Application of a risk stratification tool for familial hypercholesterolaemia in primary care: an observational cross-sectional study in an unselected urban population

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ABSTRACT

Objective The Familial Hypercholesterolaemia Case Ascertainment Tool (FAMCAT) has been proposed to enhance case finding in primary care. In this study, we test application of the FAMCAT algorithm to describe risks of familial hypercholesterolaemia (FH) in a large unselected and ethnically diverse primary care cohort.

Method We studied patients aged 18–65 years from three contiguous areas in inner London. We retrospectively applied the FAMCAT algorithm to routine primary care data and estimated the numbers of possible cases of FH and the potential service implications of subsequent investigation and management.

Results Of the 777 128 patients studied, the FAMCAT score estimated between 11 736 and 23 798 (1.5%–3.1%) individuals were likely to have FH, depending on an assumed FH prevalence of 1 in 250 or 1 in 500, respectively. There was over-representation of individuals of South Asian ethnicity among those likely to have FH, with this cohort making up 41.9%–45.1% of the total estimated cases, a proportion which significantly exceeded their 26% representation in the study population.

Conclusions We have demonstrated feasibility of application of the FAMCAT as an aid to case finding for FH using routinely recorded primary care data. Further research is needed on validity of the tool in different ethnic groups and more refined consideration of family history should be explored. While FAMCAT may aid case finding, implementation requires information on the cost-effectiveness of additional health services to investigate, diagnose and manage case ascertainment in those identified as likely to have FH.

INTRODUCTION

The National Health Service (NHS) Long Term Plan is committed to reducing cardiovascular disease with an ambition to prevent 150 000 strokes, heart attacks and dementia cases over 10 years by detecting and treating risk factors including hypercholesterolaemia.¹ Ischaemic heart disease (IHD) and strokes are among the most common causes of death in the UK² with particularly high risks where the median age-standardised prevalence of hypercholesterolaemia (>6.2 mmol/L) exceeds 20%.³ The Global Burden of Disease Study and the

WHO Global Action Plan highlight that reduction of premature cardiovascular mortality is an international priority.^{4 5}

Familial hypercholesterolaemia (FH) is a genetic disorder characterised by elevated serum low-density lipoprotein cholesterol (LDL-C).^{6 7} In individuals of European descent, FH is associated with a 10-fold greater lifetime risk of IHD and early death.⁸ Diagnosis is through clinical evaluation with validated diagnostic criteria (Simon Broome (SB) or Dutch Lipid Clinic Network (DLCN)) and consideration of genetic testing.⁹ Global cardiovascular risk scores are not applicable to patients with FH as they are already at high risk of IHD.^{8 10} Evidence supports early treatment in substantially reducing the risk of FH-related IHD and mortality. For patients with an inadequate response to standard therapies, there are expanded options from secondary care including PCSK9 inhibitors and new-in-class drugs.^{11–14} However, over 75% of estimated FH cases are undiagnosed^{15 16} representing a missed opportunity to reduce the burden of cardiovascular disease.

Existing approaches to case finding of FH in primary care are suboptimal. The National Institute of Clinical Excellence advises assessment of people considered at high risk of FH based on total cholesterol levels or reported family history.¹⁰ Time and resource constraints in primary care precludes application of the SB and DLCN assessment consistently and completely in large numbers of patients. Therefore, current approaches to case finding are associated with significant inaccuracies and have the potential for underdiagnosis of FH and referral of high numbers of false positives.

The FH Case Ascertainment Tool (FAMCAT) is an externally validated case finding tool to identify individuals likely to have FH through systematic searching of routine primary care records for lipid profiles and other contributory variables.^{17 18} Subsequent targeting of detailed clinical assessments to those at highest risk could enable more appropriate use of limited clinical resources, greater accuracy in identification of cases and improvement in case finding coverage.^{19 20} Estimates of the cohort size allow for service planning and commissioning intentions, including primary care workload, demand for genetic testing and development of specialist clinics.

OBJECTIVE

In this study, we retrospectively applied the FAMCAT to an unselected population of over 770 000 primary care patients aged 18–65 years in East London, UK, using routinely collected primary care data. We report on the risk stratification of the population by FAMCAT and the number of cases identified as likely to have FH, requiring further clinical assessment.

