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Addressing the Underdiagnosis of Familial Hypercholesterolemia: A Mixed Methods Study Exploring the Knowledge and Practice Behaviors of Cardiology Healthcare Providers

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ADDRESSING THE UNDERDIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLEMIA: A MIXED METHODS STUDY EXPLORING THE KNOWLEDGE AND PRACTICE BEHAVIORS OF CARDIOLOGY HEALTHCARE PROVIDERS

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ABSTRACT

Background. Familial Hypercholesterolemia (FH) is a common genetic disorder that is vastly underdiagnosed and undertreated. FH causes lifelong elevated low-density lipoprotein cholesterol, resulting in an increased risk for coronary heart disease, myocardial infarctions, and sudden cardiac death. Cardiology healthcare providers (CHCPs) are in an ideal position to not only screen cardiology patients for FH but also to diagnose and manage FH patients.

Objectives. Describe the practice behaviors of CHCPs in the screening, diagnosis, and management of FH, as well as gain a deeper understanding of the perspectives of CHCPs regarding FH screening and diagnostic interventions that can be implemented in cardiology clinical practice.

Methods. An explanatory mixed methods design included a quantitative survey and qualitative interviews. An adaptation of an existing FH knowledge tool guided survey development. The results of the quantitative survey, along with the Knowledge to Action framework and Theory of Planned Behavior, guided the development of the semi-structured interview protocol. Convenience and snowball sampling recruited physicians, physician assistants, and nurses in multiple subdivisions within the Division of Cardiology at Columbia University Irving Medical Center (CUIMC). Descriptive statistical analysis was performed on survey data. Qualitative interviews were conducted with survey respondents who volunteered to participate. Interviews were audio recorded, transcribed, and analyzed thematically. A descriptive review of the educational materials offered by the Division of Cardiology to CHCPs from 2018-2022 was conducted to identify the specific FH knowledge domains presented.

Results. Seventy (70) completed surveys were analyzed (30.2% response rate) for total knowledge scores (out of 19) and knowledge domain scores by professional degree/license,

subdivision, years in clinical practice at CUIMC, and years in clinical practice. CHCPs with MDs ($\bar{x}$ = 12.5), at CUIMC for 6-10 years ($\bar{x}$ = 11.7), in clinical practice for 1-5 years ($\bar{x}$ = 11.4), and within the subdivision of Inpatient Services ($\bar{x}$ = 15.5) had the highest average total knowledge scores. CHCPs with a professional degree or license of RN ($\bar{x}$ = 7.5), at CUIMC for less than 1 year ($\bar{x}$ = 9.4), in clinical practice for 6-10 years ($\bar{x}$ = 9.8), and within the subdivision of Cath Lab ($\bar{x}$ = 8.7) had the lowest average knowledge scores. Additionally, MDs scored highest across the knowledge domains of description, prognosis, prevalence, diagnostic criteria, and management, while NPs scored highest in the knowledge domain of inheritance. RNs scored lowest across the knowledge domains of description, prognosis, inheritance, diagnostic criteria, and management. PAs scored lowest with regard to prevalence of FH.

Twenty interviews were completed, and four overarching themes related to the practice behaviors of CHCPs in the screening, diagnosis, or management of FH in cardiology clinical practice were identified, including the variability in FH care; issues related to addressing FH at institutional, practice setting and individual levels; the importance of identifying FH early; and potential intervention approaches to overcome barriers to screening, diagnosing, and managing FH patients in cardiology practice. CHCPs with a professional degree of MD or with experiential knowledge of FH were the only CHCPs to describe the care of FH patients beyond the point of screening. A review of the educational materials offered by the Division of Cardiology to CHCPs from 2018-2022 revealed that only MDs, specifically fellows, were provided four lectures over the course of 4 years pertaining to FH.

Conclusions. CHCPs across all professional degrees/licenses expressed limited knowledge of FH, which served as an individual-level barrier to screening, diagnosing, and managing patients with FH. Providers with didactic or experiential FH knowledge had positive

control beliefs and higher levels of perceived behavioral control, leading them to provide FH care beyond the point of screening, such as making referrals, diagnosing, or managing FH patients.

Future FH targeted interventions in cardiology clinical practice should aim to increase didactic FH-content knowledge, improve experiential FH knowledge as well as incorporate institutional, local, and national FH resources. A proposed intervention map and implementation plan called ID-FH (Identify & Diagnose-FH), which includes the development, dissemination, implementation, and evaluation of a CUIMC-specific FH clinical practice guideline describes ways to overcome individual, practice setting, and institutional barriers to addressing FH across the Division of Cardiology at CUIMC. Improving CHCPs' ability to screen, diagnose, and manage FH patients is vital to reducing FH-related morbidity and mortality, as well as improving immediate and long-term FH health outcomes.

Keywords: Familial Hypercholesterolemia, knowledge, practice behaviors, cardiology, Theory of Planned Behavior, Knowledge to Action

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CHAPTER 1: INTRODUCTION

Overview

Familial Hypercholesterolemia (FH) is a genetic disorder that causes lifelong elevated low-density lipoprotein cholesterol (LDL-C) (Elis et al., 2011; Hendricks-Sturrup et al., 2020; Hopkins et al., 2011; Marks et al., 2003; Martinsen et al., 2019; Sturm et al., 2018). This chronic hypercholesterolemia causes individuals with FH to have an increased risk for coronary heart disease, myocardial infarctions, and sudden cardiac death (Hopkins et al., 2011; Svendsen et al., 2021). Early onset treatment and management of FH has been shown to reduce the rates of adverse cardiovascular events to that of the general population (Elis et al., 2011; Marks et al., 2003; Repas & Tanner, 2014). Thus, it is essential to initiate early intervention to reduce acute and chronic complications associated with FH.

While FH is common within the general population with a prevalence of 1 in 200 to 1 in 250, it is a vastly underdiagnosed and undertreated condition (Benito-Vicente et al., 2018; deGoma et al., 2016; Hasnie et al., 2018; Hendricks-Sturrup et al., 2020; Leren et al., 2008; Nordestgaard et al., 2013; Repas & Tanner, 2014; Zimmerman et al., 2019). Barriers to diagnosis include limited provider knowledge of FH, lack of consensus among diagnostic criteria, underutilization of genetic testing and time constraints in clinical encounters (deGoma et al., 2016; Foody, 2014; Hasnie et al., 2018; Hendricks-Sturrup et al., 2019; Pang et al., 2020; Sturm et al., 2018; Zimmerman et al., 2019).

Given the concurrence of underdiagnosis and adverse cardiovascular outcomes associated with FH, cardiology healthcare providers (CHCPs) in the United States are in an ideal position to not only screen cardiology patients for FH, but also to diagnose and manage FH patients (Foody, 2014). While the prevalence of FH within the general population is estimated at 1 in 250,

research has shown the pooled prevalence among those with atherosclerotic cardiovascular disease (ASCVD) to be 18 times higher than the general population with a prevalence of 1 in 17 (Hu et al., 2020).

Even though multiple diagnostic criteria exist for FH, and an institutional electronic health record system is in place, the Division of Cardiology at Columbia University Irving Medical Center (CUIMC) does not have a systematic way to screen, diagnose, or manage patients with FH. Developing a systematic way to screen and identify FH patients can assist CHCPs in diagnosing and managing FH and can contribute to early intervention strategies that can mitigate FH-associated adverse health outcomes.

This mixed methods research study aimed to understand current knowledge and practice behaviors among CHCPs in the screening, diagnosis, and management of FH. This study was the first comprehensive mixed methods study to explore the knowledge and practice behaviors in addressing FH, as well as potential interventions towards the systematic screening of hypercholesterolemia and diagnosis of FH cases, among CHCPs within a cardiology clinical practice. Ultimately knowledge gained from this study can inform the implementation of interventions in cardiology practice to assist with systematic screening, diagnosis, and management of FH patients.

Statement of the Problem

Literature addressing the gaps in care for patients with FH has focused heavily on primary care, universal screening, and cascade screening approaches, and lacks the perspective of CHCPs specifically (Bouhairie & Goldberg, 2015; Hopkins et al., 2011; Leren et al., 2008; Marks et al., 2000; Silva et al., 2021). No evidence-based research has been conducted exclusively within a cardiology clinical practice to explore the knowledge and practice behaviors

of CHCPs with regards to FH, as well as their perspectives on FH screening and diagnostic interventions that can be implemented in clinical care. Lack of routine FH screening can contribute to FH underdiagnosis, delayed management, and increased adverse health outcomes for patients with FH. Given the concurrence of underdiagnosis and adverse cardiovascular outcomes associated with FH, CHCPs are well positioned to screen, diagnose, and manage the clinical care of FH patients. Research has demonstrated that the prevalence of FH among those with ASCVD presenting to cardiology practice to be 18 times higher than the general population with a prevalence of 1 in 17 (Hu et al., 2020). There is a lack of understanding of current practices and potential barriers that must be addressed in order to influence practice behaviors and develop strategies to systematically identify patients with FH.

Translational Nature of the Study

The Biomedical Research Translation Continuum provides a linear conceptualization of the translational research process with four distinct phases (Drolet & Lorenzi, 2011). T1 research includes activities from basic science to humans; T2 research includes activities from human application to clinical treatment; T3 research includes activities from proven clinical treatment to clinical practice; and T4 research includes activities from clinical practice to public health impact (Drolet & Lorenzi, 2011). Translational research is a process that requires multiple steps, a variety of stakeholders, and bidirectionality between phases (Austin, 2018; Westfall et al., 2007). On the translational spectrum, this research study fell within the third translational chasm as it related to the implementation and adoption of current practice guidelines into practice (Drolet & Lorenzi, 2011). This study aimed to understand the current knowledge and practice behaviors of CHCPs in the screening, diagnosis, and management of FH, as well as understand the barriers, facilitators and needed resources of these processes to facilitate the implementation and adoption

of clinical practice guidelines. Knowledge gained from this research will aid in the development of effective practice through an intervention, program, policy, or technology that can be implemented in T3 research.

Purpose Statement and Research Questions

The purpose of this study was to describe the practice behaviors of CHCPs in the screening, diagnosis, and management of FH, as well as gain a deeper understanding of the perspectives of CHCPs regarding FH screening and identification interventions that can be implemented in cardiology clinical practice. The specific aims and accompanying research questions were:

Aim 1. Identify the current level of knowledge among CHCPs in the screening, diagnosis, and management of FH. RQ1: What is the level of knowledge among CHCPs in the screening, diagnosis, and management of FH?

Aim 2. Explore the factors that influence practice behaviors of CHCPs to screen, diagnose, and manage FH in cardiology clinical practice. RQ2: How do CHCPs describe their experiences screening, diagnosing, and managing FH in cardiology clinical practice? RQ2a: What role does provider knowledge, behavioral beliefs, normative beliefs, control beliefs, attitudes, subjective norm, perceived behavioral control and behavioral intentions play in CHCPs' screening, diagnosis, and management of FH in cardiology clinical practice? RQ2b: To what extent do these factors influence the CHCPs' perceived barriers, facilitators, and needed resources to screening, diagnosing, and managing patients with FH?

Aim 3. Use the quantitative results from the knowledge scores and themes generated from analysis of qualitative interviews to inform the development of future interventions that can be implemented in cardiology practice to assist with the systematic screening, diagnosis, and

management of FH patients. RQ3: How do the knowledge scores and CHCP interviews provide an understanding of the barriers, facilitators, and needed resources to screening, diagnosing, and managing patients with FH to inform future interventions to influence practice behaviors?

Statement of Potential Impact

The long-term goal of this research was to inform the development of tools to support CHCPs in delivering evidence-based patient-centered care for FH. The opportunity exists for CHCPs to systematically screen, diagnose and manage patients with FH to reduce the risk of long-term adverse health effects and poor health outcomes. By identifying the factors that influence the knowledge and practice behaviors of CHCPs, early intervention strategies can be employed to reduce morbidity and mortality associated with underdiagnosed and undertreated FH cases.

Conceptual Framework

This study was guided by constructs from two conceptual frameworks- the Knowledge to Action framework (KTA) and the Theory of Planned Behavior (TPB) (Ajzen, 1991; Graham et al., 2013). With an aim to better understand how the FH knowledge of CHCPs may influence the screening, diagnosis, and management of FH patients in a cardiology clinical setting, the steps within the action phase of the KTA were considered.

The first step within the action cycle identifies the knowledge to action gap, or the gap between the evidence and current practice (Graham et al., 2013). Data from the quantitative and qualitative phases aimed to elucidate gaps between evidence-based knowledge and current clinical practice. The second, third, and fourth steps of the action phase include adapting knowledge to the local context, assessing barriers and facilitators towards knowledge use, and tailoring interventions to relevant stakeholders and practice setting (Graham et al., 2013). In this

study, the qualitative phase gathered data to inform future approaches to improve FH knowledge and practice behaviors related to the screening, diagnosis, and management of patients with FH in cardiology clinical care. The outcome of this study included an intervention map and implementation plan to translate evidence-based knowledge of FH into cardiology clinical practice to improve the screening, diagnosis, and management of FH patients.

With a goal of exploring the practice behaviors of CHCPs, the TPB was used to better understand CHCPs' behaviors related to the screening, diagnosis, and management of FH patients. The TPB suggests that the motivational factors that influence behavior, known as behavioral intentions, are strong predictors of performing the behavior of interest (Ajzen, 1991; Bauer et al., 2015; Glanz et al., 2015; Graham et al., 2013; Grol, 2013; Nilsen, 2015). Behavioral intentions can be influenced by an individual's attitudes, subjective norm, and perceived behavioral control towards the specific behavior (Ajzen, 1991; Bauer et al., 2015; Glanz et al., 2015; Graham et al., 2013; Grol, 2013; Nilsen, 2015). Attitude refers to the "degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question" (Ajzen, 1991, p. 188). Subjective norm refers to "the perceived social pressure to perform or not to perform the behavior" (Ajzen, 1991, p. 188). Perceived behavioral control refers to "the perceived ease or difficulty of performing the behavior" (Ajzen, 1991, p. 183).

Additionally, the attitudes, subjective norm, and perceived behavioral control of CHCPs can be influenced by their behavioral beliefs, normative beliefs, and control beliefs (Ajzen, 1991; Bauer et al., 2015; Glanz et al., 2015; Graham et al., 2013; Grol, 2013; Nilsen, 2015). Behavioral beliefs "link the behavior to a certain outcome" (Ajzen, 1991, p. 191). Normative beliefs refer to "the likelihood that important referent individuals or groups approve or disapprove of performing a given behavior" (Ajzen, 1991, p. 195). Control beliefs "deal with the presence or absence of

requisite resources and opportunities" (Ajzen, 1991, p. 196). Behavioral, normative, and control beliefs can also be influenced by individual characteristics such as knowledge, age, and gender (Glanz et al., 2015; Graham et al., 2013). In this study, data regarding individual characteristics was gathered during the quantitative and qualitative phases. Additionally, the constructs of the TPB were explored during the semi-structured qualitative interviews within the second phase of this study.

Summary of Methodology

This study utilized an explanatory mixed methods design. During the quantitative arm, a survey (Appendix A) was distributed to CHCPs across the Division of Cardiology at CUIMC in Washington Heights, New York. Convenience sampling through CUIMC's Division of Cardiology email listserv was utilized to distribute the survey (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018). Results from the quantitative survey and the conceptual framework informed the final development of the interview protocol (Appendix B) used in the qualitative arm. Semi-structured interviews with individual CHCPs aimed to elucidate the factors that influence FH screening, diagnosis, and management at CUIMC. In addition to interview transcripts, other data sources included a document review of current protocols, training documents, and educational materials provided by the Division of Cardiology from 2018 to 2022. Quantitative survey data, qualitative interview data, and data from the document review were compared during the integrative phase of this study.

Limitations and Delimitations

Limitations

An important limitation of this research was that the findings from this case study design may not be generalizable to other clinical practice settings or among other populations. However,

the use of quantitative and qualitative data provided rich descriptions of cases and allow readers to determine if aspects of this research are transferable to other practice settings or patient populations. Another limitation was that this study did not explore, nor contributed to, the patient perspective about the experience of FH screening, diagnosis, and management processes.

Delimitations

With regards to delimitations, cases within this explanatory mixed methods research were bound by the setting of CUIMC and specialty, the Division of Cardiology. Data collection included multiple perspectives of CHCPs including training (MD, DO, PA, NP, LPN, RN) and subspeciality (i.e., electrophysiology, cardiovascular imaging, cardiac heart failure and transplant, adult congenital heart disease program). Data collection did not extend to the perspectives of administrative staff, clinical roles not involved in the delivery of FH care, and patients with FH.

Definition of Key Terms

Attitude: "the degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question" (Ajzen, 1991, p. 188).

Behavioral beliefs: "links the behavior to a certain outcome" (Ajzen, 1991, p. 191).

Behavioral intentions: "the motivational factors that influence a behavior; they are indications of how hard people are willing to try, of how much of an effort they are planning to exert, in order to perform the behavior" (Ajzen, 1991, p. 181).

Cascade screening: screening first- and second-degree relatives of patients diagnosed with FH (Bouhairie & Goldberg, 2015; Hopkins et al., 2011; Singh & Bittner, 2015).

Child-parent screening: The child serves as the initial point for screening and if the child is identified to have FH, the parent with FH may then be identified (Wald et al., 2016).

Control beliefs: “deal with the presence or absence of requisite resources and opportunities” (Ajzen, 1991, p. 196)

Familial Hypercholesterolemia (FH): Familial forms of hypercholesterolemia are a group of inherited conditions that result in elevated cholesterol levels (Elis et al., 2011; Hendricks-Sturrup et al., 2020; Hopkins et al., 2011; Marks et al., 2003; Martinsen et al., 2019; Sturm et al., 2018). For the purposes of this dissertation, FH will refer to the heterozygous form of FH.

Framework: “a structure, overview, outline, system or plan consisting of various descriptive categories, e.g., concepts, constructs or variables, and the relations between them that are presumed to account for a phenomenon. Frameworks do not provide explanations; they only describe empirical phenomena by fitting them into a set of categories” (Nilsen, 2015, p. 2).

Implementation science: “the scientific study of methods to promote the systematic uptake of research findings and other evidence based practices into routine practice to improve the quality and effectiveness of health services and care” (Nilsen, 2015, p. 2).

Normative beliefs: “the likelihood that important referent individuals or groups approve or disapprove of performing a given behavior” (Ajzen, 1991, p. 195)

Perceived behavioral control: “the perceived ease or difficulty of performing the behavior” (Ajzen, 1991, p. 183).

Subjective norm: “the perceived social pressure to perform or not to perform the behavior” (Ajzen, 1991, p. 188).

Universal Screening: evaluating family history of high cholesterol and/or premature CHD, as well as fasting lipid profile or non-fasting non-high-density lipoprotein cholesterol levels in all children and adults (Hopkins et al., 2011).

Summary

Chapter 1 provided an overview of an explanatory mixed methods case study exploring the knowledge and practice behaviors of CHCPs in the screening, diagnosis, and management of patients with FH. The chapter provided background information, explained the purpose of this study, identified the aims and research questions to be answered, described the approach that was used, and discussed the study's limitations. Chapter 2 will provide an overview of the current literature and will further describe the conceptual framework that guided this research. Chapter 3 will provide more details about the study design and methodology of this research. Chapter 4 will discuss the quantitative, qualitative, and mixed methods results of this explanatory sequential mixed methods research study. Chapter 5 will provide a discussion of the findings grounded by the study's conceptual frameworks, the KTA and TPB. Finally, study limitations, future directions for translational research, and conclusions will be discussed in Chapter 5.

CHAPTER 2: LITERATURE REVIEW

Introduction: Topic, Purpose, and Methods of Literature Review

The literature review is summarized in several sections. First a brief overview of Familial Hypercholesterolemia (FH), including clinical presentation, diagnostic criteria, treatment options and genetic background, are discussed. The second portion of the literature review examines previous literature focused on the reported barriers to diagnosing FH and interventions to improve FH identification. The final section provides an overview of the theoretical framework for this research study.

The Himmelfarb Library database, Google Scholar, and PubMed were utilized to gather articles for this literature review. Once preliminary relevant articles were identified, the reference lists of those articles were reviewed to obtain additional articles. Literature search terminology included *Familial Hypercholesterolemia (FH), FH diagnosis, FH prevalence, FH underdiagnosis, FH management, FH treatment, pathophysiology FH, barriers FH diagnosis, limitations FH diagnosis, facilitators FH diagnosis, genetic testing FH, genetics FH, FH detection, screen FH, cascade screening FH, FH cascade testing program, FH electronic alert, FH medical record, FH electronic health record, FH electronic tool, and FH precision medicine*. Abstracts were reviewed and articles that were most applicable to this research were selected. The articles selected for this literature review were published between 2000 and 2022 in English. Seminal works in the field prior to 2000 were also included in this literature review.

The literature search was expanded to SCOPUS with the same criteria applied. The majority of articles were found to be duplicates of the prior PubMed search, which indicated saturation in the literature search. Additionally, a search of clinical practice guidelines for lipid disorders from professional associations such as the American Heart Association (AHA),

American College of Cardiology (ACC) and National Lipid Association (NLA) were included in this literature review.

Description and Critique of the Scholarly Literature

Definition of Familial Hypercholesterolemia (FH)

Familial forms of hypercholesterolemia are a group of inherited conditions that result in elevated cholesterol levels. There are two inheritance forms of FH: heterozygous FH and homozygous FH (Bouhairie & Goldberg, 2015; Hopkins et al., 2011; Nordestgaard et al., 2013). Heterozygous FH occurs when an individual harbors one pathogenic mutation which causes disease onset; whereas homozygous FH occurs when an individual harbors two pathogenic mutations which results in the onset of disease (Bouhairie & Goldberg, 2015; Hopkins et al., 2011; Nordestgaard et al., 2013). While the prevalence of heterozygous FH is 1 in 200 to 1 in 250, the prevalence of homozygous FH is rarer at 1 in 500,000 (Benito-Vicente et al., 2018; Nordestgaard et al., 2013; Sturm et al., 2018). Though much less frequent, homozygous FH is a very severe form of the disease with elevated LDL-C levels from birth and CHD occurring in most affected individuals during childhood if untreated (Benito-Vicente et al., 2018; Nordestgaard et al., 2013; Sturm et al., 2018). For the purposes of this study, FH referred to the heterozygous form of FH unless otherwise specified.

Background of FH

Familial Hypercholesterolemia (FH) is a common genetic disorder with an estimated prevalence of 1 in 200 to 1 in 250 (Benito-Vicente et al., 2018; deGoma et al., 2016; Nordestgaard et al., 2013; Sturm et al., 2018). FH is characterized by lifelong elevated plasma levels of low-density lipoprotein cholesterol, or LDL-C (Elis et al., 2011; Hopkins et al., 2011; Marks et al., 2003; Martinsen et al., 2019; Sturm et al., 2018). Optimal levels of LDL-C for

adults are less than 100 mg/dL, and high levels of LDL-C in which FH should be suspected in adults are 190 mg/dL and above (Brett et al., 2018; deGoma et al., 2016; Hopkins et al., 2011; Nordestgaard et al., 2013; Wierzbicki et al., 2008).

This lifelong elevation of LDL-C levels causes affected individuals to be at an increased risk of premature coronary heart disease (CHD) (Hopkins et al., 2011; Svendsen et al., 2021). As compared to the general population, untreated patients with FH have a 20-fold increase in risk of premature CHD and a 13-fold increase in CHD mortality (Hopkins et al., 2011; Silva et al., 2021). The risk for premature CHD for untreated heterozygous FH patients is greater than 50% for men by age 50 and greater than 30% for women by age 60, with symptoms manifesting in the 40s for men and 10-15 years later for women (Ito et al., 2011; Leren et al., 2008; Martinsen et al., 2019; Nordestgaard et al., 2013). Premature CHD can manifest as myocardial infarctions and sudden cardiac death. It is estimated that 5% of myocardial infarctions in patients under 60 years old and 20% of myocardial infarctions under 45 years old are due to FH (Bouhairie & Goldberg, 2015; Hopkins et al., 2011). Patients with untreated heterozygous FH experience their first coronary event 20 or more years earlier than the general population (mean age of 42 years compared to 64 years) and are at a 2.5-fold increased risk for a recurrent myocardial infarction (Svendsen et al., 2021; Turgeon et al., 2016). It is estimated that 30% of FH patients do not survive their first myocardial infarction (Yuan et al., 2006).

Given the serious adverse health outcomes associated with FH, it is essential that treatment initiation occurs early in order to prevent associated morbidity and mortality. The ACC and AHA recommend that first line therapy includes high intensity statins for individuals with severe primary hypercholesterolemia (LDL-C $\geq$ 190 mg/dL) to reduce LDL-C levels by 50% (Grundy et al., 2019; McGowan et al., 2019). Statin use for FH patients without CHD resulted in

a 48% reduction in CHD mortality and a 25% reduction in CHD mortality for FH patients with CHD (Martinsen et al., 2019; Neil et al., 2008; Repas & Tanner, 2014). If LDL-C values remain greater than 100 mg/dL after initiation of high-intensity statins, then the cholesterol absorption inhibitor, ezetimibe, can be added to statin therapy (Benito-Vicente et al., 2018; Grundy et al., 2019; Nordestgaard et al., 2013; Turgeon et al., 2016). If this combination therapy is unsuccessful in lowering LDL-C levels below 100 mg/dL, the AHA and ACC recommend including a PCSK9 inhibitor (Grundy et al., 2019; Turgeon et al., 2016).

Elis, Zhou, and Stein (2011) examined the effectiveness of long-term intensive lipid-lowering therapy on FH in which 24% of all subjects were treated with statin monotherapy, 55% with a statin and one other agent, and 21% with a statin and two other agents. LDL-C levels were reduced by 55% to 116 mg/dL, with 30% of participants reaching an LDL-C less than 100 mg/dL, and 10% achieving an LDL-C less than 70 mg/dL (Elis et al., 2011). The introduction of PCSK9 inhibitors transformed clinical practice by providing therapies that can effectively achieve very low LDL-C levels in almost all heterozygous FH patients (Marbach et al., 2014). Patients who lack functional LDL receptors will not respond to LDL receptor therapies and require alternative approaches such as LDL apheresis, microsomal triglyceride transfer protein inhibitors, and apolipoprotein B antisense inhibitors (Marbach et al., 2014). Early onset treatment and management of FH has been shown to reduce the rates of adverse cardiovascular events to that of the general population (Elis et al., 2011; Marks et al., 2003; Repas & Tanner, 2014).

Genetics of FH

FH is associated with mutations in four genes: low-density lipoprotein receptor (LDLR), low-density lipoprotein receptor adaptor protein (LDLRAP1), apolipoprotein B (APOB), and proprotein convertase subtilin/kexin 9 (PCSK9) as can be seen in Table 2 (Martinsen et al., 2019;

Nordestgaard et al., 2013; Reeskamp et al., 2021; Sarraju & Knowles, 2019; Silva et al., 2021; Turgeon et al., 2016). Mutations in the LDLR, APOB and PCSK9 genes follow an autosomal dominant inheritance pattern, while mutations in the LDLRAP1 gene follow an autosomal recessive pattern of inheritance (Bouhairie & Goldberg, 2015; Martinsen et al., 2019; Nordestgaard et al., 2013; Sarraju & Knowles, 2019; Silva et al., 2021; Turgeon et al., 2016). More than 80% of FH cases are caused by mutations in the LDLR gene (Sarraju & Knowles, 2019). FH demonstrates approximately 90% penetrance, meaning that 90% of individuals with an FH mutation will exhibit phenotypic characteristics of the disorder (Hopkins et al., 2011; Singh & Bittner, 2015).

