A nurse-led intervention to extend the Veteran HIV treatment cascade for cardiovascular disease prevention (V-EXTRA-CVD)

NCT04545489

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Principal Investigator/Study Chair: Hayden Bosworth, PhD

Version 19, September 9, 2024

Abstract

Provide a summary of the study (recommended length: less than 500 words).

Background: The VA is the largest provider of HIV care in the United States. The ~31,000 Veterans with HIV use significantly more healthcare and have up to 2x higher risk of atherosclerotic cardiovascular disease (ASCVD) compared to uninfected Veterans. The HIV treatment cascade model includes care steps; once people obtain remission, providers should focus on preventing ASCVD. We will extend the HIV treatment cascade and focus on reducing ASCVD risk among people with HIV. Veterans with HIV have low perceived risk for ASCVD and uptake of guideline-based treatment for BP is low.

Significance/Impact: The proposed intervention has the potential to reduce ASCVD events in this population by more than a quarter and meet VA strategic priorities of: 1) improve timeliness of services; 2) focus resources more efficiently as well as address HSR&D research priorities: 1) patient centered care, care management, and health promotion; 2) healthcare access; 3) aging; 4) virtual care.
Innovation: The study is innovative: Cascade Model. By leveraging the HIV treatment cascade model, we will create a pathway for ASCVD risk reduction to be added into widespread quality improvement initiatives. Stakeholder-engaged design process. We will employ stakeholder-engaged research methods to ensure the intervention meets the needs of patients and healthcare providers. Multi-component intervention. While each of the components of our intervention have an evidence base, they have not been tested together in an HIV context. Telehealth. We will use VA Video Connect (VVC) to monitor CVD risk factors.
Specific Aims:
Aim 1: Conduct a formative evaluation to adapt intervention.
Aim 1a: Conduct qualitative interviews with Veterans with HIV and Providers to ascertain perceptions regarding CVD risk reductions to inform intervention adaptation.
Aim 1b: Adapt the intervention to the VA HIV clinic context with key stakeholder input.
Aim 1c: Conduct a retrospective review of the nationwide cohort of Veterans with HIV to evaluate hypertension care in order to inform needs for the study.
Aim 2: Evaluate the 12-month *efficacy* of an intervention to improve systolic blood pressure in Veterans with HIV. Hypothesis: We hypothesize that our intervention will result in a clinically significant 6mmHg reduction in SBP over 12 months compared to those receiving *[enhanced education + usual care]* only.
Aim 3: Conduct an evaluation of the prevention intervention.
Exploratory aim: If effective, we will conduct a budget impact analysis and simulate 10-year cost-effectiveness of the intervention.
Methodology: We will conduct qualitative interviews with care team and Veterans to adapt the intervention in an iterative design process. We will then conduct a RCT to evaluate an intervention to reduce ASCVD risk. The study will be conducted in 4 clinics among HIV+ veterans (*n*=300) on suppressive ART with confirmed SBP >140 mmHg, stratified by clinic site and hyperlipidemia status and randomized 1:1 to intervention vs. education control. The intervention will involve 4 evidence-based components based on our prior studies and adapted to veterans with HIV: (1)
interventionist-led care coordination, (2) interventionist-managed medication and adherence support (3) home BP monitoring, and (4) administered VA Video Connect (VVC). The education control will receive enhanced education and usual care. Primary outcome: difference in 12-month systolic BP in the intervention arm vs control. Secondary outcome: 12-month difference in non-HDL cholesterol. We will use a mixed-methods design to evaluate fidelity, dose delivered/received, reach, recruitment, and context of the intervention.

List of Abbreviations

Provide a list of all abbreviations used in the protocol and their associated meanings.

ACE	angiotensin converting enzyme
AMI	Acute myocardial infarction
ARB	angiotensin II receptor blocker
ART	antiretroviral therapy
ASCVD	atherosclerotic cardiovascular disease
ATP	Adult Treatment Panel
BMI	body mass index
BP	blood pressure
CDW	centralized data warehouse
CITI	Collaborative Institutional Training Initiative
CKD	chronic kidney disease
CPRS	computerized patient record system
DBP	diastolic blood pressure
DUA	data use agreement
eGFR	estimated glomerular filtration rate
EMR	electronic medical record
EPRP	external peer review process
ER	emergency room
GCP	good clinical practices
HCV	hepatitis C virus
HDL-C	high density lipoprotein cholesterol
HEDIS	healthcare effectiveness data and information set
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
HTN	Hypertension
ID	Infectious Diseases
IRB	institutional review board
ITT	Intention to Treat
JNC	Joint National Committee
JLV	Joint Longitudinal Viewer
LDL-C	low density lipoprotein cholesterol
LMM	Linear mixed-effects models
LSI	Local Site Investigator
MAR	Missing at Random
MI	myocardial infarction
mmHg	millimeters Mercury
NLA	National Lipid Association
NRI	nicotine replacement therapy
OIT	Office of Information Technology
ORD	Office of Research & Development
PC	project coordinator

PC-MHI	Primary Care - Mental Health Integration
PCP	Primary Care Provider
PHI	personal health information
PI	principle investigator
PWH	Persons with HIV
RA	research assistant
RCT	randomized control trial
RE-AIM	Reach x Efficacy - Adoption, Implementation, Maintenance
SAE	serious adverse event
SBIRT	Screening, Brief Intervention and Referral to Treatment
SBP	systolic blood pressure
SMS	short message service
VAHCS	Veterans Affairs healthcare system
VEQ	Veteran engagement quorum
VetREP	Veteran Research Engagement Panel
VVC	VA Video Connect

Contents

Protocol Title: A nurse-led intervention to extend the Veteran HIV treatment cascade for cardiovascular disease prevention (V-EXTRA-CVD)

1.0 Study Personnel

There are four VA sites {Durham VAHCS, Cleveland VAHCS, Baltimore VAHCS, Atlanta VAHCS} where research will occur. The Durham site will start first with aim 1 with support from LSIs from Cleveland and Baltimore. It is anticipated that all three sites will start aim 2 – RCT at the same time.

Principal Investigator

Name	Contact Information	Affiliations
Hayden Bosworth, PhD	Durham VA Medical Center 508 Fulton Street (152) Durham NC 27705 919-286-6936 Hayden.Bosworth@va.gov	Deputy Director for Center of Innovation (COIN) for Health Services Research in Primary Care, Durham VA Research Professor, Population Health, Duke University

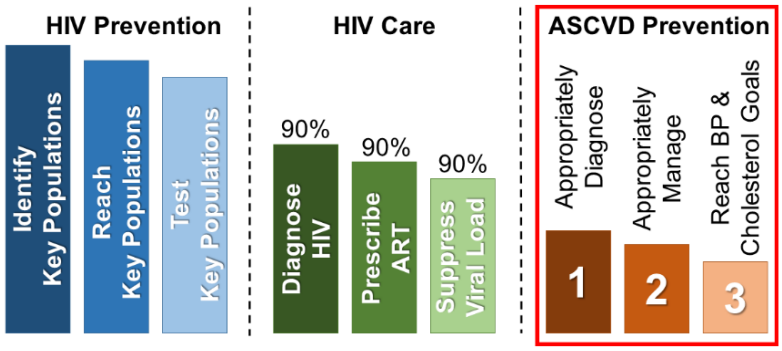
2.0 Introduction

The VA is the largest provider of medical care for patients with HIV.[1] Veterans with HIV are high users of VA healthcare and generate over 700,000 outpatient visits per year (median of 7 outpatient visits annually);[2] they are also high users of services such as hospitalizations compared to Veterans without HIV.[2] The prevalence of optimal cardiac health is low; Veterans with HIV have a twofold increased risk of myocardial infarctions[3] and a 1.5-2 times higher risk of ASCVD compared to uninfected Veterans independent of confounders.[4-6]

The CASCADE model in HIV treatment. This model was developed to assess how people with HIV access care and treatment by employing sequential care steps: (1) diagnosis, (2) prescription of appropriate antiretroviral therapy (ART), and (3) suppression of the HIV virus. This model led to large scale projects aiming to achieve 90% of people with HIV knowing their status, 90% of those on ART, and 90% of those on ART achieving virally-suppression. [7] The cascade metrics are mandated core performance measures,[8] and are a focus of nationwide HIV quality improvement initiatives. However, ASCVD prevention and treatment are currently absent in the HIV cascade model.

Why extend the treatment cascade for ASCVD prevention? For those who have achieved durable viral suppression (90% nationally), the focus of care should include prevention of ASCVD. Although HIV-specific factors play a role, traditional risk factors account for the vast majority of risk on a population level. Among the top risk factor for people with HIV with the greatest population level impact on myocardial infarction risk is hypertension, with population attributable risks far exceeding low CD4+ T-cell count or elevated viral load.[9] Unfortunately, uptake of guideline-based therapies for BP is low among people with HIV.[10-12]

Figure 1: Extended Treatment Cascade for



We will extend the HIV treatment cascade to improve uptake of guideline-based ASCVD prevention therapies. Step 1, people with HIV should have their BP and lipids screened; abnormal values should be appropriately diagnosed as hypertension as well as hyperlipidemia; Step 2, those with hypertension or hyperlipidemia should be prescribed guideline-based therapies; and Step 3, BP and lipid measurements should achieve guideline-based treatment targets; this is the focus of the study.[13] (Figure 1).

Complications of HIV infection. HIV causes chronic inflammation and immune activation, which is associated with diabetes and CVD. Long-term inflammation may elevate cholesterol levels, which can harm blood vessels and the heart. Some antiretrovirals have contributed to the development of insulin resistance leading to diabetes. HIV and the treatment can also impact the brain; more than half of people living with HIV may experience difficulties with motor skills and memory – all factors that may contribute to increased lifestyle and medication non-adherence.

Table 1: **NLA treatment goals for Veterans with HIV.**

Risk Category	Criteria	NLA goal Non-HDL-C LDL-C
Low	N/A*	N/A*
Moderate	2 major risk factors (i.e. HIV + high BP only)	<130 mg/dl <100 mg/dl
High	≥ 3 major risk factors	<130 mg/dl

Blood pressure and cholesterol targets matter. No HIV-specific BP guidelines exist; however, guidelines suggest treating to a target SBP of 140mmHg for most patients is appropriate, while acknowledging that certain groups may merit more aggressive targets (e.g. <130 systolic for diabetes).[14,15] To achieve these targets, many will require more than one drug and titrating medication. Improving self-management is thus a critical component to successful treatment of blood pressure over time.[16]

For cholesterol management, HIV-specific guidelines exist;[17,18] although, the National Lipid Association (NLA) recommendations[18] are the only current guidelines from the modern ART treatment era. In 2015, the

NLA Expert Panel on HIV recommended an approach to risk stratification and target non-HDL-C and LDL-C goals[19] (Table 1), with the additional recommendation that HIV infection may be counted as a major ASCVD risk factor for the purposes of risk stratification.

The HIV workforce is changing. Achieving ASCVD prevention targets is challenging with increased clinical demands and a changing HIV workforce. Over the past 10 years, the HIV Medicine Association [20] and the Institute of Medicine[21] have been warning of shortages of HIV specialists; numbers of HIV providers are projected to decrease due to high levels of dissatisfaction, just as attempts to improve the HIV treatment cascade bring larger numbers of patients into care.[22] Primary care providers may be able to fill the gap, but feel inadequately trained in HIV care.[23] Similarly, HIV-specialists are often uncomfortable providing primary care, including treatment for hypertension and hyperlipidemia.[24] Treating higher volumes of HIV patients is associated with more appropriate HIV management and lower overall mortality,[25] but is not associated with more appropriate cholesterol treatment for ASCVD prevention.[26]

Models that promote shared responsibilities between primary care providers and HIV-specialists exist, but their effect on primary care and non-AIDS outcomes such as ASCVD has not been rigorously studied.[27] Changing patterns of care require shifts in patient-provider trust and communication. Because of longstanding relationships, many HIV patients including those in the VA, trust their HIV provider for comprehensive care.[24,28] In one study, 84% of patients preferred having their HIV provider be their PCP.[24] However, among 1300 persons living with HIV who had anti-hypertensive and lipid-lowering medications prescribed primarily by ID specialty clinics were less likely to meet evidence-based goals for hypertension and hyperlipidemia, respectively; rates of BP control were less than 30%.[29] The impact of patient-provider trust and communication networks on ASCVD prevention efforts needs to be formally evaluated among people with HIV.

Nurse-led interventions are highly effective in high-risk individuals. The clinical role of non-physician providers is expanding in the VA, including HIV-specialist care providers in multi-disciplinary clinics.[22,30] HIV care provided by these non-physician specialists is comparable to physician specialists,[31] but the quality and comfort level of preventive care for ASCVD among these non-physicians is poorly understood. Our experiences suggests that nurse-led management of cardiovascular risk factors is highly effective.[32-35]

Key features of our prior interventions include: (1) care coordination, (2) interventionist-managed protocols and medication adherence counseling, (3) home blood pressure monitoring; and (4) integrated use of information technology tools such as video conferencing. For example, among a sample of Veterans with poorly controlled BP, home BP monitoring + behavioral counseling led to a 6mmhg reduction in systolic BP over 18 months in one of our prior studies.[35] Further, a meta-analysis of nurse-managed protocols showed a clinically significant 4mmHg reduction in systolic BP and 10-12 mg/dL reduction in cholesterol.[36]

Low perceived risk is a barrier to ASCVD preventive care. Before effective antiretroviral therapy, most people with HIV infection died of AIDS-related causes and CVD prevention was not a priority for most patients and providers. Yet, there is evidence that low perceived cardiovascular risk persists even in the ART treatment era.[37] The influence of perceived risk on ASCVD prevention behaviors are not well known.

Unknown barriers to, and facilitators, of high-quality ASCVD preventive care in the VA. Veterans with HIV and their health care team experience a number of barriers to high quality ASCVD preventive care including a historic primary focus on HIV-related issues (e.g., CD4 T-cell counts) and competing priorities (e.g., substance use, poverty, psychiatric disease, pain management). We have previously found that 135 people with HIV from various sites reported that during their health care visits, HIV was their primary health focus (i.e., HIV medications and labs).[38] In the same study, health care providers reported that it can be challenging to cover non-HIV related preventative care issues due to short visit times and other priorities.[38] Facilitators of prevention behavior included the trust that people with HIV have in their HIV providers and their ability to facilitate their decision-making and behavior.[38] While these data reveal some of the barriers and facilitators to improved care for non-AIDS co-morbidities, they are limited by not being specific to Veterans. Additional work focusing on the barriers and facilitators to ASCVD care among Veterans will yield critical and novel data that can help to inform how to best tailor and implement our ASCVD intervention.

Virtual Care in VA. The VA is rolling out two virtual modalities to help address patient access issues as well

Figure 2: VA Video Connect

The VA Video Connect (VVC) application provides encrypted and secure videoconference services to connect Veterans with their VA providers using any web-based or mobile device (e.g., iPhone, iPad).

