SYSTEMATICALLY IDENTIFYING FAMILIAL HYPERCHOLESTEROLAEMIA IN PRIMARY CARE

AN AUDIT WITHIN THE MEDWAY CLINICAL COMMISSIONING GROUP

INTERIM REPORT FOR HEART UK CONFERENCE, JULY 2-4 2014

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THE CHOLESTEROL CHARITY

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SUMMARY

Familial hypercholesterolaemia (FH) is a relatively common autosomal dominant lipid disorder that confers a lifelong risk of premature coronary heart disease (CHD) because of highly raised low-density lipoprotein-cholesterol (LDL-C). The early onset of atherosclerosis caused by FH emphasises the importance of early identification and effective therapeutic intervention.

Medway Clinical Commissioning Group (CCG) in Kent comprises 54 GP practices serving approximately 280,000 patients. In GP surgeries, technology in the form of 'Audit +' (BMJ Informatica) is being used to help practices deliver high quality care through prompts during consultations. These prompts target support for patients based on national guidance and evidence-based practice.

Although the NICE guidelines suggest referring patients with suspected FH to secondary care for genetic testing, management and contact tracing, the absence of a genetic abnormality does not exclude the diagnosis of FH, which can be made using the Simon Broome criteria. Therefore, Medway CCG instigated an FH audit using the Audit + software in an attempt to increase the diagnosis of FH.

The audit initially identified patients already diagnosed with FH or possible FH and established the baseline prevalence of FH of 0.13% (one in 750) in Medway CCG. It identified a baseline 'at risk and unscreened' prevalence of 0.59%. At re-audit after two years, there was a substantial increase in the prevalence of diagnosed FH, based on Simon Broome criteria, of 0.22% (one in 450) and showed that, despite the increase in FH diagnosis, the proportion of patients 'at risk and unscreened' remained almost unchanged at 0.58%.

In October 2013, an FH Nurse Advisor Programme was added with the aim of further improving the diagnosis of FH within the CCG. At this point, a decision was made to revise the audit and incorporate the Dutch Lipid Clinical Network Criteria (DLCNC) to define the severity of FH and support clinical management. The FH Nurse Advisor Programme further increased diagnosis in seven months, with the prevalence increasing from 0.22 to 0.26% (one in 450 to one in 375) and reduced the number of patients 'at risk and unscreened' by almost two-thirds.

The Audit + software and Medway tool and prompts can be readily integrated into other CCGs, and the nurse-led programme provides a useful model to increase diagnosis and management of patients with FH within primary care.

BACKGROUND

Familial hypercholesterolaemia (FH) is a relatively common autosomal dominant lipid disorder that confers a lifelong risk of premature coronary heart disease (CHD) because of highly raised low-density lipoprotein-cholesterol (LDL-C).[1]

Homozygous FH (HoFH) is extremely rare, occurring in one in a million people and resulting in extremely high LDL-C that requires aggressive lipid lowering therapy from a young age.[2] The more common heterozygous form of FH occurs in approximately one in 500 people, and up to one in 70 in certain ethnic groups with founder mutations.[1] Untreated, the elevated LDL-C that characterises heterozygous FH leads to a greater than 50% risk of CHD in men by the age of 50 years and at least 30% in women by the age of 60 years.[3] The early onset of atherosclerosis caused by FH emphasises the importance of early identification and effective therapeutic intervention. If primary prevention treatment is started early, the excess risk of premature vascular disease can potentially be eliminated; in patients with established disease, the benefits of preventive measures are significantly attenuated.[4]