Table 1

Genes Associated with Autosomal Dominant FH

Gene	Protein	Type of FH Mutation
LDLR	Low-density lipoprotein receptor	Loss-of-function
APOB	Apolipoprotein B-100	Loss-of-function
PCSK9	Proprotein convertase subtilisin/kexin 9	Gain-of-function

Table adapted from Sarraju, A and Knowles, W. (2019). Table 2: Overview of common monogenic FH mutations.

The presence of a pathogenic FH mutation plays an integral role in FH's risk stratification, management, diagnosis, and cascade screening. The diagnosis of FH and details of cascade screening will be discussed later in this literature review. The ability to identify a pathogenic FH mutation is variable and dependent on a variety of factors such as LDL-C level, physical symptoms, family history, and whether a clinic- or population-based approach is used. In a population-based study conducted by Khera et al. (2016), only 2% of individuals with an LDL-C > 190 mg/dL were found to have an identifiable disease-causing FH mutation. In

contrast, another research study identified a pathogenic FH mutation in 60% of patients with severe hypercholesterolemia, LDL-C > 300 mg/dL (Khera & Hegele, 2020; Wang et al., 2016). In this context, clinical guidelines strongly recommend utilizing FH diagnostic criteria to screen for FH in clinical practice when LDL-C>190 mg/dL. Thus, it is largely due to diagnosing FH cases and initiating early treatment that there is such a marked effect on reducing poor health outcomes. As noted, identification of an FH pathogenic mutation is associated with an increased risk for atherosclerotic cardiovascular disease, and individuals with an LDL-C > 190 mg/dL with an identified FH mutation have a 22-fold increased risk for atherosclerotic cardiovascular disease as compared to those with an LDL-C < 130 mg/dL and no mutation (Khera et al., 2016; Sarraju & Knowles, 2019). This increased risk for cardiovascular disease caused by a documented FH mutation can be attributed to the lifelong exposure of elevated LDL-C levels, thus necessitating aggressive early onset treatment to reduce morbidity and mortality associated with FH (Elis et al., 2011; Khera et al., 2016; Repas & Tanner, 2014; Sarraju & Knowles, 2019).

While genetic testing can offer an avenue to clinically diagnose an individual with FH, it can also be used to stratify risk for patients with a diagnosis of FH based solely on clinical findings. The risk of atherosclerotic cardiovascular disease (ASCVD) for individuals with a pathogenic FH mutation is greater than the ASCVD risk for individuals who do not harbor a pathogenic FH mutation (Khera et al., 2016). In a study by Khera et al. (2016) participants with an LDL-C greater than 190 mg/dL and a pathogenic FH mutation had a 22-times higher risk for ASCVD as compared to a 6-fold increased risk for ASCVD among participants with an LDL-C greater than 190 mg/dL and no pathogenic FH mutation (Khera et al., 2016; Sarraju & Knowles, 2019). Thus, the initiation of early treatment to lower LDL-C levels and prevent ASCVD for patients with FH is critical.

Genetic testing can also be utilized in the treatment and management strategies for patients with FH. Several new pharmacologic therapies have been developed for FH patients with novel mechanisms of action that account for the type and number of pathogenic mutations. Mipomersen has been shown to reduce LDL-C and total cholesterol levels in patients with heterozygous FH (Marbach et al., 2014). In heterozygous FH patients with CHD, LDL-C levels were reduced by 28% when treated with mipomersen (Marbach et al., 2014). PCSK9 is an enzyme that marks LDL receptors for degradation, prevents LDL-C from being broken down intracellularly, and results in elevated levels of circulating LDL-C (Benito-Vicente et al., 2018; Marbach et al., 2014; Nordestgaard et al., 2013). Gain of function mutations in the PCSK9 gene increase the activity of the PCSK9 enzyme; thus, treatment in the form of PCSK9 inhibitors such as monoclonal antibodies, have been indicated in patients with heterozygous FH in which a pathogenic mutation in the PCSK9 gene has been identified, and also other genetic forms of FH where expression of some functional LDL receptors can be unregulated (Marbach et al., 2014).

Abul-Husn et al. (2016) used electronic health data in conjunction with genomic sequence data to better understand the prevalence and clinical impact of FH pathogenic variants in a cohort of 50,726 individuals in an integrated healthcare system. Within the cohort of participants, 84.2% had LDL-C values available within the electronic health record system and 10.4% were noted to have severe hypercholesterolemia (LDL-C>190mg/dL)(Abul-Husn et al., 2016). A total of 229 individuals were identified to have a pathogenic mutation in LDLR (42.8%), APOB (44.5%), and PCSK9 (12.7%) genes, equivalent to a carrier frequency of 1 in 222 participants (Abul-Husn et al., 2016). Of these 229 participants, only 24% would have met clinical diagnostic criteria for FH (Abul-Husn et al., 2016). This highlights the need to integrate genetic testing into routine clinical screening practices for FH patients.

Diagnostic Criteria

Currently, there are three primary resources to assist in the clinical diagnosis of FH including the Dutch Lipid Clinic Network (DLCN) criteria, Simon Broome Register criteria, and Make Early Diagnosis to Prevent Early Death (MEDPED) criteria (Birnbaum et al., 2021; Hendricks-Sturrup et al., 2020; McGowan et al., 2019; Moldovan et al., 2020; Paquette et al., 2017; Yuan et al., 2006). Each of these diagnostic criteria utilizes different factors or combination of factors (i.e., LDL-C levels, family history, genetic testing results, physical signs such as tendon xanthomas or corneal arcus) in establishing a clinical diagnosis of FH (Table 1).

Table 2

FH Diagnostic Criteria Comparison

Criteria	**MEDPED**	**Simon Broom**	**DLCN**
Personal History			
Elevated LDL-C	+	+	+
Corneal Arcus			+
Tendon Xanthoma		+	+
Genetic Mutation		+	+
Premature PVD			+
Premature CAD			+
Family History			
Elevated LDL-C	+	+	+
Corneal Arcus			+
Tendon Xanthoma		+	+
Premature PVD		+	+

Premature CAD	+	+

DLCN= Dutch Lipid Criteria Network, MEDPED= Make Early Diagnosis to Prevent Early Death, LDL-C= low-density lipoprotein cholesterol, PVD= peripheral vascular disease, CAD= coronary artery disease
Table adapted from McGowan et al. (2019). Table 5: Comparison of diagnostic criteria for the diagnosis of FH.

MEDPED uses the least number of factors, including personal and family history of elevated LDL-C levels, to make a clinical diagnosis (Table 2). Mathematical models incorporating published cholesterol levels, degree of relatedness, and age for individuals in the United States and Japan were utilized to develop the MEDPED cholesterol level cutoff points (Bouhairie & Goldberg, 2015; Singh & Bittner, 2015; Williams et al., 1993). While this criterion does not account for clinical characteristics of FH such as tendon xanthomas, corneal arcus or coronary artery disease, it was found to have a specificity of 98% and sensitivity of 87% for first degree relatives with FH (Singh & Bittner, 2015; Williams et al., 1993).

The Simon Broome criteria was developed in the United Kingdom using data from FH patients in a research registry (Singh & Bittner, 2015). This criterion includes a combination of personal and family history characteristics, such as elevated LDL-C levels, tendon xanthomas, pathogenic mutation, as well as premature coronary artery disease or peripheral vascular disease (Table 2). Based on the presence or absence of specific factors, individuals can be diagnosed as definite FH or possible FH (Bouhairie & Goldberg, 2015; Martinsen et al., 2019; Singh & Bittner, 2015).

The final diagnostic criteria, known as the DLCN, is the most comprehensive of the three clinical diagnostic criteria for FH as it includes personal and family history of elevated LDL-C levels, tendon xanthomas, arcus cornealis, genetic mutation, and premature coronary artery disease or peripheral vascular disease (Table 2). The DLCN introduces a point system to categorize individuals as definite, probable, or possible FH (Bouhairie & Goldberg, 2015;

Martinsen et al., 2019; Singh & Bittner, 2015). While these and other criteria have been developed to aid in FH diagnosis, a number of barriers remain (i.e., limited provider knowledge, time in clinical encounters, lipid specialization) as described later, that prevent a timely diagnosis and initiation of appropriate treatment for patients with FH (Birnbaum et al., 2021; Hendricks-Sturrup et al., 2020; McGowan et al., 2019; Moldovan et al., 2020; Paquette et al., 2017; Yuan et al., 2006).

Improving the Diagnosis of FH

A variety of strategies have been employed in clinical practice to address the underdiagnosis of FH including universal screening, cascade screening, use of electronic health records, and implementation of clinical decision support tools.

Universal and Cascade Screening

One population-based strategy to identify individuals with FH, known as universal screening, is to perform FH screening on all individuals at a given timepoint (Bouhairie & Goldberg, 2015; Brett et al., 2018; Wald et al., 2016). Wald et al. (2016) conducted FH screening on children 1 to 2 years old during immunization appointments at general medical practices in the United Kingdom. FH screening for this study included total cholesterol and high-density lipoprotein cholesterol levels, as well as mutation analysis of 48 FH mutations (Wald et al., 2016). Of 10,095 children screened, 92 children had elevated cholesterol levels and 37 of which had an FH mutation (Wald et al., 2016).

Once a pathogenic mutation is identified within a family, then other at-risk family members can be screened for the familial mutation. This process, known as cascade screening, allows for the diagnosis of FH patients prior to the onset of symptoms (Knowles et al., 2017; Lee et al., 2019). Wald et al. (2016) invited the parents of the 37 children with a documented FH

mutation for cholesterol and genetic analysis. Thirty-two of the parents agreed and 27 of which (84.4%) were identified to harbor the same FH mutation as their child (Wald et al., 2016). This form of FH cascade screening, called child-parent screening, offers an opportunity to screen two generations at once for FH and identify FH cases at an earlier age prior to the onset of adverse FH sequelae (Alonso et al., 2020; Brett et al., 2018; Wald et al., 2016). Several limitations of cascade screening include difficulty identifying the index FH case (proband) within a family, barriers related to family communication, and geographic barriers to receiving genetic services (Hopkins et al., 2011; Nordestgaard et al., 2013; Singh & Bittner, 2015).

Researchers at the Mayo Clinic designed and evaluated a web-based tool (FH Family Share) to facilitate familial communication in order to promote cascade screening for FH (Bangash et al., 2022). The interactive website allowed genetic counselors and patients to create and distribute a genetic testing results letter to family members, build a pedigree, and learn more about FH through educational modules (Bangash et al., 2022). Researchers conducted usability testing of FH Family Share with genetic counselors and patients and found that 67% of genetic counselors were able to easily navigate the web-based tool to find information and 56% found information easy to understand (Bangash et al., 2022). With regards to patient feedback, 56% were able to find information easily on the website and 78% found information very easy to understand (Bangash et al., 2022). Additionally, all genetic counselors and patients within this study indicated that FH Family Share was worth returning to (Bangash et al., 2022). The ability for a patient with FH to easily communicate and share their genetic testing results with at-risk family members has the potential to diagnose other FH cases within a family, to initiate treatment earlier, and to prevent FH-related morbidity and mortality.

Electronic Health Records (EHRs)

The advent of EHRs has provided a means to document, store, and exchange a patient's medical information electronically. With the ability to use one synchronized medical record system, the serious underdiagnosis of FH can be addressed through EHR-based approaches (Hasnie et al., 2018; Hendricks-Sturrup et al., 2019; Lan et al., 2019; Troeung et al., 2016; Vickery et al., 2017). One strategy to detect FH cases is to utilize the measures found in diagnostic criteria such as MEDPED, DLCN or Simon Broome.

Birnbaum et al. (2021) utilized MEDPED diagnostic age-based LDL-C values within the EHR to identify FH cases within an integrated healthcare system in Northern California. Individuals identified through MEDPED underwent manual chart review to exclude secondary causes of hypercholesterolemia such as hypothyroidism or hypertriglyceridemia (Birnbaum et al., 2021). Of 1,831,658 individuals with at least one LDL-C value in the EHR, 7,468 individuals had an LDL-C value exceeding the MEDPED cut point, with a probable-FH diagnosis (Birnbaum et al., 2021). Of the 7,468 individuals with an LDL-C value exceeding the MEDPED cut point, 92.6% of individuals received care at an outside center and were not eligible for inclusion in the study, and 4.94% of individuals were excluded due to secondary causes of hypercholesterolemia. The remaining 182 patients were invited for an evaluation at the lipid clinic, 82 of whom declined (Birnbaum et al., 2021). Of the 100 individuals who received a lipid specialist evaluation, 93% were clinically diagnosed with FH, only 5% of which were previously diagnosed with FH and 45% of which were not on any lipid lowering therapy (Birnbaum et al., 2021).

Another strategy to identify FH cases within the EHR is to include additional EHR data measures, such as billing and diagnostic codes, in conjunction with clinical diagnostic criteria. Safarova, Liu and Kullo (2016) screened 131,000 individuals between 1993 and 2014 in primary

care practice using an EHR algorithm that included DLCN criteria, as well as structured and unstructured data (2016). Structured data included laboratory, medication, and administrative data. Unstructured data included clinical notes that noted presence of xanthomata and corneal arcus. Of 131,000 individuals, 5,992 patients had an LDL>190 mg/dL and no secondary causes of hypercholesterolemia (Safarova et al., 2016). Using an EHR-based algorithm, 32 definite and 391 probable FH cases were identified, only 55% of which had an existing diagnosis code consistent with FH (Safarova et al., 2016).

The FH Foundation developed a machine learning algorithm called FIND FH (flag, identify, network, deliver FH) which utilizes 75 factors such as prescriptions, laboratory data, and patient demographics to identify FH cases within the EHR (Myers et al., 2019; Sheth et al., 2021). Sheth et al. (2021) implemented FIND FH within the University of Pennsylvania Healthcare System to first, identify patients with an increased risk for FH (FIND FH score > 0.2) and second, to encourage those patients' primary care providers to make a referral to the Center for Preventive Cardiology. Of 1,607,606 eligible patients within the EHR, 8,614 were identified to have a FIND FH score > 0.2, 442 primary care providers were contacted (3,614 patients were withheld for the second phase of this study), and 153 patients had consults with the Center for Preventive Cardiology (Sheth et al., 2021). Of the 153 high risk FH patients seen in Preventive Cardiology, 46 (30.1%) were diagnosed with FH using DLCN or MEDPED criteria (Sheth et al., 2021).

Clinical Decision Support (CDS) Tools

Not only can the EHR be used to identify individuals who fulfill FH diagnostic criteria, but it can also provide evidence-based tools to assist providers in making clinical decisions to

improve patient care. Previous research has shown that clinicians are favorable to FH CDS tools (Hasnie et al., 2018; Zimmerman et al., 2019).

Bangash et al. (2020) conducted a concurrent mixed methods study in which semi-structured interviews and an implementation survey were conducted to obtain physician perspectives on two types of EHR-based CDS tools (i.e., in-basket message and best practice alert). Initially, 13 qualitative interviews were performed with physicians in community internal medicine (n=3), family medicine (n=3), obstetrics (n=1), cardiology (n=5), and vascular medicine (n=1) (Bangash et al., 2020). Following each interview, physicians were provided an implementation survey to assess the contextual barriers and facilitators that would impact CDS tool implementation (Bangash et al., 2020). A total of 13 surveys were completed, corresponding to the 13 physicians who participated in the qualitative interviews. The survey revealed that 11 physicians agreed that a CDS tool would improve early diagnosis of FH, and 12 physicians agreed that it would help healthcare providers identify and manage individuals with FH (Bangash et al., 2020).

While Bangash et al. (2020) gathered multiple forms of data, the authors recognize that a significant limitation of their research was that participants were limited to one provider type - physicians. By only incorporating the physician perspective, it is not well understood how a provider's training may impact their recommendations for an intervention aimed at addressing FH, which the proposed study addressed.

To improve the uptake and utilization of a CDS tool, it is important to also consider the content, timing, frequency, and format of the tool itself. With regards to content, research has provided recommendations for CDS tools that offer concise and straightforward information, which also incorporate evidence-based guidelines (Bangash et al., 2020; Hasnie et al., 2018). To

reduce clinician burden, the frequency of alert firing should only occur one time per provider and should not necessitate input of clinical laboratory values manually (Bangash et al., 2020; Hasnie et al., 2018). Finally, the CDS tool should allow healthcare providers to detail their decision to not act when encountering the CDS tool in an open field at the end of the tool (Bangash et al., 2020; Hasnie et al., 2018).

Barriers to FH Diagnosis

Hendricks-Sturrup et al. (2019) conducted a literature review to better understand the barriers and facilitators towards integrating FH genetic testing in the US. The authors examined 2,340 articles in PubMed/MEDLINE databases as well as eight peer-reviewed journals (Hendricks-Sturrup et al., 2019). The authors utilized the Consolidated Framework for Implementation Research (CFIR) to categorize relevant barriers and facilitators according to the five domains of CFIR including characteristics of an intervention, inner setting, outer setting, characteristics of individuals, and process (Hendricks-Sturrup et al., 2019).

A total of 26 barriers were identified across all CFIR domains (Hendricks-Sturrup et al., 2019). Barriers related to genetic testing as an intervention included the cost of testing, insurance coverage, access to testing services, privacy, and identifying family members for cascade screening (Hendricks-Sturrup et al., 2019). Limited time during clinical encounters for family history assessment, low accuracy of family history disclosure, and lack of improved diagnostic criteria utilized in the electronic health record system were identified as inner setting barriers (Hendricks-Sturrup et al., 2019). Outer setting barriers included similar findings as barriers to genetic testing itself including privacy, access to services and cost of testing (Hendricks-Sturrup et al., 2019). When considering characteristics of individuals, barriers included patient knowledge of FH, patient readiness and providers perceiving FH out of their scope of practice

(Hendricks-Sturrup et al., 2019). Finally, process barriers included FH risk stratification being based on phenotype versus genotype diagnosis (Hendricks-Sturrup et al., 2019).

While Hendricks-Sturrup et al. (2019) identified a significant number of barriers recognized in other studies, this literature review had several limitations. First, using CFIR as a guiding framework for the implementation of genetic testing may be restrictive in that CFIR does not incorporate all aspects relevant to genomic medicine (Hendricks-Sturrup et al., 2019). Second, only examining one database and eight peer-reviewed journals may exclude other pertinent literature from different disciplines (Hendricks-Sturrup et al., 2019).

Lack of Consensus Among Diagnostic Criteria

Based on the prevalence of FH, it can be extrapolated that there are approximately 14 to 34 million people worldwide and 1.5 million people in the United States with FH (deGoma et al., 2016; Nordestgaard et al., 2013). Alarmingly, with such a high burden of disease, FH remains considerably underdiagnosed and undertreated (deGoma et al., 2016; Hasnie et al., 2018; Hendricks-Sturrup et al., 2019; Leren et al., 2008; Nordestgaard et al., 2013; Repas & Tanner, 2014; Zimmerman et al., 2019). As discussed previously, the use of MEDPED, Simon Broome and DLCN can assist healthcare providers in diagnosing FH. However, there are significant differences between these diagnostic criteria. For example, the identification of a pathogenic mutation is sufficient for a definite FH diagnosis according to Simon Broome. However, the DLCN criteria requires an additional measure (i.e., elevated LDL-C level, tendon xanthoma, premature peripheral vascular disease) with a positive genetic test for a definite FH diagnosis (McGowan et al., 2019; Singh & Bittner, 2015). This lack of uniformity and complexity between diagnostic criteria can serve as a significant barrier for healthcare providers to routinely screen and diagnose individuals with FH (Alonso et al., 2020; deGoma et al., 2016).

Underutilization of FH Genetic Testing

While a person can be diagnosed through physical features alone, such as xanthomas or elevated LDL-C measurements, another way to diagnose FH is through the use of genetic testing and the identification of a pathogenic mutation. Research has shown that among individuals with suspected FH, a pathogenic mutation can be identified in 60-80% of cases (Abul-Husn et al., 2016; Knowles et al., 2017). Bellows et al. (2022) applied a regression model and DLCN criteria to estimate the yield of FH cases when combining clinical criteria and genetic testing. This study identified 3.7 FH cases using only DLCN criteria, 3.8 FH cases using only genetic testing, and 6.6 FH cases using DLCN criteria and genetic testing (Bellows et al., 2022). This research showed that incorporating genetic testing with diagnostic criteria can improve the screening and diagnosis of FH patients (Bellows et al., 2022).

While genetic testing has provided another avenue for diagnosing individuals with FH, it remains underutilized (Bouhairie & Goldberg, 2015; deGoma et al., 2016; Pang et al., 2020; Sturm et al., 2018). The first challenge towards integrating FH genetic testing into clinical practice is proband identification or identifying the first affected individual within a family (Cirino et al., 2017; Hendricks-Sturrup et al., 2019; Nordestgaard et al., 2013). Due to the misalignment of MEDPED, Simon Broome and DLCN criteria, healthcare providers experience challenges in identifying a proband when clinical diagnostic criteria are not fulfilled or are conflicting in an index patient (Hendricks-Sturrup et al., 2019).

Another challenge when considering how to incorporate genetic testing into clinical practice centers around the cost associated with FH genetic testing, including the significant cost of testing, the limited availability of financial assistance programs to cover this cost, and the lack of commercial or governmental insurers to cover the cost of genetic testing, especially when

clinical diagnostic criteria are not met (deGoma et al., 2016; Hendricks-Sturrup et al., 2019; Pang et al., 2020). Finally, the lack of pre- and post-test genetic counseling services, coupled with healthcare providers' perceptions of genetics being beyond their scope of practice, prevents the uptake and utilization of FH genetic testing into routine clinical practice (Cirino et al., 2017; Hendricks-Sturrup et al., 2019; Sarraju & Knowles, 2019; Zimmerman et al., 2019).

Limited Provider Knowledge

Since FH primarily affects the cardiovascular system, cardiologists are in an ideal position to not only screen cardiology patients for FH but also to make a clinical diagnosis (Foody, 2014). Cardiologists require the knowledge, clinical guidance, and time to facilitate the FH diagnostic process. Research has shown that healthcare providers from an array of disciplines (i.e., primary care, family medicine, cardiology) have a limited knowledge of the diagnostic criteria, clinical features, associated risks, and inheritance of FH (Foody, 2014; Hasnie et al., 2018; Hendricks-Sturrup et al., 2019; Zimmerman et al., 2019).

In 2011, the American College of Cardiology (ACC) distributed a survey to their members to assess the awareness of FH among cardiologists. The ACC found that 80% of cardiologists did not know the prevalence of FH, 0% were aware that individuals with FH are about 20 times more likely to develop premature coronary heart disease, 60% had an incomplete understanding of the risks to first-degree family members, and less than 30% were able to recognize FH when provided a clinical case example (Foody, 2014). While this survey from the ACC highlights cardiologists' limited FH knowledge, there is a lack of evidence in the literature pointing to the cause of these gaps in knowledge, such as limitations in medical school education or clinical training experience.

The Mayo Clinic conducted an explanatory mixed methods study to assess the level of FH knowledge among providers, as well as obtain feedback about a potential FH clinical decision support tool (Hasnie et al., 2018). During the first phase of the study, a survey was distributed to 1,161 physicians, including cardiologists, endocrinologists, geneticists, family medicine physicians, pediatricians, and residents across the Mayo Clinic network in five states to assess for overall FH knowledge as well as collect feedback about FH CDS preferences (Hasnie et al., 2018). Of 210 survey responses, only 5.3% of clinicians were very familiar with FH and 48.5% of clinicians correctly identified the prevalence of FH (Hasnie et al., 2018).

The second phase of the Mayo study included four qualitative focus groups with a total of thirteen cardiologists and six primary care physicians (Hasnie et al., 2018). From the focus groups four major themes emerged. The first of which was the lack of knowledge of FH and incomplete understanding of its CHD risk as well as risk to family members (Hasnie et al., 2018). The second theme revolved around the facilitators towards implementing a clinical decision support tool, which included requiring minimal manual input from providers, informing patients of their FH risk prior to the encounter to reduce the burden of discussion on the provider and including clinical guidelines on the tool (Hasnie et al., 2018). The third theme that emerged were barriers towards implementation which included limited time during clinical encounters and alerts slowing down EHR usability (Hasnie et al., 2018). The final theme that was identified centered around recommendations for the tool itself such as providing clear and succinct information about the diagnosis of FH, as well as provide management recommendations (Hasnie et al., 2018).

Several limitations addressed by Hasnie et al. (2018) included the low survey response rate (18%) and the lack of diverse specialties among the focus group participants. Not noted by

the authors, Hasnie et al. (2018) only included physician perspectives and no other provider types (i.e., RN, NP, PA). This study also examined provider perspectives from across the Mayo Clinic network in five states and did not address institution-specific barriers and facilitators towards addressing FH. Additionally, it was not clear whether those who participated in the qualitative focus groups had also completed the initial survey. This represents a major gap in this study as the FH knowledge of the providers who participated in the focus groups may not have been assessed and considered with the findings in the qualitative phase. Further while a lack of knowledge was identified among providers, the authors did not explore the factors that influence this lack of knowledge. Thus, it remains unclear how a provider's knowledge of FH may impact their attitudes and behaviors towards an intervention to improve screening for FH, such as a clinical decision support tool. The proposed study intended to fill this gap in research among a more diverse group of cardiology providers as described below.

Time Constraints in Clinical Encounters

A component in the MEDPED, Simon Broome and DLCN diagnostic criteria for FH is family history (Bouhairie & Goldberg, 2015; Singh & Bittner, 2015). As recommended by clinical guidelines, a family history should encompass a four-generation pedigree (deGoma et al., 2016). Creating a pedigree requires providers to have first, a comprehensive understanding of the clinical features of FH to elicit pertinent information and second, a knowledgebase about the inheritance of FH to appropriately identify at-risk family members. Additionally, providers need an adequate amount of time within a clinical encounter to collect, interpret, and discuss a family history. Previous research has identified a lack of time to gather a complete and detailed family history as a significant barrier to FH screening and diagnosis (Hasnie et al., 2018; Hendricks-Sturrup et al., 2019; Zimmerman et al., 2019).

Lipid Specialization

Lipidologists are physicians who specialize in diagnosing, treating, and managing patients with lipid disorders such as FH. These specialists can originate from a variety of clinical disciplines such as cardiology, endocrinology, internal medicine, and family medicine. Providers within lipid clinics can not only offer specialized treatment options, but also manage the care of this unique cohort of patients. As such, lipid specialty clinics are a prime referral site for FH patients. While lipid specialty clinics are a referral resource for clinicians, research has demonstrated that this specialization can contribute to the lack of FH knowledge among general providers as well the underdiagnosis of FH (Hasnie et al., 2018). Providers who do not specialize as lipidologists have considered FH to be out of their scope of practice, thus impacting their knowledge of FH as well as their ability to screen, diagnose, manage, as well as refer FH patients (Bangash et al., 2020; Hasnie et al., 2018; Hendricks-Sturrup et al., 2019). This lack of perceived clinical responsibility, in combination with nonuniform diagnostic criteria, limited provider FH knowledge, and time constraints of the clinical encounter contribute not only to the underdiagnosis of FH but also to FH-related morbidity and mortality (Alonso et al., 2020; deGoma et al., 2016; Hasnie et al., 2018; Hendricks-Sturrup et al., 2019; Zimmerman et al., 2019).