Benefits of VVC:

- Reduction in travel time for Veterans with limited access to VA health care facilities (e.g., living in very rural areas, have medical complexity).
- Provides quick and easy health care access.
- For vulnerable populations using encrypted video ensures the session is secure and private.

as respond to the legislative priorities such as the Choice Act and Mission Act. Two of these virtual modalities are critical for the delivery of population-level care management. The Office of Connected Care began rolling out ANNIE SMS in 2016. ANNIE SMS can incorporate two-way communication between patients and the interventionist and works with a smart phone, computer or mobile device connected to the Internet. [39] We will use this technology to collect the daily home blood pressure values. We will use video virtual care visits using VA Video Connect (VVC) to deliver the intervention (Figure 2). VVC can reduce the impact of barriers on healthcare access (e.g., distance to medical facilities), improve clinical outcomes, and is feasible and acceptable for Veterans with multi-morbidity and high healthcare utilization.[40] Blood pressures remotely monitored by a clinician through video conferences may be included in the CPRS vital signs package. Additionally, revision to the External Peer Review Process (*EPRP*) data collection instrument includes language that telehealth BPs are acceptable. Thus, we will be able to collect BP data that will directly impact the HEDIS measures of the facilities we interact with during the intervention.

PRELIMINARY DATA. Data demonstrating the importance of the project, prior experience with CVD risk reduction and implementation are presented.

SITES AND POPULATION DATA. The South accounted for half of U.S. HIV diagnoses in 2017. Minorities represent the majority of new HIV diagnoses, living with HIV, and deaths among people with HIV. Blacks have the highest age-adjusted death rate due to HIV disease throughout most of the epidemic. [41] We chose the following sites in order to provide a diverse mix of rural and urban locations. The four sites for this project include the Durham VA Heathcare system, Cleveland VA Medical Center, Baltimore VA Medical Center, and the Atlanta VA Medical Center

Risk and Perceptions of ASCVD risk among persons with HIV. Dr. Naggie using risk criteria delineated by the Adult Treatment Panel III (ATP-III) guidelines observed that 50.6% of Veterans with HIV and 33.8% of veterans with both HIV and HCV had an indication for statin therapy. However, among those meeting guideline indications, 22.7% and 31.5%, respectively, were not receiving ATP-III recommended statin therapy.[10] These results further support that veterans with HIV are not receiving adequate ASCVD care.

We observed that compared to other high-risk populations, people living with HIV report low perceived CVD susceptibility and fewer benefits from CVD prevention behaviors. Among data collected from 12 HIV healthcare providers and 18 individuals living with HIV, we observed that low perceived benefit to ASCVD prevention practices for people with HIV. Healthcare providers are more likely to identify barriers to ASCVD prevention/management than people with HIV.

Prior CVD-related interventions. 1) In a **Medicaid implementation project** among 583 Medicaid patients with diabetes, we observed that a telephone self-management intervention focused on medication adherence improved refill rates for CVD medications from 55% to 77%.[42] 2) Among 641 individuals with high CVD risk in 42 UK general practices, significant improvements **CVD risk**, BMI, SBP, DBP, increased BP medication adherence, improved diet, and increased physical activity were observed. A cohort simulation model indicated the intervention was cost effective.[43] 3) In **ACDC**, Veterans with poor diabetes control were randomized to telemonitoring and self-management support or usual care. Those in the intervention reduced HbA1c by 1.0%, SBP (-7.7 mmHg) and DBP (-5.6 mmHg) versus usual care.[44]

Interventions using Team-care to Improve Hypertension. V-STITCH (Bosworth, VA HSR&D IIR 20-034) tested a nurse-administered telephone intervention. BP control increased from 44% to 65% in the intervention group compared to 44% to 53% in the control group (p=0.03) over 24 months.[45] In the **HINTS** study (Bosworth, VA HSR&D IIR 04-426), 593 Veterans with hypertension were randomized; the medication management arm had decisions concerning their hypertension regimen made by a study physician and implemented by a nurse using a hypertension decision support system. Systolic BP improved in the combined group by 15.7 mmHg at 12 months relative to usual care.[33]

Multiple Risk Factors Projects. Cardiovascular Intervention Improvement Telemedicine Study (**CITIES**) (Bosworth, IIR 08-297) enrolled 429 at high risk for CVD. The intervention focused on both vascular disease-related behaviors and medication management and was administered via the telephone. The complier average causal effect estimates at 6 months for intervention as compared to usual care were 20-point improvement in total cholesterol and 5-point improvement in Framingham risk score. [46]

Implementation Experience. The **HTN-IMPROVE** study (Bosworth, QUERI RRP 09-196) assessed the implementation of an evidence-based telephone-administered behavioral intervention to control BP in VA primary care clinics. [47] The project was conducted in 3 diverse VAs and 800 individuals were enrolled into the program. Dr. Bosworth also participated in a CMS funded diabetes demonstration project (**SEDI**) that involved public health workers in four states implementing a telephone based intervention that reduced HbA1c by 1%.

Experiences obtained from these implementation studies provide information on the barriers and facilitators for successful implementation and sustainability.

Significance Summary: These data support the proposed approach and intervention; however, little work has investigated how to reduce CVD among Veterans with HIV. The gap between guideline-recommended CVD care and current practice among Veterans with HIV is a public health problem for the VA given Veterans' with HIV significantly increased CVD outcomes and healthcare use. If successful, V-EXTRA-CVD could become a model for optimal CVD risk management and improve quality of care.

3.0 Objectives

Our goal is to improve blood pressure (BP) treatment for Veterans with HIV to reduce ASCVD risk. Within a randomized clinical trial, we will test a VA adapted ***intervention*** to reach ASCVD guideline targets. The study will be conducted in three VA clinics that are representative of HIV specialty care in the VA**.**

Aim 1: Conduct a formative evaluation to adapt intervention.

Aim 1a: Conduct qualitative interviews with Veterans with HIV and Providers to ascertain perceptions regarding CVD risk reductions to inform intervention adaptation. Care team members and patients will participate in qualitative interviews to understand CVD risk associated with living with HIV.

Aim 1b: Adapt the intervention to the VA HIV clinic context with key stakeholder input. Care team and patients will participate in an iterative design process to adapt our intervention to the local Veteran context.

Aim 1c: Conduct a retrospective review of the nationwide cohort of Veterans with HIV to evaluate gaps in hypertension care in order to inform intervention needs. We will use data from the Corporate Data Warehouse to define hypertension care cascade among veterans with HIV who receive care at the VA.

Aim 2: Evaluate the 12-month *efficacy* of an intervention to improve systolic blood pressure in Veterans with HIV. HIV+ veterans (*n*=300) on suppressive ART with poor hypertension control (confirmed SBP >140 mmHg) will be stratified by clinic site and hyperlipidemia status and randomized 1:1 to intervention vs. education control. The intervention will consist of four evidence-based components derived from our prior studies that will be adapted to veterans with HIV: (1) interventionist-led care coordination, (2) interventionist-managed medication protocols and adherence support (3) home BP monitoring, and (4) electronic medical records (EMR) support tools. The intervention will be administered using VA Video Connect (VVC). The education control will receive enhanced education plus usual care from their providers and CVD prevention education material.

Primary outcome: difference in 12-month systolic BP in the intervention arm vs education control.

Secondary outcome: 12-month difference in non-HDL cholesterol.

Hypothesis: We hypothesize that our intervention will result in a clinically significant 6mmHg reduction in systolic blood pressure over 12 months compared to those receiving enhanced education + usual care only.

Aim 3: Conduct a process evaluation of the prevention intervention. We will use a mixed-methods design to evaluate fidelity, dose delivered/received, reach, recruitment, and context of the intervention, corresponding to the RE-AIM domains.

Exploratory aim: If effective, we will conduct a budget impact analysis and simulate 10-year cost-effectiveness of the intervention.

4.0 Resources and Personnel

There are four VA sites where research will occur: Durham VAHCS, Cleveland VAHCS, Baltimore VAHCS, Atlanta VAHCS.

Durham VAMC staff will recruit, enroll, and consent patients for all aims and house the research data. Statistical analyses will also occur at Durham

Cleveland VAMC staff will also recruit, enroll and consent patients and house research data.

Baltimore VAMC staff will also recruit, enroll and consent patients, and house research data.

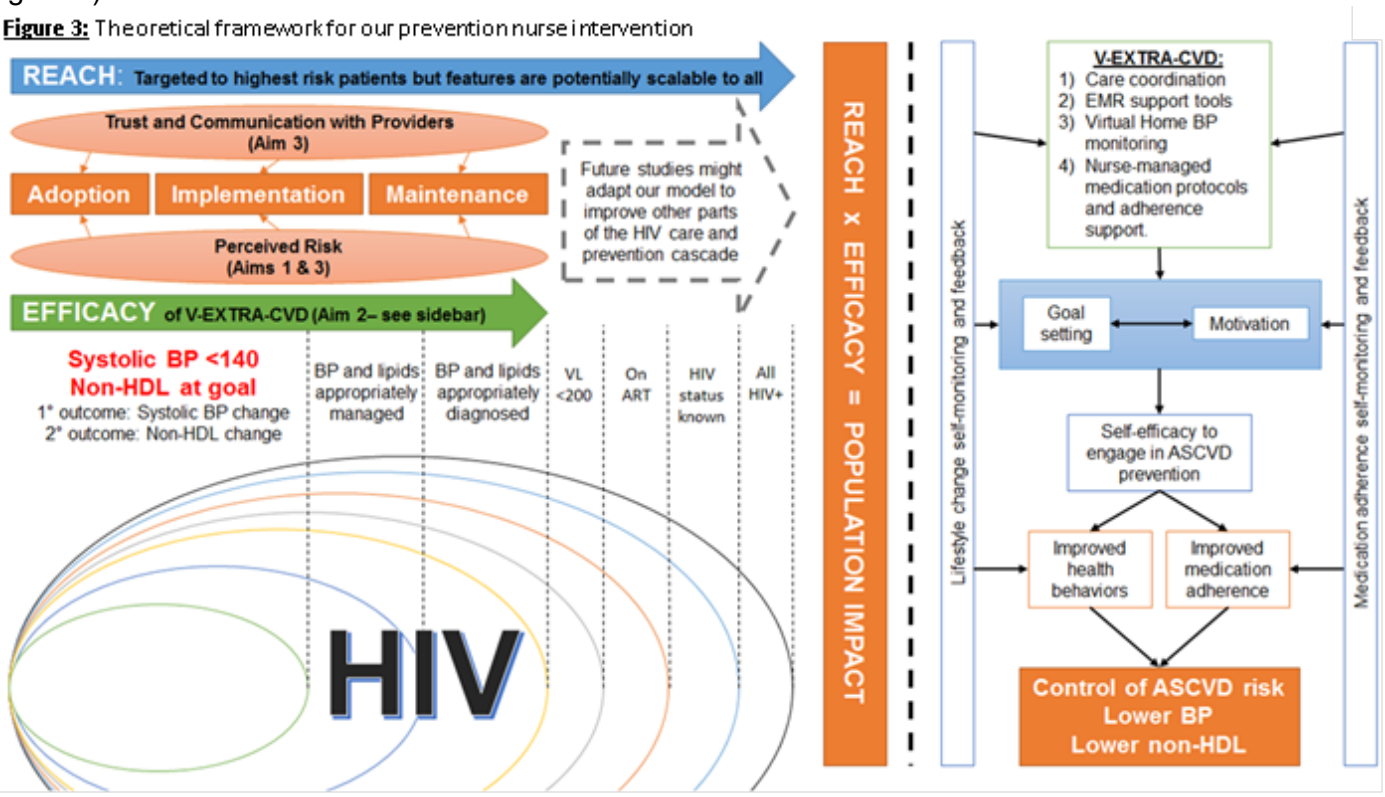
Atlanta VAMC staff will also recruit, enroll and consent patients, and house research data. Study Procedures

5.1 Study Design

Setting: The proposed study will be conducted at four VA hospitals that provide HIV specialty care for racially, ethnically, and age diverse Veterans with HIV.

Conceptual Framework: Our study utilizes the RE-AIM framework to evaluate the intervention;[48] RE-AIM stands for **R**each X **E**fficacy—**A**doption, **I**mplementation, **M**aintenance, and captures the five factors that contribute to the impact of an intervention. If proven effective for ASCVD risk factor control, the concept of a prevention interventionist may be scaled to address a broad range of preventive care services for people with HIV, thus increasing its population impact. Finally, the intervention is grounded in two models of behavior change: (1) the information-motivation-behavioral skills model and (2) self-regulatory theory.[49] These models explain how health behavior change is mediated through self-monitoring (lifestyle change and medication adherence) and acknowledge the central role that self-efficacy plays in sustained behavior change.[50] (see Figure 3).

Figure 3: Theoretical framework for our prevention nurse intervention



Part 1: Aim 1: Conduct a formative evaluation to adapt intervention.

Aim 1a: Conduct qualitative interviews with Veterans with HIV and Providers to ascertain perceptions regarding CVD risk reductions to inform intervention adaptation. Care team members and patients will participate in interviews to understand risk associated with living with HIV and CVD and trust development in care provision to modify existing intervention approach. See Appendix 2 for example interview questions informed by the theoretical framework of this study. Final interview guides will be developed collaboratively with VetREP and VEQ.

Participants*:* There are two groups of participants for aim 1

- **Healthcare providers (both ID and primary care): up to 18 health care providers** (n=6 providers from each site, a mix of provider type (MD, RN, NP, PA, PharmD) will participate
- **Veterans with HIV: up to 18 Veterans** (*n*=6 from each site) will participate

These participants (veterans and providers) will complete an informant interview with Dr. Gierisch. Veterans with HIV will be recruited by purposive sampling and provider with purposive and snowball sampling. We will first interview providers to seek their guidance on key factors on which to select our Veteran informants.

Key Informant Interviews (ID and PCP HIV Providers). We will conduct key informant interviews using a semi-structured interview guide focused on key elements of intervention adaptation consisting of open-ended questions to understand the perceptions of the clinic staff on their patients' ASCVD risk and barriers and facilitators to change, how those perceptions influence how they treat CVD risk factors, thoughts on the intervention approach, and ideas on how to adapt the intervention to the HIV clinic context.[51] We will also use these interviews to understand the various providers' knowledge and concern about ART medications and potential interactions. The guide will facilitate discussions across sites and ensure we have covered all relevant topics. These interviews will occur via phone to increase access by the staff member, and audio recordings who will later be transcribed verbatim.

Interview Procedures (Patients). We will interview Veterans with HIV about their perceptions of CVD risks, HIV medications, CVD risk reduction measures, and thoughts and adaptations needed to the intervention platform to make it more meaningful, feasible and acceptable for patients like them. To inform adaptation, we will assess barriers to, and facilitators of, improved ASCVD prevention. All interviews will take approximately 30-60 minutes and audio recordings will be transcribed verbatim. All participating Veterans with HIV will complete the following assessments self-reported survey consisting of demographics, HIV and medical history, and perceptions of CVD Risk (Health Beliefs for Cardiovascular Disease Scale[52]). Medical chart abstraction will be used to determine history of use, adherence to, and tolerance of proven CVD prevention therapies.

Aim 1b: Adapt the intervention to the VA HIV clinic context with key stakeholder input. We will use a participatory, iterative design process[53-55] including members such as: HIV providers, primary care providers, nurses, pharmacists, Veterans with HIV. We will consent all non-research staff members of the design teams verbally, and send them a welcome letter/email that includes meeting dates and details.

The design process will involve a series of up to 4 meetings over approximately 2-3 months, for about 3-4 hours each, with a goal of refining the V-EXTRA-CVD intervention within the VA environment. Design teams from each of the 3 sites will meet together, as well as breakout to discuss site-specific issues separately. Meetings will be conducted virtually, using approved VA technologies, such as Cisco Webex Meetings, VA email and MyHealtheVet secure messaging.

