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Introducing new genetic testing with case finding for familial hypercholesterolaemia in primary care: qualitative study of patient and health professional experience

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ABSTRACT

Background: Familial hypercholesterolaemia (FH) is a common inherited condition causing elevated cholesterol, premature heart disease and early death. Although FH can be effectively treated, over 80% of people with FH remain undetected.

Aim: To explore patient and health professional experiences of introducing genetic testing with case finding for FH in primary care.

Design and setting: Qualitative study in UK general practice.

Methods: Semi-structured interviews with a purposeful sample of 41 participants (24 patients and 17 health professionals) from eight practices using electronic case-finding (FAMCAT) to identify patients with higher likelihood of having FH and offered diagnostic genetic testing in primary care. Data were analysed thematically.

Results: While prior awareness of FH was low, patients were unsurprised to be identified and positive about being offered genetic testing by their practice. Patients not found to have FH were relieved, though some felt frustrated their high cholesterol lacked a clear cause. Those confirmed to have FH largely expected and accepted this outcome. Practitioners saw detection of FH as an important new opportunity for preventive care. They found the case-finding tool easy to apply and noted patients' high uptake of genetic testing. While comfortable referring appropriate patients for further specialist management, GPs sought clearer definition about responsibility for identification and longer term care of FH in future care pathways.

Conclusion: Introducing genetic testing with electronic case finding for FH in to primary care was positively experienced by patients and practitioners. Further development of this approach could help improve detection of FH in the general population.

Keywords: Familial Hypercholesterolaemia; genetic testing; genomic testing; primary care; qualitative research

INTRODUCTION

Familial Hypercholesterolaemia (FH) is one of the most common inherited conditions, causing elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) from birth, and a 13-fold greater risk of premature coronary heart disease (CHD) and early death.[1] Diagnosis to enable effective high potency lipid-lowering treatment and lifestyle advice can ensure patients with FH have healthy lives and normal life expectancy.[2] However, over 80% of people with FH have not yet been diagnosed, with around 234,000 people still unidentified in the UK.[2] In addition, the identification of index cases can enable 'cascade' testing, as 50% of first-degree relatives will also be affected by the condition.

NICE guidance in the UK[3] recommends general practices search health records for people with TC > 9.0 mmol/L if aged 30 years or older, or > 7.5 mmol/L if under 30 years, as they are at highest risk of having FH. Possible FH may also be indicated by the Simon-Broome criteria of TC > 7.5 mmol/L or LDL-C > 4.9 mmmol/L in those who also have a family history of premature myocardial infarction (aged under 60 years in first-degree relative).[3,4] Referral to specialist lipid services is then recommended for diagnostic genetic testing, further management and testing of relatives if appropriate. However most patients referred to lipid specialists do not transpire to have FH, while others don't attend after referral.[5]

The potential of exploiting genomics and identifying FH in primary care is increasingly recognised.[6, 7, 8] In the UK, a predictive clinical case finding tool to identify patients at highest likelihood of having FH (FAMCAT: 'Familial hypercholesterolaemia case ascertainment tool') has been developed [9] and validated[10] for use with patients' routine electronic health data in primary care. Readier access to genetic testing in the community, when the possibility of FH is identified by their GP, might facilitate targeted referral for lipid specialist assessment, and enable more patients with undetected FH in the general population to be diagnosed. As part of a wider evaluation of introducing FAMCAT and genetic testing for FH in primary care [11], this qualitative study explored participating practitioners' and patients' experiences of this approach.

METHODS

Context: The wider study involved 14 general practices applying a validated electronic FH case-ascertainment tool (FAMCAT) to their practice list.[11] The FAMCAT algorithm includes elements of existing clinical criteria for FH, such as Simon Broome, searching variables available from patients' electronic health records to identify those with highest likelihood of FH. It takes account of interactions between statin prescribing, family history, total cholesterol, triglycerides, LDL-cholesterol and secondary causes of elevated lipids such as diabetes and chronic kidney disease [10]. It is intended as a case-finding tool to identify those eligible for further assessment and testing for possible FH.

