UNIVERSITY OF NAIROBI

NON-COMMUNICABLE DISEASES (NCDS) BURDEN AMONG PEOPLE LIVING WITH HIV/AIDS (PLHIV) IN KENYA

BY

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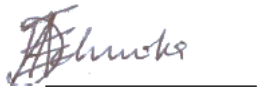
Declaration

In submission of this PhD thesis, I acknowledge that it is my original work. No part of this work has been submitted by myself, or by other persons to other institutions for other academic awards.

Signed:  **Date**: 19th November 2021

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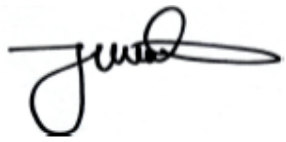
Prof. Julius O. Oyugi, MSc, PhD[1,2] University of Nairobi, Institute of Tropical and Infectious Diseases, P.O. Box 19676 – Nairobi-00202 Email: julias.oyugi9@gmail.com		19th November 2021
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Dedication

To my Children: Leon, Neema and Cyril,

As we seek to meaningfully impact society, may this work serve to inspire you and validate the traditions of intellectual integrity and excellence that we espouse as a family.

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Research Outputs

Published Work:

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Achwoka, D., Oyugi, J.O, Mutave, R., Munywoki, P., Achia, T., Akolo, M., Muriuki, F., Muthui, M., Kimani, J. High prevalence of non-communicable diseases among key populations enrolled at a large HIV prevention and treatment program in Kenya. *PLOS One*

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Submitted Articles

Achwoka, D., Mutave, R., Oyugi, J.O, Walubwa, J.A, Achia, T. A Systematic Review of Noncommunicable Disease Care Integration within HIV Care and Treatment Settings in Sub-Saharan Africa, 2013 -2018. *Global Health: Science and Practice*

Oral and Poster Communication:

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List of Abbreviations and Acronyms

AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine aminotransferase
ANC	Antenatal Clinic
ART	Anti-retroviral Therapy
BMI	Body Mass Index
CD4	Cluster of Differentiation 4
CTX	Co-trimoxazole
CDC	US Centers for Disease Control and Prevention
DICEs	Drop-In Centers
DM	Diabetes Mellitus
FDC	Fixed Dose combinations
FP	Family Planning
HAART	Highly Active Antiretroviral Therapy
HB	Hemoglobin
HPTN	Hypertension
HI	Human Immunodeficiency Virus
ICF	Intensive Case Finding
INH	Isoniazid
IPD	Inpatient Department
KP	Key Population
LSTIK II	Longitudinal Surveillance of Treatment in Kenya II
MCH	Maternal and Child Health

MOH	Ministry of Health
NASCOP	National AIDS and STI Control Program
NCD	Non-communicable Diseases
NRTI	Nucleoside Reverse Transcriptase Inhibitors
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitors
OI	Opportunistic Infection
OPD	Outpatient Department
PMTCT	Prevention of Mother to Child Transmission
PI	Protease Inhibitor
PLHIV	People Living with HIV AIDS
QA/QC	Quality Assurance/Quality Control
RNA	Ribonucleic Acid
SSA	Sub Saharan Africa
STI	Sexually Transmitted Infections
SWOP	Sex Workers Outreach Program
TB	Tuberculosis
UECs	Urea Electrolytes and Creatinine
VCT	Voluntary Counselling and Testing
VL	Viral Load
WHO	World Health Organization

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ABSTRACT

Introduction: People living with HIV (PLHIV) in Kenya are disproportionately affected by non-communicable diseases (NCDs) yet care is suboptimal.

Objectives: This study sought to determine burden of NCDs among PLHIVs in Kenya and assess benefit of NCD integrated care within HIV settings.

Materials and Methods: This study was nested and involved a component of systematic literature review and use of secondary data. For general population PLHIV data was drawn from the national longitudinal surveillance of treatment study (LSTIK II) derived from 50 comprehensive care clinics in Kenya, while key population PLHIV was drawn from Sex Worker Outreach Program (SWOP) clinics key population program in Nairobi. For LSTIK II (2003-2013), 3,340 patient records were obtained through a multistage sampling design while all 2200 patient records for SWOP (2012-2015) were considered.

Statistical Analyses: Among general population clients, we assessed distribution of NCDs by ART status and calculated incidence rate ratios for selected baseline demographic and clinical characteristics and incidence/1000 person years by ART status. We estimated prevalence of four NCD-categories among KPs, assessed distributions of co-morbidities using Chi-square test and conducted multivariate analysis to identify factors associated with NCD diagnoses.

Results: *General Population PLHIV:* We analyzed 3170 patient records; 2115 (66.3%) were from women. Close to two-thirds (63.9%) of PLHIVs were on ART. The proportion of any documented NCD among PLHIV was 11.5% (95% confidence interval [CI] 9.3, 14.1), with elevated blood pressure as the most common NCD (87.5%) among PLHIV with diagnosed NCD. At one year of follow-up 43.8% of PLHIV not on ART had been diagnosed with an NCD compared to 3.7% of patients on ART; at five years the proportions with a diagnosed NCD were 88.8% and 39.2% ($p<0.001$), respectively.

HIV-infected Key Populations: Overall, 1,478 individuals' records were analyzed; 1,392 (94.2%) FSWs and 86 (5.8%) MSMs. A total of 271, 18.3% (95% CI 16.4 -20.4%), HIV-infected KPs had an NCD diagnosis in their clinical records; 258 (95.2%) being from FSWs. Some form of cardiovascular disease (CVD) was present in 249/271, 91.8%, of KPs with a documented NCD. Chronic respiratory disease was present in 16/271, prevalence of 1.1% (95% CI: 0.62 – 1.75). Cancer was in 10/271, prevalence of 0.7% (95% CI: 0.32 -1.24). Diabetes was not reported. Significant associations between NCD diagnosis and increased age, unemployment status, BMI and CD4 of NCD diagnoses ceased on adjusted analyses.

Systematic Review: We identified 49 eligible studies. In 23 (46.9%) studies. Twenty-four (49.0%) studies were conducted among HIV-infected individuals at HIV clinics, 16 (32.7%) in general clinics, 6 (12.2%) integrated community-based screening, 2 (4.1%) applied differentiated-care models and 1 (2.0%) was at population level. For NCDs, positive outcomes of early screening and identification that forestalled complications associated with NCD progression were identified.

Conclusion: We provide estimates and draw attention to the high prevalence of NCDs among PLHIV – general and key populations living with HIV. We offer recommendations on leveraging on comparably formidable HIV healthcare delivery platforms through NCD/HIV care integration for service delivery to address the high prevalence of NCDs.

CHAPTER ONE: INTRODUCTION

Over the last decade, there have been concerted efforts at stalling the HIV epidemic – the largest communicable disease epidemic in sub-Saharan Africa (SSA). During this period, there has been an unprecedented growth globally in the coverage of HIV care and treatment programs. Global Health funding and investments towards HIV/AIDS control have also significantly risen over the years. Further, several advances in HIV research have led to expanded eligibility criteria for initiation of antiretroviral therapy (ART) to people living with HIV (PLHIV). As a result, several countries in SSA have benefited through resultant strengthened health systems. The net effect therefore, has been favorable HIV treatment outcomes with increased longevity for PLHIV.

Yet, against this optimistic backdrop, non-communicable diseases (NCDs) burden has continued to rise steadily. At a global scale, the World Health Organization (WHO) estimates that 41 million NCD-related deaths occur annually. Three quarters of these deaths are in the low and middle-income countries, presenting a disproportionate morbidity and mortality burden. Between 2000 and 2016, four major NCDs - **cardiovascular diseases** (CVDs) - including hypertension, heart attack and stroke, **cancer**, **chronic respiratory diseases** (including asthma) and **diabetes mellitus** contributed to 80% of the global NCD burden and 75% of premature deaths (WHO, 2018c). These four conditions form the underpinnings of this thesis on the merit that they make the largest contribution to both morbidity and mortality. NCDs now stand out as a leading cause of both morbidity and mortality contributing heavily to the global burden of disease.

Traditionally characterized as mainly having a communicable disease epidemic, Africa now faces a new challenge of a dual disease burden; communicable and non-communicable diseases. Home to over half of estimated PLHIV worldwide, SSA is now at crossroads. Despite increased donor funding in HIV care services, health systems across the region have remained fragile owing to the siloed approach to health programming. Many countries have now picked the call from WHO to respond urgently to the rising NCDs epidemic by attempting to leverage on investments from the HIV programs. Several

countries have now embraced multi-tasking of health care workers (HCWs) and integration of NCD services with HIV service delivery as response strategies. Countries such as Kenya have moved forward and anchored multi-tasking and task shifting among health care workers in their health policy frameworks by developing task sharing policy guidelines to assist managers in utilizing skills of different cadres of health care workers.

Statement of the Problem

Although Kenya has made strides by having an NCD policy, there is paucity of knowledge on the burden of NCDs, particularly the four aforementioned NCDs (CVD, CRD, cancer and diabetes) among PLHIVs and sub populations such as key populations who face the dual burden of disease. Several studies in Kenya have been conducted among PLHIV to determine NCD burden (Bloomfield et al., 2011; Khabala et al., 2015; Venables et al., 2016). However, these have been localized to urban and peri urban centers. They have also focused on one or two disease entities. A recent modelling study by National AIDS Control council and Imperial college London, provided a somewhat comprehensive picture of NCD burden among PLHIV (G. o. K. Ministry of Health, 2019). Therefore, there still remains a need for clear empirical data on the burden of NCDs at a national level, both among general population PLHIV and key population PLHIV, to inform robust health policy decision-making and implementation considerations in order to provide comprehensive quality care for PLHIV.

Significance of the Study

Through this work, we will add to the sparse data on prevalence and incidence on NCDs among PLHIVs including PLHIV who are key populations in SSA (Vorkoper et al., 2018). Secondly, with a burgeoning PLHIV population on lifelong ART treatment due to expanded eligibility criteria we provide important insights that will foster improvement in the HIV-NCD chronic care model integration and scale up (Kemp et al., 2018). Lastly, we add to the ever-growing NCDs research agenda with a call for programs to set up surveillance systems for NCDs among PLHIV (El-Sadr & Goosby, 2018; Vorkoper et al., 2018). As Kenya seeks to achieve ambitious UNAIDS 90-90-90 goals through

expanded treatment, strategies that ensure continued traction of health gains for PLHIVs against a backdrop of a rising burden of NCDs need to be developed (Matanje Mwagomba et al., 2018).

Scope of the Study

This study will utilize retrospective cohort data of PLHIV patients attending care in 2003-2013 from a nationally representative sample - Longitudinal Surveillance of Treatment in Kenya II (LSTIK II). Additionally, data on PLHIV who are key population will be from the University of Manitoba Prevention Nairobi Program for the period 2012 – 2015.

RESEARCH QUESTIONS

a. Does integration of NCD care within HIV settings result in improved NCD, HIV prevention, treatment and care outcomes for PLHIV?
b. What are the characteristics of the NCD burden among PLHIV attending general population ART clinics in Kenya?
c. What are the characteristics of the NCD burden among PLHIV attending key population drop in centers and ART clinics at a large key population program in Nairobi Kenya?

Four leading NCDs (cardiovascular diseases (including hypertension, heart attack and stroke), cancer, chronic respiratory diseases (including asthma) and diabetes mellitus) that contribute to the highest morbidity and mortality among PLHIV will be used to characterize NCD care in HIV settings. Outcomes from a systematic review of literature across several databases (Medline, Embase, Global Health, Scopus and Cochrane library) for the period 2000 - 2018 will be used to assess benefit of NCD-HIV integration.

RESEARCH HYPOTHESES

Owing to its retrospective design and the secondary nature of the data to be utilized, this study does not lend itself to hypothesis testing. There are no hypotheses set apriori (BMJ, 2018).

OBJECTIVES

Broad Objectives

a) To determine the burden of NCDs among PLHIVs in Kenya – both general and key populations
b) To assess the benefit of NCD integrated care within HIV settings with a view to informing implementation considerations for NCD care delivery in ART clinics.

Specific Objectives

a) To assess outcomes of integration of NCD care within HIV settings by conducting a systematic review of literature across several databases (Medline, Embase, Global Health, Scopus and Cochrane library).
b) To characterize NCD burden of the four leading NCDs that lead to the highest morbidity and mortality among PLHIV attending general population ART clinics in Kenya.
c) To characterize NCD burden of the four leading NCDs that lead to the highest morbidity and mortality among PLHIV attending key population program drop-in centers (DICEs) and ART clinics at a large HIV prevention, care and treatment program in Nairobi, Kenya

STUDY RATIONALE

Despite commendable initiatives to improve the care of PLHIV, the attention provided to NCDs has been largely inadequate. Owing to donor restrictions, many HIV programs are averse to meeting costs of NCD care even for PLHIVs. With fragile health systems and weak supply chains, many SSA countries such as Kenya are unable to meet the needs of patients suffering from NCDs.

Further, with a shrinking resource envelope, and incessant pressure from donors to embrace public health approaches such as differentiated care models, the future care of NCDs among PLHIVs continues to be uncertain.

The purpose of this study is to feed into the NCD research agenda for PLHIV. I will focus on the four major NCDs that contribute to 80% of NCD burden (CVD, CRD, cancer and diabetes). Currently many

gaps exist in the literature on what the quality-of-care PLHIV with NCD diagnosis receive. Additionally, through this research we hope to provide insights on strategies of leveraging NCD care among PLHIV on chronic HIV care models as part of health systems integration and strengthening.

CHAPTER TWO: LITERATURE REVIEW

Globally, the last decade has witnessed an unprecedented growth in the coverage of HIV care and treatment programs. Expanded criteria and early initiation of highly effective antiretroviral therapy (ART) for people living with HIV (PLHIV) has been associated with increased longevity, improved rates of viral load suppression and generally favorable treatment outcomes overall (El-Sadr & Goosby, 2018; WHO, 2016b). Incidentally, over the same period, noncommunicable diseases (NCDs) have simultaneously risen steadily to be the leading cause of death globally (WHO, 2018a).

Global Burden of NCDs

In 2016, NCDs were responsible for over 71% (41 million) of the world's 57 million deaths (WHO, 2018a). Thirty six percent of mortality cases from NCDs were considered premature since they occurred among individuals aged between the ages of 30 to 70 years. Low and middle-income countries (LMICs) bore a disproportionately huge mortality burden contributing to 78% of all NCD deaths and 85% of premature deaths worldwide, especially among the poorest and most vulnerable (Bennett et al., 2018; WHO, 2018c). In the general population, four major NCDs - cardiovascular diseases (CVDs) - including hypertension, heart attack and stroke, cancer, chronic respiratory diseases and diabetes mellitus make the largest contribution to both morbidity and mortality(WHO, 2013b).

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017 study findings reveal that the largest contribution of global disability adjusted life-years (DALYs) between the period 2007 and 2017 was from NCDs at 62% of total DALYs (Kyu et al., 2018). This was a sharp increase by 40% over the 10-year duration. The greatest number of DALY counts were estimated for ischemic heart disease (170 million), stroke (132 million) and chronic obstructive pulmonary disease (81 million) that contributed to 15% of all DALYs (Kyu et al., 2018). With age and sex specific disaggregates, GBD 2017 has revealed increased trends of NCD-associated mortality and DALYs among both males and females.

Global Action plan

The launch of the Global Action Plan for the Prevention and Control of NCDs 2013 – 2014, was a significant endorsement towards concerted efforts aimed at the control of the NCD pandemic (WHO, 2013b). Through the implementation of this action plan, it was envisioned that countries would support realization of nine voluntary NCD targets by 2025. Countries would also make significant strides towards attainment of Sustainable Development Goal (SDG) 3 on promoting health and well-being for all at all ages. Specifically, this would be in line with the SDG 3 target 4 that seeks to reduce premature mortality from NCDs by a third through prevention and treatment and also promoting mental health (Bennett et al., 2018; UN, 2018)

Further, countries signed up to achieve nine voluntary NCD targets by the year 2025 (WHO, 2013c). The main target called for a 25% relative reduction in the overall mortality from the four main NCDs (cardiovascular diseases, cancer, diabetes and chronic respiratory diseases), and a similar reduction or containment of the prevalence of raised blood pressure as per national circumstances. The rise of diabetes and obesity were to be halted. Additional targets included achieving at least 10% relative reduction in the use of alcohol, and prevalence of insufficient physical activity. A 30% reduction in mean population intake of salt and a similar reduction in the prevalence of current use in persons 15+ years. The final two targets focused on the health system's national response. This involved placing at least 50% of eligible people on drug therapy and counseling to prevent heart attacks, and having an 80% availability of affordable basic technology and essential medicines required to treat the major NCDs in both private and public facilities.

The nine voluntary targets were underpinned on a global monitoring framework to track the implementation of the nine global targets against a 2010 baseline. Countries would set national NCD targets for 2025, then develop multi-sectoral national NCD plans with an aim of reducing exposure to risk factors and facilitating a robust health system response. Countries would then finally measure results against the Global Action plan (WHO, 2013b).

Predisposing Factors and 'Best-Buys'

The GBD 2017 attributes over half of all NCD deaths to four risk factors: high blood pressure, smoking, high blood glucose and high body-mass index (Kyu et al., 2018). Obesity prevalence has risen in almost every country including LMICs leading to more than a million deaths from type 2 diabetes (Kyu et al., 2018). Fueled by increased urbanization and adoption of western lifestyles the surge of NCD risk factors has been relentless. In a bid to help countries adopt a comprehensive strategy to mitigate the burden of NCDs, WHO further broadened the 4 x 4 classification of the classic NCD risk factors to a 5 x 5 matrix. Four risk factors shared among the four main NCDs include tobacco use, unhealthy diets, physical inactivity and harmful use of alcohol. With an extension to the 5x 5 matrix, mental health was included as the fifth NCD and environmental air pollution as the fifth shared risk factor (WHO, 2018c).

The WHO further proposed 16 interventions, referred to as 'best buys', for countries' implementation based on their circumstances. Using a base year of 2010, these 'best buys' have a potential to avert 9.6 million deaths by 2025 worldwide (WHO, 2013b, 2018d) and 1.13 million deaths from cardiovascular diseases in 20 LMICs (Bertram et al., 2018). The cost-effectiveness of the 16 interventions were analyzed for LMICs using a threshold of USD 100 per Disease Adjusted Life year (DALY) averted. The 16 interventions that are less or equal to USD 100 per DALY in their implementation are presented by risk factor or disease (WHO, 2018d).

LMICs were expected to implement four 'best-buy interventions' under tobacco use. These included tax increases, smoke-free indoor workplaces and public spaces, health information and warnings and bans on tobacco advertising, promotion and sponsorship. Interventions under harmful alcohol use included tax increases, restricted access to retailed alcohol and bans on alcohol advertising. To reverse unhealthy diet and physical inactivity, LMICs would also implement salt reduction intake in food, replace trans-fat with polyunsaturated fat, and increase public awareness through mass media on diet and physical activity.

Additional interventions to curb cardiovascular disease (CVD) and diabetes would increasingly involve counselling and multi-drug therapy for people with a high risk of developing heart attacks and strokes and treatment of heart attacks with aspirin. Lastly, to address cancer, the focus would be on Hepatitis B immunization to prevent liver cancer and screening and treatment of pre-cancerous lesions to prevent cervical cancer (WHO, 2018c).

Full intervention of these 'best buys' has the potential to achieve SDG 3.4 on cardiovascular diseases (Bertram et al., 2018). Additionally, a substantial reduction of mortality from NCDs will require implementation of the WHO package of essential noncommunicable disease interventions (WHO PEN) (WHO, 2010). Finally, LMICs would require policies within the context of universal health coverage that will provide equitable healthcare, assure access to efficacious and quality care for NCDs (Bennett et al., 2018).

Intersection with HIV

The intersection of NCDs with HIV/AIDS infection is on several fronts. A key interface between NCDs and HIV could be considered from an epidemiologic standpoint. Globally, about 36.9 million people are living with HIV (UNAIDS, 2018). It is clear that Sub-Saharan Africa (SSA), which is home to over half of the estimated PLHIV worldwide, is faced with a raging yet silent, dual disease epidemic – communicable diseases and NCDs (Levitt, Steyn, Dave, & Bradshaw, 2011b; G. o. K. Ministry of Health, 2015; UNAIDS, 2016). The convergence of a dual burden of NCDs and communicable diseases in SSA is not in question (El-Sadr & Goosby, 2018; G. o. K. Ministry of Health, 2015; Peck et al., 2014; Vorkoper et al., 2018). SSA largely has a generalized epidemic with the highest incidence rates of new infections being observed among adolescent girls and young women. Investments in the care of PLHIV have led to an increased survival and longevity of PLHIV (UNAIDS, 2016). Several countries in SSA continue to report sustained and rapid scale-up of their national ART programs (Farahani et al., 2014; UNAIDS, 2016; WHO, 2016b).

Whilst the leading cause of morbidity and mortality in many countries in SSA has been traditionally from infectious causes such as HIV, a concomitant rise in incidence of NCDs and NCDs-related deaths has also been witnessed over the last decade (Miszkurka et al., 2012). Incidence of NCDs among young people has also been documented thus placing a double disease burden on this population as well (Kaneda, Naik, & Baldwin, 2015). Increased longevity of PLHIV on ART suggests likely increases in prevalence of NCDs among PLHIV in the future (Bloomfield et al., 2014; Farahani et al., 2014; National AIDS Control Council (NACC) & National AIDS/STD Control Programme (NASCOP), 2016; UNAIDS, 2016; WHO, 2016b).

Advances in the medical treatment of HIV including new highly active antiretroviral therapies (HAART) places new additional challenges for PLHIV. From a metabolic standpoint, side effects of several HAART classes such as protease inhibitors and non-nucleoside inhibitors have been associated with metabolic complications including dysglycemia that increase the risk factors of PLHIV to development of NCDs (Dave et al., 2011; Narayan et al., 2014; Patel et al., 2018). Studies have also found higher risk of conditions such as hypertension and diabetes mellitus among PLHIV on HAART as compared to PLHIV naïve patients (Dimala, Atashili, Mbuagbaw, Wilfred, & Monekosso, 2016; Patel et al., 2018; Tripathi et al., 2014).

The burden of hypertension and cardiovascular disease regardless of HIV status remains substantial (Kwarisiima et al., 2016; Miriam Rabkin, Anton Palma, et al., 2018). Previous studies show that exposure to ARVs as well as advanced HIV disease increases the risk of metabolic and cardiovascular diseases (Magodoro, Esterhuizen, & Chivese, 2016; Nduka, Stranges, Sarki, Kimani, & Uthman, 2016). Although there is evidence of increased blood pressure and hypertension among PLHIVs on ART, a distinct difference exists in the characterization of cardiovascular disease between PLHIVs and non-PLHIVs (Tilahun Nigatu Haregu, Oldenburg, Sestwe, Elliott, & Nanayakkara, 2012; Nduka et al., 2016).

Cancers are the second largest cause of NCDs-related deaths and account for about 7% of overall national mortality (G. o. K. Ministry of Health, 2015). In an era of increased access to ART, systematic reviews among PLHIV indicate steadily declining rates of AIDS defining malignancies among PLHIV with most lesions now being pre-cancerous (Tilahun Nigatu Haregu et al., 2012; T. N. Haregu, Setswe, Elliott, & Oldenburg, 2014b). Screening of cancers, such as cervical cancer remains both important and cost-effective when integrated into HIV care and treatment (Hyle, Naidoo, Su, El-Sadr, & Freedberg, 2014; Ministry of Health National AIDS & STI Control Programme, 2016).

HIV infection itself has classically been associated with increased activation of inflammatory and coagulation pathways. Despite viral suppression through use of effective HAART , elevated levels of inflammation markers such as hsCRP, IL-6, D-dimer, and cystatin C levels are observed in PLHIV (Neuhaus et al., 2010).

With the several intersections between a rising NCD epidemic in SSA, and the HIV epidemic attributable to a mix of chronic immune activation, medication side effects, coinfections and the aging process itself, PLHIV not only face a double disease burden but also a syndemic that exacerbates the disproportionate burden and prognosis of NCDs and HIV (Levitt et al., 2011b; Narayan et al., 2014). It is worth noting that HIV treatment has now become a chronic disease and the needs of PLHIV care in many ways are similar to those of NCDs (Levitt et al., 2011b).

Situational Analysis in Kenya

Non-Communicable Diseases Front

Like many other countries in SSA, Kenya is experiencing an epidemiological transition with an increasing burden of disease from NCDs (Kenya National Bureau of Statistics, Ministry of Health Kenya, & World Health Organization, 2015). Between 2005 and 2016, ischemic heart disease for instance increased by 37%. In the same period, cerebrovascular diseases increased by 20.9%. The two aforementioned conditions are now among the five top causes of mortality (Institute for Health Metrics and Evaluation, 2018). NCDs, and particularly the four main NCDs aforementioned, account for over

half of all hospital admissions and deaths in Kenya (Kenya National Bureau of Statistics et al., 2015; G. o. K. Ministry of Health, 2015).

The Kenya Health Policy 2014-2030, under policy objective number 2 acknowledges the rising burden of NCDs and seeks to halt and reverse the worrying trend (Ministry of Medical Services & Ministry of Public Health and Sanitation, 2012). The policy contends that the NCDs ought to be stemmed through a multi-pronged approach, with several sectors working together. It further urges that progress will be made under the precincts of universal equitable health coverage and through decentralization given the devolved nature of the new constitutional dispensation.

The Ministry of Health (MOH) in Kenya developed a national strategy for the prevention and control of non-communicable diseases 2015-2020 (G. o. K. Ministry of Health, 2015). This strategy is anchored within both WHO's global action plan and the Kenya health policy direction for NCDs. It carries an impetus with which all stakeholders are called to action to mitigate the economic and health losses occasioned by NCD burden. Through this strategy, MOH provides a framework for prevention and control of NCDs, and seeks to raise priority accorded to NCDs at national and county levels. Further, the strategy seeks to catalyze creation and strengthening of legislation for the prevention and control of NCDs that is in alignment with the WHO's 'best buys. Lastly, the NCD strategy promotes partnerships both locally and internationally while promoting implementation of evidence based strategies and interventions to prevent and control NCDs (G. o. K. Ministry of Health, 2015).

In 2015, Kenya conducted the WHO STEPwise approach to chronic disease risk factor surveillance (STEPS) survey (Kenya National Bureau of Statistics et al., 2015). An element of the global NCD surveillance strategy, the STEPS survey was a first one of its kind and provided baseline NCD data to guide planning in Kenya. Assessment of risk posed by combined five common and critical risk factors (current daily smokers, overweight or obese (BMI> 25kg/m^2), raised blood pressure (systolic blood pressure >140 mmHg and/or diastolic blood pressure > 90 mmHg), less than five servings of fruit and vegetables daily and low level of physical activity) was determined. A threshold of three or more

indicates a heightened risk of NCDs and their complications and warrants intervention. Only 3% of Kenyans were found to have none of these risk factors. A tenth (10.4%) of 18–44-year-olds and 25.9% of 45–69-year-olds had surpassed the threshold of three or more critical risk factors that warrant an intervention

From this survey, behavioral risk factors noted among Kenyans included: 13% of Kenyans smoke some form of tobacco (23% among men, and 4.1% among women), 19.3% of Kenyans currently drink alcohol with 13% on a daily basis and 12.7% heavy episodic drinkers. Nearly a quarter (23.2%) add salt in food while eating, 28% add sugar to beverages and 6.5% of Kenyans do not engage in recommended amounts of physical activity. More than half (56%) of Kenyans have never been measured for raised blood pressure, while 87.8% have never been measured for raised blood sugar. Only 16.4 % of women aged 30-49 years have ever been screened for cervical cancer.

On physical measurements, 27% of Kenyans are either obese or overweight (17.5% men and 38.5% women). Of the total respondents, 12% of urban respondents were obese, compared to 7% in rural settlements. Twenty-eight percent of men and 36% of women had a higher than recommended waist-hip ratio – an index used to identify individuals at increased risk of obesity related morbidity due to accumulated abdominal fat.

Using biochemical measurements, 3.1% of Kenyans have impaired fasting glycaemia, and 1.9% have raised blood glucose of ≥ 7.0 mmol/l or are currently on medication for diabetes. Close to 10% of respondents had cholesterol of ≥ 5.0 mmol/l or currently on medication for raised cholesterol.

Combining total risk of developing cardiovascular disease (CVD) was determined using a combined effect of behavioral and biological risk factors (smoking, raised blood sugar, age, and sex). Among 8% of Kenyans 40-69 years of age, the risk of developing CVD is over 30% with only 6% on current drug therapy or counseling to prevent heart attacks and strokes.

HIV Front

Kenya has made remarkable gains in the fight against HIV/AIDS. According to the 2018 Kenya National AIDS Control Council estimates, there are close to 1.5 million people living with HIV/AIDs in Kenya (G. o. K. Ministry of Health, 2018). The 2018 national HIV prevalence in Kenya is 4.8%, with a prevalence of 4.5% among adult males and 5.2% among adult females. National incidence of HIV infection is at 1.8 per 1000 individuals (G. o. K. Ministry of Health, 2018).

The burden of cardiovascular diseases among PLHIV, cancers and chronic respiratory diseases and diabetes in Kenya has been modelled by NACC and the Imperial college London in 2019. Below is a table depicting the differences in prevalence between HIV infected and HIV non-infected individuals. The prevalence of all the four conditions is poised to rise sharply between the periods 2018 – 2035.

Table 2.1 Kenya NCD Estimates Report 2019

2018 NCD	Overall		HIV positive		HIV negative	
	Prevalence	Cases	Prevalence	Cases	Prevalence	Cases
Hypertension	19.9%	5,271,172	29.9%	419,552	19.9%	4,851,620
Type 2 Diabetes	2.7%	703,760	3.1%	43,379	2.7%	660,381
High total cholesterol	8.9%	2,307,985	10.1%	141,212	8.9%	2,166,773
Chronic kidney disease	5.5%	1,446,912	8.5%	118,678	5.5%	1,328,234
Depression	3.4%	875,506	3.9%	54,187	3.4%	821,319
Cardiovascular Disease	0.7%	159,691	0.7%	9,256	0.6%	150,435
Cancer	0.4%	108,871	1.3%	17,617	0.4%	91,254

Future burden - 2035

NCD	Overall		HIV positive		HIV negative	
	Prevalence	Cases	Prevalence	Cases	Prevalence	Cases
Hypertension	23.0%	10,349,394	37.4%	961,666	23.0%	9,387,728
Type 2 Diabetes	3.3%	1,444,313	4.3%	110,243	3.3%	1,334,070
High total cholesterol	10.1%	4,435,679	12.7%	325,238	10.1%	4,110,441
Chronic kidney disease	6.4%	2,874,101	10.7%	273,739	6.4%	2,600,362
Depression	3.3%	1,454,581	3.6%	93,723	3.3%	1,360,858
Cardiovascular Disease	0.7%	326,783	1.0%	26,738	0.7%	300,045
Cancer	0.5%	255,840	2.4%	61,694	0.5%	194,146

The burden of cardiovascular diseases (CVDs) and Diabetes among PLHIV

With the advent of effective antiretroviral treatment, the life expectancy for people with HIV is now approaching that seen in the general population. Consequently, the relative importance of other

traditionally non-AIDS related morbidities has increased. Modelling studies (from the ATHENA cohort), suggest that 84% of HIV-infected patients in 2030 will have more than 1 or more comorbidities; a 30% increase from 2010. Patients with comorbidities will be higher in every age group in HIV-infected patients versus controls non infected with HIV (Smit et al., 2015).

Beyond the ageing factor, several aspects play into the pathophysiology of NCDs particularly cardiovascular diseases and diabetes among PLHIV. Some of these include: lipopolysaccharides (LPS) gut leakage that causes chronic immune activation leading to increased cytokine release, systemic inflammation and a procoagulant state; monocyte activation that leads to greater endothelial attachment and atherogenesis; cytokine–induced endothelial dysfunction; HIV-induced and ART-induced dyslipidemia (HIV lipodystrophy associated with loss of fat in limbs and truncal obesity most associated with PIs and NRTIs) and insulin-resistance and metabolic syndrome (PIs impair glucose homeostasis by inhibiting insulin-regulated GLUT4 glucose transporter into fat and muscle tissue).

Among PLHIV in Kenya, robust estimates of burden have come from the modelling report from NACC (table 2.1) and indicate a 29.9% prevalence for hypertension (compared to 19.9% for the general population). Type 2 diabetes among PLHIV, while comparable to the general HIV non infected population, is relatively high at 3.1% (c.f 2.7%) and is poised to continue to rise to 4.3% by 2035.

The burden of cancers among PLHIV.

Cancer burden is also disproportionately high among PLHIV, with the majority of the cancers being cervical cancer among women (Arbyn et al., 2019). Screening rates for cervical cancer have been low in Kenya and contributed significantly to underdiagnosis of cervical cancer (Bukirwa et al., 2015). With increasingly effective ART that is started early, classically AIDS related lymphomas, and cancers such as Kaposi Sarcoma have become rare (Herce et al., 2015). The cancer burden among PLHIV in Kenya stands at 1.3% (2018 estimates) and is poised to increase to 2.4% in 2035 (G. o. K. Ministry of Health, 2019).

The burden of chronic respiratory diseases among PLHIV

Estimates for chronic respiratory illnesses are sparse in Kenya and other parts of SSA. This is mainly contributed to the absence of screening at comprehensive care centers lacking spirometry equipment. Estimates from SSA, point to asthma being the most commonly diagnosed condition (Barr et al., 2016).

The number of new infections declined from 101,600 to 52,800 between 2014 and 2018, a 49% drop among adults. Over the same period, AIDS-related deaths decreased from 48,100 to 23,900 – a testament to the efficacy of antiretroviral therapy. The current ART coverage in Kenya is at 75% with over 1.1 million individuals on life saving ART medication.

Although predominantly a generalized epidemic, key populations in Kenya play a significant role as a bridging population for incident HIV infections. The National AIDS and STI Control Program (NASCOP) program data and the MARPs size-estimate consensus report estimate a population of 133,675 female sex workers (FSWs), 13,019 men who have sex with men (MSMs) and 18,327 people who inject drugs (PWIDs) (G. o. K. Ministry of Health, 2013).

A recent non-protocol-based remapping in 2018, estimated 157,763 FSWs, 28,344 MSMs and 16,086 PWIDs. Nairobi County contributed to 25% of all estimated FSWs, 36% of MSMs and 31% of PWIDs. The HIV prevalence among FSWs was 29.3%, while that among MSMs and PWIDs was 18.2% and 18.3% respectively. Service coverage was at 76% for FSWs, 65% among MSMs and 68% among PWIDs.

In 2016, Kenya adopted the WHO guidelines to expand ART eligibility to all persons diagnosed with HIV (Ministry of Health National AIDS & STI Control Programme, 2016). Clinical parameters of WHO stage and baseline CD4 have previously been associated with NCDs risk (Tripathi et al., 2014). In a study in Zimbabwe the factors of gender, duration of HIV sero-positive state, ART regimens received, and baseline WHO HIV disease stage, CD4 + cell counts, and each additional year of age were associated with a 6 % increased risk of NCDs (Magodoro et al., 2016). In developed countries,

mixed findings of both increased risk and no difference was noted (Rasmussen et al., 2012). Among other factors, increased risk of developing NCDs is associated with duration of and exposure to certain ARV drugs like stavudine, efavirenz and protease inhibitors (Dave et al., 2011; Oni et al., 2015; Tien et al., 2007). However, several studies in low-income countries found no significant relationships between ARV drug class or duration of exposure with risk of NCDs (Magodoro et al., 2016).

The underpinnings of Integrated NCD-HIV Care Delivery

As a response, intuitive pragmatic thinking calls for leveraging on the HIV chronic care platforms to deliver NCD care to PLHIV in LMICs such as Kenya. With sustained Global funding towards the HIV epidemic over the last decade, HIV care platforms have generally remained robust. With overall effective delivery of chronic care, HIV platforms are an attractive solution for integrated care delivery (El-Sadr & Goosby, 2018).

Integration is defined as management and delivery of health services so that clients receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system" (WHO, 2008). Common models of NCD-HIV integration identified in SSA include integrated community-based screening for HIV and NCDs in the general population; screening for NCDs and NCD risk factors among HIV patients enrolled in care; integration of HIV and NCD care within clinics; differentiated care for patients with HIV and/or NCDs; and population healthcare for all (Njuguna et al., 2018; Patel et al., 2018).

Benefits from integration of NCDs into existing HIV service delivery platforms would include: more affordable hence sustainable health service delivery by leveraging primary vertical platforms for delivery of multiple services and time and cost savings through a one-stop shop model. Additional benefits would be reduced duplication and improved cost-efficiency of health workforce, infrastructure, management and financial resources. Lastly, country ownership would be enhanced with development of country driven and country led health systems for multiple disease burdens (WHO, 2016c).

Research Agenda

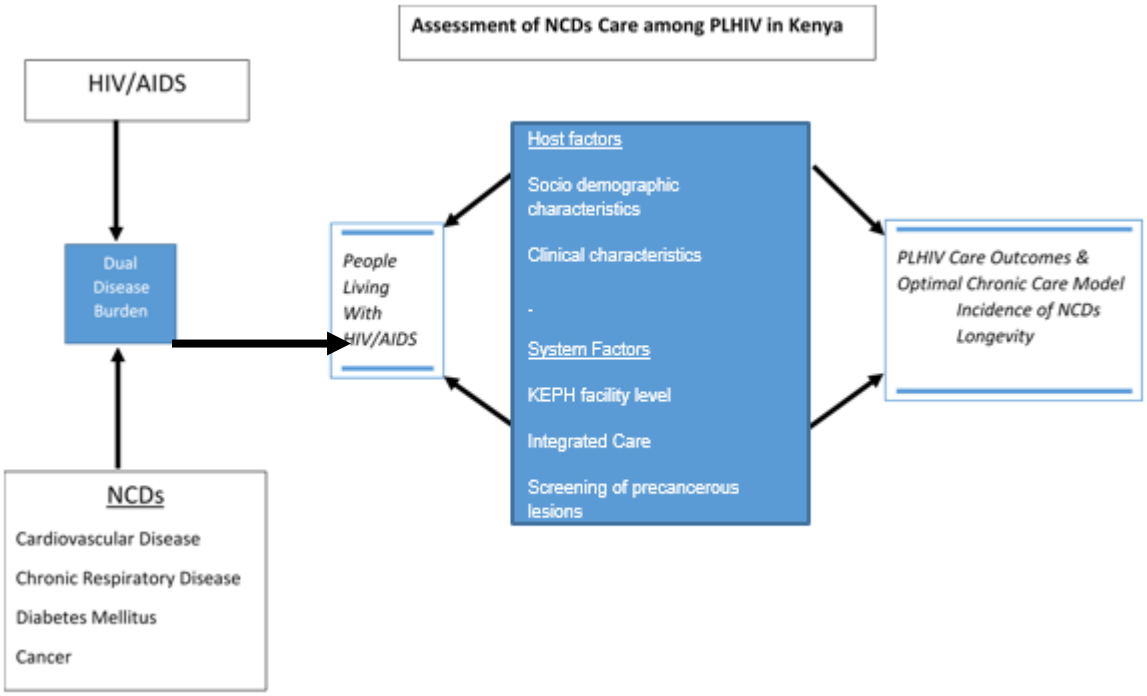
Several studies examining NCDs among PLHIV have been conducted in SSA (Edwards et al., 2015; Kagaruki et al., 2014; Kavishe et al., 2015; Magodoro et al., 2016; Peck et al., 2014). Most of these have involved cross-sectional surveys of facility level data, with smaller and less-representative samples. Previous national HIV treatment outcome studies in SSA have also not addressed NCDs among PLHIV (Farahani et al., 2014; Mutasa-Apollo et al., 2014). Study findings have shown increased prevalence of NCD risk factors among PLHIV both general and key population not on antiretroviral treatment (Patel et al., 2018; van Heerden et al., 2017). Overall incident rate for diagnosed NCDs is lower amongst those on ART compared to those not on ART. Additionally, studies describe social economic deprivation as a predictor of NCDs risk factor among PLHIV (Kagaruki et al., 2014; Zolopa et al., 2009). However, population-level data on NCD prevalence among PLHIV in SSA remain sparse (Vorkoper et al., 2018)

Further, while integration appears as the instructive strategy for NCD-HIV delivery of services, it may not be a panacea. There is paucity of data collection and surveillance of NCDs among PLHIV in LMICs necessary to inform integrated HIV/NCD care models (Patel et al., 2018). Moreover, the impact of NCDs' burden among PLHIV from early public health approaches in HIV programming such as stratifying clients in care based on declining CD4 counts has not been widely evaluated (WHO, 2013a).

Despite many attempts at integration, there is a dearth in evidence-based data on integration effectiveness and cost-effectiveness. NCD burden is much larger and complex requiring massive investments into systems and multi-stakeholder coordination. Loading NCD care delivery on existing HIV platforms may even result in a weakening of both systems.

Evaluating integrated programs is complex with commonly only process and limited outcome measures being available (WHO, 2016c). Few NCD-HIV integrated programs with screening and management approaches that are contextually appropriate for resource-limited settings exist (Patel et

al., 2018). Gaps remain in literature with even fewer studies on effectiveness, cost, and best practices for integrated chronic care platforms (Vorkoper et al., 2018).



Conceptual Framework

CHAPTER THREE: MATERIALS AND METHODS

This chapter on materials and methodology is presented by sub-sections that address each of the three distinct objectives under my PhD study.

OBJECTIVE ONE: To assess outcomes of integration of NCD care within HIV settings by conducting a systematic review of literature across several databases (Medline, Embase, Global Health, Scopus and Cochrane library)

METHODOLOGY

Search strategy and selection criteria

This was a systematic review of published studies on the effect of NCD care integration within HIV care and treatment settings on HIV program, NCD care and health systems outcomes in Sub-Saharan Africa. We considered four NCDs – cardiovascular diseases (including hypertension, heart attack and stroke), chronic respiratory diseases, cancer and diabetes mellitus, that make the largest contribution to both mortality and morbidity (WHO, 2013b). In reporting this review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009; Shamseer et al., 2015).

We completed the search in June 2019 having searched multiple databases (CINAHL, Cochrane, Embase, Global Health, Medline, PsycInfo, Pubmed and Scopus) for studies conducted over a five-year period - January 2013 to December 2018. Since both inception of the UN declaration on NCDs and launch of the Global Action Plan (GAP) for the Prevention and Control of NCDs happened in 2013, we considered 2013 a critical start point of a concerted global response to the HIV - NCD care integration implementation agenda (UN, 2012; WHO, 2013b).

The search was centered around five key concepts: PLHIV, NCD care integration, antiretroviral therapy, HIV care outcomes and SSA. For each concept, the search term was combined to the free text

search of the synonyms and derivatives of the main concept using Boolean operators "AND", "OR", and "NOT" to refine our search by combining or limiting terms. The search strategy is presented in annex 1.

Articles returned by the search were saved on EndNote X9, Clarivate Analytics (US) reference manager software for removal of duplicates. Studies were screened based on abstract information that reported HIV-NCD care integration in SSA. Two investigators (DA and JW) obtained the full text of remaining articles, reviewing them for eligibility in accordance with the following eligibility criteria.

Inclusion criteria

- Studies published in English between January 2013 and December 2018
- Studies involving PLHIV who sought HIV care and treatment in one of the countries in SSA
- Cross sectional, cohort, case control, and random control trials with outcome data on effect of HIV-NCD care integration for one or more of four NCDs - cardiovascular diseases (including hypertension, heart attack and stroke), chronic respiratory diseases, cancer and diabetes mellitus
- Conference abstracts on HIV-NCD care integration
- Studies with comparable PLHIV populations receiving NCD care in integrated vs non-integrated HIV care settings

Exclusion criteria

- Studies that did not meet one of the five identified models of HIV-NCD care integration (Njuguna et al., 2018)
- Studies from which we could not obtain relevant outcome data on HIV-NCD care integration

For cohort studies with several publications of outcome data over time, we considered for inclusion, the most recent of the studies.

Data synthesis

Data were extracted from eligible studies onto an abstraction tool produced on MS-Excel 2019 by investigator (DA) and reviewed by a second investigator (JW). The following data were abstracted: database searched, author, year, country and study setting, period of data collection, study population (PLHIV - general population or key population and specifying the typology), type of NCD, type of integration, study design, sample size, outcome measured and summary of results/recommendation. When not available, the appropriate measure of effect for the outcome were derived from the reported study data and entered onto the abstraction tool.

The exposure variable was HIV-NCD integration and was categorized as either non-integrated HIV care (standard of care) or integrated HIV-NCD care. Whereas several definitions of integration are described (Haldane et al., 2018; WHO, 2008), our framework on integration was drawn from a recent systematic review of integration models in SSA by Njuguna et al (Njuguna et al., 2018). Five models of integration were identified: Integrated community-based screening for HIV and NCDs in the general population; screening for NCDs and NCD risk factors among HIV patients enrolled in care; integration of HIV and NCD care within clinics; differentiated care for patients with HIV and/or NCDs; and population healthcare for all - UHC.