The first 3 design meetings will cover the following phases: brainstorming, conceptualization, and creation.

1. ***During brainstorming***, the team will review the data obtained during the qualitative interviews on perceptions of ASCVD risk and barriers and facilitators of ASCVD preventive care. The team will brainstorm ideas to refine the intervention in response to these data.

Targets for intervention adaptation include: (a) adjusting when, where, and to whom the CPRS alerts appear; (b) adapting the treatment algorithms to overcome barriers and maximize the facilitators; (c) targeting the staff training to include use of virtual care, care coordination and adherence support; (d) developing and tailoring staff training to facilitate acceptance, uptake, and effectiveness; and (e) helping to quickly identify and troubleshoot any problems with the implementation of the intervention.

2. ***In the conceptualization phase***, the team will evaluate advantages and disadvantages of ideas generated during the brainstorming and will develop concrete changes to the intervention.
3. ***The creation phase*** will involve the refinement of treatment protocols, manuals of procedures, and educational materials. Once the adaptation of the intervention is completed, we will conduct interviews with Veterans (up to n=12) with HIV and intervention staff from each of the three sites (up to n=9) to assess acceptability.[56] We may also present the adapted intervention to our established VEQ group for further input.

The fourth and final design meeting (revision phase) will review information from the acceptability interviews, make any final recommendations to the intervention, and discuss team members' experience of the overall design process.

Aim 1c: Conduct a retrospective review of the nationwide cohort of Veterans with HIV to evaluate gaps in hypertension care in order to inform intervention needs.

Persons with HIV (PWH) are at an increased risk of cardiovascular disease. Pre-hypertension and hypertension are both associated with an increased risk of acute myocardial infarction (AMI) in Veterans with HIV[3] . While HTN adversely affects outcomes in PWH, HIV itself has negative impact on HTN management. Persistent HIV infection is a risk factor for hypertension among PWH[57]). Integration of hypertension care into HIV care programs has shown to produce improved outcomes when compared with traditional models of HIV care[58]. HIV primary care guidelines issued by the Infectious Diseases Society of America and the VA both recommend screening, prevention and control of HTN in PWH [59,60]. However, to what extent are HTN services integrated into care of PWH and how HIV care impacts HTN care, is unknown. With over 31,000 in care, VA is the single largest provider of HIV care nationally and has an integrated nationwide electronic medical record. As such this presents a unique opportunity to investigate the relationship between HIV and HTN care. We will seek to compare the care cascades for HTN and HIV within this nationwide cohort of Veterans with HIV. While the HIV care cascade is a well-documented and widely used tool, the HTN care cascade will provide valuable framework for evaluating the quality of health service delivery for HTN by charting the proportion of persons who proceed through the stages along a defined sequence of care. Any gaps identified will define the scope of the problem and help inform future strategies for improving HTN care in this population. Comparing the HTN cascade to the HIV care cascade may function to demonstrate gaps and strengths of each program and their impact on each other.

Design:

We will collect data from the CDW files using VA provided software through VINCI using national data. The study population is the cohort of Veterans with an HIV diagnosis as defined using a validated definition. We will use demographic, ICD codes and laboratory data available in the CDW for data definitions. We will evaluate a 5 year period from January 2015 through December 2019, but will also review data from 2020 to see how the COVID-19 pandemic impacted care. We will define each step in the HIV care cascade based on widely accepted definitions. For the HIV care cascade, we will use publicly available data provided by the VA Office of Specialty Care and HIV Hepatitis and Related Conditions Office. Within this cohort of Veterans with HIV, we will then define corresponding, clinically relevant cascade steps for HTN based on the American Society of Hypertension and International Society of Hypertension clinical practice guidelines: screening, diagnosis, initiation of treatment, retention, control of HTN.

Part 2: Intervention and Process Evaluation

Aim 2: Evaluate the 12-month *efficacy* of a intervention to improve systolic blood pressure in Veterans with HIV.

We will conduct an RCT of our intervention vs. education control among HIV Veterans on suppressive ART who have hypertension. Education control participants will receive general prevention education. The primary outcome is change in systolic BP and the secondary outcome will be change in non-HDL cholesterol. As participants conclude participation in the RCT the Aim 3 Process Evaluation will be conducted with select intervention participants. Relevant information from aim 2 for the process evaluation is highlighted in yellow.

Setting: This trial will be conducted at the same sites described earlier: Durham VA, Baltimore VA, Cleveland VA, and Atlanta VA

Participants: We will enroll 300 HIV+ Veterans on suppressive ART and poor hypertension control (*n*=25-125 at each site). Inclusion and exclusion criteria is listed in section 5.4. We will include individuals who have **hyperlipidemia,** defined as non-HDL > National Lipid Association (NLA) target or on lipid-lowering medication based on the last 3 years. While 300 is our enrollment goal, we may consent and randomize up to 310, to account for site differences, withdrawals and the scheduling availability and preferences of Veteran participants.

Baseline visit: Participants will attend an in-person visit during which the informed process will be completed (see section 5.3 for informed consent procedures). Once the veteran has provided consent and enrolled in the study, the baseline visit will also consist of:

- Have in-office BP obtained by a trained research assistant using a standardized protocol[35]. If blood pressure is identified by study staff as being high (>180/110), similar to prior trials, [18,45,46] we will provide feedback to both the patient and his/her primary care provider. In terms of the Veterans' provider, we will use a developed CPRS template (requiring co-signature) and/or phone calls to notify them. If no action is taken, the study physician at each respective site will follow up with the patients' provider.
- Measurement of vitals: height, weight, waist circumference
- Have blood drawn at VA lab to measure lipid panel. If lipid panel has been completed in the past 28 days, will not need to repeat during baseline visit.
- Complete health-related surveys (see full list of measures in section 5.5). Surveys may also be administered by telephone or by mail if Veteran is unable to complete the research visit in-person, but priority will be given to in-person survey administration.
- Randomization to study arm
- Assess whether Veteran has a VA-issued BP monitor for home use; if not, will have study physician place order. This is standard of care for all veterans with hypertension.

Subsequent visits: (4,8,12 months)

- Have in-office BP obtained by a trained research assistant using a standardized protocol mentioned above.l[35]
- Complete health-related surveys (see full list of measures in section 5.5). Surveys may also be administered by telephone or by mail if Veteran is unable to complete the research visit in-person, but priority will be given to in-person survey administration.
- Measurement of vitals: weight, waist circumference
- Have blood drawn at VA lab to measure lipid panel. If lipid panel has been completed in the past 28 days, will not need to repeat during follow-up visit.

Randomization: Study statisticians will develop a 1:1 blocked randomization scheme, stratified by site and hyperlipidemia status. The project coordinator and research assistant will be blinded to the randomization schema and will randomize each subject using an automated randomization methods embedded in the study tracking software. Participants will be randomized to one of two groups:

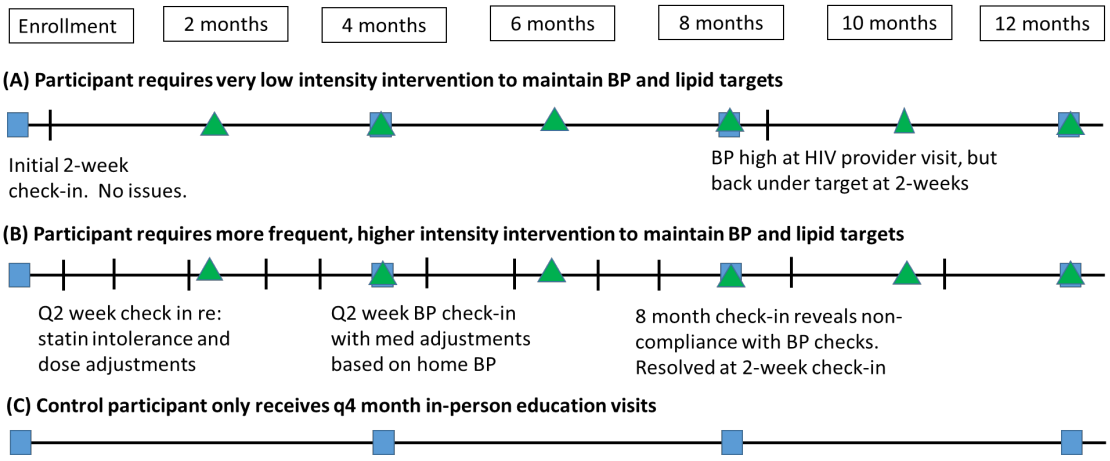
- Education control group
- Intervention

Education control group: Participants assigned to the education group at baseline will receive usual care enhanced with general prevention education delivered by the research assistant in person at lab collection times (0, 4, 8, and 12 months). Providers will not be able to see research outcome assessment of BPs since these are not placed into CPRS.
We believe it would be unethical to use a usual care comparison group. The Education control group is receiving more than usual care: education material given at each visit, BP monitored and documented in CPRS, and providers notified if BP exceeds safety thresholds, requiring their co-signature.

Intervention: Participants assigned to the intervention will also complete in-person visits every 4 months, as listed above but will also have additional contact with our interventionist who may be either a nurse or pharmacist. The in-person visits will be identical to those in the education control group, but without the in-person education material. At their baseline visit, individuals enrolled in the intervention will be invited to consent and enroll in the VA Annie program, allowing them to submit home BP readings via text message before their intervention contacts. This is an existing VA program, but will not be required to participate in the intervention.

Intervention contacts: Participants randomized to the intervention will receive a video call from the interventionist within 2-5 days of enrollment. While connected via video (using VVC) with the Veteran, the interventionist will conduct a medication assessment, including participant's knowledge of the purpose and side effects of each BP or cholesterol medication and current or potential adherence strategies. If the Veteran or Interventionist is unable or unwilling to use VVC, these contacts may also be conducted by telephone. Telephone calls may be recorded for quality control purpose only (no name will be captured on the recording, and consent would be obtained prior to any recording). At a minimum, the interventionist will have contacts at 0, 2, 4, 6, 8, 10 and 12 months(see figure 4). An initial 2-week follow-up call will ensure proper use of the home BP monitor and to address any other questions. Prior to each interventionist contact, similar to prior studies,[34,61] we will request home BP values for the past two weeks using ANNIE SMS, with the goal of using the average of at least 3 values to determine BP control. For veterans unable/unwilling to use Annie, we can collect the home BP measurements over the phone or by secure messaging to the interventionist. In addition, the interventionist will contact the intervention subjects at up to 2-week intervals as necessary to carry out the multi-component intervention. Frequency of contact will be determined by whether the participant remains above goal BP or is initiating new treatments (e.g. starting another BP medication). Regardless of contact, study outcomes are collected routinely at the same frequency for both arms.

Figure 4: Example scenarios of intervention participant contact frequency. (A) Participant with lower intensity requirements; (B) Participant with higher intensity requirement; (C) Control participant. Squares represent in-person visits and outcome assessment time points, Triangles represent Virtual visits and lines are telephone contact.



Intervention components:

1. Lifestyle Intervention. The interventionist will deliver a tailored behavioral, telemedicine intervention to improve lifestyle risks. Patients may receive up to 5 modules , based on their interest, motivation, barriers and stages of readiness to change. The lifestyle topics available for counseling include: tobacco cessation, exercise/inactivity, diet, weight, stress, sleep and alcohol misuse. The interventionist will provide resources related to these behaviors and when appropriate, refer individuals for follow-up care with Primary Care-Mental Health Integration (PC-MHI) or direct referrals to MOVE!, nutrition or smoking clinic, based on the resources available at each VA site.

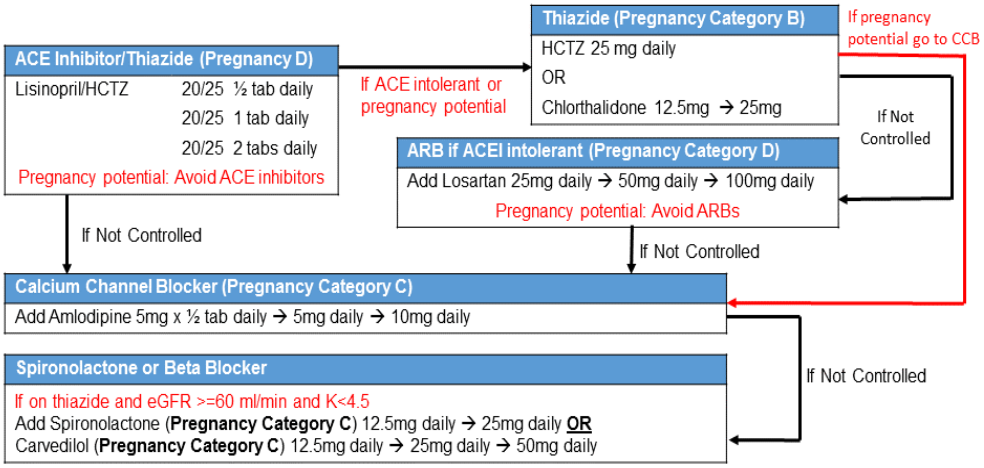
2. Care coordination. Beginning with initial enrollment, the interventionist will coordinate BP and lipid management for all participants in the intervention arm. Care coordination will consist of tailored discussions with the participant and his/her providers about which provider will take primary responsibility for BP and lipid management. The interventionist will direct management decisions to the designated provider but will facilitate communication by notifying the non-designated of any changes to medications.

3. Interventionist-managed medication protocols and adherence support. Participants with BP and non-HDL not meeting CVD goal will receive tailored medication management and adherence support. Algorithm-based care to reduce practice variation and clinical inertia has long been recommended to assure that patients are not "stuck" at sub-therapeutic doses of medications.[62] By using HIV-appropriate algorithms to guide medication titration, the prevention interventionist will make recommendations to providers to improve care by reducing clinical inertia, reducing variation, and allowing non-physician staff members to assist in care. A clear

and complete algorithm will also help simplify the medical regimen and emphasize medications that are affordable, effective, and have low side-effect profiles.

At each contact where average weekly BP based on a minimum of three values exceeds 140/90mmHg, the interventionist will review the medication list with the patient, including any potential side-effects of each medication.[63] The interventionist will provide counseling in several areas, including ways to enhance medication adherence and ameliorate side effects [as well as discuss risk factors such as physical inactivity, tobacco and alcohol misuse].[64,65] Patients may receive a personalized medication schedule (via secure link or paper) that shows when they should take their medications, if requested.