A cohort of 336 patients identified at higher likelihood of having FH by FAMCAT, and consenting to study participation, were mailed information about possible FH and invited to have blood tests for current cholesterol and genetic testing for FH. Participants also completed a family history questionnaire for the wider study. [11, 12] Genetic testing was completed by 283 patients. This followed practices' usual procedures for venesection at their surgery or local community phlebotomy clinic. On average, patients waited three months between having their blood test and receiving results by letter. Further detail on the testing used is provided in **Box A**. There were three possible results summarised in **Table 1.**

Sampling and data generation

We selected a purposeful sample, from all patients identified with possible FH and offered testing and who were willing to participate in this study, to reflect experience of differing test outcomes, family history, and diversity of social and educational background (between 20-30 patients were estimated required). Sampling of healthcare professionals included a range of roles (clinical, administrative, managerial), practice population demographic and locality (inner city/suburban/rural), and clinical experiences of FH in relation to patient identification using FAMCAT, genetic testing, referral and management (between 15-20 professionals estimated required). Professionals were interviewed after they had had at least 6 months experience applying FAMCAT and implementing genetic testing in their practice. One-to-one semi-structured interviews, using topic guides with broad prompts (appended as supplementary information) exploring patient and professional experiences,

were conducted by two post-doctoral researchers not involved in the prior development of the FAMCAT tool (LS and LC for patients; LC for healthcare professionals), either face-to-face or by telephone, according to participant preference. Prior to interview all participants provided written informed consent.

Data analysis

Interviews were digitally recorded and transcribed verbatim. Data were analysed thematically[14] and concurrently with sampling and data generation continuing until saturation of themes. Analysis followed a process of familiarisation with data, generation of initial codes, searching for and reviewing themes, defining and naming themes.[14] Data were manually reviewed and emerging themes developed by the researchers undertaking the interviews and a third senior researcher (JK), with differing disciplinary backgrounds in health psychology, health services research and general practice. JK was involved in the prior development of the FAMCAT tool, but not in its piloting in participating practices. All respondents were sent a draft summary of findings to check[15] and invite any comment on our interpretation. Responses from 11 interviewees were received confirming study findings as true to their experiences with no further comments made. These steps helped further refine analysis and check our interpretation, as a clear descriptive narrative reporting participants' experience in relation to possible FH identification and genetic testing. In addition to the latter 'member checking', we sought interim comment on the first seven patient interview transcripts and their preliminary analysis, from the study PPI advisor (who has FH); and further discussed emerging themes with three FH specialist health practitioners providing the patient telephone helpline of the national FH charity, Heart UK.

FINDINGS

41 participants were purposely selected and interviewed. This included 24 patients with a range of FH test outcomes, family history and socially diverse backgrounds and 17 primary care professional respondents (**Table 2**). Health professional respondents (10 female, 7 male) came from inner city (3), suburban (3) and rural (2) practices, with socially diverse populations and practice IMD scores ranging from 6.3 – 48.8.[16] GPs interviewed had been qualified for an average of 22 years (range 13-36 years).

The main themes generated from the data reflected the experiences and perspectives of patient and healthcare professionals during the process of case finding and genetic testing. They included: identification of higher risk of FH, experience of testing offer, testing process, experience of FH test results and experience after specialist assessment.

IDENTIFICATION OF HIGHER RISK OF FH AND EXPERIENCE OF TESTING OFFER

Both patients and GPs positively anticipated the value of improving identification of FH, recognising potential benefits for patients and their families' long-term health. Patients' motivations for having FH testing were to detect an asymptomatic condition, so they could manage it appropriately; and to enable other, especially younger, members of their family to be tested if needed.

"This is excellent because it is primary prevention and we're hoping that would have a better effect for secondary care in the future with less toll on the system if we identify these patients early so they don't have to go in to hospital with a massive MI." [GP6]

'The main reason I wanted that (test) to be done is that my children could have that sort of genetic, I was worried for myself but I thought …. it would be helpful to them to know if that was the case and then they are being made aware of it' [Patient participant 4, aged 58 years, subsequent FH mutation negative]

Primary care practitioners found the electronic search to identify people with greater probability of having FH was uncomplicated to implement on practice IT systems. Having search criteria for clinical variables already incorporated in the FAMCAT tool rather than needing to input a number of Read codes* themselves aided the process and identification of relevant patients. For example:

"[…] to run this (FAMCAT) search and then to come out with a list of "right this is what you're doing" and it was really straight forward. It was off the back of this complicated report that had been built already rather than just me trying to make sure that I've included all the Read codes recorded in the clinical systems […] that was definitely a real bonus." [Practice Nurse 3]

Practitioners reflected that seeking patients at higher risk of FH and offering relevant blood testing was similar to other screening they already routinely undertook for other conditions in general practice, such as diabetes. For example:

"[…] it doesn't seem particularly different to other areas of screening that we are involved in and it is for preventative health." [GP2]