The outcome variable was HIV care outcomes that was classified as one of three broad categories: HIV/AIDS program outcomes – improved retention in care rates, increased viral suppression, longevity and improved quality of life; NCDs care outcomes - reduction in incidence of NCDS and NCD-associated complications, including a slowing of progression of premalignant to malignant lesions; and Health System benefits including savings from averted costs and direct expenditure.

Owing to the excessive heterogeneity of population, outcome and methodology among eligible studies, we conducted a systematic review and did not conduct a meta-analysis. We prepared summary tables, grouping studies on reported parameters and providing both thematic and contextual narrative syntheses. We systematically investigated reasons for similarities and differences of study findings.

We further considered how results of studies might be affected by factors such as methodological differences, variable definitions and interventions investigated. All eligible studies were assessed by two reviewers (DA) and (JW). Any disagreements between the reviewers over the risk of bias in a particular study was resolved by discussion and involvement of a third reviewer where necessary.

Ethical considerations

The conduct of this systematic review was approved by the Kenyatta National Hospital, University of Nairobi Ethics Review Committee as part of a nested study (KNH UON ERC P720/10/2018). Data used for this review was of a secondary nature with no human subject interface.

OBJECTIVE TWO: To characterize NCD burden of the four leading NCDs that lead to the highest morbidity and mortality among PLHIV attending general population ART clinics in Kenya.

METHODOLOGY

Study design and population

The Longitudinal Surveillance of Treatment in Kenya (LSTIK) was a retrospective cohort study of HIV-infected patients aged ≥15years in Kenya, who enrolled into HIV care between October 1, 2003, and September 30, 2013. Study participants were sampled from a nationally representative random sample of 50 facilities offering ART services that had been in operation for a minimum of 15 months, and supporting at least 50 patients aged ≥15years on ART according to the 2013 NASCOP Annual Progress Report (appendix I). The LSTIK sampling process is included as appendix VIII. Our analysis was based on the cohort of patients who were enrolled in HIV care during the study period ("pre-ART cohort"), some of whom started ART in the follow-up interval between enrollment in care and data abstraction. All patients had at least 12 months of clinical follow-up prior to chart abstraction.

During the study period, there were three time periods with different ART initiation thresholds: 1st January 2003 to 31st December 2005 when the threshold for ART initiation was CD4 count <200 cells/mm^3; 1st Jan 2006 to 30th June 2010 when the threshold for ART initiation increased to CD4 <250 cells/mm^3; and 1st July 2010 to 30th September 2013 when the threshold was further increased to CD4 <350 cells/mm^3 (G. o. K. Ministry of Health, 2001, 2005, 2011).

Data collection methods

Medical records were abstracted during October 2015 –September 2016 using a standard tool on netbook computers (Mirus Innovations, Mississauga, Ontario, Canada). Data were securely transmitted electronically to a central database in Nairobi. Data cleaning and analyses were carried out using Stata 14.2 (Stata Corporation, Texas USA).

Measures

We described and restricted our analysis of co-morbidities to four major NCDs - cardiovascular diseases (including hypertension, heart attack and stroke), cancer, chronic respiratory diseases (including asthma) and diabetes mellitus. These four conditions are associated with over 60% of all NCD-related deaths. NCDs were documented at enrollment into HIV care and during patient follow-up period. Blood pressure readings were recorded from charts. Two or more measures taken within 12 months of systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg was considered as elevated blood pressure. These criteria were considered to be closely aligned with a clinical diagnosis of hypertension that involves multiple elevated blood pressure readings and consistent with classification of hypertension based on the 2003 seventh report of the Joint National Committee (JNC 7) (Chobanian et al., 2003) Unlike in the definition of elevated blood pressure, we relied on the diagnosis written in the medical records to document diabetes mellitus. No reference was made to elevated fasting blood sugar readings in patient charts.

We conducted our analysis based on the three periods of changing CD4 count thresholds for ART initiation described above. ART drugs that constituted first line regimens among adults changed over the guideline review periods and included stavudine (d4T), zidovudine (AZT), abacavir (ABC) and tenofovir (TDF). Regimens that included lopinavir (LPV/r) were considered second line.

Statistical analysis

We estimated proportions of NCDs among PLHIV at enrollment into HIV care, and during subsequent follow-up visits. We compared proportions and assessed distributions of baseline demographic and clinical characteristics by sex using Wald adjusted Pearson's χ-square test. We assessed distribution of NCDs by ART status and calculated incidence rate ratios for selected baseline demographic and clinical characteristics and incidence/1000 person years by ART status. Incidence rates were calculated and presented with their jackknife 95% confidence intervals. Data were survey-set before analysis. Data were assumed to be missing at random; we did not impute the data. All estimates were adjusted to account for sampling design and missing data. Analyses were carried out in Stata 14.2 (Stata Corporation, Texas USA).

Ethical Considerations

This study was approved by the Kenyatta National Hospital, University of Nairobi Ethics Review Committee as part of a nested study (KNH UON ERC P720/10/2018). Additional approvals for the larger LSTIK study were obtained from the Kenya Medical Research Institute's Scientific and Ethics Review Unit and the Committee on Human Research of the University of California, San Francisco. This study was reviewed according to the Centers for Disease Control and Prevention (CDC) human research protection procedures and was determined to be and approved as research, but CDC was not engaged.

OBJECTIVE THREE: To characterize NCD burden of the four leading NCDs that lead to the highest morbidity and mortality among PLHIV attending key population program drop-in centers (DICEs) and ART clinics at a large HIV prevention, care and treatment program in Nairobi, Kenya

METHODOLOGY

Study design and population

Data for this study were obtained from a medical chart review of clients enrolled in a large key populations' HIV prevention, care and treatment program in Nairobi Kenya. KPs enrolled in the Sex Workers Outreach Program (SWOP) included female sex workers (FSWs), and men who have sex with men (MSM). Those reached by SWOP team within Nairobi County are encouraged to enroll in the funded program that provides free, friendly, acceptable and accessible minimum package of HIV prevention and treatment services for sex workers as per the Ministry of Health guidelines (Ministry of Health, 2014). Due to rampant stigma and discrimination in Kenya for MSM, this group started accessing available HIV prevention and treatment services within the last 10 years. Hence, they are under-represented in health care programs providing targeted, accessible, acceptable and free health care services. Medical charts of all 2200 KPs (entire data set) living with HIV enrolled between October 2012 and September 2015 at all seven SWOP Drop-in Centers (DICEs), and on HIV treatment and care program spread across Nairobi County were included in the study. Specifically, medical charts of KPs aged 15 and above living with HIV (national antiretroviral therapy (ART) tools in Kenya classify ages ≥ 15 as adults), irrespective of ART initiation status were considered for analyses. (figure 3.1)

Study procedures and data collection

Medical records of those living with HIV enrolled in the program over the three-year period were abstracted during October and November 2018. At each of the seven constituent SWOP clinics, four trained abstractors collected data from clinic files of all HIV-infected individuals using a standardized

data abstraction tool in MS-Excel. Details of each client's clinical encounter and follow-up visit during the study period were collected. Query scripts written in structured query language (SQL) were used to extract ART care data-variables contained in the national Ministry of Health (MOH) forms. All SWOP clinics utilize the nationally approved ART electronic medical records systems that contain the national MOH ART patient care forms. Variables that fell outside the purview of the query scripts were manually extracted and double-entered into the MS-Excel abstraction tool for validation.

The team worked under the supervision of a data manager and program manager who verified abstracted data for completeness and accuracy on a daily basis to assure data quality. Data was transmitted encrypted on a daily basis and stored at a server at the central SWOP office in Nairobi. All computers used for abstraction and storage were password protected and access limited to only the data management team.

Statistical analyses

Our analyses included medical chart records of two key population typologies: FSWs and MSM who were HIV-infected. The baseline characteristics of the study participants were compared by KP type using appropriate statistics (chi-square or fisher's exact test as necessary for categorical variables and t-tests for continuous variables). Depending on the backbone antiretroviral drug molecule – nucleoside reverse transcriptase inhibitor (NRTI) or protease inhibitor (PI), antiretroviral treatment regimens were classified as either being first line or second line. The main outcome was any NCD derived from report of cardiovascular disease, diabetes mellitus, chronic respiratory diseases or cancer at enrollment and during HIV treatment and care (study period). Prevalence of the specific NCDs and any NCDs was calculated stratified by KP typology for a range of population characteristics. We conducted univariate and multivariable logistic regression to identify factors associated with NCD diagnoses. An automated stepwise backward logistic regression approach was used to identify independent predictors of NCDs retaining variables with a p-value of 0.2 from the univariate analysis. Age, gender, alcohol use and smoking were considered a priori as potential confounders and included in the final multivariable

model. Collinearity and interaction of the variables was assessed. A sensitivity check through an analysis that included missing data confirmed the assumption that data was missing at random. Missing data were not imputed. Analyses on non-clinical measures presented are based on self-reported data. We analyzed data using STATA 15 (STATA Corporation, Texas USA).

Ethical considerations

The analyses of these routine HIV treatment and care data from Nairobi County SWOP clinics was approved by the Kenyatta National Hospital, University of Nairobi Ethics Review Committee; (KNH UON ERC P258/09/2008) and as part of a nested study (KNH UON ERC P720/10/2018). Prior to accessing the required data for this study, the data manager de-identified the patients' clinical charts creating anonymity as a way of maintaining confidentiality. Upon enrollment into SWOP, all patients provided informed consent to clinical data collection that allowed use of their clinic charts to inform HIV prevention, care and treatment in Kenya. Annual approvals were granted by the Kenyatta National Hospital, University of Nairobi Ethics research committee upon satisfactory review of annual study progress reports under protocol P258/09/2008. Being of a secondary nature, there was no human subject interface during the conduct of this study.

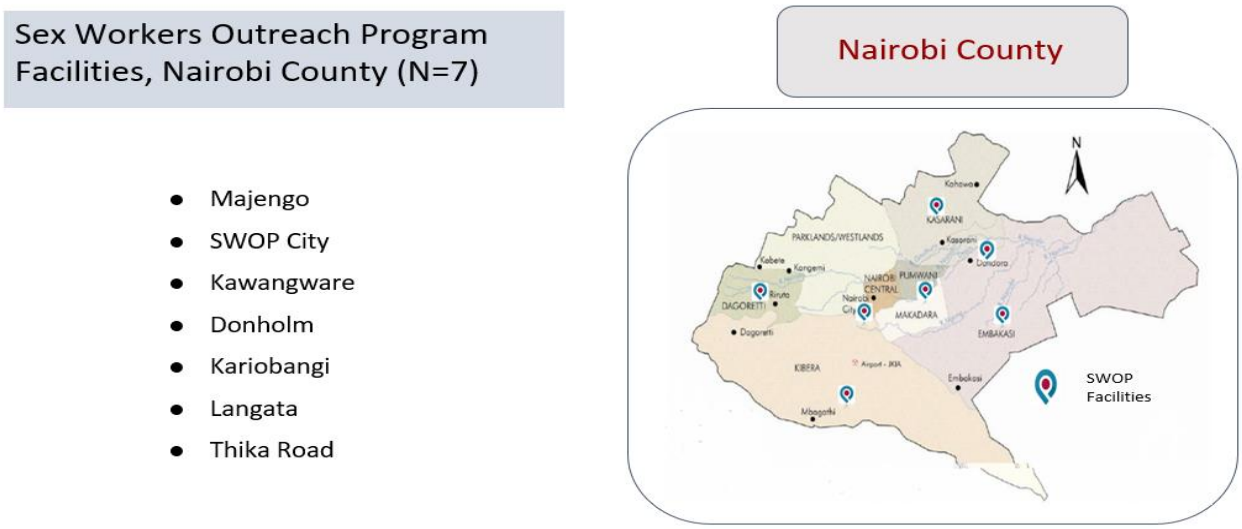


Figure 3.1:Sex Workers Outreach Program Facilities, Nairobi County

CHAPTER FOUR: FINDINGS AND DISCUSSION

The findings emanating from my PhD study and the discussion are presented in sub-sections that represent the three objectives under study. These are presented in publication format with a summary abstract and introduction leading up to the findings and discussion sections.

4.1 To assess outcomes of integration of NCD care within HIV settings by conducting a systematic review of literature across several databases (Medline, Embase, Global Health, Scopus and Cochrane library).

Publication Title: A Systematic Review of Non-communicable Disease Care Integration within HIV Care and Treatment Settings in Sub-Saharan Africa, 2013 - 2018

ABSTRACT

Background

Sub-Saharan Africa (SSA) is grappling with a growing syndemic of non-communicable diseases (NCDs) and HIV. Leveraging on robust HIV platforms to integrate HIV and NCD care is an attractive opportunity for policy makers. This systematic review assessed the effect of NCD care integration within HIV care and treatment settings in SSA at three outcome levels - HIV program, NCD care and health systems.

Methods

We searched for published studies conducted between January 2013 to December 2018 in SSA from multiple databases (CINAHL, Cochrane, Embase, Global Health, Medline, PsycInfo, Pubmed and Scopus) focusing on HIV and four NCDs - cardiovascular diseases, chronic respiratory diseases, cancer and diabetes mellitus.

Results

We identified 49 eligible studies. Eighteen (36.8%) studies were cross-sectional, 9 (18.4%) qualitative, 7 (14.3%) experimental or quasi-experimental, 6 (12.2%) cohort, 3 (6.1%) mixed- method and 6 (12.2%) applied an econometric design. In 23 (46.9%) studies, the main target condition for HIV-NCD

care integration was cancer. Fifteen (30.6%) studies addressed cardiovascular diseases including hypertension and attendant risk factors; 12 (24.5%) targeted diabetes mellitus and 2 (4.1%) targeted chronic respiratory diseases. Twenty-four (49.0%) studies were conducted among HIV-infected individuals at HIV clinics, 16 (32.7%) in general clinics, 6 (12.2%) integrated community-based screening, 2 (4.1%) applied differentiated-care models and 1 (2.0%) was at population level. For HIV, all studies recorded positive outcomes for case finding, retention, increased CD4 counts and improved quality of life. For NCDs, positive outcomes of early screening and identification that forestalled complications associated with NCD progression were identified. Resource considerations were poorly described with only a few studies reporting on program cost data. Incremental cost of HIV-NCD care integration stood at USD 3.95 - 4.00 per patient annually and represented a 6% -30% increase in total program costs for non-cancer NCDs.

Conclusion

HIV-NCD care integration is widely accepted, feasible and easily adopted by both communities and health care workers. Outcomes for both HIV and NCD care under integrated settings are generally improved. Costs associated with HIV-NCD care are modest. To achieve cost efficiencies and economies of scale during roll-out of integrated HIV-NCD care, clarity on resource requirements and specific elements of the HIV program to leverage upon is required.

INTRODUCTION

At the turn of the decade, the United Nations called for an urgent, concerted and integrated response to prevent and control HIV and non-communicable diseases (NCDs) epidemics - a double burden especially in Africa (UN, 2012). In response, WHO developed the Global Action plan framework as part of guidance to assist countries address the two colliding epidemics (WHO, 2013b). Progress has been slow, and in 2019, WHO reported non-communicable diseases (NCDs) as the leading cause of productivity losses in Sub-Saharan Africa (WHO, 2019a) - home to over 20 million people living with HIV (PLHIV)(UNAIDS, 2019a). With over 13 million PLHIV on ART, empirical evidence shows that the ageing cohort in SSA is now associated with a significant increase in NCD risk factors (Coetzee et al., 2019).

As a result of longstanding donor support to achieve HIV epidemic control and against a backdrop of weak health systems, many SSA countries have developed robust HIV service delivery systems, albeit vertically designed (El-Sadr & Goosby, 2018). Owing to the chronic nature and need for follow up for both HIV and NCDs, many countries in SSA consider leveraging on HIV's formidable care system to deliver NCD care as an attractive option (Vorkoper et al., 2018). Several countries in the region have designed innovative NCD care delivery models for both HIV infected and non-infected populations (S. Ameh, K. Klipstein-Grobusch, L. D'Ambruoso, et al., 2017; Broughton, Muhire, Karamagi, & Kisamba, 2016; Wroe et al., 2015). Scholars have developed and proposed action models to deliver HIV and NCD care in an integrated fashion (T. N. Haregu, Setswe, Elliott, & Oldenburg, 2014a). Several systematic reviews have identified multiple arrays of models developed in response to the HIV-NCD syndemics (Duffy et al., 2017; Haldane et al., 2018; Njuguna et al., 2018).

Although SSA countries remain committed to achieving the Sustainable Development Goals (SDGs) through underpinnings of Universal Health Coverage (UHC), national responses to the HIV-NCD integration agenda are characterized by hesitancy and inertia (Wagstaff & Neelsen, 2020). Several gaps preclude full scale implementation of HIV-NCD care integrated systems. Lack of robust evidence of

clinical care outcomes and costs of care including at health systems level hamper large scale implementation (Hyle et al., 2014; Matanje Mwagomba et al., 2018). Economic justification of different integration models remains unproven (R. Nugent et al., 2018). Further, modest efficiencies from some models, and caution on equilibrium conditions of infrastructure and effectiveness ratios required to achieve cost complementarities and economies of scale serves to fetter progress on integration (Obure, Guinness, Sweeney, & Vassall, 2016).

In our systematic review, we sought to plug the dearth of knowledge around HIV-NCD care integration. Based on three integration outcomes – HIV program, NCD care and health systems, and summary findings from studies conducted in SSA, we present a synthesis of commonly practiced HIV-NCD care integration models. We present feasibility and acceptability findings among HIV infected clients and general population communities. Finally, we provide cost estimates from HIV-NCD care studies to aid policy makers and program managers inform large scale implementation.

RESULTS

In figure 4.1.1, we present a flow chart summary of the study selection process outlining the number of potentially relevant studies initially identified and the number of studies finally included in the systematic review. We screened 247 studies published between January 2013 and December 2018. A total of 198 studies did not meet the inclusion criteria and were excluded. Forty-nine full-text articles were assessed for review and included in the final analysis in one of three study outcome categories (HIV program, NCD-related and Health System outcomes – costed and non-costed).

Characteristics of the studies

We conducted a systematic review of studies on HIV-NCD care integration in SSA and presented their characteristics in table 4.1. We included 49 studies: 17 from East Africa (Kenya, Uganda and Tanzania) and 32 from other regions of SSA. Eighteen (36.8%) studies had a cross sectional study design, 9 (18.4%)

were of a qualitative nature, and 7 (14.3%) were of an experimental or quasi-experimental design. There were 6 (12.2%) cohort and 3 (6.1%) mixed method design studies. Six (12.2%) studies applied an econometric study design.

In 23 (46.9%) studies, the main target condition for the HIV-NCD care integration was cancer. Other than one study from Malawi that targeted Kaposi sarcoma, the rest focused on cancer of the cervix. Fifteen (30.6%) studies addressed cardiovascular diseases including hypertension and attendant risk factors; while 12 (24.5%) targeted diabetes mellitus. Ten (20.4%) studies targeted integration of both diabetes and hypertension in HIV settings. Eight (16.3%) studies targeted all NCDs in general including mental health. Only two (4.1%) studies addressed tobacco use – a risk factor for chronic respiratory diseases.

Five integration models were analyzed (Njuguna et al., 2018). Close to a half, 24 (49.0%), of the studies were conducted among PLHIV enrolled in care at HIV clinics with some form of screening for NCDs and NCD risk factors. A third, 16 (32.7%) of studies integrated HIV and NCD care in general clinics that served both HIV infected and uninfected clients. Six (12.2%) studies, integrated community-based screening for HIV and NCDs in the general population. Two (4.1%) Kenyan studies used nurse-facilitated integrated medication adherence clubs – a form of differentiated care for patients with HIV and/or NCDs. Only one (2.0%) study applied integrated HIV-NCD care at a population level akin to universal health care.

NCD and HIV program related outcomes

Four studies reported early identification of NCDs as a positive outcome from HIV-NCD care integration (Acio et al., 2013; Afzal, Lieber, Dottino, & Beddoe, 2017; Jerene et al., 2017; Kachimanga et al., 2017). In a study in Malawi, Kachimanga et al noted that screening resulted into a tripling of the average number of patients ever enrolled for NCD care every 3 months from 40 to 114 (Kachimanga et al., 2017). Another four studies estimated prevalence of NCDs among HIV infected clients (Bekolo et al., 2016; Divala et al.,

2016; Drain, Hong, Thulare, Moosa, & Celum, 2018; Mitchell et al., 2017). One Ugandan study observed low cervical cancer screening rates despite a high prevalence of oncogenic HPV (HPV genotypes 16 or 18) (Mitchell et al., 2017). Bekolo et al. in Cameroon, observed a lower risk of cancer among HIV-infected women receiving Highly Active Antiretroviral Treatment (HAART) than the general population (Bekolo et al., 2016). This finding could not be attributed to HAART alone but to all the health benefits derived from receiving comprehensive HIV care. While contending that more work was required to identify better screening tools for diabetes, Jerene et al. used screening checklists among 2,112 patients drawn from the HIV clinics in Amhara and Oromia regions in Ethiopia and found a 1.5% prevalence with an abnormal random plasma glucose (RPG) reading (Jerene et al., 2017).

One large implementation study in Malawi diagnosed 3,448 HIV infected clients – an 11% prevalence with hypertension. At 6 months of treatment, 26% of all patients on treatment had achieved controlled blood pressure. ART adherence for hypertensive patients on treatment was similar with other patients not on hypertension treatment (80% vs 79% respectively) (Phiri et al., 2018). Two studies reported on occurrence of NCD complications among HIV infected individuals. In a cohort study in western Kenya, overall rate of treatment failure within 12 months of Loop Electrosurgical Excision Procedure (LEEP), was low at 12.8 cases per 100 person years of follow up. ART use did not significantly impact the rate of recurrence (hazard ratio: 1.24, 95% CI 0.59-2.79) (Huchko et al., 2015). Ameh et al. in a controlled interrupted time series study in primary health facilities in South Africa, found a small effect - 1% greater likelihood of controlling patient BP (coefficient =0.01; 95% CI 0.003-0.016) at pilot facilities (S. Ameh, K. Klipstein-Grobusch, E. Musenge, et al., 2017).

Two studies reported improved HIV-NCD care outcomes for the HIV program. In a cohort study at a rural district in Malawi, Herce et al. observed improved quality of care and excellent overall survival at 12 months of Kaposi sarcoma HIV infected clients. Of 114 adult HIV infected Kaposi Sarcoma patients who received ART and chemotherapy, 83% (95%CI 74-89%) were alive, and 77% were retained in care (Herce

et al., 2015). Broughton et al. in a controlled pre-post intervention study in Uganda demonstrated that through a chronic care model, it was possible to improve HIV care quality indicators. Odds of increased CD4 in the intervention group was 3.2 times higher than controls (p=0.022). Similarly, clinician-reported ART adherence was 60% (p=0.001) higher in the intervention group (Broughton et al., 2016).

Health Systems related outcomes – Non costed

Eleven studies reported that HIV-NCD care integration was feasible and acceptable to local communities (Afzal et al., 2017; Davies et al., 2018; Edwards et al., 2015; Ezechi, Gab-Okafor, Ostergren, & Odberg Pettersson, 2013; Kachimanga et al., 2017; Odafe et al., 2013; Miriam Rabkin, Anton Palma, et al., 2018; Rawat, Uebel, Moore, & Yassi, 2018; Sibanda, Ruhode, Madanhire, Hatzold, & Cowan, 2015). Five studies concluded that the HIV-NCD care integration model applied had resulted into successful outcomes (Ezechi et al., 2013; Kachimanga et al., 2017; Mwangome, Geubbels, Klatser, & Dieleman, 2016; Odafe et al., 2013; Sibanda et al., 2015). Application of the Donabedian theoretical framework provided evidence of quality systems in the integrated chronic disease management model in South Africa (S. Ameh, K. Klipstein-Grobusch, L. D'Ambruoso, et al., 2017). In addition to being feasible, HIV-NCD care integration was found to increase screening for cardiovascular disease risk factors, cervical cancer and NCD referrals (Ports, Haffejee, Mosavel, & Rameshbabu, 2015; Miriam Rabkin, Anton Palma, et al., 2018; Reid et al., 2016). Further, in a Kenyan study among 2,206 patients with 210 (9.5%) HIV infected, Edwards et al. found that NCD care for PLHIV along with HIV negative patients was feasible and achieved similar results (Edwards et al., 2015).

HIV-NCD care integration was found to reduce burden to the health system through innovative approaches that allowed for differentiated patient care. Integrated medical adherence clubs (MACs) in Kenya, demonstrated early efficacy for mixed chronic disease support through increased flexibility and a reduced burden of regular clinical review for stable patients (Khabala et al., 2015). MACs were found to offer efficient clinical management of co-morbidities and offer patients the benefit of peer support

(Venables et al., 2016). A randomized controlled study in Swaziland reported both improved CVD risk factor control and increased patient convenience (M. Rabkin et al., 2018). Increased linkages between HIV and other health services were observed in Zambia with enhanced likelihood of clients accessing additional needed health services (Hewett et al., 2016). Findings from a South African study supported integration as a method for improving continuity of care for both women and children (Clouse et al., 2018).

While noted to be feasible, several studies caution the need for a stepwise approach to HIV-NCD care integration. Phiri et al. in Malawi, recognized three factors required to overcome inertia over integration: acknowledgment of incremental resource requirements, albeit minimal, patient flow adjustments and use of data to inform future steps (Phiri et al., 2016). To increase utilization of HIV-NCD care integration, program managers require clarity on what aspects of the HIV program they are leveraging on (S. Ameh, K. Klipstein-Grobusch, L. D'Ambruoso, et al., 2017). Both adequate and a correct mix of resources are required to match needs of HIV-NCD care integration (Kumakech, Andersson, Wabinga, & Berggren, 2014; Leung et al., 2016; Pfaff, Scott, Hoffman, & Mwagomba, 2017). In a South African, pragmatic cluster randomized controlled trial with repeated cross-sectional surveys, Goudge et al. found that adding two lay health care workers to support a nurse in providing integrated chronic disease care was unlikely to have an effect on health outcomes. Necessary equipment and sufficient clinical staff to treat growing numbers of NCD clients were required to improve health outcomes (Goudge et al., 2018). Mitigating logistic challenges associated with supply chain management, overcoming the burden of developing integrated tools for HIV-NCD care and harnessing potential of patients and communities' preferences were all found to contribute positively to the success of integration (Coutinho, Nampijja, Musoke Seruma, Nambafu, & Mpiima, 2013; Pfaff et al., 2018; Van Deventer, 2015; Yuma, Giattas, & Bishanga, 2015).

Health Systems related costed outcomes

Three studies included elements of costing in their outcomes (Broughton et al., 2016; Golovaty et al., 2018; Phiri et al., 2018). In a comprehensive household integrated HIV-NCD screening program in South Africa, Golovaty et al. estimated the increase in program costs. All-inclusive NCD screening increased program costs by US Dollars (USD) 3.95 (42%) while excluding cholesterol testing lowered the increment to USD 2.24 (24%) (Golovaty et al., 2018). Broughton et al. estimated that the Ugandan chronic care model that had served 7,016 patients costed USD 1.67 per patient annually. Incremental cost effectiveness ratios of intervention compared to business as usual were USD 6.90 per additional patient with improved CD4 and USD 3.40 per additional ART patient with stable or improved adherence (Broughton et al., 2016). Phiri et al. at a large implementation study in Malawi estimated the annual cost of treatment of hypertension within PEPFAR funded HIV service delivery sites was USD 4.00 per patient (Phiri et al., 2018).

Two studies in Kenya estimated costs associated with cervical cancer screening (Vodicka et al., 2017; Zimmermann et al., 2017). Vodicka et al. found that from a societal perspective, integrating cancer of the cervix screening to HIV care would draw cost savings. Marginal per-screening costs were determined as follows: visual inspection via acetic acid (VIA) USD 3.30; careHPV USD18.28; Papanicolaou USD 24.59; and Hybrid Capture 2 screening USD 31.15. Indirect costs were cheaper for a single visit than two visit screening methods (USD 0.43 vs 2.88 respectively) (Vodicka et al., 2017). In a cost effectiveness analysis by Zimmermann et al., offering women cryotherapy VIA, Papanicolaou, and HPV at higher CD4 counts (>500 cells/ml) resulted in better life expectancies (19.9+ years) and lower costs (societal: USD 49, USD 99, USD 115 and USD 102; clinic: USD 13, USD 51, USD 71, and USD 56). VIA was most cost effective and preventative cryotherapy had the highest projected life expectancy (Zimmermann et al., 2017).

Using a quadratic cost function to examine cervical cancer screening and HIV care integration, Obure et al. found cost complementarities and modest efficiency gains. Careful considerations have to be made on service combinations when deciding what to integrate (Obure et al., 2016). Palma et al. in Malawi found increased visit durations with HIV-NCD care integration. Screening time increased from a median of 4 minutes to 15 minutes ($p<0.01$). Time on HIV care was not affected (Palma et al., 2018). Accounting for visit duration and patient flow would increase effectiveness of CVD risk factor screening and counseling into HIV programs.

PRISMA FLOW DIAGRAM

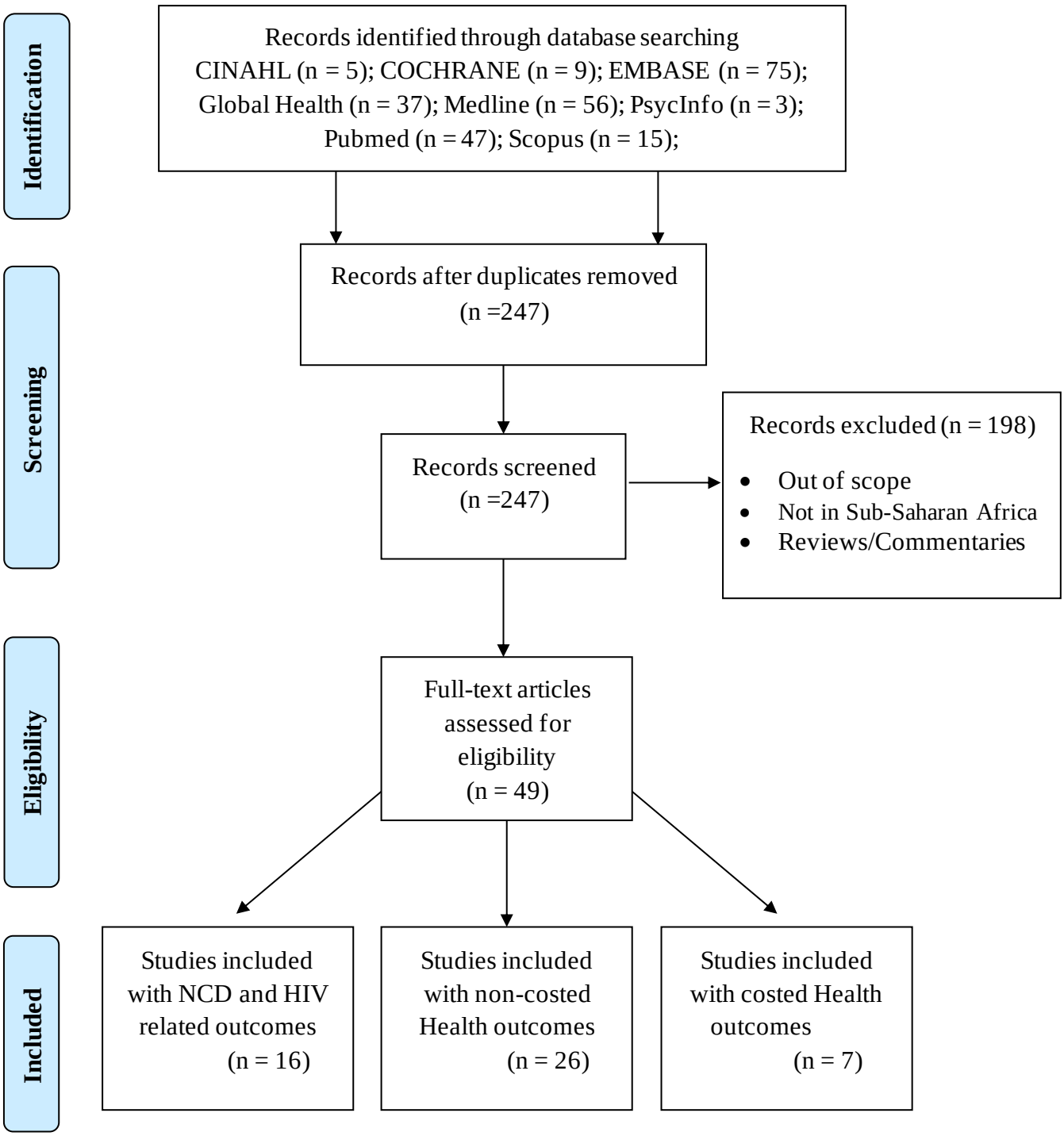


Figure 4.1.1: PRISMA flow diagram of the study selection process

Table 4.1.1: Characteristics of studies included in the Systematic Review (2013 - 2018)

Study Characteristics	n (%)
N	49
Region	
East Africa	17 (34.7%)
Other regions of Sub-Saharan Africa	32 (65.3%)
Study Type	
Qualitative	9 (18.4%)
Cross sectional/Descriptive	18 (36.8%)
Cohort	6 (12.2%)
Experimental/Quasi-experimental	7 (14.3%)
Mixed methods	3 (6.1%)
Econometric	6 (12.2%)
Target NCD*	
Cardiovascular Diseases including Hypertension	15 (30.6%)
Diabetes mellitus	12 (24.5%)
Cancer	23 (46.9%)
Chronic Respiratory Diseases	2 (4.1%)
≥ above 4 conditions	8 (16.3%)
Integration Model	
Integrated community-based screening for HIV and NCDs in the general population	6 (12.2%)
Screening for NCDs and NCD risk factors among HIV patients enrolled in care	24 (49.0%)
Integration of HIV and NCD care within clinics	16 (32.7%)
Differentiated care for patients with HIV and/or NCDs	2 (4.1%)
Population healthcare for all (Universal health care)	1 (2.0%)
Outcome Reported	
NCD and/or HIV/Program Related	16 (32.7%)
Health System: Non costed outcomes	26 (53.1%)
Health System: Costed outcomes	7 (14.2%)

**Several studies addressed more than one target NCD. Ten studies focused on both Diabetes mellitus and Hypertension; one study featured Kaposi Sarcoma.*

Table 4.1.2: Characteristics and findings from HIV/NCD integration studies reporting on HIV program and NCD-specific outcomes

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Acio, J. F., et al. (2013).(Acio et al., 2013)	Cohort study conducted in Uganda	3,500 HIV-infectedwomen	Integrated community outreach screening program - STAR- E; including home visits, treatment support meetings and referrals to lower-level health centres where screening camps were set	3450 (98.5%) WLHIV were screened for the first time; 3405 (98.7%) tested VIA negative; 45 (1.3%) tested VIA positive and were referred for cryotherapy	Integrated outreach screening programs offer access point for people at high risk for both STIs and cervical cancer. Additional benefits of STI treatment, identification of precancerous lesions, prevention education, identifying HIV-infected persons in need of care, and partner notification for STIs.
Afzal, O., et al. (2017).(Afzal et al., 2017)	Cross sectional study conducted in Limpopo province South Africa	403 participants; 306 farm workers, and 97 sex workers	see and treat" approach to screening using visual inspection with acetic acid (VIA)	83.9% of participants (32.9% sex workers and 100% farm workers) were HIV +. VIA was positive in 30.5% of participants, necessitating cryotherapy. No significant difference in VIA positivity between HIV + farm workers and sex workers. There was a positive correlation between Pap smears and VIAs results	Demonstrated successful integration of cervical cancer screening using VIA for HIV + farm workers and sex workers into an existing HIV treatment and prevention clinic in rural South Africa, addressing and treating abnormal results promptly.
Ameh, S., et al. (2017).(S. Ameh, K. Klipstein-Grobusch, E. Musenge, et al., 2017)	Controlled time series study conducted in PHC facilities in Bushbuckridge municipality, South Africa.	435 pilot and 443 control facilities	Pre/post ICDM model implementation	Six percent greater likelihood of controlling patients' CD4 counts (r = 0.057; 95% CI: 0.056 - 0.058; P < 0.001), and 1.0% greater likelihood of controlling patients' BP (coefficient = 0.010; 95% confidence interval: 0.003 to 0.016; P = 0.002) at pilot facilities.	Application of the model had a small effect in controlling patients' CD4 counts and BP, but showed no overall clinical benefit for the patients; hence, the need to more extensively leverage the HIV program for hypertension treatment
Bekolo, C. E., et al. (2016).(Bekolo et al., 2016)	Cross sectional study conducted in Nkongsamba Regional Hospital in Cameroon	302 women; 131 (43%) HIV infected and on HAART; 171 (56.6%) from community with unknown HIV status	Cervical cancer screening campaign with determination of Squamous intraepithelial lesions (SIL) by Pap smear	Cervical disease was observed in 51(16.9%) persons; 15 (11.5%) cases in HAART group and 36 (21.1%) cases in the general group(p = 0.027). After controlling for age and other covariates, women in HAART group had a 67% reduction in odds of cervical lesions compared with the community group [(aOR) = 0.33, 95%CI: 0.15-0.73, p = 0.006)	HIV-infected women receiving HAART have a lower risk of cancer than women in the general population. This finding may not be attributed to HAART alone but to all the health benefits derived from receiving a comprehensive HIV care.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Divala, O. H., et al. (2016).(Divala et al., 2016)	Cross sectional study conducted in Zomba district, Malawi,	952 PLHIV enrolled in care	Provided diagnosis for DM and HPTN at an HIV clinic	Hypertension diagnosis was associated with increasing age, higher body mass index, presence of proteinuria, being on regimen zidovudine/lamivudine/nevirapine and inversely with WHO clinical stage at ART initiation. Diabetes diagnosis was associated with higher age and being on non-standard first-line or second-line ART regimens	According to our criteria, 13.0% of HIV patients in care required drug treatment for hypertension and/or diabetes.
Drain, P. K., et al. (2018).(Drain et al., 2018)	Cross sectional study conducted in South Africa	5,428 adults	Measured a seated resting blood pressure in adults (>=18 years) prior to HIV testing, and again after receiving HIV test results,	HIV-infected adults had significantly lower blood pressure measurements and less hypertension, as compared to HIV-negative adults; while having significantly elevated blood pressures after HIV testing. HIV-infected adults had 26% lower odds of hypertension, compared to HIV-uninfected adults (aOR=0.74, 95% CI: 0.60-0.90), and HIV-infected adults with a CD4 <=200 cells/mm3 had 42% lower odds of hypertension (aOR=0.58, 95% CI: 0.38-0.89). Mean arterial blood pressure was 6.8 mmHg higher among HIV-infected adults after HIV testing (p <0.001)	Untreated HIV-infected adults, and particularly immunocompromised adults, had lower baseline rates of hypertension compared to HIV-negative adults, and that blood pressure transiently increased after receiving a positive HIV test result. Since hypertension screening may be dynamic around the time of HIV testing, hypertension screening should ideally occur before HIV testing, be repeated again after ART initiation and viral load suppression, and be continued at regular intervals.
Ezechi, O. C., et al. (2013).(Ezechi et al., 2013)	Cross sectional study conducted in Nigerian Institute of Medical Research (NIMR), Lagos, Nigeria	1,510 HIV infected women	Integrated cervical cancer screening	853 (56.2%) were aware of cervical cancer; 79.8% (1210) accepted screening; Cost of the test (35.2%) and religious denial (14.0%) were most common reasons given for refusal; having a tertiary education (OR = 1.4; 95% CI: 1.03-1.84), no living child (OR: 1.5; 95% CI: 1.1-2.0), recent HIV diagnosis (OR: 1.5; 95% CI: 1.1-2.0) and being aware of cervical cancer (OR: 1.5; 95% CI: 1.2-2.0) retained independent association with acceptance to screen for cervical cancer	Demonstrated that HIV infected women were willing to screen for cervical cancer and that integration of reproductive health service into existing HIV programs would strengthen rather than disrupt the services

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Herce, M. E., et al. (2015).(Herce et al., 2015)	A Cohort study conducted in rural Neno district, Malawi	114 adult HIV-KS patients who received ART and >/=1 chemotherapy	Protocol-guided chemotherapy, integrated antiretroviral therapy (ART) and psychosocial support delivered by community health workers	83% of patients (95% CI: 74-89%) were alive, 88 (77%) retained in care. Overall survival (OS) at 12 months did not differ by initial chemotherapy regimen (p=0.6). Among patients with T1 disease, low body mass index (BMI) (adjusted hazard ratio, aHR=4.10, 95% CI: 1.06-15.89) and 1 g/dL decrease in baseline hemoglobin (aHR=1.52, 95% CI: 1.03-2.25) were associated with increased death or loss to follow-up at 12 months	NKSC model resulted in infrequent adverse events, low loss to follow-up and excellent overall survival (OS). Our results suggest it is safe, effective and feasible to provide standard-of-care chemotherapy regimens from the developed world, integrated with ART, to treat HIV-KS in rural Malawi.
Huchko, M. J., et al. (2015).(Huchko et al., 2015)	A Prospective cohort study conducted in Western Kenya	284 HIV infected women	Follow-up colposcopy with biopsy	The 6- and 12-month rates of recurrence were 13.7 and 12.8 cases per 100 person-years of follow-up, respectively. Antiretroviral therapy use did not significantly impact the rate of recurrence (hazard ratio: 1.24, 95% CI: 0.59 to 2.79). The only significant predictor of recurrence was CD4 nadir <200 cells per cubic millimeter (adjusted hazard ratio: 3.14, 95% CI: 1.22 to 8.08).	Overall rate of treatment failure within a year of LEEP was low in this cohort of HIV-infected women. Among the women with recurrence, there was a significant amount of invasive cancer. The relatively high rate of cancer after treatment suggests that HIV-infected women merit continued close follow-up after treatment.
Jerene, D., et al. (2017).(Jerene et al., 2017)	A Cross sectional study conducted in Amhara, and Oromia regions in Ethiopia	3,439 patients; 888 Diabetes, 439 Tuberculosis; 2,112 HIV	Screening checklists for tuberculosis and diabetes, and additional risk scoring criteria to identify patients at risk of diabetes mellitus	Symptomatic patients and those with a risk score of 5 or more were about 3 times more likely to have abnormal blood glucose level. Of 2,075 HIV patients with Random Plasma Glucose (RPG) determined, only 31 (1.5%) had abnormal RPG	More work is needed to better understand interaction between HIV and Diabetes Mellitus. Research should focus on identifying the best tools and algorithms for screening Diabetes mellitus among patients with tuberculosis and HIV
Kachimanga, C., et al. (2017).(Kachimanga et al., 2017)	A Cross sectional study conducted in Neno, Malawi	14,000 adults (>= 12 years old) PLHIV and community members	Hypertension and diabetes screening	58% (n = 8133) and 29% (n = 4016) were screened for hypertension and diabetes, respectively. Nine percent (n = 716) and 3% (n = 113) were referred for further hypertension and diabetes assessment respectively. Since initiation of the screening programs, the number of patients ever enrolled for NCD care every 3 months has nearly tripled, from 40 to 114.	The screening models have shown that it is not only feasible to introduce NCD screening into a public system, but screening may have also contributed to increased enrolment in NCD care in Neno, Malawi.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Mitchell, S. M., et al. (2017).(Mitchell et al., 2017)	A Cross sectional study conducted in Uganda	87 HIV infected women	self-collection HPV testing	Of 87 WHIV offered self-collection, 40 women agreed to provide a sample at the HIV clinic. Among women tested, 45% were oncogenic HPV positive, where HPV 16 or 18 positivity was 15% overall.	High prevalence of oncogenic HPV, (HPV genotypes 16 or 18), and low knowledge of HPV and cervical cancer screening. Improved education and cervical cancer screening for WHIV are sorely needed; self-collection-based screening has the potential to be integrated with routine HIV care in this setting.
Mwangome, M. N., et al. (2016).(Mwangome et al., 2016)	A Qualitative study conducted in Tanzania	19 patients (10 HIV, 9 diabetes) and 13 family caregivers (6 HIV, 7 diabetes)	Innovative care for chronic conditions framework	HIV patients and caregivers knew more about aspects of HIV than did diabetes patients and caregivers on diabetes aspects. Continued education on care for the conditions was better structured for HIV than diabetes. Diabetes and HIV have socio-cultural and economic implications for patients and their families. The HIV program is successfully using decentralization of health services, task shifting and CHWs to address these implications.	For diabetes and NCDs, decentralization and task shifting are also important and, strengthening of community involvement is warranted for continuity of care and patient centeredness in care. While considering differences between HIV and diabetes, we have shown that Tanzania's rich experiences in community involvement in health can be leveraged for care and treatment of diabetes and other NCDs
Odafe, S., et al. (2013).(Odafe et al., 2013)	A Cross sectional study conducted in Nigeria	834 HIV infected women	Integrated screening for cervical cancer using VIA technique to HIV care and treatment services, combination of stakeholder engagement, capacity building for health workers, bi-directional referral between HIV and reproductive health (RH) services and provider-initiated counselling and screening for cervical cancer.	834 HIV+ women were offered VIA screening, and 805 (96.5%) accepted it. VIA was positive in 52 (6.5%) women while 199 (24.8%) had a sexually transmitted infection (STI)	Integrating VIA screening into the package of care offered to HIV+ women is feasible and acceptable. High burden of both HIV and cervical cancer in developing countries makes it a necessity for integrating services that offer early detection and treatment for both diseases.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Rawat, A., et al. (2018).(Rawat et al., 2018)	A Quasi-experimental study conducted in Free State, South Africa	131 PHC clinics	Integration of HIV into PHC	Trends in new diabetes patients on treatment remained unchanged. However, population-level new hypertensives on treatment decreased at +/-30 months from integration by 6/100, 000 (SE = 3, P < 0.02) and was associated with the number of new patients with HIV on treatment at the clinics	During implementation of integrated HIV care into PHC clinics, care for hypertensive patients could be compromised. Further research is needed to understand determinants of NCD care in South Africa and other high HIV-burdened settings to ensure patient-centered PHC.
Sibanda, E. L., et al. (2015).(Sibanda et al., 2015)	A Qualitative study conducted in Zimbabwe	69 HIV infected women	Integrated cervical cancer screening with HIV testing services	Women were positive about services being integrated because it enabled i) access to services under one roof; ii) information to spread. Other factors that facilitated CCS uptake were i) knowing someone who have suffered/died of cervical cancer, ii) peers iii) having suspicious symptoms iv) free services. Barriers were the same across phases; i) fear of cancer diagnosis which was greater among HIV positive women ii) concern that CCS is complex, iii) belief that the cervix is very fragile and Low risk perception was common with many believing that i) only old/HIV positive women are affected, ii) absence of signs/symptoms equates with low risk of disease	Integration has increased access to CCS while also facilitating spread of information on CCS, resulting in more positive views over time. Interventions that address myths/misconceptions are likely to improve uptake of CCS