Figure 6: Blood pressure treatment algorithm

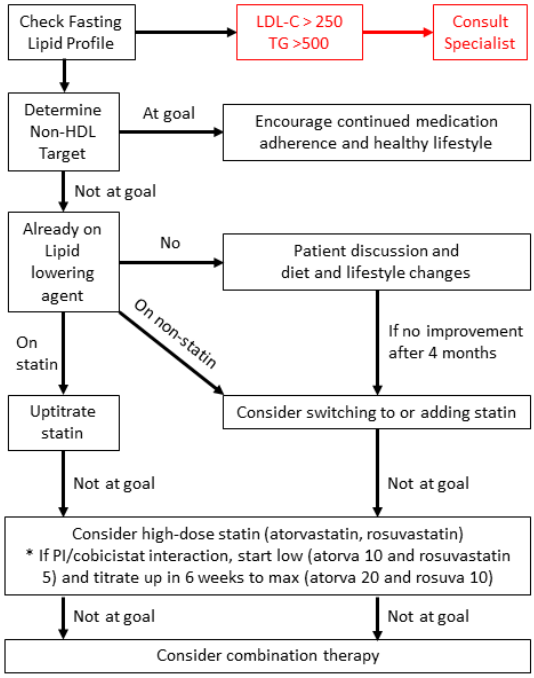


The interventionist will use a previously tested algorithm to decide on appropriate recommendations for medication changes and will approach the designated responsible provider for prescriptions and lab orders.[34,61] Any communication in CPRS between the intervention interventionist and provider will require a co-signature. The responsible provider (not a member of the study team, but the patient's provider who has been managing their hypertension, likely the PCP) will also have the option of taking the individuals OFF medication management protocols as clinically indicated (e.g. recent ASCVD events or advanced CKD), in which case the participant would continue all other components of the intervention.

Each site will have a clinical site leader who is an ID doctor familiar with current CVD/HIV treatments to reduce any potential drug-drug interactions. Our ID specialists will provide input on antihypertensive choice before initiation, although the patient's responsible provider is intended to be the one managing and prescribing these medications throughout the study.

Blood pressure. We will use an evidence-based blood pressure treatment algorithm (Figure 6) used in our prior studies, in addition to the current VA/DoD Hypertension Clinical Practice Guidelines.[66,67] A follow-up basic chemistry panel will be ordered when adding ACE/ARB, thiazide diuretic, or potassium-sparing diuretic. Medication up-titrations will be recommended at intervals of 2-4 weeks until control is achieved. Actions not shown in the figure will include, but will not be limited to: (1) adding agents such as hydralazine, terazosin, clonidine; (2) considerations for comorbid kidney disease or prior ASCVD event; (3) avoiding combination use of heart rate slowing drugs.

Figure 7: Lipid treatment algorithm.



Lipids. We will use an algorithm (Figure 7) adapted from National Lipid Association (NLA) guidelines for HIV-infected patients.[18] As recommended by the guidelines, our algorithm will address drug-drug interactions with ART, including the safe use of higher dose statins (rosuvastatin and atorvastatin) if needed, when drug interactions are present. A lipid panel (total cholesterol, triglycerides, HDL, LDL) will be checked at every in-person study visit. The interventionist will have access to all lipid fractions, but the algorithm will focus on non-HDL as the primary target. When a new lipid-lowering agent is prescribed, the prevention interventionist will call 2 weeks after initiation to discuss adherence and any possible side-effects. The interventionist will use an evidence-based approach to evaluation and management of muscle symptoms and other intolerances of statins as recommended by NLA guidelines.[68,69] This approach will include evaluation

for other causes, drug-drug interactions, checking creatinine kinase levels, trial off statin, retrial of different statin, non-daily dosing of longer acting statin (i.e. rosuvastatin), and/or referral to lipid specialist.

Relevant process evaluation data for aim 3: (1) frequency of BP and lipid algorithm use; (2) number of telephone contacts and total duration of time required to bring an elevated BP or lipid level under control; (3) Frequency of statin intolerance and proportion of intolerance cases ending in complete cessation of any statin; (4) Number of referrals to BP or lipid specialists.

4. Home BP monitoring.[35] Our justification for using home BP monitoring is that home BP measurements are reproducible with standard deviations of less than 3.1 mmHg for both systolic and diastolic measurements.[70] In addition, home BP monitors are accurate and comparable to ambulatory BP monitors,[71] a 'gold standard' of BP measurements. Home measurements have greater predictive power for mortality as compared to office-based measurements.[72] All intervention participants will receive a home BP monitor, if they do not already have one, through the VA prosthetics department. They will be trained according to a developed protocol[34] and documentation of proper usage will be recorded. The interventionist may also use video to determine if individuals are measuring their BP correctly at each intervention visit. Prior to each telephone contact, we will request BP values for the past two weeks using ANNIE with the goal of using the average of at least 3 values. Participants with poor BP control will receive interventionist calls every 2 weeks, with management changes made as described in component #4 below.

Relevant process evaluation data for aim 3: (1) Frequency of home BP checks (average checks/week); (2) Number and nature of medication changes in response to home BP data.

5. Support tools. Evidence-based tools that do not result in provider fatigue or information overload effectively improve patient outcomes.[73,74] We use these tools to assist the interventionist during the intervention phase:

- An extended treatment cascade graphic for the interventionist that appears as a recurring pdf report.
- The interventionist will regularly access names of specific patients who have fallen out of each cascade category.
- Decision support tools for the protocolized prescription of BP and cholesterol medications.
- Automatically calculated National Lipid Association treatment targets for LDL and non-HDL cholesterol.

These tools will only be available to the interventionist during the intervention phase, but will then be made available to all providers after the intervention is completed.

Relevant process evaluation data for aim 3: (1) number of times each tool is accessed; (2) proportion of subjects with missing data for NLA lipid targets tool.

6. (Optional) Participant Support Group - These will be approximately monthly drop-in groups for any Veteran randomized to the intervention arm. Study participants will be able to access the group only during their 12-month participation in the study. Groups will be for approximately 60 minutes and will be organized by a member of the study team who will function as a facilitator during the session. The purpose of these groups is for the Veterans to talk with one another about their experiences, struggles and challenges in managing their blood pressure / cardiovascular risk. The groups will not be used to seek or obtain medical advice from a medical professional. Sessions will be conducted using a VA-approved videoconferencing platform, such as Cisco Webex or Microsoft Teams, when possible, or by phone, when needed. Research staff would provide the phone number or weblink to the events by the Veteran's preferred method of communication (email, phone, mail, Annie SMS, secure messaging etc). These monthly support group sessions may be recorded (both audio and video, as is standard for Webex or Teams software) for quality control purposes only. No transcription will be done for the support group recordings; they are only for quality control purposes (e.g. to review the facilitator's methods). Participants will be eligible to continue attending monthly support groups even after their participation in the study/intervention ends, as no data is collected during these visits.

Aim 3: Qualitative Interviews for Process Evaluation

A random subset of approximately n=27-*40* intervention participants (4-*16* from each site) will complete key informant interviews at the conclusion of the intervention. Participation in these interviews will be voluntary and discussed when they provide informed consent to the intervention (aim 2). Veterans will be paid $20 for completion of interview. In addition to collecting information from Veteran participants, we will also reach out to clinicians at all 4 sites who interacted with the intervention program/staff. These will likely be ID clinicians, and

we will collect feedback related to their thoughts on the intervention delivery and future sustainability/implementation. Feedback will be collected via VA-approved methods as written or oral questions, based on clinician's preference and availability (VA encrypted email, VA REDCap survey, Microsoft Teams, and/or telephone calls). Providers/staff will not be compensated.
For the Veteran participants who complete interviews, they may also be contacted 6-12 months after completing the intervention for a second brief interview. The purpose of these interviews to hear participants' long-term perspectives from completing the study and developing a better understanding of the sustainability of the intervention.

Risk

This study is enrolling Veterans living with HIV. While this group is considered a vulnerable population, the study team has considerable experience enrolling these participants and adapting interventions that are culturally sensitive. Given the increased prevalence of ASCVD risk factors among Veterans with HIV, it is important that they are not excluded from participation in this study. We will use VA CDW to identify the initial patient sample using the inclusion/exclusion criteria. Each site's respective electronic medical record system (CPRS) will be used for a second screening level for information not readily available as normalized data in VA CDW prior to contacting patients. If investigators identify any SAE outcomes of interim findings which have the potential of affecting participants' health or welfare, the veterans as well as their PCP will be notified using secure VA notification processes.

Potential risks

a. ***Loss of confidentiality*.** The risks associated with gathering mixed methods data from participants by properly trained and supervised research assistants and technical staff is low and include risks of loss of privacy and psychological distress associated with asking questions relevant to a sensitive diagnosis like HIV.
b. ***Detection of clinically significant problems*:** Although not caused by study participation, it is possible that clinically significant problems will be detected by study staff. Subjects entering the study will have a history of hypertension so we expect to see abnormal systolic and diastolic values. All values that reach a safety threshold (<90 or >180 systolic BP, <40 or >110 diastolic BP) will be reported to the subjects' care provider as soon as possible.
c. ***Kidney disease and electrolyte imbalances*:** Some of the blood pressure agents used in the interventionist-managed protocols may cause acute kidney injury and electrolyte imbalances. Subjects with underlying kidney disease at baseline will be at higher risk.
d. ***Drug-drug and Drug-disease interactions for ART treatment***. Each site will have a clinical site leader who is an infectious disease doctor familiar with current CVD/HIV treatments to ensure that there are no drug-drug interactions.
e. ***Other medication side effects****:* All medications have potential side effects. Medications used in the interventionist managed protocols will only be recommended by the interventionist and must ultimately be prescribed by the subject's treating provider according to his/her best clinical judgement and approval. Common side effects of anti-hypertensive medication include but are not limited to: bradycardia, lightheadedness and orthostatic hypotension, lower extremity edema, kidney injury and electrolyte imbalances (see above), and myalgias.
f. ***Physical activity.*** All subjects will be encouraged to increase their physical activity, raising the possibility of musculoskeletal injury or unmasking of ischemic heart disease. Risks from increased physical activity will be minimized by encouraging moderate rather than vigorous activity. Providers will respond to these patient problems per usual medical practice.
g. ***Smoking and Alcohol Misuse*.** All subjects will be encouraged to quit smoking (if currently using), raising the possibility of withdrawal symptoms from nicotine dependence. Participants will also be screened for alcohol misuse.
h. ***Psychological risks*.** We do not anticipate any substantial psychological risks to be associated with participation in this study. As part of our assessments, we will ask participants about their demographic characteristics (i.e., race/ethnicity, socioeconomic status). It is possible that some participants may feel

uncomfortable answering some of these questions. We will only ask questions that involve data that are important for study outcomes, and we will inform patients that they may refuse to answer any interview or survey questions, but still be involved in the study. It is also possible that participants may be uncomfortable talking with the Prevention Interventionist about some topics that are included in patient-based intervention. We have not experienced any significant issues regarding this in our prior qualitative or mixed-methods studies with Veterans who are HIV+. However, subjects will be permitted to skip any topics that make them feel uncomfortable, and subjects will be informed that if they choose to discontinue the study at any time, this will not interfere with their usual medical care.

Adequacy of Protection Against Risks. The specific risk of participation are noted above; procedures for protection follow.

a. ***Protection of participants' identities and confidentiality****:* Because this study involves persons with HIV, steps must be taken to protect not only the data they provide, but also their identities. The following confidentiality-protection steps will be taken: [1] All research staff will participate in initial training, follow-up training, and ongoing monitoring and supervision to ensure their understanding of ethical issues involved in this research; [2] consent forms will be maintained in locked files with limited access, separate from any subject data and will only be accessible to the study team; and [3] any personal identifiers linked to data will be removed and replaced by code numbers in all records. These steps are not foolproof, and participants will be informed of the associated risks at the time of informed consent. Research staff will spend approximately 20 hours in initial training sessions and observed practice. Training includes reading and discussing research protocols and selected articles about interviewing, tracking, vulnerable participants and attending lecture sessions regarding emergency procedures, mandatory reporting, confidentiality, and research ethics. Training also will include how to handle transient discomfort or distress related to embarrassing or sensitive discussions as well as how to identify and respond to signs of acute distress; experienced staff will be available for immediate consultation in the event of unexpected acute psychological problems; and all staff will be made familiar with referral resources and procedures for psychological, social service, substance-use treatment, and other emergency needs. When appropriate, material specific to interacting with persons living HIV and the sensitivity of the diagnosis will be provided to research staff as part of their training curriculum.

b. ***Blood Pressure****:* All participants will have a high risk for CVD, and thus many will be prescribed hypertension medications by their health care provider at the outset of the study. It is likely that as a result of increased monitoring, we will detect more episodes of abnormal BP values. Because of potential high and low BP values, subjects in the intervention arm may have their current hypertension regimen adjusted, subjects in the education control are will be asked to contact their provider for follow-up. [We will proactively address BPs for participants in the control group. If BP is identified by study staff as being high (>180/110), similar to prior trials), we will provide feedback to both the patient and their provider via developed CPRS template and/or phone calls. If no action is taken, the study physician at each respective site will follow up with the patients' provider.] Safety monitoring of BP will occur in the context of home BP monitoring as well as BP measurement during data collection visits. An average SBP at any study visit or during home blood pressure monitoring > 180 mm Hg and/or diastolic is >110 mm Hg will be considered an alert value and will trigger assessment by the clinician. Furthermore, an average at any study visit or during a home blood pressure monitoring that is < 90 systolic or < 40 diastolic would also be considered an alert value and would trigger an assessment by a clinician. Participants who have an alert reading at home will be asked to contact the clinician directly so that she/he can assess for any cardiovascular symptoms.

   Participants who have an alert BP reading during study visits will be directly assessed for cardiovascular symptoms. Once an alert value has been confirmed, the participant will be triaged according to follow-up recommendations from Joint National Committee Recommendations (JNC 8). Participants will have access to their regular providers as well as the following study clinician investigators designated as the clinical contact for each site:. If at any time, participants have symptoms of acute end organ damage (i.e. current chest pain, dyspnea at rest, new onset of blurry vision, or new neurological deficits consistent with a stroke) in the context of an elevated BP measurement (SBP

>180, and/or DBP >110), participants will be asked to contact their clinician and will be advised and assisted in seeking emergency medical care. For participants in the intervention group whose average SBP >180 and DBP >110 or SBP < 90 or DBP < 40 but are without acute symptoms, the participant's healthcare provider will be notified and medications will be changed as deemed appropriate by the study team. Follow up contact with the study staff will occur within one week. All abnormal blood pressure results will be communicated to the clinic director at each site who will be an integral part of triage and ensuring follow up. Any change in medication management or observation of an alert value will be communicated from the interventionist as soon as possible. The prevention interventionist will then generate a note to be entered into the electronic medical record and will communicate directly with the subject's PCP. To facilitate the efficiency of this alert mechanism, the prevention interventionists will be encouraged to familiarize themselves with relevant clinic providers and staff and integrate themselves into the clinic workflow as completely as possible.

c. ***Lifestyle Interventions (Smoking Cessation, Alcohol Misuse, Physical Inactivity:*** The interventionist will explore potential barriers to meeting recommended levels of exercise using motivational interviewing techniques *as* well as setting goals for exercise. The interventionist will screen for alcohol misuse using SBIRT for Veterans who screen positive for alcohol use and make referrals to the Primary Care-Mental Health Integration (PC-MHI) program were Veterans with alcohol misuse are more likely to receive care. Screening, brief intervention, and referral to treatment (SBIRT) is an integral part of nursing practice. The interventionist will screen for tobacco cessation (smoking, smokeless, e-cig, vaping). Barriers to initiating and maintaining smoking cessation will be explored and benefits emphasized. Among those in the process of quitting smoking or recently stopped, strategies to maintain smoking cessation will be explored. The interventionist explored potential barriers to smoking cessation using motivational interviewing techniques and setting goals for smoking cessation. The interventionist will provide a direct referral to the smoking cessation clinic and ensure that the study physician puts in a prescription for NRI when appropriate. Additionally, the interventionist will provide resources related to these behaviors and when appropriate, refer individuals for follow-up care.

d. ***Medication adverse effects, including kidney and electrolyte imbalances****:* All participants who are prescribed a clinically indicated new medication according the interventionist-managed protocol will have that medication prescribed by the participant's usual health care provider, who will take primary responsibility for counseling the patient about side-effects and ordering follow-up laboratories. In addition, each participant will be counseled by the prevention interventionist about possible side effects and need for any monitoring. These protocols therefore will provide an additional level of monitoring compared to routine clinical care. Anti-hypertensive medication: Any patient prescribed an ACE-inhibitor, angiotensin receptor blocker, diuretic, or aldosterone antagonist, will be asked to return in 7-10 days for a repeat chemistry panel to check kidney function and electrolytes. The blood pressure algorithm will have special recommendations for those with more advanced chronic kidney disease (eGFR <60). Providers caring for study participants with conditions including but not limited to CKD and ASCVD, will be permitted to take their patients off of any protocolized management. Providers will take primary responsibility for the prescription of any medications in this study.

e. **Drug-Drug and Drug-disease interactions with ART.** Each site will have a clinical site leader who is an infectious disease doctor familiar with current CVD/HIV treatments to reduce any potential drug-drug interactions. Our three CVD/ID specialist and ID site specialist will provide input on antihypertensive choice before initiation. If the patient's ASCVD risk estimate is ≥5% over 10 years, based on current guidelines it is reasonable to begin moderate-intensity statin therapy. Antiretroviral therapy may adversely affect lipid levels, glycemic control, and endothelial function and has been associated with adverse changes in body composition (lipodystrophy). However, use of newer agents may lessen the metabolic derangements of antiretroviral therapy.