METHODS

Study setting

The analysis dataset included all primary care patients aged 18–65 years registered with general practitioners within three Clinical Commissioning Groups (CCGs) in East London. This comprised 127 practices (City and Hackney, $n=42$; Newham, $n=50$; Tower Hamlets, $n=35$), which use the Egton Medical Information Systems (EMIS) electronic health record. Compared with UK averages, this inner urban population has a greater proportion of individuals from black, South Asian and minority ethnic groups, younger average age, and higher levels of socioeconomic deprivation. In these CCGs, implementation of primary and secondary cardiovascular disease prevention strategies is higher than the national average. However, local levels of cardiovascular morbidities, in particular, premature cardiovascular disease, are ranked in the top 10% in the UK.²¹

Defining the study population

We included men and women aged 18–65 years old registered with a participating practice at the time of data extraction (01 July 2019). As FH is associated with premature IHD, we set the upper age limit as 65 years old. De-identified data based on Read codes in EMIS records were extracted centrally by the Clinical Effectiveness Group, Queen Mary University of London, including age, sex, ethnicity, clinical conditions (online supplemental table 1) and social deprivation. Deprivation was defined by national 2015 Index of Multiple Deprivation (IMD) quintiles derived from a geographical area comprising approximately 150 households. Blood pressure (BP) and smoking status were defined based on their most recent records. Ethnic group is self-reported and recorded in the health records and then categorised as black ethnicity including black African, Caribbean and black British; South Asian including Bangladeshi, Pakistani, Indian and other Indian subcontinent; white including white British and European; and other ethnic group including missing or not stated.

Definition of the FAMCAT variables

The FAMCAT score was devised and externally validated by Weng *et al.*¹⁷ In this study, we matched our definitions of the FAMCAT variables as closely as possible with that of the original (online supplemental table 2). For cholesterol, we considered the highest ever recorded value and if both total cholesterol and LDL-C were available, we gave preference to LDL-C. The highest triglyceride measured within 5 years of the highest cholesterol was used. In cases of missing triglyceride and/or cholesterol data, we used the mean value of the analysis sample based on patient's sex, age group of either <40 years or ≥40 years and the IHD status. In alignment with Weng *et al.*,¹⁷ outlying observations of cholesterol and triglyceride levels and data entry errors were excluded. We classed levels as 'untreated' if there was no record of prescription for lipid-lowering drugs (statin, fibrate, bile acid sequestrant, nicotinic acid) in the 90 days prior to cholesterol measurement. We categorised potency of lipid-lowering therapy into low (fluvastatin or pravastatin ≤40 mg/day; simvastatin ≤

Table 1 Characteristics of the study population aged 18–65 years and the characteristics of the FAMCAT derivation cohort aged 16 years or above

	Study population	Derivation cohort (Weng <i>et al.</i>) ¹⁷
	n (%) or mean (SD)	n (%) or mean (SD)*
Total	777 128	2 228 562
Age (years), mean (SD)†	37.2 (11.6)	49.5 (16.7)
Age during cholesterol measurement (years), mean (SD)‡§	35.7 (10.8)	57 (16.3)
Gender, n (%)		
Male	372 471 (47.9)	1 083 539 (48.6)
Female	404 657 (52.1)	1 145 023 (51.4)
Ethnicity, n (%)		Not available
White	308 694 (39.7)	
South Asian	201 957 (26.0)	
Black	104 138 (13.4)	
Other	60 601 (7.8)	
Unknown¶	101 738 (13.1)	
IMD (national quintiles), n (%)		Not available
Quintile 1 (least deprived)	5555 (0.7)	
Quintile 2	16 318 (2.1)	
Quintile 3	50 812 (6.5)	
Quintile 4	323 883 (41.7)	
Quintile 5 (most deprived)	379 446 (48.8)	
Lipid profile, mean (SD)		
Highest total cholesterol recorded, mmol/L**	5.3 (1.2)	5.8 (1.3)
Highest LDL cholesterol recorded, mmol/L††	3.5 (1.1)	3.6 (1.1)
Triglycerides during cholesterol measurement, mmol/L‡‡§§	1.7 (1.3)	1.7 (1.2)
Lipid-lowering drug usage at time of cholesterol measurement, n (%)		
Prescribed fibrate, bile acid sequestrant or nicotinic acid	730 (0.1)	9817 (0.4)
Prescribed low-potency statin	754 (0.1)	37 799 (1.7)
Prescribed medium-potency statin	21 344 (2.8)	125 315 (5.6)
Prescribed high-potency statin	33 034 (4.3)	35 582 (1.6)
Family history, n (%)		
Family history of familial hypercholesterolaemia	3440 (0.4)	12 985 (0.6)
Family history of raised cholesterol	10 176 (1.3)	8796 (0.4)
Family history of myocardial infarction	152 155 (19.6)	71 596 (3.2)
Pre-existing coronary heart disease, n (%)	7950 (1.0)	Not available
Premature onset coronary heart disease (<60 years), n (%)	6444 (0.8)	Not available
Current smoker, n (%)	157 549 (20.3)	Not available
Diabetes, n (%)	42 844 (5.5)	285 765 (12.8)
Hypertension, n (%)	59 215 (7.6)	Not available
Familial hypercholesterolaemia, n (%)	16 573 (2.1)	Not available
Stroke TIA, n (%)	3500 (0.5)	Not available
Kidney disease, n (%)	11 629 (1.5)	261 458 (11.7)