Zimmerman et al. (2019) conducted a quantitative study aimed at identifying the perceived barriers to FH diagnosis. A 12-item questionnaire examining FH knowledge, screening practices, and perceived barriers was sent to primary care physicians practicing in Minnesota (Zimmerman et al., 2019). A total of 172 physicians participated in the study from disciplines including family medicine (n=99), internal medicine (n=68), geriatrics (n=2), functional medicine (n=1) and pediatrics (n=1)(Zimmerman et al., 2019). With regards to limited provider

knowledge, only 50% of participants were able to correctly identify risk to first-degree relatives (Zimmerman et al., 2019). Indeed, 30% of participants responded that they did not know the risk to first-degree relatives (Zimmerman et al., 2019). The barriers to FH screening and diagnosis included lack of time, competing priorities in practice, lack of knowledge of FH screening practices, lack of access to a genetics professional, and genetic testing being out of the scope of practice (Zimmerman et al., 2019).

While this study added to current FH knowledge there are several limitations to note. First, participants only included primary care physicians and neglected perspectives from other provider types as well as specialties (Zimmerman et al., 2019). Additionally, this study examined provider perspectives from across the state of Minnesota and did not address institution-specific barriers and facilitators towards addressing FH (Zimmerman et al., 2019). Thus, it is not well understood how a provider's training, specialty, and institutional context may impact their knowledge and perceived barriers towards FH screening and diagnosis. The proposed study aimed to incorporate multiple training perspectives (MD, DO, PA, NP, RN, LPN) in one specialty group (cardiology) within an institution (CUIMC) to explore how these factors influence FH practice behaviors. A final limitation to the study conducted by Zimmerman et al. (2019) is its study design and collection of only quantitative data. The proposed study incorporated qualitative as well as quantitative methods to better understand the practice behaviors related to the screening, diagnosis, and management of FH.

A comparison of the most relevant studies from the literature review that informed this dissertation research can be seen in Table 3.

Table 3

Comparison of Most Relevant Studies

Authors	Study Design	Methods	Limitations
Hasnie et al. 2018	Explanatory mixed methods	Phase 1: survey to physicians in various specialties across Mayo Clinic network in five states Phase 2: qualitative focus groups among cardiologists and PCPs at Mayo Clinic-Rochester campus	Lack of diverse specialties in focus groups Limited perspectives from other provider types (i.e., PA, NP, RN) Did not address institution-specific barriers and facilitators
Bangash et al. 2020	Concurrent mixed methods	Interviews and implementation survey with physicians across various specialties at Mayo Clinic	Lack of diverse provider types (i.e., PA, NP, RN)
Zimmerman et al. 2019	Quantitative	Questionnaire to PCPs across state of MN	Lack of perspectives from other provider types and specialties Did not address institution-specific barriers and facilitators

Inferences for Forthcoming Study

This review of the literature aimed to describe what is known about FH including its prevalence, genetic contributions, adverse effects, treatment options and diagnostic criteria. Additionally, the barriers to FH diagnosis were discussed such as a lack of consensus among diagnostic criteria, underutilization of genetic testing, limited provider knowledge and time constraints in clinical encounters. This literature review highlighted that while evidence-based knowledge exists for FH, alarmingly FH remains considerably underdiagnosed and undertreated.

The concurrence of FH underdiagnosis and undertreatment, as well as the negative clinical sequalae associated with FH, places cardiology healthcare providers (CHCPs) at the front line of screening, diagnosing, and managing FH patients (Foody, 2014). While research included CHCPs as stakeholders, no studies had exclusively described the experience of CHCPs in addressing FH within cardiology clinical care (Bangash et al., 2020; Block et al., 2020; Hasnie et al., 2018). Additionally, while previous research included the perspectives of cardiology physicians, it lacked the perspectives of other CHCPs such as nurse practitioners or physician assistants, who may also be involved in the clinical care of FH patients (Bangash et al., 2020; Hasnie et al., 2018; Zimmerman et al., 2019). This represented a gap that warranted further

exploration in order to understand how FH screening, diagnosis, and management is addressed in current cardiology clinical practice and by a diverse set of providers.

With a future goal of developing interventions that address the underdiagnosis and undertreatment of FH within cardiology, it was important to first understand the institution-specific as well as specialty-specific barriers and facilitators to screening, diagnosing, and managing FH. While previous research explored the implementation of an FH CDS tool in various clinical practice areas, there was a gap in the literature as to what additional interventions were most appropriate for CHCPs in the context of cardiology clinical practice. To design and evaluate FH interventions within cardiology, this study explored the perspectives of CHCPs to understand cardiology-specific barriers and facilitators, needed resources and potential interventions targeting CHCPs.

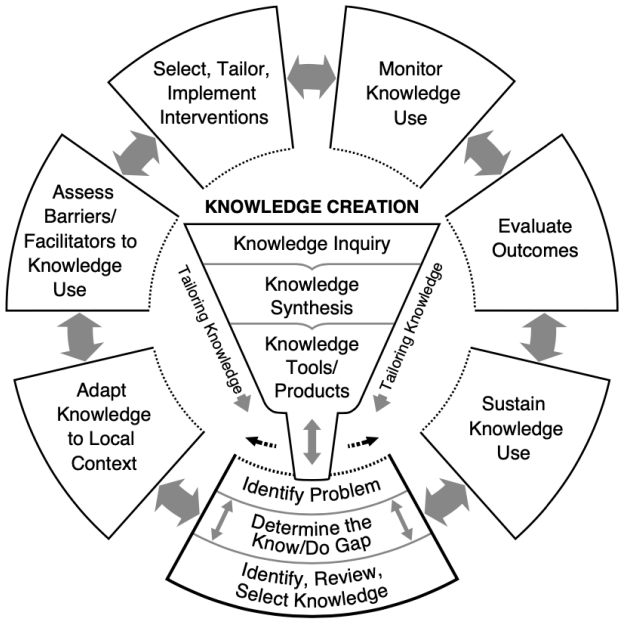
Conceptual Framework for Forthcoming Study

Knowledge to Action Framework

As this study aimed to better understand how CHCPs' knowledge of FH may influence their actions in screening, diagnosing, and managing FH patients in cardiology practice, a knowledge translation framework was employed as this study's foundational framework. The Knowledge to Action (KTA) process framework shown in Figure 1 is comprised of two main components: knowledge creation visualized as a funnel, and the action cycle displayed as the circular steps surrounding the funnel (Graham et al., 2013). When considering how to capitalize upon knowledge in a healthcare setting such as a cardiology, it was important to consider the steps within the action cycle of the KTA.

Figure 1

Knowledge to Action Framework



Note. Figure 1 from Graham, I. D., Straus, S. E., & Tetroe, J. (2013). *Knowledge translation in health care moving from evidence to practice* (2nd ed. ed.). John Wiley & Sons.

The first step within the action cycle is to identify the knowledge to action gap, meaning the gap between the evidence and current clinical practice (Graham et al., 2013). Within this research, the quantitative and qualitative phases gathered data to identify gaps between knowledge and practice behaviors of CHCPs as related to FH. To improve the uptake and utilization of knowledge within a clinical setting, it is important to consider adapting the knowledge to the local context, assessing barriers and facilitators to knowledge use, and selecting and tailoring interventions to relevant stakeholders and practice setting (Graham et al., 2013). Within this study, data collected through qualitative semi-structured interviews aimed to inform future strategies to improve FH knowledge and practice in cardiology clinical care. The outcome of this study was an intervention map and implementation plan to translate evidence-based FH knowledge and practice guidelines into cardiology practice at CUIMC with the

ultimate goal of improving the screening, diagnosis, and clinical management of FH patients and their family members.

Theory of Planned Behavior

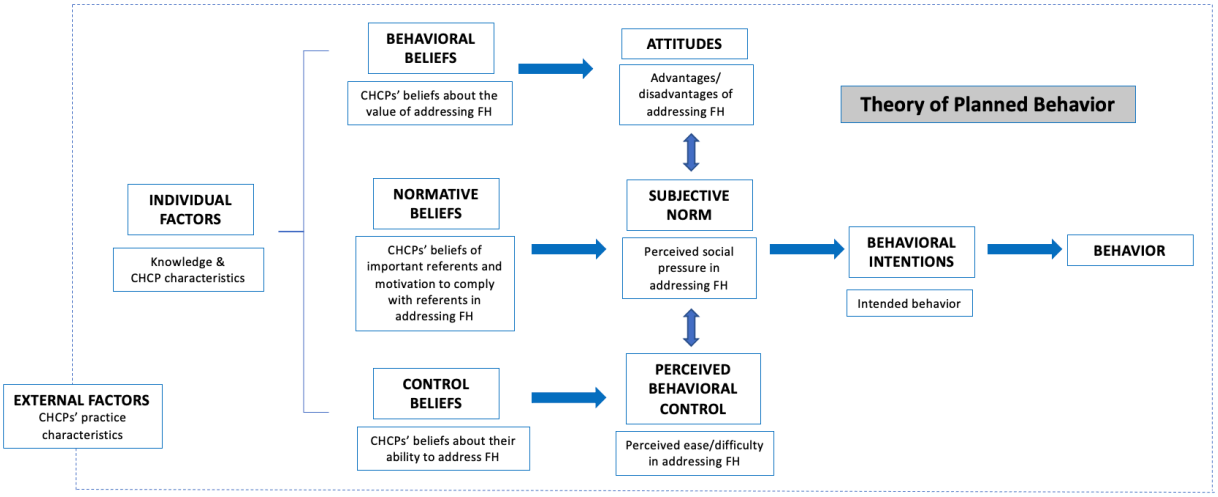
The goal of this study was to explore the practice behaviors and perceptions of CHCPs in the screening, diagnosis, and management of patients with FH. The findings from this research aimed to inform the creation of interventions targeted at CHCPs to improve practice behaviors related to the clinical care of FH patients. As such, a behavior change theory was critical to ground this research to better understand the factors that influence practice behaviors.

The Theory of Planned Behavior (TPB) can be used to not only understand but also predict behavior. Developed by Ajzen, the TPB posits that behavioral intention, or the motivational factors that influence behavior, is a strong predictor of performing the behavior (Ajzen, 1991; Bauer et al., 2015; Glanz et al., 2015; Graham et al., 2013; Grol, 2013; Nilsen, 2015). For instance, CHCPs who have a stronger intention to screen for FH will be more likely to perform FH screening among their patients.

As can be seen in Figure 2, behavioral intentions are influenced by an individual's attitudes, subjective norm, and perceived behavioral control towards the specific behavior (Ajzen, 1991; Bauer et al., 2015; Glanz et al., 2015; Graham et al., 2013; Grol, 2013; Nilsen, 2015). Attitude refers to the "degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question" (Ajzen, 1991, p. 188). Perceived behavioral control refers to "the perceived ease or difficulty of performing the behavior" (Ajzen, 1991, p. 183). Subjective norm refers to "the perceived social pressure to perform or not to perform the behavior" (Ajzen, 1991, p. 188).

Figure 2

Conceptual Framework



Note. Figure adapted from Glanz, Rimer, & Viswanath, 2015.

The attitude, subjective norm and perceived behavioral control of providers are influenced by three types of beliefs including behavioral, normative and control beliefs (Figure 2). With regards to the attitudes toward a specific behavior, a behavioral belief "links the behavior to a certain outcome" (Ajzen, 1991, p. 191). As an example, if a provider holds the belief that a diagnosis of FH will improve insurance coverage for treatment (i.e., outcome), that provider will have a more positive attitude towards the diagnostic process and be more likely to perform behaviors related to diagnosing FH. Normative beliefs refer to "the likelihood that important referent individuals or groups approve or disapprove of performing a given behavior" (Ajzen, 1991, p. 195). For instance, if a CHCP believes that an important referent (i.e., their boss or colleague) approves of FH screening, that CHCP will be more likely to comply with FH screening. Finally, control beliefs "deal with the presence or absence of requisite resources and opportunities" (Ajzen, 1991, p. 196). As an example, a provider who believes they have the

necessary resources to screen for FH will be more likely to believe that screening for FH is easy and have a higher intention of FH screening.

Behavioral, normative and control beliefs can be influenced by individual characteristics such as knowledge, age, and gender (Glanz et al., 2015; Graham et al., 2013). Figure 2 represents the foundational framework used to guide the proposed research. The framework utilized constructs of the TPB to gain a better understanding into the factors that influence practice behaviors for CHCPs in addressing FH in cardiology clinical practice.

Summary

Chapter 2 provided an overview of the current literature surrounding FH including its clinical manifestations, genetic basis, diagnostic criteria, importance of treatment, barriers to diagnosis and potential innovations to overcome diagnostic barriers. This chapter also introduced the conceptual frameworks, including the KTA and TPB, that guided this research. Chapter 3 will provide further details regarding the study design and methodology of this dissertation.

CHAPTER 3: METHODOLOGY

Background

Previous literature found that while FH is common within the general population, with a prevalence of 1 in 200 to 1 in 250, it remains vastly underdiagnosed and undertreated (Benito-Vicente et al., 2018; deGoma et al., 2016; Hasnie et al., 2018; Hendricks-Sturrup et al., 2020; Leren et al., 2008; Nordestgaard et al., 2013; Repas & Tanner, 2014; Zimmerman et al., 2019). Contributing barriers to diagnosis include lack of consensus among diagnostic criteria, limited provider knowledge, underutilization of genetic testing, and time constraints within clinical encounters (deGoma et al., 2016; Foody, 2014; Hasnie et al., 2018; Hendricks-Sturrup et al., 2019; Pang et al., 2020; Sturm et al., 2018; Zimmerman et al., 2019).

Cardiology healthcare providers (CHCPs) are well positioned to diagnose, treat, and manage patients with FH given the negative cardiovascular effects of untreated FH (Foody, 2014). However, previous research has not focused exclusively within cardiology clinical practice, nor has it taken into account diverse training among CHCPs (Bangash et al., 2020; Block et al., 2020; Hasnie et al., 2018). The primary purpose of this study was to describe the current practice behaviors, and factors that influence these behaviors, among CHCPs in the processes of screening, diagnosis, and management of FH. The long-term goal of this research was to inform future interventions that can be implemented in cardiology practice to assist with the systematic screening, diagnosis, and management of FH patients.

Specific aims and the corresponding research questions for this study included:

Aim 1. Identify the current level of knowledge among CHCPs in the screening, diagnosis, and management of FH. RQ1: What is the level of knowledge among CHCPs in the screening, diagnosis, and management of FH? (Quantitative inquiry)

Aim 2. Explore the factors that influence practice behaviors of CHCPs to screen, diagnose, and manage FH in cardiology clinical practice. RQ2: How do CHCPs describe their experiences screening, diagnosing, and managing FH in cardiology clinical practice? RQ2a: What role does provider knowledge, behavioral beliefs, normative beliefs, control beliefs, attitudes, subjective norm, perceived behavioral control and behavioral intentions play in CHCPs' screening, diagnosis, and management of FH in cardiology clinical practice? (Qualitative inquiry) RQ2b: To what extent do these factors influence the CHCPs' perceived barriers, facilitators, and needed resources to screening, diagnosing, and managing patients with FH? (Qualitative inquiry)

Aim 3. Use the quantitative results from the knowledge scores and themes generated from analysis of qualitative interviews to inform the development of future interventions that can be implemented in cardiology practice to assist with the systematic screening, diagnosis, and management of FH patients. RQ3: How do the knowledge scores and CHCP interviews provide an understanding of the barriers, facilitators, and needed resources to screening, diagnosing, and managing patients with FH to inform future interventions to influence practice behaviors? (Integrative inquiry)

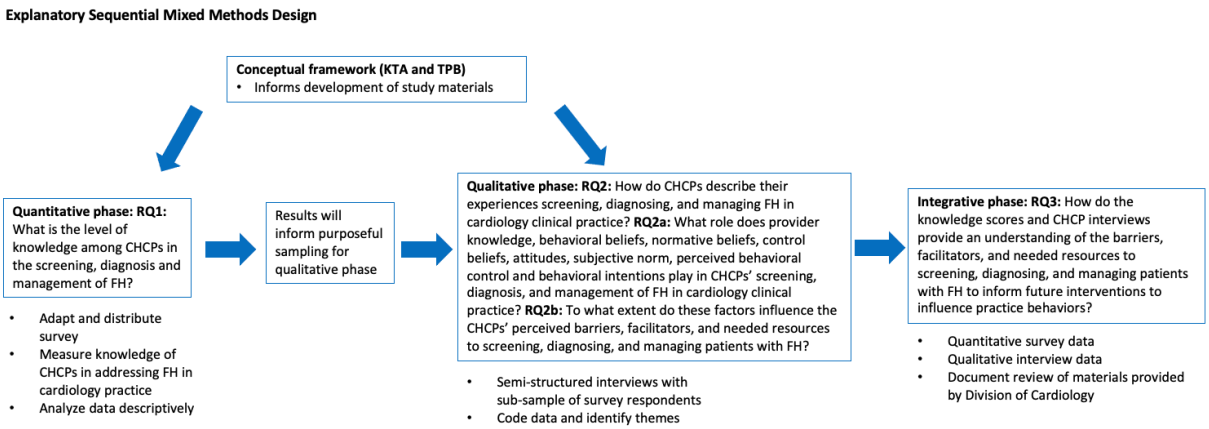
Study Design

A mixed methods, sequential, explanatory case study design was conducted to answer the research questions above. Within the quantitative phase, a survey (Appendix A) was distributed to healthcare providers across the Division of Cardiology at CUIMC. Results from the quantitative survey and the conceptual framework informed the development of interview questions (Appendix B) used in the qualitative phase of this study. The qualitative arm included semi-structured interviews with individual CHCPs who participated in the quantitative phase and

agreed to be contacted for the second phase of the study. Quantitative survey data, qualitative interview data, and other data sources including a review of current protocols, training documents and educational materials provided by the Division of Cardiology were compared within the integrative phase of this study. A visual representation of the study design is below (Figure 3).

Figure 3

Study Design



Note. KTA stands for Knowledge to Action framework and TPB stands for Theory of Planned Behavior. Figure adapted from Creswell, J.W., & Plano Clark, V.L., 2018

Participants

The study population for this research included CHCPs within the Division of Cardiology at CUIMC in Washington Heights, New York. Providers included physicians (Doctor of Medicine, MD; Doctor of Osteopathic Medicine, DO), physician assistants (PA) and nurses (nurse practitioner, NP; registered nurse, RN; licensed practical nurse, LPN). Eligibility was determined based on two questions at the beginning of the survey. Details regarding participant recruitment and sampling will be addressed further within the Methods section.

Materials

Quantitative Survey

Bell et al. (2013) utilized the TPB and KTA to develop a 19-item tool to assess the knowledge, awareness, and practice of FH among general practitioners in Australia. Of the 19-items, seven items measured knowledge, three items measured awareness, and nine items measured practice (Bell et al., 2013). This tool underwent content validation, adaptation, and face validation (Azraii et al., 2021; Azraii et al., 2018). The adapted and validated FH tool included 11 knowledge items, five awareness items, and nine practice items, consisting of a total of 25 items (Azraii et al., 2021; Azraii et al., 2018). The Kuder Richardson formula-20 internal consistency coefficient for the overall instrument was 0.79, including the following subdomains: knowledge (0.53), awareness (0.76), and practice (0.61) (Azraii et al., 2021; Azraii et al., 2018). With regards to test-retest reliability, the Cohen's kappa coefficient for the instrument was 0.76, with subdomain measurements including 0.82 (knowledge), 0.81 (awareness), and 0.76 (practice)(Azraii et al., 2021; Azraii et al., 2018).

For the purposes of this study, the survey included an adaptation of the Azraii tool. Awareness items in the tool included familiarity with FH, FH guidelines, and diagnostic criteria (Azraii et al., 2021; Azraii et al., 2018). However, these items did not align with the attitudes construct within the TPB, which includes "the degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question" (Ajzen, 1991, p. 188). FH practice behaviors were further explored during the qualitative interviews. Therefore, items measuring awareness and practice in the Azraii tool were removed. The final survey for this study included only the remaining 11 knowledge items from the Azraii tool with a total possible score of 19 with a point per correct response including multiple correct responses per question (Azraii et al., 2021; Azraii et al., 2018). The second round of adaptation included changing lipid

profile measurements as well as modifying practice guidelines and diagnostic criteria to the United States context and current clinical practice landscape. The final survey underwent expert review by lipid specialists.

Qualitative Semi-Structured Interview Protocol

Since the aim of this phase of research was to elucidate the factors that influence FH screening, diagnosis and management at CUIMC, a qualitative case study approach using a constructivist paradigm offered opportunities for a more complete, nuanced, contextual and detailed understanding of CHCPs' perceptions (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018; Levers, 2013). Final design of the interview guide (Appendix B) was informed by the results of the quantitative survey, expert review, and based on the conceptual frameworks (KTA and TPB) for this research (Ajzen, 1991; Bangash et al., 2020; Glanz et al., 2015; Hasnie et al., 2018).

Methods

Sampling and Recruitment

Convenience sampling through CUIMC's Division of Cardiology email listserv was utilized for the quantitative phase of this study (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018). The listserv included eligible participants (134 MD/DO, 57 NP/RN, and 41 PA) within 15 subdivisions in the Division of Cardiology. To increase response rate, snowball sampling was employed by asking respondents to the survey who expressed willingness to participate in the qualitative interview to forward the survey to their colleagues at CUIMC.

At the conclusion of the survey, participants were asked if they would be willing to be re-contacted for the second phase of the study. Providing contact information was not a required component of the survey and was completely voluntary. Inclusion criteria for the qualitative

semi-structured interviews included completion of the quantitative survey (and therefore meeting the initial inclusion criteria), verbal fluency in English, having access to a computer or phone, and having a valid email address.

The unit of analysis was the CHCP (MD, DO, PA, NP, LPN, RN), and each case was bound by healthcare setting (CUIMC) and specialty (cardiology). To obtain a diversity of cases, increase the richness of the data, and aim for maximum variation, a criterion sampling approach was utilized (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018; Palinkas et al., 2015). To allow for maximum variation sampling, a subsample of 20 participants from the quantitative survey was created using criteria including total knowledge score, professional degree/license, and subdivision. Snowball sampling was used to recruit participants for the qualitative interviews through professional connections at CUIMC, as well as through participants who agreed to participate in the second phase of the research study (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018).

Study Procedure

All research activities were approved by the CUIMC and GWU Institutional Review Boards (IRBs; IRB-AAAU0047). An introductory email with link to the survey (Appendix C) in Qualtrics was distributed to all members of the Division of Cardiology's email listserv. Participants were first directed to the study consent form (Appendix D). Participants who did not consent or who did not meet the study's inclusion criteria were directed to a screen thanking them for their time and consideration.

Participants who met the study's inclusion criteria and consented to continue with the survey were asked two questions: 1) if they would like to participate in the second arm of the research study which included qualitative individual interviews, and 2) if they would like to enter

to a drawing to win one of three $50 Amazon gift cards. Participants who answered "yes" to question 1, were prompted to provide their name and contact information. Participants were informed that this identifiable information would be kept confidential and only be used by the research study team for the purposes of re-contacting the participants for the second phase of the study.

Participants who answered "no" to question 1 were re-directed to question 2. If participants selected "yes" to question 2, they were re-directed to a separate gift card drawing form, which was not linked to their study survey responses. The new form asked participants to provide their name and contact information if they would like to be entered in the drawing. Participants were informed that their contact information would be kept confidential and only used for purposes of re-contacting them if they won one of the three $50 Amazon gift cards. If participants selected "no" for question 2, they were thanked for their participation and instructed to close the survey screen as the survey had been completed.

Participants who expressed interest in participating in the qualitative phase of the study were contacted via email with a request to schedule an individual interview (Appendix F). Prior to the scheduled interview, participants were provided a Study Information Sheet reviewing the purpose of the interviews, the voluntary nature of the study, the risks and benefits of study participation, and the requirement of audio recording the interview for transcription purposes (Appendix E). Participants were compensated $25 via Amazon gift card for their participation in the qualitative phase of this research.

Each participant was asked to provide verbal consent for participating in the qualitative interview as well as being audio-recorded. Interviews were audio-recorded and transcribed using Zoom software (Zoom, 2021). During each interview, fieldnotes were also gathered noting

researcher reflections on the interview process, as well as key comments and unspoken observations. In addition to interviews, educational materials and activities (i.e., lectures series, case conferences, etc) provided by the Division of Cardiology 2018-2022 were reviewed. With regards to conflicts of interest, the dissertation researcher had prior knowledge of FH, CUIMC and participants. It was crucial for the dissertation researcher to bracket this knowledge to ensure unbiased quantitative and qualitative data analysis.

Data Analytic Plan

Quantitative data from the survey instrument was analyzed using descriptive statistics. Frequency counts of provider type, subdivision of cardiology, years in clinical practice and years in clinical practice at CUIMC were calculated. Survey responses for the 11-knowledge items were added to produce a total knowledge score for each participant. A total sum knowledge score of up to 19 was calculated for each completed survey for use in data analysis for Aim 1 and the corresponding research question. The range of knowledge scores for all participants were reviewed to identify high and low thresholds and support variation among interview participants. The two-eligibility, 11-knowledge and four-demographic items were marked as mandatory for participants to complete in Qualtrics. Incomplete surveys were removed from data analysis.

Interview transcripts were single coded with Dedoose (Dedoose, 2021) software using an *a priori* coding schema that was informed by the TPB constructs (Ajzen, 1991; Creswell & Creswell, 2013; Creswell & Plano Clark, 2018). In addition to interview transcripts, other data sources included a document review of current protocols, training documents, and educational materials provided by the Division of Cardiology from 2018 to 2022. Leadership of each participant subgroup (i.e., attendings, fellows, nurses) was contacted to determine what resources (i.e., webinars, grand rounds, training documents) were provided to members within the division.

These resources were reviewed and analyzed descriptively to determine if FH content was included, and if so, what specific content areas pertaining to FH (i.e., diagnostic criteria, management options) were discussed.

Integration procedures of quantitative and qualitative data was represented at several points throughout the research process. First, quantitative results assisted in the development of semi-structured interview questions for the qualitative phase, which was presented through an interview prompts joint display (Appendix G) (Creswell & Plano Clark, 2018). The interview prompts joint display was represented as a table to delineate predetermined interview probes and questions that were identified from quantitative findings (Creswell & Plano Clark, 2018). Additionally, important factors identified in quantitative results informed aspects of the qualitative data analysis such as including predetermined codes (Appendix H) (Creswell & Plano Clark, 2018).

Statement of Subjectivity

When conducting qualitative research, it is important to recognize the potential for researcher bias to impact study findings. The statement of subjectivity provides an opportunity for the researcher to be transparent about the biases and experiences that the researcher brings to the study (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018). As a researcher engaged in a study to examine the knowledge and practice behaviors of CHCPs in the care of FH patients, the dissertation researcher had several experiences that were bracketed as a researcher to approach this study with a new perspective. First, the researcher was a CHCP with a genetics background who has a high level of FH knowledge and extensive experience working with FH patients. Second, the researcher worked with other CHCPs across the Division of Cardiology at CUIMC. Therefore, the researcher brought prior assumptions to division and institutional

barriers, facilitators, and needed resources. Third, the researcher was involved in creating and running educational FH sessions for CHCPs within the Division of Cardiology. It was important to ensure that prior knowledge of FH, participants, and CUIMC did not bias the researcher's analysis of quantitative and qualitative data.

