CURBING THE NON-COMMUNICABLE DISEASE EPIDEMIC: An evaluation of integrating rapid testing for NCD risk factors and navigated linkage to care into a standard HIV testing service platform for adults in Soweto, South Africa

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I. DECLARATION

This thesis is presented in fulfilment of the requirements for the degree of Doctor of Philosophy (PhD) in the Department of Public Health at the University of Witwatersrand. The work on which this thesis is based is original research and neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university. The contents of this doctoral thesis are entirely the work of the candidate under the supervision of Professor Glenda E Gray and Professor Tanya Doherty from the beginning of the thesis work in 2014 until its conclusion in 2021. The inclusion of two supervisors has ensured that the conceptualisation and methodology of the overall thesis and each individual chapter was sound and that the papers were written clearly and were academically appropriate. The candidate discussed the overall design of the study, secured all funding, and oversaw data collection under the guidance of these two supervisors. The candidate also discussed the data analysis and overall concept for the thesis with each supervisor. All papers were drafted in full before submission to either supervisors for their review. All revisions resulting from both the supervisor review and the peer review processes for publication were made by the candidate. The supervisors approved the final draft of each manuscript before submission for peer reviewed publication.

Five peer-reviewed journal articles included in this thesis (one, published opinion piece and four original research articles – of which three are published and one is fully drafted and within the sponsor review process for approval prior to journal submission) are directly based on research conducted to investigate the aims and objectives for this degree. All manuscripts were primarily written by the candidate and co-authored by supervisors and selected project team members. The roles and responsibilities of each author can be found below under *Peer-Reviewed Publications.*

Signature: KL Hopkins Date: 18 February 20201

II. LIST OF PEER-REVIEWED WORK

This doctoral thesis syntheses research presented in peer-reviewed manuscripts, as per general provision 6.7 in the General Rules for the Degree of PhD of the University of Witwatersrand. Each manuscript relates directly to the thesis topic, investigating the laid out aims and objectives. The candidate is the primary author on each publication included in this thesis. PhD supervisors are also contributing co-authors on these papers, due to senior expertise helping to shape each paper. Additional co-authors were included, as they were either co-investigators or heavily involved with the operations of the health screening programme from which this PhD study was embedded and data were extracted. These co-authors provided additional reviews of advanced drafts of each manuscript prior to submission to any scientific journal. The candidate formulated the study protocol, applied for and was awarded grant funding, and implemented the project with almost exclusive independence of her supervisors. She was heavily involved in all data collection, cleaning and analysis procedures; and wrote each manuscript draft with minimal input from either supervisor or co-authors. Each respective scientific journal had its own literature referencing style requirements for submitted publications and these formats are presented within this thesis.

The following publications included in this thesis, as well as additional related work and awards are as follows:

PEER-REVIEWED PUBLICATIONS

PAPER I: Hopkins KL, Doherty T, Gray G.E. Will the current National Strategic Plan enable South Africa to end AIDS, Tuberculosis and Sexually Transmitted Infections by 2022?. *S Afr J HIV Med*. 2018;19(1), a796. https://doi.org/10.4102/sajhivmed.v19i1.796

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- KL Hopkins: Conceptualisation, literature review, writing – original draft, writing – review and revision
- T Doherty: Conceptualisation, writing – review and revision
- GE Gray: Conceptualisation, writing – review and revision

PAPER II: Hopkins KL, Hlongwane K, Otwombe K, Dietrich J, Cheyip M, Khanyile N, Doherty T, Gray GE. Demographics and health profile on precursors of non-communicable diseases in adults testing for HIV in Soweto, South Africa: A cross-sectional study. *BMJ Open* 2019; 9:e030701. doi: 10.1136/bmjopen-2019-030701

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CONFERENCE PRESENTATIONS

Hopkins KL, Hlongwane K, Otwombe K, Dietrich J, Cheyip M, Khanyile N, Doherty T, Gray GE. Demographics and Health Profile on Pre-cursors of Non-Communicable Diseases in Adults Testing for HIV in Soweto, South Africa. 13th INTEREST Workshop 2019; Accra, Ghana. Abstract accepted for Poster Presentation, 14 May 2019.

Hopkins KL, Hlongwane K, Otwombe K, Dietrich J, Jaffer M, Cheyip M, Khanyile N, Olivier J, Doherty T, Gray GE. Does navigated linkage to care work? A cross-sectional study of active linkage to care within an integrated non-communicable disease-HIV testing centre for adults in Soweto, South Africa. 14th INTEREST (Virtual) Workshop 2020; Windhoek Namibia. Abstract accepted for Mini Oral Presentation. 3 Dec 2020.

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III. DEDICATION

To my two, greatest accomplishments, my children. Nothing is impossible; never stop challenging yourselves.

Gordon, thank you for being patient and sharing the highs and lows of this long journey with me.

For Mom, who taught me to never stop learning; and Dad, who never wavered in his support. Although done so in a location farther away than either of you would have preferred, thank you both for encouraging me to chase my dreams.

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VI. ABSTRACT

BACKGROUND:

The top causes of death and disability worldwide are chronic non-communicable diseases (NCDs), such as cardiovascular disease (CVD) and diabetes mellitus (DM), which contribute to more than three in five deaths. South Africa is also the epicentre of the human immunodeficiency virus / acquired immune deficiency syndrome (HIV/AIDS) epidemic, containing the world's highest prevalence of HIV-1. People living with HIV (PLHIV), now living longer while on treatment, are becoming increasingly at-risk for non-HIV-related chronic conditions similar to the HIV-uninfected population. In understanding the expected impact of NCDs on both the general population and amongst PLHIV, it becomes critical to pursue healthcare strategies that effectively and efficiently prevent, diagnose, treat, and control NCDs for both HIV-infected and uninfected persons.

AIMS:

This study aimed to provide an overall evaluation of integrating counsellor task-shifted rapid diagnostic testing (RDT) for NCD risk factors with optional peer-navigated linkage to care within an HIV Testing Services (HTS) centre in Soweto, South Africa.

Specifically, this study sought to, 1) determine the prevalence patterns of NCD risk factors amongst adult HTS clients by age, sex, HIV-status and ART-use; 2) describe the client level of satisfaction with integrated NCD-HTS, as compared to standard of care HTS; 3) assess the quality and feasibility of task-shifting RDT for NCD risk factors to counsellors; 4) determine the proportion of integrated NCD-HTS clients linked to care and initiated on treatment using peer-navigated linkage to care, as compared to standard of care HTS clients using passive referral; and 5) investigate the barriers to integrated NCD-HTS client linkage to care and initiation of treatment across chronic diseases.

METHODS:

This study was a prospective evaluation which consisted of a two-phase longitudinal study design to compare targeted study measures between the three-month standard of care HTS phase utilising passive referral for HTS clients with abnormal/positive results (19 February to 14 June, 2018) against a subsequent nine-month integrated NCD-HTS phase with optional peer-navigated referral (18 June 2018 to 28 March 2019). Standard of care HTS provided counsellor-led height, weight and BP measurements; symptoms screening for sexually transmitted infections (STIs) and tuberculosis (TB); and HIV rapid testing. Integrated NCD-

HTS further included counsellor-led BMI categorisations and RDT for blood glucose (both RPG and average HbA1c) and TC services.

Walk-in, adult clients at the PHRU Zazi HTS Centre who consented to the health screening programme were enrolled and had HTS client files opened. These paper files collected data on socio-demographics; health risk behaviour (alcohol and tobacco use); previous health screening history and treatment use for hypertension (HT), DM, hypercholesterolemia, and HIV; health screening results; clinic flow start and stop times; number of correct and incorrect counsellor-provided referrals; and peer-navigated referral uptake. These clients were then able to consent into an embedded study, comprised of HTS client clinic exit surveys and linkage to care follow-up surveys (only for clients with at least one referral for an abnormal result with follow-up conducted up to three month post-clinic visit). Surveys included both open and closed-ended questions using a five-point Likert scale to investigate HTS client satisfaction with HTS clinic flow time and services provided; time to linkage to care and treatment initiation; and reasons for not choosing peer-navigated referral, linking to care, and/or linking to care but not initiating on treatment.