*Clinical characteristics presented in the derivation cohort for men and women were combined using the formula for combining summary statistics across two groups in Cochrane Handbook for Systematic Reviews of interventions.²⁴

†Median (IQR): 35.0 (28.0–45.0).

‡Median (IQR): 34.0 (28.0–42.0).

§Patient's age at the time of data extraction was used where cholesterol is missing.

¶Unknown ethnic group=not stated code or missing.

**Data missing/outlying for 467 007 (60.1%) of 777 128 patients.

††Data missing/outlying for 514 876 (66.3%) of 777 128 patients.

‡‡Data missing/outlying for 521 584 (67.1%) of 777 128 patients.

§§Median (IQR): 1.3 (0.9–3.1).

FAMCAT, Familial Hypercholesterolaemia Case Ascertainment Tool; IMD, Index of Multiple Deprivation; LDL, low-density lipoprotein; TIA, transient ischaemic attack.

10 mg/day), medium (fluvastatin or pravastatin 80 mg/day; simvastatin 20 mg/day or 40 mg/day; atorvastatin ≤ 10 mg/day; rosuvastatin 5 mg), or high (simvastatin 80 mg; atorvastatin ≥ 20 mg/day; rosuvastatin ≥ 10 mg/day) intensity.

Calculation of FAMCAT risk

FH risk was calculated through application of the FAMCAT regression equations to our study population with variables defined as outlined. Estimates were based on probability thresholds of both 1 in 250 and 1 in 500 population prevalence of FH.^{16 22} We categorised risk stratification resulting from this analysis as unlikely, may or likely to have FH. A relative population risk of <1 indicated the individual was unlikely to have FH, a relative population risk from 1 to 5 indicated the individual may have FH, and a relative population risk of >5 indicated the individual is likely to have FH. We present these results for the whole cohort and separately for individuals with premature IHD (onset before age 65 years).

We performed a sensitivity analysis without imputations using the other variables to estimate the risk of FH where cholesterol and triglyceride were missing (see online supplemental table 3).

Patient and public involvement

Patients and the public were not involved in the design, conduct or outcome of this work.

RESULTS

Baseline population characteristics

The analysis sample comprised 404 657 women and 372 471 men with mean age (SD) of 37.2 (11.6) years (range 18–65 years). The population was ethnically diverse including white (308 694, 39.7%), South Asian (201 957, 26.0%), and black Caribbean and African (104 138, 13.4%) ethnic groups (table 1). Levels of deprivation were high relative to UK national averages with $>90\%$ of patients in the two most deprived IMD quintiles. The prevalence of smoking, diabetes, hypertension, chronic kidney disease (CKD) and stroke were 157 549 (20.3%), 42 844 (5.5%), 59 215 (7.6%), 11 629 (1.0%) and 3500 (0.5%), respectively. Prevalence of pre-existing IHD was 7950 (1.0%), with IHD recorded prior to the age 60 years in 6444 (81%) of these patients.

Level of recording of required data

Table 2 shows the level of data recording. Cholesterol was recorded for 82.5% (6558) of patients with IHD and 39.5% (303 921) of patients without IHD. Of the 16 573 with coded FH, 14.5% (2,397) did not have cholesterol recorded. Recording of cholesterol was more frequent for individuals aged 40 years and older.

