A novel approach to screening for familial hypercholesterolemia in a large public venue

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Abstract The primary aim of this study was to test the feasibility of a public health screening program to identify individuals at high risk of familial hypercholesterolemia through a novel screening approach at a large public venue. A fingerprick, non-fasting lipid panel was obtained, and a survey which consisted of 44 open- and close-ended questions divided into four sections: medical and family history of FH, opinions of cascade genetic testing, patient activation, and demographics was completed. A total of 971 participants met criteria and completed a cholesterol screen. In total, five individuals met either the Simon Broome Register or the Dutch Lipid Clinic Network criteria for possible familial hypercholesterolemia. Participants were generally positive towards genetic testing, and the vast majority listed they had no barriers to communication of genetic testing information to family members. However, the most common barrier listed was lack of communication skills. Our results suggest that a public health screening program for FH is viable at a large public venue. We argue that further research is needed to expand this study to a fully operational screening program.

Keywords Cholesterol · Genetic communication · Genetic information · Genetic screening · Genetic testing · Familial hypercholesterolemia

Introduction

Heart disease is the leading cause of death for both men and women in the USA leading to an estimated 600,000 deaths annually (Murphy et al. 2013). Risk factors for coronary heart disease (CHD) are both environmental (i.e., diet, exercise) and genetic (i.e., LDLR mutations) (Go et al. 2014). Familial hypercholesterolemia (FH) is a group of genetic forms of high cholesterol caused from mutations in genes in the low density lipoprotein recycling pathway that lead to a twofold increased level of serum low-density lipoprotein (LDL), increased risk of atherosclerosis, and ultimately negative cardiac events (Hobbs et al. 1992; Goldstein et al. 2001; Goldberg et al. 2011). Furthermore, if untreated, individuals with FH have up to a 22-fold increased risk for coronary artery disease and a 4–13-fold increased risk to die from cardiovascular disease in which 85% of males and 50% of females will suffer a coronary event before the age of 65, leading to a 20-year reduction in life expectancy relative to the general population (Miettinen and Gylling 1988; Hirobe et al. 1982; Mabuchi et al. 1989; Group. 1991; WHO. Human Genetic Program. Familial Hypercholesterolemia and Paris 1997; Hill et al. 2011; Khera et al. 2016). However, behavioral changes combined with aggressive dosing of cholesterol lowering drugs have been found to lower individuals' with FH cardiovascular disease risk to that of the general population (Simon Broome Register Group 1999).

FH is common yet highly underdiagnosed in many countries. The frequency of FH is about 1 in 300 to 1 in 500 worldwide (Goldstein et al. 2001; Benn et al. 2012). In the USA, it is estimated that FH is diagnosed in as few as 1% of individuals with the condition (Nordestgaard et al. 2013). Since effective treatments exist for managing FH, the underdiagnosis leads to an undue health burden on both individuals and the health care system. Early diagnosis to prevent this health burden and thousands of deaths from CHD each year

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is therefore desirable and potentially cost-effective (Marks et al. 2002). To address this problem, the Centers for Disease Control and Prevention has included FH in its Tier 1 genetic implementation plans and supports incorporation of screening plans into practice (Centers for Disease Control and Prevention 2015).

Screening and diagnosis of index FH cases is complex. A diagnosis can be made using several criteria including the Simon Broome criteria from the UK, the Dutch Lipid Clinic Network criteria for FH from the Netherlands, or the Make Early Diagnosis to Prevent Early Deaths (MEDPED) criteria from the USA (Broome and Group 1991; Williams et al. 1993; Nordestgaard et al. 2013). The clinical diagnoses consist of a combination of elevated cholesterol screens, positive family history of high cholesterol, genetic testing, and/or presence of xanthomas, cholesterol deposits in the tendons.

One of the most effective methods of diagnosis and disease prevention for FH is cascade genetic testing, the identification of an index case with a genetic mutation in an associated gene and the subsequent screening of family members for asymptomatic carriers (Leren et al. 2008). Cascade genetic testing significantly decreases the cost of diagnosis and may reduce the health burden (Marks et al. 2002). However, a major obstacle to cascade testing is the identification and recruitment of family members. Two main strategies have been utilized to identify, contact, and recruit family members at the population level in Europe; Norway and the Netherlands are illustrative examples with moderate and varying degrees of success at identifying and treating family members (Umans-Eckenhausen et al. 2001; Leren et al. 2008). No national screening program exists in the USA (Nordestgaard et al. 2013).