When considering aspects of trustworthiness in the qualitative arm, it was important to recognize that the researcher was a CHCP with a high knowledge of FH and extensive practice behaviors related to FH. Thus the researcher bracketed her experience to minimize bias or perceived notions about the study and its findings (Creswell & Creswell, 2013). Processes involved in bracketing included acknowledging specific areas of researcher bias, discussing strategies to manage these biases, and making an open declaration with participants at the beginning of the interview regarding the role of the interviewer as solely in a research capacity to protect any prior relationship between researcher and participant. Another strategy that was employed is member checking, in which all qualitative participants received a summarized description of interview findings and were provided an opportunity to comment if the findings were an accurate representation of their experiences (Creswell & Plano Clark, 2018). Feedback from participants confirmed the trustworthiness of the qualitative thematic findings. Researcher bracketing and member checking were employed to minimize threats to reliability and validity. Additionally, the use of multiple data sources (i.e., interviews, review of documents, fieldnotes) allowed for triangulation in the data analysis process to compare and synthesize quantitative and qualitative findings (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018; Grol, 2013).

Human Participants and Ethics Precautions

Research protocols for the quantitative and qualitative arms of this study were submitted for IRB approval at CUIMC and GWU. Participation in the quantitative survey and qualitative

interviews was voluntary with minimal risks to participants. There were no direct benefits for participants who voluntarily chose to participate in this research study. A potential benefit associated with this research was that knowledge gained would inform future interventions to improve the screening, diagnosis, and management of FH patients at CUIMC.

Participants received informed consent forms prior to participation in each arm of the study (Appendix D; Appendix E). Consent was obtained at the beginning of the survey through Qualtrics software, and verbal consent was obtained at the beginning of the semi-structured interviews. There was a risk of loss of confidentiality as the study team knew the identity of participants in the second arm of the study and had the ability to link the participant to their quantitative survey responses. In order to minimize a breach of confidentiality, each transcript was assigned a pseudonym, and all transcripts were deidentified and password protected. The link between participants and survey responses was destroyed after data analysis was completed. To protect the confidentiality of participants, individual data and identifiable information was not reported.

Summary

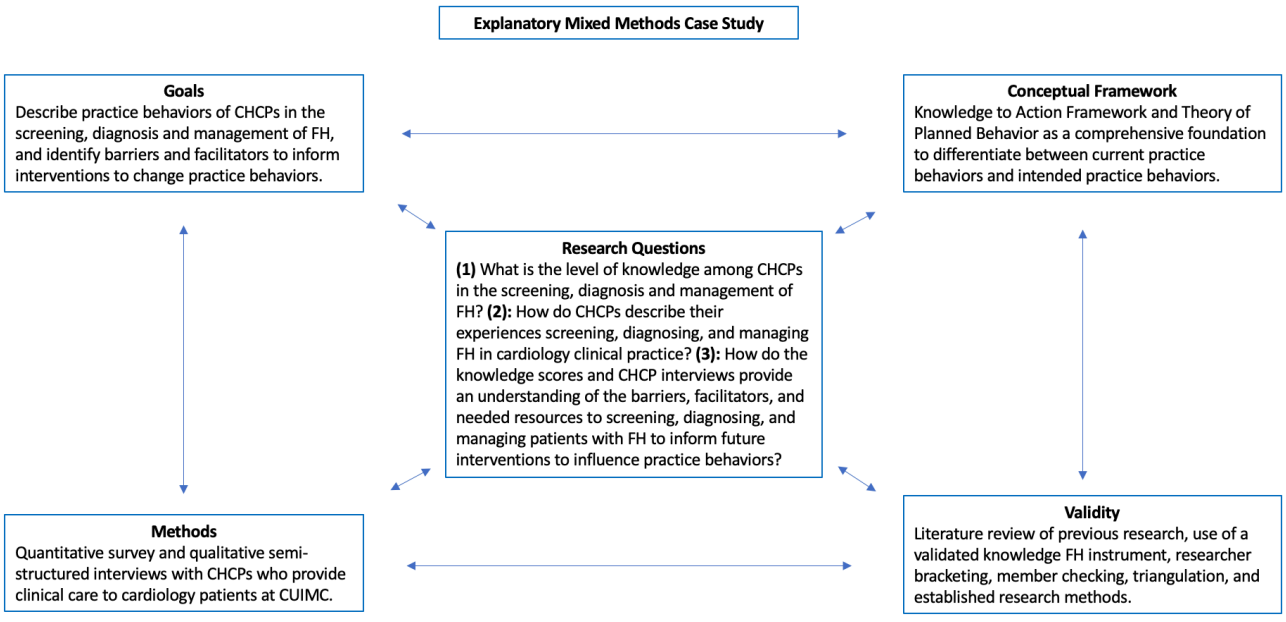
An explanatory, mixed methods, case study research design was utilized to elucidate and describe the experiences of CHCPs in the screening, diagnosis, and management of FH patients at one large medical center, CUIMC. Convenience sampling through the Division of Cardiology listserv was used as a preliminary sampling strategy for the quantitative phase, and snowball sampling was utilized as a secondary quantitative sampling strategy (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018). Results from the quantitative survey confirmed maximum variation among the qualitative interview participants based on total knowledge score, professional degree/license, and subdivision. Snowball sampling was used to recruit participants

into the qualitative phase of this research study (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018).

Data was collected from a study survey that included a modified, previously validated tool and semi-structured individual interviews were subjected to thematic analysis. A variety of strategies were employed to address the study's research questions including descriptive analysis of quantitative data collected in the survey and document review, as well as deductive and inductive coding and thematic interpretation for qualitative data. The study findings were related back to the study's research questions and conceptual frameworks. Researcher bracketing, triangulation, and member checking were employed to minimize threats to reliability and validity. Figure 4 demonstrates the alignment of the research approach.

Figure 4

Alignment of Research Approach



Note. Figure adapted from Qualitative Research Design: An Interactive Approach (3rd ed.), by J. Maxwell, 2013

CHAPTER 4: RESULTS

Introduction

The purpose of this explanatory, mixed methods, case study was to describe the practice behaviors of cardiology healthcare providers (CHCPs) in the screening, diagnosis, and management of Familial Hypercholesterolemia (FH), as well as gain a better understanding of the perspectives of CHCPs in FH screening and diagnosis interventions that can be implemented in cardiology practice. The specific aims and accompanying research questions were:

Aim 1. Identify the current level of knowledge among CHCPs in the screening, diagnosis, and management of FH. RQ1: What is the level of knowledge among CHCPs in the screening, diagnosis, and management of FH? (Quantitative inquiry)

Aim 2. Explore the factors that influence practice behaviors of CHCPs to screen, diagnose, and manage FH in cardiology clinical practice. RQ2: How do CHCPs describe their experiences screening, diagnosing, and managing FH in cardiology clinical practice? RQ2a: What role does provider knowledge, behavioral beliefs, normative beliefs, control beliefs, attitudes, subjective norm, perceived behavioral control and behavioral intentions play in CHCPs' screening, diagnosis, and management of FH in cardiology clinical practice? (Qualitative inquiry) RQ2b: To what extent do these factors influence the CHCPs' perceived barriers, facilitators, and needed resources to screening, diagnosing, and managing patients with FH? (Qualitative inquiry)

Aim 3. Use the quantitative results from the knowledge scores and themes generated from analysis of qualitative interviews to inform the development of future interventions that can be implemented in cardiology practice to assist with the systematic screening, diagnosis, and management of FH patients. RQ3: How do the knowledge scores and CHCP interviews provide

an understanding of the barriers, facilitators, and needed resources to screening, diagnosing, and managing patients with FH to inform future interventions to influence practice behaviors? (Integrative inquiry)

An online survey to assess the knowledge of CHCPs in the screening, diagnosis, and management of FH was distributed to members of the Division of Cardiology at Columbia University Irving Medical Center (CUIMC). Follow-up individual interviews were conducted via Zoom to gain a better understanding of the factors that influence FH screening, diagnosis, and management at CUIMC. This chapter provides the results related to each research question as well as provides the results of a document review including descriptive analysis of current protocols, training documents and education materials provided by the Division of Cardiology.

Quantitative Survey

A total of 232 eligible participants (134 MD/DO, 57 NP/RN, and 41 PA) received an introductory study email including the Qualtrics link (Appendix C) to recruit participants into the quantitative phase. The survey was open for four weeks. After the introductory email was distributed to the Division of Cardiology listserv on March 14, 2022, all potential participants were individually emailed with the Qualtrics survey link beginning one week after Division of Cardiology email was distributed as a reminder. Seventy-nine (79) respondents completed the inclusion/exclusion criteria. Nine (9) had incomplete responses that could not be analyzed, resulting in 70 completed survey responses that were available for analysis, corresponding to a response rate of 30.2%. Table 4 summarizes the provider characteristics of the participants. Participants of the quantitative survey had the option to enter a drawing to win one of three $50 Amazon gift cards. Of the 70 completed survey responses, 51 participants entered the drawing.

Table 4

CHCP Survey Participants' Characteristics

Characteristic	**n**	**%**
Professional Degree/License		
MD	35	50.0
PA	9	12.9
RN	17	24.3
NP	9	12.9
Subdivision of Practice		
CIVT/VALVE	12	17.1
HF/Transplant	14	20.0
EP/EKG	17	24.3
Ultrasound	1	1.4
Inpatient Services	2	2.9
Congenital	1	1.4
Faculty Practices	5	7.1
Hudson Valley	1	1.4
Fellowship	6	8.6
Research	4	5.7
Precision Medicine	1	1.4
Preventive Medicine	1	1.4
Cath Lab	3	4.3
CT Surgery	1	1.4
Other (unspecified)	1	1.4
Years at CUIMC		

Less than 1 year	5	7.1
1-5 years	23	32.9
6-10 years	12	17.1
11-20 years	19	27.1
Greater than 20 years	11	15.7
Years in Clinical Practice		
Less than 1 year	1	1.4
1-5 years	14	20.0
6-10 years	18	25.7
11-20 years	17	24.3
Greater than 20 years	20	28.6

CIVT/VALVE= Center for Interventional Vascular Therapy; HF/Transplant= Cardiac Heart Failure and Transplant; EP/EKG= Electrophysiology/Electrocardiogram; Hudson Valley= ColumbiaDoctors of Hudson Valley; CT Surgery= Cardiothoracic Surgery

Total Knowledge Scores

The survey consisted of 11-knowledge items, with one point given per each correct response; some items included multiple correct responses (Azraii et al., 2021; Azraii et al., 2018). Survey responses for the 11-knowledge items were added to produce a total knowledge score of up to 19 possible for each participant. Due to the small and unequal sample sizes of the various groups of CHCPs, inferential statistics were not performed. Instead, data is presented visually in box and whisker plots to visually present comparisons among the different groups of CHCPs.

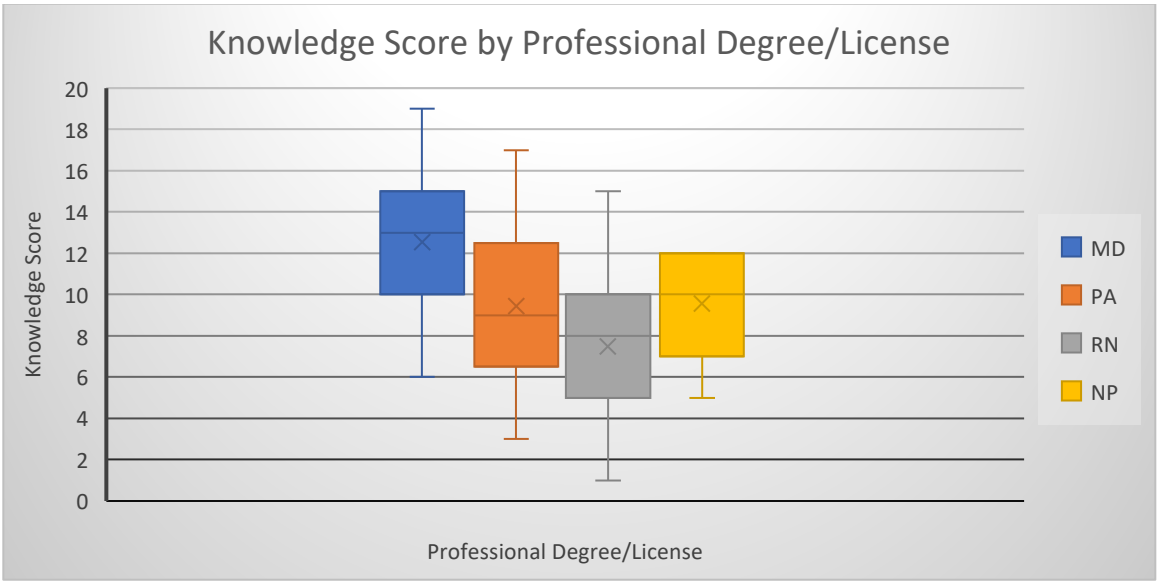
For each box and whisker plot, the minimum or the lowest score is shown at the lowest point of the bottom whisker. The lower quartile (Q1) in which 25.0% of scores fall below is

represented by the lower side of the box. The median (M) or the midpoint of the data is shown by the line that divides the box into two parts representing that 50.0% of scores are greater than or equal to this value and 50.0% of scores are less. The mean ($\bar{x}$) is the average of scores, represented by x on the box and whisker plot. The upper quartile (Q3) in which 75.0% of scores fall below is represented by the upper side of the box. The maximum or the highest score is shown at the highest point of the top whisker. The minimum or lowest score is shown at the lowest point of the bottom whisker. The interquartile range (IQR) is represented as the box showing the middle 50.0% of scores (i.e., the range between the 25th [Q1] and 75th percentile [Q3]).

Figure 5 depicts the total knowledge score by CHCPs' professional degree or license.

Figure 5

Knowledge Score by Professional Degree/License



When looking across the four groups of professional degrees (MD, PA, RN, NP), the M of 13.0 for MDs lies outside of the boxes for PAs, RNs, and NPs suggesting that there is likely to be a difference in knowledge scores between MDs and the other three professional degree

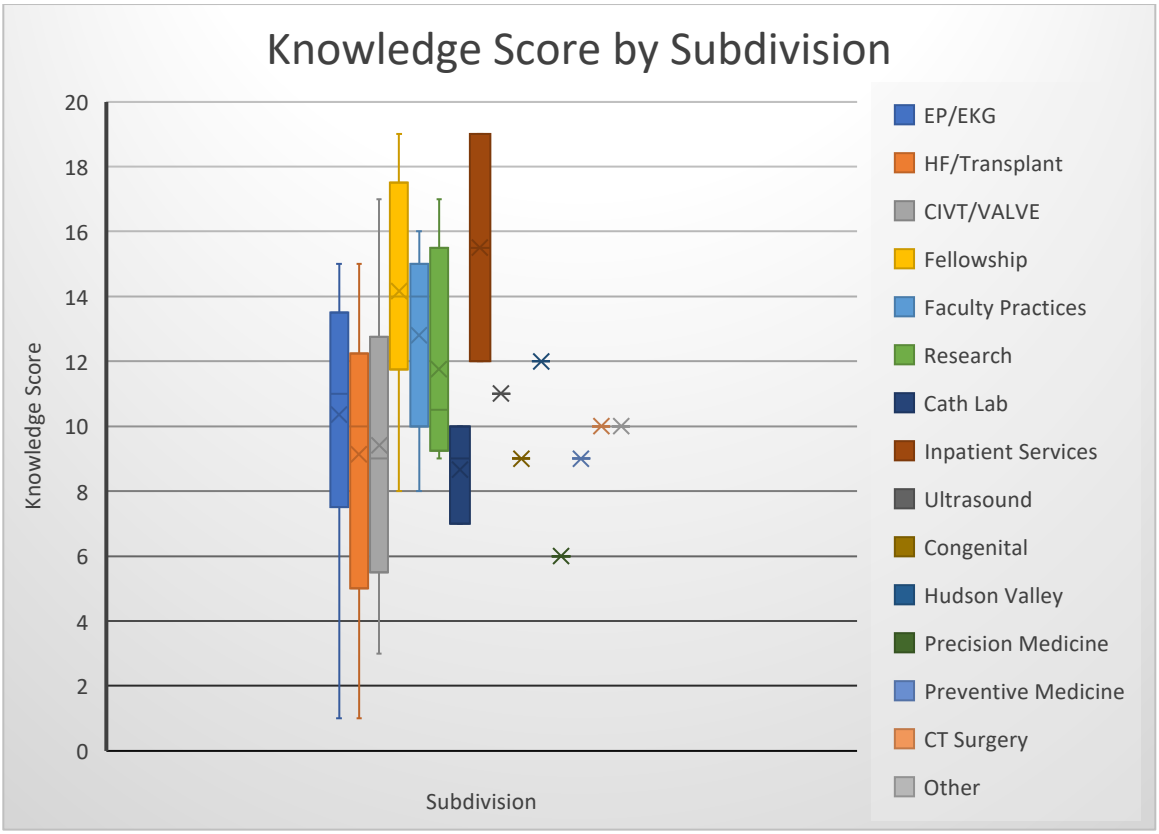
groups. Quantitative data analysis did not include inferential statistics. Descriptive statistical analysis of quantitative data was performed as this form of data analysis aligned with the study aims and research questions. Providers with a professional degree of MD had the highest maximum knowledge score, and providers with a professional degree of RN had the lowest minimum knowledge score. Similarly, MDs had the highest average knowledge score ($\bar{x}$ is 12.5), while RNs had the lowest average knowledge score ($\bar{x}$ is 7.5). Additionally, the IQRs for MDs, RNs, NPs were equal (5.0); whereas the IQR for PAs was 6.0 indicating that the PA group had a larger range of knowledge scores as compared to the other three professional degree groups. Finally, the box and whisker plots for MDs, RNs and NPs were left or negatively skewed (M is closer to Q3) meaning that the data constituted a higher frequency of low knowledge scores; the box and whisker plot of PAs was right or positively skewed (M is closer to Q1) meaning that the data constituted a higher frequency of high knowledge scores.

When comparing knowledge scores by subdivision (Figure 6), it should first be noted that only eight box and whisker plots were able to be constructed because only one CHCP was represented from the seven other subdivisions. When examining the eight box and whisker plots, CHCPs from EP/EKG, HF/Transplant, and CIVT/VALVE had the lowest minimum knowledge scores; while CHCPs from Inpatient Services, Fellowship, Research, and EP/EKG had the highest maximum knowledge scores. Additionally, CHCPs from Cath Lab ($\bar{x}$ is 8.7), HF/Transplant ($\bar{x}$ is 9.1), and CIVT/VALVE ($\bar{x}$ is 9.4) had the lowest average knowledge scores; while CHCPs from Inpatient Services ($\bar{x}$ is 15.5), Fellowship ($\bar{x}$ is 14.2), and Faculty Practices ($\bar{x}$ is 12.8) had the highest average knowledge scores. It is important to note that the IQR for CHCPs in Faculty Practices (5.0) had the smallest range of knowledge scores, and the IQRs for CHCPs in HF/Transplant (7.3) and CIVT/VALVE (7.3) had the largest range of

knowledge scores, as compared to the other subdivisions. Finally, the box and whisker plots for CHCPs working in the subdivisions of CIVT/VALVE, Fellowship and Research were right or positively skewed (M is closer to Q1) meaning that the data constituted a higher frequency of high knowledge scores. The box and whisker plots for CHCPs working in the subdivisions of EP/EKG, HF/Transplant, Faculty Practices, and Cath Lab were left or negatively skewed (M is closer to Q3), meaning that the data constituted a higher frequency of low knowledge scores.

Figure 6

Knowledge Score by Subdivision

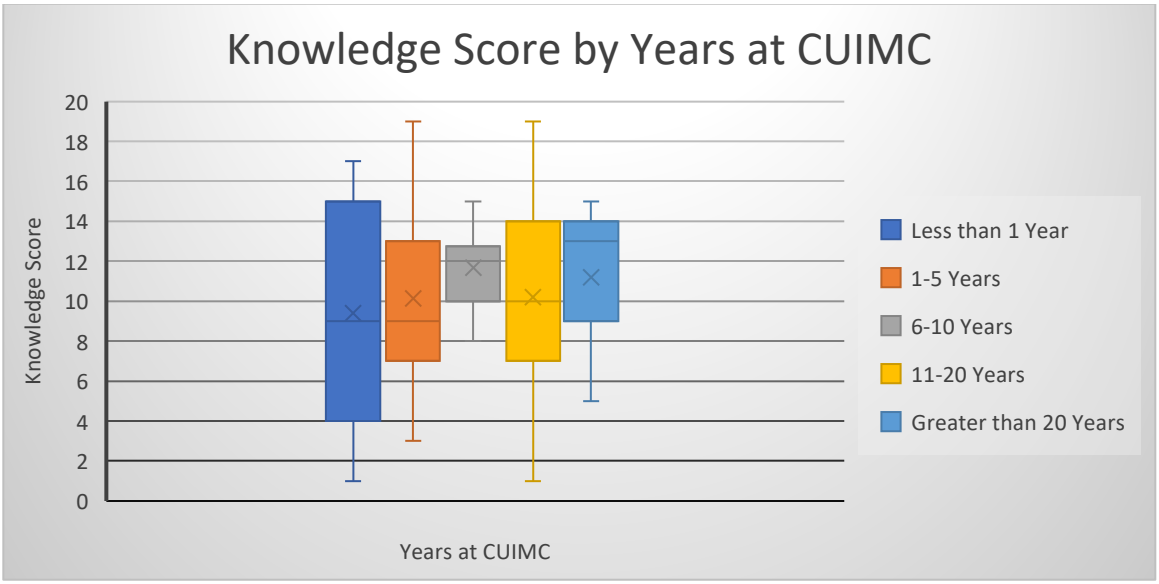


When comparing knowledge scores by years at CUIMC (Figure 7), CHCPs at CUIMC for less than 1 year and from 11-20 years, had the lowest minimum knowledge score, and CHCPs at CUIMC from 1-5 years and 11-20 years had the highest maximum knowledge scores. CHCPs at CUIMC for less than 1 year ($\bar{x}$ is 9.4) and 1-5 years ($\bar{x}$ is 10.1) had the lowest

average knowledge scores. CHCPs at CUIMC for 6-10 years ($\bar{x}$ is 11.7) and greater than 20 years ($\bar{x}$ is 11.2) had the highest average knowledge scores. It is important to note that the IQR for CHCPs who have been at CUIMC for 6-10 years (2.8) had the smallest range of knowledge scores and the IQR for CHCPs who have been at CUIMC less than 1 year (11.0) had the largest range of knowledge scores, as compared to the other provider groups. Finally, the box and whisker plots for CHCPs who have been at CUIMC for less than 1 year, 1-5 years, and 11-20 years were right or positively skewed (M is closer to Q1) meaning that the data constituted a higher frequency of high knowledge scores. The box and whisker plots for CHCPs who have been at CUIMC for 6-10 years and greater than 20 years were left or negatively skewed (M is closer to Q3), meaning that the data constituted a higher frequency of low knowledge scores.

Figure 7

Knowledge Score by Years at CUIMC

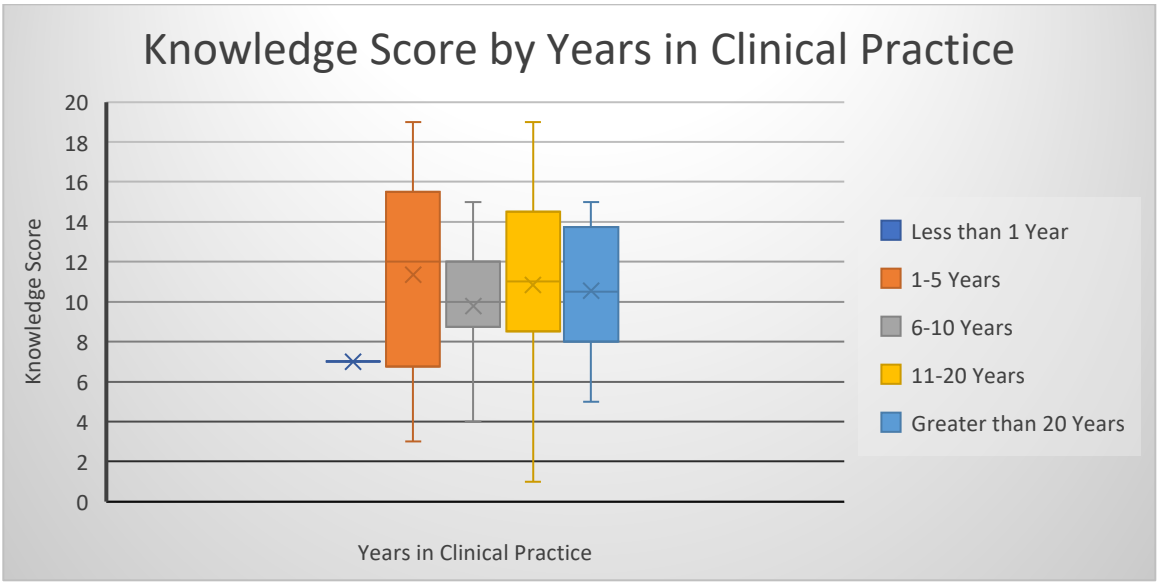


When comparing knowledge scores by years in clinical practice (Figure 8), it should first be noted that only four box and whisker plots were able to be constructed because only one CHCP represented providers with less than one year in clinical practice. Of the remaining four

CHCP groups, providers who were in clinical practice for 11-20 years had the lowest minimum knowledge score, while CHCPs who were in clinical practice for 1-5 years and 11-20 years had the highest maximum knowledge scores. CHCPs in clinical practice for 6-10 years had the lowest average knowledge score ($\bar{x}$ is 9.8), and CHCPs in clinical practice for 1-5 years had the highest average knowledge score ($\bar{x}$ is 11.4). The IQR for CHCPs who have been in clinical practice for 6-10 years (3.3) had the smallest range of knowledge scores, and the IQR for CHCPs who have been in clinical practice less than 1 year (8.8) had the largest range of knowledge scores, as compared to the other provider groups who had similar IQRs (6.0 for CHCPs in clinical practice for 11-20 years and 5.8 for CHCPs in clinical practice for greater than 20 years). Finally, the box and whisker plots for CHCPs who have been in clinical practice for 11-20 years and greater than 20 years were right or positively skewed (M is closer to Q1), meaning that the data constituted a higher frequency of high knowledge scores. The box and whisker plots for CHCPs who have been in clinical practice for 1-5 years and 6-10 years were left or negatively skewed (M is closer to Q3), meaning that the data constituted a higher frequency of low knowledge scores.

Figure 8

Knowledge Score by Years in Clinical Practice



Knowledge Score by Domain

The survey consisted of 11 knowledge questions comprising six knowledge domains (description, prognosis, prevalence, inheritance, diagnostic criteria, and management related to FH). To better understand the FH knowledge of CHCPs, the knowledge scores within the survey by domain (see Figures 9-12) were further examined. The specific knowledge domains, corresponding survey item, and total points per knowledge domain can be seen in Table 5. Average knowledge scores were calculated for each of the six knowledge domains.