All quantitative statistical analyses were conducted in SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC) using SAS/STAT procedures. Descriptive statistics (e.g. medians, means, interquartile ranges [IQR], and standard deviation) were reported for continuous variables. Frequencies and associated percentages were determined for categorical variables, stratified where appropriate by age group (18-24, 25-34, 35-44 and ≥45 years), sex, HIV status, ART use, and HTS phase. Fisher's exact or chi-square tests were conducted to test statistical significance for categorical measures stratified by HTS phase. Comparisons for descriptive statistics by HTS phase were determined using the Kruskal-Wallis test and Student's T-Test. Survey responses to close-ended and open-ended questions (once thematically sorted) were tabulated.

RESULTS:

There were 325 and 780 clients with aggregate data collected within standard of care HTS and integrated NCD-HTS, respectively. Of the 780 enrolled integrated NCD-HTS clients who were screened, 19.2% (n=149/775) were HIV-infected, 37.5% (n=289/770) were overweight/obese, 18.0% (n=139/772) had high BP, 10.8% (n=83/766) had high HbA1c (four clients had high random glucose), and 8.1% (n=62/768) had high TC. Women had significantly more overweight/obese BMI than men (46.8% [n=237/506] vs 19.7% [n=52/264]; p<0.0001); and 39.8% (n=127/319) of 18-34 year old women were overweight/obese. Males had significantly higher BP than women (23.9% [n=63/264] vs. 15.0% [n=76/508]; p=0.0023). Of 18-34 year

olds, 7.2% (n=31/433) had high blood glucose; and there were over three times as many women aged 25-34 years with high TC as compared to men of the same age group (18.2% [n=20/110] vs 5.6% [n=4/71]; p=0.0151). The majority of HIV-infected clients were female (72.5% [n=108/149]). HIV-infected clients had significantly more high HbA1c than HIV-uninfected clients (16.1% [n=24/149] vs 9.6% [n=59/614]; p=0.0223). HIV-infected individuals on ART had significantly higher TC than those not on ART (21.7% [n=10/46] vs. 4.9% [n=5/103]; p=0.0016).

Of the HIV-infected participants, 48.3% (n=72/149) already knew their HIV-status, and of those, 63.9% (n=46/72) were on ART. Of all participants screened with elevated BP, high HbA1c and high TC, 72.4% (n=97/134), 96.1% (n=73/76), and 93.3% (n=56/60) were newly diagnosed for each condition, respectively. Of the clients who self-reported as being previously diagnosed, 83.8% (n=31/37) of hypertensive clients, two (n=2/3) clients with high HbA1c, and one (n=1/4) client with high TC self-reported they had already been initiated on treatment. All clients were found to have uncontrolled disease after screening.

There were 284 and 333 HTS client clinic exit surveys analysed for standard of care HTS and integrated NCD-HTS, and therefore clinic flow time was analysed for the same sample size. Standard of care HTS clients spent significantly shorter time in minutes in the clinic from start to finish as compared to integrated NCD-HTS clients (86.0, IQR: 72.0-108.0, [n=283/284] vs 102.0, IQR: 87.0-136.0, [n=331/333]; p<0.0001). Of the integrated NCD-HTS clients, 97.9% (n=320/327) were '*very satisfied'* with integrated NCD-HTS, overall, despite standard of care HTS having significantly shorter median time for counsellor-led HTS.

Regarding quality of task-shifting RDT of NCDs to counsellors, there was one (n=1/3, 33.3%) and five (n=5/59, 8.5%) incorrect referrals made by counsellors for low and high BP, respectively. There were 2.4% (n=2/83) and 6.5% (n=4/62) incorrect referrals given for high blood glucose and blood cholesterol, respectively.

There were 82 standard of care HTS and 238 integrated NCD-HTS client study participants with at least one abnormal health screening result enrolled for follow-up. Of the 320 referrals across both HTS phases, 40.0% were HIV-infections, 11.9% STIs, 6.6% TB, and 28.8% high/low BP. Of referred integrated NCD-HTS study participants, 29.4% were referred for glucose and 23.5% cholesterol. Integrated NCD-HTS had significantly more clients linked to care for HIV (76.7% [n=66/86] vs 52.4% [n=22/42], p=0.0052) and clients linked to care within a shorter average time (6-8 days [IQR:1–18.5] vs 8–13 days [IQR:2–32]) as compared to standard of care HTS. Integrated NCD-HTS clients initiated HIV/STIs/BP treatment on average more quickly as compared to standard of care HT (5 days for STIs [IQR:1-21], 8 days

for HIV/BP [IQR:5-17 and 2-13, respectively] vs 10 days for STIs [IQR: 4-32], 19.5 days for HIV [IQR:6.5-26.5], 8 days for BP [IQR: 2–29]). The majority of participants chose passive over peer-navigated referral (89.1% vs 10.9%; $p<0.0001$). Participants rejecting peer-navigated referral preferred to go alone (55.7% [n=39/70]). Non-linkage to care was due to being busy (41.1% [n=39/95]) and not being ready/refusing treatment (31.6% [n=30/95]). Non-initiation of treatment post-linkage to care was due to normalised results assessed at clinic (49.7% [n=98/196]), prescribed lifestyle modification/monitoring (30.9% [n=61/196]), and poor clinic flow/congestion and/or further testing required (10.7% [n=21/196]).

CONCLUSIONS:

There is a chronic NCD health transition plaguing South Africa, and amongst relatively young adults (18-34 years), especially women. The current risk-factor based, gated-approach to chronic disease screening, as recommended within South African national guidelines, do not adequately allow for the most effective screening for and prevention of DM or hypercholesterolemia, or their pre-cursors amongst the general population or PLHIV.

It is feasible to integrate quality counsellor-led NCD rapid testing into standard of care HTS within historical HTS timeframes, yielding client satisfaction with HTS services and clinic flow. The integration of universal rapid HbA1c and TC screening amongst adults into standard of care practice within the public health sector, regardless of BMI categorization, HIV status or ART use, is recommended. While optional peer-navigated linkage to care did connect significantly more patients to the point of entry to care and more efficiently than standard of care passive referral, it did not translate to increased treatment. Same-day treatment initiation was not achieved across chronic diseases.

While the implementation of integrated NCD-HTS within the study site was found to be feasible and clients also deemed the clinic flow time and services provided to be highly satisfactory, the transferability and scale-up of such healthcare systems strengthening strategies within the public sector may not be as successfully. A more robust, multi-site, nation-wide study is required to determine if similar results would occur within government HTS clinics. There is a need for linkage strategies to also address various, complex levels of psychosocial and health systems barriers at the point of entry into care and treatment. A revision of current health screening and management guidelines and the implementation of cost-effective, multi-level interventions to assist in identifying individuals with unknown disease and both engaging and retaining patients in care is recommended.

KEY WORDS: Non-communicable diseases, HIV, chronic disease, HIV testing services, integrated care, health systems, active linkage to care

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X. LIST OF ACRONYMS

ACC	American College of Cardiology
ADA	American Diabetes Association
AHA	American Heart Association
AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal Care
APC	Adult Primary Care
ART	Antiretroviral Treatment
ARV	Antiretroviral drugs
BARC SA	Bio Analytical Research Corporation South Africa
BMI	Body Mass Index, as calculated by weight/(height)^2
BP	Blood Pressure
BV	Bacterial vaginosis
CAB	Community Advisory Board
CAD	Coronary Artery Disease
CCBs	Calcium Channel Blockers
CDC	The Centers for Disease Control and Prevention; the study sponsor
CDL	Chronic Diseases of Lifestyle
CD4	Cluster of Differentiation; a glycoprotein that is found primarily on the surface of helper T cells; a receptor for HIV in humans
CE	A certification mark indicating conformity with health, safety, and environmental protection standards for products sold within the European Economic Area
CHW	Community Health Worker
CI	Confidence Interval
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CT	Chlamydia Trachomatis
CVD	Cardiovascular Disease