Table 4.1.3a: Characteristics and findings from HIV/NCD integration studies reporting on Health Systems Outcomes

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Ameh, S., et al. (2017).(Ameh, Gómez-Olivé, Kahn, Tollman, & Klipstein-Grobusch, 2017)	A Cross sectional study conducted in Mpumalanga Province, South Africa	435 chronic disease patients; operational managers at seven PHC facilities in Bushbuckridge municipality	Integrated Chronic Disease Management (ICDM) model	Used a modified PSQ 8 questionnaire. Mediation pathway showed that the relationships between structure, process and outcome represented quality systems in the ICDM model. Structure correlated with process (0.40) and outcome (0.75). Given structure, process correlated with outcome (0.88). Of the 17 dimensions of care in the ICDM model, three structure (equipment, critical drugs, accessibility), three process (professionalism, friendliness and attendance to patients) and three outcome (competence, confidence and coherence) dimensions reflected their intended constructs.	The Donabedian's theoretical framework provided evidence of quality systems in the ICDM model
Ameh, S., et al. (2017).(S. Ameh, K. Klipstein-Grobusch, L. D'Ambruoso, et al., 2017)	A Qualitative study conducted in Agincourt sub-district South Africa	56 purposively selected patients >/=18 years; In-depth interviews were conducted with operational managers of each facility and the sub-district health manager General Public Patients	Integrated Chronic Disease Management (ICDM) model	Patients reported HIV stigmatization in the community due to defaulter-tracing activities of home-based carers. Managers reported treatment of chronic diseases by traditional healers and reduced facility-related HIV stigma because HIV and NCD patients attended the same clinic.	Leveraging elements of HIV programs for NCDs, specifically hypertension management, is yet to be achieved in the study setting in part because of malfunctioning blood pressure machines and anti-hypertension drug stock-outs. This has implications for the nationwide scale up of the ICDM model in South Africa and planning of an integrated chronic disease care in other low- and middle-income countries.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Bukirwa, A., et al. (2015).(Bukirwa et al., 2015)	A Qualitative study conducted in Uganda	18 HIV infected women; 6 key informant interviews with health care providers	cervical screening using Visual inspection with acetic acid and iodine (VIA and VILI)	Facilitators: Need for comprehensive assessment, diagnosis, and management of all ailments to ensure good health, fear of consequences of cervical cancer, suspicion of being at risk and the desire to maintain a good relationship with health care workers. Barriers: Myths and misconceptions such as the belief that a woman's ovaries and uterus could be removed during screening, fear of pain associated with cervical screening, fear of undressing and the need for women to preserve their privacy, low perceived cervical cancer risk, shortage of health workers to routinely provide cervical cancer education and screening, and competing priorities for both provider and patient time.	Findings highlight the need for client-centered counseling and support to overcome fears and misconceptions, and to innovatively address the human resource barriers to uptake of cervical cancer screening among HIV infected women.
Clouse, K., et al. (2018).(Clouse et al., 2018)	A Qualitative study conducted in Soweto, South Africa	25 postpartum HIV infected women	Integrated HIV-NCD care at clinic	facilitators and barriers to follow up: Barriers to follow-up included separate visit days, increased time commitment, transportation and logistics, unfamiliar clinic environments, and disrespectful staff. Factors facilitating patient engagement included social support and partner disclosure. Women were more likely to turn to friends and family for advice regarding HIV or the NCD, rather than a clinic. Women prioritized infant care after delivery, suggesting that baby care may be an entry point for improving maternal care after delivery	Findings support advocating for better integration of services at primary care level as a method to improve continuity of care for both women and children.
Coutinho, C., et al. (2013).(Coutinho et al., 2013)	A Cohort study conducted in Uganda	214 clients; both living with HIV and of unknown HIV status	Community mobilization and referrals; cervical cancer screening using VIA, treatment and management of positive lesions using Cryotherapy.	47.7% of clients were HIV positive; 19.2% positive screens for cancer of the cervix with 53.7% from HIV infected clients; from 79.9% negative results, 48.5% were HIV infected; 0.9% had suspicious lesions.	It is important to integrate cervical cancer screening within HIV/AIDS Care setting; however, HIV negative women of unknown status shun away from screening in an HIV/AIDS Care setting due to stigma.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Davies, N., et al. (2018).(Davies et al., 2018)	A Cross sectional study conducted in Johannesburg, South Africa	454 women; 91% HIV infected	Standard package of care designed to minimize HIV transmission risks; optimized pre-pregnancy health; Papanicolaou smear for eligible women; referrals for colposcopy for those with pathology prior to a pregnancy attempt.	At enrolment, 91% were HIV-positive, 92% ART and 82% virally suppressed; 83% (376/454) eligible for cervical cancer screening and 85% (321/376) completed screening. More than half had abnormal cervical pathology (185/321) and 20% required colposcopy for possible high-grade or persistently atypical lesions (64/321). Compared to HIV-negative women, abnormal pathology was more likely amongst HIV-positive women, both those on ART <2 years [aPR 2.5: 95%CI 1.2, 5.0] and those on ART >=2 years [aPR 2.1: 95% CI 1.0, 4.2].	Integrating cervical cancer screening into safer conception care was feasible with high coverage, including for HIV-positive women. Significant pathology, requiring colposcopy, was common, even amongst healthy women on ART. Safer conception services present an opportunity for integration of cervical cancer screening to avert preventable cancer-related deaths amongst HIV-affected women planning pregnancy
Edwards, J. K., et al. (2015).(Edwards et al., 2015)	A Cross sectional study conducted in Kibera, Nairobi, Kenya	2,206 patients; 210 (9.5%) HIV infected.	Integrated HIV-NCD care at clinic	Among patients with hypertension, blood pressure outcomes were similar, and for those with diabetes, outcomes for HbA1c, fasting glucose and cholesterol were not significantly different between the two groups. The frequency of chronic kidney disease (CKD) was 12% overall. Both groups responded similarly to treatment.	This study suggests that integrating NCD care for PLHIV along with HIV-negative patients is feasible and achieves similar results.
Goudge, J., et al. (2018).(Goudge et al., 2018)	A Pragmatic cluster randomized controlled trial with repeated cross-sectional surveys conducted in South Africa	4,000 participants in 8 rural clinics	adding two LHWs supporting nurses in providing chronic disease care in each intervention clinic over 18 months	While we found no improvement in BP control, the LHWs improved clinic attendance. A large and increasing numbers of patients, the dominance of the vertically funded HIV program and the poor standards of equipment in clinics compromised the quality of clinical care provided by nurses. Assistance from LHWs with booking appointments, sending reminders, prepacking medication and providing health education was insufficient to improve BP control in this environment.	LHWs can play an important role in supporting the provision of integrated chronic care. However, adding additional human resources (even if readily available and relatively inexpensive) is unlikely to have an effect on health outcomes, without the necessary equipment to accurately measure BP, and sufficient clinical staff to treat the growing numbers of chronic patients.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Hewett, P. C., et al. (2016).(Hewett et al., 2016)	A Randomized controlled trial conducted in Zambia	3,963 adult clients 18+; 1920 males, 2043 females (irrespective of HIV status)	Three study arms: 1) standard model of service provision at entry point (N = 1319); 2) an enhanced counseling and referral to add-on service with follow-up (N = 1323); and 3) components of study arm two, with additional offer of an escort (N = 1321)	Odds of clients accessing HIV testing and counseling, cervical cancer screening services among females, and circumcision services among males varied significantly by study arm at six weeks and six months; less consistent findings were observed for HIV care and treatment. Client uptake of family planning services did not vary significantly by study arm. Integrated services were found to be more efficiently provided than vertical service provision; cost-effectiveness for HIV/AIDS and cervical cancer was high in the enhanced service models.	Results provide evidence for increasing linkages and integration of a selection of HIV and sexual and reproductive health services. The study provided cost-effective service delivery models that enhanced likelihood of clients accessing some additional needed health services
Khabala, K. B., et al. (2015). (Khabala et al., 2015)	A Cross sectional study conducted in Nairobi, Kenya	1,432 patients; 1020 (71%) HIV and 412 (29%) non-communicable disease patients enrolled in 47 MACs	Integrated Medication Adherence Clubs (MACs)- nurse-facilitated mixed groups of 25-35 stable hypertension, diabetes mellitus and/or HIV patients who met quarterly to confirm their clinical stability, have brief health discussions and receive medication. Clinical officer reviewed MACs yearly, when a patient developed complications or no longer met stable criteria	Among those with NCD, 352 (85%) had hypertension and 60 (15%) had DM, while 12 had HIV concurrent with hypertension. A total of 2208 consultations were offloaded from regular clinic. During MAC attendance, blood pressure, weight and laboratory testing were completed correctly in 98-99% of consultations. Only 43 (2%) consultations required referral for clinical officer review before their routine yearly appointment. Loss to follow-up from the MACs was 3.5%.	Demonstrates feasibility and early efficacy of MACs for mixed chronic disease in a resource-limited setting. It supports burden reduction and flexibility of regular clinical review for stable patients. Further assessment regarding long-term outcomes of the MACs model should be completed to increase confidence for deployment in similar contexts.
Kumakech, E., et al. (2014).(Kumakech et al., 2014)	A Qualitative study conducted in Uganda	16: 12 Health care workers, 4 Policy makers	Integrated cervical cancer screening in HIV care	Integration of HIV and CC screening has potential to offer manifold benefits to all stakeholders in the health system, more so to the women. However, its feasibility in developing countries such as Uganda will most likely be hampered by weak and inefficient health systems	When considering HIV and CC screening integration, it is important not to only recognize the benefits but also take into account resources requirements for addressing the existing weaknesses and inefficiencies in the health systems such as limited infrastructure, insufficient drugs and supplies, inadequate and poorly motivated healthcare workers.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Kumakech, E., et al. (2015).(Kumakech, Andersson, Wabinga, & Berggren, 2015)	A Qualitative study conducted in Uganda	3 community FGDs with women and village health teams in 3 districts	Integrated cervical cancer screening in HIV care	Community members in Uganda perceive benefits of HIV and CC screening integration to outweigh the challenges; Three themes emerged from the data, namely appreciating the benefits of integration, worrying about the challenges of integration, and preferences for integration. The women endorsed the benefits.	The community members in Uganda perceive the benefits of HIV and CC screening integration to outweigh the challenges, and expect that the challenges can be minimized or managed by the women. Therefore, when considering HIV and CC screening integration, it is important to not only recognize the benefits but also take into consideration the perceived challenges and preferences of community members.
Kwarisiima, D., et al. (2016).(Kwarisiima et al., 2016)	A Randomized controlled trial conducted in Uganda	65,000 adults attending multi-disease community health campaigns in 20 rural Ugandan communities	Multi-disease community health campaigns	Hypertension prevalence was 14% overall, and 11% among HIV-positive individuals. 79% of patients were previously undiagnosed, 85% were not taking medication, and 50% of patients on medication had uncontrolled blood pressure; Viral suppression of HIV did not significantly predict hypertension among HIV-positives	Universal HIV screening programs could provide counseling, testing, and treatment for hypertension in Sub-Saharan Africa.
Leung, C., et al. (2016).(Leung et al., 2016)	A Cross sectional study conducted in Dar es Salaam, Tanzania.	14 HIV clinics	Integrated HIV-NCD care at clinic	43 % of clinics reported treating patients with hypertension; however, only 21 % had a protocol for NCD management. ECHO International Health standards for essential clinical equipment were used to measure clinic readiness; 36 % met the standard for blood pressure cuffs, 14 % for glucometers. Available laboratory tests for NCD included blood glucose (88 %), urine dipsticks (78 %), and lipid panel (57 %). 21 % had a healthcare worker with NCD training. All facilities provided some form of patient education, but only 14 % included diabetes, 57 % tobacco cessation, and 64 % weight management.	Integrated NCD and HIV care may be successfully achieved in these settings with basic measures incorporated into existing infrastructures at minimal added expense, i.e., improving access to basic functioning equipment, introducing standardized treatment guidelines, and improving healthcare worker education.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Mwanahamuntu, M. H., et al. (2013).(Mwanahamuntu et al., 2013)	A Cohort study conducted in Zambia	56,247 women attendees of Cervical Cancer Prevention Program in Zambia (CCPPZ)	Cervical cancer screening with VIA aided by digital cervicography.	HIV-seropositive women accessing services declined from 54% to 23% between 2006-2010, rates of VIA screening positivity declined from 47% to 17% during the same period (p-for trend <0.001), HIV-seropositive women were more than twice as likely (Odds ratio 2.62, 95% CI 2.49, 2.76) to screen VIA-positive than HIV-seronegative women	First 'real world' demonstration in a public sector implementation program in a sub-Saharan African setting that with successful program scale-up efforts, nurse-led cervical cancer screening programs targeting women with HIV can expand and serve all women, regardless of HIV serostatus.
Pfaff, C., et al. (2017).(Pfaff et al., 2017)	A Mixed methods study; cross sectional survey and qualitative interviews conducted in Malawi	3 NCD coordinators; 25 health centres and 5 hospitals in two rural districts in northern Malawi	Integrated HIV-NCD care at clinic	Treatment of hypertension and diabetes was predominantly hospital-based. At health centres, integrated NCD and ART care was more common, with 48% (12/25) providing ART and NCD treatment in the same consultation	Very small minority of patients with NCDs are being treated, predominantly within hospital settings rather than in health centres. Given the current workload observed, increased staff are needed to meet the demand for NCD screening and care
Pfaff, C., et al. (2018).(Pfaff et al., 2018)	A Cohort study conducted in Malawi.	6,036 adult HIV patients	integrated HIV-NCD care at clinic. Blood pressure was measured in adults at every visit and random blood glucose was determined every 2 years. Management was provided by clinical officers	765 were diagnosed with hypertension (prevalence 12.7% [95% CI 11.9-13.5); 25 were diagnosed with diabetes mellitus (prevalence 0.8% [95% CI 0.6-1.2]). Mean duration of ART visits by clinical officers increased from 80.5 to 90 min during the first quarter following HIV-NCD integration but returned to 75 min the following quarter.	The robust vertical HIV system made the design of integrated tools demanding. Challenges of integrated HIV-NCD care were related to patient flow, waiting times, NCD drug availability, data collection, clinic workload and the timing of diabetes and hypertension screening. Integrated HIV-NCD services provision was feasible in our clinic
Phiri, S., et al. (2016).(Phiri et al., 2016)	A Cross sectional conducted in Lilongwe, Malawi	6,000 PLHIV women	Step-wise integration of sexual and reproductive health (SRH) services	21% of eligible female patients received cervical cancer screening: 11% (166 women) had abnormal cervical findings during screening for cervical cancer and underwent further treatment. Proportion of women at Lighthouse using some form of modern contraception was 45% higher than at Lighthouse's sister clinic where services were not integrated (42% vs 29%),	Overcoming initial concerns about integration. First, integrated services required minimal additional resources over those needed for provision of HIV care alone. Second, patient flow improved during implementation, reducing a barrier for clients seeking multiple services. Lastly, higher contraceptive use with integration provided further evidence for promotion of SRH/ART integration.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Plotkin, M., et al. (2014).(Plotkin et al., 2014)	A Cross sectional study conducted in Tanzania	24,996 women; 21 govt health facilities in 4 regions of the country	Integration of HIV testing within newly introduced cancer of the cervix screening and treatment services	Integrating HIV testing into cancer of the cervix screening services was highly acceptable to clients and was an effective means of reaching HIV-positive women who did not know their status; Almost all women offered (94%) accepted testing, and 5% of those tested (582 women) learned for the first time that they were HIV-positive; effectiveness was limited, however, by shortages of HIV test kits at facilities.	Integration of HIV testing into cervical cancer screening services should be prioritized in HIV-endemic settings, but more work is needed to eliminate logistical barriers. The coverage of cervical cancer screening among HIV care and treatment-enrolled women in Tanzania may be low and should be examined.
Ports, K. A., et al. (2015).(Ports et al., 2015)	A Mixed methods study conducted in Durban, South Africa	67 women – structure interviews; 12 Key informant interviews	Integrated HIV and cervical cancer care	Participants had low cervical cancer knowledge, but desired more information. Relevant themes included the normalization of HIV and beliefs that cervical cancer might be worse than HIV. A comprehensive community clinic was desired by most, even if HIV-positive patients were treated there.	Integrating cervical cancer screening with HIV clinics may increase cancer screening among South African women.
Rabkin, M., et al. (2018).(Miriam Rabkin, Anton Palma, et al., 2018)	A Mixed methods Implementation science study conducted in Swaziland	1,826 HIV infected clients	Screening for hypertension, diabetes, hyperlipidemia, and tobacco smoking among patients at least 40 years and on ART	684 (39%) had at least one CVD risk factor	CVD risk factor screening was feasible and prevalence of risk factors in people living with HIV at least 40 years was high
Reid, M. J., et al. (2016).(Reid et al., 2016)	A Cross sectional conducted in Botswana	926 consults; 835 patients; 25% (209) HIV infected, 49% negative, 26% unknown status	Integrated NCD care by HIV outreach program	926 outpatient consults, involving 835 patients; 25% (n=209) HIV infected, (49%, n=410) HIV negative and (26%, n=216) unknown HIV status. Noncommunicable disease referrals were as common at primary- and district-level facilities (90% [n=459] versus 93% [n=301]; P=.22)	Demonstrates how HIV programming in Botswana can be leveraged to improve access to specialist medical services for patients with NCDs.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Rabkin, M., et al. (2018).(M. Rabkin et al., 2018)	A Randomized controlled trial conducted in Swaziland	240 HIV infected clients	Two arms: Integrated vs. referred CVD risk factors management for adults on ART	240 participants; Median age 51 years, 66% were female, 97% had hypertension, 17% had DM and 14% had HL; baseline characteristics were similar in both arms. Linkage to CVD risk factors care within 1 month was achieved by 85% and 84% of pts in the INT and REF arms, respectively. Pts in both arms attended 2.8 CVD risk factors visits on average; those in the INT arm were more likely to adhere to their assigned study arm (86% vs. 68%, risk ratio [RR]: 1.28). At 6 months, retention in HIV care was high (98%) but retention in CVD risk factors care was low (21%) with no differences between arms. Despite limited retention in CVD risk factors care, 122/193 (63%) of pts with hypertension initiated anti-hypertensive medicines; this was more likely in the INT arm (72% vs. 53%, RR: 1.35). Reductions in SBP and HbA1c occurred equally in both arms. Compared to baseline, mean ΔSBP was -15.0 mmHg (confidence interval [CI] -18.0, -11.8) in the INT arm and -15.9 mmHg (CI -19.0, -12.8) in the REF arm; mean ΔhbA1c was -0.68% (CI -1.26, -0.10) and -1.37% (CI -2.51, -0.24) in the INT and REF arms, respectively. Pts with HL in the REF arm also achieved significant reduction in TC (-0.91 mmol/L, CI -1.76, -0.65); there was no significant ΔTC in the INT arm.	Among HIV infected persons with both HIV and CVD risk factors, linkage and retention rates were similar for the integrated and referred CVD risk factors care models. Despite suboptimal retention in CVD risk factors management, pts in both arms showed improvement in CVD risk factors control. Integrated HIV and CVD risk factors services are more convenient for patients

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Van Deventer, C. (2015).(Van Deventer, 2015)	A Qualitative study conducted in North-west province, South Africa	332 patients and HCW in 9 PHC facilities	Empowerment evaluation – patient engagement in integrating and improving services for chronically ill patients (those with NCDs, mental health, HIV)	After 62 visits to 9 facilities over a year and after capturing 332 patient and health worker opinions and ideas, many interventions were implemented leading to improved flow at clinics, a heightened awareness of good services, interesting performance-measuring tools and patient/staff teams that acknowledged their symbiotic strength. Objective measurements comparing clinics that had been exposed to the Integrated Chronic Disease Model and those with the collaborative patient/staff groups showed no significant difference in clinical outcomes or waiting times	Potential of patients and patient-staff collaboration are being under-utilized in a resource strained sector where the harnessing of this potential might contribute positively towards QI in health
Venables, E., et al. (2016).(Venables et al., 2016)	A Qualitative study conducted in Kibera, Nairobi, Kenya	106 patients with HIV and /or NCDs and HCWs	MAC for HIV and NCD patients	MACs were considered acceptable to patients and health-care workers because they saved time, prevented unnecessary queues in the clinic and provided people with health education and group support whilst they collected their medication	Extending models of care previously only offered to HIV-positive cohorts to NCD patients can help to de-stigmatize HIV, allow for the efficient clinical management of co-morbidities and enable patients to benefit from peer support. Through MACs, we have demonstrated that an integrated approach to providing medication for chronic diseases including HIV can be implemented in resource-poor settings and could thus be rolled out in other similar contexts.
Yuma, S et.al (2015).(Yuma et al., 2015)	A Cross sectional study conducted in Tanzania	24,996 female patients	Integration of HIV testing within cervical cancer screening and treatment services	24,996 women screened for cervical cancer; 26% were referred in from HIV care clinics. Among the women of unknown HIV status (n=18,539), 60% offered an HIV test. Almost all women offered (94%) accepted testing and 5% of those tested (582 women) learned for the I time that they were HIV positive	It is feasible to roll out integrated services that include HIV testing and cervical cancer screening. Integrating HIV testing into cervical cancer screening services was highly acceptable and effective approach of reaching HIV positive women who did not know their status. However, its feasibility will most likely be hampered by shortage of HIV test kits for effective cervical cancer prevention service delivery. Integration of cervical cancer screening services with HIV testing should be prioritized in HIV endemic setting.

Table 4.1.3b: Characteristics and findings from HIV/NCD integration studies reporting on Costed Health Systems Outcomes

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Broughton, E. I., et al. (2016).(Broughton et al., 2016)	A Controlled, pre/post-intervention study conducted in Uganda	46 randomly sampled patients receiving HIV services at three control sites and 56 patients from three intervention sites	Two group training sessions and monthly coaching visits from improvement experts over 1 year, implementing the chronic care model (CCM)	Odds of increased CD4 in the intervention group was 3.2 times higher than controls (P = 0.022). Clinician-reported ART adherence was 60% (P = 0.001) higher in the intervention group. The intervention cost $11 740 and served 7,016 patients ($1.67 per patient). Incremental cost-effectiveness ratios of the intervention compared to business-as-usual was $6.90 per additional patient with improved CD4 and $3.40 per additional ART patient with stable or improved adherence.	For modest expenditure, it is possible to improve indicators of HIV care quality using CCM. We recommended implementing the CCM in Uganda; it may be applicable in similar settings in other countries.
Golovaty, I., et al. (2018).(Golovaty et al., 2018)	An Econometric/ Mixed methods study conducted in Kwa Zulu Natal, South Africa	570 adults in households	Integrated HIV-NCD screening (for HIV, diabetes, hypertension, hypercholesterolemia, obesity, depression, tobacco, and alcohol use), counseling, and linkage to care to all adults in households	Integrating all-inclusive NCD screening as part of home-based HTC in a high HIV prevalence setting increased program costs by $3.95 (42%) per person screened (from $9.36 to $13.31 per person). Integrated NCD screening, excluding point-of-care cholesterol testing, increased program costs by $2.24 (24%). NCD screening integrated into HTC services reduced the number of persons tested by 15%-20% per day.	Integrated HIV-NCD screening has the potential to efficiently use resources compared with stand-alone services. Although all-inclusive NCD screening could increase the incremental cost per person screened for integrated HIV-NCD services over 40%, a less costly lipid assay or targeted screening would result in a modest increase in costs with the potential to avert NCD death and disability. Our analysis highlights the need for implementation science studies to estimate the cost-effectiveness of integrated HIV-NCD screening and linkage per disability-adjusted life year and death averted.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Obure, C. D., et al. (2016).(Obure et al., 2016)	An Econometric study (Quadratic cost function) conducted in Kenya and Swaziland	40 health facilities	Integrated cervical cancer screening and SRH in HIV care	HIV counselling and testing services were characterized by service-specific economies of scale; cost complementarities between cervical cancer screening and HIV care	Contrary to expectation, efficiency gains from the integration of HIV and SRH services, if any, are likely to be modest. Efficiency gains are likely to be most achievable in settings that are currently delivering HIV and SRH services at a low scale with high levels of fixed costs. The presence of cost complementarities for only three service combinations implies that careful consideration of setting-specific clinical practices and the extent to which they can be combined should be made when deciding which services to integrate.
Palma, A. M., et al. (2018).(Palma et al., 2018)	An Econometric (time-motion study) conducted in Swaziland	172 patients	Observed HIV visits with and without screening and measured time spent on HIV and CVD risk factor screening activities	Screening increased total visit time from a median (range) of 4 minutes (2 to 11) to 15 minutes (9 to 30) ($p < 0.01$). Time spent on HIV care was not affected: 4 (2 to 10) versus 4 (2 to 11) ($p = 0.57$); at exit interviews, all of whom indicated that they would recommend screening to others	Provision of CVD risk factor screening more than tripled the length of routine HIV clinic visits but did not reduce the time spent on HIV services. Programme managers need to take longer visit duration into account in order to effectively integrate CVD risk factor screening and counselling into HIV programs
Zimmermann, M. R., et al. (2017).(Zimmermann et al., 2017)	An Econometric study (Cost effectiveness analysis) conducted in Nairobi, Kenya.	498 HIV infected women	Integrating cervical cancer screening in HIV clinic	Costs of cryotherapy, VIA, Pap, and HPV for women with CD4 200-500 cells/mL were $99, $196, $219, and $223 from a societal perspective and $19, $94, $124, and $113 from a clinic perspective, with 17.3, 17.1, 17.1, and 17.1 years of life expectancy, respectively. Women at higher CD4 counts (>500 cells/mL) given cryotherapy VIA, Pap, and HPV resulted in better life expectancies (19.9+ years) and lower cost (societal: $49, $99, $115, and $102; clinic: $13, $51, $71, and $56). VIA was less expensive than HPV unless HPV screening could be reduced to a single visit	Preventative cryotherapy was the least expensive strategy and resulted in highest projected life expectancy, while VIA was most cost-effective unless HPV could be reduced to a single visit.

Author, Year	Study Design, Country	Sample size, Subjects	Intervention	Key Findings	Conclusion
Phiri, S., et al. (2018).(Phiri et al., 2018)	An Econometric/Implementation Science study conducted in Lilongwe, Malawi	29,359 PLHIV	Integrated hypertension screening and management program using standardized hypertension treatment protocols and cohort monitoring with HIV service delivery	From 2/15 to 7/16, 29,359 adults >20 years old [median age 38 (IQR: 32-45) and 61% female] were screened for hypertension at two clinics. Of those screened, 3,448 (11%) were diagnosed with hypertension, of whom 85% were given lifestyle modification advice or started on treatment. Severe disease (BP >180/110) requiring immediate treatment with >= 2 drugs was noted in 38%. Of all patients on antihypertensive treatment for 6 months, 26% had achieved controlled BP. Of the 3,448 persons diagnosed with hypertension, 53% were male, of whom 46% were 40-49 years of age; 200 men aged 40-49 received treatment for six months and 25% achieved BP control. ART adherence for hypertensive patients receiving hypertension medications was similar with patients not on hypertension medications (80% vs. 79%, respectively). The annual cost of treatment of the entire cohort with hypertension was approximately $14,000 or $4/patient.	Hypertension screening and management can be successfully integrated into PEPFAR-funded HIV service delivery sites at low cost and with moderate blood pressure control rates. These findings support integration of NCD and HIV services to enhance HIV care as well as to target middle-aged men
Vodicka, E. L., et al. (2017).(Vodicka et al., 2017)	Econometric/ Mixed methods study (time-and-motion study was performed, and semi-structured interviews) conducted in Coptic Hope Center and Kenyatta National Hospital, Kenya	148 female HIV infected clients and 23 clinic staff	Integrating cervical cancer screening in HIV clinic	VIA was associated with the lowest estimated marginal per-screening costs ($3.30), followed by careHPV ($18.28), Papanicolaou ($24.59), and Hybrid Capture 2 screening ($31.15). Laboratory expenses were the main cost drivers for Papanicolaou and Hybrid Capture 2 testing ($11.61 and $16.41, respectively). Overhead and patient transportation affected the costs of all methods. Indirect costs were cheaper for single-visit screening methods ($0.43 per screening) than two-visit screening methods ($2.88 per screening).	Integrating cervical cancer screening into HIV clinics would be cost-saving from a societal perspective compared with non-integrated screening. These findings could be used in cost-effectiveness analyses to assess incremental costs per clinical outcome in an integrated setting.

DISCUSSION

In this systematic review, we synthesized findings from studies conducted in SSA region that addressed HIV-NCD care integration models. Owing to their growing significance and disproportionately high contribution to preventable deaths in LMICs (Bennett et al., 2018; WHO, 2013b), out attention was drawn and limited to studies that addressed bi-directional integration between HIV and four main NCD conditions – cardiovascular diseases, diabetes mellitus, chronic respiratory diseases, and cancers. Our study comes at a time when nations in the SSA region are reaffirming their commitments to provide improved health care services at a population level through universal health coverage (UHC) – a fundamental underpinning to attainment of the sustainable development goals (SDGs) (UN, 2018; WHO, 2019b). Effective implementation of UHC will benefit from additional data points on HIV and NCD care outcomes and health system costs obtained from HIV-NCD care integration models studied in this review.

From our systematic review, integration of HIV and NCD care was widely accepted by communities (Afzal et al., 2017; Ezechi et al., 2013; Kachimanga et al., 2017; Mwangome et al., 2016; Odafe et al., 2013). Five HIV-NCD integration models as described by Njuguna et al. were reviewed and all found feasible (Njuguna et al., 2018). As some studies demonstrated, community engagement was critical to the success of HIV-NCD integration for two reasons. First, through engagement with communities, feasibility of integration models that worked best was determined. Perceptions varied; while some communities found it acceptable to integrate services with HIV care (S. Ameh, K. Klipstein-Grobusch, L. D'Ambruoso, et al., 2017; Edwards et al., 2015; Ports et al., 2015), a study from Uganda highlighted stigma as a major deterrent to HIV-NCD care integration (Coutinho et al., 2013). Secondly, community engagement identified contribution of community members as essential to successful HIV-NCD care integration (Mwangome et al., 2016). While the literature demonstrated widespread acceptability and feasibility, only a few studies in Malawi, Zambia and South Africa described implementation of HIV-NCD care integration

at scale (Mwanahamuntu et al., 2013; Phiri et al., 2018; Van Deventer, 2015). Ministry of Health was identified as a lead in one HIV-NCD care integration model in South Africa (Van Deventer, 2015).

The paucity of HIV and NCD health outcomes data obtained from integrated care contributes to the inertia of SSA national health systems to implement HIV-NCD care integration. Literature on integration is fraught with gaps on health outcomes and cautions on unintended consequences that would weaken fragile health systems in SSA (Hyle et al., 2014; Petersen, Yiannoutsos, Justice, & Egger, 2014; Vorkoper et al., 2018). In our review, we identified studies that addressed health outcomes for both HIV and four selected NCD conditions. For HIV, all studies recorded positive outcomes for case finding, retention in care, increased CD4 counts and improvements in quality of life (Acio et al., 2013; Broughton et al., 2016; Herce et al., 2015). Early NCD screening and identification, prevalence estimates, and forestalling of NCD related complications were identified for NCDs (Davies et al., 2018; Edwards et al., 2015; Khabala et al., 2015; Kwarisiima et al., 2016; Zimmermann et al., 2017). Innovative differentiated care models that increase patient centered care, such as integrated medication adherence clubs, as described by Venables et al. and Khabala et al. were found to improve both HIV and NCD care outcomes (Khabala et al., 2015; Venables et al., 2016).

Costs and cost-effectiveness data for integration is an important data piece to inform roll out of HIV-NCD care integration at scale. However, in SSA, there exist significant gaps in literature on program cost data. A recent systematic review in Africa found that only a few studies reported cost data, with no study assessing the cost of long-term chronic disease management. The incremental cost of HIV-NCD care integration represented a 6% -30% increase in the total program costs for non-cancer NCDs (R. Nugent et al., 2018). Our systematic review found similar gaps with few studies reporting either cost effectiveness or cost data. Studies that reported cost data found that the incremental costs for HIV-NCD care integration were modest at USD 3.95 – 4.00 per patient annually for hypertension (Golovaty et al., 2018; Phiri et al., 2018) and USD 3.30 using VIA for cervical cancer screening (Vodicka et al., 2017; Zimmermann et al.,

2017). Cost variability was exhibited by type of screening tests, and patient characteristics (Golovaty et al., 2018). Better life expectancies (19.9+ years) and lower costs were observed for women with CD4 counts above 500 cells/ml (Zimmermann et al., 2017).

The resource considerations for HIV-NCD care integration remain complex and poorly described. From our systematic review, beyond leveraging on the robust vertical HIV service delivery systems for NCD care delivery, clarity on what components of the HIV platform to leverage upon was critical to the success of integration (Goudge et al., 2018). Modest gains have been documented depending on what components are integrated, level of fixed costs and existing infrastructure (Obure et al., 2016). Further, beyond adequate numbers, successful HIV-NCD care integration was also attributed to a correct cadre-mix of human resources for health (Goudge et al., 2018). Functional equipment and infrastructure, and a strengthened supply chain system to assure consistent supplies of both screening kits and medication added to the success of HIV-NCD care integration (Acio et al., 2013; Phiri et al., 2018; Yuma et al., 2015). Harnessing the potential of patients, through their knowledge and linkages in the community, not only served to assure the success of HIV-NCD care integration but also strengthened the health system (Mwangome et al., 2016).

To overcome the inertia of HIV-NCD care integration, some authors propose a stepwise approach that accounts for the additional resources, takes into consideration patient flow and utilizes routine data (Phiri et al., 2016). Development of integrated tools for HIV-NCD care and monitoring has been described as demanding yet a necessary pre-requisite for successful integration (Pfaff et al., 2018). Unintended consequences of HIV-NCD care integration, such as increased wait times and increased costs of seeking care have been described (Hyle et al., 2014). In a time-motion study that integrated CVD screening into HIV care in Swaziland, program managers factored in increased visit times into the program design which contributed to safeguarding the gains of improved CVD outcomes (Palma et al., 2018). Quality of care and balancing indicators using Donabedian quality improvement models serve to assure improved

program quality (Soter Ameh et al., 2017). Integrated HIV-NCD care models could also be considered a form of differentiated care that promotes patient focus. By reducing clinic burdens for health care workers, differentiated care models such as MACs allow for increased visit times for sick clients. This promotes efficient clinical management and as such are worth implementing at scale (Venables et al., 2016).

Our study is not without limitations. While we sought to accrete evidence on four selected NCD conditions, very few studies were noted to address two of the four conditions – chronic respiratory diseases and diabetes mellitus (Jerene et al., 2017; Mwangome et al., 2016; M. Rabkin et al., 2018; Rawat et al., 2018). This comes in the backdrop of a recent systematic review in SSA by Coetzee et al. who found a 5.8% prevalence of diabetes among PLHIV (Coetzee et al., 2019) . That the two conditions are underrepresented is an important gap to inform future research agenda. Due to the heterogeneity of study populations, methodology and outcome findings from the studies examined, we did not conduct a meta-analysis to pool estimates. The robustness of inferences made from cost estimates presented in this review is therefore limited. Lastly, since very few studies included in this review were implemented at a public health scale, we recommend a cautious interpretation on the generalizability of our findings.

Conclusion and Recommendations

Caught between the raging HIV and NCD epidemics (Gouda et al., 2019), SSA is experiencing a watershed moment. Beyond political goodwill and reaffirmation to offering improved health care to its people through UHC, SSA nations ought to consider making urgent decisive steps to address the HIV-NCD syndemic. With the incremental cost (6-30%) for non-cancer NCDs, and the benefits accrued – both on HIV care continuum and NCD forestalling of complications, scale up of integrated HIV-NCD care programs is worthwhile in Kenya.

The evidence adduced from this systematic review indicates that while integration is the ideal, it may not be our panacea. HIV programs are robust based and can support other fragile components of the health

system. Coupled with well-trained health care workers and efficient supply chain systems, the aforementioned serve as opportunities for countries such as Kenya to leverage upon. To mitigate against overloading the health care workers, integration options that involve use of lay cadres including community health volunteers should be considered. Task shifting of screening for NCDs to volunteers and peers at clinics presents an excellent opportunity to scale up NCD care. Use of integrated reporting tools and cross training approaches will ensure that commodity security is assured. Lastly, decanting clinics through multi disease community adherence clubs and ART groups and multi month dispensing will serve to advance HIV/NCD integration in Kenya.

Annex 4.1.1. Database Search Strategy (January 2013 – December 2018)

Database	Strategy
Pubmed (Medline)	HIV* OR AIDS OR human immunodeficiency virus
(OVID)	AND
1946-	Noncommunicable disease* OR non-communicable disease* OR noninfectious disease* OR non-infectious disease* OR Noncommunicable illness* OR non-communicable illness* OR noninfectious illness* OR non-infectious illness* OR Noncommunicable condition* OR non-communicable condition* OR noninfectious condition* OR non-infectious condition* OR cardiovascular disease* OR (chronic ADJ5 disease*) OR (chronic ADJ5 illness*) OR (chronic ADJ5 condition*) OR heart disease* OR stroke* OR neoplasm* OR cancer* OR diabet* OR comorbid* OR co-mordid* OR respiratory disease* OR respiratory illness* OR COPD OR pulmonary disease
	AND
	(integrat* ADJ5 care) OR (intergrat* ADJ5 health) OR (coordinated ADJ5 care) OR comprehensive care OR seamless care OR transmural care OR collaborative care OR (differentiated ADJ5 care) OR (integrat* ADJ5 screen*) OR (integrat* ADJ5 test*) OR (integrat* ADJ5 model*) OR (integrat* ADJ5 approach*)
Embase	HIV* OR AIDS OR human immunodeficiency virus
(OVID)	AND
1947-	Noncommunicable disease* OR non-communicable disease* OR noninfectious disease* OR non-infectious disease* OR Noncommunicable illness* OR non-communicable illness* OR noninfectious illness* OR non-infectious illness* OR Noncommunicable condition* OR non-communicable condition* OR noninfectious condition* OR non-infectious condition* OR cardiovascular disease* OR (chronic ADJ5 disease*) OR (chronic ADJ5 illness*) OR (chronic ADJ5 condition*) OR heart disease* OR stroke* OR neoplasm* OR cancer* OR diabet* OR comorbid* OR co-mordid* OR respiratory disease* OR respiratory illness* OR COPD OR pulmonary disease
	AND
	(integrat* ADJ5 care) OR (intergrat* ADJ5 health) OR (coordinated ADJ5 care) OR comprehensive care OR seamless care OR transmural care OR collaborative care OR (differentiated ADJ5 care) OR (integrat* ADJ5 screen*) OR (integrat* ADJ5 test*) OR (integrat* ADJ5 model*) OR (integrat* ADJ5 approach*)

Database	Strategy
PsycInfo	HIV* OR AIDS OR human immunodeficiency virus
(OVID)	AND
1967-	Noncommunicable disease* OR non-communicable disease* OR noninfectious disease* OR non-infectious disease* OR Noncommunicable illness* OR non-communicable illness* OR noninfectious illness* OR non-infectious illness* OR Noncommunicable condition* OR non-communicable condition* OR noninfectious condition* OR non-infectious condition* OR cardiovascular disease* OR (chronic ADJ5 disease*) OR (chronic ADJ5 illness*) OR (chronic ADJ5 condition*) OR heart disease* OR stroke* OR neoplasm* OR cancer* OR diabet* OR comorbid* OR co-mordid* OR respiratory disease* OR respiratory illness* OR COPD OR pulmonary disease
	AND
	(integrat* ADJ5 care) OR (intergrat* ADJ5 health) OR (coordinated ADJ5 care) OR comprehensive care OR seamless care OR transmural care OR collaborative care OR (differentiated ADJ5 care) OR (integrat* ADJ5 screen*) OR (integrat* ADJ5 test*) OR (integrat* ADJ5 model*) OR (integrat* ADJ5 approach*)
Global Health	HIV* OR AIDS OR human immunodeficiency virus
(OVID)	AND
1973-	Noncommunicable disease* OR non-communicable disease* OR noninfectious disease* OR non-infectious disease* OR Noncommunicable illness* OR non-communicable illness* OR noninfectious illness* OR non-infectious illness* OR Noncommunicable condition* OR non-communicable condition* OR noninfectious condition* OR non-infectious condition* OR cardiovascular disease* OR (chronic ADJ5 disease*) OR (chronic ADJ5 illness*) OR (chronic ADJ5 condition*) OR heart disease* OR stroke* OR neoplasm* OR cancer* OR diabet* OR comorbid* OR co-mordid* OR respiratory disease* OR respiratory illness* OR COPD OR pulmonary disease
	AND
	(integrat* ADJ5 care) OR (intergrat* ADJ5 health) OR (coordinated ADJ5 care) OR comprehensive care OR seamless care OR transmural care OR collaborative care OR (differentiated ADJ5 care) OR (integrat* ADJ5 screen*) OR (integrat* ADJ5 test*) OR (integrat* ADJ5 model*) OR (integrat* ADJ5 approach*)
CINAHL	HIV* OR AIDS OR "human immunodeficiency virus"
(Ebsco)	AND
	"Noncommunicable disease*" OR "non-communicable disease*" OR "noninfectious disease*" OR "non-infectious disease*" OR "Noncommunicable illness*" OR "non-communicable illness*" OR "noninfectious illness*" OR "non-infectious illness*" OR "Noncommunicable condition*" OR "non-communicable condition*" OR "noninfectious condition*" OR "non-infectious condition*" OR "cardiovascular disease*" OR (chronic N5 disease*) OR (chronic N5 illness*) OR (chronic N5 condition*) OR "heart disease*" OR stroke* OR neoplasm* OR cancer* OR diabet* OR comorbid* OR co-mordid* OR "respiratory disease*" OR "respiratory illness*" OR COPD OR "pulmonary disease"
	AND
	(integrat* N5 care) OR (intergrat* N5 health) OR (coordinated N5 care) OR "comprehensive care" OR "seamless care" OR "transmural care" OR "collaborative care" OR (differentiated N5 care) OR (integrat* N5 screen*) OR (integrat* N5 test*) OR (integrat* N5 model*) OR (integrat* N5 approach*)

Database	Strategy
Scopus	TITLE-ABS-KEY(HIV* OR AIDS OR "human immunodeficiency virus") AND TITLE-ABS-KEY("Noncommunicable disease*" OR "non-communicable disease*" OR "noninfectious disease*" OR "non-infectious disease*" OR "Noncommunicable illness*" OR "non-communicable illness*" OR "noninfectious illness*" OR "non-infectious illness*" OR "Noncommunicable condition*" OR "non-communicable condition*" OR "noninfectious condition*" OR "non-infectious condition*" OR "cardiovascular disease*" OR (chronic W/5 disease*) OR (chronic W/5 illness*) OR (chronic W/5 condition*) OR "heart disease*" OR stroke* OR neoplasm* OR cancer* OR diabet* OR comorbid* OR co-mordid* OR "respiratory disease*" OR "respiratory illness*" OR COPD OR "pulmonary disease") AND TITLE-ABS-KEY((integrat* W/5 care) OR (intergrat* W/5 health) OR (coordinated W/5 care) OR "comprehensive care" OR "seamless care" OR "transmural care" OR "collaborative care" OR (differentiated W/5 care) OR (integrat* W/5 screen*) OR (integrat* W/5 test*) OR (integrat* W/5 model*) OR (integrat* W/5 approach*))
Cochrane Library	(HIV* OR AIDS OR "human immunodeficiency virus"):ti,ab
	AND
	((Noncommunicable NEXT disease*) OR (non-communicable NEXT disease*) OR (noninfectious NEXT disease*) OR (non-infectious NEXT disease*) OR (Noncommunicable NEXT illness*) OR (non-communicable NEXT illness*) OR (noninfectious NEXT illness*) OR (non-infectious NEXT illness*) OR (Noncommunicable NEXT condition*) OR (non-communicable NEXT condition*) OR (noninfectious NEXT condition*) OR (non-infectious NEXT condition*) OR (cardiovascular NEXT disease*) OR (chronic NEAR/5 disease*) OR (chronic NEAR/5 illness*) OR (chronic NEAR/5 condition*) OR (heart NEXT disease*) OR stroke* OR neoplasm* OR cancer* OR diabet* OR comorbid* OR co-mordid* OR (respiratory NEXT disease*) OR (respiratory NEXT illness*) OR COPD OR "pulmonary disease"):ti,ab
	AND
	((integrat* NEAR/5 care) OR (intergrat* NEAR/5 health) OR (coordinated NEAR/5 care) OR "comprehensive care" OR "seamless care" OR "transmural care" OR "collaborative care" OR (differentiated NEAR/5 care) OR (integrat* NEAR/5 screen*) OR (integrat* NEAR/5 test*) OR (integrat* NEAR/5 model*) OR (integrat* NEAR/5 approach*)):ti,ab

4.2 To characterize NCD burden of the four leading NCDs that lead to the highest morbidity and mortality among PLHIV attending general population ART clinics in Kenya

Publication Title: Noncommunicable disease burden among HIV patients in care: a national retrospective longitudinal analysis of HIV-treatment outcomes in Kenya, 2003-2013

ABSTRACT

Background: Over the last decade, the Kenyan national HIV treatment program has grown exponentially, with improved survival among people living with HIV (PLHIV). In the same period, noncommunicable diseases (NCDs) have become a leading contributor to disease burden in the country. There is limited data on the burden of NCDs among PLHIV in Kenya.

