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ORIGINAL ARTICLE

Barriers to the identification of familial hypercholesterolemia among primary care providers

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Abstract

Familial hypercholesterolemia (FH) is severely underdiagnosed in the USA. Primary care providers are well-positioned to identify FH cases; however, universal FH screening is not routinely implemented in practice. The aim of the present study was to identify perceived barriers to FH screening among primary care physicians in Minnesota. A questionnaire assessed FH screening practices, knowledge, and perceived barriers to FH screening. The questionnaire, sent electronically to internal and family medicine physicians in Minnesota ($N = 1932$) yielded a conservative estimated response rate of 9% ($N = 173$). Although 92% of participants reported themselves responsible for identifying individuals with FH, 30% did not routinely perform screening in practice. Only 50% of participants were able to correctly identify the risk of FH to first-degree relatives of individuals with FH. Challenges incorporating lipid and family history data was the most frequently endorsed barrier to FH screening (34%). A majority of participants endorsed a clinical decision support system that flags individuals at high risk for FH (62%) and an algorithm with cholesterol levels and lipid disorders (56%) as means of facilitating FH screening. Although the generalizability of the findings is unknown, the results underscore the need for increased provider education regarding FH and suggest an FH screening strategy incorporating a clinical decision support system, screening algorithm, and support from other healthcare providers.

Keywords Familial hypercholesterolemia · Provider education · Universal screening · Cholesterol screening · Heart disease · Hypercholesterolemia

Introduction

Familial hypercholesterolemia (FH) is a group of genetic disorders caused by mutations in at least four genes associated with low-density lipoprotein (LDL) receptor function (Soutar and Naoumova 2007). FH is characterized by severely elevated blood LDL cholesterol levels and increased risk for atherosclerosis and coronary artery disease (Brown and Goldstein 1986; Hobbs et al. 1992; Soutar and Naoumova 2007). FH is one of the most common genetic conditions, with a prevalence of 1/250–1/500 in the USA, affecting between 630,000 and 1.2 million individuals (Goldstein et al. 1973; de Ferranti et al. 2016). FH exists in both heterozygous and homozygous forms. Individuals with heterozygous FH have a two- to threefold increase in plasma LDL levels, and individuals with homozygous FH have a six- to eightfold increase (Hobbs et al. 1992). The risk for fatal or non-fatal coronary heart disease (CHD) for individuals with heterozygous FH is over 50% for men by age 50 and nearly 60% for women by age 60 (Slack 1969). The majority of individuals with untreated homozygous FH experience a cardiovascular event and death by the second decade of life (Raal et al. 2011).

Underdiagnosis of FH in the USA

FH is severely underdiagnosed, with fewer than 1% of cases identified in the USA (Nordestgaard et al. 2013). This

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underdiagnosis places an immense undue health burden on individuals and the healthcare system. In the USA, approximately 5% of all myocardial infarctions, or 13,000 cardiovascular events, are caused by FH each year (Mozaffarian et al. 2015). Individuals who are treated early in life with cholesterol-lowering medication have a significantly lower risk of CHD that is comparable to the general population (Versmissen et al. 2008). Data from the national CASCADE-FH registry of over 1200 adults with heterozygous FH demonstrated a median age of FH diagnosis in the USA of 47 years (deGoma et al. 2016). Individuals who receive a midlife FH diagnosis or no diagnosis at all are denied the benefits of early intervention with cholesterol-lowering medications and the subsequent CHD risk reduction.

Universal screening for FH: guidelines and implementation

Universal screening for FH has been proposed, and efficacy in detecting FH cases outside the USA has been demonstrated (Klančar et al. 2015). Effective screening for FH relies on assessment of family history, clinical history, and lipid levels (World Health Organization 1999). A number of scientific organizations have issued recommendations for universal lipid screening in adults and children. The National Lipid Association recommends universal screening for elevated cholesterol levels in adults beginning at 20 years of age (Goldberg et al. 2011). Similarly, the US Preventive Services Task Force recommends screening for lipid disorders in all adult men beginning at age 35 years and women who are at increased risk for CHD beginning at age 45 years (US Preventive Services Task Force 2008).