Table 5

Domains for Knowledge

Knowledge	**Survey Item**	**Total Points**
Description	1	1
Prognosis	5, 6	3
Prevalence	3	1
Inheritance	4	1
Diagnostic Criteria	2, 7, 9, 10	9

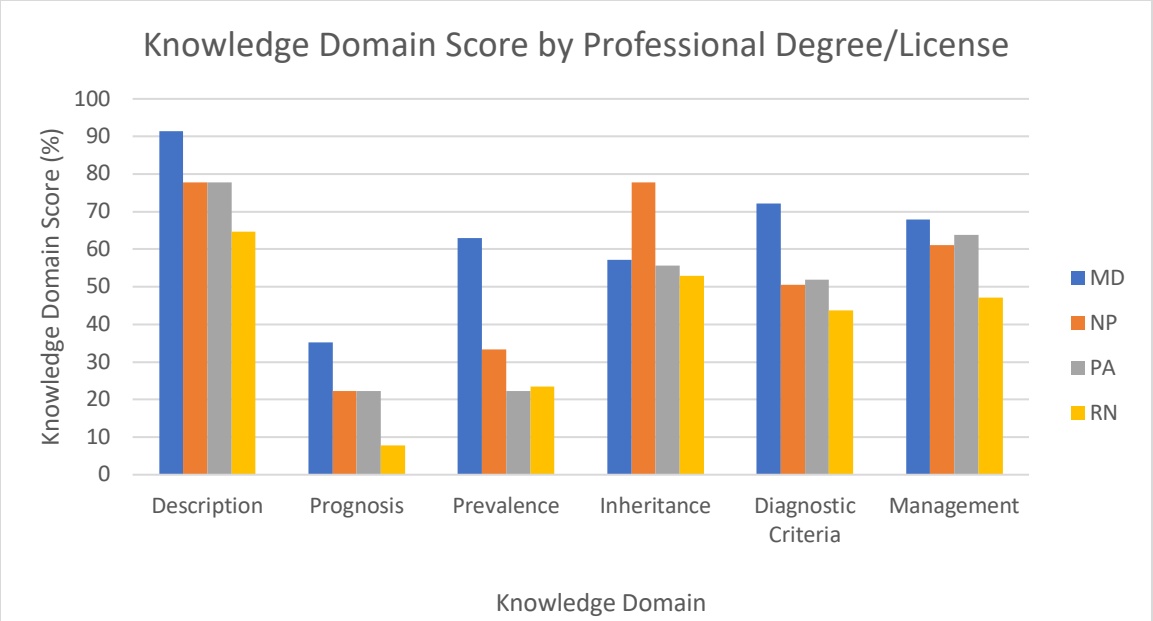
Management	8, 11	4

The survey consisted of 11 knowledge items, with a total possible score of 19 with a point per correct response, with some items having multiple correct responses (Azraii et al., 2021; Azraii et al., 2018).

When comparing the knowledge domain scores by CHCPs' professional degree or license (Figure 9), RNs scored lowest across the following knowledge domains: description (64.7%), prognosis (7.8%), inheritance (52.9%), diagnostic criteria (43.8%), and management (47.1%). PAs scored lowest with regards to the prevalence of FH (22.2%). MDs scored highest across the knowledge domains of description (91.4%), prognosis (35.24%), prevalence (62.9%), diagnostic criteria (72.1%) and management (67.9%). NPs scored highest within the knowledge domain of inheritance (77.8%). When observing the σ across the six knowledge domains, it can be noted that the knowledge domain of management had the lowest σ (9.0) meaning that there was the smallest dispersion of scores from the mean with regards to management. Whereas the knowledge domain of prevalence had the highest σ (18.9), indicating that there was the greatest dispersion of scores from the mean with regards to prevalence.

Figure 9

Knowledge Domain Score by Professional Degree/License



When comparing the knowledge domain scores by CUIMC subdivision (Figure 10), the lowest score with regards to the description knowledge domain was obtained by CHCPs in Cath Lab (33.3%). Looking at prognosis, CHCPs in Ultrasound, Congenital, Preventive Medicine and CT Surgery scored 0%. With regards to the knowledge domain of prevalence, Congenital, Precision Medicine, and CT Surgery scored 0%. For inheritance, CHCPs in Ultrasound and Precision Medicine scored 0%. Finally, CHCPs in Precision Medicine scored lowest for knowledge domains of diagnostic criteria (33.3%) and management (25.0%).

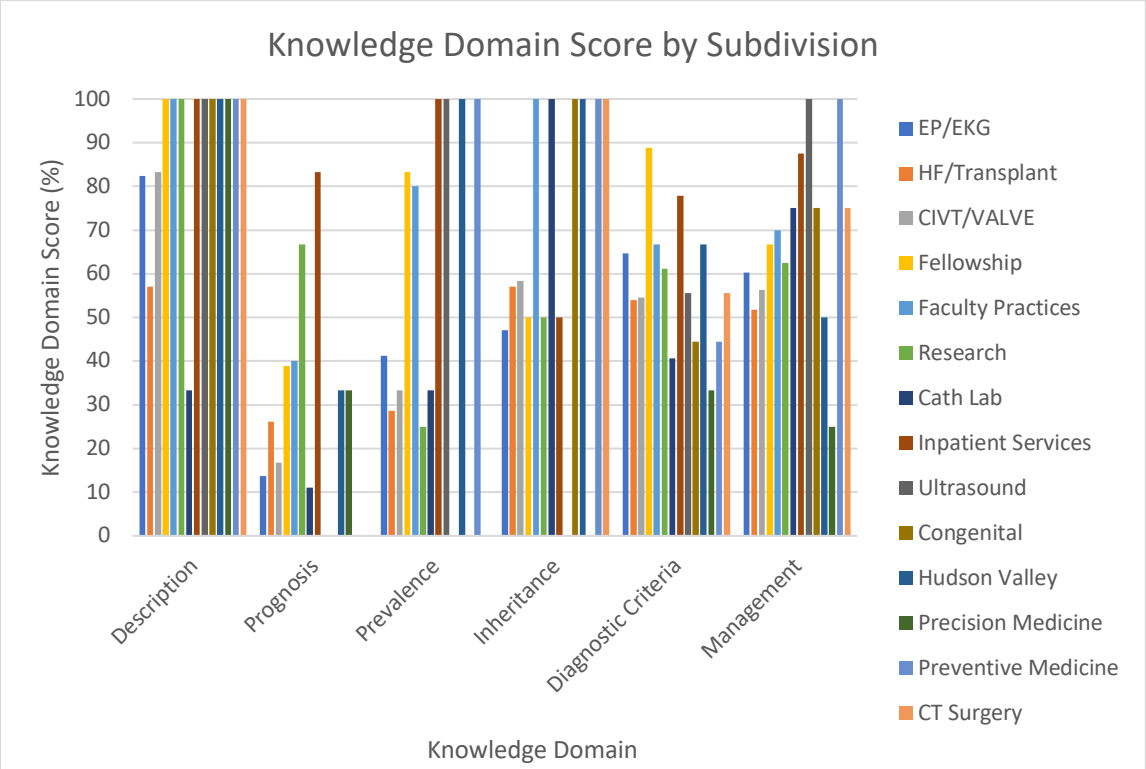
The highest score with regards to the description knowledge domain was obtained by CHCPs in Fellowship, Faculty Practices, Research, Inpatient Services, Ultrasound, Congenital, Hudson Valley, Precision Medicine, Preventive Medicine, and CT Surgery (100.0%). Looking at prognosis, CHCPs in Inpatient Services scored highest (83.3%). With regards to the knowledge domain of prevalence, CHCPs in Inpatient Services, Ultrasound, Hudson Valley, and Preventive Medicine scored 100%. For inheritance, CHCPs in Faculty Practices, Cath Lab, Congenital, Hudson Valley, Preventive Medicine and CT Surgery scored highest (100.0%). CHCPs in

Fellowship scored highest for diagnostic criteria (88.9%). Finally, CHCPs in Ultrasound and Preventive Medicine scored highest for management (100.0%).

When looking at the σ across the six knowledge domains, it can be noted that the knowledge domain of diagnostic criteria had the lowest σ (14.9) meaning that there was the smallest dispersion of scores from the mean with regards to the diagnostic criteria for FH. Whereas the knowledge domain of prevalence had the highest σ (40.4), indicating that there was the greatest dispersion of scores from the mean with regards to prevalence.

Figure 10

Knowledge Domain Score by Subdivision



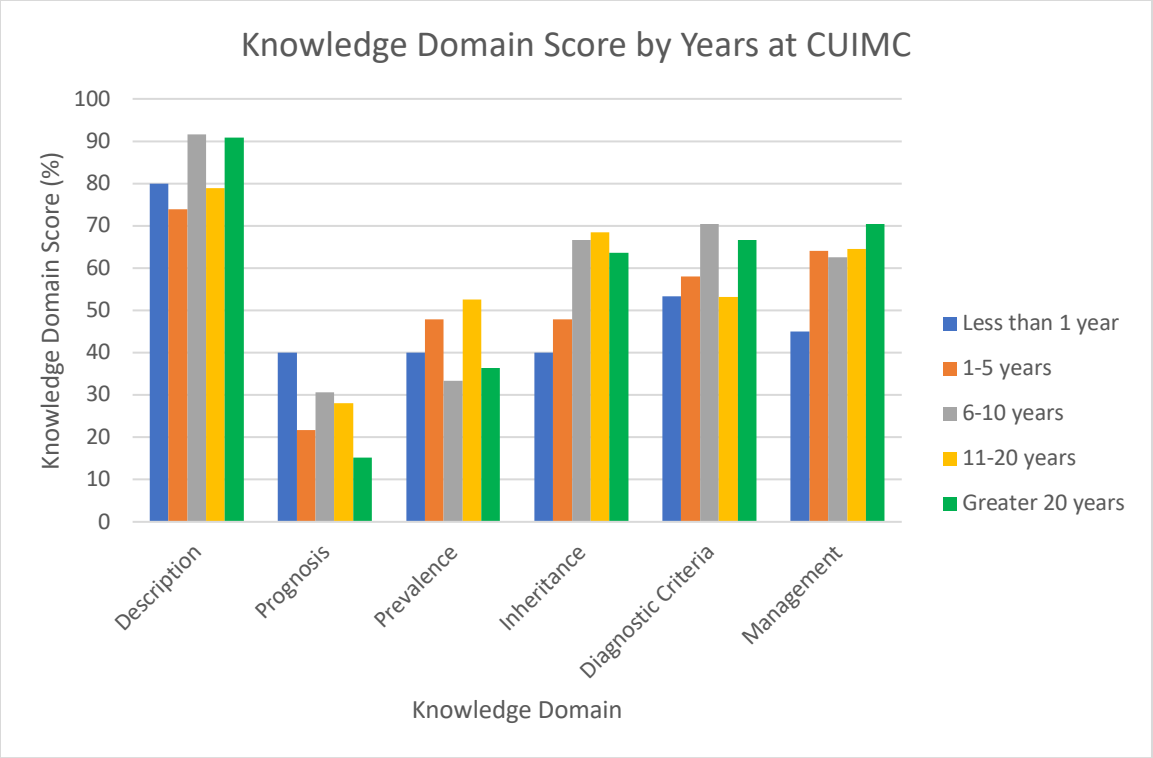
When comparing the knowledge domain scores by years at CUIMC (Figure 11), CHCPs with less than 1 year at CUIMC scored lowest in the knowledge domain of inheritance (40.0%) and management (45.0%). CHCPs with 1-5 years at CUIMC scored lowest on the knowledge

domain of description (73.9%), while those at CUIMC for 6-10 scored lowest with regards to prevalence (53.2%). CHCPs at CUIMC for 11-20 years scored lowest on the knowledge domain of diagnostic criteria (53.2%), and those at CUIMC for greater than 20 years scored lowest on prognosis (15.2%). With regards to the highest scores, CHCPs at CUIMC for 11-20 years scored highest on the knowledge domains of prevalence (52.6%) and inheritance (68.4%). Additionally, CHCPS at CUIMC for less than 1 year scored highest on prognosis (40.0%), for 6-10 years on description and diagnostic criteria of FH (91.7%), and for greater than 20 years on management (70.5%).

When looking at the σ across the six knowledge domains, it can be noted that the knowledge domain of description had the lowest σ (7.8) meaning that there was the smallest dispersion of scores from the mean with regards to the description of FH. Whereas the knowledge domain of inheritance had the highest σ (12.7), indicating that there was the greatest dispersion of scores from the mean with regards to inheritance.

Figure 11

Knowledge Domain Score by Years at CUIMC



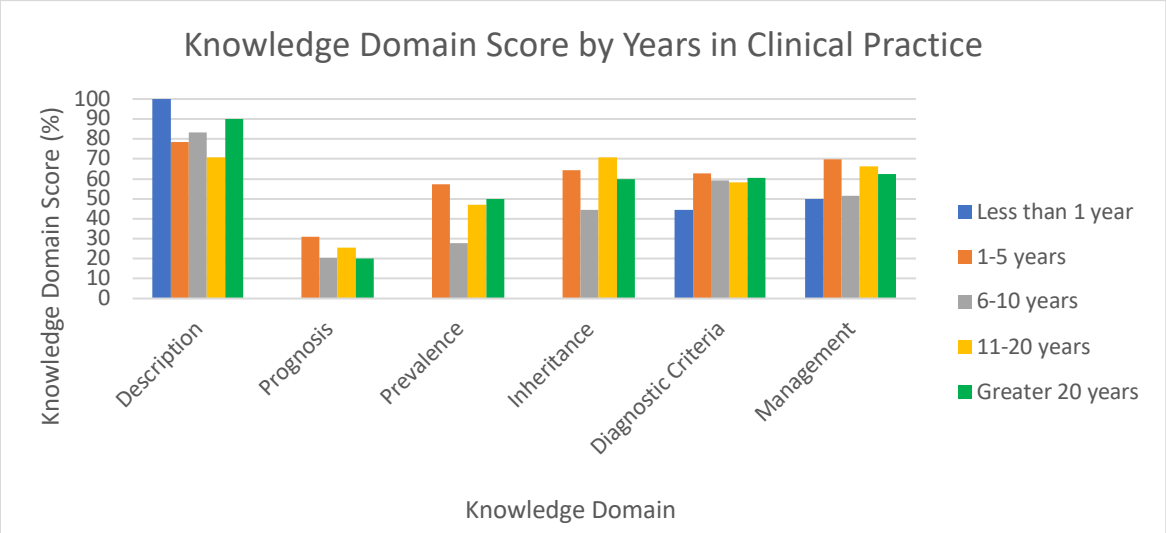
When comparing the knowledge domain scores by years in clinical practice (Figure 12), CHCPs who have been in clinical practice for less than 1 year scored the lowest across five knowledge domains including prognosis (0%), prevalence (0%), inheritance (0%), diagnostic criteria (44.4%), and management (50.0%). It is important to note that a bar was not displayed for CHCPs in clinical practice for less than one year with regards to the knowledge domains of prognosis, prevalence, and inheritance because all three knowledge domain scores were 0%. Further CHCPs who have been in clinical practice for 11-20 years scored lowest on the description knowledge domain (70.6%). With regards to the highest scores across knowledge domains, CHCPs who have been in clinical practice for 1-5 years scored the highest across four knowledge domains including prognosis (31.0%), prevalence (57.1%), diagnostic criteria (62.7%), and management (69.6%). CHCPs who have been in clinical practice for less than 1 year scored 100% with regards to the description knowledge domain, and CHCPs who have been

in clinical practice for 11-20 years, scored the highest score (70.6%) for the knowledge domain of inheritance.

When looking at the σ across the six knowledge domains, it can be noted that the knowledge domain of diagnostic criteria had the lowest σ (7.2) meaning that there was the smallest dispersion of scores from the mean with regards to the diagnostic criteria of FH. Whereas the knowledge domain of inheritance had the highest σ (28.4), indicating that there was the greatest dispersion of scores from the mean with regards to inheritance.

Figure 12

Knowledge Domain Score by Years in Clinical Practice



Quantitative Phase Summary

Seventy completed surveys were analyzed (30.2% response rate) for total knowledge scores and knowledge domain scores by professional degree/license, subdivision, years in clinical practice at CUIMC and years in clinical practice. CHCPs with MDs ($\bar{x}$ of 12.5), at CUIMC for 6-10 years ($\bar{x}$ of 11.7), in clinical practice for 1-5 years ($\bar{x}$ of 11.4), and within the subdivision of Inpatient Services ($\bar{x}$ is 15.5) had the highest average total knowledge scores. Additionally, MDs scored highest across the knowledge domains of description, prognosis,

prevalence, diagnostic criteria, and management, while NPs scored highest in the knowledge domain of inheritance. CHCPs with a professional degree or license of RN ($\bar{x}$ is 7.5), at CUIMC for less than 1 year ($\bar{x}$ is 9.4), in clinical practice for 6-10 years ($\bar{x}$ is 9.8), and within the subdivision of Cath Lab ($\bar{x}$ is 8.7) had the lowest average total knowledge scores. RNs scored lowest across the knowledge domains of description, prognosis, inheritance, diagnostic criteria, and management. PAs scored lowest with regards to prevalence of FH.

Qualitative Interviews

Interview Participant Recruitment

Twenty-four CHCPs who completed the quantitative survey expressed interest in participating in follow-up individual semi-structured interviews. A subsample consisting of twenty-one participants were selected to confirm maximum variation among study participants. Twenty-one participants were contacted via email to schedule the qualitative interview via secure Zoom audio conferencing (Zoom, 2021). Twenty CHCPs responded, scheduled, and completed an interview corresponding to a 95.2% response rate.

Quantitative survey results were used to confirm maximum variation was obtained among the qualitative sample population. A total sum knowledge score was calculated for each completed survey. Surveys with a total knowledge score of zero to nine, receiving a score of 50.0% or less, were categorized as low knowledge. Surveys with a total knowledge score from 10 to 19, receiving a score of greater than 50.0%, were categorized as high knowledge. Interview participants were equally distributed by total knowledge score (i.e., 10 interviews were conducted with CHCPs with high knowledge scores and 10 interviews were conducted with CHCPs with low knowledge scores). Table 6 presents participants characteristics including professional degree/license, years at CUIMC, and years in clinical practice.

Table 6

Participant Characteristics

Characteristic	n	%
Professional Degree/License		
MD	5	25.0
PA	6	30.0
RN	3	15.0
NP	6	30.0
Years at CUIMC		
Less than 1 year	2	10.0
1-5 years	11	55.0
6-10 years	3	15.0
11-20 years	2	10.0
Greater than 20 years	2	10.0
Years in Clinical Practice		
Less than 1 year	1	5.0
1-5 years	6	30.0
6-10 years	7	55.0
11-20 years	2	10.0
Greater than 20 years	4	20.0

Interview Data Collection

Twenty interviews were completed over Zoom. Average interview length for all participants was 18.8 minutes. Interviews were audio-recorded and transcribed using Zoom software. Zoom transcriptions (total page length of 100) were reviewed, checked, and verified against the recordings by the researcher. Participants were assigned pseudonyms to protect their confidentiality and all transcripts were de-identified and password protected.

Thematic Analysis

Using both deductive and inductive coding, four overarching themes related to the practice behaviors of CHCPs in the screening, diagnosis, or management of FH in cardiology clinical practice were identified. Each theme is represented below with supporting evidence. Appendix G displays the preliminary coding schema that informed the four primary themes.

Theme 1: Variability in FH Care. The ability to provide comprehensive care to FH patients is highly dependent on the ability of CHCPs to first identify patients at risk for FH. Since FH causes elevated LDL-C levels, the lowest threshold for identification is through a lipid panel, or a blood test to screen for cholesterol measurements. Given the clinical practice setting of cardiology and the use of the lipid panel as a screening tool for cardiovascular disease risk, CHCPs frequently discussed the use of the lipid panel in clinical practice. However, CHCPs acknowledged the lack of standard practices for ordering a lipid panel and using the results.

> "Aside from your basic lipid panel and looking at whether or not they have higher LDL's, there's not a super great process to be completely honest. And perhaps my colleagues may disagree with me, but I worked with every single physician in our practice, and there's not really a standard way of looking for FH. Every physician is different in their clinical practice. So, they all kind of pick and choose when they want to draw a lipid panel very differently." (High Knowledge, RN)

Several CHCPs discussed other ways, beyond the use of a lipid panel, to identify patients at risk for FH such as through the collection of a detailed family history.

> "We get a family history…most of our patients who come to us with coronary artery disease, we know that we have to do bypass anyway, we know they need surgery, so we do get an extensive family history." (High Knowledge, NP)

Another CHCP described using findings from a comprehensive physical exam to identify patients at risk for FH.

> "If you're suspecting it, you probably already know what their cholesterol is. I would do physical exam to look for xanthomas and take a good family history." (Low Knowledge, MD)

While both can be used to diagnose patients with FH using the Simon Broome criteria and DLCN, participants described family history and physical exam in the context of screening for FH cases. Once patients at risk for FH are identified, a diagnosis can be made based on diagnostic criteria (i.e., MEDPED, Simon Broome, DLCN) using a variety of factors such as LDL-C levels, family history, physical exam, and genetic testing. All CHCPs with a professional degree of MD as well as non-MDs with experiential knowledge of FH (i.e., having previously cared for FH patients), were the only CHCPs to describe the care of FH patients beyond the point of screening.

> "How I care for them is multi-tiered in the sense that the approach is to not only to treat the patient, but also to give them the understanding that there is a genetic basis or concern, and that this extends to family screening as well, and offering that to them as far as giving them the information to relay to their family members. First you do a pedigree analysis and make sure that they meet the diagnostic criteria and then offering them the

various treatments, such as statin therapies or combination therapies, and offering them genetic testing." (High Knowledge, MD)

FH care beyond the point of screening also included provider descriptions of referring patients at risk for FH to specialists.

"If we think that they have familial hypercholesterolemia, if I'm sort of the first person to think of that, I would send them for genetic testing because it's important to advance our knowledge of it, and also for the children potentially. But also, I would try to send them to a lipid specialist because I don't feel comfortable myself managing that level of hypercholesterolemia." (Low Knowledge, MD)

CHCPs with experiential FH knowledge also described the use of genetic testing in the care of FH patients to inform medical management.

"I think it's important to get the genetics, because then you take the extra step. You do two things. You can tell them they have a genetic disorder of a single gene, try to explain what genetics are, that their parents have one bad mutation and one normal allele, etc., and that each of their children have a 50% chance of inheriting the same problem, and when do they want to screen the children for either LDL or for the genes. And then we talk about why we need to be aggressive. And depending on age obviously, and a lot of other things, we want to start early, we want to be aggressive and, depending on their age we even want to do a cardiovascular workup if that's never been done." (Low Knowledge, MD)

Theme 2: Importance of Identifying FH Early. To better understand how the behavioral beliefs and attitudes of CHCPs could influence the care of FH patients, the importance, advantages, and disadvantages of screening, diagnosing, and managing FH in

clinical practice were explored. CHCPs had both positive behavioral beliefs and attitudes toward addressing FH. CHCPs emphasized the importance of addressing FH as it would impact their day-to-day practice.

> "We would anticipate earlier that they would be resistant to certain therapies and that we would have to uptitrate at a little bit more aggressive manner. We would start thinking about more aggressive measures earlier. Instead of spending three months talking about diet and exercise, we might immediately seek medical therapy in the beginning instead of going on this slower titration of where they should be and what they probably need in the long run […] If you have this knowledge, and you see that they have these genetics, that it would be a way that it could focus your care and put it at the forefront." (High Knowledge, NP)

Participants also described how screening, diagnosing, and managing FH in clinical practice was important as it would impact their clinical decision-making in the care of patients with other indications.

> "The safety of what we can offer patients with arrhythmias is critically dependent on the absence or the presence of coronary artery disease. The best example of that would be a whole class of anti-arrhythmic drugs that otherwise could be effective, would be contraindicated in patients with high cholesterol, high LDL, familial hypercholesterolemia, or simply very high LDL levels in the presence of coronary artery disease…I need to know this kind of background, not just for efficacy of treatment, but for the safety of the treatment." (High Knowledge, MD)

A major benefit to addressing FH in clinical practice highlighted by CHCPs was the ability to practice preventive medicine. This concept of prevention was first discussed in the context of secondary prevention or reducing the impact of disease in an already affected patient.

> "Screening for FH is definitely advantageous for preventative measures. If you can get somebody on a statin sooner than later, or on the other types of cholesterol medications out there, then that could help prevent further hospitalizations and further ACS [acute coronary syndrome] events down the line, which aren't that far down the line, given these patients with premature CAD [coronary artery disease]." (High Knowledge, PA)

This idea of secondary prevention was further highlighted by CHCPs in the context of preventing the need for surgery.

> "I think that preventative medicine is super important. We're in the business of surgery so we have to fix things that are often due to unchecked underlying diagnoses or other comorbidities, so I think that the advantage in catching and treating these disease processes sooner, is that the hope is at some point we could prevent the surgery needing to be done." (High Knowledge, NP)

The second way that CHCPs highlighted preventive medicine as an advantage for addressing FH in clinical practice was through primary prevention or preventing the onset of disease.

> "It would be great because this way at least if you learn more about FH, you could help the whole family and not just your patient, as well as you can provide some sort of feedback to the patient and if they have kids, most of the time, that's when they're really worried to see what else we can give them, or how we can prevent coronary artery disease in them." (Low Knowledge, PA)

Primary prevention was most often discussed in the context of FH patients' family members.

> "As an adult cardiologist you're just seeing the adults but making sure that attention is also paid to the pediatric population, because patients have families and family members comprised of various ages and we want to get to them earlier, in order to prevent the onset of the pathology." (High Knowledge, MD)

Theme 3: Institutional, Practice Setting, and Individual Issues to Addressing FH. Even though CHCPs held positive behavioral beliefs and attitudes towards screening, diagnosing, and managing FH, their practice behaviors varied greatly. To better understand this gap, the normative beliefs, subjective norm, control beliefs, perceived behavioral control, and individual and external issues were further explored. A number of barriers and facilitators for CHCPs in the care of FH patients were identified. These barriers and facilitators were organized by institutional-level, practice setting, and individual-level issues.

Institutional Issues

With regards to institutional-level barriers, CHCPs described not only a lack of awareness of institutional resources but also unfamiliarity with referral mechanisms.

> "I would say probably lack of information or lack of access to cholesterolemia specialists. I'm not necessarily aware of them, so I would say that's probably the disadvantage- not knowing the protocol, how to treat these patients, where to send them." (Low Knowledge, PA)

CHCPs with MDs were more aware of institutional resources and referral mechanisms.

> "I'm fortunate to be in a tertiary care center and have the opportunity to avail myself to various colleagues who have expertise in all areas. If I personally don't have the

> wherewithal, I know that I have the ability to refer my patient to get what is the care that they need and the treatment that they need to undergo. I don't think there is any disadvantage [to addressing FH], especially when you think of yourself, not as the one person guiding a patient's care, but that you are part of a community and therefore, you have the ability to tap into all the information that's available to you." (High Knowledge, MD)

CHCPs with the professional degree of MD described how working at a large academic medical center was a facilitator to providing comprehensive care to FH patients.

> "These are big academic centers, and they have experts. If I cannot, by my prescription, by my simple following of guidelines, bring their cholesterol levels down by whatever is available, then I have a very low threshold to refer them for expert opinion to somebody whose career focus is lipidology. So that is one of the…the greatest attraction to practice medicine in an academic center for me is to be able to interact ideas and exchange patients with this kind of expertise which is fortunately available in most of the major academic centers." (High Knowledge, MD)

Practice Setting Issues

CHCPs in this study provided clinical care in a variety of practice settings (i.e., subspecialties, inpatient versus outpatient, night shift versus day shift). Across practice settings, CHCPs described several barriers to providing care to FH patients including a lack of guidance from leadership, time within a clinical encounter, prioritization of clinical care, workflow and responsibilities, and the prior authorization process.

The first practice setting barrier discussed was the lack of messaging provided to CHCPs regarding if and how to screen, diagnose, or manage patients with FH.

"I think that it's pretty clear that really there is no message given about what we should be doing or how we should be practicing differently to care for FH patients." (Low Knowledge, RN)

This lack of guidance from leadership negatively influenced participants' normative beliefs and subjective norm.

"I don't think we really talk about it all that much to be completely honest. I mean, we do address hyperlipidemia, but in regards to FH specifically, we really don't do a ton of proactive work within FH specifically to be completely honest." (High Knowledge, RN)

A second practice setting barrier addressed by CHCPs was the context of the clinical encounter. Participants described how specific clinical practice settings were less amenable to caring for patients with FH.