DALYs	Disability-Adjusted Life Years
DOH	Department of Health
DM	Diabetes Mellitus
EASD	European Association for the Study of Diabetes
EEA	European Economic Area
FP	Family Planning
FPG	Fasting Plasma Glucose
FSW	Female Sex Workers
GBV	Gender Based Violence
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
GTIs	Genital Tract Infections
HAART	Highly Active Antiretroviral Therapy
Hb	Haemoglobin
HbA1c	A diagnostic method for Diabetes Mellitus; a form of hemoglobin that is measured to signify the average blood glucose concentration over a three month period
HCT	HIV Counselling and Testing
HCW	Healthcare Worker
HDL	High-Density Lipid
HIV	Human Immunodeficiency Virus
HPCSA	Health Professions Council of South Africa
HPV	Human Papilloma Virus
HREC	University of the Witwatersrand Research Ethics Committee
HSFSA	Heart and Stroke Foundation South Africa
HSP	Human Subjects Protection
HT	Hypertension
HTS	HIV Testing Services
ICDM	Ideal Clinic Monitoring System
ICSM	Integrated Chronic System Management
IDF	International Diabetes Foundation
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
IPT	Isoniazid Preventive Therapy

IPV	Intimate Partner Violence
IQR	Interquartile Range
IRB	Institutional Review Board
ISH	International Society of Hypertension
ISHP	Integrated School Health Policy
LDL	Low-Density Lipid
LIS	Laboratory Information System
LMICs	Low and Middle-Income Countries
MDGs	Millennium Development Goals
M&E	Monitoring and Evaluation
MG	Mycoplasma genitalium
MMC	(Voluntary) Medical Male Circumcision
MSM	Men who have sex with men
NAAT	Nucleic Acid Amplification Test
NCDs	Non-Communicable Diseases
NDoH	National Department of Health
NDP	National Development Plan
NG	Neisseria gonorrhoeae
NGSP	National Glycohemoglobin Standardization Program
NHI	National Health Insurance
NHLS	National Health Laboratory Service
NIMART	Nurse-Initiated Management of ART
NRTIs	Nucleoside Reverse Transcriptase Inhibitors
NSPs	National Strategic Plans
PCA	Principal Component Analysis
PCOS	Polycystic Ovarian Syndrome
PEPFAR	President’s Emergency Plan for AIDS Relief
PHCs	Primary Health Care
PhD	Doctorate of Philosophy
PHRU	Perinatal HIV Research Unit, PhD study site
PIs	Protease Inhibitors
PICT	Provider-Initiated Counselling and Testing
PLG	PanLeucogating; method for CD4+ T-cell enumeration
PLHIV	People Living with HIV/AIDS

PMTCT	Prevention of Mother-to-child Transmission of HIV
POC	Point-of-care
POCT	Point-of-care testing
PrEP	Pre-Exposure Prophylaxis
QA	Quality Assurance
QC	Quality Control
RDT	Rapid Diagnostic Test
REDCap	Research Electronic Data Capture
RPG	Rapid Plasma Glucose
SABSSM V	South African National HIV Prevalence, Incidence, Behaviour and Communication Survey
SADHS	South African Demographics and Health Survey
SAMRC	South African Medical Research Council
SANDoH	South African National Department of Health
SANHANES	South African National Health and Nutrition Examination Survey
SAHS	Southern Africa Hypertension Society
SD	Standard Deviation
SDGs	Sustainable Development Goals
SDI	Same-Day Initiation
SOP	Standard Operating Procedure
SSA	Sub-Saharan Africa
SSP	Stop Stockouts Project
STIs	Sexually Transmitted Infections
TB	Tuberculosis
TC	Total Cholesterol
TMHD	Transdisciplinary Model of Health Decision-Making
TV	Trichomonas vaginalis
UKDPS	United Kingdom Diabetes Prevention Study
UNAIDS	Joint United Nations Programme on HIV/AIDS
UN	United Nations
UTT	Universal Test and Treat (Policy)
VCT	Voluntary Counselling and Testing
WBOTs	Ward-Based Outreach Teams
WHC	The Wits Health Consortium

WHO	World Health Organization
WHR	Waist-Hip Ratio
WISH	Women’s Initiative in Sexual Health Study

XI. DEFINITIONS OF KEY TERMS

Acceptability: The perception amongst stakeholders (for this context, healthcare providers and clients/patients) that an intervention is agreeable.

Active linkage to care (e.g.; navigated linkage to care): The method of referral or linkage to care in which healthcare providers assist the patient with linking to care and treatment services. It is a more pro-active approach, with various strategies (e.g.; physically accompanying the patient to care and treatment, telephonic reminders, payment incentives, etc.).

Continuum of care: Depicts the cascade of events or steps taken in the healthcare system from patient diagnosis of disease to the patient reaching care and treatment services. The continuum of care is an important public health tool that can provide critical insights into the progression of patients through the healthcare system, within and across countries and diseases. It can highlight the patient attrition within prevention, care and treatment services.

Feasibility: The extent to which an intervention can be carried out in a particular setting or organisation.

Health transition: Health – or epidemiologic – transitions refer to a shift in population health trends, such as population age distributions, life expectancy, fertility, and both mortality and causes of mortality.

Health systems strengthening: Strategies combatting health systems failures, specifically which strengthen prevention, care and treatment services, are considered health systems strengthening strategies.

Horizontal healthcare system: The horizontal healthcare system takes on a more community-oriented and/or comprehensive, patient-centred primary healthcare approach. Rather than focus on a single health burden, such as HIV, comprehensive healthcare systems aim to tackle overall healthcare problems within a community through the permanent establishment of accessible, institutional infrastructure for 'general health services'.

Integrated care: The coordination, co-location, or simultaneous delivery of services to patients who need it, when they need it.

Lay provider: Any person who performs functions related to health-care delivery and has been trained to deliver specific services, but has received no formal professional or paraprofessional certificate or tertiary education degree.

Non-communicable diseases (NCDs): Long-term, chronic diseases linked to morbidity or acute illnesses causing sudden mortality (e.g.; diabetes, hypertension, obesity). Chronic diseases of lifestyle (CDL) are defined as a group of NCDs sharing comparable risk factors stemming from long-term exposure to traditional health-risk behaviour, such as smoking, poor diet, harmful substance use, and adoption of sedentary lifestyles.

Passive linkage to care: Referring a patient to care and treatment services without any further contact. A patient may only receive a referral letter with names and contact information for care and treatment services. Passive referral or linkage to care is widely employed across all health domains within South Africa.

Peer-navigators: Trained personnel (e.g.; nurses, lay counsellors, peers) who help patients overcome modifiable barriers to care and achieve their care goals by providing a tailored approach to addressing individual needs. In the context of this study, peer-navigators physically accompanied diagnosed patients to their care and treatment clinic.

Point-of-care testing: Medical diagnostic testing performed at the time and place of patient care.

Quality: In healthcare, quality means providing the care or service the patient needs when the patient needs it, in an affordable, safe and effective manner.

Rapid diagnostic testing: A medical diagnostic testing that is quick and easy to perform, often allowing for rapid results provision to the patient.

Satisfaction: A measurement in terms of an end user's (in this case, patient's) level of happiness with a product or service. A satisfaction rating can help the provider determine how best to improve or change its products or services.

Successful linkage to care: When a newly-identified HIV-infected person (or person with chronic disease) engages with a healthcare provider for care and treatment within 30 days of diagnosis.

Task-shifting (a.k.a.; task-sharing): The rational redistribution of tasks between cadres of healthcare providers with longer training, and those with shorter training, such as trained lay providers.

Verticalised healthcare system: The verticalised healthcare system focuses on a singular disease-oriented approach (e.g.; malaria or TB or HIV) with the aim of providing the greatest coverage for the majority in need. This method concentrates on the shorter-term stance of solving a selected health problem through the implementation of targeted measures. For example, the HIV/AIDS epidemic has created a plethora of verticalised service programmes aimed at the prevention, diagnosis, care and treatment of a single disease.

XII. PREFACE

After earning my Masters in Public Health at Boston University School of Public Health in the US, I was young and eager to exercise my newfound global health skills 'in the field'. A few years into my career, I found myself reporting to Prof Glenda Gray, managing the scientific operations of clinical research sites affiliated with the HIV Vaccine Clinical Trials Network (HVTN). Little did I know, this would be the foundation of an incredible journey towards earning a PhD under her supervision.

Encouraged to conceptualise an ancillary study using HVTN data, in 2014, I authored my first, first-authored publication investigating predictors associated with the immunogenicity of a specific HIV vaccine regimen. Interestingly, Prof Gray and I found overweight/obese BMI as a significant predictor of immune response. Shortly thereafter, I found myself in a boardroom with Prof Gray and other PHRU directors brainstorming research proposals to run through our unit's HIV testing centre, Zazi. Discussions of BMI and immunogenicity led to queries about the prevalence of other NCD risk factors in our community and the effects of those conditions on PLHIV. I remember the feeling of excitement growing as I shared more ideas of how to transform Zazi, and then hearing, '*BOOM! And that is Kate's PhD!*' Talk about being at the right place, at the right time, with the right people.

