Mixed methods formative research and pilot testing of a task-shifted adaptation of the WHO-PEN intervention to address cardio-metabolic complications in people living with HIV in Zambia

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Ethical reviews by other institutions

The protocol has been submitted for review to the Institutional Review Boards (IRBs) of the University of Zambia and University of North Carolina—Chapel Hill.

Acronyms

ART	Antiretroviral Therapy
CIDRZ	Centre for Infectious Disease Research in Zambia
DM	Diabetes mellitus
EMR	Electronic Medical Record
FGD	Focus group discussions
GRZ	Government of the Republic of Zambia
HCW	Health Care Workers
HTN	Hypertension
HTS	HIV testing services
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
IDI	In-depth interviews
KII	Key informant interview
MOH	Ministry of Health
NCD	Non-communicable disease
NPHW	Non-physician health workers
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
QA/QC	Quality Assurance/Quality Control
UNZA	University of Zambia

Key Concepts

Implementation Science	The scientific study of the use of strategies to adopt and integrate evidence-based health interventions into clinical and community settings in order to improve patient and population outcomes.
Non Communicable Diseases (NCD	Diseases that are not transmissible directly from one person to another. They tend to be of long duration and are the result of a combination of genetic, physiological, environmental and behavioural factors.
Cardio-metabolic complications of H	Health problems that arise from a combination of metabolic dysfunctions mainly characterized by insulin resistance, impaired glucose tolerance, dyslipidemia, hypertension, and central adiposity. These tend to be more common in people living with HIV.
Non-Physician Health Workers	Health care workers who are licensed to provide health services that complement or supplement those provided by a physician.
WHO Package of Essential Communicable Disease Interve (WHO PEN)	An innovative and action-oriented set of cost-effective interventions for the control of NCDs in primary health care, that can be delivered to an acceptable quality of care, even in resource-poor settings. Also known as "WHO PEN" for short.
TASKPEN	TASKPEN is the name of the package of implementation stra proposed by the investigators that are intended to deliver the PEN intervention in routine HIV clinical practice settings in Z TASKPEN has five components, which are described in deta Table 2 (below), and which will be the subject of stake consultation and adaptation in this formative research protocol.
Implementation Strategy	Highly specified, systematic processes used to implement evi based treatments or interventions, often at the clinic level, into care settings.

1. Introduction

a. General information on the research topic

Non-communicable diseases pose an urgent global health threat Globally, non-communicable diseases (NCDs) pose a significant public health and economic threat due to the associated disability, loss of productivity, and premature deaths from conditions like cardiovascular diseases (CVD) and diabetes [1]. Among the NCDs, cardiovascular conditions are the leading cause of mortality globally. By 2017, 17 million of the 56 million NCD-related deaths were attributed to CVDs [2].

b. Overview of the research and research gaps

Increased burden of NCDs, particularly cardiometabolic complications, among PLWH in SSA. With the increasing availability and widespread use of antiretroviral medications in SSA, efforts to stem the HIV pandemic have transitioned from major focus on preventing early mortality and managing opportunistic infections (OI's) to now also facilitating long-term quality of life, which requires addressing chronic complications. Complex interactions between HIV, antiretroviral drugs, nutritional and other lifestyle factors, insulin resistance, systemic inflammation, dyslipidaemias, and other chronic disease risk factors contribute to the development of chronic complications involving a number of organ systems (Fig 1).

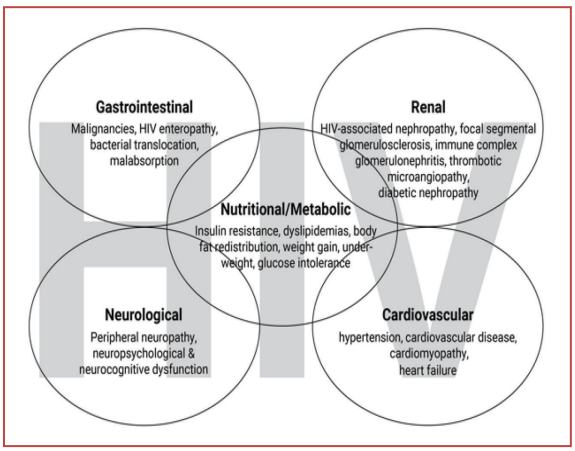


Fig 1: HIV related NCDs and cardiometabo

Zambia, like many sub-Saharan African countries, is experiencing a transition of economic conditions and lifestyle, with an expanding middle class, more sedentary lifestyle, and increasingly Western-style diets and tobacco use [3]. Whereas undernutrition formerly predominated, Zambia's nutrition-related challenges now range from malnutrition and undernutrition to obesity, hyperlipidaemias, hypertension, diabetes, cancers, and other chronic conditions [4,5]. Unhealthy alcohol use is on the rise in Zambia and other countries and is a risk factor for multiple NCDs. Recent research has linked inflammation and other factors to dyslipidaemia, with low high-density lipoprotein cholesterol and increased oxidized LDL-C associated with increased innate immune activation [6]. Insulin resistance and diabetes mellitus are other cardiometabolic complications increasing in HIV patients in Sub-Saharan Africa, with prevalence estimates approaching 26% and 47% for diabetes mellitus and prediabetes mellitus, respectively [7]. In Zambia, the prevalence of insulin resistance was estimated to be at 30% and often associated with virologic failure among PLWH enrolled in the national HIV treatment programme [8]. Diabetes mellitus has been linked to CVD in HIV such that PLWH with diabetes mellitus have a 2.4-fold increased risk of coronary heart disease events [9]. ART regimens complicate CVD risk, with newer drugs in the Zambian treatment arsenal, such as dolutegravir, associated with weight gain and others, such as protease inhibitors, with dyslipidaemia [8]. Changes in body composition associated with some antiretroviral agents, including excess visceral adipose tissue, have been linked to increased mortality [10,11].

Feasibility of HIV/NCD Integration due to common chronic care elements

HIV/NCD integration requires a focus on evidence and assessment of available resources. This is particularly true in the context of overburdened health systems [12]. Integrated care systems are more convenient for patients, decrease stigma associated with healthcare, and could be more efficient for government and non-governmental funders. Several integration approaches within HIV platforms have

been piloted for NCD screening [13,14] and HIV Care and treatment [15,16]. However, most studies have mainly focused on cancer and mental health [17].

Task shifting is common and effective in HIV care in SSA, but has not yet been widely extended to other chronic conditions [18,19]. In the emergency response to the HIV epidemic, the lack of doctors and limited number of nurses was circumvented using task shifting within HIV clinics. Because the professional workforce remains limited, task shifting hypertension care to nurses or community health workers (CHWs) has the potential to synergize resources and knowledge to support NCD care 18,20. Just as non-physicians now have strong capacity to provide HIV care in a public health approach, hypertension care can be provided by non-physician health workers (NPHWs), who provide knowledge of the benefits of a healthy lifestyle to patients almost as often as physicians 18,21.

WHO-PEN package for NCDs has potential to be used in HIV/NCD integration in SSA
The World Health Organization (WHO) has developed a *Package of Essential Noncommunicable Disease Intervention for Primary Care (WHO-PEN)* for LMICs which includes: clinical decision support for management of CVD via easy-to-follow algorithms; lifestyle counselling curriculum; and streamlined drug treatment protocols delivered by community health nurses [22]. Its efficacy at improving blood pressure control is well proven in LMICs [23,24]. Despite its established evidence base, implementation of WHO-PEN is rare in SSA, and its potential to be integrated with HIV services has not been explored. This provides an opportunity for using task-shifting and other implementation strategies to adapt and introduce WHO-PEN into the existing HIV program in Zambia. If shown to be feasible and effective, such an approach may serve as a model for other LMICs in which an adapted version of WHO-PEN can be used to train nurses and CHWs to manage hypertension and other CVDs within the HIV service delivery platform [25].

Implementation science theory and strategy can support successful introduction of evidence-based practices for HIV/NCD integration into routine HIV care settings.
It is well recognized that most efficacious interventions are not effective when introduced in real-world settings, particularly in overburdened health systems or new contexts, without appropriate adaptation [12]. Implementation science theories and strategies can help close the so-called 'know-do gap' and improve implementation of efficacious interventions, technologies, and approaches to achieve health impact at scale [12]. The Interactive Systems Framework (ISF) [26], Consolidated Framework for Implementation Research (CFIR) [27-29] the Normalisation theory (NPT) [30,31] and RE-AIM (Reach, Evaluation, Adoption, Implementation and Maintenance) are all implementation oriented and empirically supported frameworks for adapting, introducing, and evaluating evidence-based interventions in routine practice settings, such as the PEPFAR-supported HIV program in Zambia. We will use these frameworks concurrently in the formative work, WHO-PEN adaptation, and pilot testing proposed here to deliver and evaluate our integrated HIV/NCD intervention (i.e., TASKPEN).

c. Overall purpose of the research and area where the research will be conducted

The overall purpose of the formative research proposed herein is to adapt the *WHO Package of Essential Noncommunicable Disease Interventions* (WHO-PEN) approach for the Zambian public health system, and to pilot test an adapted, streamlined, and task-shifted package of integrated HIV/NCD services collectively called "TASKPEN." Specifically, this protocol is designed to adapt and pilot-test TASKPEN to manage cardiovascular disease risk factors and the cardiometabolic complication of HIV among persons living with HIV in Lusaka, Zambia. Using local data and implementation science theory, TASKPEN will address challenges faced by HIV patients who have cardio-metabolic complications related to HIV or its treatment. TASKPEN will enable productive interactions between activated, informed patients and proactive, prepared health care professionals by

task shifting most of the care to NPHWs who will be supported by the additional training and adapted screening and treatment protocols based on WHO-PEN protocols. If successful, TASKPEN's clinical effectiveness and implementation factors in Zambia would then be evaluated in a larger program.

2. Statement of the Problem

a. Short summary of the background on the problem

Despite a high NCD burden in low- and middle-income countries (LMICs), including Zambia, health systems in these countries are often tailored towards fighting infectious diseases and have limited capacity to address highly morbid cardiometabolic conditions such as hypertension, dyslipidaemia, and diabetes [32-37]. Although current evidence suggests an urgent need to leverage HIV resources at various health system levels to address the growing NCD burden among PLHIV in SSA, there still remains a critical evidence gap to identify a feasible, impactful, and cost-effective model of HIV/NCD integration for wide adoption in Zambia.

b. Importance / relevance of the research

The proposed research is important because formative evidence is lacking on how best to develop a feasible, integrated package of HIV/NCD services for Zambia's national HIV program. The study will also form the basis for a larger follow-on trial that will rigorously test the effects of the TASKPEN intervention on important dual clinical and implementation outcomes for NCDs and HIV, including dual or individual control of HIV and/or NCDs, linkage to and retention in care for those with a dual HIV/NCD diagnosis, and sustainability and cost-effectiveness of the intervention.

3. Rationale/ Justification

a. Contribution of the study to science or body of knowledge

We hope that this study will contribute new evidence on how best to integrate NCDs and HIV services in African settings with high HIV/NCD burden and limited financial and human resources, and on how NPHWs can contribute to service delivery in these settings. While the formative research proposed here focuses on adapting and defining an integrated care package for cardio-metabolic co-morbidities in PLHIV, the strategies studied will be relevant to other NCDs, like mental health, and can advance the field by rigorously documenting implementation outcomes for our strategies of interest. The study will also fill critical knowledge gaps on the following: 1) the effects of pilot testing HIV/NCD integration on HIV clinical outcomes such as viral suppression and risk of cardio-metabolic complications such as myocardial infarction; 2) the health system consequences of integration; and 3) optimal ways to apply implementation science theories to develop HIV/NCD service integration models in SSA [12].

b. Changes to be made by the study

The overarching objective of this mixed methods formative research study is to define a package of integrated HIV/NCD services and the associated implementation strategy for pilot testing, collectively referred to as the TASKPEN intervention. We plan to use pilot testing to adapt, improve, and refine TASKPEN, as well as the related training curricula and algorithms for nurses, pharmacists, community liaison officers, community health workers, treatment supporters, and other non-physician cadres. Thus, this formative research is intended to lead to a finalized TASKPEN intervention to be tested in a follow-on pragmatic stepped-wedge hybrid effectiveness-implementation trial. That trial will be designed to generate new programmatic insights that enable delivery of high-quality integrated HIV/NCD care, which may promote improved long-term outcomes of cardiovascular morbidity

reduction, HIV care retention, and viral suppression for PLHIV. Thus, findings from this study will be used to make impactful recommendations to improve integrated non-communicable disease care undertaken by GRZ and partners in Zambia.

c. Evidence supporting the justification

Table 1. Summary of literature on WHO-PEN package gaps and strategies to address them:

Evidence Intervention	Barrier	Strategy	References
WHO-PEN pa	1. Lack integrated guidelines to manage HIV and NCDs [38]	Promote adaptation Adoption of the integrated model in Zamb	International Association of Pr of AIDS Care (IAPAC) [39] Powell, Waltz [40]
	2. Lack of adequate technical skills in NCD management [5,41]	Adopt and tailor the skills and training mater Zambia	Powell, Waltz [40]
	3. Low number of doctors [41]	Revise professional ro Task shifting NCD mana to NPHW	Powell, Waltz [40]
	4. Lack of decision support [41,42]	Develop an integrated d support tool/ automatic using SMARTCARE platform to remind and clinicians	Powell, Waltz [40]
	5. Silos: HIV and NCDs [43]	Integrate HIV and NCD ca	International Association of Pr of AIDS Care (IAPAC) [39]
	6. Lack of data collection tools [5]	Develop and adapt tools f quality mon SMARTCARE E-First/ platform [44]	Powell, Waltz [40] Munthali, Musonda [45] Ministry of Health Zambia [46]
	7. Lack of basic diagnostic and vital sign equipment [47]	Provide basic NCDs diag laboratory, and vital equipment	WHO [48]

4. Theoretical / Conceptual Framework

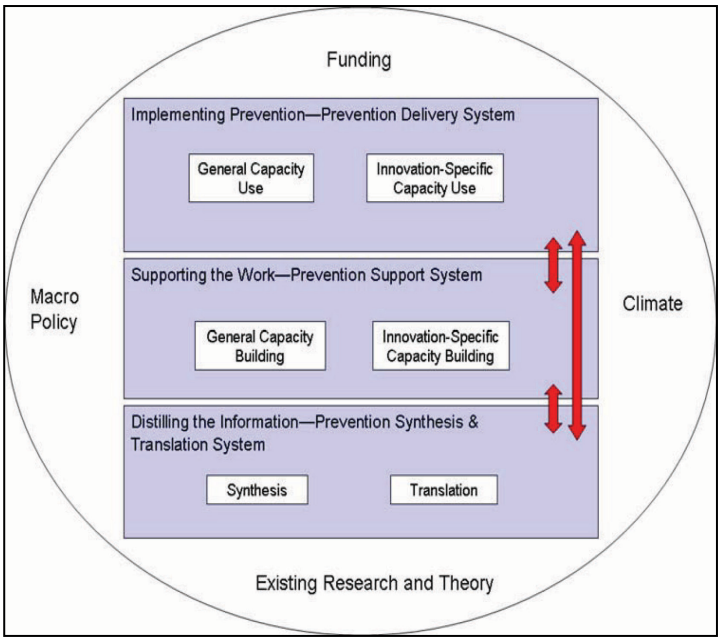


Figure 2: The interactive systems framework for disseminat

The Integrated Systems Framework (ISF, figure 2) is a theory intended to help researchers move research into practice. The ISF proposes and organizes several implementation strategies to achieve evidence-based intervention adaptation, including dissemination, implementation processes, integration, capacity building and scale up. Figure 2 shows how this can happen. The three large boxes all represent a collection of activities, broadly defined, termed "systems". The "Distilling the Information" box reflects the importance of distilling information about innovations down to their essential components and preparing them for use by end users such as health workers or program managers. It is the foundation upon which the other two boxes or "systems" are placed. The "Supporting the Work" box notes the importance of supporting the work of those end users who will put an innovation into practice, such as health workers or program managers. This can be accomplished through strategies like supportive supervision, audit and feedback, and coaching. The "Implementing Prevention" box, while focused on prevention for illustrative purposes, is about optimizing the individual, organizational, and community-level capacity of practice settings to carry out activities necessary to deliver the innovation. Importantly, these systems should optimally interact and collaborate to ensure successful dissemination and implementation of an innovation, which is reflected by the three double-headed arrows between the systems. These various systems all operate within a context that affects implementation of innovations and reflects a combination of funding availability (e.g., from government or bilateral donors), the policy environment (e.g. willingness of governments to support an intervention), the implementation climate (e.g., readiness of key stakeholders to emphasize or support an innovation), and existing research and theory (e.g., acceptability of research findings to practitioners and end-users). We will apply this theoretical foundation and the strategies revealed by the ISF at different levels of the healthcare system to ensure local adaptation and introduction of TASKPEN into the routine HIV care practice setting in Lusaka, Zambia.

