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ORIGINAL ARTICLE

Systematic Detection of Familial Hypercholesterolaemia in Primary Health Care: A Community Based Prospective Study of Three Methods

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Background Familial hypercholesterolaemia (FH), a co-dominantly inherited disease of cholesterol that markedly increases risk of premature coronary artery disease (CAD), is significantly under-diagnosed. Primary health care is increasingly seen as a setting in which to increase the detection rate of index cases. We report a prospective study of three methods of case detection using pre-existing primary health care services in one community.

Methods Three methods of case detection were tested: pathology laboratory database search, workplace health checks and general practice database search. People identified at risk by each of the three screening methods were offered detailed assessment for FH using the Dutch Lipid Clinic Network Criteria score (DLCNCS).

Results 1316 participants underwent detailed assessment for FH. The proportion of at risk people identified for further assessment was in decreasing order: GP (659 of 2494, 26.4%), workplace assessment (60 of 268, 22.4%) and pathology database (597 of 4517, 13.2%) $p < 0.001$. Eight-six (6.5%) were identified as clinical FH (DLCNCS > 5) of which 59 had genetic testing and 11 of 59, 18.6%, were confirmed to have a mutation causing FH. Pathology database detected the greatest number of clinical FH (51 of 86, 59.3%) and mutation positive participants (8 of 11, 72.7%).

Conclusion Screening within primary health care was successful in detecting participants with FH. An integrated case detection model combining screening of pathology and GP databases is proposed.

Keywords Familial hypercholesterolaemia • Primary health care • General practice • Screening • Case detection • Preventative cardiology

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Introduction

Familial Hypercholesterolaemia (FH) is a co-dominantly inherited disorder of cholesterol metabolism causing premature coronary artery disease (CAD). Resulting from mutations in the low density lipoprotein (LDL) receptor gene [1], FH occurs with an estimated frequency of 1 in 500 in the general population [2] and at higher rates due to founder effects in selected populations [3]. Primary Health Care (PHC) is increasingly seen as important for detection of new index cases of FH [4–7]

Individuals with FH have early atherosclerosis from childhood and the only evidence that they may be at risk may be a family history of premature CAD. Given the usual age for screening for CAD is 45 years and over [8] these individuals may have significant cardiovascular disease before they are considered for screening.

FH is a condition that is detectable, treatable and potentially cost-effective for screening [9]. Diagnosis of FH is made on clinical history, examination, biochemical findings and DNA testing. In Australia the DLCN criteria [10] are preferred for phenotypic diagnosis because they combine clinical findings, biochemical results and DNA results without relying on any one feature exclusively [11].

Cascade screening is the most cost-effective means of screening for FH [12]. However, detection of new cases is limited by identification of index cases. Estimates of the percentage of diagnosed FH within the community range from 10% [11] to 25% [13], meaning that the majority of cases remain undiagnosed. In Australia there may be as many as 45,000 undiagnosed cases of FH [14].

The role of PHC and in particular general practice in screening for FH has been recognised by a number of authors [5,6,11,13,15–17]. In Australia 83% of the population sees the general practitioner GP at least once a year [18]. Up to 92% of all cholesterol tests may be requested by GPs [19]. However, low awareness and gaps in GP knowledge on FH [20] reflect inadequate diagnosis and identification of index cases.

To date there are limited numbers of studies of the best screening strategies for FH in PHC. We report a case detection study using three different screening strategies based in PHC.

Methods

This study was a prospective comparison of three screening methods for the detection of FH. The study comprised three phases: Phase 1 initial screening in PHC settings, Phase 2 case detection in a primary care setting by a research nurse and general practitioner, and Phase 3 specialist clinical follow up of high-risk cases. Research participants were recruited between January 2010 and December 2012. Clinical follow-up of high-risk cases continued until June 2013.

Three PHC settings were used in screening for possible risk of FH: community pathology laboratory databases (PLD), work place based occupational health assessment (WPA) and general practice patient databases (GPD).

PLD screening method involved three community pathology providers who performed a data extraction of records of all patients 18 to 60 years with total cholesterol > 7.5 mmol/l or LDL-C > 4.5 mmol/L over the previous five years from South West Australian postcodes (6200-6299). The pathology laboratories contacted patients by mail and they were recruited when they contacted the research office for a primary care assessment.

WPA screening method involved the workforce at a large local mineral processing operation. Workers were offered a short five-question questionnaire on CAD risk (Figure 1), administered as part of their annual health assessment. Information about the condition and the consequences of a positive response to the questionnaire and of the diagnosis of FH were given and informed consent taken prior to the

	Questions
1	Have you ever had any of the following: Heart Attack, Stroke, By-pass Artery Operation, Blocked Arteries or Bad Circulation
2	Have you ever been told that your blood cholesterol is high (over 7)?
3	Have you ever been advised to take medicine to lower your blood cholesterol?
4	Has any BLOOD relative (grandparent, brother, sister, or child) aged 60 years or below, had any of the following: Heart Attack, Stroke, By-pass Artery Operation, Blocked Arteries or Bad Circulation anywhere in the body?
5	Has any BLOOD relative (grandparent, brother, sister, or child) had "high" cholesterol or cholesterol over 7?

Figure 1 WPA CAD risk questionnaire.