The road to securing funding was a trial in perseverance. For better or for worse, when passionate about something, I am quite stubborn. I set to work writing a grant proposal to include support for the *Evaluation of Zazi Study* as a study activity within the SAMRC/CDC CoAg. A 100-page protocol followed, which was stripped and re-written no fewer than five times due to shifting CDC CoAg aims and objectives. After three years of protocol writing and review, and in-person meetings and conference calls; during which time I wrote my PhD thesis opinion piece; grant funding was awarded and the study could be implemented.

This study was the first opportunity I was given to truly have full autonomy over my work. While a massive learning curve, I loved every moment. I enjoyed holding trainings and empowering study staff, as well as the synergy created amongst unit syndicates, all whilst giving back to our community. For the entirety of this study, I felt awakened professionally, and we were churning out high-quality, evidence-based data. This journey saw me presenting data at conferences, to the SAMRC, and our local community; and attending a national NCD

symposium. I also felt emboldened as a professional woman, as this journey also included my two pregnancies and the not-so-small task of raising two, young children as a working mother. I wrote the concluding two chapters during a global pandemic lockdown while also home-schooling my kids. Though hard at times, I have learned anything is possible.

I am so glad I did, because when my PhD supervisors and I saw the NCD screening results, we were, for the lack of a better word, gobsmacked. South Africa is in deep, deep trouble. This thesis presents a clear picture of the overwhelming burden of NCD risk factors – specifically obesity, HT and hyperglycaemia – currently affecting the adult population of Soweto, South Africa. It presents a multifaceted policy and programme challenge, which calls for urgent evidence-based interventions – such as those implemented within the study.

This thesis adopts a modern publication style of thesis writing, which incorporates an integrating narrative with five scientific publications – four of which contain original research. It is therefore divided into two parts: Part One comprises six sections to synthesise the thesis publications in a holistic manner. It presents the background and rationale for the PhD study, overall research approach and key findings, outlines the contribution of this thesis to current knowledge and discusses the implications of the findings for policy and practice. Part Two subsequently presents the five publications which form part of this PhD.

1.0 INTRODUCTION AND PHD THESIS OVERVIEW

A comprehensive literature review was undertaken throughout the creation of this thesis for the degree of Doctor of Philosophy (PhD). The literature review was conducted to provide the background and rationale for this research. Both published and grey literature (i.e.; research reports, policy documents, strategic documents, and government-commissioned assessments) were reviewed. Numerous online databases were utilised to ascertain published literature, including: Google Scholar, PubMed, and Web of Science. The literature review assisted in describing the burden of non-communicable diseases (NCDs), NCD risk factors, and human immunodeficiency virus (HIV) among populations of interest; depicting the evolution of HIV testing services (HTS) and the different approaches to health care delivery - horizontal and vertical; providing a review of current national health screening policies and practice; identifying existing gaps in the current public health care system; and outlining how integration and task-shifting of health screening services, and linkage to care and treatment services are defined, summarising different examples of the implementation of these strategies and how they are measured. Google was used as the search engine to identify grey literature, which was supplemented by a search of the South African National Department of Health (SANDoH), South African Medical Research Council (SAMRC), the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) websites, specifically to investigate the prevalence of disease and current health screening policies. A list of key words and phrases were used to search online, which included but were not limited to terms used to: a) investigate prevalence of disease: NCDs, hypertension (HT), diabetes mellitus (DM), obesity, body mass index (BMI), HIV; b) describe health systems and disease platforms: integrated, horizontal, vertical, fragmented, HTS; c) describe health system gaps and strategies: task-shifting, 'point-of-care testing' (POCT), 'rapid diagnostic testing' (RDT), '[passive and active] linkage to care'; and d) determine how implemented strategies are monitored: feasibility, satisfaction, quality. The literature review focusses primarily on published research on low and middle-income countries (LMICs), with grey literature specific to the context of South Africa.

1.1 PROBLEM STATEMENT

The disease profile of South Africa is changing rapidly, with the prevalence of NCDs predicted to cause almost three-quarters as many deaths as communicable, maternal, perinatal, and nutritional disease combined by 2020, exceeding them as the most common causes of death by 2030 in Africa.[1]

NCDs are defined as, *long-term, chronic diseases linked to morbidity or acute illnesses causing sudden mortality*. Within the general population, South Africa is seeing an increased prevalence of chronic diseases of lifestyle (CDL). CDLs are defined as a group of NCDs sharing comparable risk factors stemming from long-term exposure to traditional health-risk behaviour, such as smoking, poor diet, harmful substance use, and adoption of sedentary lifestyles.[2-4] CDLs may contribute to the high mortality rates associated with coronary heart disease, stroke, heart attack, renal failure, chronic bronchitis, both tobacco- and nutrition-induced cancers, emphysema, and many others.[5, 6] In South Africa, NCDs account for 40% of deaths annually; 18% of which is from cardiovascular disease (CVD), 7% from cancer, and 2% from DM (i.e.; a grouping of metabolic syndromes in which a person has high blood glucose due to lack of pancreatic production of or cellular response to insulin).[2] As this epidemic evolves, the poor are affected the most in both high and LMICs. Of concern is the fact that in LMICs, CVD is occurring in younger individuals than in the developed countries.[7] South Africa has interlocking epidemics of chronic NCDs (e.g.; HT, DM) and communicable disease (e.g.; HIV, tuberculosis [TB], sexually transmitted infections [STIs]). The nation has become the epicentre of the HIV/acquired immunodeficiency syndrome (AIDS) epidemic, reporting the highest prevalence of HIV-1, globally.[8] There are approximately 36.7 million people living with HIV (PLHIV) across the globe,[9] and over 20% (7.9 million) reside in South Africa as of 2017.[8, 10-12]. The colliding epidemics are expected to produce a higher prevalence of individuals with HIV-NCD comorbidities, and may confound treatment outcomes, negatively impacting survival.[1, 13, 14] This increased prevalence of NCDs among PLHIV is attributable to multiple elements, including increased lifespan of PLHIV and prevalence of established NCD risk factors, and direct corollaries of HIV infection and treatment.[15]

Successful antiretroviral therapy (ART) programmes enable PLHIV to reach a near-normal life expectancy,[20] and HIV infection is now considered a chronic condition requiring long-term management, just like NCDs.[16] Table 1-1 shows the trends of increased life expectancy paired with decreased adult mortality in South Africa. With HIV becoming a chronic disease, PLHIV become at-risk for other chronic comorbidities, such as CVD, depression, cancers, DM, and lipodystrophy.[15] Numerous studies indicate that HIV infection itself increase NCD risk due to the intensification of inflammatory markers and adverse events, such as metabolic outcomes, associated with ART.[21][4, 17-19] These factors induce the need for serious

attention towards effectively preventing, diagnosing, treating and controlling NCDs not only among the general population, but also among PLHIV.

Table 1-1. Estimated Life Expectancy at Birth and Adult Mortality, 2012-2017[16]

INDICATOR	2012	2013	2014	2015	2016	2017
Life expectancy at birth Total	61.2	62.2	62.9	63.4	63.8	64.2
Life expectancy at birth Male	58.5	59.4	60.0	60.3	60.8	61.2
Life expectancy at birth Female	64.0	65.1	65.8	66.4	66.9	67.4
Adult mortality Total	38%	36%	34%	34%	33%	33%
Adult mortality Male	44%	42%	40%	40%	39%	38%
Adult mortality Female	32%	30%	28%	28%	27%	26%

In light of its converging epidemics, South Africa has both revised current and developed new national plans and policies to support global targets to reduce and/or eliminate health-related morbidity and mortality.[20] This progress includes two, separate national strategic plans (NSPs) - one to combat NCDs and the other focuses on communicable disease.[2, 21] However, there still remains compelling evidence of health system challenges creating barriers towards the prevention, care and treatment of patients with chronic conditions including comorbidity. Some of the most compelling challenges are as follows: 1) health systems fragmentation, 2) shortage of human resources, 3) syndromic management of disease, 4) long wait time for health screening results, and 5) passive linkage to care. Each of these factors contribute to attrition within the cascade of prevention, care and treatment.