"[Subdivision] is a very procedural area, so we don't really get a lot of time to actually talk about cholesterol with them. In [subdivision], because it's a short term…it's a same day procedure essentially and patients usually leave within 24 hours. So, we don't really get to spend too much time with them, and they're always post-procedures, so they are usually sleeping or not really able to comprehend after having anesthesia for four or five hours, so it's hard to have a full-blown conversation with them about anything." (Low Knowledge, PA)

Additionally, CHCPs described how the prioritization of care within a clinical encounter could serve as a barrier to addressing FH in practice. For instance, CHCPs could have higher priority acute problems to address within an inpatient setting as opposed to an outpatient clinical encounter.

"It's because of the workflow. They come to us with a new event, we prescribe them Lipitor, and it's very much in the acute setting where you're not necessarily following up on them as an outpatient to see whether or not there's been a drop in their LDL and if you meet the goals for secondary prevention. It's not so much an actual real barrier to prescribe more medications, we just happen to see them at such a small phase, and we prescribe to them what they actually need in that timeframe." (High Knowledge, NP)

Another CHCP noted the acute practice setting as an issue in addressing the possibility of FH:

"Well, I think it's important but also, we deal with a lot of emergencies and things that would take priority over…Not saying that it's not important, but we're an inpatient setting. We deal with acute coronary syndrome like MIs [myocardial infractions]. Since we only have patients for a few days, and they are a lot more acutely sick. I think it's more important to make sure they have the right follow up." (High Knowledge, PA)

While CHCPs viewed FH to be out of their scope of practice due to their lack of lipid specialization or knowledge of FH, CHCPs also emphasized a deferral of FH care based on the workflow and responsibilities of particular practice settings.

"It's very much in the hands of the cardiologist who is seeing them as an outpatient. I have never sent anyone to a lipidologist on the inpatient side." (High Knowledge, NP)

Another CHCP described that in addition to working in the inpatient setting, that working the night shift could cause lipid problems to be out of the scope of practice for CHCPs.

"I'm a full-time night PA, so I actually don't refer anyone anywhere. It would be the day team." (Low Knowledge, PA)

Finally, CHCPs described the arduous process of prior authorizations to be a significant barrier in FH care.

> "I think that some of the new hyperlipidemia medications are becoming formulary. But if you start it in-house, you have to make sure that those medications are affordable for the patient. So, obtaining prior authorization is hard in an inpatient work environment because that could take several days, and the patient may be gone. It should be the outpatient follow-ups responsibility to get these prior authorizations, but we do our best by trying to initiate that when time permits." (High Knowledge, PA)

FH patients require lipid-lowering medications for their medical management, which often necessitates a healthcare provider to obtain approval from insurance companies prior to medication initiation. This process can be not only cumbersome with documentation but also requires a great deal of time. Therefore, clinical practice settings that do not have the administrative support to assist with prior authorizations view this process as a substantial practice setting barrier.

> "You have to have somebody in your office who will continually appeal. I've gotten on the phone with people who make a little extra money working for the insurance companies to do a peer evaluation. The prior approval paperwork is not easy. They make it difficult in terms of what they ask. The people looking at the paperwork are not physicians and not medical personnel. They're just given a script and they check off boxes, and if you have the wrong box checked off, they'll deny it. It's always denial until the last possible chance of denying is used up and then they'll say okay. So, we often have to send in two or three times to get a patient approved." (Low Knowledge, MD)

While CHCPs described many practice setting barriers to providing care for FH patients, one facilitator that was discussed was addressing FH in practice settings where FH could be the underlying reason for the clinical encounter.

> "In cath lab is where I would actually try to focus more on management and talking more about FH. Because when patients come for cardiac catheterization, they're always worried about their cholesterol because of the plaque that actually will cause coronary artery disease." (Low Knowledge, PA)

Providers discussed how FH care could be targeted to clinical practice settings such as cardiac catheterization, interventional cardiology, or surgery where the adverse effects of hypercholesterolemia are addressed, as opposed to electrophysiology or congenital heart disease in which chronic hypercholesterolemia is not the primary cause of the visit.

> "If I was back in interventional or surgery where I was trying to prevent that from reoccurring, hands down and make sure that they weren't coming in for a procedure, this would be higher up on our list. Because it's also…I'm dealing with them as an inpatient, I might have a chance of seeing them routinely." (Low Knowledge, PA)

Individual Issues

In addition to institution-level and practice setting issues, CHCPs also described barriers and facilitators at the individual-level. CHCPs highlighted both CHCP and patient-related issues that influenced their ability to provide FH care. With regards to barriers at the patient level, CHCPs described how a patient's insurance coverage affects a provider's ability to screen, diagnose, or manage FH in clinical practice.

> "I mean we always somehow try to maneuver a way to get them what they need, but cost is always a barrier, especially in these patient populations…The medicines end up being

expensive regardless. So, it's difficult to say that you need something when they can't financially afford it." (High Knowledge, NP)

Another patient-level issue that CHCPs discussed to be a barrier to addressing FH in clinical practice was a patient's health literacy level.

"One thing that is challenging, especially in [subdivision] clinic, because a lot of patients have typically lower health literacy and lower adherence to medications, sometimes it's hard to tell if they are compliant with their medications or if it's truly that their lipids are out of control, even on statins […] The question of whether people's lipids are out of control because of non-adherence issues or due to the fact that they need escalation therapy." (High Knowledge, MD)

Finally, a patient's hesitancy to begin medication and medication compliance was described by CHCPs to be a barrier to providing comprehensive FH care in clinical practice.

"Sometimes it takes a while for them [patients] to feel like they want to be on a statin if it's a new diagnosis or the thought process of being on a new medicine is obviously scary to some people, so sometimes it does take multiple draws or a few months to actually get them started on medication therapy." (High Knowledge, NP)

Participants also discussed CHCP-specific issues that serve as barriers to providing FH care such as feelings around prescribing medications.

"There's a little bit of hesitation on the provider side to order these drugs, knowing the barriers that will occur and the costs that will be involved. So I think if there was some laxness about how much money it is, we might be more inclined to order these meds more frequently and have them under better control." (High Knowledge, MD)

Another provider-specific barrier to providing comprehensive FH care in practice described by CHCPs was the difficulty of managing complex cases.

> "Whether I also check their lipid profile or not, honestly that may fall through the cracks one in five or one in six times. That shouldn't happen, but it does happen with too many details to worry about." (High Knowledge, MD)

Additionally, CHCPs discussed how finding FH-specific information served as a provider-level barrier to screening, diagnosing, or managing FH patients in practice.

> "A lot of things in cardiology are not simplistic. There's a lot of data that you have to parse through. So I guess that would be the barrier is trying to find what is specific to the questions that you have." (Low Knowledge, NP)

The final barrier for CHCPs to address FH in clinical practice was their lack of didactic and experiential knowledge of FH.

> "Honestly, prior to receiving the survey and the information, I did not know much about FH. It's not something I've really been exposed to in my nursing career." (Low Knowledge, RN)

This lack of FH knowledge negatively influenced providers' control beliefs and perceived behavioral control to screen, diagnose, and manage FH patients.

> "I think that my knowledge is quite limited, to be honest. When I was filling out the questionnaire ahead of time I was like, 'Oh man, I don't think I know. I feel like I got all of these wrong.' So, on a very nuanced level or a detailed level, I don't think I have a solid knowledge base of FH." (High Knowledge, NP)

In addition to individual-level barriers, CHCPs also highlighted facilitators at the individual level that influenced a CHCP's ability to provide FH care. With regards to a patient-

level facilitator, CHCPs described how a diagnosis of FH could reduce barriers related to the prior authorization process, insurance coverage, and cost of medications.

> "Right now we have some treatments which are so expensive. For example, PCSK9 inhibitor. If the patient cannot achieve the therapeutic goal after we put [them] on all the oral lipid medication, then the next step is, we will go to PCSK9 inhibitor. In order to get the insurance approved, the genetic testing results to confirm this is an FH patient is very helpful. I can say with the genetic result, it's 99.5% we'll get insurance approved." (Low Knowledge, NP)

Another individual-level facilitator that arose from the qualitative interviews was CHCPs' interpersonal relationships with other CHCPs as well as with pharmaceutical sales representatives. Specifically, CHCPs described how their relationships with other CHCPs address institution, practice, and individual-level barriers such as understanding institutional resources, mechanisms for referral, guidance from leadership, and knowledge of FH.

> "The attending physician and NP relationship is so important because we collaborate on everything, and I use them as a resource for questions and they're more experienced than I am. So, I lean on them for certain management questions." (Low Knowledge, NP)

CHCPs also described how their interpersonal relationships with pharmaceutical sales representatives can assist them in addressing barriers to FH care such as insurance coverage, cost of medication, prior authorization processes, and knowledge of FH.

> "We have started prescribing this more. Once again, there were a lot of barriers with it, with insurance, but it's starting to become a little easier. And the [pharmaceutical] reps are determining ways to make it easier for us to prescribe it, by sending it to this specific

pharmacy, and then they will help in whatever legal way they can to make prior authorizations easier to obtain." (Low Knowledge, PA)

Theme 4: Overcoming Barriers. CHCPs discussed several institutional, practice, and individual-level barriers to addressing FH in a cardiology clinical setting. To better understand how to overcome these barriers, potential interventions to assist with the screening, diagnosis, and management of FH patients were explored further in the qualitative interviews. CHCPs described several ways to overcome these barriers including the use of a referral system, education, standardized processes, and EHR applications. Further explanations of the advantages and disadvantages of possible interventions were also explored.

A need for a referral system was described by CHCPs outside of lipidology (i.e., CHCPs who wanted to refer patients to a lipid clinic), as well as CHCPs within a lipid specialty (i.e., CHCPs working in the lipid clinic who described a need for a higher patient volume).

"I think the best practice would really be a referral. Having some sort of referral process or consult to somebody a little bit more specialized so they can help guide the treatment." (Low Knowledge, RN)

Another CHCP emphasized the need for a seamless referral system to lipid specialists.

"I think the best intervention is a very easy way to refer patients that you think might have FH to genetic and lipid specialists. If there was a one-stop number that you could call to plug patients in, they'd probably get plugged in easier." (Low Knowledge, MD)

A CHCP specializing in lipids described the benefit of a referring system.

"If there's a referring system, they can directly refer to us. Especially in our clinic we have a [nurse] who is full time and scheduling time is more flexible, so the waiting time for a patient will be shorter. So, I think it's all about the referring and scheduling, and also

make people in the hospital, the other providers, aware that we exist. That we are specialists, and we are here to help, and if there's a system like that to make referring easier that'd be great. The most important thing is, we need to let the people in the hospital know we are here and honestly, we can spend more time with a patient. To explain FH in more detail. We don't have to rush. We have time and I think we can build a trust relationship [with the patient], and then the whole family eventually will come to us and, finally, we can help the FH patient. This is not something we can treat like taking antibiotics for seven days. This is lifelong, and this is a family genetic problem. It really takes time. You cannot do it rushing in a 15-minute or 10-minute phone call. […] So, if we have all the providers identify the patient…if they don't have time…if they don't know how to treat the patient, I think the best is that they refer to the lipid specialist to take care of the patient." (Lipid Specialty CHCP)

Another intervention often described by CHCPs was the use of educational initiatives such as lecture series, continuing medical education events, or case studies to improve the individual level-barrier of CHCPs' low FH knowledge.

"Having a lecture series. You need to be exposed to the disease and how to diagnose it and manage it. And exposure only comes if there's knowledge that's being disseminated. The best way to do that is from either a CME event or lecture series or case series. I think that would be the biggest intervention for other providers, including myself, is to have the ability to attend something that is either a workshop that's targeted towards genetic diseases and cardiovascular health, such as FH. So that people have the exposure and do know what's readily available to them. Not only what they can do themselves as providers, but where they can turn to and refer patients to." (High Knowledge, MD)

Participants noted that providing education to CHCPs may offer opportunities to address practice-setting barriers as well.

> "A grand rounds session, something that's educational or a topic that's included in a cardiovascular conference. A lot of the sessions that are about lipidology and lipid management talk in general population guidelines. And then it would end with 'Unless the patient has FH, that would be different then.' It's not discussed. What if they have FH? What am I going to do then? There's the general population and then there's FH, and the treatment for FH is different, but I don't think a lot of people shed light on that." (High Knowledge, NP)

When considering the advantages of educational interventions, CHCPs described how education can overcome individual-level provider barriers such as increasing cognitive awareness and knowledge of FH.

> "It's helpful in that there's always new therapies being initiated and then new recommendations in the guidelines that are good to stay abreast to, like checking lipoprotein a levels. Every time that you do have a seminar, it brings it fresh in your mind and so you're more aware of it. Also, having a lot of repetition in your education is really helpful and that helps solidify your knowledge of things." (High Knowledge, MD)

CHCPs also discussed how education provides ease of access to current practice guidelines.

> "If I am busy as a [subspecialist type] and if I hear, what I otherwise would spend hours to find out, in half an hour from an expert in the field, that's ready-made information to deliver to me on a silver plate, so that's easy." (High Knowledge, MD)

CHCPs recognized that a significant disadvantage to these educational initiatives includes planning, organizing, and scheduling these events to maximize participant attendance.

> "Well, we're all busy. If you do it too early, nobody goes. If you make it too late, everybody's tired. The problem with the seminar, although conceptually is probably the best idea, is finding a time that maximum number of people can attend." (High Knowledge, MD)

Another disadvantage of educational events addressed by CHCPs included the voluntary nature of these activities, and how voluntariness can affect attendance.

> "We get so many of those [educational seminars], and they're optional. So, most people will not go to it, even if it's 20 minutes because they don't have 20 minutes to sit down and listen to the whole thing in one session." (Low Knowledge, PA)

CHCPs also expressed a desire to have an intervention that aimed to standardize care such as using a protocol, checklist, or algorithm.

> "Education and some sort of standardized process or screening tool, to keep everybody on the same page. Because care can differ so much, so I would say continued education and standardization of a process." (Low Knowledge, RN)

Another CHCP described how a protocol or algorithm may be a useful intervention in screening and identifying patients at risk for FH.

> "I think to streamline, have an algorithm- this is the protocol, this is exactly who you can send them to for genetic testing or you could refer them outpatient to this cholesterolemia specialist, inpatient first line is high dose statin and then…yeah more of an algorithm." (Low Knowledge, PA)

Lastly, CHCPs described using EHR technology to assist with the screening, diagnosis, and referral of FH cases.

> "I would put something into the EHR that is an alarm, as a flag for the physicians to think about FH. They can use the [LDL of] 190, it's not perfect, but it's reasonable, and if a patient has an LDL over 190, an alert comes up and says, 'This is what you should do based on FH guidelines'." (Low Knowledge, MD)

Participants most often discussed using an alert within the EHR system Epic.

> "Some kind of EMR [electronic medical record]-related tool where you could pull in all of their lipid levels, even if it was from outside institutions, and then also you have to enter in people's family history and then enter in if they've had a cardiac event before and then the date…so there should be some way for Epic to integrate all that information and potentially create an alert for high-risk or low-risk and then give you the ability to then refer to lipid clinic, or genetic counseling. […] You could probably integrate something similar for the Dutch lipid criteria and that way you could plugin things and then get a likelihood of FH, and then maybe if it's high, then it could alert you to refer. Then for patients who already have an established diagnosis of FH, some kind of tool where you could track their progress in terms of lipid control and then it would alert you with suggestions like 'This needs to be under better control or consider referring', that would help." (High Knowledge, MD)

CHCPs described how this alert could assist in identifying patients based off LDL-C alone, stratifying low and high-risk patients, diagnosing patients using diagnostic criteria such as DLCN criteria, and managing patients previously diagnosed with FH.

"Some kind of a screening tool, where we would put in the patient data in terms of their age and some history and some lab results and press the magic button and then it would tell us, 'Oh this patient qualifies for a screening of FH', and then it follows from there." (Low Knowledge, RN)

One of the main advantages addressed by CHCPs for using an alert system as an EHR application to improve the care of FH patients was that alerts were part of providers' clinical workflow.

"If that is within Epic or within part of my workflow…it's very applicable. It's like 'oh here are signs to look out for, here are things to look out for.' And while I'm documenting, while I'm in the visit, it would be more useful to be able to just have that information right in front of me while I'm seeing the patient." (High Knowledge, NP)

Another advantage of using an alert system described by CHCPs was that alert systems increase the cognitive awareness of FH for providers.

"When we are in clinic and ordering labs, you're in a routine of doing things the way you've been doing it. And there's a little bit of 'Wait, why don't you think about this, or this number looks…have you thought about genetic testing?' I think that's helpful because it prompts you to start thinking in that way when I haven't been." (High Knowledge, NP)

CHCPs also discussed how an alert system prevents providers from deferring FH care based on individual, practice setting, or institutional barriers.

"It [an alert] keeps the physician from denying…kicking the can down the road…saying to the patient 'Are you sure you're taking your statin? Your numbers are not that great. What's your diet? Let's get another blood in six months.' And then that gets to be a

repetitive process of not doing anything different. So, I think those alerts can overcome inertia." (Low Knowledge, MD)

While CHCPs recognized that an FH alert could be valuable for improving the care of FH patients, they also addressed the disadvantages of using alerts in the EHR. The first disadvantage of using an alert system was the experience of alert fatigue.

"We have such alert fatigue that no one reads those boxes anymore. If there's a way to x out of them, we will find a way to x out of them." (High Knowledge, NP)

The second disadvantage described by CHCPs was not having the baseline knowledge of FH to understand the purpose of the alert.

"The disadvantage is not really knowing why you're ordering them. […] Why are you ordering it? What is the test? What are the results going to mean if you don't know enough about FH?" (High Knowledge, PA)

Qualitative Phase Summary

Twenty interviews were completed, and four overarching themes related to the practice behaviors of CHCPs in the screening, diagnosis, or management of FH in cardiology clinical practice were identified. First, the variability in FH care; second, issues related to addressing FH at institutional, practice setting and individual levels; third, the importance of identifying FH early; fourth, potential intervention approaches to overcome barriers to screening, diagnosing, and managing FH patients in cardiology practice.

Document Review

A review of the educational materials from 2018-2022 was conducted to determine the educational resources offered by the Division of Cardiology to CHCPs. These materials were reviewed and analyzed descriptively to determine if FH content was included, and if so, what

specific knowledge domains pertaining to FH (i.e., diagnostic criteria, management, prevalence, inheritance) were discussed. The Division of Cardiology at CUIMC offers three main educational opportunities including Cardiology Grand Rounds, Cardiovascular Seminar Series, and a fellowship lecture series.

Cardiology Grand Rounds is a series of lectures offered to a wide variety of CHCPs including MD, DO, PA, NP, LPN, and RNs. Over the course of four years from 2018 to 2022, a total of 60 lectures were provided and none contained content pertaining to FH. Another lecture series offered by the Division of Cardiology is called the Cardiovascular Seminar Series. The audience of this series is CHCPs with professional MD and DO licenses. From 2018 to 2022, a total of 71 lectures were provided and none contained content related to FH.

Finally, the fellowship lecture series was offered to MD and DO CHCPs within the Division of Cardiology. From 2018-2022, CHCPs were provided a total of 210 presentations within the fellowship lecture series. Of 210 presentations over the course of four years, four lectures (1.91%) provided educational content related to FH. One FH presentation was given annually from 2018 to 2022. The FH knowledge domains presented within this lecture included a general description of FH, prognosis, prevalence, inheritance, diagnostic criteria, and management options.

Mixed Methods Results

During the integrative phase of this study, three sources of data were compared to address research question three. This data included quantitative survey data, qualitative interview data, and a document review of materials provided by the Division of Cardiology. The use of multiple data sources allowed for triangulation in the data analysis process to compare and synthesize

quantitative and qualitative findings, as well as minimize threats to reliability and validity (Creswell & Creswell, 2013; Creswell & Plano Clark, 2018; Grol, 2013).

Data Integration

Results from the document review and qualitative interviews explained some key findings from the quantitative survey in this explanatory sequential mixed methods study. The primary objective of this research was to describe the practice behaviors of CHCPs in the screening, diagnosis, and management of FH, as well as gain a deeper understanding of the perspectives of CHCPs regarding FH screening and diagnosis interventions that can be implemented in cardiology clinical practice. Exploring the factors that influence the knowledge and practice behaviors of CHCPs contributes to knowledge to better understand the role of CHCPs in the care of FH patients and target early intervention strategies to reduce morbidity and mortality associated with underdiagnosed and undertreated FH cases.

When examining quantitative survey results regarding total knowledge score, CHCPs with MDs ($\bar{x}$ of 12.5), at CUIMC for 6-10 years ($\bar{x}$ of 11.7), in clinical practice for 1-5 years ($\bar{x}$ of 11.4), and within the subdivision of Inpatient Services ($\bar{x}$ is 15.5) had the highest average knowledge scores. Additionally, MDs scored highest across the knowledge domains of description, prognosis, prevalence, diagnostic criteria, and management, while NPs scored highest in the knowledge domain of inheritance. CHCPs who have been in clinical practice for 1-5 years scored the highest across four knowledge domains including prognosis, prevalence, diagnostic criteria, and management. CHCPs who have been in clinical practice for less than 1 year scored highest with regards to the description knowledge domain, and CHCPs who have been in clinical practice for 11-20 years scored had the highest score for the knowledge domain of inheritance.

Data from the qualitative interviews and document review helped to interpret the quantitative results. CHCPs with an MD or experiential knowledge of FH were the only providers to describe FH care beyond the point of screening such as taking a detailed family history, performing a thorough physical exam, or referring to lipid specialists. Additionally, CHCPs with a professional degree of MD were the only provider type to describe how working at an academic medical center was a facilitator to providing comprehensive care to FH patients through knowledge of institutional resources and referral mechanisms. Review of the educational material provided by the Division of Cardiology further highlighted that CHCPs with a professional degree of MD were provided lectures through the fellowship lecture series pertaining to the prognosis, prevalence, inheritance, diagnostic criteria, and management options for FH.

When examining quantitative survey results regarding total knowledge score, CHCPs with a professional degree or license of RN ($\bar{x}$ is 7.5), at CUIMC for less than 1 year ($\bar{x}$ is 9.4), in clinical practice for 6-10 years ($\bar{x}$ is 9.8), and within the subdivision of Cath Lab ($\bar{x}$ is 8.7) had the lowest average knowledge scores. Additionally, RNs scored lowest across the knowledge domains of description, prognosis, inheritance, diagnostic criteria, and management. PAs scored lowest with regards to prevalence of FH. CHCPs who have been in clinical practice for less than 1 year scored the lowest across five knowledge domains including prognosis, prevalence, inheritance, diagnostic criteria, and management. Further CHCPs who have been in clinical practice for 11-20 years scored lowest on the description knowledge domain.

CHCPs with a professional degree of RN or PA discussed using a lipid panel routinely in clinical practice, but not utilizing the lipid panel to screen or diagnose patients with FH.

Additionally, RNs and PAs often described receiving education in school or training pertaining to hypercholesterolemia in general, but not specifically to FH. One CHCP highlighted:

> "Well, in general, it's not something that…maybe it's just not my experience, but I don't think it's something that was taught or even specified in my school as a nurse, specifically for familial disease. But in general, we know what's the normal cholesterol and what drugs to use, but it's not really specified in school" (Low Knowledge, RN).

Review of the educational material provided by the Division of Cardiology further highlighted that while CHCPs with a professional degree of RN or PA attended Grand Rounds, there was no education at Grand Rounds pertaining to FH.

Summary

Chapter 4 discussed the quantitative, qualitative, and mixed methods results of this explanatory sequential mixed methods research study. The chapter provided quantitative survey analysis by total knowledge score and knowledge score by knowledge domain. Additionally, thematic analysis from interview data, descriptive analysis of the document review, and an integrative analysis of mixed methods results were presented. Chapter 5 will provide a discussion of the findings grounded by the study's conceptual frameworks, the KTA and TPB. Finally, study limitations, future directions for translational research, and conclusions will be discussed in Chapter 5.

CHAPTER 5: DISCUSSION

Introduction

Familial Hypercholesterolemia (FH) is among one of the most common genetic disorders; however, it is significantly underdiagnosed and undertreated (Benito-Vicente et al., 2018; deGoma et al., 2016; Hasnie et al., 2018; Hendricks-Sturrup et al., 2020; Leren et al., 2008; Nordestgaard et al., 2013; Repas & Tanner, 2014; Zimmerman et al., 2019). Given the concurrence of underdiagnosis and adverse cardiovascular outcomes associated with FH, cardiology healthcare providers (CHCPs) are well situated to screen and diagnose patients with FH (Foody, 2014). The goal of this research was to explore factors and potential interventions that may support CHCPs in the processes involved with screening, diagnosis, and management of patients with FH who present for cardiac care.

The aim of this chapter was first to discuss the major findings of this research in the context of the study's conceptual frameworks, study aims, and research questions. Second, present an intervention map, implementation plan, and recommendations for translational research. Third, address the limitations of this research.

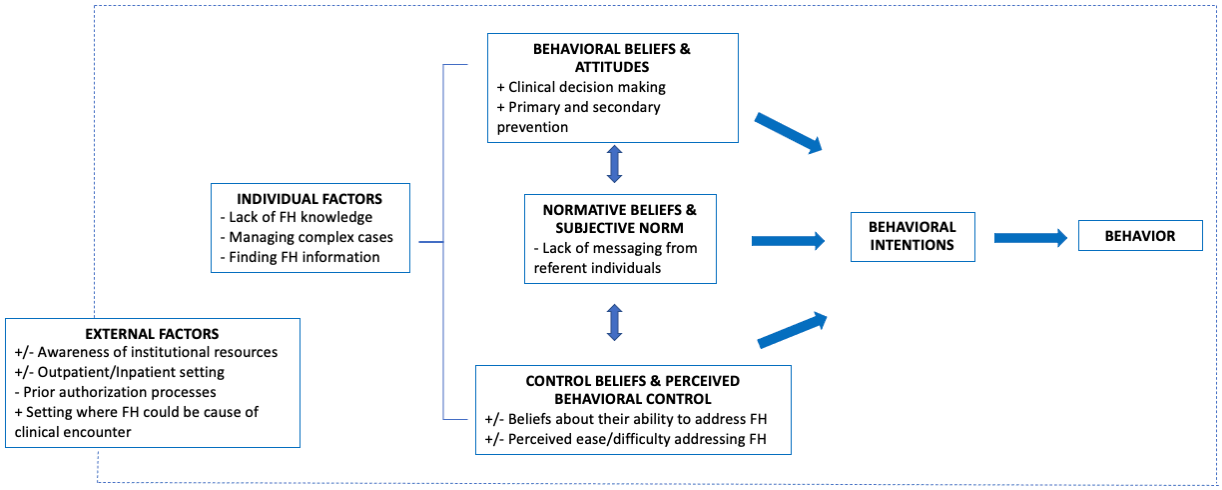
Major Findings

This research was one of the first known studies in the United States that exclusively explored the knowledge and practice behaviors of CHCPs in the screening, diagnosis, and management of patients with FH. The study population included MDs, PAs, NPs, and RNs across 15 subdivisions in the Division of Cardiology at Columbia University Irving Medical Center (CUIMC) in Washington Heights, New York. While CHCPs expressed the importance of addressing FH in clinical practice, there was a wide range of practice behaviors related to the care of FH patients. Figure 13 highlights the individual, practice setting, and institutional issues

identified in this research. Understanding the barriers and facilitators that may influence FH practice behaviors can contribute to the development of future interventions and implementation strategies to help CHCPs address FH in cardiology clinical practice.