"Yes definitely, it's been the same [process] for diabetes and lots of other conditions."[GP 9]

Very few patient participants were previously aware of FH as a condition. However most were unsurprised their practice had invited them to be tested. Receiving information about possible FH, with an invitation for and having blood testing, were regarded as straightforward. This was understood given their personal history of elevated cholesterol, or family history of the same or of heart disease, and felt familiar given their prior experience of cholesterol monitoring and review. For example:

'To be honest when I received the (invitation for testing) letter I wasn't overly surprised because quite a lot of people in my family have high cholesterol, so I wasn't surprised to have been identified' [Patient participant 21, 40 years old, subsequent FH mutation negative with 'polygenic result/ prone to high cholesterol']

'I had never heard of it (FH) before but obviously we have a lot of heart trouble and everything in the family, it felt something that I could take part in …' [Patient participant 7, 60 years, subsequent FH mutation negative]

Well at the time I certainly didn't know anything about it (FH), obviously when I received the letter I thought, because I have had such high cholesterol levels in the past, I thought maybe I ought to go for this test and just see really, but at the time I didn't really know anything about it. [Patient participant 17, 59 years, FH mutation positive]

Patients appreciated testing of their relatives might be needed depending on the outcome of their own test. Many discussed their invitation for testing with partners, siblings, children, and sometimes their own parents, to ask about family history. While this had not caused concern for most, some anxiety about possible family implications could arise:

'As soon as I did mention it (testing) to my daughter in law… she said to me 'oh would it be passed on to the children?' …meaning the grandchildren, and I said 'well nothing has come back (to say) I have actually got it so until that does, I wouldn't worry yourself about it'. So they were a bit… a few alarm bells going off …..'[Patient participant 4, 58 years old, subsequent FH mutation negative]

There was some initial scepticism among practitioners about likely patient engagement among some respondents, particularly in inner city practices with previous experience of low response rates to invitations for preventive health checks. However this was confounded by positive experience of generally high uptake of testing among patients invited, which was attributed to overall awareness of cholesterol as a health issue and existing lipid-lowering treatment.

"Sometimes you just do it [arranging appointments for blood testing] and you don't actually think that anyone will show up do you? But yes, it is good that it [attendance] shows that it is working. And that is something that we enjoy as well…
High cholesterol…. has been in the news and papers a lot more hasn't it and dietary advice is changing isn't it" [Practice Nurse 2]

"When will I get my results?", they were quite looking forward to the process so they [the patients] seemed to be more engaged [Practice Nurse 1]

TESTING PROCESS

Patients felt that the written information on FH accompanying their invitation for testing was adequate and did not feel the need to discuss this further with their GP prior to having blood testing. However the considerable time they waited to receive results was noted and this caused a degree of concern for some respondents.

'I did think it was a long time [waiting for result] … A little bit anxious but not too bad, obviously I wanted the result but yes, I wasn't too bad no' [Patient participant 17, 59 years old, subsequent FH mutation positive]

Communicating general information about possible FH and genetic testing to patients wasn't perceived to further impact on practice resources with patients routinely attending for testing following their invitation. Although offering genetic testing for FH was viewed as a positive development for patient care with simple blood testing, there was some concern its organisation could encroach on practice staff time and cause inefficiencies within their existing workload. Testing required scheduling of appointments for blood samples so they could be sent to the laboratory within 48 hours of collection:

"Anything that is time or cost neutral for the practice and has a clear benefit for people we'll generally say yes, we will go for it and if it can be really clear that that is the case then we go for it big time […but]our staff are quite overloaded with work […]." [Practice manager 1]

"…the taking of the bloods is not a problem, it is just the practicalities" [Practice Manager 2]

EXPERIENCE OF FH TEST RESULTS

Most patients who received a result letter indicating they did not have FH were relieved for themselves and their family, and were untroubled. However some felt surprised or perplexed they were not shown to have FH, given their family histories of cardiovascular disease, and had hoped for an explanation for their pattern of high cholesterol.