The aims of this study were to identify individuals at high risk of FH through a novel screening approach that includes collection of medical and family history information as well as cholesterol levels at a large public venue, the Minnesota State Fair. We aimed to assess participants' attitudes towards genetic testing and cascade testing for FH as well as patient activation, the extent a participant feels in control of their health and their ability to adhere to a prescribed health routine. The Minnesota State Fair was chosen as a unique source of participants given that it attracts a diverse population of ~1,800,000 visitors each year primarily from throughout the state of MN and therefore provides a means to quickly assess a large, cross-sectional convenience sample of the population. The results of this study will document the feasibility as well as potential strengths and obstacles to this public health screening approach for FH in the USA.

Materials and methods

Participant enrollment

The study was approved by the University of Minnesota Institutional Review Board. Recruitment of participants occurred at the 2014 Minnesota State Fair (August 21–September 1). Study staff actively recruited fairgoers outside of the research building and passively through signs at the research booth. Participants were eligible to participate if they were between the ages of 18 and 65 and aware of their biological medical family history. Participants were excluded if they had any of the following diseases: type 2 diabetes, cholestatic liver disease, nephrotic syndromes, kidney or renal failure, hypothyroidism, or morbidly obese, drank >5 drinks a day, or took seizure, high blood pressure (i.e., thiazides), or acne (i.e. isotretinoin) medications or adrenal steroids, as these factors may affect cholesterol levels but are unrelated to FH. Individuals on cholesterol lowering drugs were not excluded from participation but this was noted on the survey.

Survey

The survey consisted of 44 open- and close-ended questions divided into four sections: medical and family history of FH, opinions of genetic testing and cascade testing, patient activation, and demographics. The medical and family history portion of the survey contained items that were used in the Simon Broome and the Dutch Lipid Clinic Network criteria for making a phenotypic diagnosis of FH in adults. Questions on participants' opinions focused on whether or not participants would pursue genetic testing, if they would feel comfortable communicating genetic information regarding a hypothetical positive result and what they perceived as barriers to communicating their genetic testing results. Ability and willingness to complete healthy lifestyle behaviors, or patient activation, was assessed using the Patient Activation Measure® 13 (PAM-13) survey from Insignia Health (Hibbard et al. 2005). This measure has been validated in diverse populations for a variety of health outcomes, including heart health and cholesterol outcomes (McDermott et al. 2011). Participants are scored using statements about health behavior initiation including concepts of personal responsibility for health, ability to maintain healthy behaviors through times of stress, and the ability to initiate conversation with their physician about health concerns. Scores are calculated and participants received stages 1, 2, 3, or 4. Lower stages indicate that the individuals are more passive about their health and lack self-confidence to personally affect their own health outcomes. Higher stages indicate an active role in their health and a self-confidence to positively affect their own health outcomes. Surveys were completed either online using Qualtrics research software or on paper depending on the participants' comfort level with

technology or the availability of electronic tablets (2015). Paper survey data was input by two independent research staff and then checked for accuracy.

Cholesterol screen

A finger-prick, non-fasting lipid panel was obtained using Cardiochek® ver. 1.2 handheld devices. A non-fasting cholesterol screen was the only feasible means to collect cholesterol levels. Non-fasting cholesterol levels are supported by the European Atherosclerosis Society and the European Federation of Clinical Chemistry and Laboratory Medicine for routine use for the assessment of plasma lipid profiles (Nordestgaard et al. 2016). The calculation of LDL cholesterol using the Friedewald equation can be altered by an increase in triglycerides that occur after eating a fatty meal, so those who screened positive in our sample would require a repeat fasting cholesterol as recommended by the American College of Cardiology/American Heart Association (ACC/AHA) (Stone et al. 2014). Participants were given their total cholesterol results at the time of completion as an incentive for study participation.

