      | 4.1      | 4.1      | 4.1          |
| 4.0         | 4.0      | 4.0      | 4.0      | 4.0      | 4.0          |
| 3.9         | 3.9      | 3.9      | 3.9      | 3.9      | 3.9          |
| 3.8         | 3.8      | 3.8      | 3.8      | 3.8      | 3.8          |
| 3.7         | 3.7      | 3.7      | 3.7      | 3.7      | 3.7          |
| 3.6         | 3.6      | 3.6      | 3.6      | 3.6      | 3.6          |
| 3.5         | 3.5      | 3.5      | 3.5      | 3.5      | 3.5          |
| 3.4         | 3.4      | 3.4      | 3.4      | 3.4      | 3.4          |
| 3.3         | 3.3      | 3.3      | 3.3      | 3.3      | 3.3          |
| 3.2         | 3.2      | 3.2      | 3.2      | 3.2      | 3.2          |
| 3.1         | 3.1      | 3.1      | 3.1      | 3.1      | 3.1          |
| 3.0         | 3.0      | 3.0      | 3.0      | 3.0      | 3.0          |