FH is caused by mutations in the LDL receptor *(LDLR)*, of which more than 1200 have been identified, and less commonly by mutations in apolipoprotein B *(APOB)* and proprotein convertase subtilisin/kexin type 9 *(PCSK9)*[5], which encode for proteins critical for the normal removal of excess LDL-C from the bloodstream.[6] In populations in which no founder effect has occurred, such as the UK, approximately 40% of people with clinically suspected FH carry an identifiable mutation.[5] Recently, it has been shown that mutation-negative FH patients can be caused by an accumulation of common small-effect LDL-C-raising alleles or so-called polygenic FH.[7] But even when polygenic cases are combined with proven mutations, there remains a substantial proportion of phenotypic FH cases that do not have a genetic diagnosis. Nonetheless, in view of the morbidity and mortality associated with FH, for mutation-negative patients with the FH phenotype, cascade testing based on LDL-C and clinical criteria is still warranted, even if it is less sensitive and specific.[5]

Under-diagnosis of FH - a major gap in coronary disease prevention

In the past, it was generally accepted that the prevalence of heterozygous FH was about one in 500, based on calculations using the Hardy-Weinberg equation and the frequency of FH homozygotes; however, recent data suggest that this is an under-estimate.[2] The Copenhagen General Population Study used the Dutch Lipid Clinical Network Criteria (DLCNC) to establish the clinical diagnosis of FH and determined that the prevalence in individuals classified as definite or probable FH approached one in 200.[2, 8]

Extrapolations from this range of one in 500 to one in 200 suggest that there are between 120,000 and 300,000 people with FH in the UK. The European Atherosclerosis Society has estimated that around 15,000 patients are diagnosed with FH in the UK.[2] This estimate matches closely with a survey in 2008, which showed that ~15,000 adults and ~500 children with FH were being managed in UK lipid clinics, and points to severe under-diagnosis and under-treatment of FH in the UK.[9]

Despite the 2008 National Institute for Health and Care Excellence (NICE) guidelines recommendation for genetic testing of index cases and cascade screening,[3] and the publication of NICE Quality Standards for the management of FH in August 2013 (QS41),[10] no systematic diagnostic screening programme has yet been introduced in England, although there are active programmes in Scotland, Wales, and Northern Ireland.[11]

The diagnosis of FH

The presence of an FH-causing mutation provides a definitive diagnosis of the disorder; testing of close relatives, who carry a 50% risk of the disorder, is a recommended and cost-effective approach to diagnosing new patients.

Clinical diagnostic algorithms for FH are well defined. In the UK, the Simon Broome criteria[1, 12] are recommended to evaluate patients with raised LDL-C, especially if there is a personal or family history of premature CHD. A definitive FH diagnosis is made based on total cholesterol >6.7 mmol/L or LDL-C >4.0 mmol/L in a child (<16 years) or total cholesterol >7.5 mmol/L or LDL-C >4.9 mmol/L in an adult plus the presence of tendon xanthomas in the patient, a first-degree or second-degree relative. A diagnosis of possible FH is made if there are no tendon xanthomas but a family history of myocardial infarction (aged <50 years in a second-degree relative or <60 years in a first-degree relative) or a family history of raised total cholesterol (>7.5 mmol/L in an adult first- or second-degree relative or >6.7 mmol/L in child or sibling aged <16 years). In Europe, the DLCNC is widely used and categorises patients as definite, probable or possible FH, depending on clinical parameters.[1]

SYSTEMATICALLY IDENTIFYING FH IN PRIMARY CARE

Medway Clinical Commissioning Group (CCG) in Kent comprises 54 GP practices serving approximately 280,000 patients. In GP surgeries, technology in the form of 'Audit +' (BMJ Informatica) is in use, helping practices deliver best practice care through prompts during consultations. These prompts target support for patients based on national guidance and evidence-based practice.

Across Medway CCG, the recorded prevalence of FH is below the level predicted. Whilst the NHS Health Check programme will identify raised cholesterol in those who attend, those with undiagnosed FH would benefit from earlier diagnosis and treatment.

Although the NICE guidelines suggest referring patients with suspected FH to secondary care for genetic testing, management and contact tracing, the absence of a genetic abnormality does not exclude the diagnosis, which can be made using the Simon Broome criteria. Therefore, Medway CCG created an audit tool using the Audit + software and instigated an FH audit across the CCG to attempt to increase the diagnosis of FH. The audit software is compatible with multiple GP clinical platforms.