Data analysis

Descriptive statistics were used to review demographic data, genetic testing opinions, and diagnostic criteria for FH. Participants' total cholesterol and self-reported personal and family history data were used to assess the Simon Broome Register criteria and the Dutch Lipid Clinic Network criteria. Risk assessments were completed independently by two research staff and reviewed by the last author for consistency. An inductive content analysis was performed to identify categories of participant responses to an open-ended question on the barriers to communication of genetic testing information (Patton 2002). An inductive approach allows research findings to emerge from the principal themes inherent in raw data without a structured methodology. The method incorporates in-depth readings of text, and then identification of text segments that contain meaning units which are then labeled with a new category (code) into which the text segment is assigned. The first author reviewed all text responses and created a series of codes. The last author then used the codebook established by the first author to independently code the text responses. Both authors then met to discuss discrepancies in codes and reach agreement on all discrepancies to create a final list of codes and categories.

Results

Information on participant demographics is summarized in Table 1. A total of 971 participants met criteria, consented to

participate, and completed a cholesterol screen. A majority of participants were female (58.6%), had a college degree or higher (62.5%), and earned \$75,000 or more per year (53.45%). Most participants were married or in a marriage-like relationship (60.4%), had biological children (48.7%), and had body mass index in the normal category (48%) or overweight category (35 %). Fifty-two participants (5.3%) were on cholesterol lowering medications, and all but two had total cholesterol levels (<290 mg/dl) at the time of the screen. To assess the representativeness of our sample, we compared our study sample to Minnesota Census data (2010). State fairgoers who participated in this study were statistically significant different from the MN population in all categories examined (Table 1).

In total, five individuals met either the Simon Broome Register or the Dutch Lipid Clinic Network criteria for possible FH (~1/200), of whom two were previously treated. Using the Simon Broome Register Group criteria, no participants were classified as definite FH and two participants met criteria for possible FH. The first participant reported a father who had a myocardial infarction at age 38 as well as a paternal grandmother and uncle with CAD. The participant had a total cholesterol level of 371 mg/dl and was on a cholesterol lowering medication. The other participant reported a maternal grandfather who had a myocardial infarction at age 56 as well as a mother and maternal grandmother with elevated cholesterol levels and CAD. The participant's total cholesterol was 303 mg/dl. Using the Dutch Lipid Clinic Network criteria for diagnosing FH, no participants were identified with definite FH or probable FH, but three participants were identified with possible FH. Of the three that had possible FH, one participant had slightly elevated cholesterol levels (210 mg/dl), arcus cornealis, and reported both parents with high cholesterol. The second participant who met criteria had premature coronary artery disease, premature cerebral or peripheral vascular disease, was on cholesterol lowering medication (total cholesterol = 194 mg/dl), and reported a father with known premature coronary and vascular disease at age 48. The last participant reported known premature coronary and vascular disease in his/her mother at age 49 and father at age 36 as well as a child under the age of 18 with high cholesterol. This participant had a normal total cholesterol screen (151 mg/dl) and was reportedly not on cholesterol lowering medication.

Based upon family history data, an additional fifteen participants out of 52 who were on cholesterol lowering medications would have met Simon Broome Register Group criteria for possible FH based if their untreated total cholesterol levels were above 290 mg/dl or LDL levels were above 190 mg/dl.

Table 1. Demographic differences between Minnesota residents and study participants

Variable	State of Minnesota		State fair		<i>P</i> value
	<i>n</i> = 5,303,925	%	<i>n</i> = 971*	%	
Gender					
Female	2,671,793	50.4	569	58.6	<i>P</i> < 0.001
Male	2,632,132	49.6	387	39.9	
Age					
<20	1,426,670	26.5	34	3.5	<i>P</i> < 0.001
20–29	721,410	13.4	209	21.5	
30–39	689,108	12.8	116	11.9	
40–49	726,794	13.5	159	16.4	
50–59	780,630	14.5	262	27.0	
>60	1,039,046	19.3	111	11.4	
Education					
Some high school	414,541	7.7	9	0.9	
High school graduate or equivalent	1,421,286	26.4	70	7.2	
Some college, no degree	1,195,172	22.2	238	24.5	
College graduate (bachelor/associate)	565,284	10.5	349	35.9	
Graduate/professional degree	1,200,556	22.3	258	26.6	
NR	586,819	10.9	33	3.4	
Relationship status					
Married or in a marriage like relationship	2,821,038	52.4	586	60.4	
Never married	1,690,470	31.4	280	28.8	
Divorced	532,982	9.9	62	6	
Separated	64,604	1.2	10	1.4	
Widowed	279,950	5.2	14	1	
Income					
<\$10,000	296,101	5.5	50	5.1	<i>P</i> < 0.001
\$10,000–49,999	1,916,583	35.6	203	20.9	
\$50,000–99,999	1,776,608	33.0	323	33.2	
\$100,000–150,000	823,700	15.3	210	21.6	
>\$150,000	565,284	10.5	134	13.8	
Cholesterol lowering medication use					
No			919	94.6	
Yes			52	5.4	
BMI					
Normal (<25 kg/m ²)			427	48	
Overweight (25–30 kg/m ²)			309	34.7	
Obese (>30 kg/m ²)			154	17.3	