Objectives: We sought to characterize the burden of four major categories of NCDs (cardiovascular diseases, cancer, chronic respiratory diseases and diabetes mellitus) among adult PLHIV in Kenya.

Methods: We conducted a nationally representative retrospective medical chart review of HIV-infected adults aged ≥15 years enrolled in HIV care and treatment facilities in Kenya during the period October 1, 2003 through September 30, 2013. We estimated proportions of the four NCD categories among PLHIV at enrollment into HIV care, and occurrence and management during subsequent HIV care and treatment visits. We compared proportions and assessed distributions of co-morbidities using the Wald adjusted Pearson's χ-square test. We calculated NCD incidence rates and their jackknife confidence intervals in assessing cofactors for developing NCDs.

Results: We analyzed 3170 patient records; 2115 (66.3%) were from women. Slightly over half (51.1%) of patient records were from PLHIVs aged above 35 years. Close to two-thirds (63.9%) of PLHIVs were on ART. The proportion of any documented NCD among PLHIV was 11.5% (95% confidence interval [CI] 9.3, 14.1), with elevated blood pressure as the most common NCD (87.5%) among PLHIV with

diagnosed NCD. Although serial elevated blood pressures were detected among 343 patients, only 17 had a documented diagnosis of hypertension in their medical record. The differences in overall NCD incidence rates for men and women were not statistically significant (42.3 per 1000 person years [95% CI 35.8, 50.1] and 31.6 [95% CI 27.7, 36.1], respectively). No differences in NCD incidence rates were seen by marital or employment status. At one year of follow up 43.8% of PLHIV not on ART had been diagnosed with an NCD compared to 3.7% of patients on ART; at five years the proportions with a diagnosed NCD were 88.8% and 39.2% ($p<0.001$), respectively.

Conclusions and recommendations: PLHIV in Kenya have a high incidence of NCD diagnoses. In the absence of systematic screening, NCD incidence is likely underestimated in this population. In the context of a rising national burden of NCDs and increased survival among PLHIV, Kenya should consider maximizing ways to integrate HIV-NCD screening and care.

INTRODUCTION

The last decade has witnessed an unprecedented growth in coverage of HIV care and treatment programs globally. Expanded criteria for initiation of highly effective antiretroviral therapy (ART) for people living with HIV (PLHIV) has been associated with increased longevity and favorable treatment outcomes (El-Sadr & Goosby, 2018; WHO, 2016b). Over the same period, noncommunicable diseases (NCDs) and associated deaths have risen steadily. At a global scale, WHO estimates 31 million NCD-related deaths occur on an annual basis. Three quarters of these deaths are in low and middle-income countries. In the general population, four major –CDs - cardiovascular diseases (including hypertension, heart attack and stroke), cancer, chronic respiratory diseases and diabetes mellitus make the largest contribution to both morbidity and mortality (WHO, 2013b).

Sub-Saharan Africa (SSA), which is home to over half of the estimated PLHIV worldwide, is faced with a dual disease epidemic – communicable diseases and NCDs (Levitt et al., 2011b; G. o. K. Ministry of Health, 2015; UNAIDS, 2016). While several countries in SSA continue to report rapid scale-up of their national ART programs (Farahani et al., 2014; UNAIDS, 2016; WHO, 2016b), a concomitant rise in incidence of NCDs and NCDs-related deaths is also observed over the last decade (Miszkurka et al., 2012). NCDs, and particularly the four aforementioned, account for over half of all hospital admissions and deaths in Kenya (Kenya National Bureau of Statistics et al., 2015; G. o. K. Ministry of Health, 2015). Increased longevity of PLHIV on ART suggests likely increases in prevalence of NCDs among PLHIV in future (Bloomfield et al., 2014; Farahani et al., 2014; National AIDS Control Council (NACC) & National AIDS/STD Control Programme (NASCOP), 2016; UNAIDS, 2016; WHO, 2016b).

Several studies examining NCDs among PLHIV have been conducted in SSA (Edwards et al., 2015; Kagaruki et al., 2014; Kavishe et al., 2015; Magodoro et al., 2016; Peck et al., 2014). Most of these have involved cross-sectional surveys of facility level data, with smaller and less-representative samples. Previous national HIV treatment outcome studies in SSA have also not addressed NCDs among PLHIV

(Farahani et al., 2014; Mutasa-Apollo et al., 2014). Additionally, there is paucity of data on the impact of NCDs' burden among PLHIV from early public health approaches in HIV programming that stratified clients in care based on declining CD4 counts (WHO, 2013a). PLHIV in care with low CD4 counts as per prevailing national guidelines were considered eligible for HIV treatment and had ART included in their care accordingly. These "ART cohorts" were different from the corresponding clients in "pre-ART cohorts" who had higher CD4 counts than the then established thresholds for ART initiation.

Using a nationally representative sample, we sought to estimate the burden of NCDs among PLHIV enrolled in HIV care and treatment in Kenya between 2003 and 2013.

RESULTS

Study Population Characteristics

A total of 3170 patient records were analyzed (figure 4.2.1), with over two thirds of records (2115) constituting women. At the time of data abstraction, slightly over half (52.1%) of patients were under the age of 35 years with women being significantly more than men ($p< 0.001$). The majority (68.3%) of patients were employed; men were more likely to be documented as having formal or informal employment than women ($p< 0.001$). Half (51.1%) of patients were married or cohabiting, 12% were widowed, 7.8% divorced/separated, and 13.5% single or never married. There was a significant difference in marital status between men and women ($p<0.001$) with 64.7% (95% CI: 55.9, 72.7) of men being married as compared to 44.2% (95% CI: 39.9, 48.7), of women (Table 4.2.1).

In this cohort, (63.9%) of patients had initiated ART by the time of data abstraction, with no significant differences by sex ($p=0.874$). Just over half of patients were enrolled in care during 01 January 2006 to 30 June 2010 (54.3%). Only 9% of patients had been enrolled during the 01 Jan 2003 to 31 Dec 2005 guideline period. No differences were observed by sex across the three guideline enrollment periods ($p=0.070$). Almost similar proportions of patients had been on d4T and TDF containing regimens, (36.5%

vs 35.8% respectively). A quarter of the patients (26.9%) had been on an AZT containing regimen. Only 0.4% and 0.5% of patients were on an LPV/r or ABC containing regimen respectively at the time of data abstraction. No significant difference was noted in regimen type between men and women (p=0.05). Most patients did not have a documented WHO stage (74.7%) or CD4 count (85.4%) (Table 4.2.1).

NCDs among PLHIV

In this cohort, 387/3170 (11.5%) (95% CI: 9.3, 14.1), had evidence of any NCD in their HIV clinical care record. There was no difference between men and women in proportion with a NCD (p=0.308) (Table 4.2.1).

The proportion of patients with a documented diagnosis of an NCD among PLHIV not on ART rose sharply in the first few years of follow-up compared to the otherwise smooth trajectory and longer duration observed for PLHIV on ART (p<0.001). PLHIV who had not yet initiated ART were more likely to have a NCD diagnosis at one and five years of follow up. At one year of follow up 43.8% of PLHIV not on ART had been diagnosed with an NCD compared to 3.7% of patients on ART; at five years the proportions with a diagnosed NCD were 88.8% and 39.2% (p<0.001), respectively (Figure 4.2.2).

Overall NCD incidence was 35.1 per 1000 person years. Men had an overall NCD incidence of 42.3 per 1000 person years (95%CI: 35.8, 50.1) compared to 31.6 (95%CI: 27.7, 36.1) in women. The highest incidence rates were observed among 45-54 and ≥55-year-olds at 57.5 (95%CI: 46.7, 70.9) and 55.0 (95%CI: 38.5, 78.7) per 1000 person years respectively. The 15–24-year age band had the lowest incidence rate at 21.0 per 1000 person years (95%CI: 13.8, 31.9). No significant differences in NCD incidence rates were seen based on marital or employment status, (Table 4.2.2).

Among the 387 PLHIV with a NCD, the crude incidence rate ratio (crude IRR) for development of NCDs during follow up was 2.47 (95%CI: 1.6, 3.6) for PLHIV not initiated ART as compared to PLHIV who

initiated ART [p<0.001]), (Figure 4.2.3). Crude IRR for NCDs among men was similar to that among women (IRR=1.02, p=0.84). There was no difference in NCD crude IRR between PLHIV aged <35 years compared to PLHIV aged ≥35 years (p=0.51). No difference was detected between single/never married PLHIV and those who were married/cohabiting (IRR=1.08, p=0.62). Similarly, crude IRR of developing NCDs was no different among PLHIV who were not employed during follow up versus PLHIV who were gainfully employed (IRR=1.29, p=0.08). WHO staging comparing advanced disease staging (stage III/IV) to early disease staging (stage I/II) had a crude IRR of 0.85 (p=0.5). Age-adjusted analysis revealed no further effect for all IRRs previously described.

NCDs burden

Elevated Blood pressure: Among PLHIV with any recorded NCD, 343/387, 87.5% (95%CI 80.1, 92.4) were found to have two or more elevated blood pressure readings taken <12 months apart (our proxy measure of hypertension). Among patients with comorbidity, elevated blood pressure was more frequent in persons on ART 92.8% (95%CI 88.9, 95.4) vs 50.6% (95%CI 26.5, 74.5) not on ART respectively (p=0.03), (Table 2.3). Although serial elevated blood pressures were detected among 343 patients, only 17 (0.5%) had a documented diagnosis of hypertension in their medical record (results not shown).

Diabetes Mellitus: Only 9/387, 2.1% (95%CI: 0.9, 4.7) of PLHIV with NCD had documented diabetes mellitus. Compared by ART status, no significant difference was observed between PLHIV on ART and those not on ART, (p=0.44) (Table 2.3).

Chronic respiratory diseases: We found 9/387, 2.3% (95%CI 1.1, 4.9) of PLHIV with NCD had a documented diagnosis of asthma. Compared to patients on ART, there was no difference in documented asthma among non-ART patients; 1.3% (95%CI 0.5, 3.4) vs 9.3% (95%CI 3.2, 24.5) respectively, (p=0.15) (Table 2.3).

Cancer: Any form of cancer was documented among 3/387, 1.1% (95%CI 0.2, 4.8) of PLHIV with NCD with no statistical difference between patients on ART 1.2% (95%CI 0.2, 5.6) and those not on ART 0%, (p=0.28) (Table 4.2.3).

DISCUSSION

This evaluation describes burden of NCDs among pre- ART and ART patients from a nationally representative survey of HIV care and treatment in Kenya. This is in context to a rising burden of NCDs in Africa against a backdrop of a rapid scale up of antiretroviral therapy coverage that has contributed to increased life expectancy among PLHIV (El-Sadr & Goosby, 2018; Magodoro et al., 2016; May et al., 2014; Trickey et al., 2017; Vorkoper et al., 2018). In this study overall incident rate for diagnosed NCDs was lower amongst those on ART compared to those not on ART. This is in keeping with other study findings that have shown increased prevalence of NCD risk factors among PLHIV not on antiretroviral treatment (Patel et al., 2018; van Heerden et al., 2017). Compared to other studies that suggest social economic deprivation as a predictor of NCDs risk factor among PLHIV (Kagaruki et al., 2014; Zolopa et al., 2009), our study did not detect a difference based on employment status.

WHO's recommendation to expand ART eligibility to all persons diagnosed with HIV was adopted in Kenya in 2016 (Ministry of Health National AIDS & STI Control Programme, 2016). Clinical parameters of WHO stage and baseline CD4 have previously been associated with NCD risk (Tripathi et al., 2014). In a study in Zimbabwe the factors of sex, duration of HIV sero-positive state, ART regimens received, and baseline WHO HIV disease stage, CD4 + cell counts, and each additional year of age were associated with a 6 % increased risk of NCDs (Magodoro et al., 2016). In our study, WHO staging and baseline CD4, showed no significant associations with NCDs risk, although documentation was incomplete.

In high-income countries, mixed findings of both increased risk of developing NCDs and no difference have been noted (Rasmussen et al., 2012). Among other factors, increased risk of developing NCDs is

associated with duration of and exposure to certain ARV drugs like stavudine, efavirenz and protease inhibitors (Dave et al., 2011; Oni et al., 2015; Tien et al., 2007). However, several studies in low-income countries, including our own, found no significant relationships between either ARV drug class or duration of exposure with risk of NCDs (Magodoro et al., 2016). PLHIV who initiated ART during the follow up period were found to have a lower incidence of NCDs compared to PLHIV who did not initiate ART.

The convergence of a dual burden of NCDs and communicable diseases in SSA is not in question (El-Sadr & Goosby, 2018; G. o. K. Ministry of Health, 2015; Peck et al., 2014; Vorkoper et al., 2018). The burden of hypertension and cardiovascular disease regardless of HIV status remains substantial (Kwarisiima et al., 2016; Miriam Rabkin, Anton Palma, et al., 2018). Previous studies show that exposure to ARVs and advanced HIV disease independently increase risk of metabolic and cardiovascular diseases (Magodoro et al., 2016; Nduka et al., 2016). Although there is evidence of increased blood pressure and hypertension among PLHIVs on ART, a distinct difference exists in the characterization of cardiovascular disease between PLHIVs and non-PLHIVs (Tilahun Nigatu Haregu et al., 2012; Nduka et al., 2016).

By using two elevated blood pressure readings 12 months apart as a proxy for hypertension, our study found elevated blood pressure as the most common (87.5%) among the 4 NCDs in our study population. In comparison, only 0.5 % of these patients had a recorded diagnosis of hypertension. The population of PLHIV in care that had been diagnosed with diabetes mellitus was comparable to that of the general population with raised blood glucose (2.1% vs 1%) (Kenya National Bureau of Statistics et al., 2015) . Our study findings are similar to several studies and population based NCDs surveys in SSA (Kavishe et al., 2015; Kenya National Bureau of Statistics et al., 2015; Kwarisiima et al., 2016). There is need to emphasize cardiovascular risk factor assessment at all clinical visits especially for PLHIV aged more than 40 years (G. o. K. Ministry of Health, 2015; Peck et al., 2014; Sander et al., 2015).

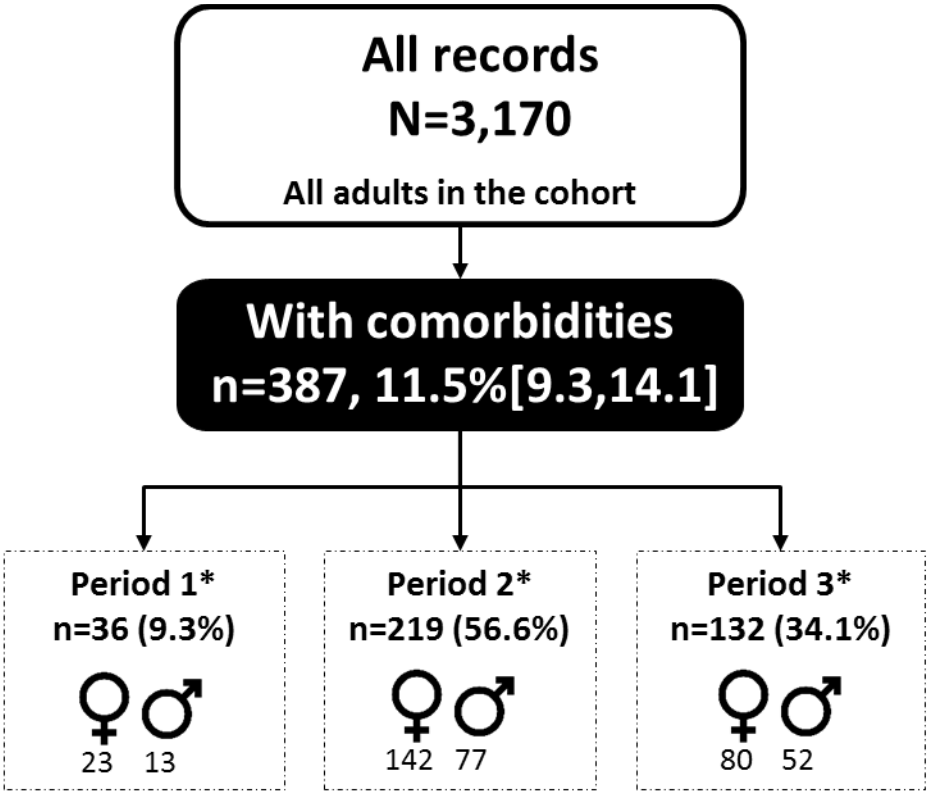
Our study found a lower prevalence of chronic respiratory diseases, including asthma, among PLHIV enrolled in care when compared to the general population (2.3% vs 8.5%) (Kenya National Bureau of Statistics et al., 2015). Although noted to be a lower prevalence, deliberate screening for findings and risk factors associated with chronic respiratory conditions such as smoking and occupational hazards should be incorporated in routine screening (K. Juma et al., 2018).

Cancers are the second largest cause of NCDs-related deaths and account for 7% of overall mortality in Kenya (G. o. K. Ministry of Health, 2015). In our study, the prevalence of cancer among PLHIV enrolled in care was 1.1%. This is higher than the general population and HIV negative individuals whose rate is 0.4% (G. o. K. Ministry of Health, 2019). In an era of increased access to ART, systematic reviews among PLHIV indicate steadily declining rates of AIDS defining malignancies among PLHIV with most cancer diagnoses now being pre-cancerous (Tilahun Nigatu Haregu et al., 2012). Screening of cancers, such as cervical cancer, however remains important and cost-effective when integrated into HIV care and treatment (Hyle et al., 2014; Ministry of Health National AIDS & STI Control Programme, 2016).

The cross sectional design of our study limited our analysis of risk factors for NCDs among PLHIV that would have bolstered our study findings and allowed us to make robust comparisons to other nationwide NCDs surveys (Petersen et al., 2014) . Additionally, patients with high mortality conditions such as stroke, myocardial infarction and severe heart failure may have died before reaching care and therefore been missed by this survey. Diagnosis of NCDs was as recorded in the charts from the HIV care clinics. As is common with program level data the absence of standardized screening and reporting of NCDs would result in an underestimate of NCD burden. As an example, most of our patients identified with an NCD were based on our review of serial blood pressure measurements instead of documented history of hypertension in the medical record. Instances of missing data and possibility that associated NCD records would have been in other clinics could result in underreporting. Additionally, infrastructural challenges in

diagnosis of NCDs such as heart failure and various forms of chronic lung disease at the HIV care clinics may have accentuated underreporting.

We present important findings including estimates of the prevalence and incidence of NCDs among PLHIVs in SSA (Vorkoper et al., 2018). We identified that there is likely substantial underdiagnoses of at least some categories of NCDs among PLHIV through our comparison of repeated elevated blood pressures and documented hypertension. Systematic screening using objective measures and criteria as well as treatment of NCDs should be integrated into HIV care and treatment programs (El-Sadr & Goosby, 2018; Vorkoper et al., 2018). As Kenya seeks to reach the ambitious UNAIDS 90-90-90 goals through expanded treatment, strategies need to be developed that ensure health gains for PLHIVs are not eroded by a rising burden of NCDs (Matanje Mwagomba et al., 2018).



* **Guidelines periods:** Period 1 - 01Jan2003 to 31Dec2005; Period 2 - 01Jan2006 to 30Jun2010; Period 3 - 01Jul2010 to 30Sep2013

Figure 4.2. 1: Proportion of patients by ART status, Longitudinal Surveillance of Treatment in Kenya, 2016

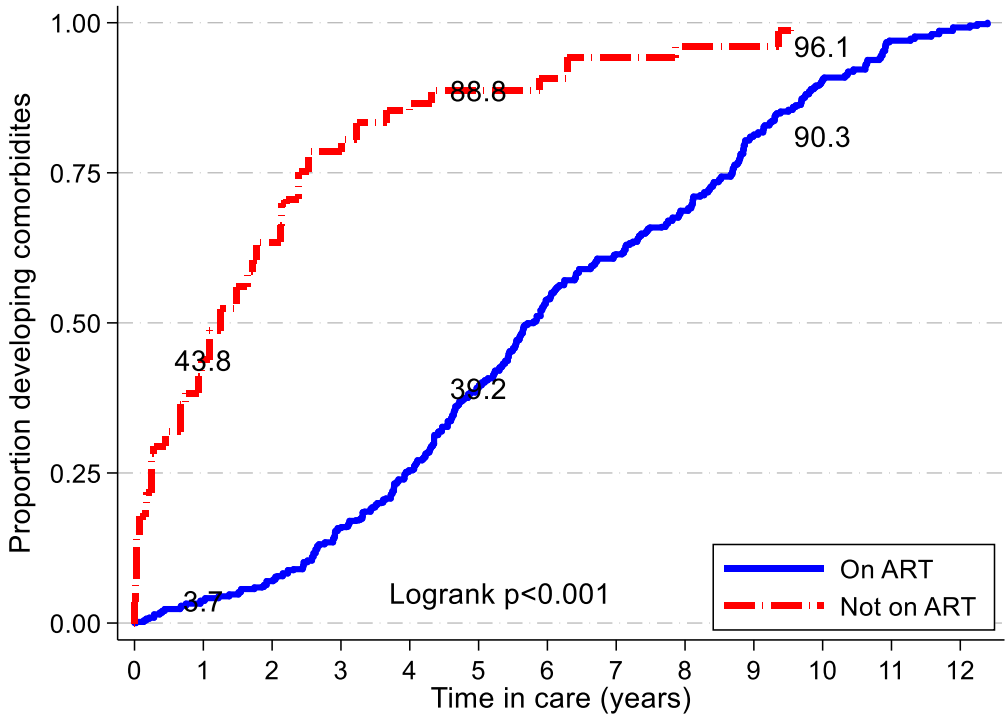


Figure 4.2.2: Proportion of patients developing comorbidities any time and during follow-up by ART status, Longitudinal Surveillance of Treatment in Kenya, 2016 (N=3170)

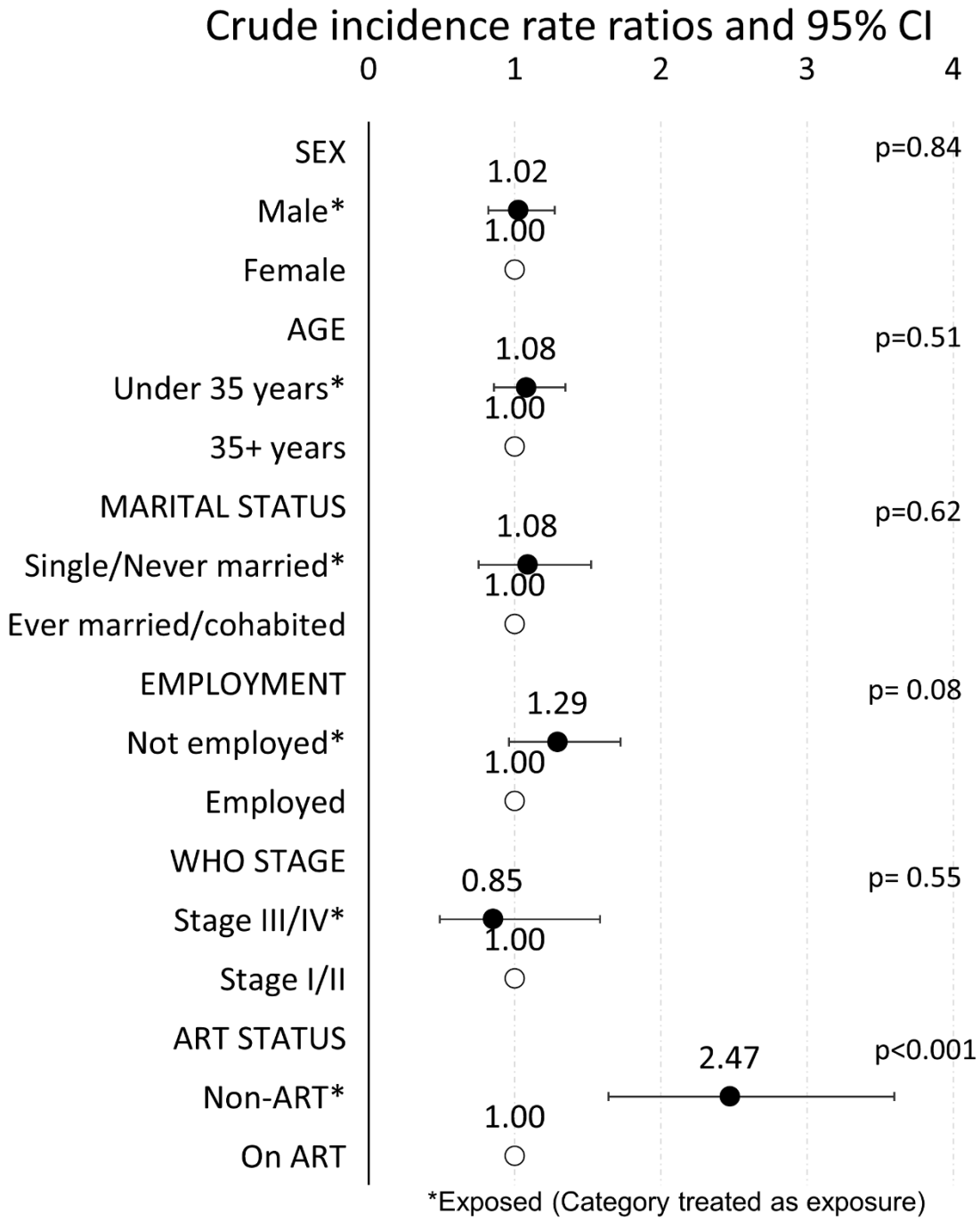


Figure 4.2. 3 Crude incidence rate ratios for Non-Communicable Diseases (NCDs) during follow-up by selected characteristics among those who have any NCD, Longitudinal Surveillance of Treatment in Kenya, 2016 (n=387)

Table 4.2.1: Distribution of characteristics of adults in care by sex, Longitudinal Surveillance of Treatment in Kenya, 2016 (N=3170)

Characteristics	Total		Women		Men		p-value
	No.	Col % [95% CI]	No.	Col % [95% CI]	No.	Col % [95% CI]	
Total	3170	100	2115		1055		
Age (years)							<0.001
Under 35 years	1658	52.1[49.5,54.6]	1250	58.6[56.0,61.2]	408	39.1[35.4,42.9]	
35+ years	1512	47.9[45.4,50.5]	865	41.4[38.8,44.0]	647	60.9[57.1,64.6]	
Employment							<0.001
Formal and informal employment	881	68.3[62.5,73.5]	507	60.8[55.3,66.2]	374	81.4[73.3,87.5]	
Unemployed	446	31.7[26.5,37.5]	351	39.2[33.8,44.7]	95	18.6[12.5,26.7]	
Marital status							<0.001
Married/cohabiting	1693	51.1[45.8,56.4]	979	44.2[39.9,48.7]	714	64.7[55.9,72.7]	
Widowed	399	12[9.5,15.0]	346	15.6[12.2,19.7]	53	4.8[3.4,6.8]	
Divorced/separated	254	7.8[6.3,9.6]	192	8.9[7.2,11.0]	62	5.5[4.0,7.6]	
Single/Never married	416	13.5[11.1,16.3]	313	15.6[12.6,19.1]	103	9.3[7.2,12.1]	
Missing marital	408	15.6[9.2,25.3]	285	15.7[10.1,23.4]	123	15.6[7.5,29.6]	
Entry point							0.435
OPD/TB clinic	2077	64.4[57.6,70.7]	1385	64.1[57.1,70.6]	692	64.9[57.7,71.5]	
IPD**	341	11.2[8.0,15.5]	225	10.8[7.5,15.2]	116	11.9[8.4,16.7]	
Others/not documented	752	24.5[18.6,31.5]	505	25.1[18.9,32.5]	247	23.2[17.4,30.2]	
WHO stage							0.131
Stage I/II	127	3.8[2.3,6.2]	85	3.9[2.4,6.2]	42	3.7[2.1,6.5]	
Stage III/IV	716	21.5[18.0,25.4]	435	20.1[16.8,24.0]	281	24.1[19.4,29.6]	
Missing WHO	2327	74.7[70.4,78.6]	1595	76[71.9,79.6]	732	72.2[66.0,77.6]	
CD4 categories							0.036
< 200	138	4.4[3.3,6.0]	75	3.5[2.6,4.7]	63	6.3[4.2,9.4]	
200-250	37	1.1[0.8,1.6]	24	1.1[0.7,1.6]	13	1.2[0.6,2.2]	
251-350	41	1.3[0.9,1.8]	25	1.1[0.7,1.8]	16	1.6[0.8,3.0]	
351-500	79	2.8[2.1,3.7]	49	2.6[1.8,3.7]	30	3.1[1.9,5.1]	
> 500	145	5[3.9,6.3]	112	5.6[4.3,7.2]	33	3.7[2.5,5.7]	
Missing	2730	85.4[82.6,87.9]	1830	86.1[83.2,88.6]	900	84.1[80.1,87.5]	
ART status							0.874
On ART	2170	63.9[57.2,70.0]	1440	64[58.5,69.2]	730	63.6[53.9,72.3]	
Non-ART	1000	36.1[30.0,42.8]	675	36[30.8,41.5]	325	36.4[27.7,46.1]	
Regimen							0.050
D4T containing regimen	758	36.5[31.8,41.5]	506	36.9[32.3,41.8]	252	35.7[29.4,42.6]	
AZT containing regimen	606	26.9[23.1,31.0]	417	28.4[24.3,32.8]	189	23.8[19.3,29.0]	
ABC containing regimen	7	0.5[0.2,1.2]	4	0.5[0.1,1.7]	3	0.5[0.1,1.5]	
LPV/r containing regimen	8	0.4[0.1,0.9]	8	0.6[0.2,1.4]	0	0	
TDF containing regimen	778	35.8[30.7,41.1]	496	33.6[28.7,39.0]	282	40[32.8,47.6]	
Enrolment guidelines period							0.070
01Jan2003 to 31Dec2005	243	9[6.7,12.0]	175	9.3[6.8,12.6]	68	8.5[5.8,12.3]	
01Jan2006 to 30Jun2010	1681	54.3[49.8,58.8]	1132	55.4[50.6,60.2]	549	52.2[47.1,57.2]	
01Jul2010 to 30Sep2013	1246	36.6[31.3,42.3]	808	35.3[30.1,40.9]	438	39.3[33.2,45.8]	
Comorbidities at any time							0.308
With comorbidities	387	11.5[9.3,14.1]	245	11.1[8.7,14.0]	142	12.4[9.9,15.4]	
Without comorbidities	2783	88.5[85.9,90.7]	1870	88.9[86.0,91.3]	913	87.6[84.6,90.1]	

Table 4.2.2: Incidence rates of Non-Communicable Diseases (NCDs) per 1000 person years by ART status, Longitudinal Surveillance of Treatment in Kenya, 2016 (N=3170)

Characteristics	**On ART**		**Incidence/1000 person years [95%CI]**		
	n/N	Percent [95% CI]	All	On ART	Non-ART
All	2170/3170	63.9[57.2,70.0]	35.1[31.6, 38.9]	34.5 [31.0, 38.5]	42[29.4-60.1]
Sex					
Female	1440/2115	64[58.5,69.2]	31.6[27.7, 36.1]	31.1 [27.0, 35.7]	38.4[24.8-59.5]
Male	730/1055	63.6[53.9,72.3]	42.3[35.8, 50.1]	41.7 [35.1, 49.7]	52[28-96.6]
Age at enrolment (years)					
15-24	261/456	53.2[46.3,59.9]	21.0[13.8, 31.9]	19.7 [12.4, 31.2]	30.2[11.3-80.4]
25-34	794/1202	61.3[54.5,67.8]	26.1[21.4, 31.8]	25.0 [20.3, 30.9]	38.5[21.3-69.6]
35-44	678/935	67.5[59.1,74.8]	35.9[30.0, 43.0]	34.8 [28.8, 42.0]	55.4[29.8-103]
45-54	319/428	70.1[59.7,78.8]	57.5[46.7, 70.9]	57.0 [46.0, 70.7]	66.9[27.9-160.8]
55 +	118/149	76.2[67.4,83.2]	55.0[38.5, 78.7]	59.4 [41.5, 84.9]	no data
Marital status					
Ever married/cohabited	1717/2346	70.6[66.6,74.3]	36.9[33.0, 41.3]	36.3 [32.3, 40.8]	45.7[30.6-68.2]
Single/Never married	271/416	64[57.4,70.1]	31.9[23.1, 44.0]	32.6 [23.4, 45.4]	23.1[5.8-92.4]
Employment					
Formal and informal employment	666/881	72.7[67.0,77.8]	43.8[37.5, 51.2]	43.8 [37.4, 51.3]	45.1[21.5-94.6]
Unemployed	329/446	71.9[64.0,78.6]	45.9[36.2, 58.2]	42.8 [33.2, 55.1]	100.2[50.1-200.3]

Table 4.2.3: Distribution of Non-Communicable Diseases (NCDs) during care by ART status, Longitudinal Surveillance of Treatment in Kenya, 2016 (n=387)

Comorbidities	Total		On ART		non-ART		p-value
	No.	Col% [95% CI]	No.	Col% [95% CI]	No.	Col% [95% CI]	
Total	387		346		41		
2+ high BP <12m apart*							0.030
Normal	44	12.5[7.6,19.9]	27	7.2[4.6,11.1]	17	49.4[25.5,73.5]	
High BP	343	87.5[80.1,92.4]	319	92.8[88.9,95.4]	24	50.6[26.5,74.5]	
Diabetes Mellitus							0.437
Without Diabetes	378	97.9[95.3,99.1]	339	98.5[96.7,99.4]	39	93.7[68.6,99.0]	
With Diabetes	9	2.1[0.9,4.7]	7	1.5[0.6,3.3]	2	6.3[1.0,31.4]	
Chronic Respiratory Diseases							0.147
Without asthma	378	97.7[95.1,98.9]	340	98.7[96.6,99.5]	38	90.7[75.5,96.8]	
With asthma	9	2.3[1.1,4.9]	6	1.3[0.5,3.4]	3	9.3[3.2,24.5]	
Cancer							0.278
Without Cancer	384	98.9[95.2,99.8]	343	98.8[94.4,99.8]	41	100	
With cancer	3	1.1[0.2,4.8]	3	1.2[0.2,5.6]	0	0	

4.3 To characterize NCD burden of the four leading NCDs that lead to the highest morbidity and mortality among PLHIV attending key population program drop-in centers (DICEs) and ART clinics at a large HIV prevention, care and treatment program in Nairobi, Kenya

Publication Title: Non-communicable disease burden among Key Population on Care and Treatment: a retrospective cross-sectional analysis of HIV-care outcomes from the Sex Workers Outreach Program in Kenya, 2012-2015

ABSTRACT

Introduction

People Living with HIV bear a disproportionate burden of noncommunicable diseases (NCDs). Despite their significant toll across populations globally, the NCD burden among Key Populations (KP) in Kenya remains unknown. We evaluated the burden of four NCD-categories (cardiovascular diseases, cancer, chronic respiratory diseases and diabetes) among female sex workers (FSWs) and men who have sex with men (MSMs) at the Sex Workers Outreach Program (SWOP) clinics in Nairobi Kenya.

Methods

We conducted a retrospective medical chart review at the SWOP clinics amongst KP clients ≥15 years living with HIV enrolled between October 1, 2012, and September 30, 2015. The prevalence of the four NCD-categories were assessed at enrollment and during subsequent routine quarterly follow-up care visits as per the Ministry of Health guidelines. We determined prevalence at enrollment and assessed distributions of co-morbidities using Chi-square and t-tests as appropriate during follow-up visits. Univariate and multivariate analysis was also conducted to identify factors associated with NCD diagnoses.

Results

Overall, 1,478 individuals' records were analyzed; 1,392 (94.2%) were from female sex workers (FSWs) while 86 (5.8%) were from men who have sex with men (MSMs) over the three-year period. FSWs' median age was 35.3 years (interquartile range (IQR) 30.1 – 41.6) while MSMs were younger at 26.8 years (IQR 23.2 – 32.1). At enrollment into the HIV care program, most KPs (86.6%) were at an early WHO clinical stage (stage I – II) and 1462 (98.9%) were on first-line anti-retroviral therapy (ART). A total of 271, 18.3% (95% confidence interval (CI): 16.4 – 20.4%), KPs living with HIV had an NCD diagnosis in their clinical chart records during the study period. Majority of these cases, 258 (95.2%) were noted among FSWs. Cardiovascular disease that included hypertension was present in 249/271, 91.8%, of KPs with a documented NCD. Using a proxy of two or more elevated blood pressure readings taken < 12 months apart, prevalence of hypertension rose from 1.0% (95% CI: 0.6 – 1.7) that was documented in the charts during the first year to 16.3% (95% CI: 14.4 – 18.3) in the third year. Chronic respiratory disease mainly asthma was present in 16/271, a prevalence of 1.1% (95% CI: 0.6 – 1.8) in the study population. Cancer in general was detected in 10/271, prevalence of 0.7% (95% CI: 0.3 – 1.2) over the same period. Interestingly, diabetes was not noted in the study group. Lastly, significant associations between NCD diagnosis with increasing age, body-mass index and CD4 + cell-counts were noted in univariate analysis. However, except for categories of ≥ BMI 30 kg/m^2 and age ≥ 45 years, the associations were not sustained in adjusted risk estimates.

Conclusion

In Kenya, KP living with HIV and on ART have a high prevalence of NCD diagnoses. This calls for scaling up focus on both HIV and NCD prevention and care in targeted populations at increased risk of HIV acquisition and transmission. KP programs ought to consider including integrated HIV-NCD screening and care in their guidelines.

INTRODUCTION

The Global Burden of Disease Study 2017 ranked non-communicable diseases (NCDs) as the number one cause of mortality worldwide (Kyu et al., 2018). In Sub-Saharan Africa (SSA), NCDs now account for 37% of productivity losses overtaking communicable diseases and heralding an epidemiologic shift from infectious causes (Ibrahim & Damasceno, 2012; Kirigia & Mwabu, 2018; WHO, 2019b). People Living with HIV (PLHIV) are disproportionately affected by the dual disease burden (Patel et al., 2018). There is renewed focus to address NCDs among PLHIV (Bloomfield et al., 2011; Garrib et al., 2018), yet key populations (KPs) who are an important segment of this population continue to lag behind in spite of their risky lifestyle choices.

The World Health Organization (WHO) identifies key populations as defined groups who, due to specific higher-risk behaviors, are at increased risk of HIV irrespective of the epidemic type or local context. Often, key populations have legal and social issues related to their behavior that increase their vulnerability to HIV infection (WHO, 2016d). The Joint United Nations Programme on HIV and AIDS (UNAIDS) considers five key population groups as being particularly vulnerable to HIV infection namely men who have sex with men (MSM), sex workers (SWs), people who inject drugs (PWIDs), transgender people and prisoners (UNAIDS, 2019b).

KPs, including those in SSA, carry a disproportionate burden of HIV; yet they have been under-represented wherever studied – particularly for HIV (Baral & Phaswana-Mafuya, 2012; Caceres, Brody, & Chyun, 2016; Caceres et al., 2017). NCD burden of four main categories – cardiovascular diseases, diabetes mellitus, chronic respiratory diseases and cancer has been estimated in the general population living with HIV in SSA (Achwoka et al., 2019; Bloomfield et al., 2011; Patel et al., 2018). The four aforementioned categories are noted to contribute 80% of premature deaths (Bennett et al., 2018). Despite being excluded from many primary HIV surveillance systems, KPs account for 25% of new HIV infections in SSA (UNAIDS, 2019b, 2019c). Further, risk factors such as harmful alcohol use, tobacco smoking and

injecting drug use predispose KPs to both HIV infection and acquisition and progression of NCDs (Caceres et al., 2017; Kuteesa et al., 2019).

Despite evidence on benefits of harm reduction among KPs, NCD-HIV care has received little attention (Awungafac, Delvaux, & Vuylsteke, 2017). In SSA countries, where KPs are recognized, NCD-HIV care packages have similarly lacked an emphasis on NCD-care (Burrows, McCallum, Parsons, & Falkenberry, 2019). Biomedical interventions aimed at NCD-HIV care such as cancer screening are considered as desirable rather than mandatory (Ministry of Health, 2014).

Using program data from a large key populations program in Nairobi, Kenya, we sought to describe the NCD burden among two key population groups – female sex workers (FSWs) and MSM living with HIV enrolled in the SWOP clinics. For this paper, we only evaluated four main NCD categories – cardiovascular diseases, diabetes mellitus, chronic respiratory diseases and cancer recorded in the patient's clinical notes over a three-year period.

RESULTS

We analyzed medical records of key populations living with HIV receiving care from seven SWOP facilities distributed across Nairobi County. Clinical encounters from October 2012 to September 2015 were analyzed for 1,478 clients who met the inclusion criteria. Among these individuals, 1,392 (94.2%) were female sex workers (FSWs), while 86 (5.8 %) were men who have sex with men (MSM) (Table 3.1).

Table 4.3.1: Baseline characteristics of key populations living with HIV attending SWOP clinics by typology, 2012 – 2015 (N=1,478)

Characteristics	Total (N=1,478)		Key Population Typology			
			FSW (n=1,392)		MSM (n=86)	
	No.	%	n	%	n	%
Age (years)						
Mean [SD]	35.8	[8.5]	36.2	[8.4]	28.2	[6.7]
15 – 25	138	9.3	102	7.3	36	41.9
25- 34	601	40.7	565	40.6	36	41.9
35-44	512	34.6	501	36	11	12.8
45+	224	15.1	221	15.9	3	3.5
Facility						
Donholm	125	8.5	118	8.5	7	8.1
Majengo	367	24.8	367	26.3		N/A[1]
SWOP City	331	22.4	273	19.6	58	67.4
Kariobangi	193	13.1	181	13	12	14
Kawangware	201	13.6	196	14.1	5	5.8
Langata	111	7.5	107	7.7	4	4.7
Thika Road	150	10.2	150	10.8		N/A
Marital Status						
Married	220	14.9	202	14.5	18	20.9
Widowed	72	4.9	71	5.1	1	1.2
Divorced	484	32.8	479	34.4	5	5.8
Single	689	46.6	627	45.0	62	72.1
WHO Stage at Enrolment						
I-II	1279	86.6	1198	86.1	81	94.2
III – IV	123	8.3	121	8.7	2	2.3
Undocumented	76	5.1	73	5.2	3	3.5
CD4 T-Cell Count						
<200	257	17.4	251	18	6	7
200-349	405	27.4	369	26.5	36	41.9
350-499	326	22.1	305	21.9	21	24.2
500+	404	27.3	388	27.9	16	18.6
Undocumented	86	5.8	79	5.7	7	8.1
Antiretroviral Treatment Regimen						
First line (NRTI based)	1462	98.9	1376	98.9	86	100.0
Second line (PI based)	16	1.1	16	1.2	0	0

[1]N/A -Not applicable since the facility was an FSW only clinic and did not enroll MSM during the study period.