Potential Benefits of the Proposed Research to the Subject and Others

Potential benefits for subjects may include improved lifestyle and lower blood pressure with

a consequent reduction in cardiovascular risk. In our previous experience, subjects in biobehavioral research studies have generally found participation to be a positive experience and they often feel good about helping provide information that has the potential to help others like them. Potential benefits to others include the possibility that this research will lead to the development of more efficient and effective clinical treatments for patients with cardiovascular disease, with the expectation that this would lead to consequent reduction in subsequent, cardiovascular complications and death.

5.2 Recruitment Methods

Aim 1: Formative Interviews and Design Team Meetings:

Participants: There are two groups of participants for aim 1

- **Healthcare providers (both ID and primary care)**. **up to 18 health care providers** (n=6 providers from each site, a mix of provider type (MD, RN, NP, PA, PharmD) will participate. Providers will be recruited by purposive and snowball sampling. We will first interview providers to seek their guidance on key factors on which to select our Veteran informants.
- **Veterans with HIV: up to 18 Veterans** (n=6 from each site) will participate. They will be enrolled by purposive sampling.

We will use nonprobability sampling techniques of purposive and snowball to recruit participants for this aim.

A purposive sampling strategy is a "judgmental or expert sample" and is a type of nonprobability sample. The objective of purposive sample is to produce a sample that can be logically assumed to be representative of the population. This is often accomplished by applying expert knowledge of the population to select, in a nonrandom manner, a sample of elements that represents a cross-section of the population. To achieve representative, yet nonrandom sample of patients for our qualitative interviews, we will first query the context experts on the study team and at the site level to ascertain key variables (eg., age, race/ethnicity, sex, comorbidities) upon which to sample the eligible population of patients with HIV and CVD risk. Based on these typologies, we will query CDW based on these variables and then develop a purposive sample based on these characteristics. In some instances, we will also use direct nominations by site leaders and providers, when feasible.

We will then mail introductory letters to Veterans who meet these criteria using a strategy whereby Veterans may call a toll-free number to opt out. The letters are on VAMC letterhead and signed by the study site PIs (attached). If patients meet telephone screening criteria and are interested in participating, we will complete the informed consent process by telephone before scheduling the qualitative interviews.

For providers, we will predominantly use a snowball sampling (ie., chain sampling, chain-referral sampling) which is another a nonprobability sampling technique. In snowball sampling, existing study participants help identify future participants from among their social network such that the sample group is said to grow like a rolling snowball. For this protocol, we will work with site leads to identify a beginning set of site providers. We will then ask these providers to nominate others they see as important to the implementation of the intervention while balancing mix of providers (eg. MD vs NP). In order to protect the identity of providers who are contacted, we will create a firewall between the study and management – that is, there will be no record for which management can be aware of which providers were contacted nor which providers agreed to participate. We will contact providers by encrypted email, with introductory information about the study (attached). Research staff will reach out to providers after the emails are sent to assess interest in participation, and will conduct the

informed consent process by phone before scheduling any interviews. Participation with providers can be done by all authorized communication methods approved by VA, such as email, Microsoft Teams, phone call.

For Aim 1b (design meetings), we plan to consent approximately 10-20 design team members across the 3 VA sites: a mix of healthcare providers, and Veterans with HIV. These healthcare providers and Veterans will most likely be those who already participated in the Aim 1a qualitative interviews and expressed interest in the design meetings, but they will undergo another verbal consent process with specific details to the design meeting process.

See table below regarding payment to Veterans for participation in the project. Providers/staff will not be compensated.

Aim 2: Evaluate the 12-month efficacy of interventionist intervention

Participants: We plan to enroll 300 HIV+ Veterans who are on suppressive ART with **HIV-1 RNA <200 copies/ml** checked at least twice within the prior year if they have hypertension and receive care at the 4 clinic sites. Our plan is to enroll approximately 100 from each of the following sites the Durham VA Healthcare System, Cleveland VA Healthcare system, Baltimore VA HealthCare System and the Atlanta VA Healthcare System. We may enroll more or less at the different sites depending on acceptance of study at the sites. Since site is one of our randomization strata enrolling more at one site will not impact analysis. Additionally, while 300 is our enrollment goal, we may consent and randomize up to 310, to account for site differences, withdrawals and the scheduling availability and preferences of Veteran participants.

The study programmer and statistician in Durham will use VA Corporate Data Warehouse to identify a sample population at each facility for Veterans enrolled in care at through either primary care clinics or infectious disease clinics. ICD-10 diagnostic and procedure codes will be used to identify patients meeting the inclusion/exclusion criteria. Research assistants will use each site's respective electronic medical record system (CPRS) for a second screening level for information not readily available as normalized data in VA CDW prior to mailing letters. Research assistants will also be able to conduct chart reviews, to assess eligibility, for other study sites using Joint Longitudinal Viewer (JLV).

The primary outcome is change in systolic BP and the secondary outcome will be change in non-HDL cholesterol. Separately for hypertension and hypercholesterolemia, we will then examine changes in the three extended treatment cascade categories (1) % appropriately diagnosed, (2) % appropriately managed, and (3) % at treatment goal. We chose BP as the primary outcome because the V-EXTRA-CVD intervention components were designed primarily to address BP management, with cholesterol management being an important but secondary consideration. For the purposes of determining cascade level #1, we will use the following table to search for diagnosis of high cholesterol or blood pressure in the medical record.

Table: Diagnosis terms for high cholesterol and high blood pressure for the purposes of determining cascade category from chart review.

High Cholesterol	High Blood Pressure
Hyperlipidemia	Hypertension
Dyslipidemia	Essential Hypertension
Hypertriglyceridemia	Secondary Hypertension
Hypercholesterolemia	Hypertensive end-organ disease
Elevated LDL	High blood pressure
Elevated Triglycerides	
Elevated Cholesterol	
Familial Hypercholesterolemia	

DO NOT include the following:	**DO NOT include the following:**
Low HDL	Pulmonary hypertension
	Intracranial hypertension
	Venous hypertension
	Pre-eclampsia or Maternal Hypertension
	Portal hypertension
	Ocular hypertension

Specific recruitment strategies may vary at each site depending on the preferences of the clinic providers and Veteran populations, but will include a mix of the following methods:

1. The research team will mail introductory letters to Veterans who meet eligibility criteria using a strategy whereby Veterans may call to opt out. The letters are on VAMC letterhead and signed by the study site PIs.
2. Medical providers in their clinics may talk to their patients about the study and refer potentially eligible and interested patients to the site's research assistant.
3. Study-specific flyers and brochures will be made available at each of the site's clinics, allowing Veterans to self-select and call the research team for more information.

The research assistant will contact potentially eligible Veterans and administer a screening questionnaire to further assess eligibility. This may be done by phone, or in-person (if a patient is already on-site for an appointment and able to meet with the research team). If patients meet screening criteria and are interested in participating, we will schedule an enrollment visit to coincide with an upcoming clinic appointment or the availability of the Veteran. If ≥ 30 days pass between initial chart review and date of consent, chart review may be repeated to confirm eligibility at time of consent.

All enrolled participants will complete a baseline assessment which includes in-office BPs, lipid panels, and several health-related surveys (see section 5.5 study evaluations). On return visits at 4, 8 and 12 months all participants will similar assessments. Participants will be randomized during the baseline visit.

Participants in both study arms will be paid a total of $150: $50 for completion of the baseline questionnaires at the enrollment visit and $50 for completion of the 12-month blood pressure and lab outcome assessment and questionnaires. They will be paid $25 for completion of the 4 & 8 month blood pressure and lab outcome assessment. These are the only study sessions that require in-person visits. If due to unforeseen reasons or closures, we are unable to obtain BP by study personnel, we may conduct VVC visit with study participant to observe the collection of self-monitored BP and schedule patient for lab collection within next 4 weeks. The research assistant completing the assessments will submit the payment voucher following each visit after we receive the results of labs.

Aim 3: Process Evaluation

Participants: A random subset of approximately n=27-40 intervention participants (4-16 from each site) will complete key informant interviews at the conclusion of the intervention. Participation in these interviews will be voluntary and discussed when they provide informed consent to the intervention (aim 2). Selection of VA providers will be based on those currently employed in ID or Primary Care clinics at the 4 study sites, and those who interacted with the study team during the intervention (most likely ID physicians whose patients enrolled in the study, and were responsible for making changes to medications after health coach recommendations). Veterans will be paid $20 for completion of interview. Providers/staff will not be compensated.

Exploratory Aim: Cost Evaluation

Participants: If effective, we will conduct a budget impact analysis and simulate 10-year cost-effectiveness of the interventionist intervention. The entire cohort of Aim 2 will be used in the budget impact analysis and the intervention cohort will be used in the 10 year cost effective analysis.

Participant payments:

The research assistant completing the assessments will submit the payment voucher following each visit. Providers/staff will not be compensated.

Aim 1 – Formative evaluation & adaptation	Formative interview (n=18) Design Meetings to adapt intervention (n=6) Phone interview to review acceptability of intervention revisions (n=12)	$20 $120 per meeting ($480 total) $20
Aim 2 – Interventionist-led intervention	In-person study outcome assessments (n=300) Months 0, 12 Months 4, 8	 $50 each $25 each
Aim 3 – Process evaluation	Post-intervention qualitative interview (n=27-40), as well as 6-12 month post-intervention sustainability interview	$20 each

5.3 Informed Consent Procedures

Subjects for each aim will go through the informed consent process to participate in the study. Research staff (RA or PC) will read, review, and discuss consent documents with all potential participants prior to obtaining consent. If the veteran appears confused or indicates a lack of understanding, the interviewer will attempt to identify the misunderstanding and to explain the study again. Any veteran who still does not comprehend the consent process and study will be excluded from the study. Veterans who understand the consent process and study and agree to participate in the study will be asked to provide consent either verbal or written. For those participants who provide written informed consent, the research assistant will keep the original signed and dated consent documents and will provide a copy of the signed documents to the subject. No veterans who have impaired decision-making abilities will be enrolled in any phase of the study. These consent procedures will take place in a private room or office. Written consent and HIPAA forms will be kept in a locked filed cabinet within a secure office at each of the 3 sites. Verbal consent will be documented in RedCap & tracking database.

Aim 1: Formative Evaluation/Qualitative Interviews and Design Team Meetings. These interviews and meetings will be done by telephone, with no in-person contact, therefore we will request a waiver of documentation of informed consent as well as waiver of HIPAA. Research staff (RA, PC, or investigator conducting the interviews) will collect verbal informed consent from both the veteran and provider participants for Aim 1. Date of verbal consent obtained will be documented in tracking database or REDCap along with the name of the person who obtained consent.

Aim 2: Intervention. Once the veteran is screened and agrees to enroll, then written informed consent and HIPAA authorization will be obtained at the baseline visit. These visits will be handled by the research assistant at each of the 3 sites. The project coordinator is also trained and able to assist with these visits. All research staff (RAs and PCs) will be up to date on all CITI training and how to obtain and document informed consent.

Aim 3: Process Evaluation: Participation in this aim will be a voluntary addition when providing informed consent for the intervention (aim 2). It will be covered by the same written consent and HIPAA authorization as Aim 2. For clinicians contacted for their feedback, language will be provided (by VA encrypted email or verbally on Microsoft Teams/telephone) related to providing consent

All study personnel will maintain certification of completed training in research ethics and confidentiality, data privacy and security. The study/site PIs will meet with research staff before the study begins to review eligibility and study procedures including obtaining informed consent and documentation of informed consent and authorization. If required by local site IRB/R&D/RCO, the research assistant will enter the research consent note into CPRS within 24 hours of the subject signing the consent and attach the scanned informed consent, HIPAA authorization as soon as possible but no later than 14 days from the signed consent.

5.4 Inclusion/Exclusion Criteria

The same inclusion and exclusion criteria is used for Veterans enrolled in all aims.

	Inclusion Criteria	**Exclusion Criteria**
Veterans with HIV Aim 1: N= 18 Aim 2: N= 300 Aim 3: N = 27	1. Age ≥ 18 years 2. Confirmed HIV+ diagnosis 3. Undetectable HIV viral load: defined as the most recent HIV viral load < 200 copies/mL, checked within the past 18 months (assessed via chart abstraction) 4. Hypertension: defined as having 2 recent outpatient BP measurements in the last 18 months to show systolic BP ≥ 130 and/or diastolic ≥ 90 mmHg OR being prescribed anti-hypertensive medication (assessed via chart abstraction) 5. Veteran at one of the sites participating in the study	1. Severely hearing or speech impaired, or other disability that would limit participation 2. In a nursing home at baseline and/or any long-term care facility. Individuals will be censored at the point of entering nursing home care 3. In-patient psychiatric care 4. Diagnosis of dementia or active psychosis 5. Terminal illness with life expectancy < 4 months (ex. Metastatic cancer, Hospice care,) 6. Recent (<90day) hospitalization for CABG, MI, stroke) 7. Pregnant, breast-feeding, or planning a pregnancy during the study period 8. Planning to move out of the area in the next 12 months. 9. No reliable access to telephone services 10. Currently enrolled in a competing research study (e.g. an intervention that may impact BP management)
Providers (infectious disease and primary care) Aim 1: N= 18 (2 HIV MDs, 2 PCPs, 2 RNs per site) Aim 3: N = 6	1. Have a panel of at least 10 veterans with HIV.	1. Not a provider at one the 3 participating facilities 2. PI is a co-investigator on the study.

