QUALITY OF CARDIOVASCULAR DISEASE PREVENTION FOR PEOPLE LIVING WITH HIV

Charles Muiruri

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Approved by:
John E. Paul
Antonia V. Bennett
Mark Holmes
Leah L. Zullig
Morris Weinberger
John A. Bartlett
ABSTRACT

Charles Muiruri: Quality of Cardiovascular Disease Prevention for People Living with HIV  
(Under the direction of John E. Paul)

The objective of this dissertation was to assess the quality of cardiovascular disease (CVD) prevention among people living with HIV (PLHIV) in the United States. Using semi-structured interviews, we explored infectious diseases (ID) specialists’ CVD care perceptions. Using retrospective data from the Duke University Medical Center, we assessed the association between combined care provision by primary care providers (PCP) and ID specialists compared to ID specialist only and time to being prescribed primary and secondary CVD prevention therapies.

Analytical approaches included template and survival analysis.

In our first analysis, two themes emerged: (1) ID specialist attitudes and perceptions towards CVD risk factor management; and (2) healthcare system factors that influenced CVD prevention in HIV care.

The second analysis assessed differences in the rate of prescribing antihypertensive and statins for PLHIV who saw an ID specialist plus their PCP versus those who only saw an ID specialist. Hypertensive patients who saw an ID specialist and PCP were more likely to be prescribed antihypertensive compared to those who only saw an ID specialist (hazard ratio [HR] =1.404, 95% confidence interval [CI] 1.016-1.942). There were no differences in the rate of being prescribed statins (HR =1.404, 95% CI 0.715-1.523).

Third analysis assessed use of secondary CVD prevention therapies among PLHIV and whether there were differences in the rate of prescribing therapies between PLHIV who saw an ID specialist and PCP compared to those who saw an ID specialist only. Out of 340 eligible patients, 50% and 25% had been prescribed antiplatelet agents and beta blockers, respectively. Compared to those who only saw an ID specialist, those who saw an ID specialist and PCP were more likely to be prescribed beta blockers (HR =1.69, 95% CI 1.02 – 2.80) and antiplatelet agents (HR=2.28, 95% CI 1.58 – 3.27).
These findings suggest that there is room for improvement in the quality of CVD prevention among PLHIV. Future research and interventions should focus on, strategies to encourage appropriate management of CVD risks by ID specialists, reduction of barriers in HIV care settings that impede CVD prevention and interventions to improve time to prescription for CVD risk factors.
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<tr>
<td>AAHIVM</td>
<td>American Academy of HIV Medicine</td>
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<tr>
<td>AB</td>
<td>Antonia Bennett (Investigator)</td>
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<tr>
<td>AIDS</td>
<td>Acquired immune deficiency syndrome</td>
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<td>AHA</td>
<td>American Heart Association</td>
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<td>AMC</td>
<td>Academic Medical Center</td>
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<td>Antiretroviral Treatment</td>
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<td>ASCVD</td>
<td>Atherosclerotic Cardiovascular Disease</td>
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<td>Duke University Medical Center</td>
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<td>Primary Care Provider</td>
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<tr>
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<td>People Living with Human Immunodeficiency Virus</td>
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CHAPTER 1. INTRODUCTION

Overview

More than 1.2 million people in the United States are living with human immunodeficiency virus (HIV) infection and this number is anticipated to increase.1 The incidence of AIDS-defining opportunistic infections and associated mortality among people living with HIV (PLHIV); however, has been dramatically reduced due to the availability of antiretroviral therapy (ART).2 As a result of the decreased mortality from HIV infection, PLHIV are increasingly diagnosed with chronic conditions as they age, including cardiovascular disease (CVD).3,4 Studies have found that PLHIV have a higher risk for major CVD events than the general population due to effects of both the HIV virus and ART.4-13 For example, in the Veterans Aging Cohort study, researchers found that after adjusting for traditional CVD risk factors, comorbidities, and substance abuse, HIV-infected veterans had an increased risk of incident myocardial infarction (MI) compared with uninfected veterans (HR =1.48; 95% CI, 1.27–1.72).11 PLHIV have an estimated 4.5-fold greater risk for sudden cardiac death.14 Further, studies have found that 8 to 22% of deaths among PLHIV are attributed to CVD, which has become the second most common cause of non-AIDS–related mortality in this population.5,6 The incidence of traditional CVD risk factors such as hypertension, dyslipidemia, obesity, and tobacco use among PLHIV are higher compared to the general population.15-17 The presence of traditional CVD risk factors, coupled with the unique CVD risks associated with the HIV virus and its treatment, position PLHIV in particular need of CVD-risk-reducing interventions. Despite an increased risk of CVD, however, such patients often receive suboptimal CVD care as measured compliance to clinical guidelines.18-24 For example, Burkholder et al. found that only 17% of HIV-infected patients at the University of Alabama’s 1917 clinic who qualified for long-term aspirin therapy per U.S. Preventative Task Force Guidelines received it.18 Clements et al. found that among United States veterans eligible for statins and infected with HIV, hepatitis C (HCV), or HIV/HCV co-infection, 22.7%, 30.5%, and 31.5%, respectively, did not receive an Adult Treatment Panel-III (ATP III) recommended statin.24 The reasons for the observed low quality of care for PLHIV with CVD are poorly
understood. Based on the Andersen Behavioral Model of health services use, we hypothesized that low use of CVD preventative care may be related to the healthcare system, healthcare provider, and patient characteristics.25

In the past three decades, a high proportion of PLHIV have received their care from infectious diseases (ID) specialists at ID clinics.26 However, little is known about ID specialists’ attitudes toward CVD risk prevention and factors that may influence CVD prevention in HIV care settings. For some patients seen at these ID clinics, non-ID primary care providers (PCP) have also been involved in their care. Traditionally, the role of PCP has been to help patients prevent, understand, and manage illness, navigate the health system, and set health goals.27 However, there is a gap in our understanding of how the specialty (e.g., primary care or ID) is associated with receipt of primary and secondary CVD prevention. Prior studies have also found that the type physician responsible for the management and long-term care of a patient may affect the use of preventative care.28-23 Therefore it is vital to evaluate if there are differences in provision of primary CVD preventative care between different physician specialties that provide ongoing care to PLHIV.

The long-term goal of this dissertation is to influence clinical care and policies aimed at improving quality of CVD care for PLHIV. The first objective of this research was to explore ID specialists’ perceptions and attitudes regarding the management of CVD risk factors among PLHIV. Second, we assessed the association between combined expertise of PCP and ID specialists compared to ID specialist alone on the quality of primary CVD risk prevention among PLHIV. Finally, we assessed the association between the combined expertise of PCP and ID specialists compared to ID specialist alone on the quality of secondary CVD risk prevention among PLHIV. The central hypothesis for the two quantitative studies was that PLHIV who received care from both ID specialists and PCPs would have an increased the likelihood of being prescribed medicines for primary and secondary CVD prevention. This dissertation used multiple-methods approach to explore the research objectives. The first aim employed qualitative research approach to explore ID specialists’ perceptions and attitudes regarding the management of CVD risk factors among HIV-infected patients. The other aims used quantitative methods to examine whether there was a difference in the rate of prescribing medications for primary prevention of CVD between PLHIV who received care from ID specialists alone versus those who were seen by both
an ID specialist and a PCP. For those PLHIV who had established CVD, we examined whether there were differences between the two groups in prescription patterns for secondary CVD prevention.

The study addressed the following specific aims:

**Aim 1:** Identify ID specialists’ perceptions and attitudes regarding the management of CVD risk factors among PLHIV through individual semi-structured interviews administered to a sample of ID specialists in the United States.

*Approach:* We recruited members of the American Academy of HIV Medicine and conducted 30 minutes semi-structured interviews with ID specialists from different healthcare systems in the United States. Open-ended questions focused on providers' overarching views about the quality of CVD preventative care, resources available to support CVD preventative care, and reflections on appropriate strategies to enhance optimal preventive care for PLHIV. Interviews were conducted until theme saturation was reached.

**Aim 2:** Determine whether there was a difference in the rate of prescribing medications for two common CVD risk factors (hypertension and dyslipidemia) between PLHIV without established CVD who received care from an ID specialist alone versus those that saw an ID specialist and their PCP at an academic medical center’s ID clinic between 2000 and 2017.

*Hypothesis:* Compared to those who received care from ID specialists only, those who received care from an ID specialist and a PCP would have an increased likelihood of being prescribed a statin or antihypertensive if they had a diagnosis of dyslipidemia or hypertension, respectively.

*Approach:* The study used Duke University Medical Center (DUMC) Adult ID Clinic from routine clinic visits from January 2000 to February 2017. These electronic medical record data were then linked to claims data that included the specialty of healthcare providers and insurance status. To test the hypothesis, we used the Kaplan-Meier method to plot time-to-event curves for PLHIV who received care from an ID specialist alone versus those who were seen by an ID specialist and their PCP. We used Cox proportional hazard models to examine the hazards of being prescribed the recommended medications for the two groups of PLHIV.

**Aim 3:** Determine whether there was a difference in the rate of prescribing secondary CVD prevention medications for PLHIV with established CVD who received care from an ID specialist
alone versus those that saw an ID specialist and a PCP at an academic medical center’s ID clinic between 1997 and 2017.

Hypothesis: Compared to those who received care from ID specialists only, PLHIV with established CVD who received care from their ID specialist and a PCP would have an increased likelihood of being prescribed antiplatelet or beta blockers.

Approach: To test the hypothesis, data source and analytical methods used in Aim 2 were employed but with a different eligibility criteria.

Conceptual Model

This project used a conceptual model informed by the behavioral model of healthcare use (Figure 1.1).25 This model posits that environmental factors, healthcare system, and population characteristics influence health services use. Specifically, the model suggests the healthcare system in the context of provider-related factors and population characteristics including predisposing characteristics, enabling resources, and needs influence the receipt of CVD risk–reduction therapies. That is, *PLHIV’s need for CVD primary and secondary prevention is determined by the healthcare system, type of healthcare providers overseeing their care, patient-level predisposing factors, and is mediated by enabling resources.* We adapted the model to focus on the context in which CVD risk prevention occurs within HIV care (Figure 1.2). Specifically, we included external environmental and provider-related factors that influence patients’ use of CVD risk preventive strategies. The first Aim was focused on provider and environmental-related factors. For the external environmental factors, we focused on the health delivery systems such as resources, policies, and practices at the ID clinic. Provider-related factors included patient factors that may be influenced by providers (e.g., a patient’s regular source of primary care) as well as provider characteristics that interacted with patient characteristics (e.g., specialist or generalist) to influence use of CVD risk prevention.

Examining the context within which use of CVD prevention occurs—specifically, provider characteristics that interact with patient characteristics to influence use of primary and secondary CVD prevention—is important.31 Researchers have found that a providers’ specialty influences the level of comfort in management of CVD risk factors in PLHIV. Fultz et al. found that compared to non-HIV internists, ID-certified physicians at ID clinics reported less comfort in prescribing medications for
hyperlipidemia, diabetes, hypertension, and depression despite a substantial prevalence of these conditions in their patient population.\textsuperscript{32} Additionally, low levels of compliance to CVD prevention guidelines by providers have been reported in previous research that found that specialty training may influence use of preventative services and that much of the variation in patient usage rates may be due to physician decision-making.\textsuperscript{28-30} Training and experience with caring for PLHIV combined with training and experience in primary and secondary prevention of CVD is expected to be associated with an increased likelihood of receiving quality CVD preventative care.