Missing values for State of Minnesota Census data were not reported

^a Missing values for state fair participants: gender (*n* = 15), age (*n* = 80), education (*n* = 14), married (*n* = 19), children (*n* = 53), and total household income (*n* = 51)

Genetic testing opinions

Overall, participants held positive opinions of genetic testing for FH (Table 2). Questions were assessed using a 4-point Likert scale (1 = strongly agree, 2 = agree, 3 = disagree, 4 = strongly disagree). Most participants responded that they would like to know if they had a genetic form of high cholesterol (mean = 1.59, SD = 0.6). Additionally, participants

responded that they felt comfortable sharing their results with their family (mean = 1.54, SD = 0.6) and would not prefer a physician or genetic counselor to discuss their results with family members (mean = 2.90, SD = 0.7). Participants were also generally positive about opinions that genetic testing would be useful (mean = 1.71, SD = 0.7) and would be a positive experience (mean = 1.85, SD = 0.7).

Table 2. Participant opinions towards hypothetical genetic testing experience

Question	Mean $\pm$ Std. Dev. ^a	Median
I would like to know if I had a genetic form of high cholesterol.	1.59 $\pm$ 0.6	Agree
I feel genetic testing is useful for me.	1.71 $\pm$ 0.7	Agree
I would feel anxious about my possible results.	2.81 $\pm$ 0.7	Disagree
I feel that knowing my results could positively affect my life.	1.85 $\pm$ 0.7	Agree
I feel that knowing my results could negatively affect my life.	2.95 $\pm$ 0.7	Disagree
I would encourage my family to get tested.	1.61 $\pm$ 0.6	Agree
I would feel comfortable discussing my results with my family.	1.54 $\pm$ 0.6	Agree
I would prefer a physician discuss this topic with my family.	2.90 $\pm$ 0.7	Disagree

^a (4-point Likert scale: 1 = strongly agree, 2 = agree, 3 = disagree, and 4 = strongly disagree)

Modes of and barriers to communication of genetic information for cascade testing

Participants were first asked which of the following communication methods they felt comfortable using to relay genetic information to family members. Participants comfort varied by mode of communication with the highest comfort with communicating in person ($n = 591$, 64%), followed by telephone ($n = 468$, 51%), email ($n = 460$, 50%), letter ($n = 230$, 25%), link to website ($n = 220$, 24%), or conversation through a physician or genetic counselor ($n = 209$, 23%). Participants were then asked to rank the methods they had selected in the previous question by most preferred method to least preferred method. The most preferred mode of communication of genetic testing information was in person followed by telephone. Email was the third most preferred method. The options of letter, link to website, and conversation with physician were markedly less preferred than the first three modes of communication.

A majority of participants in our study ($n = 773$, 79%) did not provide barriers to communicating their hypothetical FH results with their families, either by directly stating that there were no barriers ($n = 376$, 39%), or by leaving the question blank ($n = 397$, 40%). However, 21% ($n = 197$) of participants noted 206 perceived barriers. The most common barrier listed was one of communication skills ($n = 66$, 32%) (Table 3). Within this category, individuals most often commented that they were concerned with their perceived lack of knowledge and were uncomfortable discussing the information with family members. Participants described concern regarding how their family members may react to the risk of FH ($n = 55$, 27%) and that their family may lack concern or even be hostile to both the information and the participant bringing the information. Other participants felt their family would be unwilling to make changes to their lifestyles. For some participants, logistical issues such as location and time were a barrier to communication ($n = 39$, 19%). Participants expressed concern with getting the family together in person to discuss the information due to distance or a large number of family members. Seventeen participants felt emotional concerns such as anxiety

and blame would be barriers to communication. Privacy was a concern for thirteen participants, and sixteen miscellaneous concerns were raised including religion and the participant not feeling personal responsibility to inform their family.