Table: Antihypertensive Medications –

Beta Blockers	CARVEDILOL ESMOLOL METOPROLOL TIMOLOL BISOPROLOL NADOLOL ACEBUTOLOL	ATENOLOL BETAXOLOL LABETALOL PINDOLOL PROPRANOLOL NEBIVOLOL PENBUTOLOL SOTALOL
Alpha Blockers	SILODOSIN TAMSULOSIN TERAZOSIN	DOXAZOSIN ALFUZOSIN PRAZOSIN
Calcium Channel Blockers	AMLODIPINE NICARDIPINE AMLODIPINE/CELECOXIB CLEVIDIPINE ISRADIPINE NISOLDIPINE	AMLODIPINE/ATORVASTATIN DILTIAZEM NIFEDIPINE VERAPAMIL FELODIPINE NIMODIPINE
Antihypertensive Combinations	ALISKIREN/HYDROCHLOROTHIAZIDE AMLODIPINE/PERINDOPRIL ATENOLOL/CHLORTHALIDONE CANDESARTAN/HYDROCHLOROTHIAZIDE CAPTOPRIL/HYDROCHLOROTHIAZIDE HYDROCHLOROTHIAZIDE/IRBESARTAN HYDROCHLOROTHIAZIDE/LOSARTAN HYDROCHLOROTHIAZIDE/METHYLDOPA HYDROCHLOROTHIAZIDE/PROPRANOLOL AMLODIPINE/BENAZEPRIL BENDROFLUMETHIAZIDE/NADOLOL EPROSARTAN/HYDROCHLOROTHIAZIDE FOSINOPRIL/HYDROCHLOROTHIAZIDE HYDROCHLOROTHIAZIDE/LISINOPRIL HYDROCHLOROTHIAZIDE/METOPROLOL HYDROCHLOROTHIAZIDE/MOEXIPRIL HYDROCHLOROTHIAZIDE/TELMISARTAN	TRANDOLAPRIL/VERAPAMIL AMLODIPINE/OLMESARTAN AMLODIPINE/VALSARTAN AZILSARTAN/CHLORTHALIDONE BENAZEPRIL/HYDROCHLOROTHIAZIDE BISOPROLOL/HYDROCHLOROTHIAZIDE ENALAPRIL/HYDROCHLOROTHIAZIDE HYDRALAZINE/ISOSORBIDE SACUBITRIL/VALSARTAN AMLODIPINE/HYDROCHLOROTHIAZIDE/OLMESARTAN AMLODIPINE/HYDROCHLOROTHIAZIDE/VALSARTAN AMLODIPINE/TELMISARTAN HYDROCHLOROTHIAZIDE/OLMESARTAN HYDROCHLOROTHIAZIDE/QUINAPRIL HYDROCHLOROTHIAZIDE/VALSARTAN
Antihypertensives, other	CLONIDINE METHYLDOPATE RIOCIGUAT TADALAFIL GUANABENZ GUANFACINE MECAMYLAMINE	LOFEXIDINE MACITENTAN METHYLDOPA METYROSINE HYDRALAZINE ILOPROST SILDENAFIL

	MINOXIDIL	SODIUM NITROPRUSSIDE
Peripheral Vasodilators	ISOXSUPRINE PAPAVERINE	
Thiazides / Related Diuretics	HYDROCHLOROTHIAZIDE CHLOROTHIAZIDE CHLORTHALIDONE	INDAPAMIDE METOLAZONE
Loop Diuretics	FUROSEMIDE ETHACRYNIC ACID TORSEMIDE BUMETANIDE	
Carbonic Anhydrase Inhibitor Diuretics	DICHLORPHENAMIDE METHAZOLAMIDE ACETAZOLAMIDE	
Potassium Sparing / Combination Diuretics	HYDROCHLOROTHIAZIDE/SPIRONOLACTONE HYDROCHLOROTHIAZIDE/TRIAMTERENE AMILORIDE	AMILORIDE/HYDROCHLOROTHIAZIDE EPLERENONE SPIRONOLACTONE TRIAMTERENE
Diuretics, other	CAFFEINE/MAGNESIUM SALICYLATE MANNITOL SPIRONOLACTONE PAMABROM	
ACE Inhibitors	BENAZEPRIL CAPTOPRIL ENALAPRIL FOSINOPRIL QUINAPRIL	LISINOPRIL MOEXIPRIL RAMIPRIL ENALAPRILAT TRANDOLAPRIL PERINDOPRIL
Angiotensin II Receptor Antagonists	AZILSARTAN CANDESARTAN EPROSARTAN IRBESARTAN	LOSARTAN OLMESARTAN TELMISARTAN VALSARTAN

5.5 Study Evaluations

The table below lists which measures are collected from participants at each time point in the study. Data is recorded by the research assistant into secure study tracking SQL database or RedCap. The study team will develop an acceptable standardized time window for data collection around each timepoint.

Study visits/interactions:

Aim 1: Formative Evaluation	

Qualitative Interview	x	
Adaptation Virtual meeting	x	
Revision Qualitative Interview	x	
Aim 2: Intervention	Intervention	Usual Care
Enrollment Visit (baseline measurements)	x	x
Intervention Call – 1 week after enrollment visit with Interventionist	x	
Follow-up Intervention Call – 2, 4, 6, 8, 10,12 month after first call with Interventionist	x	
Adhoc check in call/video visits for BP/Statin med adjustments	x	
4, 8, 12 month outcome measurements –in person visit* with RA (to include measuring height, weight, BP, waist, and lipid panel at lab)	x	x
Aim 3: Process Evaluation Feedback on the intervention collected by phone.	x	
*Note: * if in-person study visits are discontinued for reasons out of our control or for pandemic closure we will convert them to VVC visits to capture BP outcome and schedule participants for labs with 4 weeks of BP collection. We will accept clinical labs for same lab if they have been collected within time frame.*		

Patient surveys for each time point are attached at the end of this document.

Data element	**Source(s)**	**Time period**
Aim 1: Formative Evaluation		
Perceptions of the self-management for CVD, HIV. Lifestyle change and medication adherence.	Audio recordings and field notes from qualitative interviews	Aim 1:
Aim 2: Intervention/ Survey		
Chart Abstraction/Review and screening	Site CPRS medical records/CDW	Pre enrollment
Hypertension diagnosis	Site CPRS medical records/CDW	0, 12
HIV + diagnosis, HIV history (prior labs, treatment and appointments), recent hospitalizations and ED visits, MOVE program participation	Site CPRS medical records/CDW	0
Demographics, family history of CVD, health literacy, prior home BP use, technology use, life chaos, loneliness, pain, housing and food insecurity, financial strain, anxiety and depression, physical function	Self-reported survey responses	0
Medications, comorbidities, labs, alcohol use	Site CPRS medical records/CDW	0, 4, 8, 12
Health behaviors such as physical activity, diet, tobacco use, medication adherence, sleep, stress,	Self-reported survey responses	0, 12

Data element	Source(s)	Time period
alcohol and substance use		
Aim 3: Qualitative Interviews		
Perceptions of CVD risk, self-management strategies and barriers, and intervention delivery strategy. *For example, we will ask participants which aspects of the intervention were most and least helpful, appropriateness of the number and length of telephone sessions, and ways we may be able to further improve the intervention.*	Audio recordings and field notes from semi-structured interviews	12
Optional sustainability interviews: 6-12 months after completing intervention, *to hear participants' long-term perspectives from completing the study and developing a better understanding of the sustainability of the intervention*	Audio recordings and field notes from semi-structured interviews	18 - 24 months
Exploratory Aim: Cost Impact Analysis		
Hospitalizations, Labor & Capital cost	CDW/Self-reported data	0, 12

5.6 Data Analysis

Aim 1: Formative Evaluation. Data will be analyzed by the Qualitative team in collaboration with PI.

Analysis for Aim 1a: Quantitative data (e.g., medical history, perceptions of CVD risk) will be summarized and used to describe study samples. After redacting all identifying information, verbatim transcriptions of recorded interviews will be entered into NVivo 12. A quality assurance protocol for qualitative analysis will be built into data management and analysis; 25% of the transcripts will be checked to verify accuracy of the transcriptions and 10% will be double-coded to ensure inter-coder reliability of 80% or greater.[75]

All responses will be analyzed using standard thematic analytic techniques for qualitative data: identification of themes/domains;[76] coding or classification of participants' responses by these themes performed independently by two team members; resolution of any coding discrepancies will be done by a third team member.[77] To ensure consistency, a codebook and dictionary will be developed to create universal definitions for each code. The architecture of the interview guide domains - informed by our theoretical lens of RE-AIM, Self-Regulatory Theory, and the Information-Motivation-Behavioral skills model - will drive the initial coding of our data. Yet, significant inductive (emerging) codes will also be identified. Coded items will be grouped together into distinct themes. Finally, the analytic team will work from the coded data to merge findings into a report of findings to aid in the intervention development.[28,38,78] Key findings will be abstracted into a matrix and mapped to existing intervention components to aid integration and map adaptation to inform participatory, iterative design process in Aim 1b. This method of data reduction encompassing a multidisciplinary team-based analysis creates a robust iterative process through which the data are thoroughly discussed and analytical consensus achieved. Findings from these interviews will be presented back to the study team and site leadership to inform context-specific adaptation of the intervention.

Analysis for Aim 1b: We will use a participatory, iterative design process as the analytic approach for Aim 1b.[53-55] .. The results will be a documentation of key adaptations of the evidence-based practices to inform intervention redesign to optimize clinical impacts and feasibility and acceptability of innovation uptake.

During brainstorming, the team will review the data obtained during the baseline assessment on perceptions of ASCVD risk and barriers and facilitators of ASCVD preventive care obtained during Aim 1a. The team will brainstorm ideas to refine the intervention in response to these data. Ideas will be captured in a structured, written format for the next phase.

In the conceptualization phase, the team will evaluate advantages and disadvantages of ideas generated during the brainstorming phase, and will develop concrete changes (ie., adaptations) to the intervention. For example, if the team decides to include the name of the provider (PCP or HIV specialist) responsible for BP and lipid management in the intervention program, we will discuss its feasibility. All final adaptations will be captured in a structured, written form to aid in implementation in the revision phase.

The creation and revision phases will involve the refinement of treatment protocols, manuals of procedures, and educational materials. Once the adaptation of the intervention is completed, we will present the adapted model to our Veteran Engagement Quorum and up to 9 intervention staff from each of the three sites to assess acceptability.[56] We will document any further adaptations resulting from these engagements in a structured written format to be implemented into the treatment protocols, manuals of procedures, and educational materials.

We will also analyze the perspectives from design team members in the final meeting about their experience participating in the Human Centered Design process. Content analysis of individual surveys and group discussions will be performed by the qualitative staff members and coded based on emergent themes captured. Core outcomes of interest for the surveys and discussions will include: a) previous design team experience; b) comprehension of the design team experience; c) thoughts on the design team process for the intervention; d) reflections on each phase of the human-centered design approach; and e) perceptions of the final intervention model.

Analysis for Aim 1c:

We will describe the HTN care cascade among PWH over a period of 5 years based on data definitions described above. To estimate proportions along each cascade, we will conduct descriptive analyses and obtain frequencies and percentages of Veterans at each previously defined step compared with the preceding step. We will conduct univariate analyses to describe demographic and baseline characteristics of the cohort. Means and SDs will be obtained for continuous variables, whereas percentages and frequencies will used to describe categorical variables. We will stratify the data into 2 subpopulations: HIV and HIV/HTN and compare baseline characteristics of these 2 subgroups.

Aim 2: intervention. Data will be analyzed by PhD & Master Statistician in collaboration with PI

Analysis*:* The primary outcome will be systolic BP at 12 months and secondary outcome will be non-HDL cholesterol at 12 months, both measured at 4 time-points (0, 4, 8, and 12 months). All BPs used for outcomes will be obtained by a research assistant and cholesterol levels will be measured by lab personnel who are also blinded to treatment group. Because the outcomes are continuous, linear mixed-effects models[79] (LMM) will be used to examine the differences over time between the study arms. LMM will allow us to implicitly account for the correlation between a patient's repeated measurements over time. The general mean structure of the LMM we will use to examine the hypotheses

$$Y_{ij} = \beta_0 + \beta_1 * I(month = 4) + \beta_2 * I(month = 8) + \beta_3 * I(month = 12) + \beta_5 * arm *$$

is, $I(month = 4) + \beta_6 * arm * I(month = 8) + \beta_7 * arm * I(month12),$

where Y_{ij} represents the outcome of interest (i.e., SBP or non-HDL) for patient i at time j. We will fit a common intercept and arm is the intervention group indicator. Similarly, time will be classified, where for example, $I(month = 12)$ is a dummy variable equal to 1 for the 12 month time point. Random intercepts will be included for each individual to account for correlation among repeated measurements over time. The primary analytic model will adjust for clinic site and hyperlipidemia status. The mixed effects model parameters will be estimated and tested using SAS PROC MIXED (SAS Institute, Cary, NC), and the hypothesis of between-arm differences over time will be tested using estimate statements within PROC MIXED. In particular, β_7, the estimated difference in outcome between arms at 12 months, will be the primary effectiveness outcome

assessed. All analyses will be conducted following an intention to treat (ITT) principle.

Missing data. We will assess mechanisms for missing data in this study. LMM, implicitly accommodates missingness when the response is Missing At Random (MAR); that is, when missingness is due either to treatment, to prior outcome, or to other baseline covariates included in the LMM.

Our primary analysis will include all available study-collected data. A sensitivity analysis will be conducted by filling in missing data in the following manner:

1. Use all available study-reported data.
2. If missing study-reported value → use the SBP or non-HDL cholesterol value if available in the EMR in a 2 month window from the target data for that time point
3. If missing EMR-reported value → assess whether the outcome has >10% missing remaining.
   a. If yes, ≥10% missing → use multiple imputation
   b. If no, <10% missing → do not use multiple imputation, include only study- and EMR-reported values

The final determination whether to use multiple imputation is separate for SBP and non-HDL cholesterol outcomes; SBP could meet the criteria and non-HDL does not, or vice versa.

If multiple imputation is indicated, we will use multiple imputation procedures as described by Schafer. Once missing values have been imputed, each multiply-imputed data set can be analyzed using the LMM. Final parameter estimates and their standard errors will be calculated using Rubin's formula.

We will analyze our data and report final study results and carefully examine and describe any discrepancies found between the primary and missing data analyses.

Attrition bias. As part of our examination of missing data, we will assess differences in baseline characteristics (e.g., clinic site, demographics, clinical values, medical history) by retention at each follow up time point. We will use two sample t-tests (or Wilcoxon rank sum tests) for continuous variables and χ^2 tests for categorical variables.