Baseline characteristics of the study population

Overall, majority of medical records were obtained from two SWOP facilities: Majengo (24.8%) and SWOP City (22.4%). Majengo facility served over a quarter (26.3%) of FSWs while slightly over two thirds (67.4%) of MSM sought services at SWOP City. The rest of the five SWOP clinics constituted slightly over a half of the medical records (52.8%). Median age of FSWs was 35.3 years (interquartile range (IQR) of 30.1 – 41.6) and that of MSM was 26.8 years (IQR 23.2 – 32.1). Close to half (46.6%) of

all KPs were single, 32.8% were divorced, 14.9% married and 4.9% were widowed. The proportion of FSWs that was single was lower than that of MSM (45.0% vs 72.1% respectively) (Table 4.3.1).

At entry into SWOP, 97.7% of KPs in this study cohort were HIV infected. Sixteen clients across both KP typologies (11 FSW and 5 MSM), initially HIV-uninfected at entry into SWOP, seroconverted during follow up. Seroconversion among FSW was 0.8% while that of MSM was 5.8% (results not shown). At the time of enrollment into HIV care, most KPs (86.6%) were at an early (stage I – II) WHO clinical stage. Less than a fifth (17.4%) of all clients had a CD4 T-cell count of less than 200 cells/mm^3. Over a quarter (27.9%) of FSWs and 18.6% of MSM had a CD4 count of 500 cells/mm^3 and above. Nearly all (98.9%) clients enrolled were initiated on a first line antiretroviral regimen (Table 4.3.1).

Prevalence of NCDs among Key populations living with HIV

A total of 271, 18.3% (95% confidence interval (CI): 16.4 – 20.4), KPs living with HIV had an NCD diagnosis in their clinical chart records. The vast majority, 95.2% (258 cases) of all the NCDs were from the FSW. About a third (33.9%) of the NCDs were reported from Majengo, where 25.1% (95% CI: 20.7 – 29.8) of FSW at this facility had an NCD diagnosis. – A similar proportion of MSM had an NCD diagnosis in their medical charts at Kariobangi 25.0%, (95% CI: 5.5 – 57.2). KPs aged between 35- 44 years had the highest number of NCD diagnoses 108/271, 21.1% (95% CI: 17.6 – 24.9) (Table 4.3.2). FSWs' NCD prevalence rose steadily with age, 7.8% (95% CI: 3.5 – 14.9) among the under 25 years of age to 33.0% (95% CI: 26.9 – 39.7) among those aged 45 years and above. MSM NCD prevalence was highest among those aged 35 – 44 years, 18.2 % (95% CI: 2.3 – 51.8) and lowest among those aged between 25 and 34 years 11.1% (95% CI: 3.1 – 26.1) (Fig 4.3.1a).

Table 4.3.2: Prevalence of Non-Communicable Diseases (NCDs) among Key Populations living with HIV by selected characteristics at SWOP clinics, 2012 – 2015

Characteristics	Categories	N	Overall		FSW		MSM	
			n	*% [95% C.I]*	*n*	*% [95% C.I]*	*n*	*% [95% C.I]*
Facility	Donholm	125	19	15.2 [9.4 – 22.7]	18	15.3 [9.3 – 23.0]	1	14.3 [0.4 – 57.9]
	Majengo	367	92	25.1 [20.7 – 29.8]	92	25.1 [20.7 – 29.8]		N/A
	SWOP city	331	58	17.5 [13.6 – 22.1]	49	18.0 [13.6 – 23.0]	9	15.5 [7.4 – 27.4]
	Kariobangi	193	27	14.0 [9.4 – 19.7]	24	13.3 [8.7 – 19.1]	3	25.0 [5.5 – 57.2]
	Kawangware	201	32	15.9 [11.2 – 21.7]	32	16.3 [11.4 – 22.3]	0	0
	Langata	111	4	3.6 [1.0 – 9.0]	4	3.74 [1.0 – 9.3]	0	0
	Thika Road	150	39	26.0 [19.2 – 33.8]	39	26.0 [19.2 – 33.8]		N/A
Age bands (years)	<25	138	15	10.9 [6.2 – 17.3]	8	7.8 [3.5 – 14.9]	7	19.4 [8.2 – 36.0]
	25-34	601	75	12.5 [9.9 – 15.4]	71	12.6 [9.9 – 15.6]	4	11.1 [3.1 – 26.1]
	35-44	512	108	21.1 [17.6 – 24.9]	106	21.2 [17.7 – 25.0]	2	18.2 [2.3 – 51.8]
	45+	224	73	33.0 [22.5 – 35.8]	73	33.0 [26.9 – 39.7]	0	0
Body Mass Index (kg/m^2)	<18.5	80	8	10.0 [4.4 – 18.8]	8	11.3 [5.0 – 21.0]	0	0
	18.5 – 24.9	647	79	12.2 [9.8 – 15.0]	69	11.8 [9.3 -14.7]	10	15.9 [7.9 – 27.3]
	25-29.9	420	83	19.8 [16.1 – 23.9]	80	19.6 [15.9 – 23.8]	3	25.0 [5.5 – 57.2]
	30+	301	98	32.6 [27.3 – 38.2]	98	32.8 [27.5 – 38.4]	0	0
Sex partner type	Casual client	282	51	18.1 [13.8 – 23.1]	46	18.3 [13.7 – 23.6]	5	16.7 [5.6 – 34.7]
	Regular client	78	8	10.3 [4.5 – 19.2]	8	11.4 [5.1 – 21.3]	0	0
	Regular; Casual clients + Partner	620	116	18.7 [15.7 – 22.0]	114	18.8 [15.7 – 22.1]	2	15.4 [1.9 – 45.5]
	Regular partner	15	2	13.3 [1.7 – 40.5]	1	50.0 [1.3 – 98.7]	1	7.7 [0.2 – 36.0]
	Undocumented	482	94	19.5 [16.06 – 23.3]	89	19.35 [15.8 – 23.3]	5	22.7 [7.8 – 45.4]
Condom use	No	10	1	10 [0.3 – 44.5]	1	25.0 [0.6 – 80.6]	0	0
	Yes	1102	194	17.6 [15.4 – 20.0]	186	17.9 [15.6 – 20.3]	8	12.9 [5.7 – 23.9]
	Undocumented	365	76	20.8 [16.8 – 25.4]	71	20.5 [16.3 – 25.1]	5	27.9 [9.7 – 53.5]
Alcohol consumption (Cage per day)	0	419	70	16.7 [13.2 – 20.6]	67	17.1 [13.5 -21.2]	3	10.7 [2.3 – 28.2]
	1	871	162	18.6 [16.1 – 21.3]	156	18.7 [16.1 -21.5]	6	15.4 [5.9 – 30.5]
	4	106	18	17.0 [10.4 – 25.5]	15	15.3 [8.8 – 24.0]	3	37.5 [8.5 – 75.5]
	Undocumented	79	21	26.6 [17.3 – 37.7]	20	29.4 [19.0 – 41.7]	1	9.1 [2.3 – 41.3]
Smoking (Packs per day)	0	920	160	17.4 [15.0 – 20.0]	147	17.5 [15.0 – 20.2]	13	17.1 [9.4 – 27.5]
	1	87	21	24.1 [15.6 – 34.5]	21	25.0 [16.2 – 35.6]	0	0
	2	29	2	6.9 [0.9 – 22.8]	2	8.0 [1.0 – 26.0]	0	0
	Undocumented	444	88	19.8 [16.2 – 23.8]	88	20.0 [16.3 – 24.0]	0	0
Drugs use	No	1337	250	18.7 [16.7 – 20.9]	237	18.9 [16.8 – 21.2]	13	16.1 [8.8 – 25.9]
	Yes	125	16	12.8 [7.5 – 20.0]	16	13.2 [7.8 – 20.6]	0	0
CD 4 cells/mm^3	<200	258	34	13.2 [9.3 – 18.0]	34	13.5 [9.6 -18.4]	0	0
	200-349	404	82	20.3 [16.4 – 24.5]	76	20.6 [16.6 – 25.1]	6	16.7 [6.4 – 32.8]
	350-499	325	67	20.6 [16.3 – 25.4]	63	20.6 [16.3 – 25.6]	4	19.1 [5.5 – 41.9]
	500+	404	84	20.8 [16.9 – 25.1]	81	20.8 [16.9 – 25.3]	3	18.8 [4.1 – 45.6]
ART Regimen	First line	1464	268	18.3 [16.4 – 20.4]	255	18.5 [16.5 – 20.7]	13	15.1 [8.3 – 24.5]
	Second line	16	3	18.8 [4.1 – 45.7]	3	18.8 [4.1 – 45.7]		0

Key: FSW, female sex workers; MSM, Men who have sex with men; ART, antiretroviral therapy; N, total number of participants in each category; n, number of participants with NCD; %, percentage with NCDs

At enrollment into HIV care, 34/271, 12.5%, KPs living with HIV and with an NCD diagnosis had advanced disease with a CD4 of less than 200 cells/mm3. All 34, were FSW and had an NCD prevalence of 13.5% (95% CI: 9.6 – 18.4). Thirty one percent of KP clients living with HIV and diagnosed with an NCD had an enrollment CD4 of 500 cells/mm3 and above. For both KP typologies, NCD prevalence for the 500 cells/mm3 CD4 category was close to a fifth; 20.8% (95% CI; 16.9 – 25.3) for FSW and 18.8% (95% CI; 4.1 – 45.6) for MSM respectively. Nearly all, 268/271, 98.9%, of KPs with an NCD diagnosis were currently on an NRTI-based first line ART regimen. Three FSWs were on a protease inhibitor (PI) based second line regimen and had an NCD prevalence of 18.8% (95% CI: 4.1 – 45.7). Two thirds, (66.8%) of KPs living with HIV and with an NCD diagnosis had a body mass index (BMI) range of either being overweight 83/271, 30.6% or obese 98/271, 36.2%. Prevalence of NCD among overweight FSWs was 19.6% (95% CI: 15.879 – 23.8). Overweight MSM had an NCD prevalence of 25.0% (95% CI: 5.5 – 57.2) (Table 4.3.2).

Most KP clients living with HIV and an NCD diagnosis, 116/271, 42.8% reported a mixed profile of sexual partners that included both regular and casual sexual clients as well as an intimate sexual partner. Among FSWs with a mixed profile of partners, NCD prevalence was 18.8% (95% CI: 15.7 – 22.1). Close to two fifths (38.5%) of HIV-infected MSM with an NCD diagnosis had a casual client and an NCD prevalence of 16.7% (95% CI: 5.6 – 34.7). Vast majority (99.4%) of both FSWs and MSM reported consistent use of condoms with casual clients (Table 4.3.2).

Almost two thirds, 180/271, 66.4%, of KPs living with HIV and with an NCD diagnosis consumed alcohol with 18/180, 10%, screening positive on the CAGE tool for excessive drinking. NCD prevalence among FSWs and MSM who screened positive for excessive drinking was 15.3% (95% CI: 8.8 – 24.0) and 37.5% (95% CI: 8.5 – 75.5) respectively. However, a quarter, 70/271, 25.8%, of KPs living with HIV and with an NCD diagnosis did not take alcohol. A majority of KPs living with HIV and with an NCD diagnosis, 160/271, 59.0%, did not smoke. Close to a tenth, 23/271, 8.4%, smoked tobacco cigarettes; all were FSWs.

NCD prevalence for FSWs who smoked more than one pack a day was 8.0% (95% CI: 1.0 -26.0). Drug use was reported among 5.9% of KPs living with HIV and with an NCD diagnosis cohort, all being FSWs. NCD prevalence among 16 FSWs who reported drug use was 13.2% (95% CI: 7.8 – 20.6) (Table 4.3.2).

Cardiovascular disease

Among KPs living with HIV and with a documented NCD, 249/271, 91.8%, had a form of cardiovascular disease (CVD) that included hypertension. CVD was more frequent in FSWs than MSM 17.0% (95% CI: 15.1 – 19.1) vs 14.0% (95% CI: 7.4 – 23.1) respectively. Among FSWs, CVD prevalence was lowest in the under 25 years age band 5.9% (95% CI: 2.2 – 12.4) and rose across age bands to 31.7% (95% CI: 25.6 – 38.3) in those aged 45 years and above. Among MSM, the highest CVD prevalence was in the under 25 years age band while the lowest was in the 25-34 years age band 19.4% (95% CI: 8.2 – 36.0) vs 11.1% (95% CI: 3.1 – 26.1) (Fig 4.3.1b).

Prevalence of hypertension as documented in reviewed KP medical records was 1.0% (95% CI: 0.6 – 1.7) with all cases being from FSWs. When two or more elevated blood pressure readings taken <12 months apart were considered, prevalence of elevated blood pressure was 16.3% (95% CI: 14.4 – 18.3). Our proxy measure was based on the Seventh Joint National Commission on hypertension (JNC 7) definition. Elevated blood pressure readings were more common among FSWs than MSM 16.5% (95% CI: 14.5 – 18.6) vs 14.0 (95% CI: 7.4 – 23.1) respectively. While serial elevated blood pressure readings were detected in 233/249 KP medical records, only 15/249 had a documented diagnosis of hypertension. Other CVD diagnoses such as atherosclerotic heart disease and congestive heart failure were made in 5/249 cases of CVD with a prevalence of 0.3% (95% CI: 0.1 – 0.8) (Table 4.3.3).

Table 4.3.3: Prevalence of Non-Communicable Diseases (NCDs) among Key populations living with HIV at SWOP clinics in Nairobi, Kenya, 2012-15

	Total (N=1478)		*FSW (n=1392)*		*MSM (n=86)*	
NCD type	*n*	*% [95% C.I]*	*n*	*% [95% C.I]*	*n*	*% [95% C.I]*
Any	*271*	18.3[16.4 - 20.4]	*258*	18.5 [16.5 - 20.7]	*13*	15.1[8.3 - 24.5]
Cardiovascular Disease (CVD)	249	16.9 [15.0 - 18.9]	237	17.0 [15.1 - 19.1]	12	14.0 [7.4 - 23.1]
Elevated Blood Pressure[1]	233	16.3 [14.4 -18.3]	221	16.5 [14.5 - 18.6]	12	14.0 [7.4 - 23.1]
Hypertension Diagnosis[2]	15	1.0 [0.6 - 1.7]	15	1.1 [0.6 - 1.8]	0	0
Other CVD Diagnoses	5	0.3 [0.1 - 0.8]	5	0.4 [0.1 - 0.8]	0	0
Chronic Respiratory Disease	16	1.1[0.6 - 1.8]	16	1.2 [0.7 - 1.9]	0	0
Cancer	10	0.7 [0.3 -1.2]	9	0.7 [0.3 - 1.2]	1	1.2 [0.0 - 6.3]

[2]Elevated blood pressure is calculated based on two elevated blood pressure readings taken <12 months apart in line with JNC 7 definition; [2] Hypertension diagnosis denotes documented hypertension diagnosis found in medical charts; [3] Diabetes mellitus is not shown on the table since no record of the condition was found in the entire study population

Chronic respiratory disease

A total of 16/271 medical records of KPs living with HIV reviewed were found to have a documented chronic respiratory disease (CRD). Overall prevalence of CRD was 1.1% (95% CI: 0.6 – 1.8). All cases reviewed were documented cases of asthma among FSWs (Table 4.3.3). The highest CRD prevalence was observed among FSWs aged 25-34 years 1.4% (95% CI: 0.6 – 2.8) (Fig 4.3.1c).

Cancer

We found a total of 10/271 records of KPs living with HIV had documentation of a cancer diagnosis. Overall prevalence of cancer was estimated at 0.7% (95% CI: 0.3 -1.2). Nine of the ten cancer diagnoses were of cervical cancer among FSWs. Cervical cancer diagnoses were made at two SWOP facilities – Donholm and Kawangware. The type of cancer was not specified for the one cancer diagnosis made on an MSM. Although 8 of the 10 cancer cases reported a mixed profile (regular clients, casual clients and a regular partner) for their sexual partner, all were found to have consistent condom use (results not shown). Majority of cervical cancer diagnoses (5/9) were made among the 25-34 years age-band. The one MSM who had a cancer diagnosis was in the 35-44 years age band (Fig 4.3.1d).

Diabetes mellitus

In this cohort of KP clients living with HIV, we did not find any FSWs or MSM who had a documented diagnosis of diabetes mellitus in their medical records.

Predictors of NCD among Key populations living with HIV at SWOP

On univariate analysis, increased age among KPs living with HIV was associated with an NCD diagnosis. The unadjusted odds ratio (OR) for 35-44 years age band was 2.19 (95% CI: 1.23 – 3.90) (p=0.008) and that of 45 years and above 3.96 (2.17 – 7.26) (p=0.001). Increased body mass index (BMI) was associated with an NCD diagnosis among KPs living with HIV. A BMI of 25-29.9 kg/m^2 (overweight) among the HIV- infected KP was associated with an OR 2.22 (95% CI: 1.03 – 4.78) (p=0.042) while those with a

BMI of 30 and above (obese) had an OR 4.34 (95% CI: 2.01 – 9.38) (p=0.001). Similarly, increasing CD4 cells/mm^3 was associated with a documented NCD diagnosis. Odds among CD4 counts of 200 – 349 cells/mm^3 was OR 1.67 (95% CI: 1.08 – 2.57) (p=0.022). CD4 counts of 500 cells/mm^3 and above had an OR 1.72 (1.11 – 2.66) (p=0.014) (Table 4.3.4).

Other predictive variables considered in the univariate analyses (sex, smoking, alcohol use, drug use, current ART regimen, sexual partner profile, and previous history of TB) were all not significant at a p-value of 0.2. Even though increased age, BMI and CD4 were associated with NCD diagnosis in unadjusted analyses, significant association with NCD diagnosis in the adjusted analyses remained only for categories of BMI 30 kg/m^2 and above, and ages 45 years and above (borderline statistically significant) (Table 4.3.4).

Table 4.3.4: Risk factors for NCDs among Key Populations living with HIV at SWOP Clinics in Nairobi, Kenya, 2012-15

Characteristics	Categories	N	Any NCD		Unadjusted Odds Ratio		Adjusted Odds Ratio	
			n	*% [95% C.I]*	*OR [95% CI]*	*p-value*	*OR [95% CI]*	*p-value*
Age in years	15-25	138	15	10.9 [6.2 - 17.3]	Reference		Reference	
	25-34	601	75	12.5 [9.9 - 15.4]	1.17 [0.65 - 2.11]	0.602	0.87 [0.45 - 1.67]	0.672
	35 - 44	512	108	21.1 [17.6 -24.9]	2.19 [1.23 - 3.90]	0.008	1.53 [0.79 - 2.95]	0.209
	45+	224	73	32.6 [26.5 - 39.2]	3.96 [2.17 - 7.26]	0.001	2.10 [0.98 - 4.49]	0.055
Sex	Female	1392	258	18.5 [16.5 - 20.7]	Reference		Reference	
	Male	86	13	15.1[8.3 - 24.5]	0.78 [0.43 -1.43]	0.428	1.39 [0.69 - 2.79]	0.354
Smoking	No	918	160	17.4 [15.0 - 20.0]	Reference		Reference	
	Yes	116	23	19.8 [13.0 - 28.3]	1.17 [0.72 -1.91]	0.524	1.17 [0.67 - 2.04]	0.583
Alcohol Use	No	420	70	16.7 [13.2 - 20.6]	Reference		Reference	
	Yes	979	180	18.4 [16.0 -21.0]	1.13 [0.83 - 1.53]	0.442	0.95 [0.66 - 1.38]	0.794
Drug Use	No	1336	250	18.7 [16.7 - 20.9]	Reference		Reference	
	Yes	125	16	12.8 [7.5 - 20.0]	0.64 [0.37 -1.10]	0.104	1.25 [0.66 - 2.39]	0.5
Body Mass Index (kg/m^2)	<18.5	80	8	10.0 [4.4 -18.8]	Reference		Reference	
	18.5 – 24.9	647	79	12.2 [9.8 - 15.0]	1.25 [0.58 - 2.70]	0.566	1.21 [0.49 - 3.00]	0.680
	25 – 29.9	420	83	19.8 [16.1 - 23.9]	2.22 [1.03 - 4.78]	0.042	1.73 [0.69 - 4.39]	0.246
	30+	301	98	32.6 [27.3 - 38.2]	4.34 [2.01 - 9.38]	0.001	2.87 [1.11 - 7.41]	0.029
ART Regimen	NRTI based	1462	268	18.3 [16.4 - 20.4]	Reference		N/A	
	PI based	16	3	18.8 [4.1 - 45.6]	1.03 [0.29 - 3.63]	0.966		
CD4	<200	257	34	13.2 [9.3 - 18.0]	Reference		Reference	
	200-349	405	82	20.3 [16.4 - 24.5]	1.67 [1.08 - 2.57]	0.022	1.42 [0.86 - 2.35]	0.171
	350-499	326	67	20.6 [16.3 - 25.4]	1.70 [1.08 - 2.66]	0.021	1.25 [0.72 - 2.16]	0.431
	500+	404	84	20.8 [16.9 - 25.1]	1.72 [1.11 - 2.66]	0.014	1.08 [0.63 - 1.86]	0.780
Previous TB history	No	1471	269	18.3 [16.3 - 20.4]	Reference		N/A	
	Yes	6	1	16.7 [0.4 - 64.1]	0.89 [0.10 - 7.68]	0.918		
Sex Partner Type	Casual client	282	51	18.1 [13.8 - 23.1]	Reference		N/A	

	Regular client	78	8	10.3 [4.5 - 19.2]	0.51 [0.23 - 1.14]	0.103
	Regular client + Partner +Casual Client	621	116	18.7 [15.7 - 22.0]	1.04 [0.72 - 1.50]	0.831
	Regular Partner	15	2	13.3 [1.7 - 40.5]	0.70 [0.15 - 3.18]	0.641

Key: NCD: Non communicable diseases. CI: Confidence interval.

DISCUSSION

In this study, we described burden of NCDs among Key populations (KPs) living with HIV enrolled at a large prevention and treatment program in Nairobi, Kenya. We determined prevalence of four NCD conditions: cardiovascular diseases, diabetes mellitus, chronic respiratory illnesses and any form of cancer among two KP typologies – FSWs and MSM living with HIV at seven SWOP clinics in Nairobi. Further, we explored distribution of prominent NCD risk factors and associated correlates among the two KP typologies. Our study comes against a backdrop of a rising NCD epidemic in SSA among PLHIV in the context of an evolving HIV epidemic with high unmet response for KPs (Beyrer et al., 2016; Shannon et al., 2018). In our study, we found a high overall prevalence of any of the four NCDs (18.3%) among both HIV-infected FSWs and MSM. Amidst a heightened impetus to refocus on populations at increased risk for both NCDs and HIV infection , studies similar to ours among key populations living with HIV remain rare (Brown & Peerapatanapokin, 2019). Nonetheless, systematic reviews outside SSA suggest that sexual minorities exhibit higher rates of NCDs (Caceres et al., 2017). Contrastingly, study findings from SSA point to comparably lower prevalence rates of NCDs (4.7%, 11.5% and 21.2%) among general population PLHIV clients (Achwoka et al., 2019; Coetzee et al., 2019; Kansiime, Mwesigire, & Mugerwa, 2019; Patel et al., 2018).

Study findings from concentrated HIV epidemics that are driven by an increased prevalence of HIV among key populations, point to high prevalence of NCDs among PLHIV (Chhoun, Ngin, et al., 2017). In a Cambodian study among PLHIV, close to half (47.8%) of total study participants had one or more NCDs with 75% unaware of their disease condition prior to the study (Chhoun, Tuot, et al., 2017). A recent modeling report from Kenya estimated 33% of HIV negative individuals and 36% of PLHIV to have at least one NCD. Further, prevalence of hypertension among HIV negative individuals was projected to grow from 19.9% in 2018 to 23% in 2035. This was in stark comparison to a growth from 29.9% to 37.4% among PLHIV over a similar period (G. o. K. Ministry of Health, 2019). These findings enunciate the excess NCDs burden among key populations and point to the need for routine active screening to increase early identification.

Evidence around cardiometabolic risk factors for NCDs among PLHIV is mixed. While some studies suggest that HIV infection is associated with lower BMI, triglycerides and blood pressure readings (Dillon et al., 2013; Ramsay et al., 2018), several others point to an increased prevalence of hypertension and obesity (Bloomfield et al., 2011; Brennan et al., 2018; Patel et al., 2018). There are mixed associations with ART use on the prevalence of NCDs with some studies suggesting no associations with hypertension (Coetzee et al., 2019; Dimala, Blencowe, & Choukem, 2018) while others finding an increased odds for hypertension, dyslipidemia and other cardiovascular conditions (Brennan et al., 2018; Ciccacci et al., 2019; Dillon et al., 2013). Although chronic immune activation contributes to increased hypertension among PLHIV, the inflammatory milieu is poorly understood (Masenga et al., 2019). ART associated endothelial dysfunction (Nduka et al., 2016), increasing age and longevity on ART treatment have also been associated with increased prevalence of NCDs among PLHIV (Brennan et al., 2018; Ciccacci et al., 2019; Coetzee et al., 2019). In our study, close to two thirds of KPs living with HIV who had an NCD diagnosis, were either obese or overweight. A majority were FSWs. A higher prevalence of NCD diagnoses was observed with increased age.

In our study, we found 1.0% prevalence of hypertension from clinical records. Using our proxy for hypertension of two or more blood pressure readings taken less than 12 months apart, the prevalence of hypertension rose to 16.3%. Further, we found a low prevalence of other CVD diagnoses (0.3%). Similar discrepancies have been reported in other studies in SSA (Achwoka et al., 2019; George, McGrath, & Oni, 2019). In a South African study, prevalence of hypertension was higher during the day of the interview than when compared to both self-report and client records (George et al., 2019). While the underdiagnosis in this latter study may be attributed to 'white coat hypertension', we consider our study as having a much more robust estimate of hypertension prevalence. However, while other studies reported high prevalence of other CVD diagnoses, isolating confounders of central nervous system (CNS) infections especially among ART naïve immunosuppressed clients proved difficult (Hyle et al., 2017). In our case, low prevalence of other CVD diagnoses, chronic respiratory diseases (1.1%), and diabetes mellitus (no cases) could have been attributed to absence of routine

screening against a backdrop of a non-integrated NCD and HIV care system (Fiseha & Belete, 2019; Maganga et al., 2015).

ART treatment for KPs has generally followed a similar trajectory to that of the general population. (WHO, 2016a). Expanded ART eligibility over recent years has seen KPs with higher CD4 levels initiating ART through the Test and Treat platform. In this study, less than a fifth of KPs had advanced disease (less than CD4 count of 200 cells/mm^3) demonstrating benefits of the adopted test and treat strategy. We did not find a significant association between an NCD diagnosis and CD4 measurement. This is similar to findings in SSA (George et al., 2019). We consider that the underdiagnoses of NCDs that was common in our study, may have contributed to the absence of an association between NCD diagnosis and CD4 measurements.

Key Populations engage in risky behavior that increase their risk for NCDs. Studies have documented harmful consumption of alcohol, smoking tobacco, illicit drug use, and risky sexual behaviors among KPs as factors that increase their risk for NCDs (Bello, Fatiregun, Oyo-Ita, & Ikpeme, 2010; Johnston & Corceal, 2013; Lancaster et al., 2017). A systematic review among KPs in SSA, found a median prevalence of alcohol misuse based on AUDIT/CAGE of 32.8%; and that of illicit drug use ranging from 0.1% to 97.1% for injecting drug users (Kuteesa et al., 2019). Difficult social conditions, including criminalization of sex work, uneven coverage of biomedical interventions and stigma impact negatively on NCDs among KPs (Beyrer et al., 2016; Caceres et al., 2017; Shannon et al., 2018). In our study, we observed a high prevalence of NCDs (18.7%) among FSWs who screened positive for excessive drinking. Among MSM, the prevalence was close to 2.5 times as high, albeit drawn from a small sample size. A tenth of the KPs smoked and had an NCD prevalence of less than 10%. Illicit drug use was reported by about one in twenty KPs, who also reported a low NCD prevalence. Close to a half of all KPs living with HIV who had an NCD diagnosis reported a mixed profile of sexual partners but with near universal condom use. Although sex work remains criminalized in our study setting, KPs receiving care at SWOP had good access to biomedical interventions including prevention and treatment services at both fixed clinics and through peer outreach models.

A recent systematic review on the Global burden of disease indicates that cancer cases have increased in developing countries of SSA and contribute significantly to years of life lost to disability (Fitzmaurice et al., 2019). Utilizing registry data from Malawi, an earlier study pointed to a high burden of AIDS defining cancers -predominantly Kaposi sarcoma and cervical cancer that were associated with late initiation of ART - WHO stage III and IV (Horner et al., 2018). In our study, we found a low prevalence of cancer (0.7%) with cervical cancer as the predominant cancer type. The low prevalence of cancer could have been attributed to early initiation and test and treat ART policies. In our study only 13.2% of KPs had a CD4 of <200 cells/mm3 at initiation of ART further explaining the low prevalence of AIDS-defining malignancies including Kaposi sarcoma. Additionally, introduction of cervical cancer screening towards the end of the study period in early 2015 could serve to explain the low number of cancer cases. Studies among HIV-infected FSWs in similar settings have found human papilloma virus (HPV) 51 and 52 showing independent associations with abnormal cervical cytology among FSWs (Menon, van den Broeck, Rossi, Ogbe, & Mabeya, 2017). Studies among MSM elsewhere found high rates of HPV type 16 infection that was associated with anal intraepithelial neoplasia (AIN) and anal cancer (Mendez-Martinez et al., 2014). Records of our cases lacked both staging details and any associations with HPV serotypes thus limiting our ability to further characterize the cancer burden.

Our study represents some of the earliest attempts at quantifying NCD burden among KPs living with HIV in the SSA setting. However, our study was not without limitations. The cross-sectional nature of our study design limited the inferences we could adduce. While several studies, particularly from general population PLHIV demonstrate increased incident NCD cases (Brennan et al., 2018; Coetzee et al., 2019), our study design limited the description of incidence, and outcomes following ART treatment.

Although our paper highlights the prevalence of key NCDs in a group of female and male sex workers enrolled in a funded HIV prevention and treatment program in Nairobi Kenya, majority of those with conditions of interests were women. Similar to many other countries in SSA, sex work and same sex

relationships in Kenya are not only generally criminalized but also highly stigmatized (Shannon et al., 2018).Females who sell sex however seem to be more tolerated than MSM engaged in the trade. The latter suffer double stigma and their position is further worsened by being HIV infected. Therefore, females were over represented in the study sample as fewer men out of the many closeted MSM have taken that leap of faith to enroll in ongoing HIV prevention and treatment programs. We acknowledge that the over representation of women in our sample limits generalizability of our results to key populations experiences in Kenya or the region. That notwithstanding, our data provides important insights into NCD burden in this marginalized population that has not been reported elsewhere.

Several studies indicate high levels of discrimination and uneven access for KP to HIV/NCD and SRH services (Lafort et al., 2016; Stockton, Giger, & Nyblade, 2018; Wanyenze et al., 2017). However, being in an urban set-up and operating KP only services, with linkages to legal support systems, KPs in our study were considered emancipated with improved access to HIV care. The absence of routine glucose monitoring at SWOP clinics could have contributed to the absence of any reported cases of diabetes. Similarly, our detection of hypertension based on updated guidelines that require a 24-hour mean blood pressure reading was limited owing to operational challenges at SWOP clinics (Whelton et al., 2018).

CONCLUSION

This study found a high prevalence of NCDs among KPs living with HIV on ART at a large prevention and treatment program in Nairobi Kenya. Our study results call for an urgent shift in refocusing HIV and NCD prevention in key populations targeted by ongoing programs in the face of a changing HIV epidemic. With integrated HIV/NCD care models being considered to address the growing syndemic for general population PLHIV, KPs will require similar strategies. Efforts to operationalize HIV/NCD integration through strengthening workforce strategies and revision and simplification of HIV tools to include NCD screening are an urgent priority. Differentiated approaches to delivering KP services and overcoming regulatory barriers to legitimize lay and peer approaches as part of the healthcare system warrant consideration. Strengthening data collection and surveillance of NCDs among both the general

population and KP PLHIV are necessary to inform effective HIV/NCD integration prevention and treatment models and policies.

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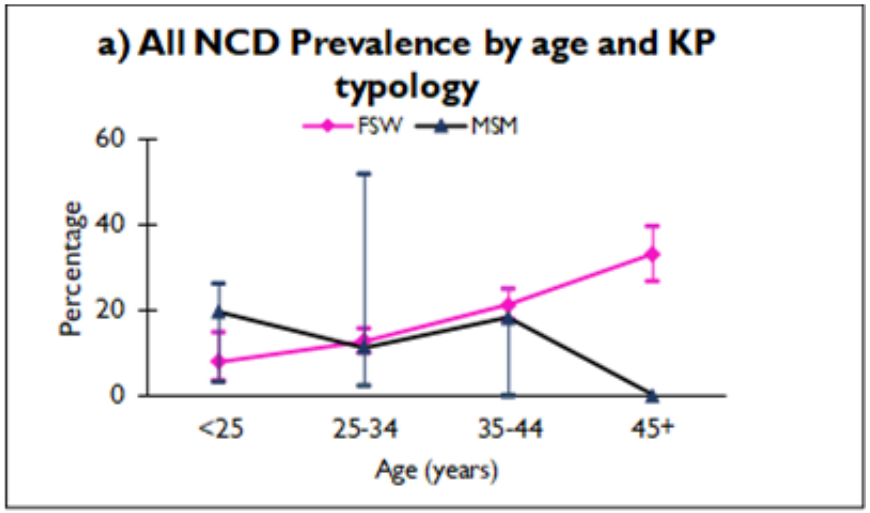

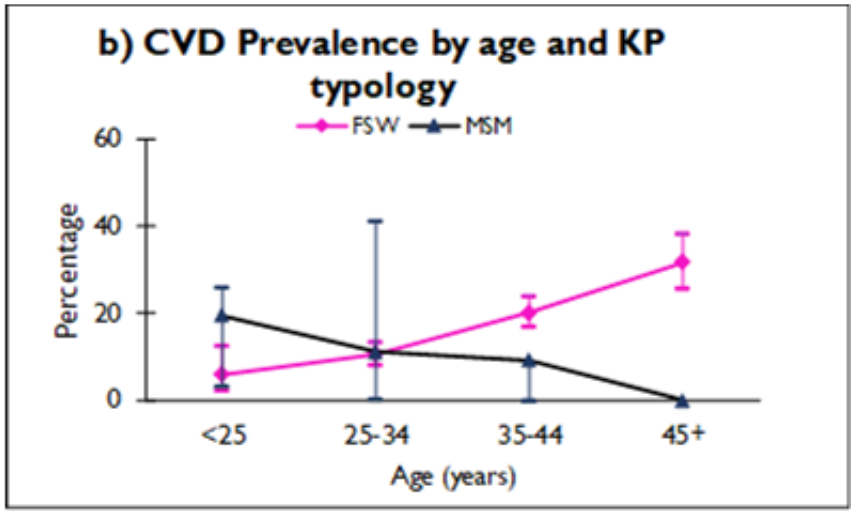

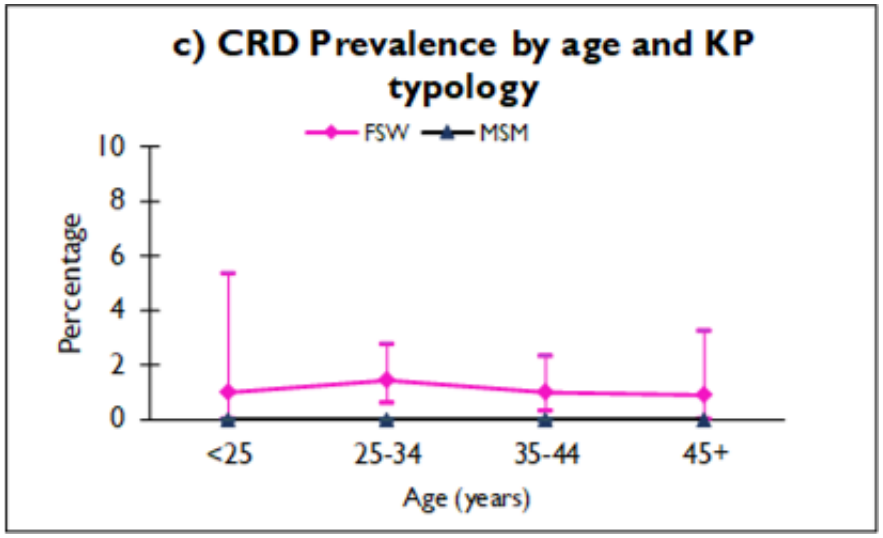

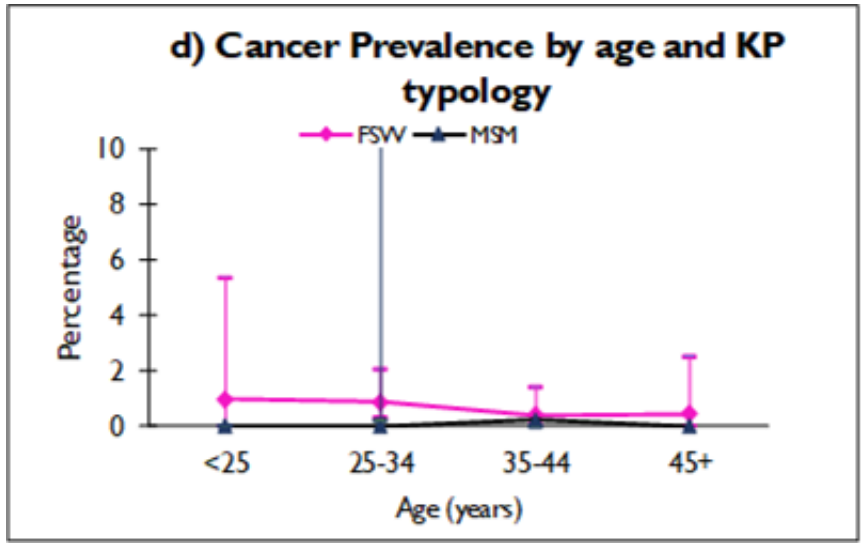

Figure 4.3.1: Distribution of NCDs among HIV-infected KP by typology at SWOP Clinics 2012-15

CHAPTER FIVE: SUMMARY RECOMMENDATIONS AND CONCLUSION

This chapter serves as a capstone to this thesis. Herein, I present a summary of major findings emanating from the study and discuss their implications. I highlight gaps in our study, and finally make recommendations that could be considered for policy and public health practice.

Through this study we sought to determine the burden of non-communicable diseases (NCDs) among both the general population and key populations living with HIV in Kenya. All PLHIV who participated in this study were enrolled into HIV prevention and care program. Two key population typologies – MSM and FSW were included in our study. We further assessed NCD-HIV care service delivery in SSA through integrated models from a HIV care setting context and measured outcomes at three levels: HIV program, NCD care and at health systems levels.

Specifically, we estimated burden of four main NCD categories -cardiovascular diseases, chronic respiratory diseases, cancer and diabetes mellitus, that contribute 80% of premature deaths using two study populations. The first was 3340 patient records of clients drawn from a nationally representative sample of 50 comprehensive HIV care clinics in Kenya that also constituted the National Longitudinal Surveillance of Treatment Outcomes in Kenya (LSTIK II) cohort 2003-2013. The second study population was 2200 patient records of key populations enrolled between 2012 and 2015 at seven clinics and Drop-in Centers (DICEs) of University of Manitoba SWOP key population program in Nairobi. A total of 3,170 patient records from the LSTIK II cohort and 1,478 patient records from the SWOP cohort were analyzed.

We conducted a retrospective cohort study among PLHIV drawn from the general population and a cross sectional study among the key populations infected with HIV. Assessment of NCD/HIV integration was through a systematic review across several databases (Medline, Embase, Global Health, Scopus and Cochrane library) spanning over five years (2013 -2018). Among general population clients, we assessed distribution of NCDs by ART status and calculated incidence rate ratios for selected baseline demographic and clinical characteristics and incidence/1000 person years by ART

status. We calculated incidence rates and presented 95% confidence intervals then graphically illustrated incidence of NCDs by ART status over time through Kaplan-Meier survival curves.

We estimated prevalence of four NCD-categories among KPs at enrollment, and subsequent management at follow-up care visits. We compared prevalence and assessed distributions of co-morbidities using Chi-square and t-tests as appropriate. We conducted univariate and multivariate analysis to identify factors associated with NCD diagnoses. All our analyses were conducted using Stata 14.2 (Stata Corporation, Texas USA).

Major findings

General Population PLHIV: We analyzed 3170 patient records; 2115 (66.3%) were from women. Slightly over half (51.1%) of patient records were from PLHIVs aged above 35 years. Close to two-thirds (63.9%) of PLHIVs were on ART. The proportion of any documented NCD among PLHIV was 11.5% (95% confidence interval [CI] 9.3, 14.1), with elevated blood pressure as the most common NCD (87.5%) among PLHIV with diagnosed NCD. Although serial elevated blood pressures were detected among 343 patients, only 17 had a documented diagnosis of hypertension in their medical record. The differences in overall NCD incidence rates for men and women were not statistically significant (42.3 per 1000 person years [95% CI 35.8, 50.1] and 31.6 [95% CI 27.7, 36.1], respectively). No differences in NCD incidence rates were seen by marital or employment status. At one year of follow up 43.8% of PLHIV not on ART had been diagnosed with an NCD compared to 3.7% of patients on ART; at five years the proportions with a diagnosed NCD were 88.8% and 39.2% ($p<0.001$), respectively.

HIV-infected Key Populations: Overall, 1,478 individuals' records were analyzed; 1,392 (94.2%) FSWs and 86 (5.8%) MSMs. FSWs' median age was 35.3 (interquartile range (IQR) 30.1-41.6) while MSMs was 26.8 years (IQR 23.2 – 32.1). At enrollment into HIV care, most KPs (86.6%) were at an early (stage I-II) WHO clinical stage; 1462 (98.9%) were on first-line ART. A total of 271, 18.3% (95% confidence interval (CI): 16.4 -20.4%), HIV-infected KPs had an NCD diagnosis in their clinical

chart records; 258 (95.2%) being from FSWs. Some form of cardiovascular disease (CVD) that included hypertension was present in 249/271, 91.8%, of KPs with a documented NCD. Using a proxy of two or more elevated blood pressure readings taken < 12 months apart, prevalence of hypertension rose from 1.0% (95% CI: 0.6 -1.7) that was documented in charts to 16.3% (95% CI: 14.4 -18.3). Chronic respiratory disease – mainly asthma was present in 16/271, prevalence of 1.1% (95% CI: 0.6 – 1.8). Cancer was in 10/271, prevalence of 0.7% (95% CI: 0.3 -1.2). Diabetes was not reported. Significant associations between NCD diagnosis and increased age, unemployment status, BMI and CD4 of NCD diagnoses were not sustained on adjusted analyses, except for categories of ≥ BMI 30 kg/m2 and age ≥ 45 years.

Systematic Review: We identified 49 eligible studies. Eighteen (36.8%) studies were cross-sectional, 9 (18.4%) qualitative, 7 (14.3%) experimental or quasi-experimental, 6 (12.2%) cohort, 3 (6.1%) mixed- method and 6 (12.2%) applied an econometric design. In 23 (46.9%) studies, the main target condition for HIV-NCD care integration was cancer. Fifteen (30.6%) studies addressed cardiovascular diseases including hypertension and attendant risk factors; 12 (24.5%) targeted diabetes mellitus. Twenty-four (49.0%) studies were conducted among HIV-infected individuals at HIV clinics, 16 (32.7%) in general clinics, 6 (12.2%) integrated community-based screening, 2 (4.1%) applied differentiated-care models and 1 (2.0%) was at population level. For HIV, all studies recorded positive outcomes for case finding, retention, increased CD4 counts and improved quality of life. For NCDs, positive outcomes of early screening and identification that forestalled complications associated with NCD progression were identified. Resource considerations were poorly described with only a few studies reporting on program cost data. Incremental cost of HIV-NCD care integration stood at USD 3.95 - 4.00 per patient annually and represented a 6% -30% increase in total program costs for non-cancer NCDs.