Patient characteristics such as age, body mass index (BMI), and diagnosis of CVD risk factors may influence the provider’s decision to provide preventative CVD care. Severity of HIV disease, substance abuse, and alcohol dependence may also increase the likelihood of providing CVD risk factor management by the healthcare providers. Other variables that may increase the likelihood of providers’ provision of CVD prevention include gender and race.\textsuperscript{33, 34} Socioeconomic status such as access to health insurance coverage, education, employment, and others may influence preventive healthcare use for PLHIV. In HIV care, there are public assistance programs to help with obtaining antiretroviral drugs, but they may not provide drugs to address CVD risk.\textsuperscript{35} Clinical characteristics such as presence of other traditional CVD risk factors and family history of CVD may influence the perceived need for CVD risk prevention (Aim 2). After a cardiac event, patients require longitudinal management of CVD risk factors to prevent subsequent cardiac events and this may influence the need for secondary CVD prevention (Aim 3).

\textbf{Rationale}

\textbf{Significance}

This study is significant in several ways. First, the incidence and mortality associated with deadly opportunistic infections among PLHIV has dramatically dropped compared to the early years of the epidemic.\textsuperscript{2} As a result, PLHIV are increasingly diagnosed with chronic conditions including CVD.\textsuperscript{3, 4} Furthermore, CVD is the second most common cause of non-AIDS-related mortality in an aging HIV population.\textsuperscript{5, 6} Given the current HIV care demands, identifying health systems and health provider factors that facilitate primary and secondary prevention of CVD in PLHIV is of great importance.\textsuperscript{36, 37} Accordingly,
our study proposes to examine ID specialists perceptions and attitude toward CVD prevention along with assessing if there is a positive association between two different care models in HIV care settings.

Second, by 2015, in the United States, more than half of PLHIV were aged 50 or older. Because risk of a cardiac event climbs considerably after age 50, we can expect increases in the demand for CVD care as the PLHIV population ages. The high incidence of traditional CVD risk factors like smoking, hyperlipidemia, obesity, and diabetes in this population also increases the need to focus on prevention of CVD. Further, given that non-ID outpatient primary care providers have been reported to have higher levels of comfort in managing these comorbidities in PLHIV compared to ID specialists, our findings are instrumental in informing future research on care models that have potential to increase the quality of CVD in this population.

Third, while studies on the quality of CVD care for PLHIV have reported suboptimal quality of care, none have included type of specialty of the healthcare providers. Because clinical specialty may influence use of preventative services and much of the variation in patient usage rates have been shown to be due to physician decision-making, it is vital to quantify net treatment benefit of different providers in the quality of CVD care. Further, the results of this dissertation will extend the current knowledge in the generalist-specialist care models. The results of the project have potential significant implications for clinical care and policy. For example in the qualitative study, the results will contribute to the current knowledge in the evolving HIV care landscape by elucidating ID specialists’ current perceptions and attitudes regarding CVD prevention. In the quantitative aims the results will elucidate whether leveraging different healthcare providers will lead to care optimization for non-AIDS-defining condition such as CVD among PLHIV.

The focus on CVD reflects its importance as the leading cause of morbidity and mortality in the United States and where studies have reported 6-15% of deaths among PLHIV attributed to CVD. Adequate CVD risk factors management has potential to reduce the likelihood of advanced atherosclerosis and subsequent cardiac events. Our findings may also influence the development of novel care models that are patient-centered for PLHIV to improve the utility and management of chronic conditions such as CVD. Finally, findings of this dissertation may be instrumental in providing a platform
for future research in development and optimization of decision support, evaluation of care coordination, and patient-reported outcomes in PLHIV.

**Innovation**

This proposal was innovative in several ways. First, the research question is novel. No known studies in this research area have included provider-related variables to estimate use of CVD preventative care in PLHIV. We identified only one study that addressed the use of provider-related variables in assessing quality of care for PLHIV. Landon et al. used providers’ specialization status to assess the quality of primary care provided to 5247 PLHIV treated in 64 ID clinics and found that general internists who considered themselves “experts” in HIV care were just as likely as ID specialists to meet the study’s predetermined quality measures. However, the quality measure did not include CVD care.

Second, the study approach is novel for this area of research. Use of clinical data within the ID clinic population in the study provided the opportunity to measure quality of care in a comparable population. Published studies in this area have been observational and have compared infected and uninfected persons. The use of uninfected persons as comparison groups may not accurately estimate quality of care because these two populations have distinct differences. PLHIV are different because of a) the presence of chronic immune activation even after achieving control of HIV replication; b) the inability to eliminate the reservoir of latent HIV-infected cells; and, c) the need for long-term antiretroviral therapy to maintain viral suppression. Accordingly, my dissertation’s comparator group for Aims 2 and 3 were only PLHIV.

Finally, the use of multiple methods to capture multilevel factors that influence the quality of CVD care for PLHIV in clinical practice is innovative. Interviews with ID specialists who deliver care across diverse healthcare settings in ID clinics provided important insights about strategies to improve quality of CVD outcomes in PLHIV. Taken together, this dissertation elucidates factors that future clinical and policy interventions can target to increase the quality of care in PLHIV.

Figure 1.1. Behavioral model of health services use.


Figure 1.2. Adapted behavioral model of health services use.
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CHAPTER 2. INFECTIOUS DISEASES SPECIALISTS’ PERCEPTIONS AND ATTITUDES REGARDING CARDIOVASCULAR DISEASE PREVENTION AMONG PEOPLE LIVING WITH HIV: A QUALITATIVE STUDY

Background

Antiretroviral therapy (ART) has significantly increased survival rates for human immunodeficiency virus (HIV)-infected persons. Approximately 8–22% of deaths in people living with HIV (PLHIV) are attributed to cardiovascular disease (CVD), which is the second most common cause of non-AIDS-related mortality in an aging HIV-infected population. Due to the effects of the HIV virus and some ARTs, PLHIV have nearly 50% higher risk for major CVD events compared to the general population. PLHIV have also higher incidence of traditional CVD risk factors such as hypertension, smoking, diabetes, and dyslipidemia.

Despite their increased CVD risk, PLHIV often receive suboptimal CVD preventative care. For example, Burkholder et al. found that only 17% of patients who qualified for long-term aspirin therapy per U.S. Preventative Task Force Guidelines were receiving it. In the HIV Outpatient Prospective Study, where 74.2% of 2005 patients had hypertension and 70.5% had low high-density lipoprotein (HDL-C) levels, only half of the patients were treated for hypertension and 2% to 11% were treated pharmacologically for low HDL-C. The reasons for the observed low levels of compliance in HIV care are poorly understood. Low use of CVD preventative care may be related both provider and healthcare system barriers. It is important, therefore to explore these barriers in the context of where HIV care takes place.

In the past three decades, a high proportion of PLHIV received their primary care from infectious diseases (ID) specialists at ID clinics, however little is known about ID specialists’ attitudes toward CVD risk prevention and factors that may influence CVD prevention in HIV care settings. To elucidate these factors, we conducted a qualitative study to examine ID specialists’ perspectives and attitudes toward CVD care in HIV care settings in the United States.
Methods

Setting

We recruited participants from the American Academy of HIV Medicine (AAHIVM) membership through a weekly AAHIVM newsletter for four consecutive weeks in April 2016. Those interested were encouraged to contact the principal investigator (CM) by e-mail or phone to ensure that they met eligibility criteria (below) and schedule face-to-face or telephone-based interviews.

Participants

Eligible participants were those who held an MD or equivalent degree, had formal ID fellowship training, and reported having an active panel of HIV-infected patients. Once the interviews were scheduled, an informed consent form was e-mailed to the ID specialist. Only those who provided informed consent were interviewed.

Conceptual Model and Interview Guide

The interview guide was developed based on the Behavioral Model of Health Services Use. This model posits that individual health status is a function of their use of health services, which is explained by environment and population characteristics. Phillips et al., found that external environmental and provider-related factor were underutilized in studies which used the Behavioral Model of Health Care use. Even though this model is based on patient behavior, studies have found that different clinical specializations may influence use of preventative services and much of the variation in patient use rates have been shown to be due to physician decision-making. For this study, we adapted the model to focus on the context in which CVD prevention occurs within HIV care (Figure 2.1). In our adapted model, we focused external environmental factors that interact with patients’ predisposing characteristics to influence patients’ use of CVD preventive strategies. External environmental factors included health delivery systems such as resources, practices, and policies at the ID clinic. Provider-related factors included provider characteristics that interact with patent characteristics (e.g., specialist or generalist) to influence use of CVD prevention.

The semi-structured interview guide was based on the adapted model and included open-ended questions eliciting general perspectives of CVD prevention in HIV care settings. We also inquired about available resources for CVD prevention and ongoing professional education on CVD in HIV-infected
persons. We asked about the ease of implementation of current clinical practice guidelines for CVD prevention in practice. Participants were asked about patient characteristics that influenced their decisions to provide CVD preventative care and finally, the role of primary care providers in the management of CVD risk factors (Appendix A).

**Data Collection**

Interviews were conducted between April and October 2016. Recruitment continued until thematic saturation was achieved. One author (CM) conducted ~30 minute interviews either in person or by telephone. All interviews were digitally recorded, professionally transcribed, de-identified, and transferred to NVivo 11 for analysis. Additional information was collected from participants, which included number of years post-ID fellowship training, HIV practice setting, and U.S. region of practice were collected during the interview or abstracted from their curriculum vitae.

**Analyses**

We used template analysis, which combines inductive and deductive approaches by allowing a priori codes to be modified, removed, and augmented. The a priori codes, which were derived from the interview guide, included provider perspectives and attitudes on CVD prevention, healthcare system factors such as availability of resources to support CVD prevention, and external environment factors such as policies and practices for achievement of goals for quality of CVD risk factor management.

We applied the initial coding template to the first five interview transcripts using NVivo 11. Then we revised the initial template and emergent thematic codes were added in a hierarchical fashion to create a final coding template that was applied to all transcripts. Two authors (CM and TG) coded all transcripts. Coders checked for consistency in applying the coding template to the transcribed interviews through discussion and reconciliation. A third member of the author (AB) reviewed discrepancies between coders and provided input to the final codebook.

**Human Subjects Research**

The Institutional Review Boards at the University of North Carolina-Chapel Hill and Duke University Health System approved this study.
Results

We interviewed 19 ID specialists who had provided consent. 58% were male; 31% had > 20 years of experience and 37% had 5-9 years’ experience practicing HIV care; and 52% practiced in academic medical centers (AMC). The majority of interviews (74%) were conducted in person and the remainder by telephone. Sixty-three percent of the participants were from North Carolina while others were from Kentucky, Georgia, Alabama, and the state of Washington (Table 2.1).

Two major themes emerged from the analysis: (1) ID specialist attitudes and perceptions toward CVD risk factor management; and (2) healthcare delivery system factors. Saturation was reached after 15 interviews. (Table 2.2)

Theme 1: ID Specialist Attitudes and Perceptions Toward CVD Risk Factor Management

We found five sub-themes in the first major theme. These included: (1) pre-eminence of HIV, (2) comfort and confidence in managing CVD risk factors, (3) consultation time, (4) keeping up with current literature on CVD prevention among HIV-infected persons, and (5) knowledge of patients’ other predisposing characteristics. We discuss each sub-theme below.

1. **Pre-eminence of HIV:** Seventeen of 19 ID specialists interviewed reported that the main priority was managing their patient’s HIV infection. For example, one participant from an AMC said,

   My first priority is still the HIV. I would have to say that their HIV needs to be under some control. Not for me to pay attention to because I'll pay attention to it if their hypertension is out of control.

   Another participant from a public health clinic said,

   Again, it depends what the incentive is. If there is no incentive to do that and I just had to focus on getting the viral load undetectable, I would say, 'Oh, well that's some other guy's job for that stuff. I'm doing my job. I'm providing quality care, as measured by this person having an undetectable viral load.