FAMCAT risk applied to the whole cohort

Within the study population (777 128), 11 736–23 798 (1.5%–3.1%) patients were estimated to be likely to have FH, depending on the prevalence assumed (figure 1). A total of 36 630–80 372 (4.7%–10.3%) patients were estimated they may have FH (table 3). For individuals with IHD (7950), 552–938 (6.9%–11.8%) were likely to have FH and 1253–1842 (15.8%–23.2%) may have FH. For those without IHD (769 178), 11 184–22 860 (1.5%–3.0%) were likely to have FH. In total, between 48 366 and 104 170 people were estimated that they may or were likely to have FH who may need further investigation (between 6.2% and 13.4% of our total cohort). The computation of FAMCAT risk with and without missing data for both IHD and non-IHD

Table 2 Completeness of data recording

	N	%
Age 18–65 years	777 128	
Cholesterol recorded*	310 436	40.1
BP recorded	676 855	87.1
IHD	7950	1.0
Age 18–39 years	490 482	
Cholesterol recorded*	106 404	21.7
BP recorded	399 078	81.4
IHD	252	0.1
Age 40–65 years	286 646	
Cholesterol recorded*	204 032	71.2
BP recorded	277 070	96.7
IHD	7698	2.7
With familial hypercholesterolaemia	16 573	
Cholesterol recorded*	14 173	85.5
BP recorded	16 522	99.7
IHD	1240	7.5
With IHD	7950	
Cholesterol recorded*	6556	82.5
BP recorded	7938	99.8
Without IHD	769 178	
Cholesterol recorded*	303 880	39.5
BP recorded	668 210	86.9

*Patients with non-missing or non-outlying LDL or total cholesterol values.

BP, blood pressure; IHD, ischaemic heart disease; LDL, low-density lipoprotein.

resulted in changes of less than 1% in all categories of risk (online supplemental table 3).

FAMCAT risk in ethnic groups

Table 4 describes risk of FH by ethnic group. A total of 39.7% of the study population were in white ethnic groups. Among individuals of white ethnicity who had IHD, 7.8%–13.2% were estimated they were likely to have FH, compared with 6.8%–11.6% of South Asians and 5.2%–9.9% of black African/Caribbean individuals. In white ethnic groups without IHD, 1.2%–2.5% were likely to have FH compared with 2.5%–4.8% in South Asian and 1.1%–2.8% in black African/Caribbean groups.

DISCUSSION

In this large study of 777 128 primary care patients, we demonstrated the feasibility of application of the FAMCAT algorithm to aid case finding of FH using routinely recorded primary care data. Our analysis identified between 48 366 and 104 170 (6.2%–13.4%) people who may or were likely to have FH who would therefore warrant further assessment and potentially genetic testing and specialist services. These findings have important implications for care and service planning in primary and secondary care.

In our population, 1 in 30 to 1 in 100 were likely to have FH according to FAMCAT risk stratification, compared with estimates of disease prevalence from 1 in 250 to 1 in 500.^{16 22} Among individuals with pre-existing IHD, this increased to 6.9%–11.8%, suggesting that targeting testing and treatment for FH in this latter group would have a higher positive case yield.^{19 20}

A total of 2.1% of this population were found to have a code for FH, which is higher than previously reported estimates of FH prevalence. The prevalence in our study may be inflated due to coding errors where patients with high cholesterol and/or family history of high cholesterol were incorrectly coded as 'FH'

Figure 1 Risk of familial hypercholesterolaemia (FH) in inner East London calculated using FAMCAT algorithm, assuming population prevalence of 1 in 500 and 1 in 250. IHD, ischaemic heart disease; PP, population prevalence.

without further scrutiny to determine a correct diagnosis. Of those coded as having FH, 47.5% were identified by FAMCAT as unlikely to have FH (online supplemental table 4). Further clarification on the accuracy of these diagnoses is needed. This would require a case note review, which was not available in this study.

FAMCAT in ethnic groups

The risk of FH varied by ethnicity. In those with IHD, FH likelihood was highest in white and lowest in black ethnic groups. In people without IHD, the FH likelihood was highest in South

Asian and lowest in black groups. This may suggest that FH is a more important factor in development of IHD for white ethnicities. Alternatively, our observations may indicate lower sensitivity of FAMCAT in detecting FH in black and South Asian ethnic groups. Indeed, lower predictive accuracy of the FAMCAT in these groups has been previously highlighted.¹⁸ Further research is needed on potential ethnicity differential disease patterns of FH and the performance of risk prediction tools including the FAMCAT for informed clinical application in ethnically diverse populations.