5. Literature Review

a. Cardio-metabolic complications in people living with HIV

Cardio-metabolic complications in HIV can occur in isolation or in combination. One of the commonly observed combination is called metabolic syndrome. The metabolic syndrome comprises a group of cardiovascular risk factors that include high blood pressure (hypertension), abdominal obesity, dyslipidaemia and insulin resistance [49]. In addition to cardiovascular disease, individuals with metabolic syndrome are susceptible to a wide variety of conditions such as diabetes [50], cancers [51], polycystic

ovary syndrome [10], and asthma [52,53]. Today, the widely used guideline for diagnosis of metabolic syndrome is the harmonized one which was suggested in 2009 by different organizations [54].

In sub-Saharan Africa, the burden of metabolic syndrome has been shown to be highly variable among HIV positive individuals who are ART-experienced and -naïve. A cross-sectional study among individuals aged ≥ 18 years on ART in Ghana found the prevalence of metabolic syndrome to be at 24.5%, 48.3% and 42.3% according to WHO, NCEP-ATP III and IDF criteria, respectively [55]. The study also found that the prevalence of metabolic syndrome in patients on ART was higher than those not on ART. Similar conclusion was drawn in a study which was conducted in South-West region of Cameroon [56]. A lower prevalence (18%) of metabolic syndrome was observed in a study conducted in Burkina Faso [57]. Muyanja, Muzoora [58] revealed that more than half (58%) of study individuals on ART in Southwestern Uganda had metabolic syndrome. A meta-analysis by Nguyen, Peer [59] found a wide range (13% to 58%) of the prevalence of metabolic syndrome in Africa. In Kenya, the prevalence of metabolic syndrome was 19.2% among adults living with HIV, of whom 98.6% of the study population were on ART [60]. Osoti, Temu [61] in the same country, found no significant difference in the prevalence of metabolic syndrome between ART-experienced (16.9%) and ART-naïve (15.2%) groups. In Southern Ethiopia, using IDF criteria, metabolic syndrome was diagnosed in 25% and 22.5% of individuals on ART and in the ART-naïve group, respectively [62]. Further, using ATP criteria, the study found that the prevalence of metabolic syndrome in the ART group was 18.1% and 15.6% in the ART-naïve group. The authors observed that patients on ART had raised triglycerides, cholesterol, LDL-c and glucose levels, making these factors the major contributors to metabolic syndrome [62].

In a narrative review in Africa, Husain et al. found a wide range of prevalence of metabolic disorders in the HIV-positive population: diabetes 2.1% to 26.5%, pre-diabetes 20.2% to 43.5%, metabolic syndrome 13% to 58% and dyslipidaemia 13% to 70% [63]. In Feleke, Fekade [64] cross-sectional study in Ethiopia, the prevalence of hyperlipidaemia was 56.9% in patients on ART for greater ≥ 1 year and among these, 38.2%, 54.2% and 17.8% had hypercholesterolemia, high LDL-c and hyperglycaemia, respectively. A study in a hospital setting in Cameroon showed that the prevalence of hypertension in patients on ART was twice that of ART-naïve patients (38% vs. 19%) [65]. A longitudinal study in Senegal which had a median follow-up of 9 years for patients on ART found that 28% and 14% of them had hypertension and diabetes, respectively [66]. In a study which assessed the burden of cardiometabolic risk factors among untreated HIV-positive Cameroonians, the prevalence of impaired fasting glucose, diabetes and metabolic syndrome was higher in ART-naïve than in healthy individuals (47% vs. 27%, 26% vs. 1%, and 47% vs. 21%, respectively) [67]. However, the prevalence of hypertension was high and comparable in both groups (41% vs. 44%). A longitudinal study in South African young women following them for 3 years after HIV infection showed that metabolic syndrome was 8.7% and 19.2% at HIV diagnosis and over 36 months, respectively [68]. These data suggest that on its own, HIV has an effect on the metabolic syndrome.

There are no published estimates of the prevalence of metabolic syndrome among adults living with HIV in Zambia. However, in a study where metabolic syndrome was evaluated among patients with type 2 diabetes, the burden was 73% using NCEP-ATP III criteria [69], and higher in women as compared to men. A population-based survey found that the prevalence of hypertension, impaired glucose tolerance, and obesity were 34.8% (Goma et al., 2011), 4% [70] and 14.2% [71], 19% [72] respectively. These findings may be different if focused on HIV-positive patients on ART. A cross-sectional survey at the Department of Medicine at University Teaching Hospital in 2017-2018 found that 19% of admissions involved cardiovascular disease; CVD was a leading cause of hospitalization in people with HIV and high CD4 counts during ART.

b. Risk factors for metabolic syndrome in HIV

The occurrence of metabolic syndrome among people living with HIV (PLHIV) has been associated with a number of factors. Published studies showed strong associations of changes in fat or adipocyte function with metabolic syndrome [73,74]. In the US, elevated glycated haemoglobin (HbA1c) and high total sugar consumption have been found to be associated with metabolic syndrome, accounting for 30% of the prevalence [75]. Morimoto, Simão [76] revealed that individuals who had metabolic syndrome and were using ART had significantly higher CD45(+), CD3(+), and CD4(+) T cell counts compared to patients without metabolic syndrome and using ART. In Poland, it was shown that CD4 counts less than 350 were a strong predictor of metabolic syndrome [77]. PLHIV in Barcelona with metabolic syndrome displayed a higher levels of C-reactive protein (CRP) and leptin, and lower adiponectin [78], and metabolic syndrome was associated with a substantial increase in the prevalence of type 2 diabetes. In young South African women, one year after HIV diagnosis, the chance of having metabolic syndrome increased by 47% [68]. In another study, a $\log_{10}$ increase in HIV-VL was independently associated with metabolic syndrome [79]. Individuals who had a smoking history, HIV-1 infection, higher body mass index (BMI) [80,81] and higher trunk-to-limb fat ratio (Jacobson et al., 2006) had higher likelihood of developing metabolic syndrome [82]. Lipodystrophy was also shown to be associated with metabolic syndrome in adult patients on ART [57].

Metabolic syndrome was shown to be higher in women than men in Ethiopia [62], Burkina Faso [57] and Uganda [58]. However, this finding was contrary to that of Rogalska-Płońska, Grzeszczuk [77]. In Poland where more males had metabolic syndrome compared to females. In Brazil, metabolic syndrome among males was associated with physical activity and education status [80]. However, in Kenya, physical activity and education status were found to be factors associated with metabolic syndrome in both males and females [60]. Other studies revealed that older age was a strong predictor of metabolic syndrome [57,58,77,81,82] . Education status has also been mentioned as a factor that affects the incidence of metabolic syndrome. In the US, among HIV-positive adults in the Healthy Living (NFHL) study, it was revealed that the incidence of metabolic syndrome was lower among the college-educated persons [74].

Metabolic syndrome was found to be higher in ART compared with non-ART users in a meta-analysis and varied significantly by age, duration of HIV diagnosis, severity of infection and use of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) [59]. Further, it has been noted that the prolonged use of ART, especially protease inhibitors (Pis) [78; 83] such as lopinavir/ritonavir [57,74,81,83], was associated with metabolic syndrome components i.e., dyslipidaemia, insulin resistance (IR), and changes in body fat compartmentalization (i.e., peripheral lipoatrophy and central fat accumulation), which are all risk factors for CVD [84,85]. In Southern Ethiopia, individuals who were taking stavudine-lamivudine-efavirenz (d4T-3TC-EFV) had increased odds of metabolic syndrome [62]. Antiretroviral therapy has also been associated with the development of severe metabolic complications which includes, lipodystrophy, dyslipidaemia, and insulin resistance [78] In addition, Nguyen et al.' meta-analysis showed that use of ART is strongly associated with metabolic syndrome [59]. Patients on ART have been known to have elevated lipid profile and glucose metabolism disturbances [86] more frequently than ART-naïve patients [62]. Systematic review and meta-analyses have found hypertension to be significantly more prevalent among patients on ART when compared to HIV-positive persons who are ART- naïve [87,88].

c. Service delivery models and implementation strategies from LMICs for integrated HIV/NCD Care

Evidence from both developed and developing countries supports integrating prevention, management and surveillance of NCD into other models of chronic care. HIV care platforms have commonly been used for integrating NCD management [16,89]. This is because decades of funding for HIV programs have

resulted in established structures and human resource capacity. In addition, the advent of ART treatment has transformed HIV into a chronic condition, and the prevalence of NCDs among the HIV positive population has also increased [90]. An integrated approach in chronic care is therefore an attractive option especially in the LMIC contexts where resources are scarce.

Provision of integrated care requires a multidisciplinary response with engagement of various cadres of health workers. Critical to provision of integrated chronic care in resource constrained environments is implementation of a task sharing strategy. Task sharing is premised on the fact that most health facilities in LMICs have inadequate numbers of trained health workers (especially doctors) to meet the demand of the population. Therefore, uncomplicated aspects of prevention, management and surveillance of chronic conditions typically conducted by doctors can be assigned to other non-doctor health workers in order to free up the few available doctors for complicated cases. Integrated care of NCD with task shifting to nurses, pharmacists and community health workers has been shown to be effective across several settings in LMICs. Task shifting approaches for the management of hypertension typically involves non-physician health workers like nurses, community health workers and pharmacists providing lifestyle modifications through education, home based follow-up care, algorithm-based clinical management, non-physician drug prescription, referrals, and organisations of care [91].

Engaging community health workers in cardiovascular disease risk assessment, patient referral to physicians and patient follow ups resulted in decreased systolic blood pressure of 8.8mmHg in the treatment group in a trial in India [92]. Task shifting to nurse care coordinators who generate prescriptions using a clinical decision support system on a mobile phone was found to reduce systolic blood pressure by 14·6 mm Hg [93]. A multidisciplinary team comprising nurse conducting cardiovascular risk management and community health workers making patient follow-ups resulting in a mean reduction of 27·2 mm Hg. Nurses providing cardiovascular risk assessment, lifestyle counselling, and initiation/titration of antihypertensive medications coupled with health insurance resulted in better control of hypertension in Ghana [94]. In Nigeria, pharmacy staff were involved in blood pressure measurements and lifestyle consultation using an mHealth application and in consulting with a cardiologist achieved a mean reduction of 9·9 mm Hg [95].

Integrated chronic care should be context specific and conducted systematically if it to be successful. WHO has provided guidance on integrating NCD management into other models of chronic care. Critical steps in the integration process include stakeholder identification and engagement, review of existing status, developments of a service delivery model, capacity building, monitoring and evaluation and review [48].

6. Research Question

The main study question is the following: “Is it feasible, acceptable, and appropriate to task-shift the delivery of an evidence-based package of integrated cardio-metabolic health services for PLHIV within Zambia’s national HIV program?”

7. Research Aims, General Objectives and Specific Objectives

The general objective of this research is to adapt WHO-PEN for a task-shifted locally-informed intervention for screening and management of cardio-metabolic co-morbidities for Zambian PLHIV, and to pilot-test it in preparation for a larger evaluation of clinical effectiveness and implementation

outcomes. To facilitate rapid formative evaluation and to initiate the stakeholder conversation on a package of integrated HIV/ NCD services for Zambia, we will begin by proposing that the five core components/ strategies from Table 2 (below) be considered for TASKPEN. To achieve this general objective, we will pursue the following specific objectives:

1. **Adapt WHO PEN into a package of integrated HIV/NCD services known as "TASKPEN" and prepare TASKPEN for pilot testing in Lusaka.**
   i. Conduct health facility assessments to: document current HIV infrastructure, laboratory capacity, and human resources to support integrated NCD management by NPHWs; characterize gaps in existing patient and clinic flows for optimized integrated HIV/NCD service delivery; and collect data to support pilot site identification (for objective #2).

   ii. Prepare data collection tools and methods to enable TASKPEN outcome ascertainment during pilot testing and the follow-on trial, including for the WHO quality of life data collection instrument (WHOQOL-HIV BREF) and an NCD module for the SmartCare electronic medical record.

   iii. Engage key stakeholders through formative research to: align WHO PEN algorithms to national NCD guidelines; generate feedback on proposed TASKPEN components, clinic processes and patient flows, and training materials; and obtain consensus on pilot sites (for objective #2).

2. **Pilot test the TASKPEN intervention and related outcome ascertainment at two PEPFAR-supported health facilities in Lusaka, Zambia.**

8. Methodology

Study design overview

Using local data and implementation science theories we will adapt WHO-PEN for Zambia and refine the proposed TASKPEN core intervention components. TASKPEN will focus on addressing challenges faced by PLHIV who have cardio-metabolic complications related to HIV or its treatment (e.g. hypertension, diabetes, dyslipidaemia). TASKPEN aims to improve detection and management of these complications. We expect the total impact of this process to result in reduced cardiovascular disease risk.

We will engage stakeholders at all levels of the Zambian health system, including front-line nurses and community health workers who will lead the intervention. Using data from stakeholders, we will adapt and finalize the TASPKEN intervention, and pilot test it at two high-volume health facilities in Lusaka, Zambia using a "mini" stepped-wedge trial design that will mimic the approach for the future larger trial. As the individual components of TASKPEN are already recommended by Zambia national guidelines, the pilot study will be done as an integral part of routine HIV care. Therefore, the TASKPEN intervention is evidence-based and not investigational.

In Table 2 below, we summarise the core intervention components/ strategies that we will assess, integrate, and adapt under this protocol to constitute the TASKPEN intervention, including the expected outputs from each activity.