The Centers for Disease Control and Prevention Office of Public Health (Centers for Disease Control and Prevention 2014a) have classified FH screening as a tier 1 genomic application. This means that existing evidence supports the clinical validity and utility of screening and its implementation in practice (Centers for Disease Control and Prevention 2014b; Sturm 2016). Yet, despite existing guidelines and support from the public health sector, FH screening is not routinely being implemented in practice. Through a chart review of over 175,000 internal medicine patients, Gonzalez Santos and Underberg (2011) identified 596 adult FH cases using the Dutch Lipid Network Clinical Criteria (an established FH diagnostic tool) (World Health Organization 1999), of which only 0.5% were correctly assigned a diagnosis of FH (Gonzalez Santos and Underberg 2011).

Barriers to FH Screening among primary care providers

Despite the high utilization of primary care services in the USA, the underdiagnosis of FH and gaps in the implementation of screening guidelines suggest the existence of barriers to FH screening in the primary care setting. Perceived barriers to lipid screening in a primary pediatric population include lack of familiarity with lipid screening guidelines and normal pediatric lipid levels, in addition to discomfort in addressing lipid disorders with patients and families (Dixon et al. 2014). A recent systematic review of 38 studies published between 2001 and 2012 revealed the most prevalent barriers to the provision of genetics services within primary care were those related to knowledge and skill (Mikat-Stevens et al. 2015).

Understanding primary care physicians' (PCP) knowledge and management practices regarding FH is vital. The American Academy of Family Practice defines a PCP as "a physician in Family Medicine, Internal Medicine or Pediatrics who provides definitive care to the undifferentiated patient at the point of first contact." (American Academy of Family Medicine Physicians 2017). Researchers in Australia, Asia, and the UK have conducted studies on the topic (Bell et al. 2014; Pang et al. 2015; Kwok et al. 2016a). The findings of these studies have consistently demonstrated gaps in FH knowledge and awareness among PCPs. While these studies suggest lack of FH knowledge among PCPs comprises a barrier to FH screening, the findings may not be generalizable to healthcare systems in the USA.

The present study sought to identify perceived barriers to the diagnosis of FH cases among PCPs in the USA, specifically Minnesota. By surveying family and internal medicine physicians, we assessed FH screening practices, knowledge of FH, and perceived barriers to implementation of FH screening. The identification of barriers to FH screening is essential in the development of strategies to overcome these barriers with the ultimate goals of increased FH identification, early intervention, and reduced disease burden.

Materials and methods

Participants, instrumentation, and procedures

Upon receipt of approval from the University of Minnesota Institutional Review Board, an online survey was administered to a sample of PCPs licensed in the state of Minnesota. Family medicine and internal medicine physicians licensed in Minnesota were identified using an online commercial mailing list service (Dr. Bill LLC, Charlotte, NC) which compiles physician data from the US Centers for Medicare and Medicaid National Provider Identifier records. Provider names, mailing addresses, email addresses, subspecialties, and active license status were verified using the publicly available Minnesota Board of Medical Practice website. Exclusion criteria included an inactive Minnesota medical license, non-physician provider, or a subspecialty certification (with the exception of geriatric medicine).

The survey contained 12 questions, including questions pertaining to FH screening practices, barriers to the identification of FH cases, knowledge, and demographics. All questions consisted of checklists of response options with the exception of one demographic question (number of years in practice) and a question regarding willingness to participate in a follow-up interview, which gave participants an option to provide a name and preferred email address. Several questions were adopted from a previous survey of primary pediatricians' lipid screening practices (Dixon et al. 2014). The survey was reviewed by two lipidologists with expertise in FH and piloted for clarity with a family medicine physician, and the final version contained their suggested edits.