The aim of the audit tool was to enable the identification of patients from primary care electronic databases who are at risk of FH based on elevated cholesterol levels, but who have not been screened and diagnosed, and to highlight these patients for assessment, diagnosis and appropriate management.

Phase 1 - Establishing the baseline and improving FH diagnosis

At the outset, there was no Read Code for 'possible FH'. Read Codes are the current primary care, NHS-wide, alpha-numeric coding system, designed to record the everyday care of a patient and enable computerised patient records to be electronically searched. The Read Code for possible FH was provided to the NHS in June 2010 and the audit was planned.

The audit first identified patients already diagnosed with FH or possible FH, thus providing a baseline prevalence. Next, all patients with either a cholesterol >7.5 mmol/L or an LDL-C >4.9 mmol/L were identified and those previously assessed using the Simon Broome criteria were excluded. From this, the audit tool produced a list of patients 'at risk and unscreened' for each practice and added prompts to these patients' notes which appeared when the clinician saw the patient, recommending them to be assessed using the Simon Broome criteria. Those who met the criteria were diagnosed as having FH or possible FH. In addition, the audit contained a series of triggers which encouraged further management steps at the point of consultation allowing opportunistic patient evaluation and screening (see Table 1).

The Audit + software was loaded onto GP clinical systems remotely, requiring no additional work for the practices or clinicians.

The audit was piloted in a single practice in September 2011, and rolled out across the CCG (then a Primary Care Trust) in October 2011 and re-audit was performed at two years.

Table 1. Triggers and prompts within the Medway FH audit tool

Trigger	Prompt
Patients with FH or possible FH whose family has not been informed	Have relatives been informed regarding FH?
Patients with FH, possible FH or probable FH whose latest total cholesterol >5 mmol/L	Up-titrate statins or consider referral
Patients whose latest cholesterol is >7.5 mmol/L or LDL-C >4.9 mmol/L who have had a positive genotype test	Diagnose FH
Patients whose latest cholesterol is >7.5mmol/L or LDL-C >4.9 mmol/L and have a family history of premature CHD and/or hypercholesterolaemia and have not had a Simon Broome assessment	Consider possible FH
Patients whose latest cholesterol is >7.5 mmol/L or LDL-C >4.9 mmol/L, have not had a Simon Broome assessment and have a family history of CHD but no details of the age of the relatives	Ask patient if MI <50 years of age in second degree relative or MI <60 years of age in first degree relative **Yes:** Consider FH **No:** Assess using Simon Broome criteria

Note: Prompts contain further information along with relevant read codes, which can be added directly into the patient record from the prompt screen.

RESULTS

Baseline findings

Baseline FH prevalence: The audit identified patients already diagnosed with FH or possible FH and established the baseline prevalence of FH within Medway CCG of **0.13%** (one in 750) (Figure 1; Table 2).

Baseline 'at risk and unscreened': The audit identified the baseline 'at risk and unscreened' prevalence of FH within Medway CCG of **0.59%** (Figure 1; Table 2).