Comparison with FAMCAT validation population

The FAMCAT validation population¹⁷ ran from 1999 to 2013, while our population was more contemporaneous comprising those currently registered in 2019. Our population was, on average, younger than that studied by Weng *et al*, with a mean age of 37.2 vs 49.5 years.¹⁷ The average age at first cholesterol

Table 3 Predicted number of cases of familial hypercholesterolaemia assuming population prevalence of 1 in 500 and 1 in 250

	1/500		1/250	
	N	%	N	%
All patients	777 128		777 128	
Likely to have familial hypercholesterolaemia	23 798	3.1	11 736	1.5
May have familial hypercholesterolaemia	80 372	10.3	36 630	4.7
Unlikely to have familial hypercholesterolaemia	672 958	86.6	728 762	93.8
Patients with IHD	7950		7950	
Likely to have familial hypercholesterolaemia	938	11.8	552	6.9
May have familial hypercholesterolaemia	1842	23.2	1253	15.8
Unlikely to have familial hypercholesterolaemia	5170	65.0	6145	77.3
Patients without IHD	769 178		769 178	
Likely to have familial hypercholesterolaemia	22 860	3.0	11 184	1.5
May have familial hypercholesterolaemia	78 530	10.2	35 377	4.6
Unlikely to have familial hypercholesterolaemia	667 788	86.8	722 617	93.9

IHD, ischaemic heart disease.

Table 4 Comparison of risk of FH estimated by FAMCAT by ethnicity

	Total	FH 1/500		FH 1/250	
		Number	%	Number	%
Patients with IHD	7950	938	11.8	552	6.9
White	2562	337	13.2	199	7.8
South Asian	3718	431	11.6	251	6.8
Black African/Caribbean	776	77	9.9	40	5.2
Other	438	45	10.3	32	7.3
Unknown*	456	48	10.5	30	6.6
Patients without IHD	769 178	22 860	3.0	11 184	1.5
White	306 132	7640	2.5	3591	1.2
South Asian	198 239	9571	4.8	5046	2.5
Black African/Caribbean	103 362	2850	2.8	1157	1.1
Other	60 163	1309	2.2	642	1.1
Not stated/missing*	101 282	1490	1.5	748	0.7

*Unknown ethnic group=not stated code or missing.

FAMCAT, Familial Hypercholesterolaemia Case Ascertainment Tool; FH, familial hypercholesterolaemia; IHD, ischaemic heart disease.

measurement was higher in the Weng *et al* cohort (57 vs 35.7 years) as was the prevalence of diabetes and CKD (12.8% vs 5.5%, 11.7% vs 1.5%), which is likely to be due to older age of participants in their cohort. There is a difference in the mean total cholesterol, while the mean LDL is similar between our study populations. However, the standard deviations of the means overlap, indicating that this difference is not statistically significant. Our population had a higher proportion of people with a recorded family history of myocardial infarction: 19.6% vs 3.2% in the Weng *et al* cohort. Recording of family history is integral to the national NHS Health Check programme in East London which may be the main reason for high levels of documentation, though the accuracy of these recordings is unknown.²³ FAMCAT only considers family history of IHD as a binary score and does not consider kinship or prematurity of onset. The relevance of accurate family history of premature IHD is an outstanding issue for further research as it is an essential element of further case identification. A comparison cannot be made between ethnicity and deprivation as they were not reported in the Weng *et al* paper. In keeping with Weng *et al*, patients on ezetimibe alone had their levels classed as 'untreated'. We also observed less missingness in all variables of interest for individuals aged over 40 years, corresponding to the 40–74 years of eligibility threshold for the NHS Health Check since 2009 and the inclusion of BP in the national Quality and Outcomes Framework for people over 40 years since 2013.

Implications for clinical practice

The 23 798 patients who were likely to have FH represent a large group of patients within which FH cases may exist, and these have been relatively easily identified through a data-driven approach. Use of the FAMCAT algorithm could allow primary care practices to generate a list of patients who may have FH, where the diagnosis has not yet been considered or excluded, using routinely recorded data. These at-risk individuals could be reviewed in more detail to determine an up-to-date FAMCAT risk and, if appropriate, clinical evaluation using the DLCN or SB criteria and genetic testing to confirm their disease status.