South Africa and other LMICs largely provide government health care through vertical programmes of dedicated staff operating within separate physical spaces amongst facilities offering various targeted services (i.e.; HIV, TB, NCDs). Although services exist under one health facility roof, the need for a patient to attend multiple clinics or healthcare providers acts as a deterrent to clients, limiting the reach of preventative screening efforts and/or linkage to care and treatment.[23]

The WHO estimates that sub-Saharan Africa (SSA) has a deficit of 4.2 million health workers, which is estimated to increase to 6.1 million by 2030.[24] Furthermore, the WHO clearly shows

the paucity of doctors and nurses in South Africa compared to developed countries. Per 100,000 population, there are 69.2 vs. 230 doctors and 388 vs. 1212 nurses in South Africa compared to the United States, respectively.[25] South Africa has significantly less doctors in comparison to other income-comparable countries.[26] It is worth noting that the provider:population ratio for other SSA countries were even smaller. The Health Professions Council of South Africa (HPCSA) reported there are only an approximate one anatomical pathologist and virologist per two million South Africans. There are about 500,000 people for each haematologist and chemical pathologist in the country. These figures highlight the tremendous absence of medical laboratory specialists in the country.[27] Additionally, the country has a gross shortage of other health care professions (e.g.; psychologists, oral hygienists and dental therapists, nurses and pharmacists, and rehabilitation therapists).[21]

South African healthcare largely relies on a system based on syndromic management. Health providers will ask patients what symptoms they may be experiencing, and if there are symptoms, they are treated. However, patients who remain asymptomatic (i.e.; without the production of symptoms) will not report any symptoms and most likely not seek out health service facilities, unless to address other concerns, leaving them open to disease-related morbidity and mortality. For example, hypercholesterolemia (high blood cholesterol) is often referred to as '*the other silent killer'*, second to HT (elevated blood pressure [BP], commonly known as '*the silent killer'*), as it has no other signs or symptoms. It is one of the leading risk factors for atherosclerotic heart disease, causing unexpected heart attack or stroke.[28] Many people have not accessed screening and are not aware of their status until they have a cardiovascular event.[29]

In South Africa, the standard practice is to send blood samples to the laboratory for tests like CD4 count, cholesterol and glycated haemoglobin (HbA1c). The samples are processed and results are then returned to the clinic to be communicated to the patient. A study conducted at a public-sector HIV/AIDS treatment facility in Johannesburg, South Africa, demonstrated that 65% of HIV-infected walk-in patients to the HTS program did not return for their CD4 test results within 12 weeks, if at all.[30] It could be assumed that similar delays could occur for the collection of other non-rapid screening test results; which in turn, is associated with further delays or fallout in patient retention within prevention, care and treatment services.[8, 30]
Lastly, passive referral (e.g.; only providing names and contact information for care and treatment services) is widely employed across all health domains within South Africa.[31] The

National HTS Policy and Guidelines reported that the large-scale HIV counselling and testing (HCT) drive in 2010, which tested 13 million South Africans in 18 months, did not increase the number of people in HIV care or on treatment.[23] In low-resource settings, such as SSA, at least 40% of PLHIV who are diagnosed with HIV are not successfully linked to treatment services.[32-34] Other PLHIV who are linked to care, commonly cycle in and out of care with varying levels of adherence.[33] Healthcare-seeking behaviour may be positively or negatively influenced by numerous factors at complex levels: individual (e.g.; acceptance of result, coping ability), relationship (e.g.; social support, risk of intimate partner violence [IPV]),[35] community (e.g.; stigma) and health systems (e.g.; prior experiences with the health system).[36]

Each of the aforementioned health care system deficiencies attribute to fallout in the care continuum of prevention, care and treatment, creating a cascade-like effect. Figure 1-1 depicts the steps within the care continuum for HIV. The main goal of HTS is the timely detection of HIV and the subsequent linkage to prevention, care and treatment services. For HIV-infected individuals, the goal is to have them rapidly initiated on ART, retained in care, and reach viral suppression, which means the quantity of virus in the body is undetectable by viral load testing (<200 copies/mL). The care continuum is an important public health tool that can provide critical insights into the cascades of care within and across countries and diseases.[37]

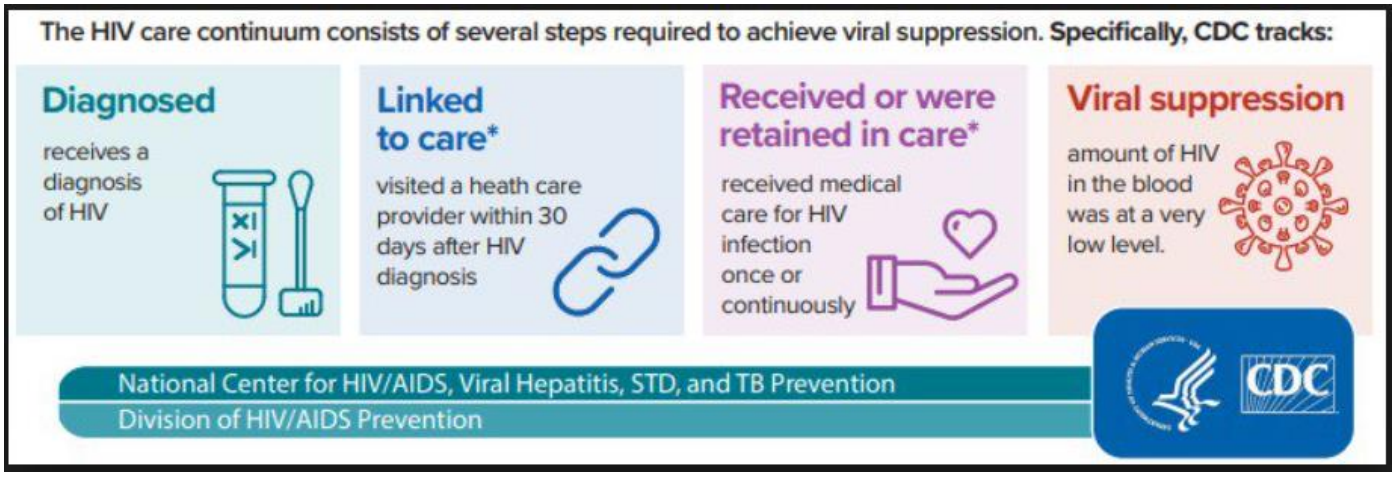


Figure 1-1. The HIV Care Continuum[38]

For example, since 2015, the Joint United Nations Programme on HIV/AIDS (UNAIDS) has been driving the elimination of HIV by 2030 through its fast-tracked 90-90-90 targets with its first benchmark to diagnose 90% of all HIV-infected persons, rapidly provide ART for 90% of those diagnosed, and achieve sustained viral suppression for 90% of those treated by 2020.[39]

As of 2017, South Africa's progress in the prevention, treatment and control of HIV falls below the 90-90-90 target. While 84.9% of all PLHIV within South Africa know their status, which is promising; only 59.9% of all PLHIV in South Africa are on ART and 52.4% of all PLHIV are virally suppressed.[12] This data highlights a main failure within the HIV care continuum as being severe patient attrition from HIV-diagnosis to treatment initiation. Downstream effects are delayed treatment initiation, which increase morbidity and mortality, and additional, preventable transmissions of the virus.[40] This fallout in the care cascade is not unique to just HIV. Many of the barriers towards retention in the treatment cascade are consistently reported across both chronic communicable and non-communicable diseases, alike.[41]

While national and global policies stress the integration of screening for NCDs within established disease programmes, such as HIV, to address the rising epidemic,[23, 42] notably there has yet to be a standard of care NCD screening protocol rolled out. Furthermore, data-based evidence on the surveillance and integration of NCDs in clinical practice is scarce.[43-45] There is a paucity of current literature evaluating health system strengthening efforts on clinical-related outcomes.

1.2 STUDY JUSTIFICATION

Innovative strategies are needed to overcome health systems deficiencies attributing to the increasing burden of NCDs and NCD-comorbidity within South Africa. There is evidence of strategies to combat the aforementioned barriers to the health system, and they are as follows: 1) a shift from vertical to horizontal health care systems (i.e.; integrated care), 2) task-shifting to lay providers, 3) RDT with the provision of same-day results, and 4) active linkage to care.