Patient activation measure (PAM-13®)

Participants consistently had high mean patient activation scores with 280 participants (28.8%) at the highest level stage 4 (maintaining behavior and pushing further) and 443 participants (45.6%) at stage 3 (taking action). The remaining participants scored at stage 2 ($n = 120$, becoming aware but still struggling) and stage 1 ($n = 104$, disengaged and overwhelmed), and 43 were not scored due to inadequate responses.

Discussion

Our research aimed to evaluate three aspects of a public health, cross-sectional genetic screening approach for FH. For a program to be effective, the target population must be willing to participate in genetic screening, individuals must be willing to discuss their results with their families to facilitate additional at-risk individuals being screened, and individuals must be willing to modify lifestyles and adhere to medical recommendations such as taking cholesterol lowering medication. The results of this pilot study suggest that a public health screening program for FH at a large venue such as the state fair may be feasible in MN. First, Minnesotans are willing to participate in screening for FH. Nearly 1000 individuals agreed to complete both a survey and cholesterol screen. Using the Simon Broome Register Group criteria and the Dutch Lipid Clinic Network criteria, we identified five possible FH cases. An additional fifteen participants would likely meet possible criteria if untreated. Of the participants, most responded favorably regarding genetic testing for FH. Our results are consistent with a previous study of ~150 individuals with FH and their family members in which 84% of respondents were in favor of screening to identify individuals

Table 3. Perceived barriers to communicating health information to family members

Barrier categories (<i>n</i> = 206) ^a	Definition
Communication (<i>n</i> = 66)	
Participant perceived lack of knowledge (<i>n</i> = 32)	Participant feels they do not have sufficient knowledge or understanding to accurately relay the information to their family.
Language barrier (<i>n</i> = 9)	Participant feels that communicating information is hindered by either medical terminology or differences in languages spoken within their family.
Discomfort with topic (<i>n</i> = 9)	Participant does not feel comfortable bringing up or discussing genetic information with family due to awkwardness of topic.
Not in contact with family (<i>n</i> = 8)	Participant is not in contact with family due to things such as physical distance or lack of cell phone service.
General communication concerns (<i>n</i> = 4)	Participant has unspecified concerns regarding communication.
Prefer doctor to explain (<i>n</i> = 4)	Participant feels this conversation would be better done by a physician.
Importance (<i>n</i> = 1)	Participant does not feel able to sufficiently stress the importance of this information.
Concern regarding family reaction (<i>n</i> = 55)	
Family lack of concern (<i>n</i> = 23)	Participant believes family will not care enough about topic to make changes to their lifestyle.
Family not willing to listen (<i>n</i> = 9)	Participant believes family will not listen to them regarding genetic information.
Family hostility towards advice (<i>n</i> = 9)	Participant is concerned that their family will be hostile towards medical advice.
Family not believe participant (<i>n</i> = 5)	Participant is concerned that they will not be believed as truthful by family members.
General concern regarding family reaction (<i>n</i> = 4)	Participant has unspecified concerns regarding family reaction.
Family lack of understanding (<i>n</i> = 3)	Participant believes family will not understand the information presented.
Family may not agree to testing (<i>n</i> = 2)	Participant is unsure they could convince their family to have genetic testing.
Logistics (<i>n</i> = 39)	
Location (<i>n</i> = 22)	Participant and family do not live close and therefore talking in person would be difficult, but optimal.
Time (<i>n</i> = 10)	Participant believes that the logistics of finding time to get together with family would be a barrier.
Finances (<i>n</i> = 4)	Participant is concerned that finances will either stop them from talking to their family or their family from acting upon genetic information.
Insurance concerns (<i>n</i> = 2)	Participant is concerned that insurance rates will go up with diagnosis.
General logistical concerns (<i>n</i> = 1)	Participants feels it will be logistically difficult to relay genetic information although how is unspecified.
Emotional response (<i>n</i> = 17)	
Anxiety (<i>n</i> = 8)	Participant believes that telling family may create undue anxiety over health outcomes.
Blame (<i>n</i> = 2)	Participant believes telling their family will place blame on someone in the family for this genetic condition.
Embarrassment (<i>n</i> = 2)	Participant is embarrassed that they have a potential health problem.
Sadness (<i>n</i> = 1)	Participant believes telling their family will trigger sadness in their family.