I didn't really feel anything [when receiving result]. I was either going to have the gene, a faulty gene or not and I happened to not - so it didn't really make me feel anything particularly' [Patient participant 13, 41 years old, FH mutation negative]

'I honestly thought I had got this FH but the letter said that I didn't so .., I was a bit confused …. I was really expecting it to say 'yes you have got it' (…) because (family members) they have all had heart attacks, strokes (…) and I thought well there has got to be something in the gene …. so I was quite surprised' [Patient participant 23, 66 years, FH mutation negative, prone to high cholesterol]

Two respondents expressed more negative emotions they had not inherited FH, for example, feeling at fault for developing hypercholesterolaemia:

'If you had told me it was because of my mother, I would have been happier now, I would have thought well there is nothing I can do about that, I have inherited this and I ought to tell my daughter… but actually when the letter came back saying that it was negative I thought well, that just must mean that it was my fault, so I must admit (that) has made me more miserable' [Participant 3, 58 years, FH mutation negative]

Mailed results confirming FH or identifying possible FH, both with need for specialist referral, were accepted and largely expected by those receiving this result (a third of our purposeful sample). Confirmation of FH was perceived to have had modest impact, noting their significant personal and family history of CVD, prior awareness of their elevated cholesterol and that they were already using lipid-lowering treatment to tackle the problem:

'It has not made a lot of difference to me because I was already having my cholesterol (treatments) before and tried to bring it down' [Patient participant 16, 56 years, FH mutation positive]

'I think I probably knew … that I had that gene. I kept thinking because of my history and then my family history it made me realise that it wasn't just… there is something there, … and obviously the wee bit more was the gene ' [Patient participant 11, 69 years old, FH mutation positive]

Most practitioners felt communicating information about possible FH, with invitation for genetic testing for the condition, was realistic. However the on-going clinical management of those awaiting the results of their genetic testing for FH was queried by some:

" […] given that there is then quite a gap until they get the genetic results, are we supposed to treat them in the meantime? As we would do normally by looking at their other risk

factors […] or do we just sort of wait, put things on hold until they have got the genetic result and then may need referral to the lipid clinic?" [GP4]

GPs were comfortable referring patients with results suggesting FH or indicating a variant of unknown significance (VUS) for specialist assessment, but sought greater understanding about interpreting and communicating the range of possible test results, and more in-depth guidance on longer term care of FH. This included the importance of treating elevated cholesterol more aggressively, and what lipid specialists may do beyond prescribing lipid-lowering therapy.

"It would be useful to know what further assessment are we talking about here at the hospital, what is it they would do for a VUS? So we need to know a reason why we are referring them." [GP8]

As approaches to improving identification of FH developed, GPs also anticipated a need for clearer guidance about evolving roles at the primary-secondary care interface. In particular who may have what clinical responsibilities or duty of care related to genetic testing for FH, and communicating and acting upon results appropriately.

"If you have done a test you're responsible for the result, ….. and that is a duty of care and it does fall back to responsibility …. and following up on a result that you've actioned". [GP7]

EXPERIENCE FOLLOWING SPECIALIST ASSESSMENT

Patients referred for specialist assessment with a confirmed FH mutation felt informed and reassured after being prescribed new medications with subsequent improvement in their cholesterol.

'I have been on medication for cholesterol for some years and have struggled to get the cholesterol level below… ... but then after attending the clinic I was prescribed some different medication to go alongside my existing (treatment) and my levels have improved since so I think about it less and less…' [Patient participant 24, 52 years old, FH mutation positive]

However, for some others notably with a VUS result, their outcome remained unclear and they had not emerged understanding if they had FH or not or if there were possible implications for family members:

'Most of it (seeing specialist) was questions, questions…., he didn't explain …how I am ever going to find out whether I have got this condition or whether I ought to be telling my sons to be tested and what's more important my new granddaughter to be tested' [Patient participant 5, 62 years old, VUS]

Several patients with confirmed FH mutation had spoken to their relatives about testing after advice from the lipid specialist but families subsequently experienced differing management. One patient with FH had contacted his siblings and daughter himself, and they had subsequently been referred by their GP for testing. In contrast, another was concerned her son's GP did not arrange referral for testing:

'I discussed it with my eldest who (lives elsewhere)… he did actually approach the doctor (his GP) and the doctor more or less laughed him out of the office and said ' Don't worry, you're too young to worry about things like that (…) so I am getting a bit concerned in case he does need this test' [Patient participant 10, 49 years-old, FH mutation positive, son aged 19 years]

DISCUSSION

This study has found introducing genetic testing with electronic case finding for FH in to primary care was positively experienced by patients and practitioners. Although patients' prior awareness of FH was low, their existing experience of cholesterol monitoring and treatment or family histories, meant they were unsurprised and positive about being offered testing having been identified as having a higher probability of FH. They saw this as helpful for themselves and to establish potential implications for family members, and found the process straightforward. However those confirmed to have FH highlighted challenges for onward communication and testing in their families.