We used stratified random sampling methods. These methods consisted of dividing the mailing list alphabetically into three arbitrary sections and selecting the first 1000 physicians in each category (internal, family medicine) with listed names and verified email addresses. Next, we reviewed each listing to determine eligibility. Eligibility criteria were physician with an active Minnesota license as verified by the MN Board of Medical Practice with a family practice or internal medicine primary specialty, a listed email address (either on the Board of Medical Practice site or commercial mailing list), and no listed sub-specialty, with the exception of geriatric medicine. The first 1000 physicians in each category (internal, family medicine) who met the eligibility criteria were included in the sample. An introductory recruitment email was sent that contained a brief description of the study, risks and benefits of study participation, details on the confidential and voluntary nature of the study, and a link to the web-based survey, administered through the online platform Qualtrics (Provo, UT). Three weeks following the introductory email, a postcard notification containing a link to the survey was sent to all eligible physicians. Email reminders and a survey link were sent to all eligible physicians who did not opt out of participation at 2 weeks, and again at 4 weeks.

Data analysis

Descriptive statistics consisting of frequencies, means, and standard deviations were calculated for responses to the survey. Written responses for "Other" categories were coded and discussed among two of the investigators to reach concordance.

Results

Participant demographics

Of the 2000 primary care providers selected, 1932 were eligible for participation. Forty-eight physicians did not meet the eligibility criteria and were removed from the sample. Four physicians who received a survey invitation sent emails indicating they were no longer providing patient care and were subsequently excluded. An additional 16 physicians indicated in their survey responses that they practiced in a non-primary care specialty or were retired from practice, and they were also removed from the final sample. Thirty-two physicians declined to participate. A total of 173 responses were received from eligible study participants (conservative estimated response rate, 9%). Table 1 contains a summary of participant demographics. Across participants, the predominant medical specialty was family medicine followed by internal medicine. Five participants selected "Other" for their medical specialty and listed specialties including geriatrics, functional medicine, and medicine-pediatrics. Participants had a mean of 23 years of experience (SD = 11.27).

FH screening practices

Although 92% of participants reported they believed themselves to be responsible for identifying individuals with FH, 30% did not routinely perform FH screening in their practice. Participants who reportedly did not perform routine FH screening ($n = 51$) were asked about referral practices for FH screening. Of the paricipants who responded to this question ($n = 50$), half (50%) did not refer patients for FH screening. Of the participants who did refer patients for FH screening, most reported referring patients to a cardiologist (28%), followed by lipid specialist (16%), and geneticist (6%).

Participants were asked about actions they would take if seeing a patient with premature coronary artery disease. The most frequently reported actions included initiating lifestyle changes (97%), ordering a lipid profile (95%), and initiating statin therapy (87%). Over half of the participants indicated they would look for clinical signs of FH such as corneal arcus and tendon xanthoma (54%). Fifty percent of participants indicated they would refer the patient to a specialist, and 23% of participants would screen the patient's close relatives for FH. Fourteen physicians (8%) specified other actions including recommending screening for the patient's family members ($n = 6$); assessing other risk factors (e.g., tobacco

Table 1 Participant demographics ($N = 173$)

Variable	Number of responses, *n* (%)
Primary medical specialty ($n = 172$)	
Family medicine	99 (57.6)
Internal medicine	68 (39.5)
Other*	5 (2.9)
Variable	Mean (standard deviation)
Number of years in practice ($n = 172$)	22.86 (11.27)

*Other: geriatrics ($n = 2$), functional medicine ($n = 1$), medicine-pediatrics ($n = 1$), unspecified ($n = 1$)

use, family history) ($n = 4$); initiating non-statin therapy (e.g., acetylsalicylic acid, chelation therapy, nitroglycerin) ($n = 3$); and ordering genetic testing ($n = 1$). Table 2 contains a summary of participants' FH screening practices.

FH knowledge

Participants were asked about the risk of FH to first-degree relatives of an individual with FH (Table 3). Only half of the sample correctly identified the 50% risk to first-degree relatives. Nearly 30% of participants responded that they did not know the risk to first-degree relatives. The remainder of the sample incorrectly identified the risk to first-degree relatives, with the majority of these participants underestimating the risk.