   When probed about CVD risk factor management, almost all respondents said that traditional CVD risk factors (e.g., smoking, obesity) influenced their decision to provide CVD preventative care. Almost all participants (18) said that neither HIV status nor the type of ART prescribed influenced their decision to provide CVD preventative care. After further probing for the reasons for not including the type of ART into consideration for CVD risk prevention, participants cited the lack of conclusive evidence to support the association between ART and CVD. For example, a participant from a public health clinic said
I'm not totally sold on the data out there that certain ARVs are more prone to or more associated with MI than others. I struggled with this when the D.A.D (Data Collection on Adverse events of Anti-HIV Drugs) study came out a few years back...

In explaining their decision-making steps about screening for CVD as it relates to ART, one participant at an AMC said,

Of course, the whole Abacavir story with the D.A.D study and a slight increase in cardiovascular events comes up. Does it mean if someone is on Abacavir, I am more likely to screen them? Probably don't, but maybe I should. I think it is more the reverse. I think if someone has a high risk profile for cardiovascular events already, then I am probably less likely to put them on Abacavir or maybe even take them off of Abacavir.

2. Comfort and confidence: ID specialists considered themselves as consultants even though the majority said they were the primary care provider (PCP) for some of their patients. ID specialists reported low levels of confidence and comfort in managing CVD risk factors for their patients. For example, a participant at a community health clinic said,

There are some of the things that you want to screen for or some of the things that you want to evaluate when you see this person as a primary care provider because to be honest with you, as a specialist, I like doing the ID part. That's why I did a fellowship. I like the ID part. ... I don't really want to do the diabetes management. I don't really want to do the hypertension management even though we do it, and I do it.

In relation to comfort in managing CVD risk factors, a participant at a VA Medical Center said,

Generally I guess if, generally if there one thing that is out of control, whether or not it is diabetes or blood pressure, cholesterol, whatever it is, I tend to then I feel fairly comfortable taking that on, at least as a first pass. In general, if there is more than one or two that is when I say, "You really need a primary care doctor."

Some ID specialists thought that an internist's expertise was superior to theirs when it came to CVD risk factor management. For example, a participant at a community health clinic said,

If I could wave a magic wand, I would really love to have an internist that I would co-practice with that would help monitor those things.
3. *Time for Consultation:* The short visits with patients also influenced the ability of the providers to focus on CVD prevention strategies. For example, a participant who practiced at a community health clinic said,

So, all these patients have insurance. Yay! But it's still a 10 minute visit!

Yet another one who practiced at an AMC said,

Right now, our visits seem to be very focused. If I have to see 20 people in the course of the day, I'm going to be asking them about their HIV. They're going to be telling me about complications. I don't have a lot of other time to start talking to them about exercising more or diet modifications or smoking cessation and things like that each and every time. I think if I wanted to do that I'd have to have an hour-long visit with patients.

4. *Keeping up with CVD literature:* Participants reported that they were not up to date with current CVD literature among HIV-infected persons. For example, a participant at an AMC said,

I'm probably a little behind the most recent guidelines to be honest in terms of knowing all of the current standards. I've sometimes found it a little bit hard to tease out quite why there needs to be unique HIV clinical practice guidelines [for CVD] separate to other patient populations.

Most of them relied on the knowledge they gained during their residency training or when they were on general medicine consult rotation. For example, one participant at an AMC said,

It seems like whenever I go onto internal medicine, I do internal medicine 4 weeks a year, the residents are constantly naming some new scoring system, that I'm like, "Oh, my God, I didn't have that in my training."

5. *Patient’s predisposing characteristics:* ID specialists’ knowledge of individual patients’ clinical and social predisposing characteristics influenced CVD prevention. ID specialists described tradeoffs and other considerations for their patients that influenced their inability to provide CVD prevention. For example, a participant at a community health clinic said,

Sometimes it's a trade-off between, do we give them something that's more lipid-friendly? Or do we give them something that will maintain their virus and be more robust against the potential evolution of mutations?

Another participant from an AMC said,
To try and hold them, to try and help them for their drug abuse, for their financial problems, for their counseling, for the many things that are associated with HIV but those things are not as strong in my mind to get them linked in with good cardiovascular care.

**Theme 2: Healthcare Delivery System Factors**

We also found that healthcare delivery system challenges influenced CVD risk factor management in HIV care settings. This second major theme had five sub-themes: (1) System-wide policies and protocols, (2) clinical practice guidelines for CVD prevention, (3) resources, (4) clinical information systems, (5) Communication with patient’s primary care provider.

1. **System-wide policies and protocols:** Only study participants who practiced at the VA ID clinics were aware of CVD prevention guidelines that existed at their clinics or health system. Participants from VA clinics mentioned that the VA had developed system-wide clinical practice guidelines and quality measures for CVD prevention. However, all other participants we interviewed were not aware of clinic or system-wide guidelines. For example, one participant at an AMC said,

   ...the other thing that concerns me a little bit about our clinic, again, being an academic center, we’re all sort of on a different agenda, we’re not all working on the same protocol. We don’t even really have a clinic protocol.

   Furthermore, there were no internal assessments for CVD prevention in these clinics. For example, the same participant said,

   I don't know exactly how well we do because there really hasn't been an assessment of that internally.

   ID specialist practicing at the VA clinics had scorecards for CVD preventative care. When probed for their attitudes toward the scorecards, participants did not find them useful. For example, one participant said,

   We have these little quality measure report cards that we get that are called happy face reports… Many times I feel like those are not as meaningful to me as sub-specialist providers as many of the measures are really focused on things that aren't related to my patient population and what I'm responsible for them.
2. **Clinical practice guidelines for CVD prevention:** Providers used different guidelines for CVD prevention. The most cited guidelines were from the American Heart Association (AHA), the Atherosclerotic Cardiovascular Disease (ASCVD), and the Infectious Diseases Society of America (IDSA). When probed for the ease of implementation of these guidelines, participants found them hard to implement for their lack of incorporating HIV as a risk factor. For example, a participant at an AMC said,

I think that we have guidelines that just point out the association between the two, but I think that they are wanting for specific recommendations on the use of medications that modify those outcomes. For example, the risk calculator for vascular disease, it doesn't even ask about HIV status and doesn't ask if you're HIV positive, are you undetectable or not. … I mean I think that the people who put together these risk calculators aren't thinking a lot about HIV as a comorbid risk.

3. **Resources:** Participants reported diverse types of resources available at ID clinics to promote CVD prevention. Available resources differed by health system and clinic. All the participants reported that their clinics had smoking cessation programs and were able to refer patients these programs. One participant said that they had a weekly metabolic syndrome clinic and few had access to a nutritionist. Adequate staffing to support preventive care was lacking in many clinics. For example, a participant at an AMC said,

Our clinic is chronically understaffed for the number of physicians. We don't have enough nursing staff to do it properly.

For those participants practicing in rural areas, there were challenges with referral systems. For example, a participant at a community health clinic said,

For providers like me who are in rural communities, who are in community-based organizations who are not directly attached to a university, you don't even really have access to qualified specialists that you feel comfortable sending your patients to for evaluation for a host of reasons, number one being their level of expertise in taking care of people that are co-infected.

4. **Clinical Information Systems:** Participants felt that the clinical information systems could be optimized with practice alerts and CVD risk calculators to improve overall CVD prevention. For example, one participant at an AMC said,
Make Epic [a clinical information system] work for us. Half the data is already in there. … It's just a matter of telling the computer to do the work for us and tell us what someone's risk is or at least prompt us to it regularly. I think that would be an easy way to routinize screening for cardiovascular risk. It needs to do some work for a change instead of telling me what to do.

Another one at a different AMC said,

It seems like we do a lot of unnecessary check boxes stuff in the clinic that probably does not have nearly the impact on patient outcomes that more a checkbox cardiovascular prevention approach could have.

Participants said that clinical information systems were embedded with outdated CVD guidelines. For example, a participant at a VA ID clinic said,

Honestly the reminders we have are probably all from 10 years ago. As we discover new data, maybe we should be checking more frequently. They're not updated. They're very old. It would be nice to have a group that was continuously updating them at least on a yearly basis to be sure that our electronic reminder system was actually consistent with current guidelines.

5. Communication with patient's PCP: For those patients who had a PCP, participants said that they faced multiple problems with communication. These challenges were less problematic when the PCP and ID specialist were in the same healthcare system. For example, a participant at a VA ID clinic said,

I feel like when you see people outside the VA that is the big challenge, to figure out what the hell medications are they on now because the patients sure as hell never know. It is as hard for me to find them as it is for them to find me.

Another participant from a community health clinic said,

That is very, very hard to do if you're in a community setting, and you're depending on people, a provider from different health care systems. It's very hard to do.

There was also a sense that by having a primary care provider coupled with poor communication, patient’s quality of care was not optimized. For example, a participant at an AMC said,

It's very challenging. I have one in my practice who has a separate primary care provider and I feel like things are redundant.
Discussion

Through interviews with ID specialists providing care for HIV-infected patients in diverse healthcare settings, we found that the use of CVD risk prevention strategies is influenced by: (1) ID specialist attitudes and perception of their role and (2) healthcare delivery factors. Consistent with previous studies,\textsuperscript{36-37} ID specialists considered themselves as consultants and therefore prioritized the management of HIV infection in their practice. However, all respondents reported that they also served as the PCP for some of their patients. Respondents reported low levels of comfort and confidence in managing CVD risk factors. This finding is consistent with one study that found that ID-certified physicians and general medicine–certified physicians at ID clinics in VA ID clinics reported less comfort prescribing medications for common comorbid conditions compared with generalist physicians at general medicine clinics.\textsuperscript{24} However, that study did not examine healthcare delivery factors.

With respect to healthcare delivery systems, we found that most participants were not aware of any CVD prevention guidelines or protocols at their clinics or health systems. They relied on their experience and training during residency and their current interactions with internists, especially at AMCs. Participants from the VA were aware of system-wide clinical guidelines and quality metrics because the VA has published guidelines for CVD risk factors for PLHIV.\textsuperscript{46} Participants generally did not keep up as well as they wanted with the HIV/CVD literature. Participants also reported challenges implementing current CVD prevention guidelines. We found that the current clinical information systems were not optimized for decision support intended to improve the quality of CVD risk prevention. For the systems that had quality assessment tools, ID specialists did not find score cards useful. Finally, ID specialist communication with patients’ separate primary care providers faced significant barriers.

Our findings raise concerns that the identified factors may negatively impact CVD risk prevention for HIV-infected patients and thereby lower the quality of care for persons living with HIV, a worrisome narrative in this high-risk population for CVD events. Because different clinical specializations may influence patients’ use of preventative services and much of the variation in patient use rates of health care have been shown to be due to physician decision-making, these findings are of great importance in designing interventions and in maintaining the significant advances in HIV prognosis.\textsuperscript{37-39} Identifying models of care that incorporate HIV care and CVD risk prevention is critical to support the aging HIV-
infected population.\textsuperscript{40-41} In the current situation where ID specialists focus almost exclusively on HIV management, when they serve as \textit{de facto} primary care providers, CVD prevention care may not receive the required attention. Strategies such as continuous training of ID specialists in CVD risk factor management have been previously suggested previously.\textsuperscript{42-43} Nurse-led interventions for CVD prevention have been found to be cost effective in CVD prevention.\textsuperscript{44-45}

\textbf{Limitations}

There are several limitations to this study. First, although we made a concerted effort to recruit a broad swath of ID specialists, our findings have limited generalizability. As with other qualitative studies, our results highlight important themes but are not able to quantify or compare other factors such intensity, proportions, or impact of the themes that we identified. However, the findings are useful in developing hypotheses for future research.