Healthcare professionals perceived this as an opportunity to enhance cardiovascular disease prevention, similar to their existing screening for other disease. Noting some logistic challenges for required timing of blood sampling, they otherwise found electronic case finding and genetic testing were uncomplicated and were open to further adoption of this approach in practice. They sought further guidance to better support detection and longer term care of FH, including clearly defined future clinical pathways with lipid specialists.

Strengths and limitations

To our knowledge, this is the first research to investigate experience of introducing genetic testing with case finding for FH with patients from the general adult population identified at higher possibility of FH by their general practice, and of practitioners using this approach in primary care. Our sample was purposefully selected including patients from diverse social and educational backgrounds, with a range of genetic test outcomes for FH; and healthcare

professionals with different team roles from a range of practices. However we recognise respondents were self-selecting and findings must be interpreted with regard to the sample as described. Patients willing to be interviewed who did not take up the offer of testing were sought but could not be identified as the vast majority of patients offered the opportunity had testing.

Interviews were conducted by two researchers with backgrounds in social science, health services research and health psychology, and analysis was developed jointly by both interviewers with a third senior clinical researcher, all of differing disciplinary backgrounds. Steps to further enhance trustworthiness of analysis and check interpretation were also used, including member-checking as described. Wider quantitative evaluation of the approach has recently been published.[11]

Comparison with existing literature

This study adds to earlier work on detection of possible FH in general practice as patient or practitioner experience has not been qualitatively reported, nor involved the use of genetic testing in primary care practice.[17-23] Our findings are consistent with wider research on what might help exploit genetics in the community setting such as use of family history,[24] guidelines and risk assessment tools.[25] Reflecting on detection of FH, our practitioner respondents also highlighted opportunity to widen cardiovascular prevention for patients and its similarities with established routine screening for other disease, such as diabetes. Practitioners sought more specific guidance on results and future management for FH, consistent with relative lack of understanding about this condition.[26,27] It is noteworthy that examples of inappropriate advice to relatives of confirmed FH patients occurred in relation to cascade testing. Respondents underlined the importance of having clear protocols that might be shared at the primary care - lipid specialist interface to underpin effective identification and management of FH.

The current findings in primary care accord with previous research in specialist genetic and lipid settings with more selected patients with FH or their relatives[28-31] where genetic testing for FH was well accepted and did not cause significant anxiety. Participants where an FH mutation was found in the current study mostly expected this. Most others felt relieved

they did not have the condition, though a negative result was more problematic or unsatisfactory for some, with lack of a genetic cause putting the emphasis for high cholesterol on the individual and their lifestyle. As we found here, this may make people feel responsible and even guilty.[29,31,32] Like other work[33] the hereditary nature of FH and its impact for families was a further key concern for our patient respondents, including the need to protect children and grand-children.[34]

Implication for practice, policy and further research

Failure to detect FH leads to either no treatment or inadequate treatment of people wrongly thought to have commoner 'life-style related' elevated cholesterol. This study highlights patients' and practitioners' positive first experience of an approach with potential to help.[11] FH is a current focus for policy to prevent avoidable premature disease and early deaths, and so is the only inherited disorder with a specific target to identify undiagnosed cases (25% of patients in next 5 years) in the long-term NHS plan.[35] Use of automated electronic case finding tools such as FAMCAT in the current study,[10,11] or others[36], could help, and exploit transferable skills in secondary prevention in primary care that are already well established, for example in diabetes.

Raising public and health professional awareness of FH is needed. Should wider genetic testing in primary care be developed[11] then avoiding delays in receiving results or specialist assessment will be required. Patients may expect genetic testing to detect a mutation and provide an explanation for their elevated cholesterol because of their personal or family histories of this or of heart disease. Prior to testing it may be helpful for patients to be advised a negative result is the most common outcome. Practitioners should check understanding and be prepared to acknowledge a variety of patient responses, mostly of relief but also including surprise, guilt or disappointment when FH is not identified. Practitioners should clarify that while a genetic cause (with implications for family members) has not been found, addressing lifestyle causes and the need for treatment remain.

As genomic testing becomes more available, future research might also explore if still being found more prone to high cholesterol (polygenic hypercholesterolaemia) may help people make more sense of their own experience and family history. Finally, challenges and support

for patients in communication of their results to wider family should be anticipated. In particular, clear processes to facilitate and ensure coordinated further testing for relatives of those with genetically confirmed FH are needed across service pathways.