Barriers to the identification of FH cases

Reported barriers to screening patients for FH included challenges combining lipid and family history data (34%), patient opposition to screening (13%), discomfort addressing genetic lipid disorders (12%), and poor reimbursement for lipid screening (9%) (Table 4). The responses provided by participants who selected "Other" ($n = 30$, 18%) identified barriers across a wide variety of themes. Among these participants, the most frequently reported barriers were lack of time ($n = 4$); multiple competing priorities in practice ($n = 4$); limited family history information ($n = 4$); advanced age of the patient population ($n = 4$); and lack of awareness of FH ($n = 4$),

Table 3 Self-reported FH knowledge ($N = 173$)

Provider response	Total, *n* (%)
First-degree relatives of an individual with FH have what percentage chance of having FH themselves?*	
50%	88 (50.9)
25%	29 (16.7)
75%	8 (4.6)
100%	1 (0.6)
0%	0 (0)
I do not know	47 (27.2)

*Correct response, 50%

Table 2 Self-reported FH screening practices ($N = 173$)

Provider response	Total, *n* (%)
Do you routinely perform screening for FH in your practice? ($n = 173$)	
Yes	122 (70.5)
No	51 (29.5)
To whom do you refer patients for FH screening? (select all that apply) ($n = 56$)	
I do not refer patients for FH screening	28 (50.0)
Cardiologist	14 (25.0)
Lipid specialist	8 (14.2)
Geneticist	3 (5.4)
Other*	3 (5.4)
Do you believe that you, as a primary care provider, have a responsibility for identifying individuals with FH? ($n = 173$)	
Yes	159 (91.9)
No	14 (8.1)
If you see a patient with premature symptomatic CAD, what action(s) would you typically take? (select all that apply) ($n = 173$)	
Initiate lifestyle changes	168 (97.1)
Order lipid profile	164 (94.8)
Initiate statin therapy	150 (86.7)
Look for clinical signs of FH (i.e., corneal arcus, tendon xanthoma)	95 (54.9)
Refer patient to specialist	70 (40.5)
Screen patient's close relatives for FH	40 (23.1)
Other**[a]	14 (8.1)

CAD, coronary artery disease

*Other: provider reportedly performs lipid screening; no referral specified ($n = 2$), other ($n = 1$)

**Other: recommend screening for patient's family members ($n = 6$), assess other risk factors ($n = 4$), initiate non-statin therapy ($n = 3$), other ($n = 2$)

[a] Select responses categorized under multiple domains

specifically a perceived low prevalence of FH and lack of need for screening. Three individuals reported a lack of knowledge of FH screening procedures. Additional barriers to FH screening included patient fasting status ($n = 2$) and insurance coverage ($n = 2$). Two participants identified barriers related to genetics services, including genetic testing being out of the provider's scope of practice and lack of access to a genetics professional in a rural practice setting. Over 47% of participants reported no barriers to screening patients for FH.

Sixty-three percent of the sample indicated a clinical support system that flags patients at high risk for FH would assist them in screening for FH (Table 4). A majority of participants (56%) also indicated that an algorithm with cholesterol and lipid disorders would facilitate FH screening. Other reported facilitators of FH screening included more time to assess patients (37%), increased training on genetic and lipid disorders (33%), and consultation with genetics experts (9%). Four physicians reported no facilitators of FH screening, with two of these participants indicating that screening is routinely performed in their practices. Three participants indicated a need for more data demonstrating the benefits of FH screening and treatment. Two physicians indicated that more education regarding FH and screening procedures would assist them in identifying FH cases.

Sixty-five percent of participants reported being comfortable identifying patients with FH (Table 4). While a majority of the sample was also comfortable identifying at-risk family members of patients with FH, the percentage was lower (55%) compared to comfort identifying patients with FH. Finally, 46 participants (25%) expressed willingness to participate in a follow-up study regarding FH screening implementation.

Discussion

The present study explored FH screening practices, knowledge of FH, and perceived barriers to FH screening among primary care physicians in Minnesota. The findings show that FH screening among PCPs surveyed was suboptimal in this sample. Over 90% of participants reported they believed

Table 4 Barriers to identification of FH cases ($N = 173$)