\textbf{Conclusions}

In summary, this qualitative study of ID specialists identified two major themes regarding CVD risk factor management in HIV care settings: (1) their attitudes and perceptions toward CVD risk factor management; and (2) healthcare delivery system factors. Improving the management of traditional risk factors in this population to reduce the incidence of CVD is critical to sustain the gains in prognosis achieved with effective ART. Future research is required to describe the implementation of clinic-wide protocols for CVD prevention and acceptability of quality assessment. Optimization of decision support tools to improve the quality of CVD care provided and ongoing training of ID specialists in CVD risk prevention are necessary. Finally, future research should also focus of care coordination between ID specialists and primary care physicians.

Figure 2.1. Adapted behavioral model of health services use.
Table 2.1. Demographic Characteristics of the Study Participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All ID specialists n = 19</th>
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<tbody>
<tr>
<td><strong>Number of years of HIV practice</strong></td>
<td></td>
</tr>
<tr>
<td>5 –9</td>
<td>7</td>
</tr>
<tr>
<td>10—14</td>
<td>3</td>
</tr>
<tr>
<td>15—20</td>
<td>3</td>
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<tr>
<td>&gt;20</td>
<td>6</td>
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<tr>
<td>Male</td>
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</tr>
<tr>
<td>Female</td>
<td>8</td>
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<tr>
<td><strong>Type of Practice</strong></td>
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</tr>
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</tr>
<tr>
<td>Academic Medical Centers (AMCs)</td>
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<tr>
<td>VA</td>
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<td>Private</td>
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<tr>
<td><strong>Interview mode</strong></td>
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<tr>
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</tr>
<tr>
<td>Telephone</td>
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<tr>
<td>GA</td>
<td>1</td>
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<td>WA</td>
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<td>NC</td>
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</tr>
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Table 2.2. Evidence of Saturation: Emergent Themes by Group of ID Specialists’ Interviews

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<th>Provider Interviews</th>
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<th>6-10</th>
<th>11-15</th>
<th>16-19</th>
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<td><strong>Provider level attitudes</strong></td>
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<td>Preeminence of HIV</td>
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<td>X</td>
<td>X</td>
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<td>Confidence &amp; Comfort</td>
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<td><strong>Consultation Time</strong></td>
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<td><strong>Keeping up with the Literature</strong></td>
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<tr>
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<td><strong>Health care delivery systems</strong></td>
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<td>Clinical Practice guidelines for CVD</td>
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<td>Resources</td>
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CHAPTER 3. DOES HAVING A PRIMARY CARE PROVIDER IMPROVE THE QUALITY OF PRIMARY CARDIOVASCULAR DISEASE PREVENTION FOR PEOPLE LIVING WITH HIV?

Introduction

In recent decades, the prevalence of AIDS-defining opportunistic infections and associated mortality among people living with HIV (PLHIV) has been dramatically reduced because of the availability of effective antiretroviral therapy (ART).\(^1\) As a result of their decreased mortality from HIV infection, PLHIV are increasingly diagnosed with chronic conditions including cardiovascular disease (CVD).\(^2,3\) In fact, approximately 8–22% of deaths among PLHIV are attributed to CVD, which is the second most common cause of non-AIDS-related mortality in this population.\(^4,5\) Because of increased CVD risk and death among PLHIV, effective preventative measures are critical to reduce CVD-related morbidity and mortality. HIV infection and some antiretroviral therapy (ART) medications are risk factors for CVD independent of traditional CVD risk factors (e.g., age, hypertension, dyslipidemia, obesity, and tobacco use).\(^6-15\) The presence of traditional CVD risk factors, coupled with the unique CVD risks associated with the HIV virus and its treatment, position PLHIV in particular need of CVD-risk reducing interventions. Despite the increased risk of CVD among PLHIV, CVD risk prevention strategies in HIV care settings (measured by level of clinical guidelines compliance) are underused.\(^16-22\) For example, Litchtenstein et al. found that 46% to 69% of patients eligible for hypertension treatment in the HIV Outpatient Study received it.\(^17\) Clements et al. found that among veterans infected with HIV, hepatitis C (HCV), and HIV/HCV co-infection and were eligible for statins, 22.7%, 30.5%, and 31.5% of veterans, respectively, were not receiving Adult Treatment Panel-III (ATP III) recommended statin.\(^22\)

The reasons for the observed low quality of care are poorly understood. Low use of CVD preventative care may be related to the healthcare system, healthcare provider, or patient characteristics.\(^44\) In the context of healthcare providers, the type physician responsible for the management and long-term care of a patient may affect the use of preventative care.\(^23-25\) Therefore it is vital to evaluate if there are differences in provision of primary CVD preventative care between different physician categories who provide ongoing care to PLHIV. Since the early 1980s, a high proportion of
PLHIV in the United States have received their primary care from infectious diseases (ID) specialists at ID clinics. For some patients seen at ID clinics, non-ID primary care providers (PCP) are also involved in their care. Traditionally, the role of PCP has been to help patients prevent, understand, and manage illness; navigate the health system; and set health goals. However, there is a gap in our understanding of how the specialty (e.g., PCP or ID) of provider overseeing long-term care for PLHIV is associated with receipt of CVD primary prevention services. For example, more than a decade ago Fultz et al. found that ID specialists reported significantly less comfort managing CVD risk factors compared to non-ID primary care providers. However, this study did not examine patient level factors or actual patterns of use of medications prescription for CVD risk factors.

Thus, the objective of this study was to determine whether there was a difference in the rate of prescribing medications for two common CVD risk factors, hypertension and dyslipidemia, between PLHIV who received ongoing care from an ID specialist alone versus those that received their care from both an ID specialist and a PCP.

Methods

Study Setting and Data Source

This retrospective study was conducted at the Duke University Medical Center (DUMC) Adult ID Clinic. The Duke ID Clinic provides medical care to 2000 PLHIV. Data from routine clinic visits were obtained from electronic medical records from January 2000 to February 20, 2017, and linked to claims data that included the specialty of health care providers and insurance status.

Human Subjects Research

The Institutional Review Boards at the University of North Carolina-Chapel Hill and Duke University Health System approved this study.

Eligibility Criteria

All patients with HIV – International Classification of Diseases, ninth revision (ICD-9) diagnostic code 042 who attended >2 separate ID clinic visits over a span of at least 12 months during the study period were eligible. Several guidelines over the past 20 years have recommended between 2 – 4 visits annually for PLHIV. Patients with a known history of CVD (acute coronary syndrome, acute myocardial infarction, myocardial infarction, stroke, peripheral vascular disease, cerebrovascular disease, coronary
heart disease, or ischemic heart disease) were excluded from the study. The exclusion diagnoses were identified by ICD-9 billing data through query of the Duke Enterprise Data Unified Content Explorer (see Table 3.1).

**Dependent Variable**

We defined the dependent variables as the time from diagnosis (hypertension or dyslipidemia) to first recorded prescription on patient medical records for antihypertensive or statins, respectively. Patients who had a negative time to event (had a prescription that predated hypertension or dyslipidemia diagnosis) were excluded. Hypertension diagnosis was determined by documentation of ICD-9 codes 401 & 405 (essential and secondary hypertension). Dyslipidemia including hyperlipidemia, hypercholesterolemia, hyperglyceridemia, and hypertriglyceridemia was determined by documentation of ICD9 codes 272 – 272.8. Medications of interest for the two risk factors are listed in Table 3.4.

**Independent Variables**

We used medical records and billing records to construct a binary variable that designated whether patients had >1 PCP visit over a span of at least 12 months during the study period. This range of visits was consistent with recommended annual preventative visit for individuals in the United States. All patients seen at the ID clinic had an assigned ID specialist. Patients whose medical records indicated that they had a PCP but no visits were categorized as having only an ID specialist.

**Control Variables**

Covariates included patient sociodemographic and clinical characteristics (see Table 3.5).

**Statistical Analyses**

We described the population using means and standard deviations (for continuous variables) and frequencies and percentages (for categorical variables). The Kaplan-Meier method was used to plot time-to-event curves for patients who received care from ID specialist and PCP and those who had an ID specialist only. To compare differences in unadjusted survival curves, we used the Log-rank and Wilcoxon tests at a 5% level of significance. Estimates whose confidence intervals excluded 1 were regarded as statistically significant.

We used Cox proportional hazard models to examine the hazards of having a prescription of recommended medication (antihypertensive or statins), hereon referred to as *being prescribed*, for
patients who received care from ID specialist and PCP and those who had an ID specialist only. We formally tested the proportional hazard assumption. The Cox proportional hazard model allowed censoring and enabled us to assess two factors simultaneously: (1) whether a patient’s prescription was recorded after diagnosis of hypertension or dyslipidemia, and (2) if they had a prescription recorded, the time to having the prescription on their medical records. For the multivariate models, we controlled for sociodemographic and clinical characteristics. The Cox proportional hazard was given by:

\[ h(t | X) = h_0(t) \exp(\beta X) \]

where \( h_0(t) \) was the baseline hazard function; \( \beta \)-regression coefficient; \( X \) were control variables.

We ran two separate models for this study; one for time to being prescribed antihypertensive medications and the other for statins as described above. We assessed proportional hazards by time interaction for the two models.

**Results**

We identified 929 PLHIV who met eligibility criteria (Figure 3.1), 723 of whom were diagnosed with hypertension, 464 with dyslipidemia, and 258 with both. Among hypertensive patients, 37% were prescribed an antihypertensive during the study period. Among patients with dyslipidemia, approximately 50% were prescribed statins during the study period. The mean time from diagnosis to being prescribed medication was 48 months (range: 0 to 239.2) and 66 months (range: 0 to 229.7) for hypertensive and statins, respectively. Sixteen percent had seen a PCP along with ID specialist, 28% were female; 58% were black or African American; and 29% had different categories of health insurance coverage (Table 3.1).

**Time to Being Prescribed Antihypertensive**

Kaplan-Meier curves had a steep decline during the initial period after being-diagnosed with hypertension among patients who received care from an ID specialist and PCP. This suggested that patients received a prescription for an antihypertensive medication the same day they were diagnosed. For patients who received care from an ID specialist and PCP, 25% had antihypertensive prescription by 33 months after their hypertension diagnosis compared to 66 months for same proportion for patients who only saw an ID specialist. This trend was consistent over the study period (Figure 3.2).
In bivariate analyses, compared to those who received care from ID specialist only, those who received care from ID specialist and PCP were more likely to be prescribed an antihypertensive (HR=1.404, 95% CI 1.016-1.942). However, after controlling for covariates specified a priori, the effect of seeing an ID Specialist and PCP decreased by 50% and was no longer statistically significant. Increasing age at HIV diagnosis (AHR=1.015, 95% CI 1.0004 -1.03) and current alcohol use status (AHR= 1.431 95% CI 1.080: 1.895) were associated with higher likelihood of being prescribed antihypertensive (Table 3.2).

**Time to Being Prescribed Statins**

Kaplan-Meier curves had a steep decline during the initial days post-diagnosis of dyslipidemia for both groups of patients. In the initial period, patients seen by ID specialists only were prescribed statins earlier post-dyslipidemia diagnosis but the difference was not significant. This trend was not consistent over the study period, as the survival curves cross multiple times (Figure 3.3).

In bivariate and multivariate analyses, there were no differences in the hazard ratios for patients who saw a PCP and ID specialist compared to those who only saw an ID specialist (HR=1.404, 95% CI 0.715-1.523) and (AHR= 0.89 95% CI 0.601 -1.317) respectively. Current alcohol use status (AHR=1.466 95% CI 1.041- 2.063), and increasing age at HIV diagnosis (AHR=1.03, 95% CI 1.013 -1.048) were again associated with increasing hazard ratios of being prescribed statins. CD4 nadir and nearest CD4 count at dyslipidemia diagnosis were marginally associated with being prescribed a statin (Table 3.3).