Table 2. TASKPEN intervention components/ strategies proposed for adaptation and expected outputs.		
Intervention Component/ Strategy & Description	Actors	Outputs
i. Adaptation of protocols, training materials, and management algorithms to the national context Review the current treatment guidelines in NCDs and other cardiometabolic diseases in Zambia and align these to the TASKPEN training materials and content, including the WHO HEARTS technical package for cardiovascular disease management in primary health care. This process will ensure consistency with MOH guidelines, culture and availability of resources of the health system. We will also ensure training materials feature an emphasis on client-centred care, which is increasingly being identified as key driver of patient retention in HIV care. Hypertension protocol: Adapt WHO PEN/ HEARTS therapy recommend based on national hypertension guidelines availability of medical supplies. Diabetes and other co-morbidities protocol: Adapt to the Zambian diabetes guidelines and practices to manage diabetes. Algorithms made suitable for NPHW to use, with guidelines when to consult or refer patien specialist physicians	Project Technical A Committee (TAC). Ministry of Health directorate of clinical ser Health workers Local experts &Patient groups	Adapted Training manual; Adapted clinical protocols algorithms for hypert diabetes and other cardiome complications to the Z settings.
ii. Strengthened diagnostic capacity for decentralized monitoring of haemoglobin A1c, cholesterol, and albumin:creatinine ratio Integrate POC diagnostics or other streamlined at health facility level to enable decentralized an shifted monitoring of NCDs/ cardiovascular risk fa	Project TAC. MOH directorate of services Health workers Local experts Patient groups	Introduction of point-of-care monitoring or other strea diagnostics at pilot sites Zambia

iii. Adapt local electronic NCD clinical data collection and decision support tool We will adapt the local EMR (SMARTCARE), a fully integrated electronic health record system, but mainly used for HIV care. We will adapt SMARTCARE to include data collection fields and clinical decision support prompts for NPHWs NCDs and other cardiometabolic complications.	Project TAC. MOH directorate of services Health workers Local experts Patient groups	SMARTCARE Module integrates HIV and NCDs an cardiometabolic complications
iv. Adapt and leverage HIV infrastructure and systems to support NCD integration We will evaluate the current configurations and as needed, the physical structure and/or equ (e.g., changing the layout of a room, adding equi to best accommodate the targeted integration and NCDs including patient flow, laboratory c and human resources. This will include creating **stop shop"** for HIV/ NCD co-management in th or OPD clinics. We will also harmonize NCD care to take advantage of existing innovations in the health system for HIV care, including for medication distribution, fast-tracked clinical evaluation, and integrated adherence support and back-to-care services.	Local clinicians, Nurses Laboratory specialists Patients groups	Agreed patient and laborato that integrates HIV and NCDs
v. Task shift and task share responsibilities CHWs based at the facility will conduct blood pr screening, height and weight measuremen random blood glucose monitoring. CHWs will s health education, including delivery of brief mec adherence and smoking cessation counselling. will also support community tracing and back t activities for PLHIV with cardio-metabolic compli who are late or disengagement from care. Nurses will be trained on the aforementioned pr and will be enabled to prescribe medicatic hypertension, diabetes, and dyslipidaemia.	Nurses Community health worke Patients groups	Guidelines for nurse prescribi Agreed CHW work flow

Specific Objective #1:

a. Overview

The activities described below involve a combination of programmatic activities (i.e., "non-human subjects research" or "NHSR" under i. & ii. below) and formative mixed methods research (iii. below). Where applicable, we have explicitly indicated activities that are NHSR below. Specific objective #1 will yield the following outputs in preparation for specific objective #2: Treatment guidelines and algorithms (both in SmartCare and on paper); Defined service delivery package and patient flow; Training materials and work flow for NPHW; Agreed sites where we will pilot test; Data collection tools both for MOH/program and the study (e.g. the WHOQOL-HIV instrument); Agreed indicators that if achieved will provide sufficient evidence to move to a larger program.

b. Study design

i. Health facility assessments (Non-human subjects research)

Health facility assessments will follow WHO recommendations for data collection and a previously adapted version of the WHO PEN site readiness assessment tool. Health facility assessments will take place at approximately 15 sites selected purposively from among health facilities in Lusaka, Zambia with high-volume (i.e., more than 3,000 HIV-positive patients in care) and that have CDC/PEPFAR-supported ART clinics. Sites include:

1	Matero Reference
2	Kanyama 1st Level Hospital
3	Chipata 1st Level Hospital
4	Chawama 1st Level hospita
5	Chelstone Urban Health Center
6	George urban health center
7	Chilenje 1st level hospital
8	Kalingalinga Urban Health
9	Matero Main Urban Health
10	Kamwala Urban Health Center
11	Makeni Urban Health Center
12	Mtendere health center
13	Railway Urban Health Center
14	Kabwata Urban Health Center
15	Ng'ombe Urban Health Center

At a subset of sites—Chawama 1st Level hospital, Chilenje 1st level hospital, George urban health center and Mtendere health center—we will conduct a more comprehensive assessment using a structured observation. Criteria for selecting these 4 sites include: 1) Patient volume— at least 3,000 patients on ART in the past 12 months so we have increased opportunity to encounter recipients of HIV care who also have cardio-metabolic co-morbidities; 2) Health facility level—we aimed to include facilities representing both primary health care level and higher level (level I hospital) heath services in order to capture heterogeneity in the health system and a variety of contextual implementation challenges; 3) Models of NCD integration—we aimed to include facilities that had either nonintegrated ART and outpatient/ NCD services and sites that were already working towards integration; 4) Catchment population socioeconomic status—we targeted sites with a mix of low, middle, and higher socio-economic status for the Lusaka catchment population; and 5) Data Quality—we selected a combination of sites with both high and low data non-missingness (defined as above or below 60% non-missingness) for variables of interest (i.e., at least one documented blood pressure measurement

and BMI in the past 12 months). These 4 sites will include the 2 sites where we will pilot our intervention pending stakeholder agreement.

Structured observations will describe how NCDs for PLHIV are being managed, who are managing them, which cardio-metabolic complications are being addressed, what medications, equipment, and lab tests are available and which are not, and how patients are being managed, communicated with, and referred across departments within the same facility and between various levels of the health system to coordinate care. Structured observations will generally consist of: directly observing encounters between patients and healthcare workers or lay cadres (i.e. treatment supporters and community health workers); reviewing facility and program registers and records; and generally observing the flow, wait times, and dynamics for NCD and integrated HIV/NCD service delivery activities in selected facilities. The data will be formalized into research memos and will contribute to building a picture—alongside other data collection activities for Specific Objective #1—of services supporting or impeding integration of HIV/NCD care and management of cardio-metabolic risk factors and co-morbidities for PLHIV in Lusaka, Zambia.

Structured observations will involve a trained study team member as a passive observer in public observable zones within health facilities, such as waiting areas, departmental registry rooms and vitals measurement stations. In all instances, permission to be based in these areas will be established with the overall-in charges (for facilities) prior to the commencement of study activities. Informed consent will not be sought out for structured observations since they will take place in open publicly available areas and will not collect any protected or identifying health information, and will not create generalizable knowledge. This activity is simply intended to document existing service delivery for integrated HIV/NCD care in the local Lusaka context. Based on a list of themes outlined in a Structured Observation tool (Appendix B), the trained observer will sit or stand in an unobtrusive location to observe client flow, one-on-one and group interactions involving HCWs, and other elements of day-to-day operations. Each 'block' of observation will last 1-2 hours. As far as possible, the observer will not participate in conversations or activities although where necessary may answer direct questions.

Observations will be conducted over approximately 2–3 days per facility and will be scheduled to occur on different days of the week and at different times of the day to better reflect the timing and variation of services and practices affecting NCD care and HIV/NCD integration. Structured observations will incorporate time spent in facility departments that affect patient and NPHW flow for management of NCDs in PLHIV, particularly the ART clinic, the Outpatient Department (OPD), the laboratory, and pharmacy. The study observer(s) will introduce themselves to all HCWs and staff, accompanied by the facility in-charge, in a general round of introductions at the beginning of the observation-period, and subsequently sit in a single space (as much as possible) in departments of interest, making shorthand notes related to their observations of health facility operations, healthcare worker interactions, patient-provider interactions and informal conversations. Notes will be structured under general thematic headings, including environment and workflow for NCD care, NCD patient care services, Equipment and Lab services, Medications, HCW work patterns & behaviours, with a particular focus on NPHWs, and communication and rapport-building patterns, among others. Short hand notes will be recorded on sub-thematic areas, including the following: operations; equipment and medication availability; waiting times; record keeping; communication patterns; referral systems; and interactions among healthcare workers and patients. Notes will be expanded in full at the end of the day (or as soon as possible thereafter), and formalized into a summary memo, which will be stored in an electronic log for later analysis. No personal identifying information such as names will be documented in notes or reports to protect confidentiality of staff and patients.

ii. Preparation of data collection tools (Non-human subjects research)

Piloting of WHOQOL-HIV Brief

WHOQOL-HIV BREF is an essential tool to assess quality of life, considered the '4th' 95-95-95 HIV indicator (i.e., beyond viral suppression), which will be a secondary outcome for the pilot and the later follow-on trial. As such, under this sub-aim, we will use the WHOQOL-HIV instrument previously adapted to the Zambian context, and pilot the WHOQOL-HIV BREF items focusing on ensuring semantic equivalence and assessing known group validity.

To confirm semantic equivalence, two trilingual (English, Bemba, Nyanja) study staff will back translate WHOQOL-HIV BREF items into English from Nyanja and Bemba. A consensus discussion will then be held between the translators and the MPIs to discuss difficult items with questionable clarity, which will then be resolved by consensus and the WHOQOL-HIV BREF revised accordingly. The final version for assessing known group validity will be called "WHOQOL-HIV-BREF-Zam."

Preparation of the SmartCare NCD module

We will work with a CIDRZ program developer hired by the study team, and with the stewards of the national EMR, SmartCare, which comprise CIDRZ, MOH, CDC/PEPFAR, and BroadReach, to adapt SmartCare to include an NCD module and automatic decision-support prompts for non-physician health workers. We envision that this may include a rather simple adaptation of an existing "outpatient department" module already available in SmartCare.

We will test this adapted version of SmartCare using an innovative approach known as "theatre testing". Theatre testing is a visual consultative process for obtaining rapid feedback on a new service or product from end-users. For this non-human subjects research component, we will use a voluntary sign-up sheet posted at health facility-level to invite ~10-15 adapted NCD SmartCare module end users, including a mix of NPHWs, from CIDRZ-supported sites to observe a demonstration of the module in action and/or use the module themselves. As this will be a convenience sample of SmartCare end users, we cannot exclude the possibility of selection bias among volunteers who agree to participate in theatre testing. However, since the intention of theatre testing is to improve the quality of the NCD module for local implementation, and not to create generalizable knowledge, we do not consider this a substantive methodological limitation. Following the theatre testing, a brief questionnaire (Appendix D. ii) will be administered to obtain feedback on the module that will feature the simple 12-item implementation survey (incorporating empirically supported measures for acceptability, feasibility, and appropriateness) mentioned above, among other implementation-relevant items [98]. Data from the theatre testing surveys will be summarized using descriptive statistics, and the results used to further refine and finalize the SmartCare module in advance of the pilot in objective #2.

While theatre testing will involve brief interactions with human volunteers to administer a 12-item survey, no identifiable private information or biospecimens will be obtained, used, studied, analysed, or generated during theatre testing. Moreover, the information obtained from the surveys will be recorded in such a manner that the identity of the volunteers cannot readily be ascertained, directly or through identifiers linked to the volunteers, and the investigators will not try to re-identify or contact the volunteers. Finally, any disclosure of the volunteers' responses outside theatre testing would not reasonably place the volunteers at risk of criminal or civil liability or be damaging to their financial standing, employability, educational advancement, or reputation. As such, theatre testing is considered to be research exempt from U.S. federal regulations, category 2 (exemption 2).

iii. Engage key stakeholders (Formative research)

All the formative research activities described under this sub-section are intended to generate generalizable knowledge about how diverse stakeholders in settings heavily burdened by HIV and cardio-metabolic NCDs perceive the need and urgency for HIV/NCD service integration, as well as the changes to the health system and implementation context necessary to realize integration.

Focus group discussions

We will prepare the strategies described in Table 2 for pilot implementation through consultative focus group discussions (FGDs) and brief surveys to create generalizable knowledge. These data collection activities will be guided generally by phases of the ADAPT-ITT approach [96] In order to get views from relevant stakeholders about the acceptability, appropriateness, and applicability of the strategies described in table 1 above, we will conduct the following 9 consultative focus group discussions (FGDs) within each of the following levels of the health system, including: Provincial and District Health Offices (x1) involving senior program managers, technical staff and coordinators; Health facilities (x 4) with high-volume ART clinics meeting WHO PEN criteria for becoming a demonstration site (i.e. have district and provincial government approval) involving front-line non-physician health workers (e.g. nurses, clinical officers, and pharmacists); and community level (x4) involving CHWs/ lay health providers and treatment supporters from the 4 purposively selected facilities for collection of formative data. Consultative FGDs will involve 4-8 participants each (i.e., 36-72 total), during which we will present the training materials, management algorithms, and patient and clinic flows, as appropriate, using vignette-style semi-structured guides to depict the core components of the proposed TASKPEN intervention. We will invite participants (Appendix A. i) to discuss how these do or do not fit with the local implementation context, and provide feedback for improvement.

Sampling for participation in consultative FGDs will be purposive for MOH headquarters (such as MoH staff already dedicated to cardiometabolic NCD issues) and provincial and district health offices staff and opportunistic for non-physician health workers and CHWs and lay health providers based on an open invitation. A few screening criteria will be applied for FGDs with NPHWs and CHWs/ lay health providers, which will be verified using a brief screening and eligibility case reporting form to confirm that participants are: ≥18 years of age; a non-physician professional or lay/ peer HCW involved with HIV and/or NCD service delivery at one of the study sites; and generally familiar with health services and operations at their facility.

A small team of trained FGD moderators will conduct all FGDs using semi-structured discussion guides (Appendix C. i, ii and iii) that will explore domains adapted from the Consolidated Framework for Implementation Research [97], including: *complexity* (i.e. the perceived difficulty of implementing TASKPEN intervention components in terms of time required, the disruptiveness of TASKPEN activities to average HCW work flow, the number of steps required to complete steps along the patient care pathway, and preferences for models of facility-level service integration of varying complexity, etc.); *perceived patient needs and resources* (i.e. the extent to which perceived patient needs, as well as factors that enable or hinder satisfying those needs are known to FGD participants and prioritized by their respective organizations); *perceived HCWs challenges* (i.e. perceived individual and system-level challenges and their context that may hinder delivery of TASKPEN); *structural characteristics* (i.e. the number and scope of professional NPHW and lay/ peer HCWs tasked with or otherwise organized into units that can support the TASKPEN intervention): *knowledge and beliefs* (i.e. individual attitudes regarding and value placed on supporting integrated HIV/NCD services, as well as familiarity with evidence and other facts surrounding the importance of integrated HIV/NCD services for improving the health of PLHIV); *planning* (i.e. the extent to which established procedures or strategies are in place to

manage cardio-metabolic risk factors and co-morbidities among PLHIV); *engaging* (i.e. the types of leaders among MOH management and frontline HCWs, including facility-level physicians, focused on NCD and/or cardio-metabolic complication management); and *executing* (i.e. the extent to which plans exist to support NCD and/or cardio-metabolic complication management for PLHIV); among others. Within this thematic framework, questions will be open-ended to allow the moderator to probe for emerging major and minor themes. The discussion guides will include a standard opening statement for use by the moderator to clarify FGD processes and participant roles, will present a description of the proposed TASKPEN intervention, and will be structured such that participants are encouraged to respond mostly to the moderators and not one another. FGDs will last approximately 1 to 2 hours each. FGDs will be conducted in a private room in the health care facility or other neutral setting.

Implementation surveys

At the conclusion of each consultative FGD, we will administer a simple 12-item survey (Appendix D. i) incorporating three empirically supported measures for the acceptability, feasibility, and appropriateness of the final package of proposed TASKPEN training materials, protocols, standard operating procedures, and processes [98]. Each measure will contain 4 questions that are scored on a Likert scale from 1 (completely disagree) to 5 (completely agree) that ask respondents to rate the TASKPEN intervention on the aforementioned implementation domains. Guided by the Integration and Training Phases of ADAPT-ITT, we will use results from the surveys and consultative FGDs to refine and finalize TASKPEN implementation strategies and related outputs in readiness for the pilot testing in specific objective #2.

Key informant interviews

We will engage senior MOH stakeholders and policy makers through key informant interviews (KIIs). KII participants will be identified and contacted by phone, email, or in-person by the MPIs or one of the co-investigators and will be given detailed information regarding the purpose of the KIIs, and will then be asked if they would be willing to participate (Appendix A. ii). KII interview guides (Appendix C. iv.) will be semi-structured and follow the same Consolidated Framework for Implementation Research[9] domains described for the FGDs.

Patient in-depth interviews

We will engage patients as our final key stakeholder group through in-depth interviews (IDIs) (Appendix C. v.). For IDIs, we will purposively select approximately 20 PLHIV with cardio-metabolic NCDs (i.e., diabetes, hypertension, dyslipidaemia, etc.) from the 4 sites where structured observations will be done. IDIs will examine patient experiences accessing both HIV and NCD services. We believe this number will be sufficient to identify major and minor themes, and achieve saturation on patient thoughts on ways to adapt and introduce the TASKPEN intervention for the pilot sites in specific objective #2. To ensure balanced representation across sex, age band, and major NCDs of interest, study staff will purposively select IDI participants by manually reviewing existing clinic registers and SmartCare records. For all potential IDI participants, study staff will approach them in person to see if they might be interested in learning more about the study using a recruitment script (Appendix E). If interested, study staff will then speak with the potential participant to sensitize them about the study and ask if they might be willing to participate in the interview (Appendix A. iii). Where a potential participant declines to learn more about the study or to provide consent, we will identify a replacement from among other potential participants until we achieve the enrolment targets summarized below.