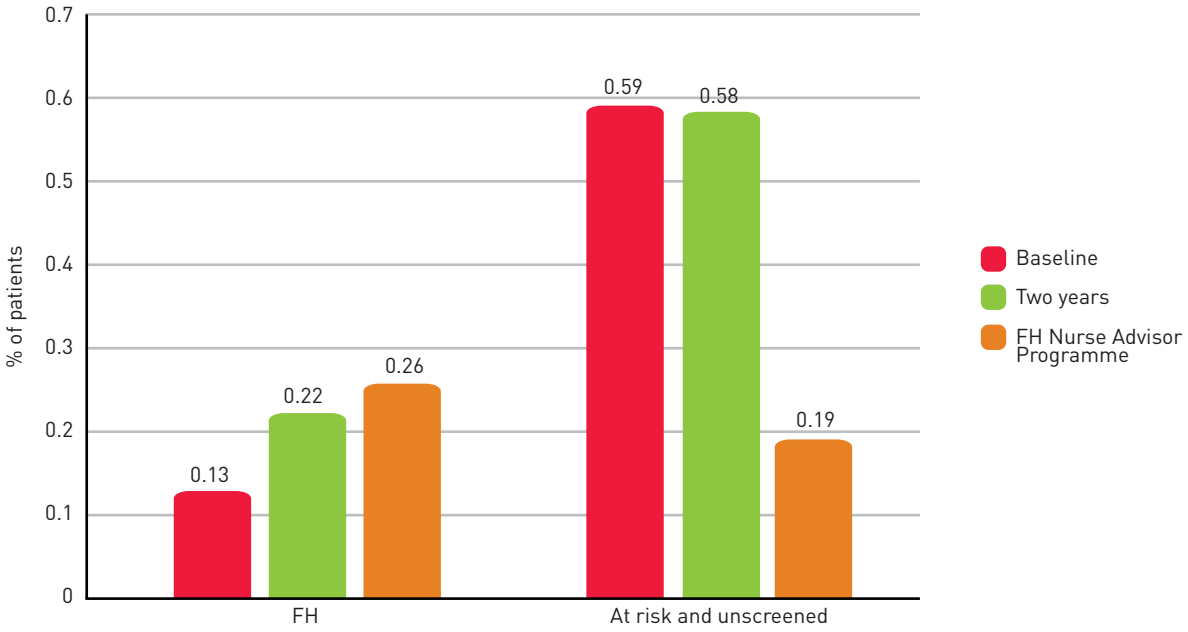
Estimated diagnostic workload: In the context of a GP practice with a population of 10,000 patients, the 'at risk and unscreened' patient numbers would be approximately **60 patients**.

Re-audit at two years

FH prevalence after two years: Re-audit showed a substantial increase in the prevalence of diagnosed FH, increasing to 0.22% (one in 450) (Figure 1, Table 2).

'At risk and unscreened': Despite the increase in FH diagnosis, the proportion of patients 'at risk and unscreened' remained almost unchanged at 0.58% (Figure 1, Table 2).

Figure 1: Summary of the Medway FH audit results at baseline, after two years and after the introduction of the FH Nurse Advisor Programme



FH (definite, probable and possible)
* Patients were considered to be 'at risk and unscreened' if they had a total cholesterol >7.5 mmol/L and/or LDL-C >4.9 mmol/L and had not been assessed using the Simon Broome criteria.

Table 2: Summary of the Medway FH audit tool results

Audit stage	Time-point	FH (definite, probable and possible) (% of patients)	At-risk and unscreened (% of patients)
Baseline	October 2011	343/262,030 **(0.13)**	1,553/262,030 **(0.59)**
Two years§	October 2013	442/199,346 **(0.22)**	1,164/199,346 **(0.58)**
FH Nurse Advisor Programme	June 2014*	742/280,450 **(0.26)**	536/280,450 **(0.19)**

§ Denominator (and numerator) is lower than previous time-point; data could not be extracted from all EMIS (Electronic medical information systems) at this time.
* Data cut-off 30.05.2014

Phase 2 - Active review of GP audit lists via the FH Nurse Advisor Programme

In October 2013, an FH Nurse Advisor Programme was introduced within the CCG with the aim of further improving the rate of diagnosis of FH in Medway. At this point, a decision was made to revise the audit and incorporate the DLCNC to define the severity of FH and support clinical management. The six sections of the Medway FH audit tool are shown in Box 1.

The FH Nurse Advisor Programme was conducted in three stages - an initial meeting and sign-up with each practice; a review of 'at risk and unscreened' patients, and calculation of DLCNC scores; and a nurse-led patient advice clinic (Figure 2).