Power. The power calculation for this study was based on our prior nurse-led BP intervention,[35] a meta-analysis of lipid-lowering medication adherence interventions,[80] and baseline BP and cholesterol data from our clinic sites. Power estimates were derived empirically via simulation in SAS 9.4. Simulated data were generated based on estimates from prior studies, such that we assumed a mean SBP at baseline of 145 mmHg for both arms, with a reduction in the education control arm of 1 mmHg by 12 months. For the intervention arm, we evaluated effect sizes (differences from education control at 12 months) of 5-7 mmHg. We estimate that 15% of patients may drop out by the 12-month time point, and incorporated missing values into the simulated data based on a uniform pattern of 5% missing at 4 months, 10% at 8 months, and 15% at 12 months. The drop-out rate is consistent with prior interventions at our sites (80-88% retention at 12 months).[33,35,81] We conservatively estimated variance components assuming a total standard deviation of 17 and a within-individual correlation of 0.4 among repeated SBP measurements. Similarly, for the secondary non-HDL outcome, we assumed a baseline value of 132 mg/dL with a standard deviation of 41 and a within-individual correlation of 0.7, and evaluated sample size needed over effect sizes ranging from 10-20 mg/dL. After generating 1,000 simulated datasets under these assumptions, we fit the LMMs described above to each and assessed the effect of interest using two-sided tests with a type I error rate of 0.05. Based on results, we will have >80% power to detect a 6 mmHg lower systolic BP and >90% power to detect a 15 mg/dL lower non-HDL cholesterol in the intervention arm vs. education control. Table 4 displays the sample sizes needed to detect a range of plausible ***clinically significant*** BP and non-HDL effects. A 6 mmHg improvement in systolic BP is associated with a ~20% decrease in ASCVD events,[82] and a 15 mg/dL improvement in cholesterol is associated with ~10% decrease in clinical ASCVD events.[83]

Pre-specified sub-group analyses of the primary and secondary outcomes will include clinic site, sex, and baseline ASCVD risk category (10-20%, >20% or prior ASCVD). For each category, we will examine the interactions with intervention arm and time. Generally, the modeling approach will mirror that described above

Table 4: Sample size estimates to detect a range of plausible and *clinically significant* effect sizes

	BP Effect Size	*Non-HDL Effect Size*

	5mmHg	*6mmHg*	*7mmHg*	*10mg/dL*	*15mg/dL*	*20mg/dL*
70% Power	278	190	140	248	110	64
80% Power	350	234	178	310	148	80
90% Power	466	340	232	424	184	104
Green cells represent sample sizes that are less than our proposed sample size (n=300).						

for each outcome. Three separate analyses for each outcome will be conducted to assess the effect of each potential moderator. Models will be fit in SAS PROC MIXED, as described above, and the moderating effect of each of the three factors will be assessed via the hypothesis test of the three-way interaction among subgroup, treatment, and time at 12 months.

Analysis for Aim 3: The Process Evaluation: Data will be analyzed by the Qualitative team in collaboration with PI. The analysis for this aim will use a mixed-methods approach. We describe these by outcome below.

ASCVD Risk: We will assess changes in the perceived ASCVD risk scale between intervention and control group using t-tests and will examine correlations between changes in perceived risk and changes in clinical outcomes.

Additionally, we will collect additional data on the context of the intervention by assessing changes in perceived ASCVD risk and care team networks. In a group of up to 27 participants, we will evaluate how perceptions of ASCVD risk qualitatively changed over the course of the intervention. As above, qualitative interviews with participants will be analyzed using standard thematic analytic techniques for qualitative data: identification of themes/domains;[76] coding or classification of participants' responses by these themes performed independently by two team members; resolution of any coding discrepancies will be done by a third team member.[77] To ensure consistency, a codebook and dictionary will be developed to create universal definitions for each code.

Process Outcomes analysis: The process evaluation will collect data on key implementation measures across the following six categories: **fidelity** (quality), **dose delivered** (completeness), **dose received** (exposure and satisfaction), **recruitment**, **reach** (participation rate), and **context**.[84] Key measures of interest for each component of the intervention are described above under Aim 2 "Intervention components."

intervention relevant data: (1) frequency of BP and lipid algorithm use; (2) number of telephone contacts and total duration of time required to bring an elevated BP or lipid level under control; (3) Frequency of statin intolerance and proportion of intolerance cases ending in complete cessation of any statin; (4) Number of referrals to BP or lipid specialists.
Home BP monitoring relevant data: (1) Frequency of home BP checks (average checks/week); (2) Number and nature of medication changes in response to home BP data.
Support tools relevant data: (1) number of times each tool is accessed; (2) proportion of subjects with missing data for NLA lipid targets tool.

Exploratory Aim: If effective, [we will conduct a budget impact analysis] and simulate 10-year cost-effectiveness of the intervention. Data will be analyzed by the Economic team (Drs. Kaufman and Smith) in collaboration with PI.

Health economic analyses. If the intervention is effective, we will conduct a budget impact analysis of the intervention costs at 12 months and simulate cost-effectiveness at 10 years. We plan to simulate 10-year rather than lifetime outcomes due to the lack of validated data for CVD outcomes past 10-years in an HIV cohort. We will apply a VA perspective in cost evaluation. To assess the cost-effectiveness of

the intervention, we will examine the difference in average health care and intervention costs between treatment and control arms (incremental cost), and difference in average effectiveness between treatment and control arms to calculate an incremental cost-effectiveness ratio (ICER) that summarizes the relative costs and benefits of the interventionist-led intervention.

Budget impact analysis: Fixed and marginal costs over the 12-month study period will be described using VA and study data. One-way sensitivity analyses will be used to demonstrate the impact of uncertainty in resource utilization. The unit cost will be multiplied by the estimated number of people potentially eligible for the intervention to project the budget required to scale the intervention.

Cost effectiveness analysis: Ten year ICERs are defined as the incremental cost divided by the difference in Quality-Adjusted Life Years (QALYs) to enable comparisons to other interventions under consideration for broader translation. To simulate 10-year outcomes, we will leverage the existing evidence on costs and utilities associated with hypertension control as well as competing risks and utilities specific to HIV populations with ART in high-income countries.[85-87] The ACC/AHA pooled cohort equations for ASCVD risk will be applied to estimate 10 year ASCVD incident event rates. In the intervention scenario, we will apply relative risk ratios for ASCVD events associated with blood pressure-lowering therapies using the ACC/AHA systematic reviews informing the Million Hearts tool.[88] We will use TreeAge to build a cohort-based simulation model, and apply parameter values that have been validated in prior cost-effectiveness studies. Costs for CVD preventative therapies will be extended out to the end of the period, applying published adherence/maintenance rates. Discount and inflation rates of 3% will be applied to out-year costs. One-way sensitivity analyses may be used to evaluate the impact of Reach and Maintenance on 10 year cost effectiveness. We will assess variability in the estimate using a probabilistic Monte Carlo sensitivity analysis with 1000 iterations and generate an acceptability curve presenting the percentage of simulation iterations for which the intervention achieves cost-effectiveness thresholds over a range of willingness-to-pay values.

5.7 Withdrawal of Subjects

Participant withdrawal. Because this is a minimal risk study, it is unlikely subjects will be withdrawn due to safety concerns. Participants are free to withdraw from the study at any time for any reason. However, the study team will meet weekly to determine cumulative enrollment and drop-out rates, as well as charts of these rates over time so that we can detect any changes. Any individuals who decline to participate or drop out of the study will be asked to describe a specific reason for this choice. These reasons will be tracked in the study database. We will regularly review the numbers of patients who cite different reasons for refusal / drop-out, and if there are any factors that can be modified in our study approach, we will take action as appropriate. The project coordinator will also present, at each meeting, enrollment and drop-out rates according to gender, race, and clinic. If any differences are observed, we will examine refusal / drop-out reasons endorsed by these different groups to detect whether there are any systematic study-related processes that may be influencing these differences.

Investigator withdrawal: Participants should normally be withdrawn from the trial if a serious adverse event (SAE) occurs. The below are the reasons an investigator may withdraw a participant from the study.

1. The investigator considers it in the best interest of the veteran that they or she is withdrawn
2. A Veteran displays abusive behavior towards staff
3. A patient is female and becomes pregnant during the study
4. The study is suspended or cancelled

The reason and date of withdrawal will be documented by research staff in the study tracking database. For patients in the intervention arm who no longer want to participate in the intervention, they will still be eligible to complete the outcome assessments (at months 4, 8, 12) and receive payment for completion of those visits.

5.0 Reporting

***Unexpected and serious adverse event reporting*:**

Because this is a minimal risk study involving only a telehealth based intervention, we do not anticipate serious adverse events due to the study. However, safety information will be monitored at each interaction with the patient by the Interventionist via telephone sessions and the Research Assistant at outcome visits. Specific information regarding safety collected during telephone calls and visits with the research assistants will be summarized for reporting. Due to the age range and health conditions (HIV, hypertension, hyperlipidemia, cardiovascular disease, physical inactivity, smoking) of the patients identified for participation in the study, hospitalizations and other health events, including diagnosis of new medical conditions, surgeries, ER visits, MI, Stroke, falls and death, unrelated to the study are expected. Any events that fall into one of these categories will be reported at continuing review. Additionally, we expect that some patients may be uncomfortable answering survey questions or have pain and bruising as a result of blood draw for labs, which is similar to usual medical care. It is also expected that participants will miss monthly phone calls during the required time window and we will not consider either of these events protocol deviations. A study physician will be on call at all times at their site. There will not be a data monitoring committee for the study. The PI, site PIs, study Statistician, and project coordinator will serve this role. All adverse events will be reviewed by the PI and Site PIs, the study statistician, and the project coordinator. All sites will be responsible for reporting SAEs to the PI in Durham as soon as the reporting individual becomes aware of the occurrence. Durham will be responsible for conveying information from each site to the VA Central IRB. The VA Central IRB Table of Reporting Requirements will be used to guide all of our reporting decisions, with time windows given for each type of report.

6.0 Privacy and Confidentiality

Protected Health Information (PHI) will be used and disclosed among members of the study team. It will not be disclosed outside of VHA. PHI will be obtained from existing sources including medical records and clinical databases for recruitment purposes and looking at VA expenditures and utilization. PHI will be obtained directly from participants as they are screened over the phone, attend the consent visit and complete interviewers and outcome assessment. PHI will also be obtained directly from veterans through their participation with interventionist and qualitative interviews.

Of primary importance in all study activities will be the security and protection of veterans' protected health information (PHI). We will take several measures to secure the data. We will only collect the data necessary for the study. All electronic data will be stored on a secure VA server, rather than on individual desktop or laptop computers.

To further minimize any risks regarding privacy of individuals, we will take specific measures to protect both paper and electronic data. Except when required by law, participants will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records. Subjects will be assigned a random study ID and the linkage file will be stored separately from their study data. All electronic data will be stored on secure VA servers in folders and databases accessible only to study personnel whose job functions require access to this information. We will minimize the use of paper data collection by entering information from telephone screening interviews, baseline and follow-up assessments, and intervention tracking directly into a computer database. Any paper-based documents (i.e., consent form) will be stored in a locked filing cabinet in a locked office. Any paper documents that must be transported to / from clinic enrollment sites will be carried in a locked briefcase.

Training and authorization of access: Only individuals officially assigned to the study team will have access to individually identifiable information about human subjects. All study team members will have completed VA's required human subjects training, training in research ethics and confidentiality, data privacy and security. Study team members will be included on a staff listing and removed should they end

participation on the study. Prior to beginning the either the qualitative interview, a verbal consent script will be reviewed with the participant and verbal willingness to continue participation will be captured at the beginning of the audio recording. Study data will only be accessible to key personnel whose job functions require access to these data. In the event of improper use or disclosure, the VA Central IRB will be notified within one hour of becoming aware of the incident, and well as reporting the incident to the local VAHCSA Durham, Cleveland and Baltimore research oversight authorities as per local protocol in compliance with IRB, privacy and compliance officers, as well as the medical center director.

Physical controls: Software will be provided by the Durham VA Center of Health Services Research and the VINCI workspace. Recording and transcription of the qualitative interviews will be conducted utilizing VA approved software installed and configured by VA OI&T personnel. Audio recordings will be captured using WebEx or MS Teams as the software to record the audio portion of the patient interviews. WebEx/Teams recordings will be saved directly to the restricted study folder on the R drive. We will use the approved version of Audacity software (http://trm.oit.va.gov/ToolPage.aspx?tid =5566#) to edit the audio file in the study folder on the HSRD VA project server prior to it being transcribed by the SLC team. Additional, software includes packages for data management (Microsoft SQL 2012), statistical analysis (SAS), Qualitative (NVivo, Atlas.ti), Tree Age, word processing (MS Word) and other specialized software (CATI). The primary database engine technology will be Microsoft SQL 2012, a relational database management system. All of the computerized data entry systems are backed by a series of related SQL data tables that will reside on certified and accredited VA Servers that are located in the Durham VA Medical Center IRM Server Room and the VINCI data center. All data transactions within and between systems will run through controlled, secure transactions to ensure the preservation of database integrity and privacy.

The server power protection system is configured to page Office of Information and Technology (OIT) and center personnel upon detecting problems and sends a test notice weekly. Data are backed up to tape and backups are run daily. Center operating systems, database servers and internet information servers are patched monthly or more frequently for critical updates. Individual workstations, desktop PCs or laptops, are patched using the VA standard and laptops are encrypted using the VA standard tool Encryption. Workstations are equipped with anti-virus and firewall software. PHI is handled according to appropriate Health Insurance Portability and Accountability Act of 1996 (HIPAA) privacy and security regulations. Research staff who work with PHI are required to complete all appropriate HIPAA and information security training.

The information technology solution that will serve to facilitate research activity will be based on a series of asynchronously connected database applications over which a comprehensive data model is deployed. Each database application will function independently as a discrete system. All data transactions within and between subsystems will run through controlled, secure transactions to ensure the preservation of database integrity and privacy. Study data will be maintained on secure servers for the duration of the study and for a period of time after the completion of the study that will be compliant with all VA regulations in place at the time of study closure. Access to the data is only granted to IRB-approved study personnel via approved software applications used for study participant tracking, data collection, and reporting.

We do not plan to apply for a Certificate of Confidentiality. We recognize the diagnosis of HIV is a sensitive subject. The study focus is on addressing the cardiovascular needs of the patients and having a certificate of confidentiality would potentially limit our ability to provide care coordination between the research interventionist and the primary care or infection disease doctors. We also want to provide clear transparency regarding recommendations our study team is making to patients for the cardiovascular care vs other care they may be receiving. We do not believe that we are putting the veterans at more risk by not applying for a certificate on confidentiality.

Once data has been analyzed, final deidentified data sets will be created for the study. Patients who participated in the project will be sent a summary letter to thank them for their participation as well as provide them with de-identified summary information regarding study participants. We will take the following steps to ensure that the information shared maintains the protection of patient privacy.

Publications from this research will be made available to the public through the National Library of Medicine PubMed Central website within one year after the date of publication and study results will be available on

Clinical Trials.gov within 1 year of the final follow-up with last study participant. A local privacy officer and study statistician will certify that the dataset contains no PHI prior to distribution. Data will be provided to requester in electronic form. Final data sets will be maintained locally until enterprise-level resources become available for long-term storage and access. Guidance on request and distribution processes will be provided by ORD.

No date or specimens will be banked in the study.