Provider response	Total, *n* (%)
What barriers exist for screening adults for FH in your practice? (Select all that apply) ($n = 170$)	
No barriers	71 (41.8)
Challenge combining lipid and family history data	58 (34.1)
Patient opposition to screening	22 (12.9)
Discomfort addressing genetic lipid disorders	20 (11.8)
Poor reimbursement for lipid screening	15 (8.8)
Other*[a]	30 (17.6)
What would assist you in screening for FH? (Select all that apply) ($n = 166$)	
A clinical decision support system that flags patients at high risk for FH	103 (62.0)
An algorithm with cholesterol levels and lipid disorders	93 (56.0)
More time to assess patients	61 (36.8)
Increased training on genetics and lipid disorders	55 (33.1)
Consultation with genetics experts	15 (9.0)
Other**	13 (7.8)
Are you comfortable identifying patients with FH? ($n = 172$)	
Yes	112 (65.1)
No	60 (34.9)
Are you comfortable identifying at-risk family members of patients with FH? ($n = 172$)	
Yes	96 (55.8)
No	76 (44.2)

*Other: lack of time ($n = 4$), multiple competing priorities in practice ($n = 4$), limited family history information ($n = 4$), advanced age of patient population ($n = 4$), lack of knowledge of FH screening procedures, lack of awareness of FH ($n = 3$), challenges with patient fasting status ($n = 2$), lack of insurance coverage for screening ($n = 2$), genetic testing beyond scope of practice ($n = 1$), lack of access to a genetics professional ($n = 1$), other ($n = 3$)

**Other: nothing ($n = 4$), data demonstrating benefits of FH screening and treatment ($n = 3$), education regarding FH and screening ($n = 2$), other ($n = 2$)

[a] Select responses categorized into multiple domains

themselves to be responsible for the identification of FH cases, supporting the crucial role of family and internal medicine physicians in FH screening. However, only 50% of participants correctly identified the risk of FH to first-degree relatives of individuals with FH, and nearly 30% of the sample did not perform FH screening in their practice.

Challenges combining lipid and family history data was the most frequently endorsed barrier in this study. Documentation of family history of CHD occurs infrequently in a primary care setting and, when documented, is often insufficient to conduct a risk assessment (Dhiman et al. 2014). Clinical criteria incorporating both lipid and family history have been developed and widely implemented to facilitate the identification of FH cases. These include the Dutch Lipid Clinic Network (DLCN), Simon Broome Register (SBR), and Make Early Diagnosis to Prevent Early Death (MEDPED) criteria (Henderson et al. 2016). The reported challenges in combining lipid and family history data given the existence of well-established FH diagnostic criteria may suggest that there is a lack of knowledge about available FH diagnostic tools among PCPs, adequate family history information is not routinely obtained in practice, and/or time constraints prohibit conducting a risk assessment.

Lack of knowledge regarding FH was a commonly identified barrier to screening in this study. These findings are consistent with those of similar studies conducted outside the USA, with 45–51% of PCPs correctly identifying the risk of FH to first-degree relatives of individuals with FH (Bell et al. 2014; Pang et al. 2015; Kwok et al. 2016b). With one third of participants reporting that increased training on genetic and lipid disorders would assist them in FH screening, it is evident that family and internal medicine physicians themselves have recognized this need.

Strategies are needed to overcome barriers to FH screening among PCPs. A majority of participants reported that a clinical decision support system (62%) and an algorithm with cholesterol levels and lipid disorders (56%) would assist them in screening for FH. Research has demonstrated that clinical decision support systems are necessary and effective for integrating genetic tests including pharmacogenetics and cancer genetics into primary care (Blankenship et al. 1989; Overby et al. 2013; Hicks et al. 2016b, a). Clinical decision support for the screening and prevention of dyslipidemia is no exception (Souza et al. 2011). These systems utilize existing FH clinical criteria to identify at-risk patients and prompt providers to consider additional assessment (Green et al. 2016). The incorporation of algorithms to identify FH cases based on variables documented in electronic health records consistent with a diagnosis of FH can further enhance this strategy. Such algorithms have been developed and validated for use in FH case-finding in a primary care setting (Weng et al. 2015; Safarova et al. 2016). Green et al. (2016) described the implementation of the FH Audit Tool, a clinical decision support software for the detection of FH cases, in a general practitioner health group in the UK (Green et al. 2016). The FH Audit Tool was developed to flag patients with definite or possible FH based on the SBR and DLCN criteria. After 33 months, the prevalence of FH increased from one in 750 (0.13%) to one in 357 (0.28%), and the number of at-risk unscreened patients decreased from 0.59 to 0.14%. Notably, a considerable reduction in the number of unscreened at-risk individuals occurred only after the incorporation of nurse-led FH clinics.