**Discussion**

We found that PLHIV with comorbid hypertension received care from ID specialist and PCP had increased likelihood of being prescribed antihypertensive medications. This may be because PCPs are oriented toward early diagnosis and treatment of hypertension. A study by Donahue and colleagues found that generalists had a magnified perception of CVD risk without treatment and of the benefits of risk-modifying medical treatment, making them more likely to prescribe medicines earlier.

A similar pattern was not observed for statins. This may be explained by the potential for drug interactions between HIV protease inhibitors and many statins, which have led to HIV-specific guidelines for statin use in PLHIV. Therefore we might expect that patients seen by ID specialists only would be prescribed statins earlier because of the ID specialists’ exposure to the evidence base that these
medications can be safely co-administered. This evidence base might have been delayed in reaching the knowledge of PCPs who might be up to date with ID specialty literature.

There was a long duration between diagnosis and the first record of prescription in the medical records. This may also be related to the provider’s perception of their role in caring for PLHIV. In fact, qualitative studies have found that HIV providers prioritize HIV treatment and achievement or maintenance of viral suppression over other conditions. We also found that overall low proportions of PLHIV had prescribed the recommended medications during the period of the study. This finding is corroborated by other studies that have focused on underutilization of CVD preventative therapies. When we controlled for sociodemographic and clinical characteristics, increasing age at HIV diagnosis and current alcohol use increased the hazards of being prescribed antihypertensive and statins. Therefore, as individuals acquire HIV infection at later stages of their life, they may be more likely to be diagnosed and prescribed medications. With current alcohol use as the other major confounder, previous research has found that alcohol is a risk factor for both dyslipidemia and hypertension, and therefore we would expect increase in the likelihood of being diagnosed with dyslipidemia and subsequent statin prescription.

Limitations

Our study had several limitations. First, our study was conducted at a single academic medical center and thus may not reflect care in other healthcare systems or with different patient populations and practice patterns. Second, we did not include other comorbidities in our analysis; the presence of other comorbidities may influence the provision of CVD prevention strategies. Third, we lacked data on primary CVD prevention such as lifestyle modification. Fourth, the quality of EHR-derived data is limited by the quality of provider documentation and the extent to which, prescriptions were filled outside of the healthcare system. Fifth, the formal test of the proportional hazard assumption on the second model (statin) was rejected, however, the p-value of 0.05007 suggests that the assumption may not be violated. Thus, these results should be interpreted with caution.

Finally, access to a PCP and having insurance are endogenous, which may bias our results. However, in our study we restricted the sample to patients who used the access to a non-ID PCP as opposed to everyone who had a PCP in their records.
Future Research

Our findings suggest that different healthcare providers’ specialization may influence use of preventative services such as CVD primary prevention among PLHIV. Specifically, PCPs might be attuned to the need for hypertension management compared to ID specialists, and therefore development of primary care strategies within HIV care settings may increase the potential for patients to receive quality CVD prevention. Intervention strategies to encourage appropriate management of CVD risk by ID specialists are also warranted.

Future interventions may focus on quantifying the treatment effect of receiving care from an ID specialist and PCP for other modifiable CVD risk factors including tobacco use, diabetes, and others among PLHIV. Future research studies should focus on employing implementation science strategies like audit and feedback to improve time to prescription for CVD risk factors. Our findings also call for development of novel care models that are patient-centered for PLHIV to improve the utility and management of chronic conditions such as CVD.
Figure 3.1. Eligibility criteria.
Figure 3.2. Kaplan-Meier curves for time to being prescribed antihypertensive after diagnosis of hypertension for 563 PLHIV adults seen at DUMC ID Clinic 2000–2017.

Figure 3.3. Kaplan-Meier curves for time to being prescribed statins after diagnosis of dyslipidemia for 372 PLHIV adults seen at DUMC ID Clinic 2000–2017.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients n = 929</th>
<th>Saw PCP n = 146</th>
<th>No PCP n = 783</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>670 (72.12)</td>
<td>97 (66)</td>
<td>573 (73)</td>
</tr>
<tr>
<td>Female</td>
<td>259 (27.88)</td>
<td>49 (34)</td>
<td>210 (27)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>539 (58.08)</td>
<td>78 (53)</td>
<td>461 (59)</td>
</tr>
<tr>
<td>Other Races</td>
<td>390 (41.98)</td>
<td>68 (46)</td>
<td>322 (41)</td>
</tr>
<tr>
<td><strong>Insurance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>568 (63.82)</td>
<td>59 (40)</td>
<td>509 (65)</td>
</tr>
<tr>
<td>Yes</td>
<td>361 (28.86)</td>
<td>87 (60)</td>
<td>274 (35)</td>
</tr>
<tr>
<td><strong>Alcohol Use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>319 (34.34)</td>
<td>51 (35)</td>
<td>515 (66)</td>
</tr>
<tr>
<td>No</td>
<td>323 (34.77)</td>
<td>95 (65)</td>
<td>268 (34)</td>
</tr>
<tr>
<td><strong>Substance Abuse</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>80 (8.61)</td>
<td>11 (8)</td>
<td>69 (8)</td>
</tr>
<tr>
<td>No</td>
<td>536 (57.7)</td>
<td>135 (92)</td>
<td>714 (92)</td>
</tr>
<tr>
<td><strong>Tobacco use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>200 (21.53)</td>
<td>29 (20)</td>
<td>171 (22)</td>
</tr>
<tr>
<td>No</td>
<td>511 (55)</td>
<td>117 (80)</td>
<td>612 (78)</td>
</tr>
<tr>
<td><strong>Age at HIV Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>41.77 (13-81)</td>
<td>43.46 (21-67)</td>
<td>41.32 (13-81)</td>
</tr>
<tr>
<td>No</td>
<td>278.98 (1-2099)</td>
<td>278.98 (2-1674)</td>
<td>278.2 (1-2099)</td>
</tr>
<tr>
<td><strong>CD4 Nadir</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nearest CD4 at HTN Diagnosis</strong></td>
<td>503.66 (2-2451)</td>
<td>548 (5-2451)</td>
<td>495 (2-2124)</td>
</tr>
<tr>
<td><strong>BMI at nearest HTN Diagnosis</strong></td>
<td>30.08 (14.83-194.65)</td>
<td>32.19 (14.83-194.65)</td>
<td>29.64 (17.45-162.5)</td>
</tr>
<tr>
<td><strong>Nearest CD4 at Dyslipidemia Diagnosis</strong></td>
<td>632.19 (6-2451)</td>
<td>657.5 (6-2451)</td>
<td>610.7 (10-1579)</td>
</tr>
<tr>
<td><strong>BMI at nearest Dyslipidemia Diagnosis</strong></td>
<td>29.27 (17.03-156)</td>
<td>30.24 (17.03-83.86)</td>
<td>29.22 (17.45-155.9)</td>
</tr>
<tr>
<td><strong># months between HTN Dx and Antihypertensive Rx</strong></td>
<td>48 (0-239)</td>
<td>87 (0-249)</td>
<td>89 (0-247)</td>
</tr>
<tr>
<td><strong># month between Dyslipidemia Dx and Statin Rx</strong></td>
<td>66 (0-229)</td>
<td>69 (0-174)</td>
<td>63 (0-229)</td>
</tr>
</tbody>
</table>

Abbreviations: HTN - Hypertension, Dx - Diagnosis; Rx - Prescription
Table 3.2. Crude and Adjusted Hazard Ratios for Predictors of Being Prescribed Antihypertensive Among PLHIV Who Saw a PCP in Conjunction with ID Specialist Compared to Those Who Only Saw an ID Specialist at DUMC ID Clinic, 2002–2017

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude HR</th>
<th>95% CI</th>
<th>Adjusted HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>1.404</td>
<td>(1.016 - 1.942)</td>
<td>1.244</td>
<td>(0.888 - 1.743)</td>
</tr>
<tr>
<td>BMI at nearest HTN Dx</td>
<td>0.9997864</td>
<td>(.990 - 1.0096)</td>
<td>1.000928</td>
<td>(0.991 - 1.0107)</td>
</tr>
<tr>
<td>Age at HIV Dx</td>
<td>1.008</td>
<td>(.995 - 1.021)</td>
<td>1.0149</td>
<td>(1.00036 - 1.0296)</td>
</tr>
<tr>
<td>Female</td>
<td>0.8629328</td>
<td>(0.646 - 1.153)</td>
<td>0.913</td>
<td>(0.657 - 1.268)</td>
</tr>
<tr>
<td>Black</td>
<td>0.7084429</td>
<td>(.541 - 0.927)</td>
<td>0.789</td>
<td>(0.582 - 1.0696)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>2.108255</td>
<td>(1.615 - 2.751)</td>
<td>1.431</td>
<td>(1.0803-1.895)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>1.785875</td>
<td>(1.208 - 2.639)</td>
<td>1.326</td>
<td>(0.867-2.0276)</td>
</tr>
<tr>
<td>CD4 Nadir</td>
<td>1.000343</td>
<td>(0.999 - 1.000827)</td>
<td>1.000</td>
<td>(0.999-1.000362)</td>
</tr>
<tr>
<td>Nearest CD4 at HTN Dx</td>
<td>1.000487</td>
<td>(1.000145 - 1.00083)</td>
<td>1.000322</td>
<td>(0.9998-1.000825)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1.323</td>
<td>(0.9737 -1.799)</td>
<td>0.891</td>
<td>(0.634-1.252)</td>
</tr>
<tr>
<td>Uninsured</td>
<td>0.829</td>
<td>(0.636 -1.0805)</td>
<td>1.0156</td>
<td>(0.763 - 1.352)</td>
</tr>
</tbody>
</table>

Hazards Ratios are based on Cox proportional hazard model on 563 patients
Formal test of proportional hazard (HR= 0.9999882 p-value =0.992)
Table 3.3. Crude and Adjusted Hazard Ratios for Predictors of Being Prescribed Statins Among PLHIV Who Saw a PCP in Conjunction with ID Specialist Compared to Those Who Only Saw an ID Specialist at DUMC ID Clinic, 2002–2017

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude HR</th>
<th>95% CI</th>
<th>Adjusted HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>1.0437</td>
<td>(0.715-1.523)</td>
<td>0.890</td>
<td>(0.601-1.317)</td>
</tr>
<tr>
<td>BMI at nearest dyslipidemia Dx</td>
<td>0.997</td>
<td>(0.983 - 1.012)</td>
<td>1.00042</td>
<td>(0.985 - 1.0156)</td>
</tr>
<tr>
<td>Age at HIV Dx</td>
<td>1.027</td>
<td>(1.00966 -1.045)</td>
<td>1.030</td>
<td>(1.013 -1.048)</td>
</tr>
<tr>
<td>Female</td>
<td>1.160</td>
<td>(0.817 -1.647)</td>
<td>1.1200</td>
<td>(0.739 -1.701)</td>
</tr>
<tr>
<td>Black</td>
<td>1.224</td>
<td>(0.891-1.681)</td>
<td>1.204</td>
<td>(0.841-1.727)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.625</td>
<td>(1.177- 2.242)</td>
<td>1.466</td>
<td>(1.041-2.063)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>1.114358</td>
<td>(0.603- 2.060)</td>
<td>0.857</td>
<td>(0.455-1.615)</td>
</tr>
<tr>
<td>CD4 Nadir</td>
<td>0.9996251</td>
<td>(0.999 -1.000332)</td>
<td>0.999</td>
<td>(0.998-0.999)</td>
</tr>
<tr>
<td>Nearest CD4 at dyslipidemia Dx</td>
<td>1.000208</td>
<td>(0.999-1.000659)</td>
<td>1.000663</td>
<td>(1.000087-1.00124)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1.568507</td>
<td>(1.044 - 2.356)</td>
<td>1.252</td>
<td>(0.824-1.903)</td>
</tr>
<tr>
<td>Uninsured</td>
<td>1.10337</td>
<td>(0.801 -1.519)</td>
<td>1.2950</td>
<td>(0.919 -1.826)</td>
</tr>
</tbody>
</table>