The nurse reviewed practice audit lists of 'at risk and unscreened' patients. Patients for whom all parameters were known were scored according to the DLCNC. Any missing clinical parameters preventing calculation of the DLCNC score were sought via a local healthcare professional, and non-clinical parameters were sought from the patient after invitation to a clinic. The DLCNC score prompted referral to other healthcare professionals as appropriate, and/or an invitation to attend a FH nurse-led advice clinic. At these clinics, the FH nurse provided education on lifestyle modification, including advice on diet, exercise and smoking cessation if necessary, with HEART UK leaflets offered. Family history was discussed and clinical examination for xanthoma or corneal arcus was performed. Cascade screening, in the form of letters for patients to forward to first-degree relatives, was also conducted at the clinic. The nurse advisor referred patients with a DLCNC score indicating 'possible FH' back to the GP for further management, and those with a DLCNC score indicating 'definite or probable FH' on to secondary care.

BOX 1.
The six sections of the Medway FH audit tool

1. FH (definite, possible, probable)
2. High cholesterol (excluding all FH*)
3. Dutch Lipid Clinical Network Criteria score (excluding all FH*)
4. Simon Broome assessment
5. Personal history of CHD
6. Family history of FH

(*all FH = all definite, possible and probable cases)

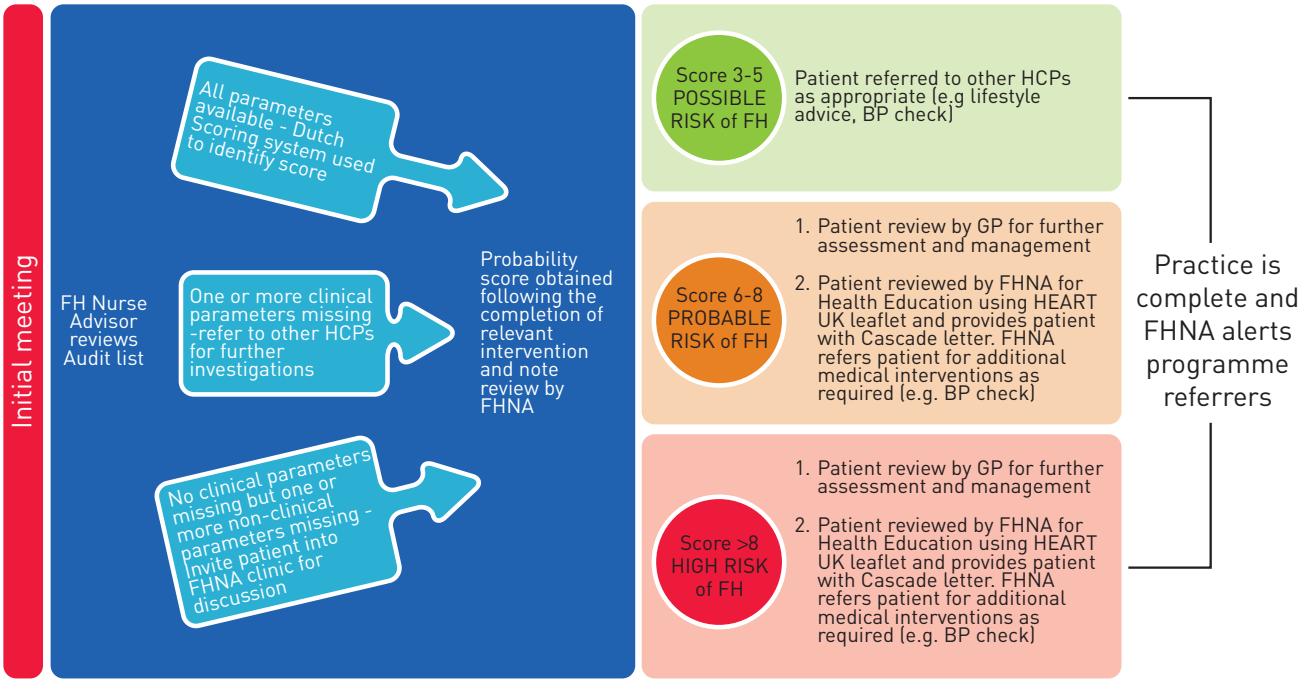
RESULTS

Baseline findings

FH prevalence: From initiation of the Nurse Advisor Programme in October 2013 to June 2014 (seven months), the prevalence of patients diagnosed with FH within Medway CCG increased to **0.26%** (one in 375) (Figure 1; Table 2).

'At risk and unscreened': Following the programme, this had reduced to **0.19%** (Figure 1; Table 2).

Figure 2: FH Nurse advisor programme



FHNA: Familial Hypercholesterolaemia Nurse Advisor
HCPs: Healthcare professionals
BP: Blood pressure

NEXT STEPS AND SUSTAINABILITY

Rolling out to other GP practices and CCGs

The Medway FH audit programme provides a transferrable model that can be used to improve the detection of FH in primary care. The Audit + software and Medway tool and prompts can be readily integrated into other GP practices and implemented within other CCGs. The FH Nurse Advisor Programme provides a useful model to increase diagnosis and appropriate referral of patients with FH within primary care.

HEART UK is currently in discussions with BMJ Informatica and relevant agencies (eg, CCGs) to make the audit tool and prompts widely available to GPs. In addition, HEART UK is seeking support to extend the FH Nurse Advisor Programme beyond the Medway region.

The full report of the Medway audit is due to be published in October 2014.

GP information packs