Discussion Summary

This study describes the burden of NCDs among PLHIV – both general population and key population living with HIV and explores the outcomes of NCD/HIV care delivered in the context of a HIV setting. The backdrop for this study is noteworthy. First, SSA is at a crossroads with a dual burden of disease posed by an ever-increasing burden of NCDs in a region traditionally prioritized for its heavy burden of HIV and other infectious diseases. Secondly, with an increased coverage of life saving antiretroviral therapy, SSA is witnessing a burgeoning number of ageing PLHIV, who now have additional risk factors for NCDs. Lastly, we highlight the fragility of health care systems in SSA and the opportunity presented by fairly robust HIV care delivery systems that we can leverage upon to deliver integrated care for NCDs and HIV.

Our study found high overall prevalence of any of the four documented NCDs among both general population PLHIV (11.5%) and key populations (MSM and FSW) living with HIV (18.3%) A majority of the population was female and aged above 35 years of age. Outside SSA, systematic reviews suggest higher rates of NCD (Caceres et al., 2017). Contrastingly, studies in SSA point to lower NCD prevalence rates (4.7%, 11.5% and 21.2%) among general population PLHIV (Achwoka et al., 2019; Coetzee et al., 2019; Kansiime et al., 2019; Patel et al., 2018). Recent modeling data from Kenya point to higher estimates with 36% of adult PLHIV suffering from one NCD in 2018. NCD prevalence is poised to grow to 55% prevalence among adult PLHIV in 2035 (G. o. K. Ministry of Health, 2019). Our findings serve to underscore the urgent need to pay attention to the rising NCD burden in an ageing PLHIV cohort.

In our study, the commonest NCD was elevated blood pressure under the main category of cardiovascular disease. While no differences were noted by sex, our study pointed to a high level of underdiagnosis across all studied NCDs. Despite a low prevalence of documented diagnosis of hypertension, proxy estimates obtained through two or more elevated blood pressure readings taken < 12 months apart increased the prevalence of hypertension significantly - 1.0% vs 16.3% among KPs infected with HIV and 87.5% of general PLHIV with documented NCD. Low proportions were noted

for chronic respiratory disease including asthma (2.3% general PLHIV and 1.1% among KPs infected with HIV) and cancer (1.1% general PLHIV and 0.7% KPs infected with HIV). While general PLHIV reported 2.1%, no cases of diabetes were reported among KPs infected with HIV. Follow up conducted among general PLHIV at five years showed an increase from 3.7% to 39.2% in the diagnoses of NCDs. These findings are consistent with the 2019 NCD estimates report in Kenya that point to hypertension and high total cholesterol as the two key drivers for the future NCD burden among PLHIV (G. o. K. Ministry of Health, 2019).

We identified five integration models from a HIV standpoint for NCD/HIV service delivery. These are: Integrated community-based screening for HIV and NCDs in the general population; screening for NCDs and NCD risk factors among HIV patients enrolled in care; integration of HIV and NCD care within clinics; differentiated care for patients with HIV and/or NCDs; and population healthcare for all – UHC. Outcomes for the HIV program were positive across the care continuum. Early identification that led to improved care was noted for NCDs thereby proffering NCD/HIV integration as being a favorable intervention. While health system benefits were noted, cost estimates were poorly described and mainly related to integrated care for cancer.

Study Limitations

Through our study, we identified four key issues that serve as study limitations. The use of routine program data placed an inherent weakness in our estimation of the burden of NCDs. With busy comprehensive care clinics that are generally under-staffed, documentation gaps by clinicians are rife. Missing data, and lost files and registers were some of the challenges that beleaguered the routine data and service statistics utilized in this study. A controlled prospective study with cohort monitoring has potential to provide better estimates of NCD burden including incidence.

Secondly, our study limited the study of NCD burden to four main NCDs that contribute to 80% of premature deaths. Health system limitations in Kenya are epitomized by lack of reagents to offer screening for glycemic control, cancer and spirometry for chronic respiratory conditions to eligible

clients at public facilities. Inferences from our study are limited by these challenges leading to underdiagnosis. Additionally, the burden of a fifth NCD – mental illness that is now noted to be of public health importance was not estimated. This is an area worth advancing future research.

Thirdly, we note that our study population, especially among the key populations infected with HIV, was mainly derived from FSWs. MSM comprised only 5.8% of the study population. It is important to recognize that sex work is criminalized in Kenya and particularly stigmatized when MSM are concerned. Whereas our study provides one of the earliest bold attempts to reach out to a hidden population we recognize the pitfalls that would arise from making inferences made from the small MSM sample and call for caution in interpreting these results.

Lastly, we present the merits of integration as the preferred route for service delivery for both NCD and HIV. While NCD/HIV care integration is an attractive option for its ability to leverage on the robust HIV platform that exists in many countries in SSA, the poor description of cost elements is a significant challenge. Costing studies beyond cervical cancer care provision in HIV settings are required. Clarity on elements of the HIV platform that offer cost-benefit and effectiveness are required in order to offer sound implementation and policy recommendations.

Conclusion and Recommendations

For many countries in SSA, tackling NCDs against a backdrop of HIV remains a formidable challenge. NCD prevalence among PLHIV is incessantly on the rise. Countries including Kenya, need to make concerted efforts to alter their policy environment and increase domestic resourcing to hasten the response on the NCD-HIV syndemic. Approaches such as integration that seek to leverage on HIV chronic care platforms for delivery of NCD care to PLHIV appear attractive. Universal health care (UHC) promises to inject some impetus in the response but needs an adjunct institutional response.

From the findings of this PhD study, I would present the following five recommendations:

a) Setting up of a routine surveillance system to measure non-communicable diseases among PLHIV.

b) Setting up of education and wellness centers within hospitals while assuring linkage with comprehensive care centers where HIV infected clients are attended to.

c) All PLHIV should be screened for NCD risk factors such as smoking, hypertension, dyslipidemia and diabetes. Simple screening tests such as random blood glucose, measuring abdominal girth, and documenting body mass index at every clinic visit should be made routine

d) With the five models of HIV-NCD integration studied, counties and health facilities should choose judiciously aspects that would work well for their individual counties. While integration works, I acknowledge that if not judiciously employed, the risk of overrunning the system through overworked health care workers and an overburdened supply chain system stand to arise. Use of lay cadres for some tasks including education and screening, and differentiated community models that decant clinics would offer reprieve to a weak health system.

e) To succeed all the four aforementioned recommendations, need to be hinged on policy and a societal shift to healthier lifestyle choices.

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REFERENCES

Achwoka, D., Waruru, A., Chen, T.-H., Masamaro, K., Ngugi, E., Kimani, M., . . . De Cock, K. M. J. B. P. H. (2019). Noncommunicable disease burden among HIV patients in care: a national retrospective longitudinal analysis of HIV-treatment outcomes in Kenya, 2003-2013. *19*(1), 372. doi:10.1186/s12889-019-6716-2

Acio, J. F., Schouten, E., Arinaitwe, M., Lukoda, N., Akurut, D., Kellerman, S., & Ssemafumu, E. (2013). Cervical cancer and STI screening: A must in the era of HIV/AIDS; increasing access for HIV infected women through community outreach screening programmes. *Sexually Transmitted Infections. Conference: STI and AIDS World Congress, 89*(SUPPL. 1).

Afzal, O., Lieber, M., Dottino, P., & Beddoe, A. M. (2017). Cervical cancer screening in rural South Africa among HIV-infected migrant farm workers and sex workers. *Gynecologic Oncology Reports, 20*, 18-21.

Allen, L. N., Pullar, J., Wickramasinghe, K. K., Williams, J., Roberts, N., Mikkelsen, B., . . . Townsend, N. (2018). Evaluation of research on interventions aligned to WHO 'Best Buys' for NCDs in low-income and lower-middle-income countries: a systematic review from 1990 to 2015. *BMJ Global Health, 3*(1), e000535. doi:10.1136/bmjgh-2017-000535

Ameh, S., Gómez-Olivé, F. X., Kahn, K., Tollman, S. M., & Klipstein-Grobusch, K. (2017). Relationships between structure, process and outcome to assess quality of integrated chronic disease management in a rural South African setting: applying a structural equation model. *BMC Health Services Research, 17*, 1-15. doi:10.1186/s12913-017-2177-4

Ameh, S., Klipstein-Grobusch, K., D'Ambruoso, L., Kahn, K., Tollman, S. M., & Gomez-Olive, F. X. (2017). Quality of integrated chronic disease care in rural South Africa: user and provider perspectives. *Health Policy Plan, 32*(2), 257-266. doi:10.1093/heapol/czw118

Ameh, S., Klipstein-Grobusch, K., Musenge, E., Kahn, K., Tollman, S., & Gomez-Olive, F. X. (2017). Effectiveness of an Integrated Approach to HIV and Hypertension Care in Rural South Africa:

Controlled Interrupted Time-Series Analysis. *J Acquir Immune Defic Syndr, 75*(4), 472-479. doi:10.1097/qai.0000000000001437

Arbyn, M., Weiderpass, E., Bruni, L., de Sanjosé, S., Saraiya, M., Ferlay, J., & Bray, F. (2019). Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *The Lancet. Global health*, S2214-2109X(2219)30482-30486. doi:10.1016/S2214-109X(19)30482-6

Awungafac, G., Delvaux, T., & Vuylsteke, B. (2017). Systematic review of sex work interventions in sub-Saharan Africa: examining combination prevention approaches. *Trop Med Int Health, 22*(8), 971-993. doi:10.1111/tmi.12890

Baral, S., & Phaswana-Mafuya, N. (2012). Rewriting the narrative of the epidemiology of HIV in sub-Saharan Africa. *SAHARA-J: Journal of Social Aspects of HIV/AIDS, 9*(3), 127-130. doi:10.1080/17290376.2012.743787

Barr, A. L., Young, E. H., Smeeth, L., Newton, R., Seeley, J., Ripullone, K., . . . Sandhu, M. S. (2016). The need for an integrated approach for chronic disease research and care in Africa. *Glob Health Epidemiol Genom, 1*, e19. doi:10.1017/gheg.2016.16

Bekolo, C. E., O'Bryan, G., Tchago, F. E., Nangue, C., Bekoule, P. S., & Kollo, B. (2016). Integrating Cervical Cancer Screening with HIV Care in Cameroon: Comparative Risk Analysis of Cervical Disease in HIV-Infected Women Receiving Antiretroviral Therapy to Women in the General Population. *PLoS One, 11*(2), e0149152. doi:10.1371/journal.pone.0149152

Bello, S., Fatiregun, A., Oyo-Ita, A., & Ikpeme, B. (2010). Dose-response relationship between alcohol use and blood pressure among drivers of commercial vehicles in Calabar, Southern Nigeria. *J Public Health Afr, 1*(1), 1.

Bennett, J. E., Stevens, G. A., Mathers, C. D., Bonita, R., Rehm, J., Kruk, M. E., . . . Ezzati, M. (2018). NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4. *Lancet, 392*(10152), 1072-1088. doi:10.1016/s0140-6736(18)31992-5

Bertram, M. Y., Sweeny, K., Lauer, J. A., Chisholm, D., Sheehan, P., Rasmussen, B., . . . Deane, S. (2018). Investing in non-communicable diseases: an estimation of the return on investment for prevention and treatment services. *Lancet, 391*(10134), 2071-2078. doi:10.1016/s0140-6736(18)30665-2

Beyrer, C., Baral, S. D., Collins, C., Richardson, E. T., Sullivan, P. S., Sanchez, J., . . . Mayer, K. H. (2016). The global response to HIV in men who have sex with men. *Lancet, 388*(10040), 198-206. doi:10.1016/s0140-6736(16)30781-4

Bloomfield, G. S., Hogan, J. W., Keter, A., Sang, E., Carter, E. J., Velazquez, E. J., & Kimaiyo, S. (2011). Hypertension and obesity as cardiovascular risk factors among HIV seropositive patients in Western Kenya. *PLoS One, 6*(7), e22288. doi:10.1371/journal.pone.0022288

Bloomfield, G. S., Khazanie, P., Morris, A., Rabadan-Diehl, C., Benjamin, L. A., Murdoch, D., . . . Hicks, C. (2014). HIV and noncommunicable cardiovascular and pulmonary diseases in low- and middle-income countries in the ART era: what we know and best directions for future research. *J Acquir Immune Defic Syndr, 67 Suppl 1*, S40-53. doi:10.1097/qai.0000000000000257

BMJ. (2018). Study Design and Choosing a Statistical Test. Retrieved from https://www.bmj.com/about-bmj/resources-readers/publications/statistics-square-one/13-study-design-and-choosing-statisti

Brennan, A. T., Jamieson, L., Crowther, N. J., Fox, M. P., George, J. A., Berry, K. M., . . . Rosen, S. (2018). Prevalence, incidence, predictors, treatment, and control of hypertension among HIV-positive adults on antiretroviral treatment in public sector treatment programs in South Africa. *PLoS One, 13*(10), e0204020. doi:10.1371/journal.pone.0204020

Broughton, E. I., Muhire, M., Karamagi, E., & Kisamba, H. (2016). Cost-effectiveness of implementing the chronic care model for HIV care in Uganda. *International Journal for Quality in Health Care, 28*(6), 802-807.

Brown, T., & Peerapatanapokin, W. (2019). Evolving HIV epidemics: the urgent need to refocus on populations with risk. *Curr Opin HIV AIDS, 14*(5), 337-353. doi:10.1097/coh.0000000000000571

Bukirwa, A., Mutyoba, J. N., Mukasa, B. N., Karamagi, Y., Odiit, M., Kawuma, E., & Wanyenze, R. K. (2015). Motivations and barriers to cervical cancer screening among HIV infected women in HIV care: a qualitative study. *BMC Womens Health, 15*, 82. doi:10.1186/s12905-015-0243-9

Burrows, D., McCallum, L., Parsons, D., & Falkenberry, H. (2019). *Global Summary of Findings of an Assessment of HIV Service Packages for Key Populations in Six Regions*. Retrieved from Washington, DC:

Caceres, B. A., Brody, A., & Chyun, D. (2016). Recommendations for cardiovascular disease research with lesbian, gay and bisexual adults. *J Clin Nurs, 25*(23-24), 3728-3742. doi:10.1111/jocn.13415

Caceres, B. A., Brody, A., Luscombe, R. E., Primiano, J. E., Marusca, P., Sitts, E. M., & Chyun, D. (2017). A Systematic Review of Cardiovascular Disease in Sexual Minorities. *Am J Public Health, 107*(4), e13-e21. doi:10.2105/ajph.2016.303630

Cao, B., Bray, F., Ilbawi, A., & Soerjomataram, I. (2018). Effect on longevity of one-third reduction in premature mortality from non-communicable diseases by 2030: a global analysis of the Sustainable Development Goal health target. *Lancet Glob Health, 6*(12), e1288-e1296. doi:10.1016/s2214-109x(18)30411-x

Chhoun, P., Ngin, C., Tuot, S., Pal, K., Steel, M., Dionisio, J., . . . Yi, S. (2017). Non-communicable diseases and related risk behaviors among men and women living with HIV in Cambodia: findings from a cross-sectional study. *Int J Equity Health, 16*(1), 125. doi:10.1186/s12939-017-0622-y

Chhoun, P., Tuot, S., Harries, A. D., Kyaw, N. T. T., Pal, K., Mun, P., . . . Yi, S. (2017). High prevalence of non-communicable diseases and associated risk factors amongst adults living with HIV in Cambodia. *PLoS One, 12*(11), e0187591. doi:10.1371/journal.pone.0187591

Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo, J. L., Jr., . . . Roccella, E. J. (2003). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *Jama, 289*(19), 2560-2572. doi:10.1001/jama.289.19.2560

Ciccacci, F., Tolno, V. T., Doro Altan, A. M., Liotta, G., Orlando, S., Mancinelli, S., . . . Marazzi, M. C. (2019). Noncommunicable Diseases Burden and Risk Factors in a Cohort of HIV+ Elderly Patients in Malawi. *AIDS Res Hum Retroviruses, 35*(11-12), 1106-1111. doi:10.1089/aid.2019.0125

Clouse, K., Motlhatlhedi, M., Bonnet, K., Schlundt, D., Aronoff, D. M., Chakkalakal, R., & Norris, S. A. (2018). "I just wish that everything is in one place": facilitators and barriers to continuity of care among HIV-positive, postpartum women with a non-communicable disease in South Africa. *AIDS Care, 30*(sup2), 5-10. doi:10.1080/09540121.2018.1470308

Coetzee, L., Bogler, L., De Neve, J.-W., Bärnighausen, T., Geldsetzer, P., & Vollmer, S. (2019). HIV, antiretroviral therapy and non-communicable diseases in sub-Saharan Africa: empirical evidence from 44 countries over the period 2000 to 2016. *J Int AIDS Soc, 22*(7), e25364-e25364. doi:10.1002/jia2.25364

Coutinho, C., Nampijja, S., Musoke Seruma, E., Nambafu, S., & Mpiima, D. (2013). Scaling up cervical cancer screening in HIV/AIDS resource limited settings: TASO Jinja experience. *Sexually Transmitted Infections. Conference: STI and AIDS World Congress, 89*(SUPPL. 1).

Dave, J. A., Lambert, E. V., Badri, M., West, S., Maartens, G., & Levitt, N. S. (2011). Effect of nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy on dysglycemia and insulin sensitivity in South African HIV-infected patients. *J Acquir Immune Defic Syndr, 57*(4), 284-289. doi:10.1097/QAI.0b013e318221863f

Davies, N., Chersich, M., Mullick, S., Naidoo, N., Makhoba, N., Rees, H., & Schwartz, S. R. (2018). Integrating cervical cancer screening into safer conception services to improve women's health outcomes: a pilot study at a primary care clinic in South Africa. *Sexually Transmitted Diseases, 10*, 10.

Dillon, D. G., Gurdasani, D., Riha, J., Ekoru, K., Asiki, G., Mayanja, B. N., . . . Sandhu, M. S. (2013). Association of HIV and ART with cardiometabolic traits in sub-Saharan Africa: a systematic review and meta-analysis. *Int J Epidemiol, 42*(6), 1754-1771. doi:10.1093/ije/dyt198

Dimala, C. A., Atashili, J., Mbuagbaw, J. C., Wilfred, A., & Monekosso, G. L. (2016). Prevalence of Hypertension in HIV/AIDS Patients on Highly Active Antiretroviral Therapy (HAART) Compared with HAART-Naive Patients at the Limbe Regional Hospital, Cameroon. *PLoS One, 11*(2), e0148100. doi:10.1371/journal.pone.0148100

Dimala, C. A., Blencowe, H., & Choukem, S. P. (2018). The association between antiretroviral therapy and selected cardiovascular disease risk factors in sub-Saharan Africa: A systematic review and meta-analysis. *PLoS One, 13*(7), e0201404. doi:10.1371/journal.pone.0201404

Divala, O. H., Amberbir, A., Ismail, Z., Beyene, T., Garone, D., Pfaff, C., . . . Oosterhout, J. J. v. (2016). The burden of hypertension, diabetes mellitus, and cardiovascular risk factors among adult Malawians in HIV care: consequences for integrated services. *BMC Public Health, 16*(1243).

Drain, P. K., Hong, T., Thulare, H., Moosa, M. Y., & Celum, C. L. (2018). Integrating hypertension screening at voluntary HIV testing in South Africa. *Topics in Antiviral Medicine, 26 (Supplement 1)*, 311s-312s.

Duffy, M., Ojikutu, B., Andrian, S., Sohng, E., Minior, T., & Hirschhorn, L. R. (2017). Non-communicable diseases and HIV care and treatment: models of integrated service delivery. *Tropical Medicine & International Health, 22*(8), 926-937.

Edwards, J. K., Bygrave, H., Van den Bergh, R., Kizito, W., Cheti, E., Kosgei, R. J., . . . Reid, T. (2015). HIV with non-communicable diseases in primary care in Kibera, Nairobi, Kenya:

characteristics and outcomes 2010-2013. *Trans R Soc Trop Med Hyg, 109*(7), 440-446. doi:10.1093/trstmh/trv038

El-Sadr, W. M., & Goosby, E. (2018). Building on the HIV platform: tackling the challenge of noncommunicable diseases among persons living with HIV. *AIDS, 32*, S1-S3. doi:10.1097/qad.0000000000001886

Ezechi, O. C., Gab-Okafor, C. V., Ostergren, P. O., & Odberg Pettersson, K. (2013). Willingness and acceptability of cervical cancer screening among HIV positive Nigerian women. *BMC Public Health, 13*, 46. doi:10.1186/1471-2458-13-46

Farahani, M., Vable, A., Lebelonyane, R., Seipone, K., Anderson, M., Avalos, A., . . . Marlink, R. (2014). Outcomes of the Botswana national HIV/AIDS treatment programme from 2002 to 2010: a longitudinal analysis. *Lancet Glob Health, 2*(1), e44-50. doi:10.1016/s2214-109x(13)70149-9

Fiseha, T., & Belete, A. G. (2019). Diabetes mellitus and its associated factors among human immunodeficiency virus-infected patients on anti-retroviral therapy in Northeast Ethiopia. *BMC Res Notes, 12*(1), 372. doi:10.1186/s13104-019-4402-1

Fitzmaurice, C., Abate, D., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdel-Rahman, O., . . . Murray, C. J. L. (2019). Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017: A Systematic Analysis for the Global Burden of Disease Study. *JAMA Oncol.* doi:10.1001/jamaoncol.2019.2996

Freiberg, M., Duncan, M. S., Kundu, S., Mumpuni, A., Epstein, E., Bedigian, A., . . . Tseng, Z. H. (2019). *Sudden Cardiac Death among HIV-Infected and -Uninfected Veterans*. Paper presented at the Conference on Retroviruses and Opportunistic Infections, Seattle, Washington. http://www.croiwebcasts.org/p/2019croi/32

Garrib, A., Birungi, J., Lesikari, S., Namakoola, I., Njim, T., Cuevas, L., . . . Nyirenda, M. (2018). Integrated care for human immunodeficiency virus, diabetes and hypertension in Africa. *Trans R Soc Trop Med Hyg*. doi:10.1093/trstmh/try098

George, S., McGrath, N., & Oni, T. (2019). The association between a detectable HIV viral load and non-communicable diseases comorbidity in HIV positive adults on antiretroviral therapy in Western Cape, South Africa. *BMC Infect Dis, 19*(1), 348. doi:10.1186/s12879-019-3956-9

Ginsberg, G. M., Lauer, J. A., Zelle, S., Baeten, S., & Baltussen, R. (2012). Cost effectiveness of strategies to combat breast, cervical, and colorectal cancer in sub-Saharan Africa and South East Asia: mathematical modelling study. *Bmj, 344*, e614. doi:10.1136/bmj.e614

Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. (2018). *Lancet, 392*(10159), 1859-1922. doi:10.1016/s0140-6736(18)32335-3

Golovaty, I., Sharma, M., Van Heerden, A., van Rooyen, H., Baeten, J. M., Celum, C., & Barnabas, R. V. (2018). Cost of Integrating Noncommunicable Disease Screening Into Home-Based HIV Testing and Counseling in South Africa. *Journal of Acquired Immune Deficiency Syndromes: JAIDS, 78*(5), 522-526.

Gouda, H. N., Charlson, F., Sorsdahl, K., Ahmadzada, S., Ferrari, A. J., Erskine, H., . . . Whiteford, H. (2019). Burden of non-communicable diseases in sub-Saharan Africa, 1990-2017: results from the Global Burden of Disease Study 2017. *Lancet Glob Health, 7*(10), e1375-e1387. doi:10.1016/S2214-109X(19)30374-2

Goudge, J., Chirwa, T., Eldridge, S., Gomez-Olive, F. X. F., Kabudula, C., Limbani, F., . . . Thorogood, M. (2018). Can lay health workers support the management of hypertension? Findings of a cluster randomised trial in South Africa. *BMJ Global Health, 3*(1), e000577.

Haldane, V., Legido-Quigley, H., Chuah, F. L. H., Sigfrid, L., Murphy, G., Ong, S. E., . . . Perel, P. (2018). Integrating cardiovascular diseases, hypertension, and diabetes with HIV services: a systematic review. *AIDS Care, 30*(1), 103-115.

Haregu, T. N., Oldenburg, B., Sestwe, G., Elliott, J., & Nanayakkara, V. (2012). Epidemiology of Comorbidity of HIV/AIDS and Non-communicable Diseases in Developing Countries: A systematic review. *The Journal of Global Health Care Systems, 2*(1).

Haregu, T. N., Setswe, G., Elliott, J., & Oldenburg, B. (2014a). Developing an action model for integration of health system response to HIV/AIDS and noncommunicable diseases (NCDs) in developing countries. *Global journal of health science, 6*(1), 9-22.

Haregu, T. N., Setswe, G., Elliott, J., & Oldenburg, B. (2014b). National Responses to HIV/AIDS and Non-Communicable Diseases in Developing Countries: Analysis of Strategic Parallels and Differences. *J Public Health Res, 3*(1), 99. doi:10.4081/jphr.2014.99

Herce, M. E., Kalanga, N., Wroe, E. B., Keck, J. W., Chingoli, F., Tengatenga, L., . . . Rigodon, J. (2015). Excellent clinical outcomes and retention in care for adults with HIV-associated Kaposi sarcoma treated with systemic chemotherapy and integrated antiretroviral therapy in rural Malawi. *J Int AIDS Soc, 18*, 19929. doi:10.7448/ias.18.1.19929

Hewett, P. C., Nalubamba, M., Bozzani, F., Digitale, J., Vu, L., Yam, E., & Nambao, M. (2016). Randomized evaluation and cost-effectiveness of HIV and sexual and reproductive health service referral and linkage models in Zambia. *BMC Public Health, 16*, 785. doi:10.1186/s12889-016-3450-x

Horner, M. J., Chasimpha, S., Spoerri, A., Edwards, J., Bohlius, J., Tweya, H., . . . Gopal, S. (2018). High Cancer Burden Among Antiretroviral Therapy Users in Malawi: a Record Linkage Study of Observational HIV Cohorts and Cancer Registry Data. *Clin Infect Dis*. doi:10.1093/cid/ciy960

Huchko, M. J., Leslie, H., Maloba, M., Zakaras, J., Bukusi, E., & Cohen, C. R. (2015). Outcomes up to 12 months after treatment with loop electrosurgical excision procedure for cervical

intraepithelial neoplasia among HIV-infected women. *JAIDS, Journal of Acquired Immune Deficiency Syndromes, 69*(2), 200-205.

Hyle, E. P., Mayosi, B. M., Middelkoop, K., Mosepele, M., Martey, E. B., Walensky, R. P., . . . Triant, V. A. (2017). The association between HIV and atherosclerotic cardiovascular disease in sub-Saharan Africa: a systematic review. *BMC Public Health, 17*(1), 954. doi:10.1186/s12889-017-4940-1

Hyle, E. P., Naidoo, K., Su, A. E., El-Sadr, W. M., & Freedberg, K. A. (2014). HIV, tuberculosis, and noncommunicable diseases: what is known about the costs, effects, and cost-effectiveness of integrated care? *J Acquir Immune Defic Syndr, 67 Suppl 1*, S87-95. doi:10.1097/qai.0000000000000254

Ibrahim, M. M., & Damasceno, A. (2012). Hypertension in developing countries. *Lancet, 380*(9841), 611-619. doi:10.1016/s0140-6736(12)60861-7

IHME. (2018). Kenya. Retrieved from http://www.healthdata.org/kenya

Institute for Health Metrics and Evaluation. (2018). IHME - Measuring what matters: Kenya. Retrieved from http://www.healthdata.org/kenya

Jerene, D., Hiruy, N., Jemal, I., Gebrekiros, W., Anteneh, T., Habte, D., . . . Sangiwa, G. (2017). The yield and feasibility of integrated screening for TB, diabetes and HIV in four public hospitals in Ethiopia. *Int Health, 9*(2), 100-104. doi:10.1093/inthealth/ihx002

Johnston, L. G., & Corceal, S. (2013). Unexpectedly high injection drug use, HIV and hepatitis C prevalence among female sex workers in the Republic of Mauritius. *AIDS Behav, 17*(2), 574-584. doi:10.1007/s10461-012-0278-y

Juma, K., Reid, M., Roy, M., Vorkoper, S., Temu, T. M., Levitt, N. S., . . . Yonga, G. (2018). From HIV prevention to non-communicable disease health promotion efforts in sub-Saharan Africa: A Narrative Review. *AIDS, 32*, S63-S73. doi:10.1097/qad.0000000000001879

Juma, P. A., Mapa-Tassou, C., Mohamed, S. F., Matanje Mwagomba, B. L., Ndinda, C., Oluwasanu, M., . . . Kyobutungi, C. (2018). Multi-sectoral action in non-communicable disease prevention

policy development in five African countries. *BMC Public Health, 18*(Suppl 1), 953. doi:10.1186/s12889-018-5826-6

Kachimanga, C., Cundale, K., Wroe, E., Nazimera, L., Jumbe, A., Dunbar, E., & Kalanga, N. (2017). Novel approaches to screening for noncommunicable diseases: Lessons from Neno, Malawi. *Malawi Medical Journal, 29*(2), 78-83.

Kagaruki, G. B., Mayige, M. T., Ngadaya, E. S., Kimaro, G. D., Kalinga, A. K., Kilale, A. M., . . . Mfinanga, S. G. (2014). Magnitude and risk factors of non-communicable diseases among people living with HIV in Tanzania: a cross sectional study from Mbeya and Dar es Salaam regions. *BMC Public Health, 14*, 904. doi:10.1186/1471-2458-14-904

Kaneda, T., Naik, R., & Baldwin, W. (2015). *Noncommunicable Diseases Risk Factors among Young People in Africa*. Retrieved from http://www.prb.org/pdf14/ncd-risk-youth-africa.pdf

Kansiime, S., Mwesigire, D., & Mugerwa, H. (2019). Prevalence of non-communicable diseases among HIV positive patients on antiretroviral therapy at joint clinical research centre, Lubowa, Uganda. *PLoS One, 14*(8), e0221022. doi:10.1371/journal.pone.0221022

Kavishe, B., Biraro, S., Baisley, K., Vanobberghen, F., Kapiga, S., Munderi, P., . . . Grosskurth, H. (2015). High prevalence of hypertension and of risk factors for non-communicable diseases (NCDs): a population based cross-sectional survey of NCDS and HIV infection in Northwestern Tanzania and Southern Uganda. *BMC Med, 13*, 126. doi:10.1186/s12916-015-0357-9

Kemp, C. G., Weiner, B. J., Sherr, K. H., Kupfer, L. E., Cherutich, P. K., Wilson, D., . . . Wasserheit, J. N. (2018). Implementation science for integration of HIV and non-communicable disease services in sub-Saharan Africa: a systematic review. *AIDS, 32*, S93-S105. doi:10.1097/qad.0000000000001897

Kenya National Bureau of Statistics, Ministry of Health Kenya, & World Health Organization. (2015). *Kenya STEPwise Survey for Non Communicable Diseases Risk Factors 2015 Report*. Retrieved from http://www.health.go.ke/wp-content/uploads/2016/04/Steps-Report-NCD-2015.pdf

Khabala, K. B., Edwards, J. K., Baruani, B., Sirengo, M., Musembi, P., Kosgei, R. J., . . . Reid, T. (2015). Medication Adherence Clubs: a potential solution to managing large numbers of stable patients with multiple chronic diseases in informal settlements. *Tropical Medicine and International Health, 20*(10), 1265-1270.

Kirigia, J., & Mwabu, G. (2018). *The Indirect cost of illness in Africa* (Vol. 11).

Kumakech, E., Andersson, S., Wabinga, H., & Berggren, V. (2014). Integration of HIV and cervical cancer screening perceptions of healthcare providers and policy makers in Uganda. *BMC Public Health, 14*, 810. doi:10.1186/1471-2458-14-810

Kumakech, E., Andersson, S., Wabinga, H., & Berggren, V. (2015). Integration of HIV and cervical cancer screening perceptions and preferences of communities in Uganda. *BMC Womens Health, 15*, 23. doi:10.1186/s12905-015-0183-4

Kuteesa, M. O., Seeley, J., Weiss, H. A., Cook, S., Kamali, A., & Webb, E. L. (2019). Alcohol Misuse and Illicit Drug Use Among Occupational Groups at High Risk of HIV in Sub-Saharan Africa: A Systematic Review. *AIDS Behav*. doi:10.1007/s10461-019-02483-y

Kwarisiima, D., Balzer, L., Heller, D., Kotwani, P., Chamie, G., Clark, T., . . . Kamya, M. R. (2016). Population-Based Assessment of Hypertension Epidemiology and Risk Factors among HIV-Positive and General Populations in Rural Uganda. *PLoS One, 11*(5), e0156309. doi:10.1371/journal.pone.0156309

Kyu, H. H., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., . . . Murray, C. J. L. (2018). Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet, 392*(10159), 1859-1922. doi:10.1016/s0140-6736(18)32335-3

Lafort, Y., Greener, R., Roy, A., Greener, L., Ombidi, W., Lessitala, F., . . . Delva, W. (2016). HIV prevention and care-seeking behaviour among female sex workers in four cities in India,

Kenya, Mozambique and South Africa. *Trop Med Int Health, 21*(10), 1293-1303. doi:10.1111/tmi.12761

Lancaster, K. E., Lungu, T., Mmodzi, P., Hosseinipour, M. C., Chadwick, K., Powers, K. A., . . . Miller, W. C. (2017). The association between substance use and sub-optimal HIV treatment engagement among HIV-infected female sex workers in Lilongwe, Malawi. *AIDS Care, 29*(2), 197-203. doi:10.1080/09540121.2016.1211244

Leung, C., Aris, E., Mhalu, A., Siril, H., Christian, B., Koda, H., . . . Hawkins, C. (2016). Preparedness of HIV care and treatment clinics for the management of concomitant non-communicable diseases: a cross-sectional survey. *BMC Public Health, 16*(1), 1002. doi:10.1186/s12889-016-3661-1

Levitt, N. S., Steyn, K., Dave, J., & Bradshaw, D. (2011a). Chronic noncommunicable diseases and HIV-AIDS on a collision course: relevance for health care delivery, particularly in low-resource settings--insights from South Africa. *Am J Clin Nutr, 94*(6), 1690s-1696s. doi:10.3945/ajcn.111.019075

Levitt, N. S., Steyn, K., Dave, J., & Bradshaw, D. (2011b). Chronic noncommunicable diseases and HIV-AIDS on a collision course: relevance for health care delivery, particularly in low-resource settings - insights from South Africa. *American Journal of Clinical Nutrition, 94*(6), 1690S-1696S.

Maganga, E., Smart, L. R., Kalluvya, S., Kataraihya, J. B., Saleh, A. M., Obeid, L., . . . Peck, R. N. (2015). Glucose Metabolism Disorders, HIV and Antiretroviral Therapy among Tanzanian Adults. *PLoS One, 10*(8), e0134410. doi:10.1371/journal.pone.0134410

Magodoro, I. M., Esterhuizen, T. M., & Chivese, T. (2016). A cross-sectional, facility based study of comorbid non-communicable diseases among adults living with HIV infection in Zimbabwe. *BMC Res Notes, 9*, 379. doi:10.1186/s13104-016-2187-z

Masenga, S. K., Hamooya, B. M., Nzala, S., Kwenda, G., Heimburger, D. C., Mutale, W., . . . Kirabo, A. (2019). Patho-immune Mechanisms of Hypertension in HIV: a Systematic and Thematic Review. *Curr Hypertens Rep, 21*(7), 56. doi:10.1007/s11906-019-0956-5

Matanje Mwagomba, B. L., Ameh, S., Bongomin, P., Juma, P. A., MacKenzie, R. K., Kyobutungi, C., . . . Berman, J. (2018). Opportunities and challenges for evidence-informed HIV-noncommunicable disease integrated care policies and programs: lessons from Malawi, South Africa, Swaziland and Kenya. *AIDS, 32*, S21-S32. doi:10.1097/qad.0000000000001885

May, M. T., Gompels, M., Delpech, V., Porter, K., Orkin, C., Kegg, S., . . . Sabin, C. (2014). Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy. *AIDS, 28*(8), 1193-1202. doi:10.1097/qad.0000000000000243

Mendenhall, E., & Norris, S. A. (2015). When HIV is ordinary and diabetes new: remaking suffering in a South African township. *Glob Public Health, 10*(4), 449-462. doi:10.1080/17441692.2014.998698

Mendez-Martinez, R., Rivera-Martinez, N. E., Crabtree-Ramirez, B., Sierra-Madero, J. G., Caro-Vega, Y., Galvan, S. C., . . . Garcia-Carranca, A. (2014). Multiple human papillomavirus infections are highly prevalent in the anal canal of human immunodeficiency virus-positive men who have sex with men. *BMC Infect Dis, 14*, 671. doi:10.1186/s12879-014-0671-4

Menon, S., van den Broeck, D., Rossi, R., Ogbe, E., & Mabeya, H. (2017). Multiple HPV infections in female sex workers in Western Kenya: implications for prophylactic vaccines within this sub population. *Infect Agent Cancer, 12*, 2. doi:10.1186/s13027-016-0114-5

Ministry of Health. (2014). *National Guidelines for HIV/STI Programming with Key Populations in Kenya*. Retrieved from

Ministry of Health, G. o. K. (2001). *Guidelines to Antiretroviral Drug Therapy in Kenya*. Retrieved from http://collections.infocollections.org/whocountry/en/d/Jh4331e/1.html

Ministry of Health, G. o. K. (2005). *Guidelines for Antiretroviral Drug Therapy in Kenya*. Retrieved from https://www.popline.org/node/276660

Ministry of Health, G. o. K. (2011). *Guidelines for Antiretroviral therapy in Kenya*. Retrieved from http://www.faces-kenya.org/files/Kenya%20Treatment%20Guidelines%202011.pdf

Ministry of Health, G. o. K. (2013). *Kenya Most At Risk Populations Size Estimate Consensus report*. Retrieved from http://www.aidsinfoonline.org/kpatlas/document/KEN/KEN_2012_PSE_Report_FSW_MSM_PWID.pdf

Ministry of Health, G. o. K. (2015). *Kenya National Strategy for the Prevention and Control of Non-Communicable Diseases 2015-2020*. Retrieved from https://www.who.int/nmh/ncd-task-force/kenya-strategy-ncds-2015-2020.pdf

Ministry of Health, G. o. K. (2018). *Kenya AIDS Response Progress Report 2018*. Retrieved from https://nacc.or.ke/wp-content/uploads/2018/11/HIV-estimates-report-Kenya-20182.pdf

Ministry of Health, G. o. K. (2019). *Kenya NCD Estimates Report 2019*. Retrieved from

Ministry of Health National AIDS & STI Control Programme. (2016). Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya 2016. Retrieved from https://www.prepwatch.org/wp-content/uploads/2016/08/Guidelines-on-ARV-for-Treating-Preventing-HIV-Infections-in-Kenya.pdf

Ministry of Medical Services, & Ministry of Public Health and Sanitation. (2012). *Kenya Health Policy 2012–2030*.

Miszkurka, M., Haddad, S., Langlois, E. V., Freeman, E. E., Kouanda, S., & Zunzunegui, M. V. (2012). Heavy burden of non-communicable diseases at early age and gender disparities in an adult population of Burkina Faso: World Health Survey. *BMC Public Health, 12*, 24. doi:10.1186/1471-2458-12-24

Mitchell, S. M., Pedersen, H. N., Eng Stime, E., Sekikubo, M., Moses, E., Mwesigwa, D., . . . Ogilvie, G. S. (2017). Self-collection based HPV testing for cervical cancer screening among women living with HIV in Uganda: a descriptive analysis of knowledge, intentions to screen and

factors associated with HPV positivity. *BMC Womens Health, 17*(1), 4. doi:10.1186/s12905-016-0360-0

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med, 6*(7), e1000097. doi:10.1371/journal.pmed.1000097

Mutasa-Apollo, T., Shiraishi, R. W., Takarinda, K. C., Dzangare, J., Mugurungi, O., Murungu, J., . . . Woodfill, C. J. (2014). Patient retention, clinical outcomes and attrition-associated factors of HIV-infected patients enrolled in Zimbabwe's National Antiretroviral Therapy Programme, 2007-2010. *PLoS One, 9*(1), e86305. doi:10.1371/journal.pone.0086305

Mwanahamuntu, M. H., Sahasrabuddhe, V. V., Blevins, M., Kapambwe, S., Shepherd, B. E., Chibwesha, C., . . . Parham, G. P. (2013). Utilization of Cervical Cancer Screening Services and Trends in Screening Positivity Rates in a 'Screen-And-Treat' Program Integrated with HIV/AIDS Care in Zambia. *PLoS One, 8*(9). doi:10.1371/journal.pone.0074607

Mwangome, M. N., Geubbels, E., Klatser, P., & Dieleman, M. (2016). I don't have options but to persevere." Experiences and practices of care for HIV and diabetes in rural Tanzania: A qualitative study of patients and family caregivers. *International Journal for Equity in Health, 15*(1). doi:10.1186/s12939-016-0345-5

Narayan, K. M., Miotti, P. G., Anand, N. P., Kline, L. M., Harmston, C., Gulakowski, R., 3rd, & Vermund, S. H. (2014). HIV and noncommunicable disease comorbidities in the era of antiretroviral therapy: a vital agenda for research in low- and middle-income country settings. *J Acquir Immune Defic Syndr, 67 Suppl 1*, S2-7. doi:10.1097/qai.0000000000000267

National AIDS Control Council (NACC), & National AIDS/STD Control Programme (NASCOP). (2016). *Kenya HIV Estimates 2015*. Retrieved from http://nacc.or.ke/wp-content/uploads/2016/12/Kenya-HIV-Estimates-2015.pdf

NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4. (2018). *Lancet, 392*(10152), 1072-1088. doi:10.1016/s0140-6736(18)31992-5

Nduka, C. U., Stranges, S., Sarki, A. M., Kimani, P. K., & Uthman, O. A. (2016). Evidence of increased blood pressure and hypertension risk among people living with HIV on antiretroviral therapy: a systematic review with meta-analysis. *J Hum Hypertens, 30*(6), 355-362. doi:10.1038/jhh.2015.97

Neuhaus, J., Jacobs, D. R., Jr., Baker, J. V., Calmy, A., Duprez, D., La Rosa, A., . . . Neaton, J. D. (2010). Markers of inflammation, coagulation, and renal function are elevated in adults with HIV infection. *J Infect Dis, 201*(12), 1788-1795. doi:10.1086/652749

Njuguna, B., Vorkoper, S., Patel, P., Reid, M. J. A., Vedanthan, R., Pfaff, C., . . . Pastakia, S. D. (2018). Models of integration of HIV and noncommunicable disease care in sub-Saharan Africa: lessons learned and evidence gaps. *Aids, 32*, S33-S42. doi:10.1097/qad.0000000000001887

Noncommunicable diseases country profiles 2018. (2018). Retrieved from Geneva:

Nugent, R., Barnabas, R. V., Golovaty, I., Osetinsky, B., Roberts, D. A., Bisson, C., . . . Watkins, D. (2018). Costs and cost-effectiveness of HIV/noncommunicable disease integration in Africa: from theory to practice. *AIDS, 32 Suppl 1*, S83-s92. doi:10.1097/qad.0000000000001884

Nugent, R., Barnabas, R. V., Golovaty, I., Osetinsky, B., Roberts, D. A., Bisson, C., . . . Watkins, D. (2018). Costs and cost-effectiveness of HIV/noncommunicable disease integration in Africa: from theory to practice. *Aids, 32*, S83-S92. doi:10.1097/qad.0000000000001884

Obure, C. D., Guinness, L., Sweeney, S., & Vassall, A. (2016). Does integration of HIV and SRH services achieve economies of scale and scope in practice? A cost function analysis of the Integra Initiative. *Sexually Transmitted Infections, 92*(2), 130-134.

Odafe, S., Torpey, K., Khamofu, H., Oladele, E., Adedokun, O., Chabikuli, O., . . . Okoye, M. (2013). Integrating cervical cancer screening with HIV care in a district hospital in Abuja, Nigeria. *Nigerian Medical Journal, 54*(3), 176-184.

Oni, T., Youngblood, E., Boulle, A., McGrath, N., Wilkinson, R. J., & Levitt, N. S. (2015). Patterns of HIV, TB, and non-communicable disease multi-morbidity in peri-urban South Africa- a cross sectional study. *BMC Infect Dis, 15*, 20. doi:10.1186/s12879-015-0750-1

Palma, A. M., Rabkin, M., Simelane, S., Gachuhi, A. B., McNairy, M. L., Nuwagaba-Biribonwoha, H., . . . El-Sadr, W. M. (2018). A time-motion study of cardiovascular disease risk factor screening integrated into HIV clinic visits in Swaziland. *J Int AIDS Soc, 21*(3), e25099.