FAMCAT has showed a high degree of discrimination (area under the receiver operating curve 0.832, 95% CI 0.820 to 0.845). Assuming a population frequency of 1 in 500, FAMCAT had a sensitivity of 84% (1028 predicted vs 1219 observed cases) and specificity of 60% (443 949 predicted vs 745 781 observed non-cases), with a positive predictive value of 0.84% and a negative predictive value of 99.2%.¹⁸ In other words, for every 119 people likely to have FH, after further investigation, 1 person would be identified with FH and 118 would not have genetically confirmed FH but would nevertheless require clinical advice on whether further treatment was required based on the family history and clinical findings.

This study demonstrates that other localities could potentially use FAMCAT to aid FH case finding, though not all areas have the digital maturity to run algorithms across the entire local population. The application of FAMCAT is likely to generate substantial additional workload for primary and secondary care services. Therefore, it is imperative to consider infrastructure requirements to accommodate the expected increase in demand in both community and secondary care settings. For instance, development of dedicated community FH facilities may be of value to reduce the burden on existing hospital lipid clinics. Such large-scale changes to specialist investigations would require

evidence of cost-effectiveness and substantial changes to current care pathways.

Those who have not had an ischaemic cardiac event but are deemed likely to have FH by FAMCAT represent a group who may not otherwise have been identified before an index myocardial infarction or stroke, and for whom testing and treatment would play an important part in positively altering their disease trajectory. An FH diagnosis will help ensure they have appropriate treatment, and is also important for their families and cascade testing. In those who have had a cardiac event, confirmation of FH would have similar implications including for first-degree relatives.

Limitations

FAMCAT is not diagnostic, it merely applies a risk estimate. As seen in this paper, this approach generates a large cohort who need further scrutiny, first in primary care with a detailed family history and examination, then in secondary care for genetic testing and clinical advice. The FAMCAT algorithm generates substantial numbers at high FH risk for further investigation and management, and this process has yet to be assessed for cost-effectiveness.

Calculating individual FH risks without cholesterol and triglyceride measurements assumes values that fall into the ideal category in the FAMCAT algorithm. This could lead to incorrect estimates. Hence, we imputed missing values using population means for IHD and non-IHD groups. This approach artificially reduces the overall variability of missing variables. In studies where the primary purpose is hypothesis testing, this approach to imputation may lower the threshold for achieving statistical significance. However, this limitation is less important for this study, as the purpose of our work is demonstration of feasibility and description of the FAMCAT.

Use of the FAMCAT relies on recording of coded data including BP, cholesterol and family history. There was less

Key messages

What is already known on this subject?

- Underdiagnosis of familial hypercholesterolaemia (FH) represents a significant missed opportunity for prevention of coronary artery disease and premature death. The FH Risk Ascertainment Tool (FAMCAT) is designed to improve case finding in primary care but has not been studied in unselected primary care settings.

What might this study add?

- The original FAMCAT Study used a national dataset of selected volunteer practices to estimate likelihood of FH from routine data in primary care electronic health records. Our study applies FAMCAT to a large, unselected and ethnically diverse urban population. We estimate the number of people with possible FH and their demographic and clinical characteristics.

How might this impact on clinical practice?

- We demonstrated that FAMCAT could be feasibly applied to routine primary care data to enhance identification of individuals with FH. This information informs planning of health service provision and highlights recording of family history and ethnicity as topics for further research and improvement.

missingness of these variables for individuals aged over 40 years old, notably of cholesterol. This is likely due to the NHS Health Check and suggests this could also be an opportunity to estimate the FAMCAT risk. A total of 60.5% of patients without IHD and 14.5% with IHD did not have a record of cholesterol measurement. A complete lipid profile is advisable for optimal accuracy of FAMCAT.

CONCLUSION

We were able to implement the FAMCAT algorithm across entire localities to estimate likely numbers of patients requiring investigation for FH and assist commissioners and health service providers to determine these approaches. However, further research on the external validity in different settings and populations is warranted for the tool to be applied more widely. The recording of key variables including first-degree family history of premature IHD and the missing data requires improvement for use in service settings. Such data-driven approaches have the potential to improve detection of FH in the general population and reduce cardiovascular morbidity and mortality, but evidence of cost-effectiveness for full implementation of such a pathway is currently lacking.

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Contributors JR and CC conceived the study. CW conducted the data extraction and the analysis. All authors contributed to the planning of the study and the manuscript.

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Patient consent for publication Not required.

Ethics approval This study is based on de-identified information obtained from routinely compiled general practitioner electronic health records and did not require ethics committee approval.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplemental information. Data are extracted from patient record systems held by GP practices. Outputs of the data extracted are collated and in the format of tables within the paper or in supplemental information.

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