To continue to support GP practices within the Medway CCG, GP practices are being provided with a primary care guidance pack from HEART UK. The packs contains information about FH, including the HEART UK FH toolkit[14], HEART UK patient information leaflets[15] and a series of four publications sponsored by HEART UK and published in the *Primary Care Cardiovascular Journal*.

Referral to secondary care

NICE guidance recommends that healthcare professionals should offer all people with a diagnosis of FH referral to a specialist with expertise in FH for confirmation clinical diagnosis with DNA testing and initiation of cascade testing of relatives in those patients with a confirmed molecular diagnosis.[3,10] Within the Medway FH Nurse Advisor Programme, referral to local lipid clinics was advised for all newly diagnosed cases of FH. However, in many cases, the patient had already been referred and managed in secondary care. Re-referral was advised if the patients' cholesterol levels were not optimised or if their cholesterol levels had risen after being transferred back to primary care.

Genetic testing

NICE guidance recommends genetic testing of all index cases and cascade screening of family members as a cost-effective method for identifying new cases of FH.[3] Genetic testing for FH is not yet routine in England and was not included as part of this audit. However, with the new NHS commissioning structure and its commitment to increased investment into genetic sequencing resources, genetic testing of all FH cases is certainly feasible.[11, 13] When available, genetic testing will allow mutation carriers to be distinguished from those with polygenic FH and focus resources on cascade testing in the 40% of clinical FH patients with an identified single gene alteration.[11]

Diagnosing FH in primary care

FH a common disorder that remains under-diagnosed and untreated.[2] Recent NICE quality standards guidance and ESC guidelines recognised this as a significant issue to be addressed.[2,10] In addition the recent Department of Health Cardiovascular Outcomes Strategy recognised improving identification of inherited cardiac conditions a strategic priority and action.[16]

The Medway Audit model provides a solution to improving diagnosis of FH within primary care. The Audit + software and Medway tool and prompts running in the background on GP IT systems improved diagnosis of FH, but the number of patients at risk and unscreened remained the same. The FH Nurse Advisor Programme not only increased the number of FH diagnoses, it also reduced the number of patients at risk and unscreened by almost two-thirds. The Medway CCG model could be adopted by other CCGs within England to improve diagnosis, awareness and management of FH in primary care.

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