Table 3. Mixed methods data collection summary for Specific Objective #1

Method	Activity Type	Activity Description	Total Participant	Approxim Time for activity
Health facility asse Structured Observations	***Non-human research***	~15 observations—1 at each purposively selected health faci Lusaka Province	n/a	1–2 hours
Theatre testing	***Non-human research***	End users participate in theatre te adapted SmartCare NCD module	n/a	~1 hour
Key Informant Interviews	***Research***	~5-10 central MOH senior policy ma technocrats	~5-10	~1 hour
Focus Group Discussions & Implementation survey	***Research***	1 FGD involving senior provincia office (PHO) and district health offic program managers, technical st coordinators	~4 – 8	~2 hours
	Research	~4 FGDs (i.e. 1 at each of 4 pu selected high-volume ART clinics in Zambia) involving frontline non-p health workers (NPHWs) such as nu	~16 – 32	~2 hours
	Research	~4 FGDs at community level (i.e. 1 of the 4 selected facilities above) CHWs/ lay health providers and t supporters	~16 – 32	~2 hours
	Research	Implementation survey done for participants at end of FGD	~36 – 72	~20 minut
In-depth Interviews	***Research***	~20 IDIs will be done with PLH cardio-metabolic co-morbidities (i.e each of 4 purposively selected high ART clinics in Lusaka, Zambia)	~20	~1 hour
Key Informant Interviews	***Research***	~8 KIIs (i.e. 2 at each of the 4 pu selected high-volume sites) conducted with clinicians at each fac	~8	~1 hour

c. Study site and population / research materials

Formative research activities will be conducted in MOH administrative settings at central, provincial and district levels in Lusaka, as well as 15 high-volume, PEPFAR-supported facilities and their surrounding catchment areas in Lusaka District (henceforth referred to as "sites"). These sites will be selected in consultation with our TAC. The study population will include a mix of MOH policy makers, program managers, non-physician health workers (e.g., nurses and clinical officers) community health workers (CHWs)/ lay health providers, and adult patients living with HIV and related NCD co-morbidities.

d. Selection of participants, sampling methods, sample size

i. Description and source of population and catchment area

For the mixed methods formative outcome evaluation, we will conduct: 1) In-Depth Interviews (IDIs) with patients; 2) Focus Group Discussions (FGDs) with Provincial Health Office (PHO) and District Health Office (DHO) program managers, technical staff and coordinators, NPHWs and community health workers participating in the delivery of the TASKPEN; 3) Key Informant Interviews (KII) with key stakeholders, such as policy makers from the Ministry of Health (MOH) and clinicians, critical to implementation of the TASKPEN intervention.

ii. Participant inclusion criteria

IDI participants must be emancipated HIV-infected adults ≥18 years of age who have a documented cardio-metabolic condition.

FGD participants must be: ≥18 years of age; a NPHW or community health worker / lay provider involved with HIV and/or NCD service delivery; or a PHO and DHO program managers, technical staff and coordinators generally familiar with HIV and/or NCD service delivery at their facility.

Implementation survey participants must be: ≥18 years of age; a NPHW involved with HIV and/or NCD service delivery; and coordinators generally familiar with HIV and/or NCD service delivery at their facility.

KII participants must be: ≥18 years of age; a senior MOH policy maker or health official working at national level in Zambia involved in managing, coordinating, and/or overseeing health services for non-communicable diseases in Zambia.

iii. Participant exclusion criteria

We will exclude any potential IDI, FGD/ implementation survey, or KII participant if they are unwilling or unable to provide informed consent.

e. Specific Objective #1 Outputs: Final TASKPEN Pilot Sites & Package for Pilot Testing

After all objective #1 data collection and analysis, we will review the data and may modify the implementation strategies and peripheral elements necessary to introduce the TASKPEN intervention, but not the evidence-based core elements detailed in Table 1. These will then be circulated to stakeholders on our Technical Advisory Committee (TAC) to get their final feedback. This will be done via email or Zoom video-conference meeting depending on TAC member availability. The outputs from Specific Objective #1 following TAC consultation will be: 1) consensus on the final TASKPEN package, including the core strategies/ components, training materials and 2) finalization of the two pilot sites for proceeding to pilot testing in specific objective #2.

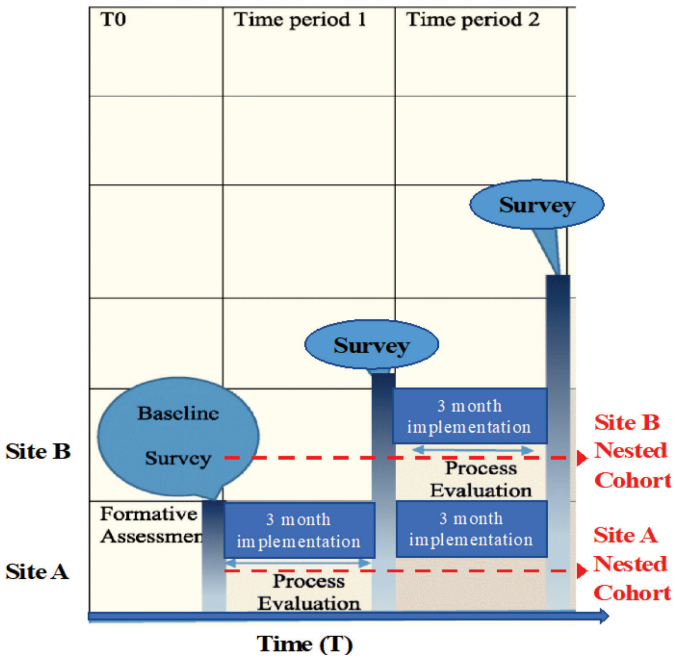
Specific Objective #2: Pilot test TASKPEN at two PEPFAR-supported health facilities in Lusaka, Zambia.

a. Overview

By completing specific objective #1, we will be fully prepared for TASKPEN pilot testing, having ready an adapted version of TASKPEN that includes all the essential implementation strategies necessary to overcome barriers to HIV-NCD integration in routine care settings. While the peripheral elements and implementation strategies used to introduce TASKPEN may undergo adaptation under specific objective #1, it is important to note that the 5 core, evidence-based components outlined in Table 1 and proposed for this pilot will not substantively change. Under specific objective #2, we will launch the TASKPEN pilot and fully task-shift our intervention to NPHWs and integrate it within the PEPFAR-supported HIV service delivery platform. Concurrently with implementation, during the pilot we will identify facilitators and barriers to TASKPEN introduction, assess preliminary implementation outcomes and patient and provider preferences related to integrated management of cardio-metabolic complications for PLHIV, ascertain early clinical outcomes for patients before and after TASKPEN piloting, and collect formative costing data.

b. Study design

***Figure**: Study schematic with "mini" stepped wedge and nested cohort.*



For this objective, we will conduct a quasi-experimental "mini" cross-sectional stepped-wedge study at the 2 pilot sites employing a mixed methods approach. First, at the two pilot sites (i.e. A and B), we will conduct a baseline assessment of select outcomes for PLHIV receiving the existing standard of care. This will involve conducting a brief bio-behavioural survey or "patient survey" among a consecutive sample of ~376 adult PLHIV presenting for routine HIV services at the two sites (i.e., ~188 PLHIV per site, see Sample Size and Statistical Power below). After this first patient survey, one randomly selected facility (i.e. cluster) will be switched to the full TASKPEN intervention. The patient survey will be repeated again with another ~376 adult PLHIV after ~3 months at both sites before switching the second site to the full TASKPEN intervention. After switching the second site, both pilot sites A and B will implement the full TASKPEN intervention for another ~3 months after which time a third and final "end line" patient survey will be conducted. Survey data will be used to estimate the pilot effect size of the TASKPEN intervention to aid in planning a future larger trial and to measure WHO PEN process indicators for all PLHIV in care who accessed routine health services during the pilot period.

Complementing the baseline, midline, and endline patient surveys will be a "nested cohort" of PLHIV with cardio-metabolic comorbidities enrolled at both sites beginning at baseline. At each site, we will enrol a subset of ~100 baseline survey participants (i.e., ~200 total) found to have at least one cardio-metabolic complication or risk factor (see below) on the baseline survey. We will then follow these nested cohort participants longitudinally for ~9 months at site A and site B. A nested cohort sample size

of 200 PLHIV was selected to represent about 50% of all baseline survey participants who are estimated to have a cardiometabolic co-morbidity at each site (i.e., ~188 PLHIV in care per site who complete a baseline survey x ~50% of survey participants with hypertension, diabetes, and/or dyslipidaemia = ~100 participants per site), consistent with estimates for the prevalence of cardio-metabolic comorbidities among PLHIV in Lusaka, Zambia. Moreover, the nested cohort sample size of ~200 total participants (~100 per site) is intended to assess the feasibility of the intervention and longitudinal follow up of study participants to inform a future larger trial; it is not intended to test a hypothesis *a priori*. By enrolling a nested cohort, we can use their data to enrich inferences made from the cross-sectional surveys and will be able to make more granular comparisons between and within sites (i.e. with an external and internal comparator group, respectively).

The "mini" stepped-wedge approach is appropriate because individual randomization is not feasible since TASKPEN is a facility-level program, and because it will help us anticipate operational challenges for the future larger trial (i.e., a stepped-wedge cluster randomized trial planned for 2023 with NIH funding). The nested cohort will also leverage existing routine data sources, including the SmartCare electronic medical record (EMR) and CIDRZ Laboratory Information Management Systems (LIMS). The MOH/CIDRZ teams implementing HIV program activities routinely collect individual-level clinical data, which as a line-listed resource can provide insights into individual outcomes for the nested cohorts.

Nested cohort data collection will include a patient quality of life questionnaire and a patient discrete choice experiment (DCE). The DCE will require patient completion of a questionnaire to elicit preferences for the different features of integrated HIV and NCD services. Stated preference methods such as DCEs have been increasingly used to quantify the relative importance and trade-offs among HIV service delivery and treatment programs. For example, recent DCEs from Zambia have examined how patients stable on ART would make trade-offs among the features of differentiated service delivery programs, including the location of service delivery and frequency of medication pick-up. In order to ensure successful uptake of integrated services for HIV and non-communicable diseases (NCDs), it is critical to incorporate patient preferences into the service design and delivery.

We will also conduct a mix of IDIs, FGDs, key informant interviews, and implementation surveys with patients and providers to evaluate feasibility, acceptability, and other implementation outcomes.

c. Study sites and population / research materials

Evaluation activities will be conducted in 2 high-volume, ACHIEVE-supported facilities and their surrounding catchment areas, henceforth referred to as the "pilot study sites" in Lusaka Province. These sites will be selected from among the 4 sites undergoing in-depth formative assessment under Objective #1. Tentatively, the pilot sites will be Chilenje 1st level hospital and George urban health centre, subject to approval by our TAC and findings from our formative assessment. The "mini" stepped wedge pilot will include all HIV-infected adults aged 18 years and older seeking care at the two pilot sites. Inclusion in the nested cohort will require documented HIV infection, age ≥ 18 years and one or more cardio-metabolic conditions or risk factors of interest described below (i.e., hypertension, diabetes/ pre-diabetes, and/or dyslipidaemia).

d. Selection of participants, sampling methods, sample size, enrolment and follow-up procedures

i. Description and source of population and catchment area

Based on existing PLHIV volumes at high-volume ACHIEVE supported sites in Lusaka, we expect to survey at least ~188 PLHIV meeting patient survey eligibility criteria at each site at baseline, midline, and endline (i.e., ~564 at each site or ~1128 participants in total) and to recruit approximately 100 baseline survey participants into the nested cohort at each site (i.e., ~200 total). For outcome ascertainment in the surveys, we will check vital signs, anthropomorphic measurements, and biomarkers. For outcome ascertainment in the nested cohort, we will review SmartCare, LIMS, and other MOH and CIDRZ registers and augment the abstraction of these routine data with study-driven primary data collection. Study-driven primary data collection in the nested cohort will include administration of the adapted WHOQOL-HIV-BREF-Zam and discrete choice experiment (DCE) questionnaire to these ~200 participants.

For the implementation outcome evaluation, we will conduct: 1) In-Depth Interviews (IDIs) with patients; 2) Focus Group Discussions (FGDs) with NPHWs and community health workers participating in the delivery of the TASKPEN; and 3) Key Informant Interviews (KII) with key stakeholders, such as policy makers from the Ministry of Health (MOH) and Clinic In-Charges, critical to implementation of the TASKPEN intervention. A brief implementation survey will be conducted with FGD participants at the end of each FGD.

ii. Participant inclusion criteria

For the cross-sectional patient surveys, we will include all adult males and females ≥18 years of age seeking routine HIV care at the two pilot sites during the pilot period.

For the nested cohort, the participant will need to be eligible and included in the patient survey done at baseline plus they will also need to have one or more of the following cardio-metabolic conditions or risk factors: 1) any current tobacco smoking; 2) hypertension as defined by WHO PEN (i.e., systolic blood pressure [SBP] ≥140 mmHg and/or diastolic blood pressure [DBP] ≥90 mmHg; 3) diabetes mellitus as defined by WHO PEN (i.e. random plasma glucose ≥ 11.1 mmol/L, fasting plasma glucose ≥ 7 mmol/L, and/or haemoglobin A1c ≥ 48 mmol/mol / ≥6.5%); 4) prediabetes (defined as having impaired fasting glucose of 6.1 to 6.9 mmol/L, impaired glucose tolerance with a two-hour, post-oral glucose tolerance test glucose ≥7.8 mmol/L but <11.1 mmol/L and a fasting plasma glucose <7.0 mmol/L, and/or haemoglobin A1c 42 to 48 mmol/mol or between 6.0–6.4%); and/or 5) dyslipidaemia (defined as total cholesterol >5.2 mmol/L or low density lipoprotein ≥3.4 mmol/L).

IDI participants must be emancipated HIV-infected adults ≥18 years of age who were enrolled in the nested cohort and had documented exposure to the TASKPEN intervention at a pilot site.

FGD / implementation survey participants must be: ≥18 years of age; a NPHW or community health worker (CHW)/ lay health provider involved with TASKPEN or integrated HIV/NCD service delivery; and generally familiar with HIV and/or NCD service delivery at their facility.

KII participants must be: ≥18 years of age; a facility-level ART or OPD clinic manager/ in-charge or policy maker at district, provincial, or national level in Zambia; and generally familiar with HIV and/or NCD-related issues in their community.

iii. Participant exclusion criteria

For the cross-sectional patient surveys, we will exclude adults who do not have documented evidence of HIV infection or who have not established HIV care at a study site. We will also exclude people unwilling or unable to provide written informed consent.

For the nested cohort component, we will exclude adults who have no documented evidence of HIV infection or a NCD of interest. We will also exclude people who did not participate in the baseline patient survey, are not likely to remain at the site for their care through the end of cohort follow-up, or unwilling/ unable to provide written informed consent.

We will exclude any potential IDI, FGD/ implementation survey, or KII participant if they are unwilling or unable to provide written informed consent.

iv. Justification of exclusion of any sub-segment of the population

We will not exclude any sub-segment of the adult population for the cross-sectional patient surveys. We have chosen to exclude infants, children, and adolescents under 18 years of age from this analysis as the mechanisms and systems built to support their care are unique, and because this population has a lower risk of cardio-metabolic complications of HIV.

v. Site sampling and randomization, including sample size and statistical power

The pilot sites for the formative evaluation will be selected based on their feasibility to deliver TASKPEN and to reflect different levels of the health system. For the mini stepped wedge study, the pilot sites will be Chilenje 1st level hospital and George urban health centre, subject to approval by our TAC and findings from our formative assessment. We will use a computer-generated allocation algorithm to randomize the time at which Chilenje and George will switch from standard of care to the TASKPEN intervention. This timing will be concealed from clusters and the trial team until ~4 weeks before the switch date.

Table 4. Study sites for the TASKPEN formative assessment.

Facility	*Annual PLHIV (TX_CUR*	% of TX_ clients with documented (within last 6 m	% of TX_CURR with a documen pressure measu (within the la months)	*Avg. No. o PLHIV enterir (TX_NEW)*	*Health Level*	*Integration of NCD a care*
Mtendere	6138	727 (11.84%)	719 (11.71%)	833	First	Partial integration (ART services available in outpatient department)
Chawama	10161	5599 (55.10%)	4485 (44.14%)	1353	Secondary	No integration
Chilenje	8083	7225 (89%)	6484 (80%)	1045	First	No integration
George	8785	1103 (13%)	38 (0.4)	1345	Primary	No integration

For the cross-sectional patient surveys, we will survey a consecutive sample of 188 eligible patients in care at each clinic at each of the 3-time points (i.e., baseline, midline, and end-line) using a stepped-wedge cluster-randomized design. Applying this design with a sample of 2 clusters (i.e., sites), 3 survey time points, 2 steps, 1 cluster switching from control to intervention at each step, and an average of 564 subjects per cluster (i.e., 188 participants per cluster per period) achieves 80% power to detect a risk ratio of 1.25 (for the risk of dual HIV/NCD control during the intervention period compared to the control period) at the 0.05 significance level with an inter-class correlation coefficient of 0.25. We assumed that

the proportion of participants achieving dual HIV/NCD control is 0.75 under the alternative hypothesis, and 0.6 under the null hypothesis, and used the two-sided Wald Z-Test as the test statistic. Based on the above calculation, we will survey 564 eligible patients at each clinic across the 3-time points (i.e., 3*188=564 eligible patients) to achieve **a total sample size of 1128 participants** for the mini stepped-wedge. It is important to note that participants previously surveyed will not be eligible for subsequent surveys—i.e., once interviewed, a patient should not be eligible for interview in subsequent surveys unless they are part of the nestd cohort. Finally, as part of the baseline, midline, and endline cross-sectional surveys, we will review de-identified routine data for all PLHIV in care at the study sites during the study period to estimate HIV viral load completeness, NCD-variable data completeness (e.g., routine weight and blood pressure measurements), and performance on WHO PEN indicators in the routine medical record.

