Audit of patient selection for Familial Hypercholesterolaemia (FH) genetic testing over a 2-year period with retrospective comparison of the Simon-Broome criteria vs the Dutch Lipid Clinic Network (DLCN) criteria vs the Wales FH service genotype scoring criteria.

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INTRODUCTION

Familial hypercholesterolaemia (FH) is a genetic disease that results in elevated levels of low-density lipoprotein cholesterol (LDL-C) and predisposes to early onset cardiovascular disease. Three main scoring systems – the Simon-Broome criteria, the Dutch Lipid Clinic Network (DLCN) criteria and the Wales FH Service genotype scoring criteria, exist to facilitate patient selection for genetic testing. NICE Guideline CG71 recommends the use of Simon Broome criteria or DLCN criteria to make a clinical diagnosis of FH in primary care settings. This audit aimed to discern which criteria performed best within a specialised lipid clinic.

METHODS

Patients that attended a consultant-led specialist lipid clinic and received genetic testing for FH between September 2019 and August 2021 were identified and scored retrospectively against the three scoring systems. Cascade tests and tests that did not have results available at the time of audit were excluded. Comparisons between the three systems were made for sensitivity, specificity, positive predictive value and negative predictive value. 70 patients were included in the final analysis. False negatives, defined as patients identified as not meet testing criteria retrospectively but had a pathogenic variant identified, were numbered and their clinical notes analysed against the three scoring systems to determine any factors that may aid in reducing false negatives.

RESULTS

10 out of 70 patients were found to have a known pathogenic variant for FH.

	Simon-Broome	DLCN criteria	Wales FH service genotype score
Number of patients who met testing criteria	40	56	17
True positives	5	9	5
False positives	35	47	12
Number of patients who did not meet testing criteria	30	14	53
True negatives	25	13	48
False negatives	5	1	5
Sensitivity	50%	90%	50%
Specificity	~41.7%	~21.7%	80%
Positive predictive value (PPV)	12.5%	~16.1%	~29.4%
Negative predictive value (NPV)	83.3%	~92.9%	~90.6%

False negatives analysis:

(LDL-C levels in mmol/L; ✓: Met criteria; ✕: Did not meet criteria)

Patient	Simon-Broome Criteria		DLCN criteria *		Wales FH service genotype score **	
1	✓		✓		LDL-C 5.9 Premature MI in 1° relative Unknown family history of high cholesterol	✕
2 (Possible family history of FH)	LDL-C **not** > 4.9 Premature MI in 1° relative Family history of high cholesterol, exact levels not known	✕	LDL-C 4.5	✕	LDL-C 4.5 Premature MI in 1° relative Family history of high cholesterol, exact levels not known	✕
3 (Possible family history of FH)	LDL-C > 4.9 No history of premature MI in 1° / 2° relative No known family history of high cholesterol	✕	✓		LDL-C 7.7	✕
4	LDL-C > 4.9 No history of premature MI in 1° / 2° relative Family history of high cholesterol, exact levels not known	✕	✓		LDL-C 7.1 Family history of high cholesterol, exact levels not known	✕
5 (Possible FH diagnosis decades ago)	LDL-C > 4.9 No history of premature MI in 1° / 2° relative Family history of high cholesterol, exact levels not known	✕	✓		LDL-C 8.0 Family history of high cholesterol, exact levels not known	✕
6	LDL-C > 4.9 No history of premature MI in 1° / 2° relative Family history of high cholesterol, exact levels not known	✕	✓		✓	

- 3/6 patients (Patient 2, 3, 5) warranted further investigations due to possible personal or family history of FH.
- 3/6 patients (Patient 4, 5, 6) would have met criteria for all three scoring systems if family history of high cholesterol was quantified and found to be out of the respective specified ranges.
- Patient 1 may have met the criteria for Wales FH service genotype score if information for all components of the family history required was available.

CONCLUSION

No scoring system was able to retrospectively pick up all patients that had a pathogenic variant on genetic testing. DLCN criteria was superior in terms of sensitivity (90%) and negative predictive value (~92.9%). Wales FH service genotype score was superior in terms of specificity (80%) and positive predictive value (~29.4%). If a patient does not meet DLCN criteria for testing, it is less likely that the patient has FH. If the patient meets the Wales FH service genotype score, it is more likely that the patient has FH. False negatives using any of the three criteria may be reduced by using clinical judgement and by obtaining a comprehensive family history. Recommendation of Wales FH service genotype score for clinical diagnosis of FH may potentially be of value in the primary care setting.