Only 9% of PCPs in the present study noted they would consult with genetics experts, and only 50% of PCPs who did not screen for FH reported making referrals to other providers. Yet, the incorporation of genetics healthcare providers into FH screening programs has been highly successful in countries such as the Netherlands (Umans-Eckenhausen et al. 2001; Defesche 2010). The Netherlands FH screening program employs specialized nurses who facilitate genetic testing for first-degree relatives of FH index cases with an identified lipoprotein receptor gene (*LDLR*) mutation. As of 2010, nearly 44,000 relatives have been contacted, and over 16,000 new cases of FH have been documented (Defesche 2010). As the above studies illustrate, a multipronged intervention strategy will likely be required for an optimally effective FH screening program.

Given the importance of cascade screening for FH, it is notable that 44% of participants in the current study did not feel comfortable identifying at-risk family members of individuals with FH. Furthermore, less than 25% of participants would screen relatives of individuals with premature symptomatic coronary artery disease for FH. These findings emphasize the need for provider education regarding FH screening or utilization of other approaches to promote cascade screening within the current US healthcare systems. Cascade screening for family members of FH index cases is an essential component of a successful screening program. A variety of cascade screening approaches with demonstrated utility exist in the Netherlands, Australia, Brazil, and the UK (Umans-Eckenhausen et al. 2001; Versmissen et al. 2008; Jannes et al. 2015; Bell et al. 2015). Some authors have proposed an approach combining elements of universal and cascade screening as the ideal method for increasing the detection of FH cases (Wald et al. 2007; Morris et al. 2012). Combined screening approaches have broad implications for other common genetic conditions, such as Lynch syndrome and hereditary breast and ovarian cancer syndrome, which can benefit from increased identification in primary care and sequential cascade screening (Roberts et al. 2018).

Study strengths and limitations

To our knowledge, this is the first study in the USA to examine PCPs' perceptions of barriers to FH screening in adults. Strengths of the present design include a fairly even representation of family and internal medicine

physicians with varying degrees of experience, ranging from 2 to over 50 years in practice. Participants were given the opportunity to provide free text responses for several survey items that allowed for the collection of more in-depth data regarding FH screening barriers and facilitators. Limitations of the study include a relatively small sample size and low response rate (9%) that could lead to potential selection bias. For instance, a high percentage of respondents believed it was their responsibility to identify individuals with FH (92%) and reported screening for FH (70%). We hypothesize that these percentages are an overestimation of actual practice. The study only included physicians practicing in Minnesota, which may limit generalizability of results to other states. Additional studies are necessary to replicate the findings and test survey question validity. Finally, the study did not include other PCPs who may be involved in FH screening, such as physician assistants, nurse practitioners, and nurses.

Practice implications and research recommendations

The present findings demonstrate that FH screening among PCPs is suboptimal, and they underscore the need for increased education among PCPs regarding FH identification and risk assessment. In addition to increased provider education, strategies to overcome barriers to FH screening will likely entail a multipronged approach incorporating clinical decision support systems, screening algorithms, and support from other providers within the primary care setting or triaging to genetics healthcare professionals. Future studies including a larger sample size, additional non-physician PCPs, and more geographic regions will contribute to the generalizability of these findings. Research on the implementation of these strategies is needed to identify the ideal FH screening program with the ultimate goals of increased FH detection, earlier treatment, and reduced cardiovascular disease.

Compliance with ethical standards

Conflict of interest All authors declare no conflicts of interest specifically related to content in this manuscript. The following unrelated relationships are disclosed for transparency. Heather Zierhut is a Senior Advisor for GeneMatters, LLC (telegenetics genetic counseling company). Pat McCarthy Veach received royalties for books co-authored—Springer Publishing Co. (1 book); Wiley (1 book); and Oxford (1 book). Daniel Duprez has served as a consultant for Amgen and Ackea and received grants from Pfizer, Sanofi, Regeneron, and Astra-Zeneca.

Human subjects and informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000(5). Informed consent was obtained from all participants for being included in the study. This article does not contain animal subjects.

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