For the nested cohort component, the total sample size of ~200 participants was selected for operational feasibility and to assess our ability to collect longitudinal cardio-metabolic data, but does not involve *a priori* hypothesis testing.

The suggested sample size for DCE surveys is estimated by the method of Orme and Johnson as N >500c/(t x a), where c is the number of analysis cells (i.e., the largest number of levels for any attribute), t is the number of choice tasks, and a is the number of options. Assuming maximum 4 levels per attribute, 10 choice tasks, and 3 options, the minimum required sample size is 67 to examine the effects in the overall study population. However, a larger sample size is necessary to measure preference heterogeneity among patients participants. Thus, administering the DCE questionnaire to all nested cohort participants is being proposed to fully assess preference heterogeneity in the patient population.

For our qualitative and costing components, we have not calculated sample sizes *a priori*, as we will not be conducting statistical hypothesis testing. The total participants listed in Table 5 (below) are meant to serve as a guide only. Additional IDIs, FGDs/ implementation surveys, KIIs, and structured observations may be added until thematic saturation is reached and no new themes are elicited from participants.

vi. Recruitment & Enrolment

For the cross-sectional patient surveys, we will coordinate with facility staff to approach, in person, consecutive PLHIV accessing routine health services at the clinic about the study. We will sensitize patients about the study at the clinic appointment desk, triage, and other waiting areas to take advantage of times when patients are queueing or otherwise awaiting health services. We will seek to conduct study activities after patients have received most of their clinic services so as not interrupt routine work and patients flows. After written informed consent procedures are completed, we will request basic locator information (e.g. phone number) to follow up with participants and administer a brief, one-time bio-behavioral survey.

For the nested cohort component, we will contact a consecutive sample of survey participants who we identify with a cardio-metabolic NCD through the survey and invite them to be followed in the cohort. For consenting participants, we will prospectively collect individual-level data, using existing routine data systems and study-specific case reporting forms, at the selected sites during the pilot period. Study staff will mention during baseline survey consent procedures that we may contact, by phone or in person, participants found to have a cardio-metabolic NCD via the survey and invite them to learn more

about the cohort at their next clinic visit. Phone recruitment for the nested cohort will be done using a recruitment script (Appendix D.i). For those interested, study staff working closely with facility staff will speak with potential cohort participants during their next clinic visit to sensitize them about the study and proceed with informed consent procedures if eligible and interested. The study procedures, risks, and benefits will be discussed in detail in Nyanja, Bemba, or English based on potential participant preference. The potential participant will have the opportunity to ask questions and deliberate before they decide whether or not they consent to participate.

For IDIs, potential participants identified to be eligible from among nested cohort participants will be contacted by phone or in person by study staff using study locator information. Study staff will ask if the potential participant might be interested in volunteering for the IDIs. IDI risks and benefits will be discussed in detail. The potential participant will have the opportunity to ask questions and deliberate before they decide whether or not they consent to the IDI. Where a potential participant declines to learn more about an IDI or to provide consent, we will identify a replacement from among other nested cohort participants until we achieve our IDI enrolment target.

For KIIs, participants identified to be eligible will be contacted by phone, email, or in-person by the MPIs or one of the co-investigators and will be given detailed information regarding the purpose of the KIIs, and will then be asked if they would be willing to participate. Because using a structured screening script may undermine the trust and personal rapport necessary to ensure key informant enrolment and honest responses to interview questions, a screening script will not be implemented for KIIs.

Enrolment of FGD/ implementation survey participants in all cases will be achieved by issuing an open invitation to all eligible non-physician health care workers (NPHWs) and community health workers (CHWs) / lay health providers. For NPHWs and CHWs, the study coordinator or co-investigator will communicate the open invitation using a recruitment script during the regularly scheduled (usually monthly) “all staff” or similar team meeting, which is scheduled in advance by the facility in-charge during the lunch hour and held in a conference room or other relatively private space at the facility. Enrolment will be on a first come, first served basis. We will coordinate scheduling of all FGDs/ implementation surveys with facility in-charges and will seek to conduct them at study sites on a weekend day or, if not feasible, during the lunch hour or late in the day on a weekday when clinical activities have wrapped up or are winding down so as to minimally impact patient care activities. For example, in many health facilities, ART clinic is only offered on certain days, or if offered daily, one day is dedicated to a specialized population (e.g. Paediatric ART Clinic) with the clinical encounters ending before lunch due to lower patient volume and workload. The investigators have experience collecting data from professional and lay healthcare workers in this way, which has enabled implementation science studies to achieve their enrolment targets without adversely affecting patient care activities. We will undertake all possible measures so as not to remove healthcare providers from their clinical duties.

vii. Nested cohort follow-up procedures

Nested cohort participants will be the only study participants having more than one encounter with the study team. As such, we will schedule study follow-up visits approximately every 3 months over a ~9-month period starting at 2 weeks from the time of the baseline patient survey. Thus, their total engagement with the study will amount to about 4 follow-up visits (at ~2 weeks and then around 3 and 6 months from the baseline survey plus one study exit visit at around 9 months). Study visits will be largely aligned with the schedule of routine clinic visits stipulated in the Zambia national HIV guidelines (i.e., every 3-6 months for established ART patients and more frequently during the first month of treatment for new ART patients) and will be scheduled mostly for times when the study teams are conducting the midline and endline surveys at the study sites. Study research assistants, who are not

providing any interventions as part of TASKPEN, will contact the participants in the nested cohort via phone call every month to check vital and clinic status (still in care at original site) and ascertain any changes in household location. If the participant is unreachable, community tracing will be done to verify whereabouts leveraging existing CIDRZ community tracing platforms in Lusaka. At the next time a survey assessment is done at the site, and before the clinic is switched from control to intervention, the nested cohort participants will be re-assessed by the team.

Study follow-up procedures will be designed so as not to disrupt routine care delivery and will include: determination of retention in integrated HIV/NCD care and referral for routinely available adherence and psychosocial counselling and back-to-care services, as appropriate; lab monitoring for cardio-metabolic NCDs (see laboratory procedures below) if not already done by the government health workers during their routine health visits; brief survey administration to assess adherence, nutritional status, tobacco and alcohol use, and other NCD-related health parameters; and completion of the quality of life and DCE questionnaires.

e. Data collection plan and tools

i. Data collection overview

As in specific objective #1, data collection activities for specific objective #2 will involve a combination of NHSR and implementation research activities detailed below.

ii. Non-human subjects research activities

Two NHSR activities will take place under specific objective #2. The first will be structured observations of TASKPEN implementation at two pilot sites once the intervention reaches steady state. For structured observations, a study observer(s) will introduce themselves and the study to all lay and professional healthcare providers, treatment supporters, and other MOH staff in the relevant ART clinic, pharmacy, or other service delivery setting where HIV/NCD services are being provided. Observers will then position themselves in an unobtrusive location within that setting in preparation for starting the observation and will take field notes using a structured observation guide.

The second NHSR data collection activity will involve a costing exercise. The costing work will focus on identifying the full range of costs involved in delivering integrated HIV/ NCD care. At the two pilot health facilities, we will collect data through a mix of reviewing patient and administrative records, as well as conducting pilot costing surveys involving ~10 MOH staff as informants. No demographic or health information will be collected directly from informants. Informants will be identified based on their knowledge of managerial and administrative issues at MOH and will be contacted by phone, email, or in-person by one of the co-investigators or study staff. Patient charts and administrative records will be reviewed for the purpose of identifying input data necessary for costing in those records. The data gathered will inform the design, adaptation and implementation plan of the full costing module for the follow-on larger study.

We will start our costing data collection activities by reviewing relevant local and regional literature on input and price data using the following sources for service delivery costs:

1. Unit costs for service delivery (cost per visit and admission)
2. Unit costs for diagnostic tests (blood test, radiography test, etc.)
3. Prices of all inputs, including salaries, allowances, per diem, medicine process, prices of medical supplies, etc.

We will then review patient charts (electronic and paper) at the two pilot sites to ascertain patient service use, frequency of visits, treatment protocols implemented for each patient, and to facilitate determination of associated costs including staff costs, costs of medications, diagnostic tests, and other costs. No identifying patient information will be collected. We will also extract cost data from routinely available MOH and project administrative records to examine the following:

1. Determine the availability and quality of cost input data in order to inform design of instruments for the future larger evaluation.
2. The material inputs and costs utilized in implementation of the TASKPEN intervention.
3. The proportion of human resource requiring training to perform the various TASKPEN intervention components.

Finally, we will administer our pilot costing survey. The survey data to be collected include:

1. What components of NCD services are offered at facilities
2. Human resources required and/or available to deliver NCD treatment and care services, and training requirements or gaps
3. Determine distribution of overheads across various centres through interviews
4. Salaries of all cadres of staff
5. Time spent by patients waiting, preparing for, or receiving integrated HIV/NCD services
6. Time spent by health care workers preparing for, and directly providing health services to, patients
7. Administrative cost data

iii. Quantitative research data collection

At both sites, during a ~1-month "run in period," we will establish basic study infrastructure to enable quantitative data collection during the patient surveys. This will involve fully equipping study offices at the sites and ensuring information technology connectivity and available computer hardware. Then, study staff will begin data collection on cardio-metabolic and implementation outcomes of interest using three cross-sectional patient surveys. The first two surveys (at baseline [0 months] and midline [3 months] will be done immediately prior to a site switching to the intervention; a final survey will be done at 6 months and serve as the "endline" assessment. The surveys will ask questions about participant socio-demographics, HIV and cardio-metabolic NCD history, and health behaviours. It will involve trained study staff administering a tablet-based questionnaire to participants, as well as taking participants' anthropomorphic measurements (e.g., height, weight, and waste circumference), vital signs (e.g., pulse and blood pressure), and a small blood sample to measure random/ fasting blood glucose, haemoglobin A1c, cholesterol levels, and other biomarkers. These laboratory tests will follow MOH recommendations and may include new point-of-care diagnostic technologies (see laboratory procedures section), and the results will be reported to patients and the clinic for clinical management. Any participant found to have newly diagnosed hypertension, diabetes/ pre-diabetes, and/or dyslipidaemia will be linked to care at the study sites. In addition, the study QA/QC nurse and study clinical scientist/ doctor will be available to act immediately on any vital sign or laboratory abnormality, including to offer patient counselling, provide warm "handoffs" to clinical staff, refer patients for acute care at the study sites, and prescribe appropriate outpatient treatment for non-acute issues in cases where MOH staff are not available (e.g., after business hours). Finally, we will ask participants to provide a phone number so we can invite those identified with hypertension, diabetes/ pre-diabetes, and/or dyslipidaemia through the survey to be followed in the nested cohort.

For nested cohort participants, study staff will ask them to provide locator information and to complete the midline and endline surveys (shortly after their routine HIV care visits) as part of their ~4 scheduled study follow up visits. Similar handling of abnormal vitals signs and lab testing values will be offered to nested cohort participants as patient survey participants. In addition, we will administer the brief

WHOQOL-HIV-BREF-Zam instrument and the discrete choice experiment questionnaire one time each during one of their ~4 follow up visits. Cohort enrolment will stop when the target number is reached. Finally, we will review cohort participants' HIV and NCD clinical data using a minimally sufficient set of identifying variables (i.e. first name, surname, date of birth, and SmartCare ART number) to follow them longitudinally in the routine medical record. To this end, we will abstract data from existing paper-based patient charts and MOH registers, as well as the electronic SmartCare EMR and LMIS systems to: 1) assess HIV and NCD outcomes (e.g., viral load); 2) evaluate WHO PEN outcome indicators of interest (e.g. proportion of PLHIV routinely screened for hypertension); and 3) monitor for efficient collection of routine data, including routine laboratory test results (e.g. viral load).

Under routine program conditions, and as a part of standard monitoring & evaluation (M&E), CIDRZ and MOH staff manually collect data from clinical and program registers and other paper-based routine records available in departments providing HIV, NCD, and other health services. These departments include the out-patient department (OPD) where some NCD services (such as hypertension management) are provided, the ART clinic and Differentiated Service Delivery Centres (where ART and HIV care is provided), and the laboratory department, among others. Paper-based records stored in these departments contain identifying information, including names, dates of birth, and addresses, and, as such, are maintained in locked rooms per MOH standard operating procedures. Trained and experienced study staff will confidentially handle these paper-based records following MOH standard operating procedures and will ensure they do not leave the secure locations where they are stored and are only accessible to authorized study and facility staff during working hours. For the purposes of this protocol, study staff will abstract existing health information from these routine paper-based data sources, including height, weight, ART start date, viral load sample collection data and results, among others, and enter them into a secure, password-protected database in REDCap, eClinical or similar web-based system stored securely on the encrypted CIDRZ server. Authorized study staff will also extract patient-level electronic data from existing electronic SmartCare and LIMS records already housed on the CIDRZ network at the CIDRZ Head Office into the secure, password-protected, web-based database. The database will be backed up automatically at regular intervals (i.e. at least once weekly) onto an encrypted password-protected CIDRZ back-up server for data security purposes. Whenever possible, electronic SmartCare and LIMS data will be linked at facility-level with data abstracted from paper-based records using the SmartCare ART number.

For nested cohort participants, we will supplement the aforementioned routinely collected data with study-specific data collected through survey and CRF administration to assess medication adherence, quality of life, nutritional status, tobacco and alcohol use, and other NCD-related health parameters. The WHOQOL-HIV-BREF-Zam (Appendix G) will be administered in Nyanja or Bemba to nested cohort participants at our pilot sites to investigate the ability of the instrument items to discriminate between those with and without active symptoms related to HIV and co-morbid NCDs, as determined by differences in mean scores. A p-value less than 0.05 will be considered significant; items with non-significant differences between the two groups may be removed from a future iteration of the instrument.

All DCE questionnaires will be conducted one-on-one in private by a trained interviewer with consenting patient and provider participants. Each DCE will be explained verbally to participants. Each questionnaire is expected to last approximately 30 minutes. Before the DCE, the interviewer will conduct a brief review of each participant's clinic file to confirm HIV status, ART regimen, most recent CD4 cell count, most recent viral load, and cardio-metabolic conditions. The DCE questionnaire will be developed in English and translated into Bemba and Nyanja and then translated back to English to

validate the translation. The DCE questionnaire will be administered using the secure REDCap Mobile App on Android tablets, which can be used offline, and later uploaded to a secure database. The DCE starts with a simple vision and literacy test to ensure internal validity and facilitate quality control as sight is necessary for full comprehension of DCE choice tasks. The DCE then proceeds to provide an introduction of each attribute and its levels. Participants will be asked to rank the levels of each attribute based on their individual preferences. Each participant will receive 8-10 choice tasks on the tablet, and will be asked to choose between three hypothetical HIV/NCD integrated service delivery programs/ scenarios with different levels of attributes per choice task.

iv. Qualitative and mixed methods data collection

We anticipate needing to complete the following number of qualitative data collection activities (Table 5, below) with the following number of participants: 1) For IDIs, ~20 cohort participants will be interviewed to explore their experiences with both usual practice and TASKPEN (~10 IDIs per facility). These participants will be purposively selected to ensure balance in gender, age band, and NCD co-morbidities; 2) For FGDs, ~4 total FGDs (or ~2 FDG per site) involving ~4-8 non-physician health workers OR ~4-8 community health workers/ lay health providers per FGD following TASKPEN implementation (or ~16-32 total participants); and 3) For KIIs, interviews with ~10 key stakeholders will be performed, including ART and OPD clinic managers/ in-charges or designee and policy makers at provincial and national MOH levels, selected purposively based on their involvement and familiarity with TASKPEN implementation and/or the NCD policy setting in Zambia. For all the above-mentioned qualitative data collection activities, we will adapt the semi-structured tools from specific objective #1 based on the CFIR and formative research findings from that objective to create the tools for specific objective #2. Finally, we will administer the same implementation survey used in objective #1 (with the addition of a clinical sustainability assessment) to FGD participants to assess measures of acceptability, appropriateness, feasibility, and sustainability. We anticipate conducting qualitative and mixed methods data assessment after both sites are exposed to the TASKPEN intervention in the mini stepped wedge pilot.