Further research, including substantive randomised trial of this approach is anticipated from parallel work[11]. This is needed to assess whether detection of FH can be improved in primary care, including whether introducing genetic testing beyond its traditionally specialised arena in to the community could enhance more targeted specialist referral and uptake, widen access to and yield more timely diagnosis to improve outcomes. This should include assessment of intervention acceptability[37] and requirements for implementation[38] prior to its potential adoption in practice. Development of meaning or explanatory insights from experience of this approach could also be anticipated within future qualitative work.

This study has found introducing genetic testing with electronic case finding for FH in to primary care was positively experienced by patients and practitioners. Further development of this approach could help improve detection of FH in the general population.

HOW THIS FITS IN

Over 80% of patients with familial hypercholesterolaemia (FH) remain unidentified, with diagnostic testing occurring in specialist lipid care. This study has found introducing electronic case-finding and genetic testing for FH into primary care was positively experienced by patients identified at high risk, and positively perceived by practitioners as important, straightforward and similar to existing preventive care. With further development and evaluation this offers a promising approach to help improve detection of FH in the general population.

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Provenance: Freely submitted; externally peer reviewed.

Competing interests: The authors have no competing interest to declare.

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* Read Codes are a coded thesaurus of clinical terms which provide a standard vocabulary for clinicians to record patient findings and procedures, in health and social care IT systems across primary and secondary care (https://digital.nhs.uk/services/terminology-and-classifications/read-codes)

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Box A: Genetic testing for FH

Next generation sequencing (NGS) was used and is now becoming more available in the UK. This identifies genetic mutation causing monogenic FH (caused by a major change in a single gene). The NGS assay identifies FH-causing genes *LDLR* (18 exons), *APOB* (28 exons), *PCSK9* (12 exons), *LDLRAP1* (9 exons). It further identifies genetic variations called 'Variants of Unknown Significance' (VUS) which may indicate the person has FH or reflect normal variation. The assay also identifies 12 point mutations (LDL-C raising single nucleotide polymorphisms). Each of these slightly increases cholesterol levels. If several are present collectively they contribute to 'polygenic hypercholesterolaemia'. This means the patient may be more prone to having raised cholesterol than the general population but does not have FH.[13]

Table 1: Genetic test results

Test result	Advice to GP	Advice to Patient
FH mutation positive	Confirms patient has FH. Refer to lipid specialist.	Patient informed has FH. Will be referred to lipid specialist.
FH mutation unclear (variant of unknown significance or 'VUS')	Result unclear. Patient may have FH. Refer to lipid specialist for further assessment.	Result unclear. May have FH. Require specialist referral and assessment
FH mutation negative	Patient does not have FH. Provide healthy lifestyle advice and leaflet. However, if positive family history of premature heart disease, the patient fulfils Simon-Broome (SB) criteria for possible FH, as per NICE guidelines. Seek specialist advice on whether further assessment needed.	Informed do not have FH. If any relative develops heart attack under 60 years may need specialist assessment, advised to see GP.
FH mutation negative with polygenic result	Patient does not have FH but genetic testing indicates more likely to have raised cholesterol than general population (see Box A). Advise regular routine cardiovascular risk assessment.	Informed do not have FH - but are more prone to high cholesterol. Advised to see GP for routine cardiovascular health check.

Table 2: Characteristics of participants

Participants	N=41
Patient FH mutation positive	8
Patient FH mutation unclear (VUS)	3
Patient FH mutation negative	7
Patient FH mutation negative, prone to high cholesterol (polygenic)	6
General Practitioner (GP)	7
Practice Nurse	4
Healthcare Assistant	4
Practice Manager	2
Patients' gender	
M	11
F	13
Patients' age	
<40	1
40-49	7
50-59	8
>59	8
Patients' ethnicity	
White British/Irish	16
South Asian	4
Black	1
Other: European	3
Patients' Index of Multiple Deprivation (IMD)*	
Quintile 1	7
Quintile 2	5
Quintile 3	7
Quintile 4	2
Quintile 5	3
Patients' highest formal educational level	
No formal qualifications	4
GCSE/O-level/CSE	5
A-level or equivalent	6
Degree	4
Other/vocational	5
Family history – 1st degree relatives	
Known Familial Hypercholesterolaemia	0
High cholesterol	17
Premature CHD events (<60 years)	8
Premature deaths from CHD (<60 years)	4
Co-morbidities (apart from elevated cholesterol):	
None	14
Cardiovascular disease	3
Other (e.g. lymphoma, asthma, hypothyroidism, hypertension, diabetes)	7

*IMD Quintile where 1 is least deprived and 5 is most deprived15 ©Crown Copyright 2006