Table 3. (continued)

Barrier categories (<i>n</i> = 206) ^a	Definition
Surprise (<i>n</i> = 1)	Participant believes family will be unpleasantly surprised by the news.
Lack of trust (<i>n</i> = 1)	Participant lacks trust in the genetic information.
Guilt (<i>n</i> = 1)	Participant feels that telling family will make some members feel guilty for causing health problems.
Lazy (<i>n</i> = 1)	Participant is concerned laziness will stop action (either their own, or their family's).
Miscellaneous (<i>n</i> = 16)	
Not sure (<i>n</i> = 4)	Participants do not know if there would be any barriers or not.
No at risk family members (<i>n</i> = 3)	Participant has no living extended family that could be at risk due to small family of deaths.
Living with disease (<i>n</i> = 3)	Participant is concerned with living the disease including symptoms of the disease, their ability to pass the disease to their children, and how FH affects other health concerns.
Actionability of results (<i>n</i> = 1)	Participant is concerned for whether or not anything can be done to address this health concern.
Participant as barrier (<i>n</i> = 1)	Participant feels they themselves are a barrier to talking to their family.
Religion (<i>n</i> = 1)	Participant is concerned that religious beliefs may hinder discussing genetic information with their family.
Not participant's responsibility (<i>n</i> = 1)	Participant feels that it is not their responsibility to deal with their family's health problem.
Privacy (<i>n</i> = 13)	
General privacy concerns (<i>n</i> = 13)	Participant had unspecified privacy concerns.

^a One hundred ninety-seven participants noted 206 barriers

in their family (Andersen et al. 1997). In a nationally representative sample of British residents, 69% of the sample was in favor of genetic testing for heart disease, and those participants with a family history of heart disease were even more interested in genetic testing (74%) (Sanderson et al. 2004). Since our study did not directly perform genetic testing, these opinions are hypothetical, and participants' attitudes may change if given the ability to actually test for the condition. Research comparing actual pre- and post-screening genetic testing opinions would better assess the experiences for future screening programs.

In order for a population-based screening approach for FH to be effective, it is important that cascade genetic testing is acceptable and a viable option for most individuals. Our results found that most individuals would be willing to speak with their families to relay genetic screening results. Individuals felt it was their responsibility to discuss their results with their family and disagreed that it was the physician's responsibility to inform the participant's family. Our results are similar to patient interviews of 38 index FH cases which showed that patients were in favor of genetic testing and cascade testing (Hallowell et al. 2011). This is consistent with other studies that conducted focus groups to obtain opinions about the process of communicating their results of genetic

testing for cancer causing genes (Forrest et al. 2003; Hallowell et al. 2005). These focus groups suggested that patients desire to moderate their own discussions of genetic results and answered specifically that they felt they only needed physicians in a support role. This approach is similar to the method of cascade screening used by the Norwegian national screening program in which patients meet with a genetic counselor and then are encouraged to communicate information with family members. Although uptake of testing in this population was less than the Netherlands program which utilizes healthcare providers to contact relatives directly, this screening method may be more useful in the USA due to a desire for patient autonomy and legal requirements of patient confidentiality which may prevent physicians from directly contacting family members (Umans-Eckenhausen et al. 2001; Leren et al. 2008). Debate surrounding the ethical implications of direct versus indirect cascade screening exists (Newson and Humphries 2005; Sturm 2016). Although indirect screening was preferable to most in our study, some participants actually preferred a direct method.

The vast majority of participants listed that they had no barriers to communication of genetic testing information, though barriers were noted by 21% of our population. This suggests that many participants feel able to manage