IDIs, KIIs, and FGDs will be tape-recorded with participant permission for subsequent transcription. An interviewer/ facilitator will guide the IDIs, KIIs, and FGDs, and a note-taker will document non-verbal cues and main points. The note-taker will also take notes to ensure no loss of information in the event of a technological failure and to provide contextual information. For FGD and KII participants, basic demographic background information about each respondent (such as title/role, age, gender, and education level) will be audio-recorded at the start of the FGD or KII, but no responses will be traced to specific individuals during analysis and reporting. At the end of all completed IDIs, KIIs, and FGDs, study staff will review all recordings to ensure they are audible and all notes for legible handwriting. Ambiguous information from interviews or FGDs will be clarified with the source. As far as practical, the field team will transcribe audio-recordings, with support from other qualitative data analysts and coders. Interviewers/facilitators will read the transcripts for completeness and fill in gaps using their interview and field notes. Transcribed interviews will be stored in password-protected files.

Table 5. Summary of mixed methods data collection activities for completing Specific Objective #2.

Method	**Activity Ty**	**Number**	**Total Particip**	**Approxir Time fo activity**

Structured Observa	***Non-human s research***	~2 observations—1 at each site included in the "mini" wedge trial	0 (Non-participat	1–2 hours
Costing survey	***Non-human s research***	Reviewing administrative records with assistance c informants	0 (Non-participat	~1 hour
Focus group discussions	***Research***	~2 FGDs total— ~1 FGD with NPHW at each site	~8 – 16	~2 hours
	Research	~2 FGDs total with CHWs/lay health providers – ~1 FGD each site	~8 – 16	~2 hours
	Research	Brief implementation survey done with all FGD participants FGD	~16 – 32	~15 minute
In-depth interviews	***Research***	~20 total from among nested cohort participants— ~10 per s	~20	~1 hour
Key informant interv	***Research***	~5 - 10 in each pilot site with key stakeholders	~10-20	~1 hour
WHOQOL-HIV-BRE survey	***Research***	~200 nested cohort participants (~100 per pilot site from cohort)	~200	~30 minute
Discrete Choice Ex (DCE) survey	***Research***	~200 nested cohort participants	~200	~30 minute

v. Study instruments, questionnaires, lab instruments, and analytic tests

Data collection tools and instruments are included in the Appendix. All patient surveys and cohort questionnaires will be programmed in REDCap and will be administered by trained study staff directly to participants using encrypted, pass-word protected tablets. The same patient survey instrument will be administered at baseline, midline, and endline.

For the DCE, we will develop a questionnaire for patients to elicit their unique preferences for integrated HIV and NCD services. Questionnaires will contain a brief section on demographic information including age, gender, education level, and average monthly income. DCEs will ask participants to choose from among three scenarios of HIV and NCD integrated service provision. Each scenario will have a set of attributes that are varied across 2 to 4 levels. The attributes and levels will be developed and refined based on the results of formative data collected under Objective #1 (above). For the DCE

questionnaire, the following attributes and levels for delivering integrated services will be explored, with modifications to be made based on the final results of qualitative analyses under Objective #1:

1. Type of clinical venue
   a. Integrated ART Clinic
   b. Integrated Outpatient Department
   c. Dedicated “Chronic Care Clinic”
2. Type of clinical provider
   a. Clinical officer
   b. Nurse
   c. Lay health worker
3. Type of visit frequency
   a. Monthly
   b. Every 3 months
   c. Every 6 months
4. Type of community psychosocial support
   a. Community adherence/ support groups
   b. Community health worker/ peer navigator visits

The DCE survey will be developed with Ngene software using a fractional factorial, balanced and orthogonal design. The balanced design indicates that each level per attribute appears for the same number of times across the choice tasks, while the orthogonal design indicates that each pair of levels appears equally often across all pairs of attributes in the survey.

Structured observation guides and costing surveys will not be used for research purposes and will be developed in English for use by professional study staff only.

All qualitative data collection activities for specific objective #2, will be adapted from the semi-structured tools used in specific objective #1 that are based on the CFIR and formative research findings from that objective. IDI guides, as well as the WHOQOL-HIV-BREF-Zam, will be developed in English and translated into *Bemba* and *Nyanja*, the two other languages that are commonly spoken in Lusaka. FGD and KII guides will be developed and administered in English since these participants speak and write fluently in English, which is the official language of health training in Zambia. IDI, FGD and KII guides may undergo minor adaptation over the life of the study to optimize participant comprehension and thematic elicitation, and to minimize any risk of psychosocial distress posed by the wording of questions and probes. Audio recording will also be used with the consent of participants. Verbatim transcripts will be transcribed and translated into English (as needed). Field guides will be piloted before data collection begins, and the tools will be further refined to improve their clarity, completeness, overall usability. Electronic devices used for data collection will be password-protected, with access restricted to authorized and trained study staff only. For sharing and analysis purposes, individual identifying information will be removed and where necessary, codes will be used. Standard operating procedures will be developed to guide and inform the usage of the developed tools.

At the conclusion of each FGD, we will administer an implementation survey incorporating three empirically supported measures for the acceptability, feasibility, and appropriateness of the final TASKPEN intervention.[98] Each measure contains 4 questions (i.e., 12 total) that are scored on a Likert scale from 1 (completely disagree) to 5 (completely agree) that ask respondents to rate the TASKPEN intervention on the aforementioned implementation domains. We will also incorporate the Clinical Sustainability Assessment Tool, which contains 35 items on 1 (To little or no extent) to 7 (To a very great extent) Likert scale to assess perceived sustainability of the TASKPEN intervention.

vi. Laboratory procedures

All patients receiving integrated HIV/NCD care at the pilot sites will receive standard laboratory tests free of charge as part of MOH-recommended routine care. This includes viral load, serum creatinine, full blood count, ALT/SGPT, Hepatitis B Surface Ag, CD4 count, urine pregnancy test, rapid syphilis testing, and random plasma glucose. The current MOH-guidelines also recommend testing total cholesterol and triglycerides in PLHIV and haemoglobin A1c in PLHIV with suspected or known diabetes. However, because of resource limitations and limited laboratory infrastructure, these latter cardio-metabolic tests are not typically available under usual practice. As such, as part of the patient surveys conducted at baseline, midline, and endline at study sites, trained study staff will directly test all PLHIV who enrol in the survey for random/ fasting glucose, haemoglobin A1c, and total cholesterol, low density lipoprotein (LDL), and high-density lipoprotein (HDL). To conduct this testing, we will equip each site with capacity to measure glycosylated haemoglobin A1c (HgbA1c), low density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol, and/or urine albumin to creatinine ratio. For testing through the survey of haemoglobin A1c, low density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol, we will collection blood, which will be no more than ~5-10 mL. If possible and feasible, a point-of-care (POC) platform (e.g., Afinion™ 2 multi-assay analyser) will be used to ensure more rapid result reporting. In this case, the volume of the blood draw will be less at approximately 3 drops of whole blood (about 20 microL). For urine, 1 mL is required for testing. Results of all testing done through the study will be given to participants and healthcare providers for clinical management and recorded in study and routine medical records to enable pilot outcome ascertainment.

vii. Outcomes

Outcomes measurement

The primary measures for the pilot are adoption, acceptability, feasibility, appropriateness, as well as the preliminary effect of the TASKPEN intervention. We will assess implementation outcomes principally using a handful of theoretical frameworks. A brief questionnaire will be administered that will feature the simple 12-item implementation survey (incorporating empirically supported measures for acceptability, feasibility, and appropriateness) mentioned above, among other implementation-relevant items[98]. We will further examine **acceptability** in our qualitative data as a construct comprising multiple dimensions[99]. We will include open-ended questions guided by established implementation science frameworks such as the CFIR to elaborate on what makes the intervention appropriate or not and acceptable or not. We will further evaluate **feasibility** in our qualitative data by applying the theoretical basis of ‘‘compatibility’’ from Rogers’ “Diffusion of Innovation” theory, among other theories[100].

We will describe implementation outcomes of **adoption** and **reach** according to RE-AIM. We will also calculate **retention** as the proportion of participants enrolled in the nested cohort and considered to be engaged in care at ~6 months. We will measure **adherence** in the nested cohort by reviewing pharmacy records at ~6 months to determine consistent access to anti-hypertensive, diabetes, and dyslipidaemia medications, as appropriate, as well as antiretroviral therapy. For the patient surveys, we will ask participants about adherence and review pharmacy records to examine medication adherence overall at the study sites.

Finally, we will pilot the feasibility, applicability, and completeness of the following measures in the cross-sectional assessments and nested cohort for adoption in the future follow-on trial:

1. ***Dual*** HIV and NCD disease control, defined as:
   a. HIV RNA level of <200 copies per milliliter on the most recent measure; ***AND***

b. The absence of the following NCD conditions as defined by the nested cohort eligibility criteria: 1) uncontrolled systolic hypertension; 2) uncontrolled diabetes mellitus; and 3) uncontrolled dyslipidaemia.

2. *10-year ASCVD risk score* (based on American College of Cardiology/ American Heart Society guidelines)
3. The HIV-specific *D.A.D. CVD risk score*: (The Data-collection on Adverse Effects of Anti-HIV Drugs) score.
4. Quality of life as measured by WHOQOL-HIV-BREF [101].
5. Number and % of patients with HIV RNA suppression (defined as <1,000 copies/ml)
6. Number and % of patients who are currently smoking (defined as smoking of any tobacco product in the last 30 days)
7. Number and % of patients with normal systolic blood pressure (<140 mmHg) among persons with HTN
8. Number and % of patients with stage III hypertension (i.e., BP >180/110) among persons with HTN
9. Number and % of patients with normal fasting blood sugar among persons with DM
10. Number and % of patients with haemoglobin A1c <7% among persons with DM

Implementation outcomes measurement

We will evaluate implementation outcomes as defined by Proctor, Silmere,[28] adapting CFIR constructs as described by Warner G et al[29] and Damschroder and Lowery [102], and using the RE-AIM framework.

Table 6. Primary implementation outcomes**.**

Implementation ou	**Description**	**Theoretical B**	**Measurement**	**Time points (Months)**
Reach	No. of people and percentage of the target population affected and the extent to which the individuals reached are representative and include those most at risk for NCD-related poor outcomes/ complications.	RE-AIM	% of PLHIV with HTN who are recruited and receive/participate in intervention at ~6 months;	~6 months
Appropriateness	The extent to which p interventions can be deliv health facilities	Theory of Diffus	Individual interviews, Focus group dis Key informant interviews. We also use measures of appropriate Weiner, Lewis [98]; WHO PEN Health Assessment questionnaire	~6 months
	Perceived fit, relevan compatibility of TA among providers and and/or perceived	Proctor et al. 2011; Weiner et al., 2017	Intervention Appropriateness M (IAM)	~6 months

	TASKPEN to the lack integration			
	Referrals for task sharing/ sh		Administrative records	~6 months
Acceptability	User and provider feedback	CFIR	IDIs, Focus group discussions guic informants	~6 months
	Extent to implementation stake perceive TASKPEN agreeable, palatable satisfactory	Proctor et al Weiner et al.	Acceptability Implementation Measure (	~6 months
Adoption	No. and percentage of participating, and the extent the settings selected representative of settings target population will use or	CFIR; RE-AIM	Focus group discussions and Key i interviews of implementation challen barriers; % of facilities and providers that intervention at ~6 months	~6 months
Feasibility	Extent to which the TA intervention can successfully used or out within a practice se	CFIR, ISF; Wei 2017	Data extraction checklist (Daily conducted related to the e interventions e.g. counselling, no. o profiled, followed up, etc.); Feasibility of Intervention M (FIM)	~6 months
Fidelity	The extent to which provi delivering TASKPEN packag the protocol/guidelines	CFIR	Structured observations of NPH community health activities during cons with clients	~6 months
Cost	Resources, inputs, and H necessary to implement T pilot		Administrative surveys	~6 months

viii. Training for all study personnel

All study staff will be certified in human subjects' protection and trained on data abstraction/collection and qualitative research procedures, including for FGDs, IDIs and KIIs. This training will include methods for the informed consent process, stressing the importance of participant privacy and confidentiality, voluntary participation, and risk mitigation. Intensive training sessions will use a mixture of methods, both didactic and case-based, including lectures, case-based learning and practice with field guides and data abstraction tools. All involved personnel will be trained to respect persons, participants' organization cultures and regulations from initial contact to dissemination. Respect for persons and organizations, which constitutes the need to respect persons and their privacy, will be

emphasized in Standard Operating Procedures. All study personnel will also be required to sign a confidentiality agreement to further promote protection of participants' data.

Patient chart, registers, LIMS and SmartCare reviews are part of routine patient monitoring systems. Study staff will be trained on research ethics and management before data is abstracted from patient charts, records or registers. They will assure confidentiality and privacy of data processed in this study. All hard copy and electronic records will be kept in a secured and locked area. All electronic data collection devices and computers storing study data will be encrypted and password protected and access restricted to authorized study staff only.

The study clinical scientist/ doctor, QA/QC nurse, and research assistants will be trained on sterile, safe, and proper finger pricking for the purposes of checking random/ fasting glucose during patient surveys. We will also train these research staff on operations of the point-of-care Afinion™ 2 multi-assay analyser platform and performing finger pricks to load a few drops of blood (~20 micoL) into the platform's testing cartridges.

All study staff, including study clinicians and mentors, interviewers, facilitators and note-takers will be trained on recruitment, consenting processes, enrolment and the conduct of their duties. In addition, qualitative research will be trained on how to set up rooms to ensure a non-coercive atmosphere conducive to dialogue and discussion, use of digital recorders, note-taking techniques and techniques for eliciting participant response. They will be trained on writing field notes and in managing, transcribing and analysing data. Finally, interviewers and facilitators will receive basic training on how to actively refer back to care those participants wishing to re-engage in care, including who to contact at the relevant facilities to arrange follow-up and how to document such interactions.

f. Data management and storage

i. Information management and analysis software

Under current programmatic conditions already in place at the study sites, SmartCare EMR data, which includes routinely collected patient identifying and health information, are stored in secure Microsoft SQL Server databases at each facility and merged into a central server located at CIDRZ head office in Lusaka at least once monthly, but often weekly, depending on the patient volume at the facility.

ii. Data entry, editing and management, including handling of data collection forms, different versions of data, and data storage, security, and disposition

For the patient surveys and nested cohort, study-specific data will be entered by study staff onto secure REDCap study forms using the REDCap application and encrypted, password-protected study tablets. REDCap has built in data logic and security functionalities to ensure high quality data collection.

For the purposes of routine data review, SmartCare and LIMS EMR data will be abstracted and merged with information from study-specific CRFs/ surveys and facility paper-based registers and records, such as NCD laboratory result registers and routine program viral load and anthropomorphic data available at the study sites. The above data will then be merged to create a final, comprehensive, and secure database in REDCap or similar system. Data in the pilot database will be organized by study number assigned to each participant that will then serve as the lone and overarching study identifier. The study number will be formatted similar to the following CIDRZ approach: SC—XXXXX—CD with "SC" serving as the 2-digit site code, "XXXXX" the participant number, and "CD" representing the 2-digit check digit. Immediately upon exportation of data from the database to create the analytical dataset, all patient identifying information will be purged from all records for the purposes of protecting patient confidentiality. We will accomplish this by programming code to automatically drop all variables that

include identifying information from the analytical dataset and recoding all identifying information in the final database to “0” or missing value.

The DCE for each participants will be identified by the aforementioned study ID. REDCap is specifically geared to support online or offline data capture for research studies and operations. After returning to the study office, study staff will upload DCE data from the REDCap Mobile App to a secure server (likely the REDCap server). The DCE data will then be merged into the study database using the REDCap API via a secure, encrypted transmission (SSL/HTTPS).