A WHO-recommended effective health programming practice is to integrate HTS with other health services; however, the routine offer of integrated services is not normalised. Integrated care is typically defined as, '*the coordination, co-location, or simultaneous delivery of services to patients who need it, when they need it'*.[22] In actual practice, this would require both the coordination and sharing of space, services and resources across various diseases programmes and provision of referrals for all diagnoses.[42] It is necessary to leverage the existing infrastructure and build integrated care capacity of staff who have supported unilateral HIV programmes.[46] In the context of the colliding HIV-NCD epidemics, it would be pragmatic to further integrate screening for NCDs into HTS and HIV care services. Intended outcomes

are a more patient-centred approach to prevention, care and treatment; improved efficiency and quality of both NCD and HTS service delivery, and increased availability and uptake of health care services amongst both geographical and socio-economic groups, resulting in increased equity.[47] Ensuring integration of NCD screening and treatment into facility-based HTS, as put forth by SANDoH NSPs, would increase the uptake of both HIV and NCD testing and treatment, if the health system includes a well-functioning supply chain.[48] While HIV and other select programmes (i.e.; TB and reproductive and sexual health) have indeed integrated through the formation of broad national policies, there is a paucity of literature on the NCD-HTS integration in clinical practice.[43-45]

The WHO Consolidated HTS Guidelines reported a strategy to cope with the shortages of trained healthcare workers - *task-shifting* (also referred to as task-sharing), defined as, *'the rational redistribution of tasks between cadres of healthcare providers with longer training, and those with shorter training, such as trained lay providers'*.[42] The WHO has defined a lay provider as, '*any person who performs functions related to health-care delivery and has been trained to deliver specific services, but has received no formal professional or paraprofessional certificate or tertiary education degree'*.[49] This method increases the effectiveness and efficiency of available personnel, expanding the role of trained lay providers, to empower the current workforce to deliver more widespread HTS.[42, 50, 51]

Furthermore, moving from syndromic management of disease in LMICs, such as South Africa, to diagnostic testing would assist in identifying patients who are asymptomatic. Where feasible, RDT should be employed to provide same-day results and immediate referral and treatment, if required. Potentially a more active approach, such as assisting patients with their referrals, could increase linkage to care and treatment services.[36]

The range of literature depicting the implementation and evaluation of integrated health screening, task-shifting, and active linkage to care strategies is limited, particularly within HIV programmes among LMICs. Additional evidence-based data is required regarding the prevalence patterns of NCDs and associated risk factors, and the evaluation of strategies to combat health systems barriers and enable the better clinical care of chronic disease and comorbid patients within the healthcare continuum. Studies on the implementation of innovative healthcare reform strategies can yield evidence-based analysis on the success or failure of an intervention, and therefore inform policymakers about the best way forward. There

needs to be an evaluation of the implementation process to further understand underlying factors which positively or negatively impact desired health-related outcomes, such as health programme screening results; and the feasibility, acceptability, and ease of transferability to practice. It is also important to include healthcare providers and patients as part of this process evaluation to assist in understanding how interventions are received, ascertaining their true implications, as well as obtaining feedback on how to optimise previously implemented strategies in practice.[52]

This thesis aims to contribute knowledge from a walk-in HTS clinic for the general population within a South African urban township to the growing body of evidence on integrated NCD-HTS models utilising task-shifting and active linkage to care and treatment strategies. The study population includes key populations of older adolescents; young, pregnant and postpartum women; men who have sex with men (MSM); and couples and partners. These data will assist the SANDoH with policy decisions and formulate recommendations on the practicality and potential scale-up of such an integrated NCD-HTS model in similar geographical and sociodemographic settings.

There are a few critical gaps in information for which this thesis aims to build knowledge. This integrated NCD-HTS model has never been implemented within the community of Soweto. Stationary and mobile clinics offering limited, integrated health screenings have been documented across South Africa. However, they were not as robust in nature regarding both screenings provided and in sample size, offered to the general population, implementing systematic data capture, or containing the joint components of task-shifting, active linkage to care, nor obtaining feedback from HTS clients.

There is a serious paucity in the knowledge of the burden of communicable and chronic NCD comorbidities within this population. Literature tends to focus on communicable disease comorbidity (i.e.; HIV-TB or HIV-STI), and there is very little data available on other comorbid combinations. Additional knowledge contributions of this thesis is the evaluation of the feasibility of integrating NCD screenings into standard of care HTS, the quality of task-shifting NCD screenings to lay providers, and the acceptability of these strategies by the end user – the HTS clients. This study also investigates the effectiveness of passive versus active linkage to care strategies within the same population.

This comprehensive study of services to the general population of Soweto is an opportunity for South Africa to lead in providing comprehensive health screening services with linkage to care for adults. The research highlights the requirement for the greater tailoring of programmes which address the overall needs of adults seeking HTS. It also highlights how the vertical structure of healthcare service delivery to adults through HIV mechanisms has limited the ability of service providers to comprehensively assist these individuals.

1.3 AIMS AND OBJECTIVES OF THE STUDY

1.3.1 OVERALL AIM

This thesis seeks to provide an overall evaluation of integrating counsellor task-shifted RDT for NCD risk factors with navigated linkage to care within an HTS centre in Soweto, South Africa.

1.3.2 SPECIFIC OBJECTIVES

Within the adult client population, aged 18+ years, seen within the Zazi HTS Centre, in Soweto, South Africa:

1. To determine the prevalence patterns of NCD risk factors (obesity, high BP, high blood glucose, high TC);
2. To describe the client level of satisfaction with integrated NCD-HTS, as compared to standard of care HTS;
3. To assess the quality and feasibility of task-shifting RDT for NCD risk factors to counsellors;
    a. *Quality* as determined by comparing the number of correct and incorrect task-shifted counsellor referrals given within integrated NCD-HTS; and
    b. *Feasibility* as determined by the amount of time integrated NCD-HTS clients spent within the clinic flow, as compared to standard of care HTS clients.
4. To determine the differences in both percentage of clients who linked to care and initiated on treatment and time from diagnosis to initiating treatment between integrated NCD-HTS clients who chose to utilise navigated linkage to care as compared to those who chose passive referral; and
5. To investigate the barriers to integrated NCD-HTS client linkage to care and initiation of treatment across chronic diseases.

1.4 THESIS THEMES

1.4.1 OVERALL THEME

The overarching theme for this thesis is the heavy burden of NCDs,NCD risk factors, HIV, and comorbidity in a resource-limited setting.

1.4.2 SPECIFIC THEMES

There are four specific themes elaborated upon within this thesis, and they are listed and defined, as follows:

1. Health transition: A health – or epidemiologic – transition refers to a shift in population health trends, such as population age distributions, life expectancy, fertility, and both morbidity and mortality and their associated causes.
2. Health systems strengthening: Improvements towards strengthen the healthcare systems are often strategies belonging to one of six core components or *building blocks*: service delivery, health workforce, health information systems, access to essential medicines, financing, and leadership/governance.[53]
3. Health screening and treatment policies/guidelines and practice: National policies direct public healthcare service implementation, and where policies do not exist, there are global guidelines which highlight the evidence-based recommended practice. There could be discordance between policies/guidelines and actual practice in the public healthcare sector.
4. Transferability of strategies: Successful interventions (e.g.; integrated NCD-HTS, task-shifting, and navigated linkage to care and treatment) could be identified in research settings, but there would need to be evidence that the strategies can be generalizable to other contexts and populations (e.g.; into the public healthcare practice).

The specific thesis themes and their relation to the four, original research papers (papers II through V) included within this thesis are highlighted within Table 1-2. In-depth description of how the themes, content and original papers are structured within the thesis can be found under Section 1.5.