Patel, P., Rose, C. E., Collins, P. Y., Nuche-Berenguer, B., Sahasrabuddhe, V. V., Peprah, E., . . . Group, f. t. N. H. N. P. D. C. T. O. (2018). Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: a systematic review and meta-analysis. *AIDS, 32*, S5-S20. doi:10.1097/qad.0000000000001888

Peck, R. N., Shedafa, R., Kalluvya, S., Downs, J. A., Todd, J., Suthanthiran, M., . . . Kataraihya, J. B. (2014). Hypertension, kidney disease, HIV and antiretroviral therapy among Tanzanian adults: a cross-sectional study. *BMC Med, 12*, 125. doi:10.1186/s12916-014-0125-2

Petersen, M., Yiannoutsos, C. T., Justice, A., & Egger, M. (2014). Observational research on NCDs in HIV-positive populations: conceptual and methodological considerations. *JAIDS, Journal of Acquired Immune Deficiency Syndromes, 67*(Suppl. 1), S8-S16.

Pfaff, C., Scott, V., Hoffman, R., & Mwagomba, B. (2017). You can treat my HIV - But can you treat my blood pressure? Availability of integrated HIV and noncommunicable disease care in northern Malawi. *African Journal of Primary Health Care and Family Medicine, 9*(1). doi:10.4102/phcfm.v9i1.1151

Pfaff, C., Singano, V., Akello, H., Amberbir, A., Berman, J., Kwekwesa, A., . . . van Oosterhout, J. J. (2018). Early experiences integrating hypertension and diabetes screening and treatment in a human immunodeficiency virus clinic in Malawi. *Int Health, 10*(6), 495-501.

Phiri, S., Feldacker, C., Chaweza, T., Mlundira, L., Tweya, H., Speight, C., . . . Haddad, L. (2016). Integrating reproductive health services into HIV care: Strategies for successful

implementation in a lowresource HIV clinic in Lilongwe, Malawi. *Journal of Family Planning and Reproductive Health Care, 42*(1), 17-23. doi:10.1136/jfprhc-2013-100816

Phiri, S., Tweya, H., Maida, A., Gupta, S., Speight, C., Giles, D., . . . Patel, P. (2018). Hypertension screening and management in two pepfar-funded clinics in Malawi. *Topics in Antiviral Medicine, 26 (Supplement 1)*, 516s-517s.

Plotkin, M., Besana, G. V., Yuma, S., Kim, Y. M., Kulindwa, Y., Kabole, F., . . . Giattas, M. R. (2014). Integrating HIV testing into cervical cancer screening in Tanzania: an analysis of routine service delivery statistics. *BMC Womens Health, 14*, 120. doi:10.1186/1472-6874-14-120

Ports, K. A., Haffejee, F., Mosavel, M., & Rameshbabu, A. (2015). Integrating cervical cancer prevention initiatives with HIV care in resource-constrained settings: A formative study in Durban, South Africa. *Glob Public Health, 10*(10), 1238-1251. doi:10.1080/17441692.2015.1008021

Rabkin, M., de Pinho, H., Michaels-Strasser, S., Naitore, D., Rawat, A., & Topp, S. M. (2018). Strengthening the health workforce to support integration of HIV and noncommunicable disease services in sub-Saharan Africa. *AIDS, 32*, S47-S54. doi:10.1097/qad.0000000000001895

Rabkin, M., Palma, A., McNairy, M. L., Gachuhi, A. B., Simelane, S., Nuwagaba-Biribonwoha, H., . . . El-Sadr, W. M. (2018). Integrating cardiovascular disease risk factor screening into HIV services in Swaziland: lessons from an implementation science study. *AIDS, 32*, S43-S46. doi:10.1097/qad.0000000000001889

Rabkin, M., Palma, A. M., McNairy, M., Simelane, S., Gachuhi, A. B., Bitchong, R. A., . . . El-Sadr, W. M. (2018). Integrated vs referred management of CVD risk factors for HIV+ patients in Swaziland. *Topics in Antiviral Medicine, 26*, 309s-310s.

Ramsay, M., Crowther, N. J., Agongo, G., Ali, S. A., Asiki, G., Boua, R. P., . . . Tollman, S. (2018). Regional and sex-specific variation in BMI distribution in four sub-Saharan African countries:

The H3Africa AWI-Gen study. *Glob Health Action, 11*(sup2), 1556561. doi:10.1080/16549716.2018.1556561

Rasmussen, L. D., Mathiesen, E. R., Kronborg, G., Pedersen, C., Gerstoft, J., & Obel, N. (2012). Risk of diabetes mellitus in persons with and without HIV: a Danish nationwide population-based cohort study. *PLoS One, 7*(9), e44575. doi:10.1371/journal.pone.0044575

Rawat, A., Uebel, K., Moore, D., & Yassi, A. (2018). Integrated HIV-Care Into Primary Health Care Clinics and the Influence on Diabetes and Hypertension Care: An Interrupted Time Series Analysis in Free State, South Africa Over 4 Years. *J Acquir Immune Defic Syndr, 77*(5), 476-483. doi:10.1097/qai.0000000000001633

Reid, M. J., Haas, M. K., Sedigeng, P., Ramogola-Masire, D., Friedman, H. M., & Ho-Foster, A. (2016). Leveraging HIV Programming to Enhance Access to Noncommunicable Disease Care in Southern Botswana. *J Int Assoc Provid AIDS Care, 15*(1), 7-10. doi:10.1177/2325957415569310

Sander, L. D., Newell, K., Ssebbowa, P., Serwadda, D., Quinn, T. C., Gray, R. H., . . . Reynolds, S. (2015). Hypertension, cardiovascular risk factors and antihypertensive medication utilisation among HIV-infected individuals in Rakai, Uganda. *Trop Med Int Health, 20*(3), 391-396. doi:10.1111/tmi.12443

Shamseer, L., Moher, D., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., . . . Stewart, L. A. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *Bmj, 350*, g7647. doi:10.1136/bmj.g7647

Shannon, K., Crago, A. L., Baral, S. D., Bekker, L. G., Kerrigan, D., Decker, M. R., . . . Beyrer, C. (2018). The global response and unmet actions for HIV and sex workers. *Lancet, 392*(10148), 698-710. doi:10.1016/s0140-6736(18)31439-9

Sibanda, E. L., Ruhode, N., Madanhire, C., Hatzold, K., & Cowan, F. M. (2015). Barriers and facilitators to uptake of cervical cancer screening among clients attending integrated

HIV/sexual and reproductive health clinics in Zimbabwe. *Sexually Transmitted Infections, 2)*, A228-A229.

Smit, M., Brinkman, K., Geerlings, S., Smit, C., Thyagarajan, K., Sighem, A., . . . Hallett, T. B. (2015). Future challenges for clinical care of an ageing population infected with HIV: a modelling study. *Lancet Infect Dis, 15*(7), 810-818. doi:10.1016/s1473-3099(15)00056-0

Stockton, M. A., Giger, K., & Nyblade, L. (2018). A scoping review of the role of HIV-related stigma and discrimination in noncommunicable disease care. *PLoS One, 13*(6), e0199602. doi:10.1371/journal.pone.0199602

Tien, P. C., Schneider, M. F., Cole, S. R., Levine, A. M., Cohen, M., DeHovitz, J., . . . Justman, J. E. (2007). Antiretroviral therapy exposure and incidence of diabetes mellitus in the Women's Interagency HIV Study. *AIDS, 21*(13), 1739-1745. doi:10.1097/QAD.0b013e32827038d0

Trickey, A., May, M. T., Vehreschild, J.-J., Obel, N., Gill, M. J., Crane, H. M., . . . Sterne, J. A. C. (2017). Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. *The Lancet HIV, 4*(8), e349 - e356. doi:10.1016/S2352-3018(17)30066-8

Tripathi, A., Liese, A. D., Jerrell, J. M., Zhang, J., Rizvi, A. A., Albrecht, H., & Duffus, W. A. (2014). Incidence of diabetes mellitus in a population-based cohort of HIV-infected and non-HIV-infected persons: the impact of clinical and therapeutic factors over time. *Diabet Med, 31*(10), 1185-1193. doi:10.1111/dme.12455

UN. (2012). Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases A/RES/66/2 Retrieved from https://www.un.org/en/ga/search/view_doc.asp?symbol=%20A/RES/66/2

UN. (2018). Sustainable Development Goals. Retrieved from https://www.un.org/sustainabledevelopment/health/

UNAIDS. (2016). *Global AIDS Update* Retrieved from http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf

UNAIDS. (2018). Global HIV & AIDS statistics — 2018 fact sheet. Retrieved from http://www.unaids.org/en/resources/fact-sheet

UNAIDS. (2019a). Fact Sheet - World AIDS Day 2019. Retrieved from https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

UNAIDS. (2019b). Key Populations. Retrieved from http://www.unaids.org/en/topic/key-populations

UNAIDS. (2019c). Key Populations Atlas. Retrieved from http://www.aidsinfoonline.org/kpatlas/#/home

Van Deventer, C. (2015). Integration of non-communicable chronic diseases (Ncds) and hiv/aids and mental health care through the involvement of chronically ill patients using empowerment evaluation. *South African Family Practice, 57*(6), 337-346.

van Heerden, A., Barnabas, R. V., Norris, S. A., Micklesfield, L. K., van Rooyen, H., & Celum, C. (2017). High prevalence of HIV and non-communicable disease (NCD) risk factors in rural KwaZulu-Natal, South Africa. *J Int AIDS Soc, 20*(2). doi:10.1002/jia2.25012

Venables, E., Edwards, J. K., Baert, S., Etienne, W., Khabala, K., & Bygrave, H. (2016). "They just come, pick and go." The Acceptability of Integrated Medication Adherence Clubs for HIV and Non Communicable Disease (NCD) Patients in Kibera, Kenya. *PLoS One, 11*(10), e0164634. doi:10.1371/journal.pone.0164634

Vodicka, E. L., Babigumira, J. B., Mann, M. R., Kosgei, R. J., Lee, F., Mugo, N. R., . . . Chung, M. H. (2017). Costs of integrating cervical cancer screening at an HIV clinic in Kenya. *Int J Gynaecol Obstet, 136*(2), 220-228. doi:10.1002/ijgo.12025

Vorkoper, S., Kupfer, L. E., Anand, N., Patel, P., Beecroft, B., Tierney, W. M., . . . Project, o. b. o. t. H. N. (2018). Building on the HIV chronic care platform to address noncommunicable diseases in sub-Saharan Africa: a research agenda. *AIDS, 32*, S107-S113. doi:10.1097/qad.0000000000001898

Wagstaff, A., & Neelsen, S. (2020). A comprehensive assessment of universal health coverage in 111 countries: a retrospective observational study. *Lancet Glob Health*, *8*(1), e39-e49. doi:10.1016/S2214-109X(19)30463-2

Wanyenze, R. K., Musinguzi, G., Kiguli, J., Nuwaha, F., Mujisha, G., Musinguzi, J., . . . Matovu, J. K. B. (2017). "When they know that you are a sex worker, you will be the last person to be treated": Perceptions and experiences of female sex workers in accessing HIV services in Uganda. *BMC Int Health Hum Rights*, *17*(1), 11. doi:10.1186/s12914-017-0119-1

Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Jr., Collins, K. J., Dennison Himmelfarb, C., . . . Wright, J. T., Jr. (2018). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*, *71*(6), e13-e115. doi:10.1161/hyp.0000000000000065

WHO. Global Action Plan for the Prevention and Control of NCDs 2013-2020. Retrieved from https://www.who.int/nmh/events/ncd_action_plan/en/

WHO. Global Health Observatory Data. NCD mortality and morbidity. 2018. Retrieved from http://www.who.int/gho/ncd/mortality_morbidity/en/

WHO. NCD Global Monitoring Framework: Ensuring progress on noncommunicable diseases in countries. Retrieved from https://www.who.int/nmh/global_monitoring_framework/en/

WHO. (2008). Integrated health services – what and why? Technical Brief No. 1. Retrieved from https://www.who.int/healthsystems/technical_brief_final.pdf

WHO. (2010). *Package of essential noncommunicable (PEN) disease interventions for primary health care in low-resource settings.* . Retrieved from Geneva:

WHO. (2013a). Consolidated Guidelines on the use of Antiretroviral Drugs for Treating and Preventing Hiv Infection Recommendations For A Public Health Approach. Retrieved from http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_eng.pdf

WHO. (2013b). *Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020*. Retrieved from https://www.who.int/nmh/events/ncd_action_plan/en/

WHO. (2013c). NCD Global Monitoring Framework: Ensuring progress on noncommunicable diseases in countries. Retrieved from https://www.who.int/nmh/global_monitoring_framework/en/

WHO. (2016a). *Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations – 2016 Update*(Vol. 2019, pp. DEFINITIONS OF KEY TERMS). Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK379697/

WHO. (2016b). *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection Recommendations for a public health approach - Second edition*. Retrieved from https://apps.who.int/iris/handle/10665/208825

WHO. (2016c). *Discussion paper on how to promote the inclusion of the prevention and control of noncommunicable diseases within other programmatic areas* Retrieved from Geneva: http://www.who.int/global-coordination-mechanism/working-groups/WHO_Background_paper_on_integration_of_NCDs_Peter_Lamptey_FOR_DISPATCH.pdf

WHO. (2016d). *Global strategy on human resources for health: workforce 2030*. Retrieved from

WHO. (2017). *Noncommunicable Diseases Progress Monitor, 2017*. Retrieved from Geneva:

WHO. (2018a). Global Health Observatory Data. NCD mortality and morbidity. 2018. Retrieved from http://www.who.int/gho/ncd/mortality_morbidity/en/

WHO. (2018b). Global Health Observatory Data. NCD mortality and morbidity. 2018. Retrieved from http://www.who.int/gho/ncd/mortality_morbidity/en/

WHO. (2018c). *Noncommunicable diseases country profiles 2018*. Retrieved from Geneva: https://www.who.int/nmh/publications/ncd-profiles-2018/en/

WHO. (2018d). *The updated Appendix 3 of the WHO Global NCD Action Plan 2013-2020.* Retrieved from http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_R11-en.pdf

WHO. (2019a). *A heavy burden: the productivity cost of illness in Africa*. Retrieved from https://www.afro.who.int/publications/heavy-burden-productivity-cost-illness-africa

WHO. (2019b). Universal Health Coverage. Retrieved from https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc)

Wroe, E. B., Kalanga, N., Mailosi, B., Mwalwanda, S., Kachimanga, C., Nyangulu, K., . . . Dullie, L. (2015). Leveraging HIV platforms to work toward comprehensive primary care in rural Malawi: the Integrated Chronic Care Clinic. *Healthc (Amst), 3*(4), 270-276. doi:10.1016/j.hjdsi.2015.08.002

Yuma, S., Giattas, M. R., & Bishanga, D. (2015). Hitting two birds with one stone: Provider initiated counseling and testing for HIV and cervical cancer. *International Journal of Gynecology and Obstetrics, 5)*, E441.

Zimmermann, M. R., Vodicka, E., Babigumira, J. B., Okech, T., Mugo, N., Sakr, S., . . . Chung, M. H. (2017). Cost-effectiveness of cervical cancer screening and preventative cryotherapy at an HIV treatment clinic in Kenya. *Cost Effectiveness and Resource Allocation, 15*(13).

Zolopa, A., Andersen, J., Powderly, W., Sanchez, A., Sanne, I., Suckow, C., . . . Komarow, L. (2009). Early antiretroviral therapy reduces AIDS progression/death in individuals with acute opportunistic infections: a multicenter randomized strategy trial. *PLoS One, 4*(5), e5575. doi:10.1371/journal.pone.0005575

SUPPLEMENTARY CHAPTER

Tackling an emerging epidemic: The burden of non-communicable diseases among People living with HIV/AIDS in sub-Saharan Africa

Chapter six is a supplementary chapter that serves to advance the importance of addressing NCDs. It articulates from a broad lens what actions could be advanced to tackle NCDs through a multi-sectoral approach. It is in press and currently in the Pan African Medical Journal.

Abstract

Sub Saharan Africa (SSA) is at a crossroads. Over the last decade, successes in the scale up of HIV Care and Treatment programs has led to a burgeoning number of People living With HIV (PLHIV) in care. At the same time, an epidemiologic shift has been witnessed with a concomitant rise in non-communicable diseases (NCD) related morbidity and mortality. Against low levels of domestic financing and strained healthcare delivery platforms, the NCD-HIV syndemic threatens to reverse gains made in care of People Living with HIV (PLHIV). NCDs are the global health disruptor of the future. In this review, we draw three proposals for Low and Middle-income countries (LMICs) based on existing literature that, if contextually adopted, would mitigate against impending poor NCD-HIV care outcomes. First, we call for an adoption of universal health coverage by countries in SSA. Secondly, we recommend leveraging on comparably formidable HIV healthcare delivery platforms through integration. Lastly, we advocate for institutional-response building through a multi-stakeholder governance and coordination mechanism. Based on our synthesis of existing literature, adoption of these three strategies would be pivotal to sustain gains made so far for NCD-HIV care in SSA

Introduction

Non-communicable diseases (NCDs) are the leading cause of death globally. In 2016 alone, of the world's 57 million deaths, NCDs contributed to 41 million (71%) (WHO, 2018b). Four NCDs in particular - cardiovascular diseases (including hypertension, heart attack and stroke), cancer, chronic

respiratory diseases and diabetes mellitus made the largest contribution to both morbidity and mortality. Low and middle-income countries (LMICs), that also carry a significant burden of HIV/AIDS, bore a disproportionately higher mortality burden. LMICs contributed to 78% of all NCD deaths and 85% of premature deaths ("NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4," 2018).

Home to about 19 million (52%) of the 37 million PLHIV (UNAIDS, 2018), Sub-Saharan Africa (SSA) has a predominantly generalized HIV/AIDS epidemic. Overall, general population have a low HIV prevalence compared to key population who contribute up to 47% of new infections. Key populations are defined as groups who due to specific higher-risk behaviors are at an increased risk of HIV. Among others, key population groups include: men who have sex with men, sex workers, people who inject drugs and prisoners. Key populations therefore, constitute an important bridging population for HIV transmission to the general population (UNAIDS, 2018). Progress towards universal coverage of highly active antiretroviral therapy (ART) for PLHIV in SSA has been exponential. Expanded ART initiation criteria for PLHIV over the last decade has been associated with increased longevity and favorable treatment outcomes (El-Sadr & Goosby, 2018).

Concomitantly, NCDs have risen steadily to become the leading cause of both morbidity and mortality (WHO). The Global Burden of Diseases, Injuries and Risk Factors Study (GBD) 2017 indicated a 40% increase between 2007 and 2017 of NCDs disability adjusted life-years (DALYs). NCDs contributed to 62% of total DALYs ("Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017," 2018).

That the two epidemics – NCDs and HIV/AIDS are not only a double burden but also on a collision path in Sub-Saharan Africa (SSA) is therefore not in question (Levitt, Steyn, Dave, & Bradshaw, 2011a). In fact, some authors have described the current intersection of NCDs and HIV epidemics as a syndemic (Mendenhall & Norris, 2015). Clearly, SSA is undergoing an epidemic transition. For

instance, in 2016, Kenya witnessed the entry of two NCDs – ischemic heart disease and cerebrovascular disease, into the top five causes of death (IHME, 2018). The losses attributed to this dual burden of NCDs and HIV call for an urgent response.

The Global Response

Through the Sustainable Development Goal (SDG) 3, the United Nation set ambitious targets to substantially roll back the tide on four main NCDs – cardiovascular diseases, chronic lung diseases, cancer and diabetes mellitus by 2030 (UN, 2018). Specifically, SDG 3 target 4 seeks to reduce premature mortality from NCDs by a third through prevention and treatment and promote mental health (UN, 2018).

Global Action plan and Commitment to achieving Nine NCD targets

Internationally, the launch of the Global Action Plan (GAP) for the Prevention and Control of NCDs 2013-2014 served to inject impetus at efforts to control the NCD pandemic. The GAP was a significant endorsement towards concerted efforts aimed at control of NCD pandemic (WHO, 2013b). By implementing the GAP, countries would not only support realization of nine voluntary NCD targets by 2025 but also position themselves to make significant strides towards attainment of SDG 3 on promoting health and well-being for all at all ages.

Further, countries signed up to achieve nine voluntary NCD targets by the year 2025 (WHO). The main target called for a 25% relative reduction in overall mortality from the four main NCDs (cardiovascular diseases, cancer, diabetes and chronic respiratory diseases), and a similar reduction or containment of the prevalence of raised blood pressure as per national circumstances. The rise of diabetes and obesity were to be halted. Additional targets included achieving at least 10% relative reduction in the use of alcohol, and prevalence of insufficient physical activity. A 30% reduction in mean population intake of salt and a similar reduction in the prevalence of current use in persons 15+ years. The final two targets focused on the health system's national response. This involved placing at

least 50% of eligible people on drug therapy and counseling to prevent heart attacks, and having an 80% availability of affordable basic technology and essential medicines required to treat the major NCDs in both private and public facilities.

The nine voluntary targets were underpinned against a global monitoring framework to track implementation of the nine global targets against a 2010 baseline. Countries would set national NCD targets for 2025, develop multi-sectoral national NCD plans with an aim of reducing exposure to risk factors and facilitating a robust health system response and finally measure results against the Global Action plan (WHO).

At the 66th UN high level meeting of the General Assembly on Prevention and control of NCDs, all WHO member states from SSA endorsed the Global Action Plan (UN, 2012). A review tracing Africa's progress towards implementing the NCD GAP 2012-2030 and the WHO's NCD Progress monitor report of 2017 however showed mixed results (WHO, 2017). Despite many countries making several political commitments towards prevention and control of NCDs, progress has remained largely insufficient and highly uneven (WHO, 2017).

Overall, more than half of African countries had not met their 2015 targets and were making slow progress towards achievement of 2016 targets. Gains were observed in implementation of national campaigns on diet and physical activity. Limited gains were noted for guidelines development for NCD management and drug therapy and counseling. Southern Africa region was least progress while Northern Africa was noted to be the most progressive.

Progress in the largest African economies have been remarkable with Nigeria achieving set NCD targets, and instituting demand-reduction measures for both harmful alcohol and tobacco use. However, efforts towards guidelines development, drug therapy and public awareness on physical activity have been limited (WHO, 2017). South Africa on the other hand has been very successful instituting unhealthy diet reduction measures but have had less progress with tobacco and harmful use

of alcohol. South Africa has not made progress with public education and awareness campaigns on physical activity (WHO, 2017).

That accelerated action for implementation of the NCD GAP is not in question (WHO, 2017). Beyond political goodwill through declarations, an accountability framework with cost estimates on NCD burden is required. Definition, coordination and characterization of a multi-sectoral approach in developing local policies and programs to address NCD burden would be essential in catalyzing NCD GAP rollout with fidelity (P. A. Juma et al., 2018).

WHO's 16 Best-Buys

The WHO further proposed 16 interventions, referred to as 'best buys', for LMICs' implementation based on their circumstances. The 'best buys' are the mainstay for WHO's strategy on NCD control (Allen et al., 2018). Using a base year of 2010, these 'best buys' have a potential to avert 9.6 million deaths by 2025 worldwide and 1.13 million deaths from cardiovascular diseases in 20 LMICs (Bertram et al., 2018). Full intervention of these 'best buys' has the potential to achieve SDG 3.4 on cardiovascular diseases (Bertram et al., 2018).

The 'best-buys' are generally classified by predisposing risk factors of tobacco use, harmful alcohol use, unhealthy diets and physical inactivity. Other interventions address cardiovascular disease, diabetes and cancer. Under tobacco use, four 'best-buy interventions' for LMICs implementation included tax increases, smoke-free indoor workplaces and public spaces, health information and warnings and bans on tobacco advertising, promotion and sponsorship. Interventions under harmful alcohol use included tax increases, restricted access to retailed alcohol and bans on alcohol advertising.

To reverse unhealthy diet and physical inactivity, LMICs would implement salt reduction intake in food, replace trans-fat with polyunsaturated fat, and increase public awareness through mass media on diet and physical activity.

Additional interventions to curb cardiovascular disease (CVD) and diabetes would involve co unselling and multi-drug therapy for people with a high risk of developing heart attacks and strokes and treatment of heart attacks with aspirin. Lastly, to address cancer, focus would be on Hepatitis B immunization to prevent liver cancer and screening and treatment of pre-cancerous lesions to prevent cervical cancer (*Noncommunicable diseases country profiles 2018*, 2018).

Similar to implementation of the NCD GAP, WHO member states' progress on 'best-buys' implementation is uneven. That the 'best buys' were mainly adopted from high income countries serves to heighten uncertainty over a prioritization index for implementation in the diverse context of LMICs. Between 2000 and 2015, risk of premature death attributed to the four main NCDs declined by 25.4% in high income countries. Such mortality declined only by 7.8% in lower-middle income countries and increased by 6% in low-income countries (Cao, Bray, Ilbawi, & Soerjomataram, 2018).

A 2018 systematic review of 'best-buys' implementation examined the WHO 'best buys' in greater detail (Allen et al., 2018). Some 33 LMICs had implemented a national campaign to create public awareness on diet and physical activity (WHO, 2017) . LMICs were found to have no evidence for any of the alcohol 'best-buys' with countries such as Gambia, Ghana, Nigeria and Uganda being aggressively targeted markets. Tobacco use was found to be on the decline in all WHO regions save for Africa.

Further, there was no evidence of five of the six dietary interventions. By 2015, five LLMICs had implemented salt reduction policies, but none was a low-income country (WHO, 2017). There were no African countries found to have evaluated cardiovascular 'best-buys'. Modelling studies however, project that 17.9 million deaths could be averted with cardiovascular polypharmacy at a cost of USD 0.75 – 1.30 per capita. Similarly, for cervical cancer, a single smear at the test age of 40 years with lesion removal and cancer treatment would avert 462 Disability Adjusted Life Years (DALYs) per million people in SSA (Ginsberg, Lauer, Zelle, Baeten, & Baltussen, 2012).

Generally, a lack of published evidence of 'best-buy' interventions in LMICs (most studies are in South East Asia) and that some interventions have not even been evaluated serves to dampen the rapid implementation of the WHO 'best-buys' in LMICs (Allen et al., 2018).

Package of Essential NCD Interventions (WHO PEN)

In addition to the Best-buys, WHO proposed a package of essential NCD interventions (PEN) for primary health care in low-resource settings ("NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4," 2018; WHO, 2010). The goal of the PEN was to close the gap between what is needed and what is currently available to reduce burden, health-care costs and human suffering due to major NCDs. The PEN outlined strategies to improve equity, efficiency, quality of care and health impact for major NCDs in primary care. Specific interventions were aligned to the WHO health system building blocks of leadership and governance, financing, medical products, health information system, health workforce, and service delivery. Finally, the PEN calls for engagement of communities and empowerment of people for self-care to improve NCD and other health outcomes.

Tailoring the Response to address NCDs among PLHIV

To achieve gains and favorable NCD care outcomes, LMICs particularly in SSA, need to tailor approaches to their specific country contexts. A looming NCD-HIV syndemic, dwindling donor support for public health programs, and increased clamor for domestic financing are realities that SSA countries will continually need to address. Indeed, SSA is at a watershed point. In this review, we suggest three generic strategies that if contextually adopted would promote and sustain positive health outcomes for NCD care among People living with HIV/AIDS.

Universal Health Coverage (UHC)

Several studies continue to place PLHIV at increased risk for NCD-related morbidity and mortality (Narayan et al., 2014). Sudden cardiac death is more common in people with HIV (Freiberg et al., 2019). Chronic obstructive pulmonary disease (COPD) doubled the risk of a heart attack among PLHIV. The tension posed by free HIV care services and paid NCD care accentuates poor NCD-HIV

care outcomes and disparity. By providing free access to all healthcare, universal health coverage (UHC) promises to turn the tide on NCD-HIV related morbidity and mortality (WHO, 2019b).

UHC is encapsulated within SDG 3 target 8 that calls for its achievement by the year 2030. Through UHC are the aspirations of achieving financial risk protection and access to quality healthcare medicines and vaccines (UN, 2018). WHO has included UHC as part of its three-prong work program for 2019 – 2023 specifically targeting UHC for an additional one billion people.

For LMICs in SSA, achieving UHC is highly desirable. Acceleration by member states to adopting a UHC political declaration is critical. Through UHC, domestic funding for healthcare is likely to increase. Further, UHC promises to catalyze policy environments in many countries to be supportive of health. A health in all policies strategy will advance provision of equitable healthcare and assure access to efficacious and quality care for NCDs. Implementation of the WHO package of essential noncommunicable disease interventions (WHO PEN) within the context of UHC promises substantial reduction of mortality from NCDs.

Whilst the attainment of UHC is desirable, maintaining quality is paramount. Healthcare delivery systems in SSA are generally poorly resourced and consequently fragile. Human resources for health are outstretched and below the capita recommendations (WHO, 2016d). Monitoring strategies and support for transition to UHC along a glide path such as through pilot studies and models are necessary to assure high quality service provision.

Integration: Leveraging on the HIV care Platform

Healthcare infrastructure and systems for public healthcare delivery in most of SSA remain strained. Contrastingly, owing to sustained global health funding over the last decade, HIV care delivery platforms have grown and are robust. As a response, to deliver NCD care to PLHIV in LMICs, intuitive programmatic thinking calls for leveraging on HIV chronic care platforms (Miriam Rabkin, Helen de

Pinho, et al., 2018). With overall effective delivery of chronic care, HIV platforms present an attractive solution for integrated care delivery (El-Sadr & Goosby, 2018).

Integration is defined as management and delivery of health services so that clients receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system. Common models of NCD-HIV integration identified in SSA include integrated community-based screening for HIV and NCDs in the general population; screening for NCDs and NCD risk factors among HIV patients enrolled in care; integration of HIV and NCD care within clinics; differentiated care for patients with HIV and/or NCDs; and population healthcare for all (Njuguna et al., 2018).

Benefits from integration of NCDs into existing HIV service delivery platforms would include more affordable health service delivery through leveraging primary vertical platforms to deliver multiple services. Additionally, through a one-stop shop model, we realize both time and cost savings. Other benefits would be reduced duplication and improved cost-efficiency of health workforce, infrastructure, management and financial resources. Finally, country ownership and sustainability would be enhanced through development of country driven and country led health systems for multiple disease burdens (WHO, 2016c).

Although integration appears as the instructive strategy for NCD-HIV delivery of services, it may not be a panacea. NCD burden is a much larger and complex challenge requiring multi-stakeholder coordination as well as massive investments into systems. Loading NCD care delivery on existing HIV platforms could result in a weakening of both systems.(WHO, 2016c).

Despite many attempts at integration, there is a dearth in evidence-based data on integration effectiveness and cost-effectiveness (Rachel Nugent et al., 2018). Surveillance and data collected on NCDs among PLHIV in LMICs lacks the veracity to inform integration of HIV/NCD care models. Evaluating integrated programs is complex with commonly only process and limited outcome measures being available. Few NCD-HIV integrated programs with screening and management

approaches that are contextually appropriate for resource-limited settings exist. Gaps remain in literature with even fewer studies on effectiveness, cost, and best practices for integrated chronic care platforms (Vorkoper et al., 2018).

Global and Regional Multi-stakeholder Partnerships for Institutional Response to NCDs

The NCD-HIV syndemic is testament of an epidemiologic shift in disease patterns in SSA. There is clear evidence that an effective response will require a coherent response from a global public health partnership from multiple stakeholders including those beyond the health sector (Bertram et al., 2018). A multi-pronged response that includes societal change towards healthier lifestyle choices, health systems that are re-engineered to address chronic care, fair trade and norms in trade and fiscal decision making are all required.

Governments would adopt an all-in health policy environment that would facilitate pre-service training of front-line healthcare workers and managers on holistic patient NCD-HIV care (P. A. Juma et al., 2018). Higher institutions of learning could add to the response by prioritizing a research agenda that includes tailored approaches to address NCDs in SSA (Vorkoper et al., 2018).

Similar to the early days of HIV, there is need to involve and engage civil society. Activism from civil society would increase the impetus with which governments develop policies that are responsive to the NCD-HIV syndemic. Additionally, against a backdrop of HIV, engagement with civil society would harmonize a response to the NCD challenge through creation of messaging and strategies around tackling NCDs.

Conclusion

For many countries in SSA, tackling NCDs against a backdrop of HIV remains a formidable challenge. Countries need to make concerted efforts to alter their policy environment and increase domestic resourcing to hasten the response on the NCD-HIV syndemic. Approaches such as integration that seek to leverage on HIV chronic care platforms for delivery of NCD care to PLHIV appear attractive.

However, empirical evidence on what works for integration remains scanty. Universal health care (UHC) promises to inject some impetus in the response but needs an adjunct institutional response. This response would include multiple players beyond the health sector with a governmental coordination mechanism. Priority ought to be placed on a sharpened research focus by higher educational and research institutions on NCD policy and holistic NCD-HIV care. Akin to the HIV epidemic's narrative, civil society groups in SSA countries need to champion for accelerated action on NCDs and a societal change towards healthier lifestyle choices.

Tables

Table 6.1: Recommendations to tackle NCD burden among People Living with HIV in Sub-Saharan Africa
1. National Implementation of Universal Health Care (UHC) • National adoption of the UHC political declaration • Catalyze policy environment to support health by increasing domestic healthcare funding • Advance provision of equitable and quality care healthcare for NCDs
2. Integration of NCD care into HIV Care and Service Delivery • Leverage on robust HIV chronic care platforms for integrated care • Foster NCDs screening and surveillance approaches within HIV programs
3. Global and Institutional NCD Responses • Adoption of all-in health policy approach by Government • Pre-service training of frontline healthcare workers on holistic NCD-HIV patient care • Higher Education Institutions prioritizing NCD research agenda • Rights based approach through Civil Society Organizations engagement

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Authors' contributions

DA compiled inputs from other authors on the initial concepts. RM, JOO, and TA guided the design and endorsed the paper. DA prepared the first draft of the paper. All authors read and approved the final version of the manuscript.

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APPENDICES

Appendix I: Longitudinal Surveillance of Treatment in Kenya (LSTIK II) Study Facilities

ID	MFLcode	Site	Nascop_region	SubCounty	County	Owner
1	11094	Thika District Hospital	Central	Thika	Kiambu	Ministry of Health
2	10698	Mary Help of the Sick Hospital	Central	Thika	Kiambu	Kenya Episcopal Conference-Catholic Secretariat
3	11259	Bomu Medical Centre - Likoni	Coast	Mombasa	Mombasa	Private Enterprise (Institution)
4	11861	Tudor District Hospital (Mombasa)	Coast	Mombasa	Mombasa	Ministry of Health
5	11520	Likoni Catholic Clinic	Coast	Mombasa	Mombasa	Kenya Episcopal Conference-Catholic Secretariat
6	11912	Zion Community Clinic	Coast	Bahari	Kilifi	Christian Health Association of Kenya
7	12438	Machakos District Hospital	Eastern	Machakos	Machakos	Ministry of Health
8	11976	Consolata Hospital (Nkubu)	Eastern	Meru Central	Meru	Kenya Episcopal Conference-Catholic Secretariat
9	12056	Kibwezi Health Care	Eastern	Makueni	Makueni	Private Enterprise (Institution)
10	12341	Kisau Health Center	Eastern	Makueni	Makueni	Ministry of Health
11	12739	Sololo Mission Hospital	Eastern	Moyale	Marsabit	Kenya Episcopal Conference-Catholic Secretariat

12	13023	Kenyatta National Hospital	Nairobi	Dagoreti	Nairobi	Ministry of Health
13	13080	Mbagathi District Hospital	Nairobi	Dagoreti	Nairobi	Ministry of Health
14	13019	FACES - Nairobi	Nairobi	langat	Nairobi	Ministry of Health
15	18743	Kariobangi-EDARP	Nairobi	Kasarani	Nairobi	Kenya Episcopal Conference-Catholic Secretariat
16	13207	Shaurimoyo-EDARP	Nairobi	Kamukunji	Nairobi	Kenya Episcopal Conference-Catholic Secretariat
17	18409	St. Veronica-EDARP	Nairobi	Kamukunji	Nairobi	Other Faith Based
18	13051	Loco Health Centre	Nairobi	Makadara	Nairobi	Other Public Institution
19	15204	Moi Teaching and Referral Hospital	North Rift	Uasin Gishu	Uasin Gishu	Ministry of Health
20	15753	Turbo Health Centre	North Rift	Eldoret West	Uasin Gishu	Ministry of Health
21	14749	Kapsabet District Hospital	North Rift	Nandi North	Nandi	Ministry of Health
22	15057	Lokichar (RCEA) Health Centre	North Rift	Turkana	Turkana	Christian Health Association of Kenya
23	13608	Homa Bay District Hospital	Nyanza	Homa Bay	Homa Bay	Ministry of Health
24	14022	Rachuonyo District Hospital	Nyanza	Rachuonyo	Homa Bay	Ministry of Health

25	13667	Kendu Adventist Hospital	Nyanza	Rachuonyo	Homa Bay	Christian Health Association of Kenya
26	13912	Nyamira District Hospital	Nyanza	Nyamira	Nyamira	Ministry of Health
27	14110	St Joseph Mission Hospital	Nyanza	Migori	Migori	Kenya Episcopal Conference-Catholic Secretariat
28	13668	Kendu Sub District Hospital	Nyanza	Rachuonyo	Homa Bay	Ministry of Health
29	13745	Macalder Sub District Hospital	Nyanza	Migori	Migori	Ministry of Health
30	14097	Sony Sugar Health Centre	Nyanza	Migori	Migori	Company Medical Service
31	13588	Got Agulu Sub-District Hospital	Nyanza	Bondo	Siaya	Ministry of Health
32	13751	Magina Health Centre	Nyanza	Homa Bay	Homa Bay	Ministry of Health
33	13688	Kibogo Dispensary	Nyanza	Nyando	Kisumu	Ministry of Health
34	13540	Ekerenyo Health Center	Nyanza	Nyamira	Nyamira	Ministry of Health
35	13521	Chemelil Dispensary	Nyanza	Nyando	Kisumu	Ministry of Health
36	14018	Rabar Dispensary	Nyanza	Siaya	Siaya	Ministry of Health
37	14123	St. Pauls Dispensary	Nyanza	Siaya	Siaya	Kenya Episcopal Conference-Catholic Secretariat
38	13972	Okiki Amayo Health Centre	Nyanza	Rachuonyo	Homa Bay	Ministry of Health

39	14120	St Monica Town Clinic	Nyanza	Kisumu East	Kisumu	Kenya Episcopal Conference-Catholic Secretariat
40	13651	Kambajo Dispensary	Nyanza	Bondo	Siaya	Ministry of Health
41	14147	Tingare Dispensary	Nyanza	Siaya	Siaya	Ministry of Health
42	13900	Nyamasare	Nyanza	Migori	Migori	Ministry of Health
43	15288	Nakuru Provincial General Hospital (PGH)	South Rift	Nakuru	Nakuru	Ministry of Health
44	15719	Tenwek Mission Hospital	South Rift	Bomet	Bomet	Christian Health Association of Kenya
45	15280	Naivasha District Hospital	South Rift	Nakuru	Nakuru	Ministry of Health
46	15212	Molo District Hospital	South Rift	Nakuru	Nakuru	Ministry of Health
47	14611	Kabazi Health Centre	South Rift	Nakuru	Nakuru	Ministry of Health
48	14394	CMF Aitong Health Centre	South Rift	Narok	Narok	Other Faith Based
49	16030	Mukumu Hospital	Western	Kakamega East (Shinyalu)	Kakamega	Other Faith Based
50	15820	Bukura Health Centre	Western	Kakamega Central (Lurambi)	Kakamega	Ministry of Health

Appendix II LSTIK II Data Abstraction Tool

MFL code…….. Facility name……County……..

Date of Abstraction……Abstractors Code……

Data source: Manual…… EMR…….