1. Lists of Data Reviewed and/or Collected for Screening/Recruitment and Conduction of Study:

The Personal Health Information that will be obtained, used, and/or shared for this study includes:

Identifier(s)	Source(s) of Health Information
☒ Names	☒ Medical history & physical exam information
☒ All geographic subdivisions smaller than a State, including street address, city, county, precinct, and zip code. Describe: Address, City, State, Zip	☒ Photographs, videotapes, audiotapes, or digital or other images
☒ All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, visit or treatment dates, etc.; and all ages over 89, Describe: birth date, admission date, discharge date, visit or treatment dates, lab date, Dx date	☒ Biologic specimens (e.g., blood, tissue, urine, saliva). Describe: blood samples to measure lipid profile
☒ Telephone numbers	☒ Progress notes
☐ Fax numbers	☒ Diagnostic / Laboratory test results
☒ Electronic mail addresses (needed for VA Video Connect & ANNIE SMS, support group technology used in intervention)	☐ Operative reports
☒ Social Security Numbers	☐ Imaging (x-ray, CT, MRI, etc.)
☐ Medical record numbers	☒ Discharge summaries
☐ Health plan beneficiary numbers	☒ Survey / Questionnaire responses
☐ Account numbers	☒ Billing records
☐ Certificate and/or license numbers	☒ HIV testing or infection records
☐ Vehicle identifiers and serial numbers, including license plate numbers	☐ Sickle cell anemia information
☐ Device identifiers and serial numbers	☐ Alcoholism or alcohol use information
☐ Web Universal Resource Locators (URLs)	☐ Drug abuse information
☐ Internet Protocol (IP) address numbers	☐ Mental health (not psychotherapy) notes
☒ Biometric identifiers, including finger & voice prints	☐ Psychological test results
☒ Full-face photographic images and any comparable images	☐ Genetic testing
☒ Any other unique identifying number, characteristic, or code, describe : Anonymous/Randomly assigned study ID# **Note: This is not the unique code assigned to otherwise de-identified health information for re-identification purposes.*	☐ Other, describe:

All non-Veterans enrolled in this study will receive the VA Notice of Privacy Practices (NOPP) and are requested to sign the acknowledgment form. The signed acknowledgment form will be maintained with the research records.

2. Data and/or Specimen Acquisition:

Data for this study will be collected through (*check all that apply*):

☒ Prospective data and/or specimen collection obtained from participants. Provide description of processes: We will survey participants during their participation in the study (in-person visits every 4 months). We will also place lab orders for each in-person visit (every 4 months) to collect lipid profile. The study requires use of some individually identifiable data, including participant names, street address, city, county, zip code, telephone number, email to enroll in ANNIE SMS and VA Video Connect and Social Security number to complete telephone screening, send recruitment letters. We will collect the minimum amount of study data required to complete study aims involving recruitment, outcome assessment and reimbursement. Screening and outcome data will be collected in the currently approved version of REDCap.

☒ Retrospective data collection and/or specimens obtained from medical chart review/data access. Describe how data will be obtained (e.g., fileman, CDW, etc.): We will use the current VA CDW/VINCI resources to identify the necessary participants with the requested inclusion/exclusion criteria. Using the real SSNs from that subset, we will retrieve current mailing addresses, telephone number, as well as the specific medical record data (using approved VA data bases) via the VHA Corporate Data Warehouse (CDW) dataset via the VINCI or another secure platform. We will perform medical chart review to assess study eligibility using CPRS or JLV.

☐ Retrospective data collection and/or specimens obtained from an IRB-approved data and/or specimen repository. Indicate the repository source including name, VA location, and IRB number: .

3. Level of Data:

The following level(s) of data will be acquired/maintained for this study (*check all that apply*):

☒ Identifiable—Data contains direct identifiers.
☒ Coded—Data linked to a specific by a code rather than a direct identifier for re-identification purposes. Only someone possessing the key to the code can link the data to a particular participant.
☐ De-Identified (all 18 HIPAA identifiers removed
- ☐ Verified Statistically

OR

- ☐ Verified by Absence or Removal of 18 HIPAA identifiers

☐ Limited Data Set
☐ Other: Describe:

4. Location of Data and/or Specimens, and Data Retention Plan:

A. Data and/or Specimen Location: Data will be stored electronically in V06.med.va.gov\Dur\HSRD\V-EXTRA_CVD_CIRB20-26 or on the VINCI servers workspace for the project. Data that will be stored electronically include patient demographics, survey data, and audio/video data from recorded qualitative interviews or virtual support group sessions. The tracking database will be located behind the VA firewall on the R drive at the Durham VA. All surveys will be done using the currently approved version of the VA REDCap survey tool, which is hosted on the VINCI servers. No study data will be stored on the hard drive of a PC.

Paper records of data include signed informed consent forms, or surveys taken during outcome assessment visits and will be stored in locked file cabinets at each of the three sites.

☒ Data will be also be placed at the VA Informatics and Computing Interface (VINCI; http://vaww.vinci.med.va.gov/vincicentral/VINCIWorkspace.aspx). The VA Informatics and Computing Infrastructure is a partnership between the VA Office of Information Technology and the Veterans' Health Administration Office of Research and Development. Researchers and operations staff can use VINCI to

access data and statistical analysis tools in a virtual working environment through a certified VHA network computer using the VA Intranet or Virtual Private Network (VPN).

B. Data Retention Plan

☒ Research records will be maintained and destroyed according to the National Archives and Records Administration, Records Schedule Number: DAA-0015-2015-0004. Records destruction, when authorized, will be accomplished using the then current requirements for the secure disposal of paper and electronic records. Currently, destruction of research records (see DAA-0015-2015-0004, section 7.6 “Research Investigator Files” for materials included in research records) is scheduled for 6 years after the cut-off (the cut-off is the completion of the research project) and may be retained longer if required by other federal agencies. Records will not be destroyed without pre-notification to the facility records manager. .

☐ Other data retention plan, describe:

5. **Data Access and Data Recipients:** Only members of our research team will have access to data. The project coordinator, research assistants, interventionist, and statisticians will have access to identifiers and coded data. This coded data can be shared with the co-investigators for analysis.

All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up-to-date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one’s password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins).

Access to study data will be removed for all study personnel when they are no longer part of the research team.

6. **Data and/or Specimen Transportation and/or Transmission for all data and/or specimens involved in the study:**

☒ Data and/or specimens will not be transported or transmitted outside of each VA site

☐ Data and/or specimens will be transmitted to other VA sites using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted disk (encryption is optional).

☐ Data are coded or contain identifiers and thus will be sent <choose method of transfer such as: PKI or RMS encrypted e-mail, FIPS 140-2 encrypted disk (with VA-authorized carrier and tracking), or FIPS 140-2 encrypted external drive (with VA-authorized carrier and tracking). You may identify a primary and secondary method>.

☐ Other, describe:

B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional).

☐ Specimens are coded or contain identifiers and thus will be sent via VA-authorized carrier with tracking.

☐ Other, describe:

I. ☐ Data and/or specimens will be transported to non-VA/VHA sites (e.g., academic affiliates, laboratories, etc.) using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted CD.

☐ Data are coded or contain identifiers and thus will be sent via <choose method of transfer such as FIPS 140-2 encrypted CD or FIPS 140-2 encrypted hard drive/flash drive> using VA—approved carrier with tracking.

☐ Data are coded or identified and will be sent via the Safe Access File Exchange (SAFE) at https://safe.amrdec.army.mil/safe/. SAFE is a secure method of exchanging files <2GB to and from individuals with a valid .gov, .mil, .com, or .edu email address. <insert information including collaborator name.>

☐ Data are coded or identified and will be uploaded to sponsor website using electronic case report form (eCRF) <insert information including sponsor name and URL and the encryption the site uses.>

☐ Other, describe:

B. Specimens

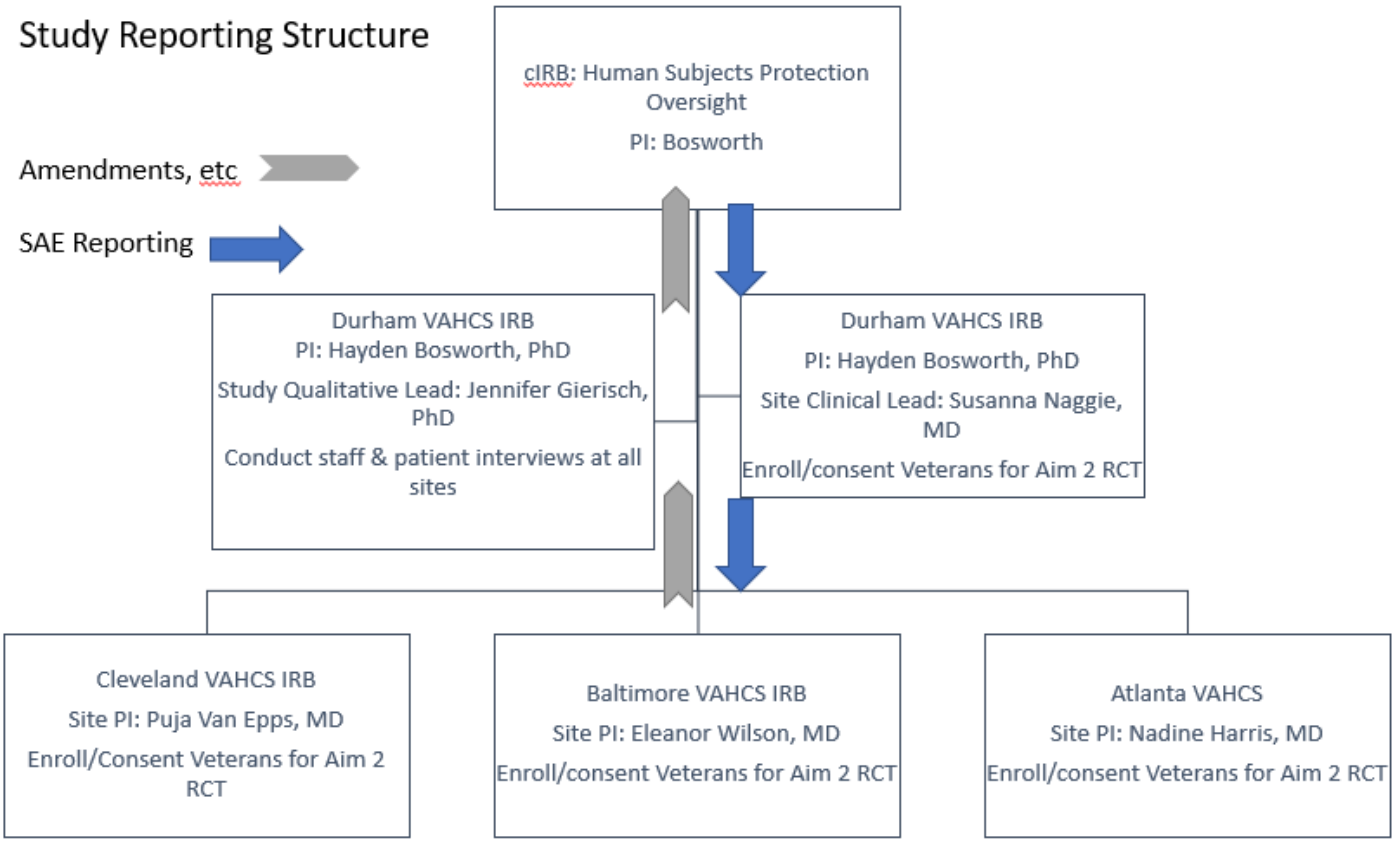
☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional) or will be hand-delivered by research study personnel. Specify method of delivery:

☐ Specimens are coded and thus will be sent via VA-approved carrier with tracking or will be hand-delivered by research study personnel. Specify method of delivery:

In accordance with the HIPAA and the Privacy Act, for any coded or identifiable data or specimens released from the Durham VAMC (with the exception of Limited Data Sets), an Accounting of Disclosure (AOD) will be maintained (e.g., in a database or spreadsheet) that includes the participant's name, date of the disclosure, description of the nature of the Individually Identifiable Information (III) disclosed, purpose of each disclosure, and the name and address of the person/agency to whom the disclosure was made.

☒ We will communicate with veterans enrolled as participants in this research study through MyHealtheVet.

7.0 Communication Plan



There are four VA sites where research will occur. All sites are considered engaged in this study: (1) Qualitative data collection and analyses will occur at Durham VAHCS. (2) Durham VAHCS staff will recruit, enroll, and consent patients for intervention and house the research data. Statistical analyses will also occur at Durham. (2) The Cleveland staff, overseen by Site-PI, will also recruit, enroll and consent patients and house research data. The Baltimore staff, overseen by Site-PI, will also recruit, enroll and consent patients and house research data. The Atlanta staff, overseen by site-PI, will also recruit, enroll and consent patients and house research data. The VA Central IRB is the IRB of record for this study.

The Site-PIs will ensure there is a Local Site Investigator (LSI) at each site from which patients are enrolled. For this study, these sites include the Durham Healthcare System (with LSI and PI Hayden Bosworth, PHD) and Cleveland VAHCS. Baltimore VAHCS. After initial review, any revisions to the protocol, informed consent or HIPAA authorization will be submitted on Form 116 to the cIRB by the Durham VAHCS. Once approved, the Durham PI will be responsible for forwarding the current documents to each of the other sites for immediate use.

The site-PIs will communicate this information to other study staff via conference call, if needed. In addition, study PIs and LSI will be regularly updated through the weekly team meetings.

Regular study meetings will occur with key members of the research team. Any issues that arise – related to IRB changes, adverse event reporting, data collection, or recruitment/enrollment concerns, can be shared among all sites and dealt with in a timely manner. The project coordinator at the Durham site will be responsible for ensuring communication between all sites

Data and Safety Monitoring

Because this is a minimal risk study involving only a telehealth-based intervention, we do not anticipate serious adverse events due to the study. However, safety information will be monitored at each interaction with the patient by the Interventionist via telephone sessions and the Research Assistants at outcome visits. All sites will be responsible for reporting SAEs to the PI in Durham as soon as the reporting individual becomes aware of the occurrence.

SAEs identified in Durham will be reported to the Durham PI who is responsible for complying with all cIRB reporting requirements. SAEs identified in Baltimore and Cleveland and Atlanta will be reported to their respective site-PI who will report all SAEs to the Durham PI who will report to cIRB, as required.

All adverse events will be reviewed by the Study PI, all four site-PIs (all of which are practicing MDs), the study statistician, and the project coordinator.

Safety Reasons that trigger immediate suspension of research

Participants should normally be withdrawn from the trial if a serious adverse event (SAE) occurs. Participants must be withdrawn from the trial if:

a. They withdraw their consent

b. Veteran subsequently meets one of the exclusion criteria for the study.

c. The investigator considers it in the best interest of the veteran that he or she is withdrawn.

d. Veteran displays abusive behavior towards staff

e. Veteran is a female and become pregnant during the study

f. The study is suspended or cancelled

The reason and date of withdrawal will be documented by research staff in the study tracking database. For patients in the intervention arm who no longer want to participate in the intervention, they will still be eligible to complete the outcome assessments (at months 4, 8, 12) and receive payment for completion of those visits.

The Durham PI will be responsible for reporting to the VA Central IRB within 5 business days any SAEs that meet the criteria, as well as any follow-up reports requested. Summary information that did not require immediate reporting will be submitted at continuing review.

The PI/SC will ensure adequate monitoring in the following ways: all study staff will have completed their required research training prior to beginning any research activity, ensuring that each member of the research team has a research scope of practice (SOP), updated annually, that clearly defines the duties in which the person is trained, qualified and allowed to perform for research purposes, and will maintain a staff listing of all personnel involved in the conduct of the study which will include their CITI and GCP training completion dates.

All non-compliance with the study protocol will be reported. Protocol deviations or protocol violations will be reported to the cIRB by the Durham PI within 5 business days after being made aware of the occurrence using Form 119 if initiated in response to an SAE or UAP, or Form 129 if the event was likely to have an adverse effect on the subjects rights, safety or welfare, their willingness to continue participation, or the integrity of the research data.

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