Table 1-2. Relation of Thesis Themes and Papers

THEMES	CONTENT	PAPERS*			
		II	III	IV	V
Health transition (Objective 1)	Prevalence of disease by age, sex, HIV status, ART use.	X	X		
Health systems strengthening	(i) Integrated HTS;	X (i)	X (i)	X (i)	X (i)

(Objectives 2, 3, 4 & 5)	(ii) (iii)	Quality of task-shifting of RDT of NCD risk factors to counsellors; and Feasibility of integrated NCD-HTS into standard of care HTS clinic flow.			(ii) (iii)	
Health screening and treatment policies and practice (Objectives 2, 3, 4 & 5)	(i) (ii) (iii) (iv)	Proportion of clients newly diagnosed; Proportion of clients with uncontrolled disease; Proportion linked to care and initiated on treatment; and Client preferred referral method and reasons not linked to care or initiated on treatment.	X (i) (ii)	X (i) (ii)		X (i) (ii) (iii) (iv)
Transferability of strategies into public practice (Objectives 2, 3, & 4)	(i) (ii) (iii) (iv) (v)	Level of client satisfaction with integrated NCD-HTS counselling and screening services; Level of client satisfaction with integrated NCD-HTS clinic flow time; Quality of task-shifting of RDT of NCD risk factors to counsellors; Feasibility of integrated NCD-HTS into standard of care HTS clinic flow; and Client preferred referral method and reasons notlinjed to care or initiated on treatment.		X	X (i) (ii) (iii)	X (iv) (v)

***See list of papers starting on page ii**
Antiretroviral therapy, ART; Human immunodeficiency virus, HIV; HIV testing services, HTS; Non-communicable diseases, NCDs; Rapid diagnostic testing, RDT.

1.5 STRUCTURE OF THE THESIS

This PhD is structured as a thesis with publications. It therefore is divided into two parts: Part One contains the integrating narrative which synthesises the entire body of work (all of the thesis papers) in a holistic manner, and Part Two consists of the five, peer-reviewed papers of this thesis (see list starting on page ii).

The integrating narrative comprises six sections: 1) Introduction and PhD Thesis Overview; 2) Literature Review; 3) Methodology; 4) Results; 5) Discussion; and 6) Conclusions, Implications, Future Research.

The review of literature elaborates upon the growing burden of NCDs and NCD risk factors globally, regionally and locally within South Africa, both separately and within the context of the HIV epidemic. Current national policies and guidelines issued to combat these public health threats are described, along with a description of the current health systems structures in place and gaps within the health system, which contribute to failures in reaching set prevention and treatment goals; along with proposed strategies to alleviate those gaps. The literature review concludes with an amplification regarding the strategy of integrating NCD screening within established HIV programmes, and a summary of past efforts of integrated HTS models implemented among LMICs and within South Africa.

The study methodology section provides a description of the study setting and population, staff trainings, data sources and management, and the study methods used. The study setting and population subsection describes the socio-demographics of the study setting; what is known of the health profile of the study population, focusing on NCDs and HIV; and basic health services available to the community. HTS programme and study-specific trainings and procedures are also detailed. The subsection on data highlights the two different data sources utilised within this thesis; and includes a description of the study sample, sampling procedures; and data collection, entry, quality control and analysis procedures. It concludes by describing ethical considerations.

Part One, section four, integrates the study results corresponding to the four thesis themes, referencing the four, original research papers (papers II through V) incorporated as part of this thesis. The first subsection presents an overview of the general sampling methods for the various studies included within this thesis and the socio-demographics of the study participants by HTS phase (i.e.; standard of care HTS and integrated NCD-HTS). Significant differences between HTS phase client populations are highlighted, with reference to papers II and III. The subsection continues to report on the socio-demographics of HTS clients participating in the thesis-related sub-studies (i.e.; HTS client clinic exit surveys and HTS client linkage to care follow-up surveys), referencing papers IV and V. The second subsection supports the theme of health transition, with reference to paper II and III, and presents an overview of the health profile of the clients from standard of care HTS and integrated NCD-HTS, by age group, sex, HIV-status and ART use. The third subsection, regarding health systems strengthening, presents results on the quality of task-shifting RDT of NCD risk factors to counsellors and the feasibility of integrating NCD screenings into HTS clinic flow, while presenting unpublished

data from this PhD study and also referencing data from Paper IV. Subsection four speaks towards the theme of health screenings and treatment policies and practice. Of those participants screened, it describes the proportion of HTS clients newly diagnosed for each condition; and of those who already knew their diagnoses, the proportion who had already been initiated on treatment and remained with uncontrolled disease. It also describes the proportion of screened and referred HTS clients linked to care and initiated on treatment within both HTS phases, reporting study participant reasons on preferred referral method (i.e.; passive vs active) and why they may not have been linked to care and/or initiated on treatment. This section references paper V. Lastly, the fifth subsection linked with the theme of transferability of strategies into public practice, references paper IV. It describes the level of HTS client satisfaction on pre- and post-test counselling, health screening services, and clinic flow time, per HTS phase. The aforementioned aspects of quality of task-shifting RDT of NCD risk factors to counsellors and the feasibility of integrating NCD screening into HTS clinic flow also pertain to the theme of transferability. However, those results will remain described under the theme of health systems strengthening.

The discussion section deliberates the results thematically, linking them to both the aims of this thesis and gaps in the literature. It compares study results against both national and international study findings, among LMICs. This section also reviews the thesis conceptual framework in regard to the study findings, and evaluates both study limitations and strengths.
Part One closes with a summary of key findings, a discussion of the implications of those findings, and recommendations for further research, policy revision, and adaptive clinical practice, in regards to combating the joint NCD and HIV epidemics, as deduced by the study.
Part Two includes five papers which the PhD candidate first-authored – one opinion piece (Paper I) and the four, original research papers (Papers II through V) containing thesis study data.

In assisting to outline the justification for the study, Paper I presents the PhD candidate's first-authored, published *opinion piece*, entitled, '*Will the current National Strategic Plan enable South Africa to end AIDS, Tuberculosis and Sexually Transmitted Infections by 2022?'*, which is largely referenced within Part One, section one and two. Rather than responding to a specific aim/objective, this paper dissects South Africa's NSP for HIV, TB and STIs (2017-2022), outlining critical components it lacks in order to reach set disease prevention/treatment targets (i.e.; gaps in funding, vague mention of prevention and treatment strategies, shortfalls in human

resources and lack of health system requirements).[48] The paper, therefore, provides some of the foundation for the interventions introduced in this study, which incorporates some of the mentioned strategies to combat the NSP shortfalls: implement active linkage to care, utilise current human resources, integrate service delivery, and incorporate real-time data capture for timely monitoring and evaluation (M&E).[48]

Paper II, entitled, '*Demographics and health profile on pre-cursors of non-communicable diseases in adults testing for HIV in Soweto, South Africa: A cross-sectional study';* supports specific objective 1. This paper presents the demographic and health profile of adults who presented to the standard of care HTS clinic during the study's baseline phase.

Paper III, entitled, '*South Africa's horrific burden of non-communicable diseases and HIV-NCD co-morbidities, especially amongst young adults: screening results from an integrated HIV testing services clinic for adults in Soweto, South Africa'*; also responds to the first specific objective. It reports on the prevalence of both previously diagnosed and undiagnosed NCD and HIV-NCD risk factor comorbidity among adults attending the clinic during the integrated NCD-HTS phase. It also presents the rates of both controlled and uncontrolled disease among those clients who were previously diagnosed and had ever been initiated on treatment.

Paper IV, '*Level of adult client satisfaction with clinic flow time and services of an integrated non-communicable disease-HIV testing services clinic in Soweto, South Africa: A cross-sectional study'*; is in response to the second specific objective regarding HTS client satisfaction of the integrated NCD-HTS model in comparison to standard of care HTS, as well as provides evidence-based data to attend to specific objective three – feasibility of task-shifting RDT of NCD risk factors to counsellors into HTS clinic flow.

Lastly, Paper V, '*Does peer-navigated linkage to care work? A cross-sectional study of active linkage to care within an integrated non-communicable disease-HIV testing centre for adults in Soweto, South Africa'*; responds to both the fourth and fifth specific objective. It details the comparison of rates of linkage to care and initiation of treatment using both the standard of care HTS passive referral approach and the integrated NCD-HTS active linkage to care approach. It also shares the voices of study participants regarding their choice of referral type, and why they were not linked to care and/or initiated on treatment.

Appendices including ethical clearance certificates and data collection tools are included towards the end of the thesis.

2.0 LITERATURE REVIEW

2.1 EPIDEMIOLOGIC TRANSITIONS RELATED TO PUBLIC HEALTH

Globally, we are currently experiencing an epidemiologic transition towards chronic non-communicable diseases; which has been denoted through the shifting models of population age distributions, life expectancy, fertility, and both mortality and causes of mortality.[54]

In 2010, only four of the top ten global causes of mortality were due to NCDs, which grew to seven of the ten top global causes of disease in 2016. Over 70% of global deaths were attributable to NCDs (e.g.; ischaemic heart disease; stroke; chronic obstructive pulmonary disease [COPD]; Alzheimer disease and other dementias; trachea; bronchus and lung cancers; and DM). There were a combined 15.2 million deaths, globally, for ischaemic heart disease and stroke, alone; and these two specific NCDs have been the leading cause of death, worldwide over the last fifteen years.[55] Figures 2-1 and 2-2 show this epidemiologic trend.