Figure 13

Summary of Major Findings



Interpretation and Discussion of Findings

Knowledge to Action Gap

One of the primary goals of this research was to understand how a CHCP's FH knowledge may influence their practice behaviors in the care of FH patients. As such the knowledge translation framework, KTA, was utilized as a guiding framework for this study. The first step in the action cycle of the KTA distinguishes between the gap in evidence-based knowledge and current practice, known as the knowledge to action gap (Graham et al., 2013). Data from the quantitative and qualitative phases aimed to highlight the FH knowledge to action gap among CHCPs in cardiology practice at CUIMC.

This study's literature review examined the existing evidence-based knowledge pertaining to the definition, prevalence, prognosis, inheritance, diagnostic criteria, and

management of FH. The quantitative survey first identified CHCPs' overall knowledge of FH by examining the total knowledge score across provider types. Total knowledge scores were highest for MDs, followed by PAs, NPs, and RNs. An examination of the gap in knowledge within each knowledge variable was also explored. MDs scored highest across description, prognosis, prevalence, diagnostic criteria, and management, while NPs scored highest in the knowledge variable of inheritance. RNs scored lowest in description, prognosis, inheritance, diagnostic criteria, and management, while PAs scored lowest in the knowledge variable of prevalence.

Qualitative interviews explored current FH practice behaviors to understand how a CHCP's level of FH knowledge influenced their care of FH patients. With regards to screening, participants described the lack of standard practices around when to order a lipid panel and the use of lipid panel results. While the use of a detailed family history and comprehensive physical exam were described to screen FH cases, neither were discussed in the context of diagnosing FH. CHCPs with a professional degree of MD or with experiential knowledge of FH were the only CHCPs to describe the care of FH patients beyond the point of screening such as referring patients to lipid specialty clinics or using genetic testing for diagnosis and management. Additionally, CHCPs across all professional degrees/licenses expressed limited knowledge of FH, which served as an individual-level barrier to screening, diagnosing, and managing patients with FH. Finally, a review of the education provided by the Division of Cardiology highlighted that only MDs who attended the fellowship lecture series were provided educational content related to FH. Analysis of quantitative, qualitative, and document review data emphasized the gap in knowledge between the evidence of FH and CHCPs' clinical practice behaviors at CUIMC.

Factors that Contribute to Knowledge to Action Gap

In order to minimize the knowledge to action gap and determine ways to translate FH evidence-based knowledge into cardiology clinical practice, it was important to first understand the factors that contribute to this gap. Figure 13 displays the major findings from the quantitative and qualitative phases that influence CHCPs' practice behaviors related to the screening, diagnosis, and management of FH.

One of the most important factors that affected a CHCP's ability to care for patients with FH highlighted through this research was a provider's knowledge of FH. As described by participants, there were two ways to obtain FH knowledge: through education (didactic knowledge) or through practice (experiential knowledge). Didactic and experiential exposure could occur in a variety of settings such as in health professional training, clinical rotations, conferences, lecture series, or on the job in clinical practice. Exposure to FH, either through didactic or experiential opportunities, was a critical first step to improve the screening, diagnosis, and management of FH. Without knowledge of the condition, CHCPs will not recognize FH in their clinical encounters, nor will CHCPs be able to screen, diagnose, or manage FH patients.

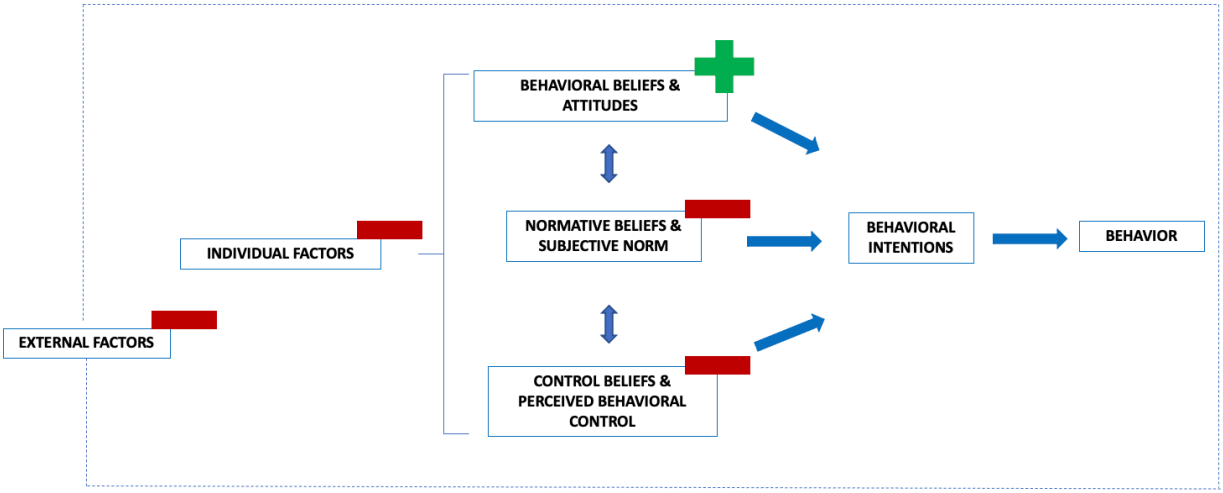
The inability to recognize FH may also influence a provider's perception of the prevalence of FH. FH is a common genetic disorder with a prevalence of 1 in 200 to 1 in 250, and is significantly underdiagnosed and undertreated (Benito-Vicente et al., 2018; deGoma et al., 2016; Hasnie et al., 2018; Hendricks-Sturrup et al., 2020; Leren et al., 2008; Nordestgaard et al., 2013; Repas & Tanner, 2014; Zimmerman et al., 2019). Given the negative cardiovascular effects associated with untreated FH, it could be reasoned that CHCPs in this study have likely encountered patients with FH in clinical practice. However, the majority of CHCPs in this study expressed having limited or no exposure to FH in their training or clinical practice. This disclosure highlighted the likelihood that patients with FH were underdiagnosed and

undertreated at CUIMC. While limited FH knowledge among CHCPs contributes to the lack of comprehensive care for FH patients, other contributing factors need to be assessed to better understand how to tailor interventions to improve FH patient outcomes at CUIMC.

Given that this study aimed to explore the practice behaviors of CHCPs in the care of FH patients, the TPB was used to better understand the factors that influence behavior. Quantitative and qualitative data from this study were used to determine how constructs from the TPB positively or negatively influence a CHCP's behavior to screen, diagnose, and manage FH patients in cardiology practice (Figure 14). It was critical to understand how the constructs from the TPB could serve as barriers or facilitators to providing FH care for CHCPs to create and tailor behavior change interventions to the audience of CHCPs and context of cardiology.

Figure 14

TPB Influences



Beyond CHCPs' level of FH knowledge, other individual issues that serve as barriers to screening, diagnosing, and managing FH in cardiology practice included providers' hesitancy about prescribing lipid lowering medications due to the perceived barriers to get these medications approved, managing complex cardiac cases and prioritization of care, and difficulty

finding FH information and resources. Individual-level facilitators for CHCPs were the interpersonal relationships with individuals who had higher levels of FH knowledge such as other CHCPs or pharmaceutical sales representatives. A key underlining aspect of these interpersonal relationships was the necessity for one party to have a high level of FH knowledge, without which these interpersonal relationships may have served as a barrier to FH care.

This research aimed to examine factors that may influence behavior change in CHCPs. Providers described several patient-level issues during the qualitative interviews that may influence CHCP practice behaviors in the screening, diagnosis, and management of FH patients. Patient barriers, as described by CHCPs, included insurance coverage, hesitancy to start new medications, health literacy level, and medication compliance. Even though CHCPs can screen, diagnose, and manage FH in clinical practice, to ensure that there are improved patient outcomes, patient issues need to be further explored. Thus, a limitation of this study and an area of emphasis for future research includes exploring the TPB constructs from the patient perspective to determine the barriers and facilitators to a patient's behavior change related to FH and to develop patient-centered behavior change interventions.

The lack of FH knowledge expanded beyond FH-specific content such as inheritance, prognosis, and diagnostic criteria, and included lack of FH institutional knowledge. Not having knowledge of institutional resources such as lipid clinics or genetic specialists, as well as mechanisms for referrals to these resources, acted as a barrier for CHCPs to provide the standard of care to FH patients. CHCPs described practice setting barriers such as limited time in a clinical encounter and FH being beyond their scope of practice, as barriers to clinical FH care. Therefore, if CHCPs don't have the resources (i.e., knowledge, time) to diagnose or manage FH,

the minimum that CHCPs could do is refer FH patients to providers with the knowledge, skills, and resources to provide comprehensive FH care.

This research highlighted that having FH content knowledge and FH institutional resource knowledge influences CHCPs' control beliefs, perceived behavioral control, normative beliefs, and subjective norm. Providers with didactic or experiential FH knowledge had positive control beliefs and higher levels of perceived behavioral control, leading them to provide FH care beyond the point of screening such as making referrals, diagnosing, or managing FH patients. Unfortunately, these CHCPs with high FH content knowledge and institutional resources knowledge were a minority in the qualitative phase of this study. The majority of CHCPs in the qualitative phase, including both low and high knowledge CHCPs, described having a limited knowledge of FH and institutional resources, which negatively influenced their control beliefs and perceived behavioral control, as these CHCPs did not feel equipped with the knowledge, skills, and resources to screen, diagnose, or manage FH patients. Additionally, CHCPs emphasized the lack of messaging from referent individuals such as subdivision leadership, other CHCPs, or Division of Cardiology leadership.

This lack of messaging negatively influenced CHCPs' normative beliefs and subjective norm. Even though participants had positive behavioral beliefs and attitudes towards providing care to FH patients in cardiology practice, the innumerable barriers at the individual, practice setting, and institutional levels negatively influenced CHCPs' normative beliefs, subjective norm, control beliefs, and perceived behavioral control (Figure 14). While CHCPs expressed the value of addressing FH in clinical practice, their lack of knowledge and resources prevented them from performing behaviors related to screening, diagnosing, and managing FH. This study

highlighted that to improve FH patient outcomes at CUIMC, CHCPs not only need to increase their content knowledge of FH but also their knowledge of FH institutional resources.

Directions for Translational Research

Intervention

When considering ways to improve CHCPs' knowledge of FH, minimize the knowledge to action gap, and translate FH evidence-based knowledge to cardiology clinical practice, it is essential to first select the knowledge to be translated. Clinical practice guidelines (CPGs) for FH have been published by the National Lipid Association, American College of Cardiology, American Heart Association, and International Family Heart Foundation (Gidding et al., 2015; Grundy et al., 2019; Jacobson et al., 2015). While CPGs deliver current scientific evidence to assist providers with clinical decision-making, the existence of multiple CPGs and inapplicability of CPGs to the local context (i.e., institution or practice setting) may serve as barriers to knowledge uptake and utilization. Guideline adaptation processes outlined by ADAPTE or CAN-IMPLEMENT can be used to select and modify FH CPGs to meet the needs of patients, CHCPs, and CUIMC's cardiology practice setting (Graham et al., 2013; Harrison et al., 2013; Straus et al., 2019).

While national and international FH CPGs provide information related to the six knowledge variables addressed in the quantitative phase of this study, they do not provide practice setting or institution-specific knowledge such as referral information to lipid specialists or genetic testing services. Using ADAPTE or CAN-IMPLEMENT processes to create tailored FH CPGs for CUIMC's Division of Cardiology can help to overcome individual, practice setting, and institutional barriers to caring for FH patients (Harrison et al., 2013). Additionally, the use of a CUIMC-specific FH CPG may positively influence CHCPs' normative beliefs and

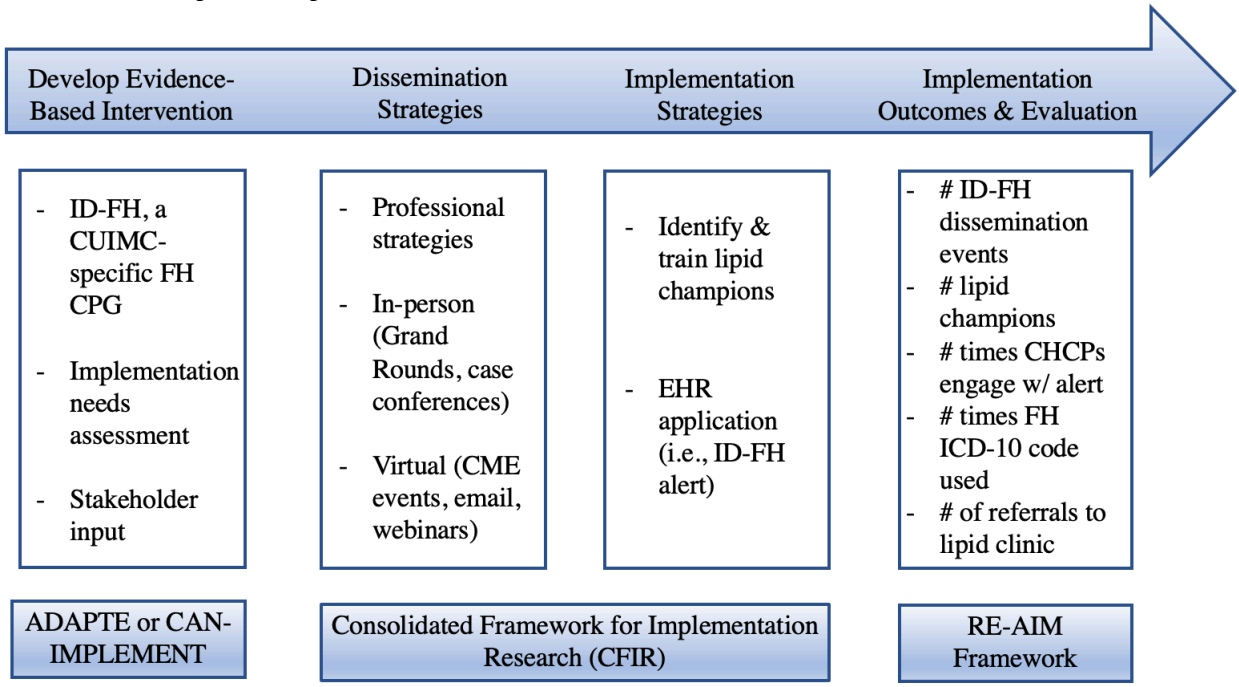
subjective norm, as well as increase CHCPs' control beliefs and perceived behavioral control. The proposed intervention, ID-FH (Identify & Diagnose-FH), includes the development, dissemination, implementation, and evaluation of a CUIMC-specific FH CPG across the Division of Cardiology. The intervention map and implementation plan related to ID-FH will be further described below.

Intervention Mapping

Implementation science is the scientific study of methods to promote the uptake of evidence-based knowledge in clinical practice (Grol, 2013; Nilsen, 2015). When considering how to create, implement, and evaluate ID-FH, implementation strategies such as intervention mapping can be utilized. Intervention mapping provides guidance using systematic processes involved in the development, adaptation, implementation, adoption, and evaluation of health promotion interventions (Bartholomew Eldredge et al., 2016; Fernandez et al., 2019; Grol, 2013). Additionally, the use of the Consolidated Framework for Implementation Research (CFIR) and Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework can play a pivotal role in guiding implementation and evaluation of ID-FH (Damschroder et al., 2009; Glasgow et al., 1999; Nilsen, 2015; Stetler et al., 2006). Processes involved in intervention mapping informed by constructs of CFIR and RE-AIM will be further elaborated to describe the intervention, implementation, and evaluation of ID-FH (Figure 15).

Figure 15

Intervention Map and Implementation Plan



ID-FH Development. The first step of intervention mapping includes conducting an implementation needs assessment (Fernandez et al., 2019). It is critical to engage all relevant stakeholders in this needs assessment to inform the creation of ID-FH. Relevant stakeholders include division and subdivision leadership, as well as CHCPs providing clinical care with varying levels of FH knowledge across different subdivisions of cardiology. It is important to include both ID-FH implementers (i.e., individuals who are providing instruction regarding how to use ID-FH) and adopters (i.e., individuals who are using ID-FH in clinical practice) in the process of intervention development to promote ID-FH utilization and adoption among CHCPs in cardiology clinical practice.

During the implementation needs assessment, barriers and facilitators to implementation should be accounted for. The five primary domains of CFIR, including intervention characteristics, individual characteristics, inner setting, outer setting, and implementation processes, can be used to guide barrier and facilitator identification (Damschroder et al., 2009).

With regards to the characteristics of ID-FH, the criteria for FH identification and diagnosis, adaptation of evidence-based FH guidelines, and complexity of ID-FH need to be assessed. As previously discussed, implementation factors related to relevant stakeholder groups, such as FH knowledge, identification within CUIMC, and attitudes about ID-FH, can affect implementation. The culture, climate, organizational readiness for change, and communication networks of CUIMC are inner setting factors that can impact ID-FH implementation (Damschroder et al., 2009; Grol, 2013). Outer setting considerations include the location of CUIMC, community resources, and governmental insurance policies. Finally, implementation processes include planning, engaging, executing, reflecting, and evaluating (Damschroder et al., 2009; Grol, 2013). Using intervention mapping processes guided by CFIR will move the intervention, ID-FH, through the action cycle of the KTA including adapting knowledge to the local context, assessing barriers and facilitators to knowledge use, and selecting and tailoring ID-FH to CHCPs and cardiology practice (Bartholomew Eldredge et al., 2016; Damschroder et al., 2009; Fernandez et al., 2019; Graham et al., 2013; Grol, 2013).

ID-FH Dissemination and Implementation. Qualitative data provided CHCP perspectives about strategies to overcome individual, practice setting, and institutional barriers at CUIMC that can be considered in the dissemination and implementation of ID-FH. As described by Grol (2013), professional strategies can be utilized to disseminate ID-FH through the Division of Cardiology listserv, division and subdivision-specific protocols, and educational meetings (lecture series, continuing medical education events, workshops, case conferences). In a study conducted by Weng et al (2018) a one-hour FH education intervention was provided to general practitioners and practice nurses across six UK general practices. This education intervention improved clinical practice in a variety of ways such as repeating cholesterol tests, assessing

family history of heart disease, diagnosing secondary cause of hypercholesterolemia, examining clinical features, and improving statin prescription for individuals diagnosed with FH using the Simon Broome criteria (Weng et al., 2018).

CHCPs at CUIMC described limitations to FH educational initiatives including the voluntary nature of educational activities, lack of time to attend, as well as planning, organizing, and scheduling these events to maximize attendance. Thus, it is critical to make ID-FH available to CHCPs virtually to minimize barriers related to access to information. Additionally, synchronous and asynchronous educational activities should be offered to maximize CHCP attendance and minimize time constraints. Providing education about ID-FH to CHCPs will aim to not only increase CHCPs' didactic knowledge of FH, but also positively influence CHCPs' normative beliefs, control beliefs, subjective norm, and perceived behavioral control with the long-term goal of improving CHCPs' FH practice behaviors.

The first proposed ID-FH implementation strategy is to utilize "lipid champions" across the Division of Cardiology to assist in the implementation and adoption of ID-FH in clinical practice. This study highlighted how CHCP interpersonal relationships were a facilitator to providing care for FH patients. Lipid champions would be CHCPs who had positive behavioral beliefs and attitudes to screening, diagnosing, and managing FH in cardiology practice. These champions would also aim to represent a variety of professional degrees/licenses, subdivisions, and years in clinical practice.

Results from the quantitative phase highlighted that CHCPs with MDs, at CUIMC for 6-10 years, in clinical practice for 1-5 years, and within the subdivision of Inpatient Services had the highest average total knowledge scores. While MDs scored highest across five of the six knowledge domains (description, prognosis, prevalence, diagnostic criteria, and management),

NPs scored highest in the knowledge domain of inheritance. This data can be used as a preliminary strategy to identify lipid champions across the Division of Cardiology.

Once lipid champions were identified, then ID-FH training could be conducted to increase their didactic and experiential knowledge of FH, as well as improve their control beliefs and perceived behavioral control to caring for patients with FH. Lipid champions would then be able to implement ID-FH in their clinical practice setting, as well as utilize their interpersonal relationships to train other CHCPs to use ID-FH. This implementation strategy would also aim to increase the normative beliefs and subjective norm of other CHCPs, as referent individuals such as colleagues, were approving of behaviors related to screening, diagnosing, and managing FH in cardiology practice.

Findings from the quantitative phase can provide guidance for ID-FH implementation through the use of lipid champions. CHCPs with a professional degree or license of RN, at CUIMC for less than 1 year, in clinical practice for 6-10 years, and within the subdivision of Cath Lab had the lowest average total knowledge scores. While RNs scored lowest across the knowledge domains of description, prognosis, inheritance, diagnostic criteria, and management, PAs scored lowest with regards to prevalence of FH. This data highlights that the target group for ID-FH implementation includes RNs, PAs, and CHCPs in Cath Lab. This implementation strategy is further supported by qualitative data in which CHCPs described Cath Lab as a practice setting facilitator since FH could be the underlying reason for the clinical encounter. Other practice setting facilitators identified in the qualitative interviews where ID-FH can be implemented include an outpatient setting, a less procedure-focused practice and during day shift.

While the use of lipid champions in the Division of Cardiology at CUIMC to improve the clinical care of FH patients is new to cardiology, the concept of best practice champions is familiar to the field of nursing. Ploeg et al (2010) conducted an exploratory mixed methods study to determine how nursing best practice champions influence the diffusion of the Registered Nurses' Association of Ontario's best clinical practice guidelines (CPG) (2009b). Qualitative and quantitative data revealed that champions disseminated CPG information through several ways including education, awareness, and serving as a resource to support and mentor nurses (Ploeg et al., 2010). Additionally, champions were found to be persuasive leaders working on interdisciplinary teams to advocate for evidence-based practice using CPGs (Ploeg et al., 2010). Finally, champions were able to tailor CPG implementation strategies to the organizational context (Ploeg et al., 2010).

Another strategy to implement ID-FH across the Division of Cardiology at CUIMC is to utilize the EHR system. While lipid champions are limited by their reach across all subdivisions of Cardiology and their interpersonal relationships with all CHCPs, the EHR system provides a unique opportunity as an implementation platform since CHCPs engage with it routinely in practice. ID-FH can be programmed within the EHR as an alert to provide CHCPs with clinical decision support during encounters with patients at risk for FH. Implementing ID-FH through the EHR will not only aim to improve CHCP didactic knowledge of FH, but also their experiential FH knowledge as CHCPs will be applying ID-FH content knowledge in real-time patient encounters.

When implementing ID-FH in the EHR it is important to consider the content, timing, frequency, and format of the alert itself. With regards to content, ID-FH can be tailored to offer concise and straightforward guidance for an EHR alert (Bangash et al., 2020; Hasnie et al., 2018;

Persson Lindell et al., 2022). To reduce CHCP burden and alert fatigue, ID-FH can be programmed to appear for specific CHCP characteristics (i.e., professional degree/license, subdivision) and patient issues (i.e., cholesterol level, age) (Bangash et al., 2020; Hasnie et al., 2018; Persson Lindell et al., 2022). The ability for the EHR alert to be programmed for specific CHCP characteristics will be dependent on to whom and where ID-FH will be rolled out. For example, if piloting ID-FH with fellows, then programming ID-FH to appear for only the professional degree of MD will be an important consideration. With regards to frequency and format, considerations should be made on how often the alert will appear for CHCPs, if the alert will be passive or active, as well as recognizing the action a CHCP should take from engaging with the alert (i.e., making a referral) (Bangash et al., 2020; Hasnie et al., 2018; Persson Lindell et al., 2022). During the pre-implementation phase, quantitative and qualitative data should be gathered to enhance the CHCP experience and EHR interface to improve uptake and utilization of the ID-FH alert.

ID-FH Evaluation. The RE-AIM framework consists of five constructs (reach, efficacy, adoption, implementation, maintenance) that can be utilized to evaluate the implementation of ID-FH in cardiology practice at CUIMC (Glasgow et al., 1999). In order to understand the reach of ID-FH, several evaluative figures can be determined across the Division of Cardiology as well as within various subdivisions. For instance, the number of educational opportunities including ID-FH content, the number of lipid champions, and the number of times CHCPs engage with the ID-FH alert can be gathered to better understand the number of individuals who receive or are affected by ID-FH (Glasgow et al., 1999; Miller et al., 2021).

To evaluate the effectiveness of ID-FH implementation, data can be collected through quantitative and/or qualitative means by exploring changes in knowledge, attitudes, behavioral

beliefs, subjective norm, normative beliefs, perceived behavioral control, control beliefs, and practice behaviors related to screening, diagnosing, and managing FH in cardiology practice after ID-FH dissemination and implementation strategies have been employed (Glasgow et al., 1999; Miller et al., 2021). To understand the adoption of ID-FH in clinical practice at the institutional level, it would be important to recognize what subdivisions provide ID-FH educational content, have lipid champions, and more often engage with the ID-FH alert (Glasgow et al., 1999; Miller et al., 2021). To evaluate the ID-FH implementation strategies at the institutional level, it would be beneficial to explore the barriers and facilitators to the use of lipid champions and the ID-FH alert in cardiology practice (Glasgow et al., 1999; Miller et al., 2021). Finally, when considering how to sustain ID-FH over time (Glasgow et al., 1999; Miller et al., 2021).

Limitations

This dissertation research had several limitations. The quantitative phase yielded a total of 70 completed surveys which may not be representative of all subdivisions of Cardiology, cardiology professional degrees/licenses, years of clinical practice, levels of FH knowledge, as well as FH experiences and practice behaviors. Further, selection bias may have occurred among CHCPs who elected to participate in the survey. CHCPs were provided a brief description of the study details in the recruitment email which identified FH as the central topic of study. CHCPs with prior knowledge or experience with FH may have been more likely to participate in the survey. Additionally, the inability to observe participants while taking the survey may have resulted in a mis-categorization of CHCPs as high or low knowledge if additional resources such as online reference tools or other CHCPs were utilized to complete the quantitative survey.

Within the qualitative phase, a total of 20 CHCPs participated in semi-structured interviews. Qualitative data provided an in-depth and nuanced understanding of the experiences

of CHCPs in the screening, diagnosis, and management of FH. While the sample of 20 individuals represented a diversity of subdivisions, levels of FH knowledge, and professional degrees/licenses, this sample cannot be considered representative of CHCPs broadly. The findings from the quantitative and qualitative phases may not be generalizable to other practice settings (i.e., primary care, pediatrics, family medicine), institutions, or patient populations. However, the use of quantitative and qualitative data provided rich descriptions of cases and allowed readers to determine aspects of this research that could be transferable to other practice setting, institutions, or patient populations. Finally, while this research explored the knowledge and practice behaviors of CHCPs, it neglected to account for the perspective of FH patients. To better understand the factors that affect the screening, diagnosis, and management of FH, the knowledge and health behaviors of FH patients should be further explored.

Future Research

While research continues to expand our knowledge of the pathology, genetic contributions, and pharmacogenomic treatment options for FH, this study highlighted the necessity for more research addressing T3 chasms of the translational spectrum. If providers on the frontline of patient care are unable to screen or diagnose FH in clinical practice, then how do T1 and T2 research efforts translate to improved health outcomes for patients with FH?

FH patients present to care in a variety of settings. While this study focused on the clinical context of cardiology specifically with CHCPs, future research needs to explore the barriers and facilitators to FH care in other practice settings (i.e., primary care, family medicine, pediatrics), as well as explore the experiences related to screening, diagnosing, and managing FH among other healthcare professionals. Additionally, like many chronic health conditions, diagnosis is simply the first step to improving long-term health outcomes. To minimize the

adverse health outcomes associated with FH, future research should explore FH patient experiences to identify patient issues such as the ability to afford medications, health literacy level, and medication compliance that may influence the screening, diagnosis, and management of FH.