The final study database comprised of study-specific data and abstracted routine data for all study sites will be stored on a secure, encrypted SQL server and will be updated with new data at least once weekly. The final database will be backed up daily onto a secure study account housed on a separate, encrypted CIDRZ server. To ensure data security and integrity, the database will be programmed to automatically back up daily to One Drive without user prompting. We will conduct regular database queries of extreme and missing values. Quality assurance and quality control procedures will be in place throughout the project, with regular assessment of missing or inconsistent records. The analytical dataset will be created as a comma-separated variable file or stored as one of the available analysis software package formats, including SAS, Stata or R. The analytical dataset will be encrypted and password protected at all times for analysis purposes. Quantitative analyses will be performed using Stata (Statacorp LLC, College Station, TX) or other comparable statistical software.

For qualitative data specifically, digital audio-files will be transferred to password-protected, encrypted study computers accessible only to trained study staff responsible for transcription. All transcriptions will be done in one translation and transcription step. Microsoft word will be used to create transcripts and Nvivo QSR™ (or comparable qualitative analytical software) will be used to manage documents and code sets for complex qualitative data derived from structured observation notes and IDI, FGD, and KII transcripts. All transcripts and research memos (from structured observations) will be stripped of any and all identifying information and will be saved as password-protected files on an encrypted CIDRZ One Drive account housed on the secure CIDRZ local area network. After completion of transcription and validation, all electronic audio-files will be immediately destroyed. Transcripts and research memos will be backed up daily and automatically to a separate location on an encrypted CIDRZ server to ensure data security and integrity.

Any study-specific paper forms, such as demographic forms, will be stored securely at study sites in locked filing cabinets in a locked room identified in coordination with the MOH department or overall in-charge. In all cases of study-specific form management, personal identifying information and study data collected during the course of IDIs, KIIs, FGDs, or structured observations will be stored separately and will only be linkable through the use of a link log kept in a separate, secure location.

At study closeout, evaluation data will be stored/ archived until at least the final analysis and reporting on the project are complete. CIDRZ will follow the recommendations of the Zambia MOH for archiving of all hard copy and electronic records (tentatively for 3 years after the completion of the analysis), as well as for the method of eventual destruction of data including the shredding of any original paper-based information and systematic deletion of original data files from CIDRZ’s servers. CIDRZ will defer to Zambia MOH guidance on the handling and management of all data to be used as part of this evaluation protocol. The MPIs will be ultimately responsible for all data security issues. All data will be stored per National Health Research Authority, UNC IRB, and University of Zambia Biomedical Research Ethics Committee guidelines and guidance.

iii. Quality control/ assurance

As a part of routine monitoring activities, data audits are performed to verify the quality of routine clinical, laboratory, and pharmacy data collected at CIDRZ-support facilities, including the facilities included for this study. CIDRZ conducts data quality monitoring activities at specific times (daily, weekly, monthly, quarterly, semi-annually and annually). Data quality audits (DQA) are conducted with reference to standard SOPs. Sites are sampled in the following fashion: (i) randomly, when conducting routine audits; (ii) targeted (objectively), when poor performance is observed; and (iii) purposively, when data manipulation is suspected. Lay Counsellors assist in manual checks of patient records during DQAs. Data Associates primarily enter data into SmartCare from patient charts, ensure data completeness, and run facility-level performance reports. Data Coordinators run validation checks, compare indicator cascades, ensure that data associates follow the laid down standard operating procedures, run data aggregations and proactively identify potentially missing data. M&E Coordinators analyse data submitted and participate in Facility and District Data Review meetings. Data Managers develop data collections tools and provide first-level data quality analysis of aggregated data. The M&E Manager coordinates SIMS and feedback to program teams (data reviews). Additionally, through its PEPFAR-funded projects, CIDRZ provides facility-level mentorship to health workers and supports collaborative quality improvement (CQI) activities.

For quantitative and mixed methods study activities, we will leverage the aforementioned data QC systems to ensure accurate and efficient data collection. The study SmartCare Developer, will run aggregate reports on the percentage of patients at study sites with missing vital signs, anthropomorphic, and laboratory data and feed this back to the site. The study Data Manager will run data logic, completeness, and consistency checks on data in the study database using programmed REDCap functionalities and feedback QC queries to the study sites for clarification and resolution.

For qualitative data, final qualitative transcripts will be reviewed for accuracy against original notes and recordings, for at least 5% of the transcripts. Any errors will be corrected by the person who conducted the interview using good clinical practice (GCP) correction procedures. Monitoring visits will be conducted on an ad hoc basis to ensure that data collection is being done well. Any retraining will be done on-site on an as-needed basis, to ensure that collected data are of high quality.

iv. Data ownership, sharing and governance

All study data will be owned by the Zambia Ministry of Health (MOH) as the stewards of the national HIV program. As the owners of the data, the Zambia MOH will ultimately be responsible for oversight of all data governance issues. Qualitative data will not be shared due to the small sample size involved and the potential for deduction. All decisions regarding data dissemination, for example at the request of a journal at the time of publication, will be made by the Zambia MOH as the owners of the data.

g. Data analysis

i. Quantitative data analysis

We will summarize background characteristics (for participants and facility) by the intervention periods (control, intervention). The preliminary effect of the TASKPEN intervention will be estimated by comparisons of the percentage of participants in the patient surveys with dual HIV/NCD control during the control period and the intervention period. We will also calculate CVD risk score based on the ASCVD, D.A.D, or similar and compare this outcome between the control and intervention periods. Binary outcomes will be analysed using generalized linear mixed logistic model with margins to estimate risk ratio and risk difference adjusted for key potential confounders. Health facilities will be specified as random effects while time will be specified as fixed effect in the model. Continuous outcomes will be analysed using linear models to estimate mean score difference in an analogous way.

Quality of life score will be analysed in a similar way. P-values less than 0.05 will be considered statistically significant. We do not plan to impute missing values. All analyses will be performed using Stata 16 MP4 (StataCorp, College Station, TX, USA).

Using baseline, midline, and endline patient survey data and routine EMR data, we will assess the implementation outcomes described in Table 6. We will calculate standardized scores for validated instruments in our implementation survey. Comparisons of proportions for the aforementioned implementation outcomes will be done by calculating prevalence ratios and associated 95% confidence intervals as appropriate. Comparisons of continuous outcomes will be done by the Z-test/ 2-sample T-test or the Wilcoxon Rank-Sum test as appropriate.

To understand patient-level outcome measures of **disease control, retention**, **adherence**, and **viral suppression**, we will analyse data from the patient surveys. We will estimate **dual disease control** as the proportion of participants in the intervention and control periods who have a HIV viral load <200 copies/ml and do not have uncontrolled systolic hypertension, diabetes, and/or dyslipidaemia. We will calculate **retention** as the proportion of participants considered to be consistently engaged in care at 6 months according to the national HIV treatment program definition (e.g., without evidence of death, default, or loss to follow up defined as ≥30 days having elapsed since a missed pharmacy refill/ clinic visit). We will measure **adherence** in the nested cohort by reviewing pharmacy records at 6 months to calculate the medication possession ratio (MPR) over that time frame for anti-hypertensive, diabetes, and dyslipidaemia medications, as well as antiretroviral therapy. We will calculate **viral suppression** as the proportion of survey participants meeting established thresholds of suppression (e.g., viral load <1,000 copies/ml or <200 copies/ml) at 6 months following ART initiation and/or study enrolment. To compare outcome measures, we will report differences and ratios with accompanying 95% confidence intervals. We will compute variance for differences and ratios using the sandwich variance estimator or appropriate resampling approaches to account for the clustered nature of the data by site.

We will leverage the rich data from the nested cohort on cardiometabolic outcomes and covariates to make more accurate inferences about the distributions of these outcomes, and their trends over time, among all survey participants, as well as the target population of all PLHIV routinely in care at the study sites. Specifically, we will use outcomes measured in the nested cohort to account for measurement error (e.g., failure to capture a NCD diagnosis) or missing data (e.g., no record of a component of a given risk score) in the survey data and routinely collected medical record data. Rather than simply excluding records with missing data, considering those without a recorded diagnosis or biomarker value to be “outcome free,” or using potentially mismeasured versions of the outcomes, we will address both measurement error and missing data using imputation approaches. These approaches fit models for the outcome of interest conditional on covariates among the nested cohort and use results to predict outcomes in the study population (i.e., survey participants) and the target population (i.e., all PLHIV in care at the study sites). We will report results from the nested cohort alone and after the imputation described above. To better understand the ability of the SmartCare EMR to capture routine NCD covariats and outcomes over time, we will also report the sensitivity and specificity of various measures obtained using the routine data only (assessed using data from the nested cohort as the gold standard) and the distribution of study-collected outcomes in the nested cohort among those with missing routine measurements.

DCE analysis: DCE questionnaire results will be analyzed by the mixed-effects logit model, which is commonly used to analyze DCE data and identify potential preference heterogeneity by the patients’ key characteristics. The mixed-effects logit model calculates the relative mean preference weights per attribute. We will compare models with different random parameters using the Akaike information

criterion (AIC), Bayesian information criterion (BIC), and likelihood ratio tests for goodness-fit-test and select the final model.

***Cost analysis*:** A micro-costing approach will be conducted from a provider perspective. The costing analysis will include the following items: (i) Staff and patient time in clinical settings, (ii) medical supplies and nonmedical consumables per procedure, (iii) type and number of laboratory and other medical investigations, (iv) capital allowance (equipment and buildings) overheads, and (v) administration (including management, M&E). In terms of calculating costs, for staff costs, data from interviews and structured questionnaires will be used to estimate average time input per consultation or procedure type per staff cadre will be used. Appropriate salary data will be used to calculate staff cost for each procedure or intervention. Personnel costs will be drawn from public sector salary scales. Staff time for non-clinical work such as administration, management, M&E shall be calculated using time allocation and staff salaries. Drugs and medical costs shall be based on prescriptions filled out and prices. Names, dosages and quantities of drugs prescribed will be multiplied by respective unit prices to obtain costs of the drug regimen. Where applicable, cost per laboratory test or other diagnostic test and number of tests will be used to calculate the costs of medical investigations for each case. Secondary data on cost per test will also be used where possible. For equipment and buildings, the share of cases in total patient volumes per year will be used. We shall apply standard recommendations on annualization of capital costs in order to obtain the equivalent annual cost using a discount rate of 3% and depreciation periods of 3-5 years for equipment and 30 years for buildings/ construction. All cost items will be aggregated into total costs. Using the outcomes estimated in the study, the average cost per case will be calculated for each intervention and the standard of care.

ii. Qualitative data analysis

We will use content analysis with a deductive directed approach guided by the CFIR and other implementation science frameworks to code, analyse, and interpret our data[104]. Nvivo (QSR International, Melbourne, Australia, version 12) will be used to support data management, coding and analysis. The first step in the analysis, after reading all transcripts, will be to develop initial coding nodes and sub nodes based on the domains and constructs of the CFIR framework, Proctor et al. implementation outcomes,[28] and possibly other frameworks[104]. In the second step, units of analysis, such as sentences or longer semantic units, will be deductively coded into the nodes and sub nodes. Third, the coded text will then be subjected to a rating process based on the recommended method described by the authors of CFIR [102]. A deliberated consensus process will be used to assign a rating to each construct obtained from TASKPEN. The ratings will reflect the valence (positive or negative influence) and the magnitude or strength of each construct that emerged in each Group based on the coded text. When all constructs are obtained from all groups, they will be rated, we will compare ratings for each construct across health facility and patient groups. We will use criteria described by CFIR developers and adapted by Gee, P.[104]

The participation of one versus multiple coders in the qualitative analysis process will depend on the volume and complexity of the data. All audio-recordings from IDIs and FGDs will be translated and transcribed directly into English in one step (in Microsoft Word) incorporating expanded field notes. The note-taker fluent in all three languages will compare transcripts to audio-recordings and assess them for accuracy, completeness and compliance with formatting requirements. Any anomalies will be addressed by the interviewer or facilitator supported by field notes. Transcripts will be transformed into projects for coding in Nvivo QSR™, which will be used to sort and organise the data to enable Framework analysis and subsequent interpretation. A thematic framework will be developed for data analysis using both inductive reasoning based on emerging themes and deductive reasoning based on *a priori* themes to capture factors that facilitate and hinder linkage to care. For IDIs and FGDs, two

independent coders (interviewer and facilitator) will code two transcripts each to refine and validate the codes and then another three transcripts each to achieve consistency in coding. They will code the remaining transcripts independently. All qualitative data will be indexed by themes as well as cases (type of respondent, gender, urban/rural, district). The analysis team will also apply a modified grounded theory perspective and will note contradictions and points of convergence in analytic memos. Indexed data will be put into matrices embedded with Nvivo corresponding to the *a priori* program inquiries on facilitators and barriers, clearly identifying the source of the data. These matrices will help identify links between theme, patterns and inherent evidence in extracted quotes. Such mapping will provide explanations that are used to develop recommendations that reflect participants' lived experiences, and perceived needs and preferences for linkage to care. Triangulation and use of multiple analysts will minimize bias in the qualitative inquiry.

9. Ethical Considerations

a. Overview

As we propose to implement MOH-recommended HIV/NCD integrated services, the risks incurred with the study activities described herein are minimal. The principal risk involved is the possibility of an inadvertent disclosure of confidential patient health information, which could include HIV status, or a minimal risk of bruising or infection from blood draws that are no different than what is encountered in routine clinical practice. At all steps of the study, we will protect participant privacy and confidentiality to reduce this risk.

This protocol will obtain ethical and regulatory approvals from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) and the University of North Carolina Internal Review Board (UNC IRB). The study team will also receive an approval letter from the Ministry of Health, National Health Research Authority. All staff who have contact with participants will receive training on the protection of human research participants prior to participating in the study.

b. Non-human subjects research activities

A number of data collection activities do not involve direct interactions with participants and are not intended to generate generalizable knowledge, namely: health facility assessments/ structured observations, costing surveys, and theatre testing. Rather, these data collection activities are intended to refine the TASKPEN package or understand its implementation in a specific, local implementation context to inform routine healthcare services.

For structured observations, since they seek to understand the scope and manner in which services are provided in a specific local context and no direct participant interactions or data collections will occur, we are seeking a non-human subjects research determination. Similarly, for costing surveys, since the goal is to collect information about the commodities, staffing, and other programmatic inputs into NCD care and services in the public sector, and no personal or otherwise identifying information will be sought or recorded, we are seeking a non-human subjects research determination. Finally, for theatre testing, since this seeks to collect information about the feasibility, acceptability, and appropriateness of modification of modules of the national SmartCare EMR, and no personal or otherwise identifying information will be sought or recorded from participants, we are seeking a non-human subjects research determination.

c. Informed consent

Discussions with prospective participants and informed consent procedures will be conducted in private

to protect confidentiality. Data collection team members will obtain written informed consent from all participants prior to completing research activities. The procedures, risks, and benefits will be discussed and the research team swill answer all questions prior to obtaining consent. Consent forms for patients (e.g., nested cohort and IDI participants) will be translated into the two most common local languages in Lusaka (Bemba, Chinyanja,) and back-translated into English to assure accurate translation. All versions of the consent forms will be approved by the relevant ethics committees prior to study initiation. For illiterate participants, a literate, impartial witness will be present during the entire consent process to ensure that all of the relevant information has been provided and the participant voluntarily gives consent. A comprehension question checklist will be used for all informed consent discussions involving nested cohort participants to evaluate and document understanding of study procedures and risks and benefits.

d. Confidentiality

Measures will be taken to ensure safety of data and confidentiality of all our study participants. The tablets together with audio tapes, field notes, and all other materials will be kept in a locked, fireproof safe cabinet at study clinics and CIDRZ headquarters. No participants nor health facility will be identified in any report or publication about this study. However, for quality control and safety purposes, collected data may be reviewed by the sponsor of this study, the ethical and regulatory committees at the University of North Carolina at Chapel Hill or the University of Zambia. Data will be stored on the CIDRZ secure server in Lusaka.

e. Potential risks

Since what we propose is consistent with recommended routine health services, just implemented with improved efficiency and fidelity, we do not expect major risks from the study participants beyond what patients experience during routine care or normal service provision. The principal risk to study participants is the possibility of an inadvertent disclosure of confidential health information. This risk will be minimized through training and supervision of all study staff. The confidentiality of all study records will be safeguarded to the maximum extent possible. To provide protection to all study participants, data security measures will be strictly adhered to, including the de-identification of data for analysis purposes and the storage of data on secure, password-protected and encrypted computers. All data analyses will be done on datasets that include the study number as the only unique identifier. We expect these procedures to adequately protect the confidentiality of participants' health information.