Hazard Ratios are based on Cox proportional hazard model on 372 patients; Formal test of proportional hazard (HR = 1.000385 p-value 0.050)
Table 3.4. Primary CVD Prevention Medications

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Dyslipidemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benazepril</td>
<td>Simvastatin</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Pravastatin</td>
</tr>
<tr>
<td>Losartan</td>
<td>Atorvastatin</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Rosuvastatin</td>
</tr>
<tr>
<td>Lisinopril</td>
<td></td>
</tr>
<tr>
<td>Atacand</td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td></td>
</tr>
<tr>
<td>Enalapril</td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td></td>
</tr>
</tbody>
</table>

Table 3.5. Control Variables

<table>
<thead>
<tr>
<th>Demographics Characteristics</th>
<th>Clinical Characteristics</th>
<th>Other characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at HIV dx</td>
<td>CD4 count at the time of hypertension or dyslipidemia diagnosis</td>
<td>Tobacco use status</td>
</tr>
<tr>
<td>Race</td>
<td>Nadir CD4 count</td>
<td>Substance abuse status</td>
</tr>
<tr>
<td>Sex</td>
<td>Body Mass Index at the time of hypertension or dyslipidemia diagnosis</td>
<td>Alcohol use status</td>
</tr>
</tbody>
</table>
REFERENCES


PMC3154840


CHAPTER 4. DIFFERENCES IN PRESCRIPTION PATTERNS FOR SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE FOR PEOPLE LIVING WITH HIV

Introduction

Following a major ischemic cardiac event, patients require long-term management of cardiovascular disease (CVD) risk factors to control disease progression and prevent subsequent cardiac events or death, also referred to as secondary CVD prevention. Studies have found that a significant number of cardiac events occur in patients previously diagnosed with CVD. For example, Kerr et al. found that 42% of cardiac events occurred in individuals who had prior CVD and that CVD risk was approximately 20% higher compared to those without prior CVD. These findings highlight the need for intensive secondary CVD prevention among average-risk patients.

There is also a need to better understand secondary prevention of CVD among patients with elevated risk such as people living with HIV (PLHIV). PLHIV have an estimated 4.5-fold greater risk for sudden cardiac death compared to the general population. In the past decade, research on CVD among PLHIV has been on understanding the epidemiology, etiology, and primary prevention of CVD in PLHIV. However, there exists a gap in knowledge on secondary prevention and long-term care for CVD among PLHIV. For example, Pearce et al. found that PLHIV were significantly less likely than uninfected patients to receive standard of care procedures for acute myocardial infarction. However, the reasons for these differences were not clear.

In addition lifestyle modification, therapeutic strategies are recommended for secondary CVD prevention. The therapeutic strategy most commonly recommended is antiplatelet agents. Also, there have been recommendations of initiating and maintaining a beta-blocker regimen for patients after an acute myocardial infarction or diagnosis of coronary atherosclerosis, intermediate coronary syndrome, or angina pectoris syndrome. Beta blockers are used to manage cardiac arrhythmias after a myocardial infarction event and to protect the heart from a subsequent event. The duration between diagnosis and filling the prescription has been shown to have a significant effect of the likelihood of subsequent CVD event or death.
Despite these guidelines, many PLHIV fail to receive potential lifesaving secondary CVD preventative therapies because of provider, patient, and health system factors.\textsuperscript{27-31} For example, with respect to healthcare providers, limited time with patients and complex medication regimens influence compliance with guidelines.\textsuperscript{28} For patients, substance abuse, mental illness, language barriers, poverty and low levels of literacy have been found to influence adherence to secondary CVD preventative care.\textsuperscript{27-30} For the health system, policies and resources, organization, and physician supply have been found to influence provision preventative care.\textsuperscript{31} In this study we focused on the healthcare providers who deliver long-term care for PLHIV. Apart from patient-related factors, studies have found that the type of physician responsible for the management and long-term care of a patient may affect the use of CVD preventative care.\textsuperscript{32-34} Therefore examining healthcare provider factors that influence use of these preventative strategies is of great importance in improving the quality of care for PLHIV.

After CVD diagnosis, the initial acute care may be provided by a cardiologist, and then over time this specialty care may be turned over their primary care provider (PCP) for long-term monitoring.\textsuperscript{35} In HIV care, for more than three decades, a high proportion of PLHIV in the United States have received their primary care from infectious diseases (ID) specialists at ID clinics.\textsuperscript{36} For some patients seen at ID clinics, other non-ID outpatient PCP are also involved in their care. One the role of PCPs is to help patients prevent and manage illness, navigate the health system, and set health goals.\textsuperscript{37} Apart from limited literature on secondary prevention, there is a dearth of literature on the effect of different specializations of physician who provide care for PLHIV as it relates to CVD secondary prevention. Thus, the objective of this study was to determine whether there was a difference in the rate of prescribing and time to being prescribed medications from diagnosis of CVD for two secondary prevention therapies, antiplatelet agents and beta blockers, between PLHIV who received care from an ID specialist alone versus those that saw an ID specialist and PCP.

\textbf{Methods}

\textbf{Study Setting and Data Source}

The study was conducted at the Duke University Medical Center Adult ID Clinic. The Duke ID Clinic consistently provides medical care to approximately 2,000 PLHIV. Data from routine clinic visits
were obtained from electronic medical records from January 3, 1997, to January 5, 2017, and claims data that included the specialty of healthcare providers and insurance status were linked in the database.

Human Subjects Research

The Institutional Review Boards at the University of North Carolina-Chapel Hill and Duke University Health System approved this study.

Eligibility Criteria

All patients with HIV – International Classification of Diseases, ninth revision (ICD-9) diagnostic code 042 who attended >2 separate ID clinic visits over a span of at least 12 months during the study period were eligible. Several guidelines over the past 20 years have recommended between 2 – 4 visits annually for PLHIV. Patients with a known history of CVD (acute coronary syndrome, acute myocardial infarction, myocardial infarction, stroke, peripheral vascular disease, cerebrovascular disease, coronary heart disease, or ischemic heart disease) were included in the study. Diagnoses were determined by clinical or final billed ICD-9 code through query of the Duke Enterprise Data Unified Content Explorer (Table 4.1).

Dependent Variable

The dependent variable was time from diagnosis of CVD to first recorded prescription on patient medical records for antiplatelet agents or beta blockers. Patients who had a negative time to event (had a prescription on record prior to CVD diagnosis) were excluded. This may have occurred because antiplatelet agents were also recommended for primary prevention of CVD during the study period but we were interested in secondary CVD prevention. Beta blockers were also recommended for primary prevention of CVD (i.e., management of hypertension) and, as mentioned above, our analysis was focused on secondary prevention. Antiplatelet agents available during the study period included cilostazol, aspirin, clopidogrel, and prasugrel. Beta blockers included atenolol, timolol, pindolol, labetalol, carvedilol, and metoprolol.

Independent Variables

We constructed a dichotomous variable indicating whether a patient had >1 PCP visit over a span of at least 12 months during the study period. This range of visits was consistent with recommended annual preventative visit for individuals in the United States. Because of their HIV infection; all patients
seen at the ID clinic have an ID specialist. Patients whose medical records indicated that they had a PCP but had no visits were categorized as receiving care from only an ID specialist.

**Control Variables**

Control variables included patient sociodemographic and clinical characteristics (Table 4.5).

**Statistical Analyses**

We described the population; using means and standard deviations (for continuous variables) and frequencies and percentages (for categorical variables). The Kaplan-Meier method was used to plot time to event curves for patients who received care from ID specialists and PCPs and those who had an ID specialist only. To compare differences in unadjusted survival curves, we used the Log-rank and Wilcoxon tests at a 5% level of significance. Estimates whose confidence intervals excluded 1 were regarded as statistically significant.

We used Cox proportional hazard models to examine the hazards of having a prescription of recommended medication (antiplatelet agents or beta blockers), hereon referred to as *being prescribed*, for patients who received care from ID specialist and PCPs and those had an ID specialist only. We formally tested the proportional hazard assumption. The Cox proportional hazard model allowed censoring and enabled us to assess two factors simultaneously: (1) whether a patient’s prescription was recorded after diagnosis of CVD, and (2) if they had a prescription recorded, the time to having the prescription on their medical records. Because the diagnosis of acute myocardial infarction requires a confirmatory test, for sensitivity analysis, we restricted the sample to only those who had acute myocardial infarction.

For the multivariate models, we controlled for sociodemographic and clinical characteristics. The Cox proportional hazard was given by:

\[ h(t | X) = h_0(t) \exp(\beta X) \]

where \( h_0(t) \) was the baseline hazard function; \( \beta \)- regression coefficient; \( X \) were control variables.

We ran two separate models for this study; one for time to being prescribed antiplatelet agents and the other for beta blockers as described above. We assessed proportional hazards by time interaction for the two models.
Results

We identified 340 PLHIV who met initial eligibility criteria (Figure 4.1) Seventy-five percent were male, 64% were black or African American, and 67% had health insurance coverage at the time of CVD diagnosis. Twenty-two percent of patients received care from their PCP and an ID specialist; 18% were using illicit drugs and the mean age at HIV diagnosis was 47.3 years (range: 20–90). Twenty-five percent had an acute myocardial infarction diagnosis, 61% had other forms of chronic ischemic heart disease, and the rest had intermediate coronary syndrome, old myocardial infarction, or angina pectoris syndrome.

The annual number of CVD diagnoses among PLHIV receiving care at Duke varied by year during the study period (1997–2017), with an annual average of 16 new diagnoses of CVD per year. The highest number of CVD diagnoses occurred between 2005 and 2009; this was also true for the sub-types of CVD diagnosis per year (Figure 4.2).

Approximately half the patients had been prescribed antiplatelet agents, while 25% had beta blocker prescriptions during the study period. The mean time between diagnosis of CVD to being prescribed an antiplatelet agent was 54 months (range: 0–214). For beta blocker the mean time was 72 months (range: 0–213). When we restricted the diagnosis codes to only acute myocardial infarction, which has a confirmatory test, the mean number of months from diagnosis to prescription was 57 months (range: 0–175) and 81 months (range: 0–197) for antiplatelet agents and beta blockers, respectively.

Time to Being Prescribed Antiplatelet

Kaplan-Meier curves showed a steep decline during the initial days following diagnosis of CVD among patients who received care from their PCP and an ID specialist. This may suggest that many patients received a prescription the same day they were diagnosed. For patients who received care from both an ID specialist and PCP, 25% had antiplatelet prescriptions by 10 months after their CVD diagnosis, compared to 60 months after their CVD diagnosis for same proportion for patients who only saw an ID specialist. This trend was consistent over the study period (Figure 4.4).

In bivariate analysis, compared to those who received care from ID specialist only, those who received care from ID specialist and PCP were more likely to be prescribed antiplatelet agents earlier (HR=2.28, 95% CI 1.58 – 3.27). However, after controlling for sociodemographic and clinical
characteristics, the effect of seeing a PCP along with ID specialist was not significant (AHR 1.49, 95% CI 0.99 – 2.23). Increasing age at HIV diagnosis (AHR=1.03, 95% CI 1.008 -1.04), year of CVD diagnosis (AHR= 1.23 95% CI 1.16- 1.30), and current tobacco use status (AHR= 1.95 95% CI 1.25 -3.02) were associated with higher likelihood of being prescribed antiplatelet agents (Table 4.3.)

