Familial Hypercholesterolaemia screening - application of genetic testing and diagnostic LDL-C cut-off values for relatives of FH patients in a Welsh population

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- Family cascade testing is an efficient way to diagnose FH and enable treatment to prevent premature coronary heart disease.

- Current British FH screening strategy is to detect relatives through cascade testing using age and gender adjusted LDL-Cholesterol values largely derived from a Dutch population.

- This study evaluated the validity of these cut-offs when applied to a Welsh population and compared these to DNA genotype testing, the diagnostic gold standard.

Methods: 30 index patients with a DNA diagnosis of heterozygous FH were recruited from Lipid Clinics in Cardiff and Bridgend.

90 relatives were then recruited to the study. LDL-C tests and DNA genotype results were available for these relatives.

The distribution of LDL cholesterol is shown for genotype positive relatives and compared with genotype negative relatives.

Overall, the Dutch-derived cut-off values performed satisfactorily on the local patients (sensitivity 91.5%, specificity 93.0%). However, sensitivity and specificity declined with increasing age, reaching 80% and 70% respectively for the 45-54 group.

This is caused by increasing baseline LDL-C values with increasing age in genotype negative patients as shown by increasing overlap in the distributions. Thus, the positive predictive value of the Dutch diagnostic cut-off values decreases with age.

Conclusion: Genetic testing should be incorporated into UK cascade testing for FH, especially in older age groups to overcome diagnostic ambiguity.

References