conversations with their families about their FH results. However, barriers may exist for a significant proportion of the population. The largest category of barriers dealt with communication skills for presenting information to families. The largest subgroup of participants stated that they did not feel that they would have understood the genetic information sufficiently to present the information to their families. One potential solution surrounding uncomfortableness with understanding the genetic information is genetic counseling. A significant percentage of participants ($n = 209$, 23%) preferred a conversation through their physician or genetic counselor similar to the Netherlands program. Genetic counselors can assist in providing additional education and communication assistance for patients to gain skills needed to discuss genetic information with family members. Additionally, written materials may help to facilitate the discussion and ensure individuals have accurate information. Although these are perceived barriers, all of the barriers had been noted in qualitative interviews of 20 individuals with inherited high cholesterol who were contemplating discussing information on diagnosis and treatment with biological relatives (van den Nieuwenhoff et al. 2007). In our study, it was found that most people believed that anxiety would not be a barrier to genetic testing, whereas Andersen et al. found that anxiety was expressed by 44% of the FH index cases and their relatives (Andersen et al. 1997). It will be important to investigate actual anxiety associated with genetic testing in future work. Several survey-based studies have found that anxieties about genetic testing vary more in cases where the test is diagnostic but the disease is untreatable and additionally have higher anxiety in cases of cancer when the test is not diagnostic than in cases where treatment is known and effective (Shaw and Bassi 2001; Gaff et al. 2005).

Lastly, in order for a FH screening program to be effective, individuals need to be willing to make behavioral changes to treat FH. These lifestyle changes may include diet and exercise modification and the addition of a cholesterol lowering medication. In this study, we used a proxy measurement of patient activation to assess self-efficacy to medical treatment. A majority of participants (74%) scored a three or higher on the PAM-13®, suggesting a willingness to take an active role in their health. This suggests that participants may be likely to make lifestyle changes should they be diagnosed with FH. PAM-13® was used as a surrogate marker for participant adherence to potential necessary lifestyle changes. While the PAM-13® has been validated in many populations, this tool does not address specific questions related to the management of FH such as diet, exercise, and cholesterol-lowering medications.

This pilot project possessed several strengths and limitations. First, the location of the screening allowed rapid recruitment of nearly 1000 participants. The self-selecting nature of the recruitment strategy at the Minnesota State Fair may have

attracted a biased sample such as individuals who were more motivated to be healthy, had a previous history of high cholesterol and/or family history, and were interested in genetic research. It is possible that the nature of our sample led to a group of individuals who were more likely to want to participate in cascade screening and had fewer barriers to communication. A systematic review of Lynch syndrome studies undergoing cascade screening found that demographic factors such as age (<50 years), female sex, parenthood, level of education, employment, participation in medical studies, and family history of the condition were positively associated with uptake of genetic testing (Sharaf et al. 2013). Despite efforts to recruit a diverse population, the study sample was somewhat homogeneous which limited our ability to generalize findings and compare categories of opinions. Additionally, data on the number of participants who declined or did not meet eligibility criteria was not able to be collected due to recruitment methodology. Several state fairgoers stated they got annual cholesterol screens. For this reason, our sample may be healthier than the overall population.

Second, the FH screening assessments combined self-reported family history information and non-fasting cholesterol levels to identify potential cases. A clinical exam, fasting cholesterol screen, and follow-up genetic testing would be optimal but were not practical given this screening approach. The ability of participants to accurately recall family history may limit the accuracy of the data. Studies comparing self-reported family history of heart disease and actual disease has shown acceptable sensitivities (>80%) and specificities (>90%) for the first degree relatives (Hunt et al. 1986; Bensen et al. 1999). Confirmation by medical records would be optimal but not practical. Participants were asked ages of a family member with tendon xanthoma, arcus cornealis, and other heart-related issues. In some cases, ages were not known or not reported. It is possible that cases were missed due to lack of detailed ages which are necessary to classify participants as definite, probable, or possible FH according to specified criteria.

Third, assessing the barriers to cascade screening was open ended in nature to elicit a variety of potential barriers. A combination of both open- and close-ended questions with potential barriers listed would likely have been more informative and could have possibly led to a higher number of individuals leaving the question blank.

This pilot study has shown that the essential components are present for a FH genetic screening program to be successful in the state. In the future, larger studies may be completed to further elucidate the possibility of public health screening program for FH in MN. We argue that further research is needed to expand this study from the conceptual to an actual screening program to assess factors such as instant FH assessments and counseling, uptake of genetic testing, communication of genetic information and cascade testing, as well as

cost-effectiveness. Ultimately, an effective screening program will address the underdiagnoses and health burden of FH in the US.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The study was approved by the University of Minnesota Institutional Review Board.

Informed consent Informed consent was obtained from all individual participants included in the study.

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