Phlebotomy conducted during patient surveys carries a small risk of pain, bleeding, bruising, and infection. The magnitude and likelihood of phlebotomy risk is consistent with those normally encountered during the course of routine medical care for healthy persons.

The topics covered in the interviews, FGDs/ implementation surveys, KIIs, and DCEs pertain to participants' experiences providing or receiving services, their experiences implementing interventions, or their preferences surrounding services, but some participants may feel uncomfortable with some questions. All participants will be informed during the consent process, and again during data collection activities, that they can refuse to answer any question they do not wish to answer or to end the interview at any time without penalty.

Coming into close contact with study team members can put participants at risk for COVID-19. All participants will be informed of this risk during the recruitment and consent processes. When appropriate and necessary, qualitative data collection for FGDs and KIIs may be done over a secure HIPAA-compliant Zoom web conferencing line to minimize direct participant contact, particularly during times when local COVID-19 public health restrictions are in place.

f. Protection against Risks

Discussions with potential participants, including informed consent procedures, will be conducted in private to protect confidentiality. Trained data collection staff will obtain written informed consent from eligible participants where needed. The procedures, risks, and benefits of participation will be discussed and all questions will be answered prior to obtaining consent.

To minimize phlebotomy risks, the following measures will be taken: (1) finger pricks will be used whenever possible; (2) only clinically trained study nurses and/or clinicians will perform or support phlebotomy activities, and only trained research staff supervised by the study QA/QC nurse will perform finger pricks; (3) the MPIs will review with study staff how to properly conduct study procedures involving blood sampling; (4) sterile technique will be used for all blood sampling; and (5) we will seek to obtain specimens at the fewest number of time points and with the smallest volumes possible.

Risks to the participant will be minimized by thorough training and supervision of all team members. All study data and forms will only be identified by a coded number to maintain participant confidentiality. All databases and digital audio files will be secured with password-protected access systems, and computer entries will be identified by coded number only. Forms, lists, appointment books, audio-recordings, and any other listings or data forms that link participant ID numbers to other identifying information will be stored in a separate, locked cabinet. All data analysis will be done on a de-identified data set or interview transcripts, which have only the participant number as a unique identifier and have removed any identifying information. It is expected that these procedures will adequately protect participant confidentiality. All study procedures carry minimal risks.

In light of COVID-19, the study team will follow MOH guidelines to protect study participants from COVID-19.[105] This includes providing and using personal protective equipment and following the procedures described above. A COVID-19 information sheet will be added to the consent process to ensure that participants are aware of potential risks and how to protect themselves. Participants will be reminded that their participation is voluntary.

g. Potential benefits

Participation carries the possibility of direct benefit to participants, including receiving free screening and diagnostic testing, and linkage to care and treatment, for highly morbid cardio-metabolic NCDs during patient surveys. Nested cohort participants who have disengaged from care who are contacted by trained study staff may decide to re-engage in HIV and/or NCD care and will receive support from study staff to do so. Future patients, and in some cases the individuals providing data themselves, may benefit if the study reveals ways to improve NCD/HIV care integration and the management of cardio-metabolic complications of HIV.

Knowledge gained from the research may serve to improve the health status of HIV patients living with NCDs. The knowledge gained from the research may also provide the government and its partners the necessary information for improving multi-sectoral NCD programs, resulting in a healthier, more productive population.

h. Consent process

For the patient surveys, study personnel will only have a one-time contact with participants, unless those participants are recruited for, and enrol in, the nested cohort and thus undergo longitudinal follow up in the study. For the nested cohort component, study personnel will have contact with individuals at the time of the baseline patient survey, and then again at about 2 weeks and about 3-, 6- and 9-months

later. For both the patient survey and nested cohort, informed consent procedures will take place as detailed under section c “informed consent” above.

For review of existing, de-identified routine NCD- and HIV-relevant data at the pilot sites, we believe a waiver of written informed consent for this component is justifiable for the following reasons: 1) the proposed review of existing, routinely collected and de-identified aggregate health data involves no greater than minimal risk, with the principal risk being potential harm from an inadvertent breach of confidentiality, for which we will institute multiple confidentiality protections to safeguard the data; 2) omitting the consent form would prevent creation of the only study-specific document that could link the participant to the research; 3) waiving written informed consents will not adversely affect the rights and welfare of individuals who have their data reviewed; and 4) conducting the quantitative component could not practically be carried out without the waiver. Permission to review individual patient data will be sought from the relevant local and international IRBs, and the MOH through protocol review procedures under the National Health Research Authority.

For FGDs and the ensuing implementation survey, participation will be completely voluntary and subject to verbal informed consent (see **Appendix**). During the informed consent process, we will make sure that NPHWs such as nurses and community health workers/ peer health educators who may be employed by MOH or a study partner know that they do not have to participate if they don’t want to and that their decision to join the study or not will in no way affect their employment or status with their employer. We will also emphasize to all NPHW participants that we will safeguard and anonymize their individual responses to minimize the risk that what they say becomes known to their employer or colleagues. Study staff will make it clear that participants do not need to answer questions that make them feel uncomfortable. All consenting participants will be provided an information sheet. No signature page will be collected from FGD participants to avoid creating documentation that connects the participants to the research.

For IDIs and KIIs, participation will be completely voluntary and subject to written informed consent in the participant’s choice of English, Nyanja, or Bemba. During the informed consent process for IDIs, study staff will review and verify with potential participants their routinely collected locator information already on file with their health facility. In addition, study staff will explain to potential IDI and KII participants during the consenting process that the interview will be audio-recorded, and that individuals who do not wish to have their voice recorded during the IDI will be ineligible to participate. Staff will also explain that participants do not need to answer any question that makes them feel uncomfortable. (see **Appendix**).

All participant information sheets for the patient surveys, nested cohort, patient IDIs, and FGDs involving lay health providers/ community health workers will be prepared in simple English then translated into Bemba and Nyanja by a professional translator who is a native speaker of the target language. The translated information sheets will then undergo back translation to ensure accuracy, consistency, and understandability of the translations. The participant information sheet will explain the purpose of the specific study procedures, its processes, inclusion and exclusion criteria, risks, benefits if any, and provide assurance of privacy and confidentiality. Further the participant information form will explain the meaning of participation; that participation is completely voluntary, and that participants have the right to withdraw at any time and with no penalty.

At encounters for the patient survey, nested cohort, patient IDIs, and lay health provider/ community health worker FGDs, staff will provide participants with the information sheet in the language of their

choice (*Bemba, English, Nyanja*), reading the form to those who are unable to read. After this process, they will paraphrase each paragraph for all participants to ensure that main points are understood. They will invite and answer questions and ask if the participant is willing to participate. If willing, study staff will obtain their signature as required. Participants will be asked for permission to be audio-recorded during IDIs, KIIs, and FGDs, as appropriate, for later transcription and analysis. Participants will receive a nominal reimbursement (ZMK 100, equivalent to ~$USD 5) after completing study activities/ visits. No reimbursement will be offered for structured observation as these will take place during the course of routine service delivery and will not require additional activities on the part of participants.

i. Physical Risks

Phlebotomy conducted during the patient surveys carries a small risk of pain, bleeding, bruising, and infection. The magnitude and likelihood of phlebotomy risk is consistent with those normally encountered during the course of routine medical care for healthy persons.

j. Psychosocial Risks

Participants may become embarrassed, worried, anxious, or uncomfortable when discussing sensitive topics during FGDs, IDIs, or KIIs. Study staff will be trained how to identify and mitigate issues that may cause psychosocial distress, and how to refer to free counselling services available at MOH health facilities and in the community.

There may be a small risk of social harm involved with contacting study participants by phone or in-person or approaching potential patient participants for procedures at the health facility. For example, if a member of staff were to inadvertently disclose confidential health information when speaking to a friend or relative who answered the phone for the number listed for a participant, this could cause stigma, discrimination, or social harm to the potential participant. These issues notwithstanding, we will take several steps to minimize these risks.

k. Methods to Minimize Risk

To ensure that confidential health information is not inadvertently disclosed during phone or in person contacts with potential participants, we will train all staff on the use of a standardized recruitment script (Appendix D.i).

All participants will be instructed during the informed consent process that they may discontinue any study procedure, including procedures for the patient surveys, nested cohort, IDIs, FGDs, DCEs, and KIIs at any time for any reason, such as experiencing psychosocial stress related to any question(s). Risks relating to psychological discomfort will be further minimized by: 1) reducing respondent burden through streamlining of IDI and FGD guides; and 2) referring participants to appropriate counselling, as necessary. We do not anticipate that focus group discussions, and KIIs will pose any risk of psychological discomfort to stakeholders beyond that encountered in the course of everyday professional conversations. However, with FGDs, since they will be in a discussion with several of their co-workers, there is a chance that what they say could get back to their co-workers, and potentially even their supervisors. Thus, due to the presence of work colleagues in FGDs and the potentially sensitive nature of questions surrounding perceptions of the functionality of the health system, we will ensure through a comprehensive written informed consent process that participants are aware of: 1) their right to withdraw; 2) their right to not respond to any question(s) they do not wish to answer; 3) the fact that their responses will not be linked back to them in any way or shared with their employers or supervisors; 4) the fact that FGD participants will be encouraged to not share anything said outside the focus group; and 5) the fact that their decision to participate or not participate in the study will in no

affect their standing or employment with the study site/ health facility, their employer, MOH, or CIDRZ.

We will strive to minimize the risk of unintended confidentiality breeches involving study-related information by: 1) conducting all study procedures in private settings that are conveniently located for participants such that all information is kept strictly confidential and not inadvertently disclosed to anyone not involved in the study activity; and 2) engaging existing MOH and CIDRZ program providers to continue offering routine stigma mitigation messaging.

All electronic and paper information reviewed or collected during the course of this study will be kept securely and confidentially and will only be handled by designated study personnel appropriately trained in the management of these data. Information entered into the study database will be kept separately from participant identifying details and protected by a password. Indeed, data security measures will be strictly adhered to, including the immediate de-identification of all data prior to analysis but after linking disparate data source across time in the final database. All data will be stored on secure, password-protected servers and encrypted computers and tablets.

Participant information will remain confidential at all times, unless we are required by law to release information. Reports about the study and results that may be published in scientific journals will not include any identifying information that would allow participants identities to be revealed or deduced.

l. Anticipated Benefits to Participants

There may be no benefit to individuals who participate in this study. However, participation in the patient survey carries the possibility of newly diagnosing undetected cardio-metabolic NCDs such as hypertension, diabetes, and dyslipidaemia, and linking these individuals to treatment and care at the study sites. If the study reveals ways to improve NCD/HIV care integration and the management of cardio-metabolic complication of HIV, then future patients, and in some cases the individuals providing data themselves, may benefit.

m. Handling of Unexpected or Adverse Events

i. Response to new or unexpected findings and to changes in the study environment

Any new, unexpected finding or change to the HIV programme operational environmental will be resolved in consultation with MOH.

ii. Identifying, managing, and reporting adverse events

Adverse events related to implementation of the TASKPEN pilot will be minimized through study mentors and facility-based champions who are experienced in providing integrated services. Study team members will report any unfavourable or adverse findings, especially in regard to quality of care, immediately to the MOH for consideration of remedial action. All health-related emergencies will be handled as per clinic guidelines, including management of abnormal vital signs and laboratory values identified through the patient surveys. The study QA/QC nurse and study clinical scientist/ doctor will be available to act immediately on these abnormalities, including to offer patient counselling, provide warm "handoffs" to clinical staff, refer patients for acute care at the study sites, and prescribe appropriate outpatient treatment for non-acute issues in cases where MOH staff are not available (e.g., after business hours).

No adverse events are anticipated as part of this study, as we are not testing any investigational interventions, pharmaceutical products, or medical devices. The most serious—but unlikely—adverse event would be related to inadvertent disclosure of confidential information. However, several measures

will be taken to safeguard against this risk, including the de-identification of analytical datasets, strict adherence to confidentiality procedures, and safeguarding study participant privacy at all times.

Any adverse events associated with the study will be handled by the MPIs and senior study staff and will be reported immediately to all regulatory authorities overseeing the study. We will utilize the HLB-SIMPLe project-wide Data Safety Monitoring Board (DSMB) led by the Research Coordinating Center (RCC) at Washington University in St. Louis, USA, and supported by NIH, for reporting purposes on general AEs, serious AEs (i.e., SAEs), unanticipated problems involving risks to subjects or others (UPIRSOs), protocol violations and non-compliance and social harm information. We will use the following procedures in the event of an AE, SAE, UPIRSO, protocol violation, or instance of non-compliance or social harm. In the case of any of these instances, the research team will alert the MPIs immediately (same day). Subsequently, the MPIs will report all SAEs or suspected UPIRSOs by an expedited written report sent via email to NHLBI and the DSMB chair or designee/ representative within 24hrs of the MPI's awareness of the event. The DSMB chair or representative, when necessary in conjunction with the full DSMB, will review reports and decide whether the event meets the definition of an unanticipated problem increasing risks to subjects or others. Events that meet these criteria will be considered unanticipated problems involving risks to participants or others, and will be reviewed by the convened, full DSMB. Copies of the written report will also be sent to UNZA BREC and the UNC IRB within 10 working days (with one exception) of events that meet the definition of an unanticipated problem involving risks to subjects or others. The exception is if the SAE involved death and indicates that participants or others are at increased risk of harm. In such a case, the MPIs will be required to submit a report to UNZA BREC and the UNC IRB within 3 working days. Any suspension or termination of IRB approval will include a statement of the reason(s) for the action and will be reported promptly to the NIH PO within 3 business days of receipt. In cases of protocol violations, staff re-trainings and other remedial actions will be taken by the MPIs in coordination with the RCC, CIDRZ Research Operations Department, and NIH, as appropriate.

CIDRZ holds organizational policies and procedures for the safety and security of its personnel and of the clientele with which CIDRZ employees interact during professional activities. Since the evaluation falls within the scope of CIDRZ's typical professional activities, these organizational policies and procedures will be relevant.

10. Sponsor Monitoring

The U.S. National Institutes of Health (NIH) is the primary sponsor for the study. As the sponsor, NIH may conduct monitoring or auditing of any study activity to ensure the scientific integrity of the study and to ensure the rights and protection of study participants. Monitoring and auditing activities may be conducted by any of the following individuals and parties: NIH staff ("internal"); Authorized representatives of NIH (e.g., a contracted party considered to be external"); Both internal and external parties.

Monitoring or auditing may be performed by on-site visit carried out at CIDRZ or study facilities or through other means of communications such as telephone calls or written correspondence. During the visit, any study-related materials may be reviewed and the MPIs, and other investigators, along with the study staff should be available for discussion of findings.

To ensure good clinical practice and compliance with national and international regulatory guidelines, the study may also be subject to inspection or review by authorized Zambian or international regulatory authorities, including the UNZA BREC, NHRA, UNC IRB, and UAB IRB.

11. Dissemination of Findings

All reports and publications of collected data will be presented in aggregate form only. The names or other identifiers of participating individuals will not be presented in any publication. Reports will be written so that no person may be individually identified, even indirectly. Results will be disseminated locally to the participating clinics, key stakeholders, including US government partners, and the Ministry of Health. Results from this study will also be presented at national, regional, and international meetings, and submitted to international peer-reviewed journals.

Study findings will be made available through appropriate local and international channels, including academic and public health research symposia. One or more publications will also be submitted to a peer-reviewed journal

12. Timeline

Milestone Plan for the TASKPEN Stu	Year 1												Year 2											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Sub-award and contracts	x	x	x																					
Protocol development		X	X	x	x																			
Ethical review			X	X																				
Recruitment & Hiring		X	X	x																				
Establishing Technical Advisory C (TAC)			X	X																				
Team orientation and training			X	X	X	X	x																	
Adaptation consultation with stak National NCD Working Group, Scientists, global actors & Others						X	X	X	X															
Validation and consolidation of the tools and guidelines						x	x	X	X	X														
Develop SOPs based on guidelines						x	x	x	X	X	X													
Baseline assessment								x	x	x	X	X	X											
Pilot implementation											x	x	x	X	X	X	X	X	X	X	x	x		
Final evaluation of pilot																				X	X	X	x	x
Dissemination & Consultative process planning																						x	X	X

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14. Appendices (Please see attached supporting documents folder)