STUDY ID:……Complete patient record ☐ YES ☐ NO

A. DEMOGRAPHIC INFORMATION	
1. Date of birth:	/ / (D D M M Y Y Y Y) ☐ Not documented
2. Age in years/Date documented	…… Date documented (Most recent)…….
3. Age at enrollment into HIV care	_ _ years ☐ Not documented.
4. Date of enrollment into pre-ART Care	/ / ☐ Not documented D D M M Y Y Y Y
5. Sex:	☐ Male ☐ Female ☐ Not documented
6. Marital status of patient	☐ Married Monogamous ☐ Married Polygamous ☐ Widowed ☐ Not documented/Not documented. ☐ Divorced ☐ Single/Never married ☐ Other…….. ☐ Cohabiting
7. Patient education level at time of enrollment into HIV Care	☐ None ☐ Primary school ☐ Secondary school ☐ Not documented ☐ Other……. ☐ University
8. Patient's employment status at the time of enrolment HIV care?	☐ Employed ☐ Not Employed ☐ Not documented
B. HIV DIAGNOSIS	

9. Date of first diagnosis of HIV-infection recorded in the chart:	/ / ☐ Not documented D D M M Y Y Y Y
10. Testing point	☐VCT ☐PMTCT ☐ TB Clinic ☐STI Clinic ☐Inpatient ☐MCH ☐ Home testing and referral ☐Outpatient Other:_____
11. Referral source	☐VCT ☐PMTCT ☐ TB Clinic ☐STI Clinic ☐Inpatient ☐MCH ☐ Home testing and referral ☐Outpatient Other:_____
C. BASELINE PRE-ART INFORMATION	
12. Weight at enrolment	__ ___ ___ . ___ Kg ☐ Not documented
13. Height at enrolment	__ ___ ___ . ___ m ☐ Not documented
14. BMI at enrolment	___ ____. ____ ☐ Not documented
15. WHO stage at enrolment	☐ I ☐ II ☐ III ☐ IV ☐ Not documented
16. CD4 count (+/- 3 months from enrolment)	___ ____ ____ cells/m^3 ☐ Not documented
17. HB at enrollment	__ ___ .___ g/dl
D. FAMILY TESTING	
18.Partner tested for HIV? Date tested	☐ YES ☐ NO ☐ Not documented ☐ Not applicable / / D D M M Y Y Y Y
19. Result of partner's HIV test	☐ POS ☐ NEG ☐ Not documented
20. Partner enrolled in care	☐ YES ☐ NO ☐ Not documented
21. How many biological children has this patient ever had?	_____ ☐ Not documented

22. Children <15years tested, Date and results

Child test result	Date of test	Enrolled in care

☐ POS ☐ NEG ☐ Not documented		☐ YES ☐ NO ☐ Not documented
☐ POS ☐ NEG ☐ Not documented		☐ YES ☐ NO ☐ Not documented
☐ POS ☐ NEG ☐ Not documented		☐ YES ☐ NO ☐ Not documented
☐ POS ☐ NEG ☐ Not documented		☐ YES ☐ NO ☐ Not documented
☐ POS ☐ NEG ☐ Not documented		☐ YES ☐ NO ☐ Not documented

E. PRE- ART FOLLOW UP

23. Pre-ART nutrition assessments (indicate for all visits if patient was seen, exclude visits for drug refill only or drug pick up on behalf of patient)

Visit date	Weight	Height	BMI
	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented
	--- --- ---- . ---- -----	--- --- ---- . ---- -----	--- --- ---- . ---- -----

	☐ Not documented	☐ Not documented	☐ Not documented
	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented
	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented
	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented
	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented
	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented	--- --- ---- . ---- ----- ☐ Not documented

24. CTX, nutrition and other support (indicate for all visits dates)

Date of visit	Cotrimoxazole provided	Nutritional support provided and Type	Other
	☐ YES ☐ NO ☐ Not documented	☐ YES ☐ Supplemental ☐ Therapeutic feed ☐ Not documented ☐ NO	
	☐ YES ☐ NO ☐ Not documented	☐ YES ☐ Supplemental ☐ Therapeutic feed ☐ Not documented ☐ NO	
	☐ YES ☐ NO ☐ Not documented	☐ YES ☐ Supplemental ☐ Therapeutic feed ☐ Not documented ☐ NO	

			☐ YES ☐ NO ☐ Not documented	☐ YES ☐ Supplemental ☐ Therapeutic feed ☐ Not documented ☐ NO	
			☐ YES ☐ NO ☐ Not documented	☐ YES ☐ Supplemental ☐ Therapeutic feed ☐ Not documented ☐ NO	

25. Adherence to CTX (indicate for all visits)

	Date of visit	Adherence status
		☐ Good ☐ Poor ☐ Action Taken (specify) … ☐ No action Taken ☐ Not Documented
		☐ Good ☐ Poor ☐ Action Taken (specify) ……☐ No action Taken ☐ Not Documented
		☐ Good ☐ Poor ☐ Action Taken (specify) ……☐ No action Taken ☐ Not Documented
		☐ Good ☐ Poor ☐ Action Taken (specify) …… ☐ No action Taken ☐ Not Documented

26. TB Screening (indicate for all clinic visit dates)

Date of visit (1st Should be enrollment date)	TB screening done	If TB suspect, Action taken
	☐ YES	☐ IPT provided ☐ Lab test

	Already diagnosed with TB prior to enrolment NO TB TB SUSPECT NO Not documented	Chest X ray TB treatment Not documented
	YES NO TB TB SUSPECT NO Not documented	IPT provided Lab test Chest X ray TB treatment Not documented
	YES NO TB TB SUSPECT NO Not documented	IPT provided Lab test Chest X ray TB treatment Not documented
	YES NO TB TB SUSPECT NO Not documented	IPT provided Lab test Chest X ray TB treatment Not documented
Most recent Visit (last one)	YES NO TB TB SUSPECT NO Not documented	IPT provided Lab test Chest X ray TB treatment Not documented

27. For females: Cervical cancer screening done ☐ Yes ☐ No ☐ Not documented

Date Screening done	Test results and type of lesion and action taken
	☐ POS Type of Lesion found:…….. ☐ Treatment provided at site ☐ No treatment provided at site ☐ Referral made ☐ NEG ☐ Not documened
	☐ POS Type of Lesion found:…….. ☐ Treatment provided at site ☐ No treatment provided at site ☐ Referral made ☐ NEG ☐ Not documened

28.Family Planning Services (indicate for all)

Date of visit	FP provided	If YES, Type of FP provided
	☐ YES ☐ NO ☐ Not documented	☐ COC ☐ Injectable ☐ Implant ☐ IUCD ☐ Condoms ☐ Surgical (vasectomy/BTL) ☐ Not applicable ☐ Not documented

	☐ YES ☐ NO ☐ Not documented	☐COC ☐ Injectable ☐ Implant ☐ IUCD ☐ Condoms ☐ Not applicable ☐ Not documented	
	☐ YES ☐ NO ☐ Not documented	☐COC ☐ Injectable ☐ Implant ☐ IUCD ☐ Condoms ☐ Not applicable ☐ Not documented	
	☐ YES ☐ NO ☐ Not documented	☐COC ☐ Injectable ☐ Implant ☐ IUCD ☐ Condoms ☐ Not applicable ☐ Not documented	

29. WHO stage during follow-up for all visits

Date of visit	WHO stage
	☐ I ☐ II ☐ III ☐IV
	☐ I ☐ II ☐ III ☐ IV
	☐ I ☐ II ☐ III ☐ IV
	☐ I ☐ II ☐ III ☐ IV

	☐ I ☐ II ☐ III ☐ IV

30. Pre ART Laboratory Markers

Date of lab test	CD4 count cells/mm^3	HB g/dl	ALT	UECS

31. OI and co-morbidity (other co-existing illnesses) at enrollment and during Pre-ART follow up (Indicate for visit dates where documented)

Date of Visit	OI documented	Co-morbidities	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____	_____	

	☐ Not documented	☐ Not documented	
32. Was patient ever diagnosed with active TB during pre-ART follow-up?	☐ Yes ☐ NO ☐ Not documented		
Date of TB diagnosis	Date started TB treatment	☐ Still on treatment Date finished treatment DD/MM/YYYY	
DD/MM/YYY	DD/MM/YYY	DD/MM/YYY ☐ Not documented	
DD/MM/YYY ☐ Not documented	DD/MM/YYY ☐ Not documented	DD/MM/YYY ☐ Not documented	
DD/MM/YYY ☐ Not documented	DD/MM/YYY ☐ Not documented	DD/MM/YYY ☐ Not documented	
33. Hospitalization at enrollment and during pre-ART follow up (indicate for all documented hospitalizations)			
Date	Reason for admission		
	---------- ☐ Not documented		
	---------- ☐ Not documented		
	----------☐ Not documented		

	----------☐ Not documented
	----------☐ Not documented
	----------☐ Not documented
	----------☐ Not documented

34. Since the last follow-up visit is patient ((chose one)	☐ Alive and still on care date of last visit D D / M M / Y Y
	☐ Lost to follow-up (3 months since last visit) date of last visit D D / M M / Y Y TCA date D D / M M / Y Y
	☐ Transferred Out Date of last Visit D D / M M / Y Y
	☐ Defaulter Date of last visit D D / M M / Y Y
	☐ ART started ART start date D D / M M / Y Y
☐ Died	☐ Date reported dead D D / M M / Y Y Y Y

F. ART CARE (Fill this section for Patients on ART only)

35 Patient previously received ART before enrollment into this Facility?

☐ Yes

☐ ART (transfer in) Date given DD/MM/YYYY ☐ Date not Documented

☐ Single dose NVP Date given DD/MM/YYYY ☐ Date not Documented

☐ HAART for PMTCT Date given DD/MM/YYYY ☐ Date not Documented

☐ PEP Date given DD/MM/YYYY ☐ Date not Documented

☐ No

36 Date of ART initiation in this facility D D / M M / Y Y Y Y
☐ Not documented

G. BASELINE ART CARE INFORMATION

37. Weight at ART start	__ ___ ___ . ___ Kg ☐ Not documented
38. Height at ART start	__ ___ ___ . ___ m ☐ Not documented
39. BMI at ART start	___ ____. ____ ☐ Not documented
40. WHO stage at ART initiation	☐ I ☐ II ☐ III ☐ IV ☐ Not documented
41. CD4 count (+/- 3 months from ART start date)	___ ____ ____ cells/m^3 ☐ Not documented

42. HB	__ ___ .___ g/dl
43. ALT	___ ____ ____
44. Creatinine	___ ___ ____
45. Pre-ART counseling	☐ Yes ☐ No ☐ Not documented
46. Adherence Counselling at ART initiation	☐ Yes ☐ No ☐ Not documented
47. Criteria for ART initiation	☐ CD4 Count __ ____ ___ cells/mm^3 ☐ WHO staging ____ ☐ TB coinfection ☐ HBV coinfection ☐ Other (specify)……..….. ☐ Not documented
48. Was patient screened for Hepatitis B at ART initiation?	☐ Yes ☐ No ☐ Not documented
49. Was patient Hepatitis B Surface Antigen Positive	☐ Yes ☐ No ☐ Not documented
50. Was patient pregnant at time of initiation of ART? Year of Pregnancy	☐ Yes year of pregnancy YYYY ☐ No ☐ Not documented ☐ N/A (male)

51. What was the initial ART regimen (Choose from the list below)

NRTI	NNRTI	PI's and Boosted PI's	FDC
☐ Zidovudine (AZT) ☐ Lamivudine (3TC) ☐ Emtricitabine (FTC) ☐ Stavudine (d4T) ☐ Abacavir (ABC) ☐ Didanosine (ddl) ☐ Tenofovir (TDF) ☐ Not documented	☐ Nevirapine (Viramune, NVP) ☐ Efavirenz (EFV) ☐ Not documented	☐ Lopinavir (LPV) ☐ Nelfinavir (NFV) ☐ Ritonovir (RTV) ☐ Saquinavir (SQV) ☐ Lopinavir/ritonovir (LPV/r) ☐ Nelfinavir/ritonovir (NFV/r) ☐ Indinavir/ritonovir (IDV/r) ☐ Saquinavir/ritonovir (SQV/r) ☐ Not documented	☐ d4T/3TC/NVP ☐ TDF/3TC/EFV ☐ AZT/3TC/NVP ☐ AZT/3TC ☐ TDF/3TC ☐ d4T/3TC ☐ Other, specify:_____ ☐ Not documented

H. ART FOLLOW UP INFORMATION

52. Have all three ARV drugs ever been stopped	☐ Yes ☐ NO ☐ Not documented

53. If Yes, indicate date of stop, Reason for stop, action taken and date restarted

Date Stopped	Reason for stopping	Action taken	Date Restarted
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	

54. Was ART regimen ever changed ☐ Yes ☐ NO ☐ Not documented

55. If Yes, indicate date of change, number of drugs changed, and final regimens			
Date of ART regimen change	Initial ART regimen	Reason for change	Final ART regimen

56. Adherence to ARVS and CTX (indicate for all visits)

	Date of visit	Adherence status
		☐ Good ☐ Fair ☐ Poor ☐ Action taken (specify) … ☐ No action taken ☐ Not documented
		☐ Good ☐ Fair ☐ Poor ☐ Action taken (specify) … ☐ No action taken ☐ Not documented
		☐ Good ☐ Fair ☐ Poor ☐ Action taken (specify) … ☐ No action taken ☐ Not documented
		☐ Good ☐ Fair ☐ Poor ☐ Action taken (specify) … ☐ No action taken ☐ Not documented

57 Was patient ever diagnosed with active TB during ART follow up?	☐ Yes ☐ NO ☐ Not documented	
58. Date of TB diagnosis	Date started TB treatment	☐ Still on treatment If completed, date finished treatment
DD/MM/YYYY ☐ Not documented	DD/MM/YYYY ☐ Not documented	DD/MM/YYYY ☐ Not documented

DD/MM/YYYY ☐ Not documented	DD/MM/YYYY ☐ Not documented	DD/MM/YYYY ☐ Not documented
DD/MM/YYYY ☐ Not documented	DD/MM/YYYY ☐ Not documented	DD/MM/YYYY ☐ Not documented

59. OI and co-morbidity at ART start and during ART follow up

Date of Visit	OI documented	Co-morbidities	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	
	_____ ☐ Not documented	_____ ☐ Not documented	

60. Hospitalization at ART start and during ART follow-up (indicate for all documented hospitalizations)

Date	Reason for admission

	---------- ☐ Not documented
	---------- ☐ Not documented
	----------☐ Not documented
	----------☐ Not documented
	----------☐ Not documented
	----------☐ Not documented
	----------☐ Not documented

61. Is client enrolled in a support group ☐ YES ☐ NO ☐ Not documented

62. Has client disclosed status to partner(s) ☐ YES ☐ NO ☐ Not documented

63. Has substance use by patient been assessed?

☐ YES, substance abuse discussed Date: DD/MM/YYYY

☐ YES alcohol, smoking, and other drug use discussed Date: DD/MM/YYYY

☐ YES, substance abuse support, counseling provided Date: DD/MM/YYYY

☐ YES, substance abuse referral provided Date: DD/MM/YYYY

☐ NO

I. MOST RECENT VISIT

64. Date of most recent visit.	DD MM Y Y Y Y ☐ Not documented
Date of next visit	DD/MM/YYYY ☐ Not documented

65. If on ART indicate the most recent regimen

NRTI	NNRTI	PI's and Boosted PI's	FDC
☐ Zidovudine (AZT) ☐ Lamivudine (3TC)	☐ Nevirapine (Viramune, NVP) ☐ Efavirenz (EFV)	☐ Lopinavir (LPV) ☐ Nelfinavir (NFV)	☐ d4T/3TC/NVP ☐ TDF/3TC/EFV

☐ Emtricitabine (FTC) ☐ Stavudine (d4T) ☐ Abacavir (ABC) ☐ Didanosine (Videx, ddl) ☐ Tenofovir (TDF) ☐ Not documented	☐ Not documented	☐ Ritonovir (RTV) ☐ Saquinavir (SQV) ☐ Lopinavir/ritonovir (LPV/r) ☐ Nelfinavir/ritonovir (NFV/r) ☐ Indinavir/ritonovir (IDV/r) ☐ Saquinavir/ritonovir (SQV/r) ☐ Not documented	☐ AZT/3TC/NVP ☐ AZT/3TC ☐ TDF/3TC ☐ Other, specify:_____ ☐ Not documented

66. Since the most recent follow up visit is patient ((chose one)	☐ Alive and still on ART date of last visit D D / M M / Y Y
	☐ Lost to follow up Date of last Visit D D / M M / Y Y TCA date D D / M M / Y Y
	☐ Transferred Out Date of last Visit D D / M M / Y Y
	☐ Defaulted Date of last Visit D D / M M / Y Y
	☐ Died Date reported dead D D / M M / Y Y Y Y

67. If patient died, what was the reported cause of death? (If documented)	☐ Respiratory (not pulmonary TB) ☐ Acute diarrhea ☐ Chronic diarrhea ☐ Malaria ☐ Cryptococcal meningitis ☐ TB (pulmonary + extra-pulmonary) ☐ Other……. ☐ Unknown

J. LABORATORY MONITORING DURING ART FOLLOW UP

68. Please record the dates of ALL CD4 counts, Hemoglobin levels, and ALT values, VL done during ART follow up and dates of the tests.

Date of visit	CD4 count cells/mm^3	HB g/dl	ALT U/l	UECS	VL Copies/ml

Appendix III: Data Abstraction Request Guide - SWOP Clinics

Variables	Variable name	Format/codes
Demographic and enrolment variables		
Facility Name	facility	
Facility MFL code	mfl	numeric
County	county	string
Pseudo patient ID (Created from MFL+ a serial number) unique for each patient	pseudoid	alphanumeric, 10 digits
Gender M/F	sex	1= Female; 0=Male
KP Typology	Kptype	1= FSW; 2= MSM; 3= PWID
Date of birth	dateofbirth	dd/mm/yyyy (if missing, age at enrollment mandatory)
Marital status	marital	1=Married, 2=Widowed, 3=Divorced, 4=Single/never married, 5=Separated, 6=Cohabiting
Employment status	employment	1=Employed, 2=Unemployed,3=Self-employed, 4=Student
Date of enrollment into care	dateenrol	dd/mm/yyyy
Age at enrollment (months)	enrolagemth	numeric (mandatory if date of birth missing)
Age at enrollment (years)	enrolageyrs	numeric (mandatory if date of birth missing)
Patient type: enrolled in this facility or transfer in	patienttype	1=Enroled in this facility; 2=Transfer-in
If transfer in, transfer in date	dateti	dd/mm/yyyy (if missing, 99/99/9999)
Entry point	entrypoint	1=VCT, 2=PMTCT, 3=TB Clinic, 4=Inpatient, 5=Outpatient, 5=ANC/MCH,

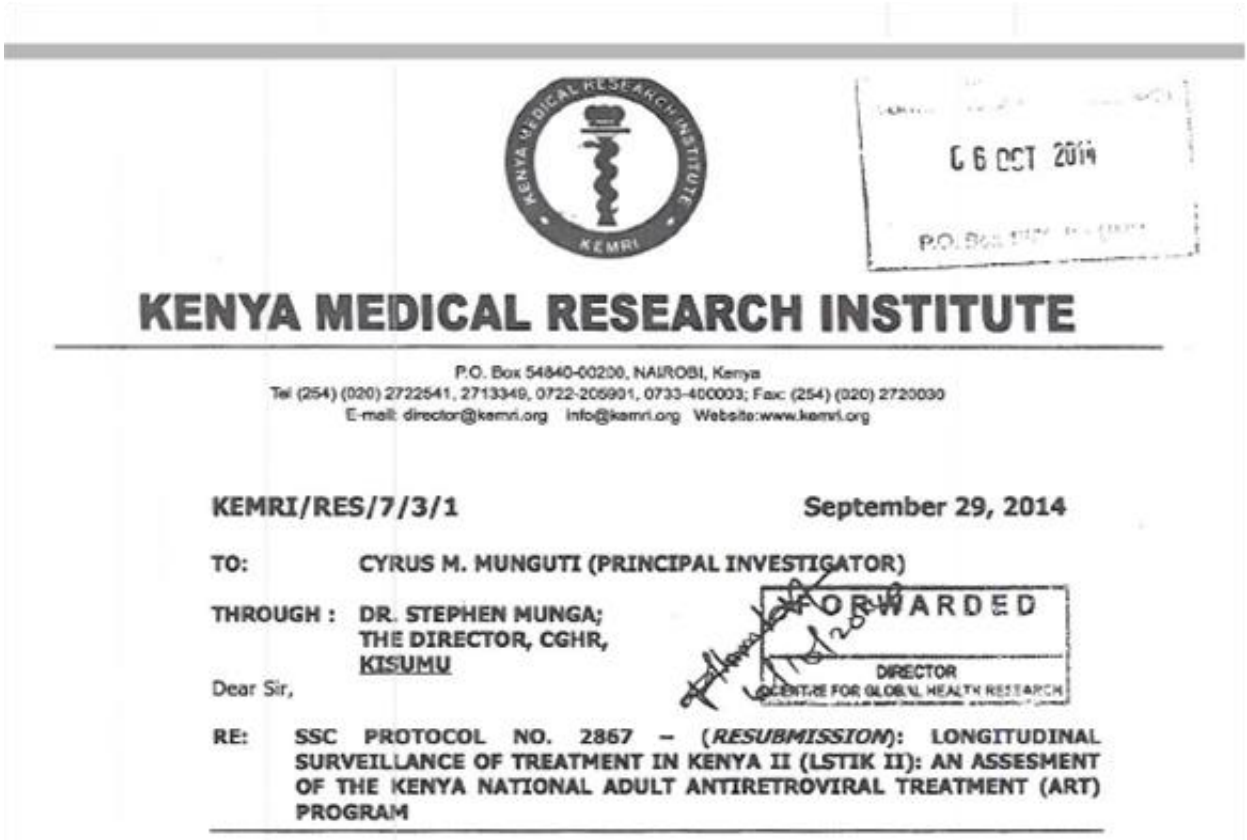
		6=HBCT and referral, 7=CCC, 9=Other

HIV care and treatment		
Pseudo patient ID	pseudoid	alphanumeric
Date of HIV diagnosis	diagdate	dd/mm/yyyy
WHO stage at enrolment	enrolwhostage	1; 2; 3; 4
Viral load at enrolment	enrolvl	numeric
CD4 at enrolment	cd4	numeric
On cotrimoxazole	ctx	1=yes; 0=no
Patient currently on ART-Yes/No	onart	1=yes; 0=no
Date of ART initiation	dateart	dd/mm/yyyy
ART regimen at initiation	startregimen	string: ABC+DDI+LPV/r ABC+3TC+EFV ABC+3TC+NVP D4T+3TC+LPV/r D4T+3TC+NVP D4T+DDI+EFV D4T+DDI+IDV D4T+3TC+EFV D4T+3TC+NFV TDF+FTC+EFV TDF+3TC+EFV TDF+3TC+LPV/r TDF+3TC+NVP TDF+NVP+LPV/r AZT+DDI+IDV AZT+DDI+LPV/r AZT+3TC+ABC AZT+3TC+EFV AZT+3TC+LPV/r AZT+3TC+LPV/r AZT+3TC+NFV AZT+3TC+NVP AZT+3TC+TDF Other Specify
Has patient ever changed ART?	everchanged	1=yes; 0=no
Date of ART change	datechanged	dd/mm/yyyy

Reason for ART change(single drug substitution, switch to 2nd line, OTHER)	reason	1=switch to 2nd line; 2=single drug substitution; 3=ADR; 4=other
Current ART regimen(at last visit)	currentregimen	string
Has patient ever had TB	evertb	1=yes; 0=no
Did patient have TB at enrolment	tbatenrol	1=yes; 0=no
Did patient have TB thereafter	tbafter	1=yes; 0=no
Has patient received IPT during followup	ipt	1=yes; 0=no
Comorbidity at enrolment	comorbidity	1=yes; 0=no
Adherence to ART Counseling Provided at Enrollment	AdherenceEnrol	1=yes; 0=no
Adherence to ART Quality	AdherenceQual	1=good; 2=fair; 3=poor
Number of Enhanced Adherence Counselling Sessions Provided	AdherenceEAC	numeric
Monitoring parameters including blood pressure		
Pseudo patient ID	pseudoid	
Visit date	visitdate	dd/mm/yyyy
Weight *option: All weights/heights	weight	kg
Height *option: All height measurement if child/once if age xx and above	height	cm
Blood pressure (systolic)	bp_s	numeric
Blood pressure (diastolic)	bp_d	numeric
WHO	whostage	1; 2; 3; 4
CD4 cell count	cd4absolute	numeric
CD4 percentage	cd4percent	numeric
Viral load cell count	vloadcopies	numeric
NCDs history		
Pseudo patient ID	pseudoid	

Visit date	visitdate	dd/mm/yyyy
Has patient ever had comorbidities?	anycomorbidities	1=yes; 0=no
Diabetes Mellitus	diabetes	1=yes; 0=no
Renal Failure	renal	1=yes; 0=no
Cervical Cancer	cervical	1=yes; 0=no
CNS (including depression)	cns	1=yes; 0=no
Tumor/cancer (both benign and malignant)	tumor	1=yes; 0=no
Lymphoma	lymphoma	1=yes; 0=no
Asthma	asthma	1=yes; 0=no
Cardiac Disease (incl congestive cardiac failure)	cardiac	1=yes; 0=no
Blood pressure*	blood	1=yes; 0=no
Depression**	depression	1=yes; 0=no
Other comorbidities	other	1=yes; 0=no
Other comorbidities (specify)	othersp	string
Outcomes		
Pseudo patient ID	pseudoid	
Date when outcome occurred. If "active in care", then last visit date	dateofoutcome	dd/mm/yyyy
Outcome (mutually exclusive)	outcome	1 - Active; 2 - Transfer out; 3 - LTFU; 4 - Dead

Appendix IV: LSTIK II KEMRI IRB (SERU) Approval



06 OCT 2014

P.O. Box

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840-00200, NAIROBI, Kenya
Tel (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1 **September 29, 2014**

TO: **CYRUS M. MUNGUTI (PRINCIPAL INVESTIGATOR)**

THROUGH : **DR. STEPHEN MUNGA;**
THE DIRECTOR, CGHR,
KISUMU

FORWARDED
DIRECTOR
CENTRE FOR GLOBAL HEALTH RESEARCH

Dear Sir,

RE: **SSC PROTOCOL NO. 2867 – (*RESUBMISSION*): LONGITUDINAL SURVEILLANCE OF TREATMENT IN KENYA II (LSTIK II): AN ASSESMENT OF THE KENYA NATIONAL ADULT ANTIRETROVIRAL TREATMENT (ART) PROGRAM**

Reference is made to your letter dated 15th September, 2014. The ERC Secretariat acknowledges receipt of the revised document on 22nd September, 2014

This is to inform you that the Ethics Review Committee (ERC) reviewed the document submitted, and is satisfied that the issues raised at the 230th meeting, have been adequately addressed.

This study is granted approval for implementation effective this **September 29, 2014.** Please note that authorization to conduct this study will automatically expire on **September 28, 2015.** If you plan to continue with data collection or analysis beyond this date please submit an application for continuing approval to the ERC secretariat by **August 15, 2015.**

You are required to submit any amendments to this protocol and other information pertinent to human participation in this study to the SSC and ERC for review prior to initiation.

You may embark on the study.

Yours faithfully,

EAB

PROF. ELIZABETH BUKUSI,
ACTING SECRETARY,
KEMRI/ETHICS REVIEW COMMITTEE

CGH HSR Tracking #: 2014-284

Request for Project Determination & Approval – Center for Global Health (CGH)

This form should be used to submit proposals to the CGH Office of the Associate Director for Science/Laboratory Science (ADS/ADLS) for research/nonresearch determination and requirements for IRB review/approval.
Approval Chain: Investigator → Branch Chief/Country Director →Division ADS → CGH Human Subjects Mailbox

☐ **New Request** ☐ **Amendment** ☐ **Laboratory Submission**

Project Title: LONGITUDINAL SURVEILLANCE OF TREATMENT IN KENYA II (L-STIK II): An Assessment of the Kenya National Adult Antiretroviral Treatment (ART) Program[D-06-2014]		Project Location/Country(ies): Kenya
CDC Principal Investigator(s): Cyrus Munguti/Isaac Zulu/Lucy Nganga		
CDC Project Officer(s): Lucy Nganga	Division: DGHA	Telephone: +254722209714
Proposed Project Dates: Start: Spetember 2014	End: September 2015	

Please check appropriate category and subcategory:

☐ **I. Activity is NOT human subjects research. Primary intent is public health practice or a disease control activity (Check one)**

- ☐ **A.** Epidemic or endemic disease control activity; if applicable, Epi-AID # GH000069
- ☐ **B.** Routine surveillance activity (e.g., disease, adverse events, injuries)
- ☐ **C.** Program evaluation activity
- ☐ **D.** Public health program activity*
- ☐ **E.** Laboratory proficiency testing

*e.g., service delivery; health education programs social marketing campaigns; program monitoring; electronic database construction and/or support; development of patient registries; needs assessments; and demonstration projects intended to assess organizational needs, management and human resource requirements for implementation.

☐ **II. Activity is research but does NOT involve human subjects (Check one)**

- ☐ **A.** Activity is research involving collection or analysis of data about health facilities or other organizations or units (NOT persons).
- ☐ **B.** Activity is research involving data or specimens from deceased persons.
- ☐ **C.** Activity is research involving unlinked or anonymous data or specimens collected for another purpose.
- ☐ **D.** Activity is research involving data or specimens from animal subjects. *

*Note: Approval by CDC Institutional Animal Care and Use Committee (IACUC) may be required.

☒ **III. Activity is research involving human subjects but CDC involvement does not constitute "engagement in human subjects research." (Check one)**

- ☒ **A.** This project is funded under a grant/cooperative agreement/contract award mechanism. Award #
  ALL of the following 3 elements are required:
  - ☒ 1. CDC employees or agents will not intervene or interact with living individuals for research purposes
  - ☒ 2. CDC employees or agents will not obtain individually identifiable private information.
  - ☒ 3. Supported institution must have a Federal wide Assurance (FWA) and project must be reviewed by a registered IRB linked to the supported institution's FWA.

Supported Institution/Entity Name:	Advancement of Public Health Practices in Kenya		
Supported Institution/Entity FWA #	FWA00006828	FWA Expiration Date (mm/dd/yyyy):	10/30/2016
Expiration Date of IRB approval:	28Sept2015	(Attach copy of the IRB approval letter)	

- ☐ **B.** CDC staff provide technical support that does not involve possession or analysis of identifiable data or interaction with participants from whom data are being collected (No current CDC funding).
- ☐ **C.** CDC staff are involved only in manuscript writing for a project that has closed. For the project, CDC staff did not interact with participants and were not involved with data collection (No current CDC funding).
- ☐ **D.** Activity is research involving linked data, but CDC non-disclosure form 0.1375B is signed. *

☐ **IV. Activity is research involving human subjects that requires submission to CDC Human Research Protection Office (Check one) ***

- ☐ **A.** Full Board Review (Use forms 0.1250, 0.1370 – research partners)
- ☐ **B.** Expedited Review (Use same forms as A above)
- ☐ **C.** Exemption Request** (Use forms 0.1250X, 0.1370 – research partners)
- ☐ **D.** Reliance**
  - ☐ 1. Request to allow CDC to rely on a non-CDC IRB (Use same forms as A above, plus 0.1371)
  - ☐ 2. Request to allow outside institution to rely on CDC IRB (Use same forms as A above, plus 0.1372)

*There are other types of requests not listed under category IV, e.g., continuation of existing protocol, amendment, incident reports.
**Exemption and reliance request is approved by CDC Human Research Protection Office (HRPO).
CGH HS Form – 12/28/2011

CGH HSR Tracking #:

Amendment: If this request is an amendment to an existing project determination. Please include a brief description of the substantive change or modification below and attach both clean and marked copies of the amended protocol or project outline.

Submission: Attach a protocol or project description (See standard format below) in enough detail to justify the proposed category. Submit your request to your branch chief (or country director for DGHA country staff).

Approval Chain
Investigator → Branch Chief/Country Director →Division ADS → CGH Human Subjects Mailbox

CGH ADS/ADLS Review **Date received in CGH ADS /ADLS office:**

[X] **Project does not require human subject research review beyond CGH at this time.**

[ ] **Project constitutes human subject research that must be routed to CDC HRPO.**

Comments/Rationale for Determination:

CDC staff will not have access to identifiable data for research purposes.

Approvals/Signatures:	Date:	Remarks:
Cyrus Munguti Investigator		
Cathy Toroitich-Ruto Digitally signed by Cathy Toroitich-Ruto DN: cn=Cathy Toroitich-Ruto, o=CDC, ou=SET, email=vto5@cdc.gov, c=KE Date: 2014.12.15 14:04:57 +03'00' Branch Chief/Country Director		
, ADJ, DGHA Division Human Research Protection Coordinator Division ADS/ADLS or Director	12/19/14	
DN: c=US, o=U.S. Government, ou=HHS, ou=CDC, ou=PIV, serialNumber=[illegible] Date: 2014.12.29 10:26:43 -05'00' CGH Human Research Protection Coordinator CGH ADS/ADLS or Deputy ADS/ADLS	12/29/2014	

Note: Although CDC IRB review is not required for certain projects (categories I,II & III) approved under this determination, CDC investigators and project officers are expected to adhere to the highest ethical standards of conduct and to respect and protect to the extent possible the privacy, confidentiality, and autonomy of participants. All applicable country, state, and federal laws must be followed. Informed consent may be appropriate and should address all applicable elements of informed consent. CDC investigators should incorporate diverse perspectives that respect the values, beliefs, and cultures of the people in the country, state, and community in which they work.

Appendix V: University of Nairobi/Manitoba Ethics Approval

19th February, 2018

Ref: KNH-ERC/R/39

Dr. Joshua Kimani
Co-Investigator
UNITID
College of Health Sciences
University of Nairobi

Dear Dr. Kimani

Re: Approval of Annual Renewal – Use of clinical care database by the University of Nairobi/University of Manitoba Research team to evaluate HIV prevention, care and treatment in Kenya (P258/09/2008)

Refer to your communication dated February 8,2018.

This is to acknowledge receipt of the study progress report and hereby grant annual extension of approval for ethical research protocol P258/09/2008.

The approval dates are 18th February 2018 – 17th February 2019.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approved period. (*Attach a comprehensive progress report to support the renewal).*
f) Clearance for export of biological specimens must be obtained from KNH-UoN- Ethics and Research Committee for each batch of shipment.

g) Submission of an *executive summary* report within 90 days upon completion of the study
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

Ensure that the ethical renewal is renewed timely as per KNH-UoN ERC requirements.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M.L. CHINDIA
SECRETARY, KNH-UON ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director CS, KNH
The Chairperson, KNH-UoN ERC

CGH HSR Tracking #: 2014-064

Request for Project Determination & Approval – Center for Global Health (CGH)

This form should be used to submit proposals to the CGH Office of the Associate Director for Science/Laboratory Science (ADS/ADLS) for research/nonresearch determination and requirements for IRB review/approval.
Approval Chain: Investigator → Branch Chief/Country Director → Division ADS → CGH Human Subjects Mailbox

☑ **New Request** ☐ **Amendment** ☐ **Laboratory Submission**

Project Title: Increasing Access to Quality Comprehensive HIV Prevention Services for Most at Risk Populations in Nairobi Province, Kenya [D-05-2013]		Project Location/Country(ies): Nairobi, Kenya
CDC Principal Investigator(s): Dr Kipruto Chesang		
CDC Project Officer(s): Dr Lawrence Gelmon, Mercy Muthui	Division: DGHA	Telephone: +2542867000
Proposed Project Dates: Start: Oct 2012	End: Sep 2015	

Please check appropriate category and subcategory:

☐ **I. Activity is NOT human subjects research. Primary intent is public health practice or a disease control activity (Check one)**

- ☐ **A.** Epidemic or endemic disease control activity; if applicable, Epi-AID # GH000069
- ☐ **B.** Routine surveillance activity (e.g., disease, adverse events, injuries)
- ☐ **C.** Program evaluation activity
- ☒ **D.** Public health program activity*
- ☐ **E.** Laboratory proficiency testing

*e.g., service delivery; health education programs social marketing campaigns; program monitoring; electronic database construction and/or support; development of patient registries; needs assessments; and demonstration projects intended to assess organizational needs, management and human resource requirements for implementation.

☐ **II. Activity is research but does NOT involve human subjects (Check one)**

- ☐ **A.** Activity is research involving collection or analysis of data about health facilities or other organizations or units (NOT persons).
- ☐ **B.** Activity is research involving data or specimens from deceased persons.
- ☐ **C.** Activity is research involving unlinked or anonymous data or specimens collected for another purpose.
- ☐ **D.** Activity is research involving data or specimens from animal subjects. *

*Note: Approval by CDC Institutional Animal Care and Use Committee (IACUC) may be required.

☒ **III. Activity is research involving human subjects but CDC involvement does not constitute "engagement in human subjects research." (Check one)**

- ☒ **A.** This project is funded under a grant/cooperative agreement/contract award mechanism. Award #
  ALL of the following 3 elements are required:
  - ☒ 1. CDC employees or agents will not intervene or interact with living individuals for research purposes
  - ☒ 2. CDC employees or agents will not obtain individually identifiable private information.
  - ☒ 3. Supported institution must have a Federal wide Assurance (FWA) and project must be reviewed by a registered IRB linked to the supported institution's FWA.

Supported Institution/Entity Name:	KH/UoN		
Supported Institution/Entity FWA #	FWA00002173	FWA Expiration Date (mm/dd/yyyy):	08/23/2017
Expiration Date of IRB approval:	02/26/2015	(Attach copy of the IRB approval letter)	

- ☐ **B.** CDC staff provide technical support that does not involve possession or analysis of identifiable data or interaction with participants from whom data are being collected (No current CDC funding).
- ☐ **C.** CDC staff are involved only in manuscript writing for a project that has closed. For the project, CDC staff did not interact with participants and were not involved with data collection (No current CDC funding).
- ☐ **D.** Activity is research involving linked data, but CDC non-disclosure form 0.1375B is signed. *

☐ **IV. Activity is research involving human subjects that requires submission to CDC Human Research Protection Office (Check one) ***

- ☐ **A.** Full Board Review (Use forms 0.1250, 0.1370 – research partners)
- ☐ **B.** Expedited Review (Use same forms as A above)
- ☐ **C.** Exemption Request** (Use forms 0.1250X, 0.1370– research partners)
- ☐ **D.** Reliance**
  - ☐ 1. Request to allow CDC to rely on a non-CDC IRB (Use same forms as A above, plus 0.1371)
  - ☐ 2. Request to allow outside institution to rely on CDC IRB (Use same forms as A above, plus 0.1372)

*There are other types of requests not listed under category IV, e.g., continuation of existing protocol, amendment, incident reports.
**Exemption and reliance request is approved by CDC Human Research Protection Office (HRPO).

CGH HSR Tracking #:

Amendment: If this request is an amendment to an existing project determination. Please include a brief description of the substantive change or modification below and attach both clean and marked copies of the amended protocol or project outline.

Submission: Attach a protocol or project description (See standard format below) in enough detail to justify the proposed category. Submit your request to your branch chief (or country director for DGHA country staff).

Approval Chain
Investigator → Branch Chief/Country Director →Division ADS → CGH Human Subjects Mailbox

CGH ADS/ADLS Review **Date received in CGH ADS /ADLS office:**

☒ **Project does not require human subject research review beyond CGH at this time.**

☐ **Project constitutes human subject research that must be routed to CDC HRPO.**

Comments/Rationale for Determination:

Approvals/Signatures:	Date:	Remarks:
Investigator		
Cathy Toroitich-Ruto Digitally signed by Cathy Toroitich-Ruto DN: cn=Cathy Toroitich-Ruto, o=CDC-Kenya, ou=Science & Ethics Team, email=vxu0@ke.cdc.gov, c=KE Date: 2014.03.10 14:53:43 +03'00' Branch Chief/Country Director		
Division Human Research Protection Coordinator Division ADS/ADLS or Director	4/1/14	
Basia Tomczyk CGH Human Research Protection Coordinator CGH ADS/ADLS or Deputy ADS/ADLS	4/16/14	

Note: Although CDC IRB review is not required for certain projects (categories I,II & III) approved under this determination, CDC investigators and project officers are expected to adhere to the highest ethical standards of conduct and to respect and protect to the extent possible the privacy, confidentiality, and autonomy of participants. All applicable country, state, and federal laws must be followed. Informed consent may be appropriate and should address all applicable elements of informed consent. CDC investigators should incorporate diverse perspectives that respect the values, beliefs, and cultures of the people in the country, state, and community in which they work.

Appendix VI: Letter of Permission from NASCOP Ministry of Health – LSTIK II Study

MINISTRY OF HEALTH

NATIONAL AIDS AND STI CONTROL PROGRAM (NASCOP)

KNH Grounds, P.O. Box 19361-00202, Nairobi, Kenya. Telephone: +254 775597297, Fax: +254 20 2710518,

E-mail: imukui@nascop.or.ke

November 22, 2018

To the Secretary,
KNH-UON Ethics and Research Committee,
Email: uonknh_erc@uonbi.ac.ke

Dear Prof Chindia

RE: Utilization of Longitudinal Surveillance of Treatment in Kenya II (LSTIK II) Data To Estimate Non-communicable Disease Burden Among People Living with HIV/AIDS in Kenya

The National AIDS & STI Control Programme conducts routine surveillance on outcomes of persons living with HIV who are in HIV care and treatment. Between 2015 and 2016, the programme in collaboration and support from Centers for Disease Control and Prevention Kenya office conducted the Longitudinal Surveillance of Treatment in Kenya study (LSTIK II) to assess outcomes of persons in HIV care and treatment across the country over the years 2003-2013. Part of this included assessing the burden of non-communicable diseases among PLHIV.

Dr. Dunstan Achwoka's was part of the team supporting implementation of this national survey by conducting monitoring and quality control aspects during data collection and participated in the writing of the study report. The purpose of this letter to affirm support to him to utilize part of LSTIK II in the assessment of non-communicable diseases among PLHIV in Kenya.

Sincerely,

Dr. Irene Mukui

Principal Investigator-LSTIK II, National AIDS &STI Control Program, Kenya

Appendix VII: Letter of Permission from University of Manitoba Research Group

UNIVERSITY OF NAIROBI
Institute of Tropical & Infectious Diseases

College of Health Sciences
Kenyatta National Hospital
Tele. 254-20-272 6765
Fax. 254-20-272 6626

P.O. Box 19676 - 00202
Nairobi – Kenya.
E-mail: unitid@uonbi.ac.ke
Website: www.uonbi.ac.ke/UNITID

Nov 30th, 2018

Prof. M.L. Chindia,
Secretary,
KNH-UON ERC
Kenyatta National Hospital
P O Box 20723 – 00202
Nairobi, Kenya

Dear Prof Chindia,
Ref: **Letter of no Objection to Use HIV Clinical Care Database**
On behalf of the University of Manitoba Research Group, Nairobi, I write to register our support for Dr. Dunstan Achwoka's application to utilize data from our SWOP program – (HIV Prevention and Care Services for Key populations in Nairobi – Grant Number: 3U2GPS002846-01W1). He has proposed to use the database to estimate the burden of non-Communicable disease among key population enrolled in our program.

Dr. Dunstan Achwoka has been a key collaborator in this project from 2010. He served as Our activity manager for the cooperative agreement. In that role, Dr. Achwoka offered Substantial technical support and oversight during the project's implementation. Collection of the said data is approved by KNH ERC under the following program Title; ***-Use of clinical care database by the University of Nairobi/University of Manitoba Research team to evaluate HIV prevention, care and treatment in Kenya (P258/09/2008).*** I Am one of grant co-recipients from CDC – PEPFAR and use of the huge database for evidence based programming is our mandate and in fact encouraged.

On behalf of the collaborative team, we wish him well and hope this note suffices.

Yours truly,

Dr. Joshua Kimani; Co- Investigator
jkimani@csrtkenya.org
+254 733 719711

Appendix VII: KNH-UoN ERC Study Approval

14th February, 2019

Ref: KNH-ERC/A/52

Dr. Dunstan Eugine Achwoka
Reg. W80/53477/2018 (PhD Candidate)
Institute of Tropical and Infectious Disease (UNITID)
College of Health Sciences
University of Nairobi

Dear Dr. Achwoka

Research proposal – An assessment of Non-Communicable Disease (NCDs) Care among People Living with HIV/AIDS (PLHIV) in Kenya (P720/10/2018)

This is to inform you that the KNH-UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 14th February 2019 – 13th February 2020.

This approval is subject to compliance with the following requirements:

g) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
h) All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
i) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
j) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
k) Clearance for export of biological specimens must be obtained from KNH-UoN ERC for each batch of shipment.
l) Submission of a request for renewal of approval at least 60 days prior to expiry of the approved period. (*Attach a comprehensive progress report to support the renewal).*
m) Submission of an *executive summary* report within 90 days upon completion of the study.
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

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Appendix VIII: Longitudinal Surveillance Of Treatment In Kenya II Study Design and Methodology

An Assessment of the Kenya National Adult Antiretroviral Treatment (ART) Program

Collaborating Institutions:

Ministry of Health, Kenya

Centers for Disease Control and Prevention, Kenya/USA

Kenya Medical Research Institute, Kenya

CoAg # *5 U19 GH000069*: **"Advancement of Public Health Practices in Kenya"**
Ministry of Public Health and Sanitation

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LSTIK II: STUDY DESIGN AND METHODOLOGY

The study comprises three independent sub-studies: 1) retrospective cohort pre-ART: 2) retrospective cohort ART; and, 3) cross-sectional VL sub-study

Study Population:

The target population is all adult and adolescent patients (aged ≥15years) who enrolled in care from October 1, 2003 through September 30, 2013. We will sample the study participants from a nationally representative random sample of 50 sites offering ART services, in operation for a minimum of 15 months, and supporting at least 50 adults on ART. All the three sub-studies will be carried out in the same sites.

Inclusion Criteria: (for study participants)

All persons 15 years and above at the time of enrollment into care who:

- For the retrospective cohort pre-ART, enrolled in care from October 1, 2003 through September 30, 2013
- For the retrospective cohort ART, initiated ART from October 1, 2003 through September 30, 2013
- Consent for the VL sub-study (For adults aged 18 and above at time of enrolment who provide informed consent, for adolescents aged 15-17 at time of enrolment whose parent or guardian provide consent and who assent to participate in the sub-study)

Sample size calculation:

The necessary sample size is calculated independently for each sub-study. For the pre-ART and ART sub-studies, the sample size calculation is based on the proportion of patients who are expected to be retained in care at 12 months. For the pre-ART population we expect that 70%[5] of the patients enrolled into care will be active while for those initiated on ART this number is expected to be around 90%.[6] On the other hand, for the VL suppression, it is expected that about 80%[2] of the patients on treatment will have VL suppression. For all sample size estimates, we shall assume a design effect of 1.5 to take into account within-facility clustering, and a desired precision of ±2% points. The sample size calculations are presented in the table below. In each sub-study we shall increase the sample size by 10% to take into account missing files and incomplete data.

[5] Kenya ART programdata
[6] Kenya AIDS Indicator Survey 2012

Table 2: Sample size calculations for the pre-ART, ART and viral load studies

Sub-study	Population Size	p	Sample size (n)[7]	Adjusted[8] sample size (Final sample size)
Pre-ART	262,992[9]	70%	3,025	3,340
ART	513,860[5]	80%	2,300	2,560
Viral Load	513,860[5]	80%	2,300	2,560

Site selection and sample size allocation:

A total of 50 facilities will be sampled from a list of facilities who reported at least 50 patients active and on ART (current on ART) to National AIDS and STI Control Program (NASCOP) for the Annual Progress Report (APR) in 2013. The sites will be sampled using a multistage sampling design; first the sites will be stratified by the volume of patients that they support. The APR 2013 data will be stratified into four quartiles. Within each stratum, the facilities will be allocated purposively such that the strata with the largest number of facilities being allocated the most facilities while the strata with

[7] n = [DEFF*Np(1-p)]/ [(d2/Z21-α/2*(N-1)+p*(1-p)]

[8] Sample size is adjusted by 10% to care of the missing files and rounded off to get wholes numbers for the stratum allocation

[9] Source: Data from PEPFAR Annual Progress Report 2013

the least number of facilities being allocated the least number of facilities (Allocation is not proportional to stratum sizes). The facilities within each will be selected using a probability proportion to number of adults on ART. On the other hand, each stratum will be allocated the same number of patient files to abstract and the files will be distributed equally to the facility within each stratum.

Summary of strata and sampling allocation, LSTIK

Stratum no	Patient Volume cut-off	Number of facilities	Allocation	Pre-ART
01	>=2,908	25	8	835
02	2,908-1,171	72	11	835
03	1,171-442	180	14	835
04	442-51	733	17	835

LSTIK II Study Sites

County	n	Site Names
Bomet	1	Tenwek
Homa Bay	6	Homa Bay, Rachuonyo, Kendu Adventist, Kendu SDH, Magina, Okiki Amayo
Kakamega	2	Mukumu, Bukura
Kiambu	2	Thika level 5, Mary Help of the sick
Kilifi	1	Oasis Medical Center
Kisumu	3	Kibogo, Chemelil GOK, St Monica
Machakos	1	Machakos level 5
Makueni	2	Kibwezi, Kisau SDH
Marsabit	1	Sololo Mission
Meru	1	Consolata (Nkubu)
Migori	4	St. Joseph, Macalder, Sony, Nyamasare
Mombasa	3	Bomu (Likoni), Tudor, Likoni Catholic
Nairobi	7	KNH, Mbagathi, KEMRI VCT, Kariobangi (EDARP), St Joseph (EDARP), St Veronica (EDARP), Loco Dispensary
Nakuru	4	Nakuru PGH, Naivasha DH, Molo DH, Kabazi HC
Nandi	1	Kapsabet DH
Narok	1	CMF Aitong
Nyamira	2	Nyamira DH, Ekerenyo SDH
Siaya	5	Got Agulu, Rabar, St Paul, Kambajo, Tingare
Turkana	1	Lokichar (RCEA)
Uasin Gishu	2	MTRH, Turbo Health Center
20	50