**Time to Being Prescribed Beta Blockers**

Kaplan-Meier curves showed a moderately steep decline during the initial days post-diagnosis of CVD in both groups of patients, suggesting that most patients in both groups did not have a prescription in their medical records that same day. For patients who saw a PCP in conjunction with ID specialist, 25% had beta blocker prescriptions by 100 months after their CVD diagnosis compared to 150 months for same proportion for patients who only saw an ID specialist. This trend was consistent over the study period (Figure 4.2).

In bivariate analysis, compared to PLHIV who received care from ID specialist only, those who received care from both an ID specialist and their PCP were more likely to be prescribed beta blockers earlier (HR =1.69, 95% CI 1.02 – 2.80). In the adjusted model, the effect of a PCP was not significant (AHR= 1.46 95% CI 0.66 -1.96). Increasing age at HIV diagnosis (AHR= 1.025 95% CI 1.003- 1.05), BMI at CVD diagnosis (AHR= 1.04 95% CI 1.003 – 1.04), and year of CVD diagnosis (AHR = 1.16 95% CI 1.09 – 1.25) were associated with higher likelihood of being prescribed beta blockers (Table 4.4).

**Discussion**

We found that PLHIV with established CVD who saw their PCP in conjunction with an ID specialist had increased likelihood of being prescribed antiplatelet agents and beta blockers medications compared to those who only saw an ID specialist. This observation may reflect the differences between the roles of a PCP and that of an ID specialist when it comes to preventative care. Even though ID specialists were de facto primary care providers for the patients who did not have their PCPs, their practice patterns differed. We also found that, overall, low proportions of PLHIV had been prescribed the recommended medications during the period of the study. In the general population in high-income settings, around 60% of patients are prescribed antiplatelet therapy and 50% beta-blockers for secondary prevention. In the United States, Muntner et al. estimated that among patients with established CVD, only 44.5% receive an antiplatelet agent prescription. However, given that HIV patients are at a higher
risk for CVD events than the general population, underuse of preventative strategies may increase the likelihood of death in this PLHIV.

Our study also found long delays in being prescribed secondary CVD therapies. These delays were also experienced by those who had a diagnosis of acute myocardial infarction. In a population-based study, Jackevicius et al. found that patients who filled none of their discharge prescriptions within 120 days after myocardial infarction had an 80% increased odds of death and those who filled only some of their prescriptions had a 44% increased odds of death compared with those who filled most of their prescriptions.\textsuperscript{26} Although this was related to filled prescriptions and not provider ordering of medications, this underscores the need to reduce the duration between diagnosis and prescription. When we controlled for sociodemographic and clinical characteristics, it was unsurprising that increasing age at HIV diagnosis increased the hazards of being prescribed antiplatelet agents and beta blockers given that CVD risk increases with age. Current tobacco use at the time of CVD diagnosis was also found to increase the likelihood of being prescribed antiplatelet agents, whereas increasing body mass index (BMI) was found to increase the likelihood of being prescribed beta blockers. This may be because tobacco use and higher BMI have been found to be risk factor for CVD and because the patients already had a CVD diagnosis, there was an increased likelihood of being prescribed these therapies to reduce the risk of reoccurrence.\textsuperscript{34} Finally, a one year increase in the year of CVD diagnosis was associated with higher likelihood of being prescribed antiplatelet agents and beta blockers. This observation may reflect the evolution of HIV treatment in the United States. With the availability of ART in 1995, the prognosis of PLHIV dramatically improved, and therefore in subsequent years, the likelihood of being diagnosed with CVD increased. We also observed that the highest frequency of CVD diagnoses annually occurred between 2005 and 2009, which is when landmark studies described the association of ART with increased CVD risk.\textsuperscript{4, 6, 42-46} Subsequently, providers may have been more aware of CVD among PLHIV, thereby influencing their diagnosis recognition.

Limitations

Our study had several limitations. First, our study was conducted at a single academic medical center and thus may not reflect care in other healthcare systems or with different patient populations and practice patterns. Second, we did not include other comorbidities in our analysis; the presence of other
comorbidities may influence the provision of CVD prevention strategies. Third, we lacked data on primary CVD prevention such as lifestyle modification. Fourth, the quality of EHR-derived data is limited by the quality of provider documentation and the extent to which, prescriptions were filled outside of the healthcare system. Fifth, we did not control for the type of ART regimens. Sixth, we did not have data on over-the-counter antiplatelet therapy. However, our study did not assess prescription fills but rather documentation of prescription.

**Future Research**

Our study findings suggest that PCPs might be more attuned to the need for antiplatelet agents and beta blocker therapies compared to ID specialists. Therefore, intervention strategies to encourage appropriate management of secondary CVD risk by ID specialists are warranted because a high proportion of PLHIV see only ID specialists. Further, because of the involvement of a cardiologist soon after a cardiac event, future research should focus on adapting innovative care models such as the “model for shared care of elderly patients with cancer.” Future interventions should focus on quantifying the treatment effect of seeing a PCP for other CVD risk factors management including smoking cessation, which have been found to be an important CVD risk factor in this population. Innovative models of care for multiple chronic conditions are needed to improve the quality of secondary CVD prevention. To support utility and timely prescription of secondary CVD therapies, strategies such as audit and feedback are necessary.
Figure 4.1. Eligibility criteria.
Figure 4.2. Annual number of CVD diagnosis for PLHIV and seen at DUMC ID Clinic, 1997–2017.

Figure 4.3. Kaplan-Mieir curves for time to being prescribed antiplatelet agents after diagnosis of CVD for 247 PLHIV adults seen at DUMC ID Clinic, 1997–2017.
Figure 4.4. Kaplan-Meier curves for time to being prescribed beta blocker agents after diagnosis of CVD for 267 PLHIV adults seen at DUMC ID Clinic, 1997–2017.

Table 4.1. ICD-9 Codes Used to Determine Eligibility and Their Distribution

<table>
<thead>
<tr>
<th>ICD-9 Code</th>
<th>Diagnosis name</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>410.X</td>
<td>Acute myocardial infarction</td>
<td>86</td>
<td>25%</td>
</tr>
<tr>
<td>411.X</td>
<td>Other Acute and Subacute forms of ischemic heart disease</td>
<td>17</td>
<td>5%</td>
</tr>
<tr>
<td>412</td>
<td>Old myocardial infarction</td>
<td>15</td>
<td>4%</td>
</tr>
<tr>
<td>413.x</td>
<td>Angina pectoris</td>
<td>16</td>
<td>5%</td>
</tr>
<tr>
<td>414.x</td>
<td>Other forms of chronic ischemic heart disease</td>
<td>206</td>
<td>61%</td>
</tr>
</tbody>
</table>
Table 4.2. Demographic and Clinical Characteristics of HIV-Infected Persons eligible for Secondary Prevention of CVD at Duke University Medical Center ID Clinic, 1997–2017

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients n =340</th>
<th>ID Specialist &amp; PCP n =75</th>
<th>ID Specialist Only n = 265</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>254 (75)</td>
<td>56 (75)</td>
<td>198 (75)</td>
</tr>
<tr>
<td>Female</td>
<td>86 (25)</td>
<td>19(25)</td>
<td>67 (25)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>216 (64)</td>
<td>39 (52)</td>
<td>180(68)</td>
</tr>
<tr>
<td>Other Races</td>
<td>124 (36)</td>
<td>36 (48)</td>
<td>85(33)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>113(33)</td>
<td>32 (43)</td>
<td>81 (31)</td>
</tr>
<tr>
<td>Yes</td>
<td>227 (67)</td>
<td>43 (57)</td>
<td>184 (69)</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>74 (22)</td>
<td>28 (37)</td>
<td>46 (17)</td>
</tr>
<tr>
<td>No</td>
<td>266 (78)</td>
<td>47 (63)</td>
<td>219 (83)</td>
</tr>
<tr>
<td>Substance Abuse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (8)</td>
<td>9 (12)</td>
<td>18 (7)</td>
</tr>
<tr>
<td>No</td>
<td>313 (92)</td>
<td>66 (88)</td>
<td>247 (93)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60 (18)</td>
<td>16 (21)</td>
<td>44 (17)</td>
</tr>
<tr>
<td>No</td>
<td>280 (82)</td>
<td>59 (79)</td>
<td>221 (83)</td>
</tr>
<tr>
<td>Age at HIV Diagnosis (years)</td>
<td>47.3 (20 -90)</td>
<td>48.4 (26 - 77)</td>
<td>47 (20 -90)</td>
</tr>
<tr>
<td>CD4 Nadir</td>
<td>204 ( 1 - 1403)</td>
<td>233 (2- 1015)</td>
<td>195 (1-1096)</td>
</tr>
<tr>
<td>Nearest CD4 at CVD Diagnosis</td>
<td>424 (1 - 1096)</td>
<td>501.5 (7- 1327)</td>
<td>402.3 ( 1- 1832)</td>
</tr>
<tr>
<td>BMI at nearest CVD Diagnosis</td>
<td>27.7 (15.1-55.7)</td>
<td>27.7 (15.1- 45.8)</td>
<td>27.6 (16.3 - 55.8)</td>
</tr>
</tbody>
</table>

Abbreviations : CVD= cardiovascular disease; Dx =Diagnosis; Rx - Prescription
Table 4.3. Crude and Adjusted Hazard Ratios for Predictors of Being Prescribed Antiplatelet Agents Among PLHIV Who Received Care from Their PCP in Conjunction with ID Specialist Compared to Those Who Only Saw an ID Specialist at DUMC ID Clinic, 1997–2017

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude HR</th>
<th>95% CI</th>
<th>Adjusted HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>2.28</td>
<td>(1.58 - 3.27)</td>
<td>1.49</td>
<td>(0.99- 2.23)</td>
</tr>
<tr>
<td>BMI at nearest CVD Diagnosis</td>
<td>1.008</td>
<td>(0.98 -1.02)</td>
<td>1.01</td>
<td>(0.99 - 1.04)</td>
</tr>
<tr>
<td>Age at HIV diagnosis</td>
<td>1.020</td>
<td>(1.01 - 1.03)</td>
<td>1.04</td>
<td>(1.02 - 1.05)</td>
</tr>
<tr>
<td>Year of CVD dx</td>
<td>1.24</td>
<td>(1.18 - 1.30)</td>
<td>1.23</td>
<td>(1.16 - 1.30)</td>
</tr>
<tr>
<td>Male</td>
<td>1.26</td>
<td>(0.98 -1.64)</td>
<td>1.380</td>
<td>(0.83 - 2.27)</td>
</tr>
<tr>
<td>Black</td>
<td>0.87</td>
<td>(0.68 - 1.11)</td>
<td>0.810</td>
<td>(0.53 - 1.23)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>2.24</td>
<td>(1.75 - 2.87)</td>
<td>1.270</td>
<td>(0.83 - 1.94)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>2.15</td>
<td>(1.52- 3.05)</td>
<td>1.530</td>
<td>(0.86 - 2.73)</td>
</tr>
<tr>
<td>CD4 Nadir</td>
<td>1.0013</td>
<td>(1.0008 - 1.002)</td>
<td>0.999</td>
<td>(0.999 - 1.001)</td>
</tr>
<tr>
<td>Nearest CD4 at CVD Diagnosis</td>
<td>1.001</td>
<td>(1.0007 - 1.0013)</td>
<td>1.0005</td>
<td>(0.999 - 1.001)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>2.15</td>
<td>(1.66 - 2.78)</td>
<td>1.95</td>
<td>(1.25 - 3.02)</td>
</tr>
<tr>
<td>Insurance</td>
<td>0.93</td>
<td>(0.73 -1.18)</td>
<td>0.73</td>
<td>(0.49 - 1.01)</td>
</tr>
<tr>
<td>tvc p-value = 0.893</td>
<td>1.000645</td>
<td>p=0.414</td>
<td>0.9998937</td>
<td>p=0.414</td>
</tr>
</tbody>
</table>