This research aimed to elucidate the factors that influence the clinical care of FH in cardiology practice at a single academic medical center. The knowledge gained from this study may be translated to other demographic regions, practice settings, and patient populations. Future research centered on addressing T3 and T4 gaps in FH knowledge can not only bridge translational chasms and inform future research, but also make significant progress in addressing the underdiagnosis and undertreatment of FH.

Summary

Chapter 5 provided a discussion of the major findings of this dissertation research in the context of the study's aims, research questions, and conceptual frameworks. Additionally, Chapter 5 presented an intervention map, implementation plan, and recommendations for translational research to support CHCPs in the screening, diagnosis, and management of FH patients who present for care in cardiology practice. Finally, this chapter addressed the limitations of this dissertation research.

Conclusion

This research utilized an explanatory mixed methods research design guided by the KTA and TPB to better understand how the knowledge and practice behaviors of CHCPs influence the screening, diagnosis, and management of FH in cardiology practice. Given the negative sequelae associated with FH, and the vast underdiagnosis and undertreatment of FH, CHCPs play an important role in the care of FH patients. Results from this study provided an intervention map

and implementation plan to overcome individual, practice setting, and institutional barriers to addressing FH at CUIMC. Interventions should aim to implement, adopt, and evaluate CUIMC-tailored and cardiology-specific FH guidelines. Addressing CHCPs' ability to screen, diagnose, and manage FH patients is critical to reducing FH-related morbidity and mortality, as well as improving immediate and long-term FH health outcomes.

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APPENDICES

Appendix A. Survey Instrument

Pre-survey questions to capture inclusion/exclusion criteria

1. Are you a licensed physician (MD or DO), physician assistant (PA), or nurse (NP, LPN or RN)?
    a. Yes
    b. No

2. Have you provided clinical care to patients in the Division of Cardiology at Columbia University Irving Medical Center?
    a. Yes
    b. No

The survey will only continue after the participant responds "Yes" to each of these questions. If the participant responds "No" to any of these questions, they will receive a message that they do not meet the inclusion criteria to continue the survey (see below).

We're sorry. You do not meet the eligibility criteria for participating in this survey. Thank you for your interest and time.

Validated FH KAP Questionnaire

1. Which one of the following descriptions best describes Familial Hypercholesterolemia (FH)?
    a. The presence of family members with diagnosed high cholesterol
    b. A genetic disorder that is characterized by very high cholesterol and a family history of premature heart disease
    c. The presence of multiple lipid abnormalities that may be genetic in nature
    d. An ultra-rare, potentially fatal condition caused by cholesterol levels that can be up to six times the normal level
    e. Don't know
    f. Other (please specify)
        i. Open text box

2. Which one of the following lipid profiles is most consistent with the diagnosis of FH? (Reference intervals: TC<99.0mg/dL; TG<30.6mg/dL; HDL-C>18.0mg/dL; LDL-C<63.0mg/dL)
    a. TC 108.0mg/dL; TG 61.2mg/dL; HDL-C 14.4mg/dL; LDL-C 68.4mg/dL
    b. TC 113.4mg/dL; TG 219.6mg/dL; HDL-C 18.0mg/dL; LDL-C not reported
    c. TC 144.0mg/dL; TG 19.8mg/dL; HDL-C 18.0mg/dL; LDL-C 117.0mg/dL
    d. TC 97.2mg/dL; TG 23.4mg/dL; HDL-C 30.6mg/dL; LDL-C 55.8mg/dL
    e. TC 127.8mg/dL; TG 18.0mg/dL; HDL-C 63.0mg/dL; LDL-C 57.6mg/dL

3. What is the prevalence of FH globally?
    a. 1 in 100 persons
    b. <u>1 in 250 persons</u>
    c. 1 in 1,000 persons
    d. 1 in 2,000 persons
    e. 1 in 5,000 persons
    f. Don't know

4. What is the likelihood that first-degree relatives (i.e., parents, siblings, and children) of someone who has FH will also have the condition themselves?
    a. 0%
    b. 25%
    c. <u>50%</u>
    d. 75%
    e. 100%
    f. Don't know

5. How much greater is the risk of premature coronary artery disease (CAD) in untreated FH patients compared to the general population?
    a. 2 times greater
    b. 5 times greater
    c. 10 times greater
    d. <u>20 times greater</u>
    e. 50 times greater
    f. Don't know

6. When you are assessing a patient's family history, at what cut-off age for males and females do you consider CAD to be "premature"? Leave blank if you wish to answer "Don't know".
    a. Premature CAD in males (years of age or younger): _____ **<u>(55)</u>**
    b. Premature CAD in females (years of age or younger): _____ **<u>(65)</u>**

7. Is the following statement true or false? An accurate diagnosis of FH can only be made via genetic testing.
    a. True
    b. <u>False</u>
    c. Don't know

8. What is the target LDL-C following maximum tolerated dose of high intensity statin for patients diagnosed with FH?
    a. Less than 32.4mg/dL
    b. Less than 46.8mg/dL
    c. Less than 61.2mg/dL
    d. <u>Greater than 50% reduction from baseline LDL-C concentration</u>
    e. Greater than 30% reduction from baseline LDL-C concentration
    f. Don't know

9. Which of the following are important to obtain from the family history in patients with FH? *Please select all that apply*
    - **a. <u>Consanguinity</u>**
    - **b. <u>Family history of premature CAD (age of onset)</u>**
    - **c. <u>Family history of hypercholesterolemia (TC and/or LDL-C)</u>**
    - **d. <u>Family history of tendon xanthomas</u>**
    - **e. <u>Family history of childhood unexplained death</u>**
    - **f. <u>Three generation pedigree/family history chart</u>**
    - g. None of the above
    - h. Don't know

10. Which of the following would exclude the diagnosis of FH? *Please select all that apply*
    - a. Normal LDL-C concentration before puberty
    - b. Absence of clinical signs (i.e., tendon xanthoma)
    - c. Absence of mutation on genetic testing
    - d. Absence of ultrasound finding of tendon xanthoma
    - **e. <u>None of the above</u>**
    - f. Don't know

11. Which of the following are the management options for FH patients? *Please select all that apply*
    - a. Lifestyle modification is a substitute for lipid lowering medication
    - **b. <u>Ezetimibe co-administered with statin therapy is recommended as an option for adult heterozygous FH</u>**
    - **c. <u>Lipid lowering drug therapy is considered by the age of 10 years</u>**
    - d. Lipid modifying therapy should be continued during pregnancy
    - **e. <u>Progress of cascade screening in FH patients should be recorded</u>**
    - f. None of the above
    - g. Don't know

<u>Provider Characteristics</u>

1. What professional degree and/or license do you hold? *Please select all that apply*
    - a. MD
    - b. DO
    - c. PA
    - d. NP
    - e. RN
    - f. LPN
    - g. Other (please describe)
        - i. Open text box

12. Within which subdivision of the Division of Cardiology do you currently work in? *Please select all that apply*
    - h. Center for Interventional Vascular Therapy (CIVT/VALVE)

i. Cardiac Heart Failure and Transplant
j. Electrophysiology/EKG
k. Cardiovascular Imaging (Nuclear)
l. Cardiovascular Ultrasound (Echocardiography)
m. Cardiology Inpatient Services
n. Adult Congenital Heart Disease Program
o. Women's Heart Health
p. Cardiology Faculty Practices
q. ColumbiaDoctors of the Hudson Valley
r. ColumbiaDoctors Medical Group
s. Fellowship
t. Cardiovascular Research
u. Center for Behavioral Cardiovascular Health
v. Cardiology Precision Medicine
w. Other (please describe)
    i. Open text box

2. How many years have you been in clinical practice (include residency and/or fellowship years) at Columbia University Irving Medical Center?
    a. Less than 1 year
    b. 1-5 years
    c. 6-10 years
    d. 11-20 years
    e. Greater than 20 years

3. How many years have you been in clinical practice (include residency and/or fellowship years)?
    a. Less than 1 year
    b. 1-5 years
    c. 6-10 years
    d. 11-20 years
    e. Greater than 20 years

Thank you for participating in this survey!

A follow up phase of this study will involve an individual 30-minute virtual interview with co-investigator of the study, Isha Kalia, MS, MPH, CGC, to further explore cardiology healthcare providers' current clinical practice behaviors regarding FH and discuss potential future innovations to address the screening, diagnosis, and management of FH. If you choose to participate in the interview, you will be given a $25 Amazon gift card as a token of appreciation.

1. Would you be interested in participating in a 30-minute virtual interview?
    - Yes (will be directed to question 2 below)
    - No (will be directed to question 3 below)

2. Thank you for agreeing to be recontacted for a 30-minute virtual interview. Please provide your contact information below. Your contact information will be kept confidential and only used for purposes of requesting your participation in a follow up phase to this research. Your responses from the survey will be linked to your contact information below. Your contact information will not be shared for other research or other purposes.

- Name (open text box)
- Email (open text box)

3. Thank you for participating in this survey! If you would like to be entered to win a drawing for one of three $50 Amazon gift cards, please click the survey link below. If you are not interested in entering to win a drawing, thank you for your participation! You can close this survey tab as the survey is completed.

(Qualtrics drawing survey link that is different from the original Qualtrics survey link)

The survey link will direct participants to a new page with the information below:

Thank you for participating in this research study! To enter to win a drawing for one of three $50 Amazon gift cards, please provide your information below. Your contact information for purposes of the drawing will not be linked to your responses from the survey. You will be contacted by the co-investigator of the study, Isha Kalia, MS, MPH, CGC, from email address ik2417@cumc.columbia.edu, if you win one of the three $50 Amazon gift cards.

Name:

- Open text box

Email:

- Open text box

Appendix B. Qualitative Interview Guide

Knowledge:

1. How did you acquire your knowledge about FH?
2. What would have helped you increase your knowledge about FH? Why?

Current Practice Behaviors:

1. Can you tell me a little bit about the clinical setting that you work in?
    a. How are you are currently addressing FH in your patient population?
2. How do you screen patients in your practice for FH?
    a. What tests do you perform to screen patients for FH?
    b. What informs the tests you select?
3. Can you tell me how you diagnose patients in your practice with FH?
    a. What diagnostic criteria do you use?
    b. What tests do you perform to diagnose someone with FH?
    c. What informs the tests you select?
4. How do you manage patients with FH?
    a. What informs your management plan?
5. What specialists do you engage with to address FH?
    a. Are there any referral practices that you engage in?
    b. What is that process?

Intended Practice Behaviors and Needed Resources:

6. What current practice behaviors related to FH might you like to change? Why?
    a. What FH screening practices would you like to change? Why?
    b. What FH diagnostic practices would you like to change? Why?
    c. What FH management practices would you like to change? Why?

Attitudes/Behavioral Beliefs:

7. On a scale of 1 to 10, with 1 being not important and 10 being very important, how important is it that FH is addressed in your clinical practice? Why?
    a. What factors influenced your rating?
8. What are your thoughts about the advantages of addressing FH?
9. What are your thoughts about the disadvantages to addressing FH?

Normative Beliefs/Subjective Norm:

10. What message do you believe is given to you regarding if and how you should address FH among your patients?
    a. From whom does this message come from (i.e., peer colleagues, division chair, department chair, institution as a whole)?

External Factors/Control Beliefs/Perceived Behavioral Control

11. What factors influence your ability to address FH?
    a. How do these factors influence you?
12. What makes addressing FH easier?
13. What makes addressing FH harder?

Intervention:

14. If you were to create an intervention that could help cardiology providers address FH in their practice, what type of intervention would you introduce? Why?

Appendix C. Email to Cardiology Listserv

Subject Line: Calling all cardiology healthcare providers!

Dear Colleagues,

As a member of the Division of Cardiology at Columbia University Irving Medical Center, we would like to invite you to participate in a survey about your experience with patients who are at risk for Familial Hypercholesterolemia.

The data collected from this study will be used to create interventions to help our cardiology patients.

This survey should take no more than 10 minutes, and to thank you for your time, you can enter to win a **$50 Amazon gift card.**

You can find the survey link here:
https://columbiangwu.co1.qualtrics.com/jfe/form/SV_0xL8zrpCsfrL1Ea

Please complete this survey by **April 30, 2022.**

Thank you in advance for participating in this project!

Sincerely,

Dr. Muredach Reilly
Director of the Irving Institute for Clinical and Translational Research

Appendix D. Consent Form for Survey Instrument

COLUMBIA UNIVERSITY MEDICAL CENER INFORMED CONSENT FORM

Protocol Title: Exploration of FH Practice Behaviors Among Cardiology Healthcare Providers
IRB # AAAU0047

Contact	Contact Type
Dr. Muredach Reilly	Principal Investigator
Isha Kalia	Investigator

What is on this form?
We are asking you to take part in a research study because you are a healthcare provider working in the Division of Cardiology. We would like to learn more about your experience providing clinical care to patients with Familial Hypercholesterolemia. We hope to use this information to improve clinical practices at Columbia University Medical Center.

This form explains why we are doing this research study and what you will be asked to do if you choose to participate in it. It also describes the way we would like to use this information we learn from you. Please take the time to read this consent form.

If at any time you have questions about this form or the research study, please ask a member of the research study team. Take all the time you need to decide whether you want to take part in the research study. Participation is voluntary; you do not have to participate if you do not want to.

Key Points of This Form

- The purpose of this research study is to understand the practice behaviors of cardiology healthcare providers in the care of patients with Familial Hypercholesterolemia at CUIMC
- If you participate in this research study, we will ask you to complete an eleven-item survey. Detailed information about research study participation is in "What will happen if I participate in this study?"
- You might want to participate in this research study to help us better understand the clinical practice behaviors for patients with Familial Hypercholesterolemia in the Division of Cardiology. There may be no direct benefits to you for participation. For a complete description of possible benefits, please see "What are the benefits of being in the study?" section below
- You might not want to participate in this research study. All of the known risks are listed in "What are the risks of being in the study?"
- Your participation in other research studies will not change whether or not you participate in this research study. More information is in "What alternatives are available?"
- If you are interested in learning more about this research study, please read the details below

Research Study Purpose
You are invited to participate in a survey assessing the knowledge and practice behaviors of cardiology healthcare providers in the screening, diagnosis, and management of Familial Hypercholesterolemia. The goal of this work is to inform future interventions to support cardiology healthcare providers in the systematic screening, diagnosis, and management of patients with Familial Hypercholesterolemia.

What will happen if I participate in this study?
If you agree to take this survey that takes approximately 15 minutes to complete, you will be asked questions about your demographic and professional backgrounds, as well as questions pertaining to your knowledge and practice behaviors for patients with Familial Hypercholesterolemia.

Will I be paid to participate?
After completing the entire study survey, you may provide your contact information to be entered to win one of three $50 Amazon gift cards. If you withdraw before the end of the survey, you will not qualify to be entered into the drawing nor eligible to receive one of the three $50 Amazon gift cards.

What alternatives are available?
The alternative is to not participate in the study.

What are the benefits of being in the study?
There are no direct benefits to participating in the study. The study's goal will be to assess the level of knowledge and practice behaviors of cardiology healthcare providers in screening, diagnosing, and managing patients with Familial Hypercholesterolemia. The long-term goal of this research is to provide cardiology healthcare providers with tools to support the delivery of evidence-based patient-centered care for FH. In this indirect way, patients and their family members may benefit from the study.

Your decision about whether or not to participate in this study will not affect your employment/medical care. Your personal information will NOT be shared directly with Columbia University Irving Medical Center.

What are the risks of being in the study?
Participants will not receive treatments or procedures related to this research project, so this research poses no risk of physical injury or side effects. We will assign identifiers (study IDs) to subjects and only include those study identifiers in all data records. Confidential information such as subject name will be maintained in a password protected file on a secure drive and destroyed once data analysis activities are completed. Only the investigators and study staff will have access to protected health information (PHI).

You will be given an opportunity to provide your name and contact information to demonstrate your interest in participating in the second phase of this study involving individual interviews. If you choose to be re-contacted for the second phase of this study, your identifiable information will be connected to your survey responses. You will be given an opportunity to

provide your contact information to be entered to win one of three $50 Amazon gift cards. Your contact information for the drawing will not be connected to your survey responses. The risks associated with this study are lack of anonymity (other coworkers you know may be participating).

How will information about me be protected?
Your data will be stored on password protected computers and identified with anonymous ID numbers. Once all data are collected, your responses will be reported in aggregate. What we find from this study may be presented at meetings or published in papers, but individual responses or identifiable personal information about participants will not be disclosed in these presentations or papers.

What are my rights if I participate in this research study?
Taking part in this research study is your choice. You can decide not to take part or stop being in the research study at any time. If you decide to withdraw from the research study before it is finished and no longer want to be contacted by the researchers, you will need to notify in writing one of the researchers listed on the first page of this consent form.

Who do I call with questions?
You may contact Isha Kalia, MS, MPH, CGC if you have any questions or concerns about this research study. If you have any questions about your rights as a research participant, or if you have a concern about this research study, you may contact the office below.

Human Research Protection Office
Institutional Review Board
Columbia University Irving Medical Center
154 Haven Ave, 1st Floor
New York, NY 10032
Telephone: 212-305-5883
Email: irboffice@columbia.edu

Statement of Consent
I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered.

Do you consent to participate in this research study?
- Yes
- No

Appendix E. Study Information Sheet

COLUMBIA UNIVERSITY MEDICAL CENER INFORMED CONSENT FORM

Protocol Title: Exploration of FH Practice Behaviors Among Cardiology Healthcare Providers
IRB # AAAU0047

Contact	Contact Type
Dr. Muredach Reilly	Principal Investigator
Isha Kalia	Investigator

What is on this form?
We are asking you to take part in a research study because you are a healthcare provider working in the Division of Cardiology. We would like to learn more about your experience providing clinical care to patients with Familial Hypercholesterolemia. We hope to use this information to improve clinical practices at Columbia University Medical Center.

This form explains why we are doing this research study and what you will be asked to do if you choose to participate in it. It also describes the way we would like to use this information we learn from you. Please take the time to read this consent form. We will also talk with you about taking part in this research study.

If at any time you have questions about this form or the research study, please ask a member of the research study team. Take all the time you need to decide whether you want to take part in the research study. Participation is voluntary; you do not have to participate if you do not want to.

Key Points of This Form

- The purpose of this research study is to understand the practice behaviors of cardiology healthcare providers in the care of patients with Familial Hypercholesterolemia at CUIMC
- If you participate in this research study, we will ask you to complete an interview by phone that will take approximately 30 minutes. Detailed information about research study participation is in "What will happen if I participate in this study?"
- You might want to participate in this research study to help us better understand the clinical practice behaviors for patients with Familial Hypercholesterolemia in the Division of Cardiology. There may be no direct benefits to you for participation. For a complete description of possible benefits, please see "What are the benefits of being in the study?" section below
- You might not want to participate in this research study. All of the known risks are listed in "What are the risks of being in the study?"
- Your participation in other research studies will not change whether or not you participate in this research study. More information is in "What alternatives are available?"
- If you are interested in learning more about this research study, please read the details below

Research Study Purpose
You are invited to participate in an interview to understand the practice behaviors of cardiology healthcare providers in the screening, diagnosis, and management of Familial Hypercholesterolemia. The goal of this work is to inform future interventions to support cardiology healthcare providers in the systematic screening, diagnosis, and management of patients with Familial Hypercholesterolemia.

What will happen if I participate in this study?
If you agree to participate in this research study, you will complete a 30-minute interview to discuss your perspectives on the screening, diagnosis, and management of Familial Hypercholesterolemia. The goal of this work is to inform future interventions to support cardiology healthcare providers in the systematic screening, diagnosis, and management of patients with Familial Hypercholesterolemia, so we will offer participants the opportunity to see aggregated results that can be shared back with their teams and healthcare administrators.

We are asking you to allow us to record the audio of the Zoom interview. No facial features will be recorded, and your name will not be used in the audio recording. The recordings will be used for analysis by the researchers of this study. The audio will be transcribed (written out) and any identifying information including your name will be removed from the transcript. The transcript will be analyzed by the researchers to identify common themes across the interviews. The results of the analysis may be published in a scientific journal. Quotes from the interview may be included but no identifying information about you, such as your name, will be published so you cannot be identified.

The audio recording will be stored on a password protected encrypted file. It will be destroyed after the transcription is complete. The transcription will be stored on a password protected encrypted file.

Unfortunately, you are not eligible to participate in the qualitative interview if you are not willing to be audio recorded.

Will I be paid to participate?
Participants will be compensated for their time participating in the qualitative interviews with a $25 Amazon gift card.

What alternatives are available?
The alternative is to not participate in the study.

What are the benefits of being in the study?
There are no direct benefits to participating in the study. The study's goal will be to understand cardiology healthcare providers experience screening, diagnosing, and managing patients with FH. The long-term goal of this research is to provide cardiology healthcare providers with tools to support the delivery of evidence-based patient-centered care for FH. In this indirect way, patients and their family members may benefit from the study.

Your decision about whether or not to participate in this study will not affect your employment or status at Columbia University Irving Medical Center. Your personal information will NOT be shared directly with Columbia University Irving Medical Center.

What are the risks of being in the study?
Participants will not receive treatments or procedures related to this research project, so this research poses no risk of physical injury or side effects. We will assign identifiers (study IDs) to subjects and only include those study identifiers in all data records. Confidential information such as subject name will be maintained in a password protected file on a secure drive and destroyed once data analysis activities are completed. Only the investigators and study staff will have access to protected health information (PHI). The risks associated with this study are lack of anonymity (other coworkers you know may be participating).

How will information about me be protected?
Your data will be stored on password protected computers and identified with anonymous ID numbers. What we find from this study may be presented at meetings or published in papers, but individual responses or identifiable personal information about participants will not be disclosed in these presentations or papers.

Your registration information (containing personally identifiable information) and interview data will be stored in a password-protected, encrypted computer system with limited access. Your personally identifiable data associated with this study would be accessible only to the research team and IT personnel who maintain the data and the secure electronic systems where the data is housed.

The research team will adhere to the laws and policies in place to protect the confidentiality of your personal information. Your personal information will NOT be shared directly with CUIMC. However, your information will become part of a database that is maintained within the secure conditions disclosed above. A limited number of staff will have access to identifiable data: the study investigator; dissertation researcher and IT personnel responsible for maintaining data and secure electronic systems. Data released to the team above will be deidentified by removing any personal identifying information including demographic data. The deidentified data may be shared in academic publications. None of your answers will be connected to you.

What are my rights if I participate in this research study?
Taking part in this research study is your choice. You can decide not to take part or stop being in the research study at any time. If you decide to withdraw from the research study before it is finished and no longer want to be contacted by the researchers, you will need to notify in writing one of the researchers listed on the first page of this consent form.

Who do I call with questions?
You may contact Isha Kalia, MS, MPH, CGC if you have any questions or concerns about this research study. If you have any questions about your rights as a research participant, or if you have a concern about this research study, you may contact the office below.

Human Research Protection Office

Institutional Review Board
Columbia University Irving Medical Center
154 Haven Ave, 1st Floor
New York, NY 10032
Telephone: 212-305-5883
Email: irboffice@columbia.edu

Statement of Consent
I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered.

Do you consent to participate in this research study?
- Yes
- No

Appendix F. Recruitment Email for Qualitative Phase

Hello,

Thank you for participating in the survey about your experience with patients who are at risk for Familial Hypercholesterolemia. At the end of the survey, you indicated you would be interested in participating in our follow-up interview.

To review, the purpose of this interview will be to better understand your practice behaviors in the care of patients at risk for Familial Hypercholesterolemia. These interviews will occur over Zoom and will require audio recording. The interview should last approximately 30 minutes.

Please find attached to this email, the consent form for the interview. At the beginning of the interview, I will obtain your verbal consent to participate. As a thank you for participating in the interview, you will receive a $25 Amazon gift card after the interview.

Please review the attached consent form, and feel free to reach out to me if you have any questions.

If you are interested in participating in the interview, please let me know a few days and times in the coming weeks that you are available to speak.

Again, thank you for your time and consideration in participating in this research study.

Best,
Isha Kalia

Appendix G. Interview Prompts Joint Display

Quantitative Construct	Qualitative Interview Question
Total Knowledge Score	How did you acquire your knowledge about FH? What would have helped you increase your knowledge about FH? Why?
Screening FH	How do you screen patients in your practice for FH? What FH screening practices would you like to change? Why?
Diagnosing FH	Can you tell me how you diagnose patients in your practice with FH? What FH diagnostic practices would you like to change? Why?
Managing FH	How do you manage patients with FH? What informs your management plan? What FH management practices would you like to change? Why?

Appendix H. Predetermined Codes

Code	**Definition** *(TPB construct)*
Knowledge	How the participant acquired their FH knowledge *(individual factors)*
Importance_Rating	The numerical importance rating CHCPs provided related to the importance of screening, diagnosing, or managing FH *(behavioral beliefs)*
Importance_Reasoning	The reasoning behind CHCPs' importance rating *(behavioral beliefs)*
FH_Advantages	The advantages of screening, diagnosing, or managing FH *(attitudes)*
FH_Disadvantages	The disadvantages of screening, diagnosing, or managing FH *(attitudes)*
Message	The message given to CHCPs regarding if and how to screen, diagnose, or manage people with FH *(normative beliefs, subjective norm)*
Factors_Easier	The factors that make it easier for the CHCP to screen, diagnose or manage FH *(control beliefs, perceived behavioral control, external factors)*
Factors_Harder	The factors that make it harder for the CHCP to screen, diagnose or manage FH *(control beliefs, perceived behavioral control, external factors)*
Intended Practice	The FH screening, diagnostic, or management practices that the CHCP would like to change *(behavioral intentions)*

Appendix I. Preliminary Coding Schema

Parent Code	Child Code	Definition	Examples
Variability in FH Care	*Identification*	Utilization of screening tools to identify FH cases	Lipid panel, physical exam, family history, identification of xanthomas
	Post-Identification	Clinical care provided after identification of those at risk for FH	Genetic testing, pedigree analysis, referral to lipid clinic, genetic counseling
Importance of Addressing FH	*CHCP decision-making*	Any way that knowledge of FH impacts CHCP's decision-making	Medical management of hypercholesterolemia, safety, and efficacy of treatment
	Prevent disease progression (patient)	How FH knowledge can prevent disease progression in patient	Decreased hospitalizations, decreased coronary events, aggressive treatment
	Prevent disease onset (family)	How FH knowledge can prevent disease onset in patient's family members	Primary prevention in family, cascade screening, inheritance, and risk to family members
Barriers and Facilitators	*Institutional Issues*	Considerations specific to working at an academic medical center	Access to lipid specialists, referral practices, institution-specific resources
	Practice Setting Issues	Descriptions of how clinical practice setting impacts FH care	Time in encounters, priority of cases, prior authorization processes
	Individual-Level Issues	CHCP and patient issues related to providing care for FH	Insurance coverage, cost of treatment, medication compliance, FH knowledge
Overcoming Barriers	*Referral System*	How a referral system overcomes FH barriers	Consult to lipidologists or genetic specialists
	Education	Ways that educational initiatives can address FH barriers	Advantages (increasing cognitive awareness); disadvantages (attendance)
	Standardize Processes	How FH processes can be standardized	Protocol, checklist, algorithm, screening tool
	EHR Applications	Descriptions of how EHR applications can be used to address barriers to FH practice	Alert to prompt referral, advantages (part of workflow), disadvantages (alert fatigue)