Hazards Ratios are based on Cox proportional hazard model on 247 PLHIV
Table 4.4. Crude and Adjusted Hazard Ratios for Predictors of Being Prescribed Beta Blockers Among PLHIV Who Received Care from Their PCP in Conjunction with ID Specialist Compared to Those Who Only Saw an ID Specialist at DUMC ID Clinic, 1997–2017

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude HR 95% CI</th>
<th>Adjusted HR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>1.69 (1.03 - 2.8)</td>
<td>1.460 (0.66 - 1.96)</td>
</tr>
<tr>
<td>BMI at nearest dyslipidemia diagnosis</td>
<td>1.020 (0.993 - 1.05)</td>
<td>1.04 (1.004 - 1.07)</td>
</tr>
<tr>
<td>Age at HIV diagnosis</td>
<td>1.010 (0.994- 1.03)</td>
<td>1.030 (1.003 - 1.05)</td>
</tr>
<tr>
<td>Year of CVD dx</td>
<td>1.19 (1.11 - 1.27)</td>
<td>1.17 (1.09 - 1.25)</td>
</tr>
<tr>
<td>Male</td>
<td>1.190 (0.73 -1.96)</td>
<td>1.2800 (0.68 - 2.38)</td>
</tr>
<tr>
<td>Black</td>
<td>0.780 (0.49- 1.23)</td>
<td>0.980 (0.55 - 1.71)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.210 (0.71 - 2.05)</td>
<td>0.810 (0.45 - 1.6)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>1.3 (0.58 - 3.09)</td>
<td>0.890 (0.37 - 2.16)</td>
</tr>
<tr>
<td>CD4 Nadir</td>
<td>1.000 (0.999 -1.002)</td>
<td>1.000 (0.998 - 1.002)</td>
</tr>
<tr>
<td>Nearest CD4 at CVD Diagnosis</td>
<td>1.00037 (.999 - 1.001)</td>
<td>1.00002 (.999 - 1.001)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1.49 (0.87- 2.54)</td>
<td>1.300 (0.71 - 2.38)</td>
</tr>
<tr>
<td>Insurance</td>
<td>1.06 (0.65- 1.30)</td>
<td>0.7900 (0.46 - 1.37)</td>
</tr>
<tr>
<td>tvc</td>
<td>1.000645 (0.4698937)</td>
<td>p-value = 0.893 (p-value 0.414)</td>
</tr>
</tbody>
</table>

Hazards Ratios are based on Cox proportional hazard model on 267 PLHIV
Table 4.5. Control Variables

<table>
<thead>
<tr>
<th>Demographics Characteristics</th>
<th>Clinical Characteristics</th>
<th>Other characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age at HIV dx</td>
<td>• CD4 count at the time of hypertension or dyslipidemia diagnosis</td>
<td>• Tobacco use status</td>
</tr>
<tr>
<td>• Race</td>
<td>• Nadir CD4 count</td>
<td>• Substance abuse status</td>
</tr>
<tr>
<td>• Sex</td>
<td>• Body Mass Index at the time of hypertension or dyslipidemia diagnosis</td>
<td>• Alcohol use status</td>
</tr>
<tr>
<td>• Health Insurance status</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


REFERENCES

1. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation.


CHAPTER 5. SUMMARY OF FINDINGS AND IMPLICATIONS FOR POLICY, PRACTICE, AND RESEARCH

Findings from this dissertation provide insights to the factors that influence cardiovascular disease (CVD) prevention among people living with HIV (PLHIV) in the United States. Specifically, utilizing the Andersen Behavioral Model and multiple methods this dissertation illuminated the importance of evaluating contextual factors that influence CVD prevention for PLHIV.

**Infectious Disease Specialists' Perceptions and Attitudes**

In the qualitative study, we found that infectious disease (ID) specialists considered themselves consultants whose central focus was management of HIV even though they were also the *de facto* primary care physician (PCP) for majority of their patients. For patients who had their own PCP, ID specialists cited multiple challenges when communicating with the PCPs, especially when the PCP was not in the same healthcare system. This finding suggests that poor care coordination between the ID specialist and the PCP may negatively affect CVD outcomes. ID specialists also reported lower levels of comfort and confidence in managing CVD risk factors in their patient panels. This was related to the length of time allocated to see a patient and also access to CVD literature for PLHIV. Therefore future research should focus developing interventions to include CVD prevention in HIV care settings; assessing the provision of ongoing education for CVD prevention among PLHIV to ID specialists and improvement of care coordination between ID specialist and PCP.

**Healthcare Delivery Systems Factors**

In this study we found that majority of ID specialist were not aware of any CVD prevention guidelines or protocols at their clinics or health systems. Most of them used guidelines for uninfected populations and that posed challenges in implementation. Additionally, the clinical information systems deployed for patient care were not optimized to aid in decision support for CVD prevention for PLHIV. These findings highlight the need to implement current research findings of the association between HIV and CVD in clinical practice and also the development of guidelines for CVD prevention in PLHIV. We also found that resources to support CVD prevention in HIV care settings differed by healthcare system...
and clinic. This finding has clinical practice implications and also poses a challenge in the general evaluation of performance from one HIV care setting to another. Therefore future research should focus on the development of a minimum set of resources that ID clinics should have to optimize CVD prevention. Taken together the qualitative study illuminated the need for research and interventions focused on reducing barriers found in HIV care settings to improve the quality of CVD prevention.

**Types of HIV Care Provider and Time to Being Prescribed CVD Risk Factors Therapies**

In the quantitative studies that focused on primary prevention of CVD, we found that PLHIV with comorbid hypertension who received care from an ID specialist and their PCP were more likely to be prescribed antihypertensive medications earlier. PLHIV with a diagnosis of dyslipidemia who received care from an ID specialist and a PCP were less likely to be prescribed statins earlier, but the results were not statistically significant. These findings underscore the need for collaboration between ID specialists and PCPs in CVD prevention for PLHIV.

With respect to PLHIV with established CVD, those who received care from an ID specialist and their PCP were more likely to being prescribed beta blocker and antiplatelet agents. These findings may reflect the differences between the roles of a PCP and that of an ID specialist when it comes to preventative care. Therefore, future research and interventions should focus on development of primary care strategies within HIV care settings, which may increase the potential for patients to receive quality CVD prevention. Intervention strategies to encourage appropriate management of CVD risk factors by ID specialists are also warranted. Future research should also focus on quantifying the treatment effect of receiving care from an ID specialist and a PCP for other modifiable CVD risk factors including tobacco use, diabetes, and other chronic conditions.

There was a long duration between diagnosis and the first record of prescription in the medical records. Employing implementation science strategies like audit and feedback to improve time to prescription for CVD risk factors may also support the quality of CVD prevention in PLHIV. Because patients who have established CVD may also receive care from a cardiologist, future research should focus on adapting innovative care models such as the “model for shared care of elderly patients with cancer” proposed by Cohen."
Policy Relevance

With current United States healthcare policy move toward population health and models of care that incentivize high-value care, the findings of this dissertation provide a valuable first step for stakeholders in developing interventions that will improve the quality of CVD prevention in PLHIV. To improve the prognosis for PLHIV primary and secondary CVD prevention is critical to control disease progression and prevent subsequent cardiac events or death. Overall, a complex array of factors influences utilization of CVD prevention in PLHIV. In HIV care settings where ID specialists are generally the de facto PCP, there is a need to develop interventions that support CVD prevention. Before developing such interventions, future studies should seek to uncover the reasons for the differences using a population-based datasets for PLHIV.

Future Directions

Focusing on primary and secondary prevention of CVD risk factors in PLHIV reflects the importance for this population of a leading cause of morbidity and mortality in the United States. This study is an important first step in a continuum of research focused on quality of care for PLHIV. It provides a foundation for future research, including

1. Extending research to other CVD risk factors such as diabetes and smoking;
2. Extending research into investigation of optimal care coordination between ID specialists and PCPs;
3. Extending research in evaluation of effectiveness of nurse or other mid-level provider interventions for CVD prevention;
4. Extending research to patient-reported outcomes on CVD prevention by PLHIV;
5. Development of interventions to optimize electronic medical records as decision support tools in CVD prevention for PLHIV; and
6. Developments of HIV care models that incorporate the management of multiple chronic conditions.

To achieve these goals, it will be vital to access large cohort datasets like the Veteran Aging Cohort Study (VACS), and the Multi Center Cohort Study (MACS) from the Centers for AIDS Research (CFAR) to improve external validity.
In summary, through the framework of the Andersen Behavioral Model and multiple method approaches this dissertation was able to illuminate provider and health system factors that affect the utility of CVD preventative strategies. Although epidemiologic studies have compared infected and uninfected populations, this dissertation is the first one to compare differences in the quality of care between different groups of PLHIV. Taken together, this dissertation was able to elucidate factors that future clinical and policy interventions can target to increase the overall quality of care for PLHIV.
REFERENCES

APPENDIX A. SEMI-STRUCTURED INTERVIEW GUIDE

Hello, I’d like to thank you for your time and interest in our research project. Your participation is very important to us. My name is CM. The purpose of this research is to find out about your experience with primary and secondary prevention of cardiovascular disease in an HIV Clinic population.

Your opinions as an HIV health care provider are extremely valuable as we try to better understand factors that influence the provision of primary and secondary CVD preventive care for HIV infected person in clinical practice. This information will assist in designing interventions that will improve the quality of CVD care in HIV infected persons.

We are interested in your ideas, comments and suggestions. Please feel free to share your thoughts and talk candidly during the discussion. We have provided you a consent form for your review. Do you agree to participate? Do you have any questions before we begin?

1. First I would like to hear your general thoughts about prevention of CVD in the ID clinic population.
   PROBE IF NECESSARY – Are there specific reason why you think about this topic that way?

2. One of the measures that health services researchers use to describe quality of care is concordance with Clinical Practice Guidelines (CPGs). What are your personal thoughts about CPGs prevention of CVD for the HIV infected persons?
   PROBE IF NECESSARY –
   - How about their implementation in your patient pool?
   - How do you keep up with current literature on the topic?
   - Are CMEs routinely provided?

3. What kind of resources (Tests for CVD risk factors, staff, etc) do you have at the ID Clinic to facilitate prevention of CVD?
   PROBE IF NECESSARY – what would facilitate/enable providers to increase the likelihood of providing CVD risk reduction for the HIV infected persons at the ID clinic?

4. Conceptually, patient characteristics may influence provider’s decision to provide optimal primary and secondary CVD care. Think about the past year, what were the main clinical characteristics of your patients that would have influenced your decision to provide primary and secondary CVD risk reduction care?
   PROBE IF NECESSARY:
   - what were the top three? Any particular reasons for these characteristics?
   - Are there specific HAART or Traditional CVD risk factors that influence you decision making?

5. Now let us move on to the provider mix. Think about the traditional role of a family physician (non-HIV primary care provider - PCP). In your opinion, what benefits can your patients draw from additional routine care that can ideally be provided by a PCP?
   PROBE if NECESSARY- How much Primary care does a ID specialist want to provide? (if not discussed in 1)
   - How would this combined ID/PCPC care ideally work?

6. Finally, think about an ideal world. What would be require to optimize recognition and prevention of CVD other chronic diseases for HIV INFECTED persons in the ID clinic?
PROBE IF NECESSARY:
- How would you change anything from the current status of affairs? (if not discussed in 1)
- Should these kind of services be in or out of the HIV care system (ID clinics) (if not discussed in 1 and 5)
- Should the tracked measures of quality of HIV care include overall health of the patient?

7. What are your final thoughts about how we can improve recognition and prevention of CVD strategies for HIV INFECTED persons?

Thank you very much for participating in these interviews.