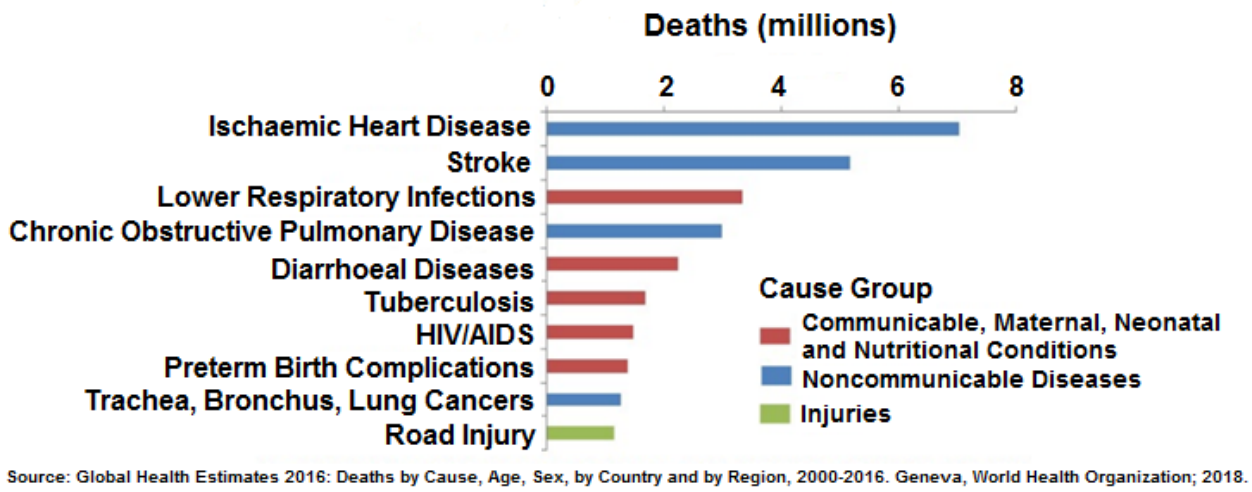


Figure 2-1. Top 10 Global Causes of Death, 2000

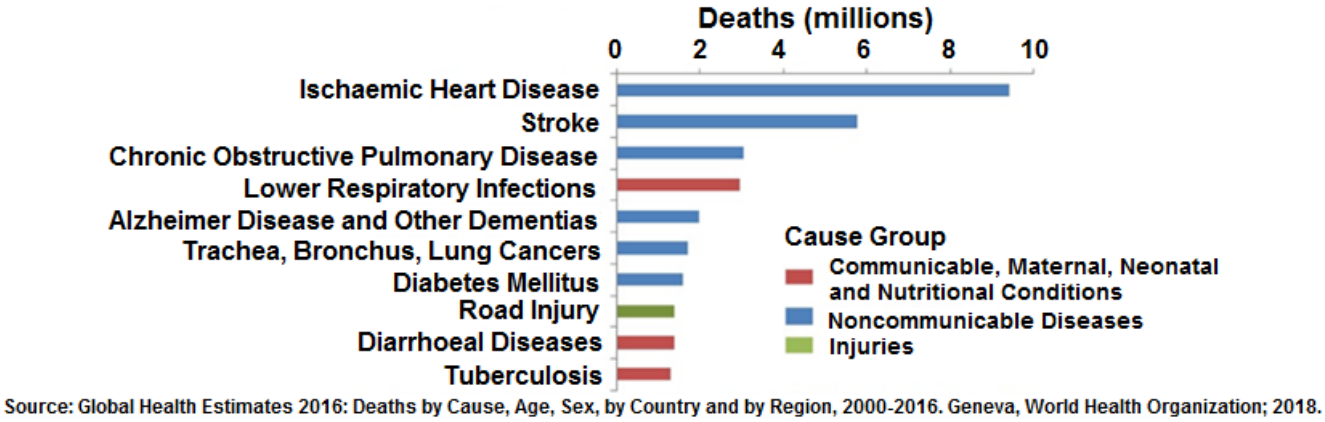


Figure 2-2. Top 10 Global Causes of Death, 2016

When looking at the absolute number of NCD deaths globally in 2016, 78% occurred among LMICs.[55] Figure 2-3 depicts the current chronic disease epidemic among LMICs. Today, even amidst the constant threat of infectious disease epidemics heavily burdening LMICs, it is understood NCDs will soon become the most common cause of mortality in Africa, most likely by 2030.[1] Quite urgently, prevention, care and treatment/control programmes need to be created and/or strengthened to curb the NCD epidemic, especially for resource-limited settings.

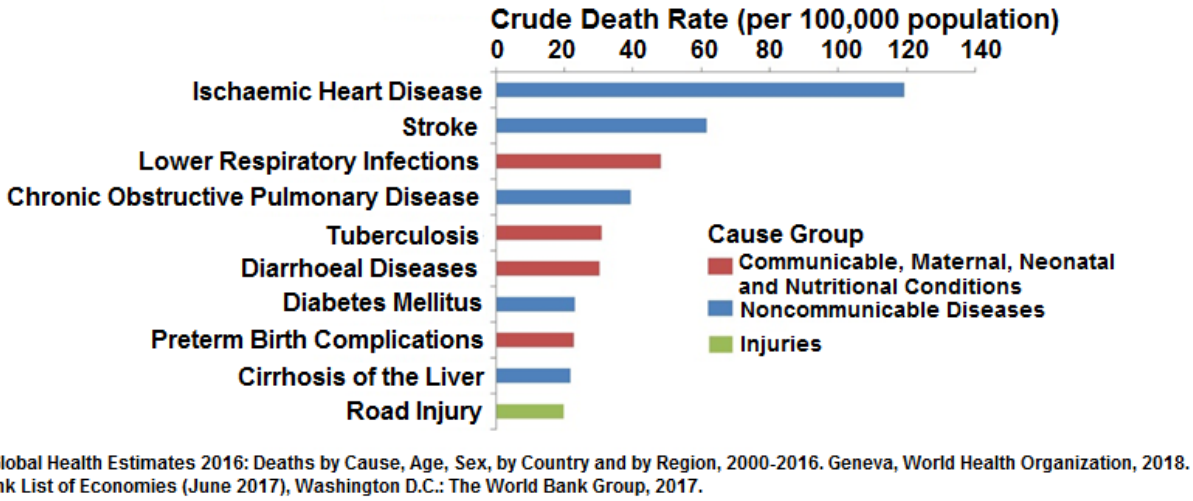


Figure 2-3. Top 10 Causes of Death in LMICs, 2016

2.2 NON-COMMUNICABLE DISEASES AND THEIR RISK FACTORS

Chronic NCDs are typically of long duration and slow progression over one's lifespan. They are linked to morbidity and/or acute illnesses causing sudden mortality. The four most common types of NCDs, globally, are CVD (e.g.; heart attacks and stroke), cancer, chronic respiratory diseases (e.g.; chronic obstructed pulmonary disease and asthma), and DM.[56] Studies have

shown two of the main NCDs accounting for the greatest comorbidity among LMICs are CVD and DM;[15] and therefore, for the purpose of this thesis, CVD and DM will be the focus. Specifically in South Africa, NCDs account for 40% of deaths annually; 18% of which is from CVD and 2% from DM.[2]

Cardiovascular Disease

CVDs cover a plethora of heart diseases, which include but are not limited to the following: coronary artery diseases (CAD) (e.g.; angina and myocardial infarction [i.e.; heart attack]), stroke, heart failure, abnormal heart rhythms, aortic aneurysms, and venous thrombosis.[57, 58]

Globally, CVD accounts for more deaths than HIV, TB and malaria, combined. There were a reported 422.7 million cases of CVD and 17.9 million CVD deaths, globally, in 2015.[59] The Heart and Stroke Foundation South Africa (HSFSA), states that CVD is the second leading cause of mortality in South Africa, after HIV/AIDS, accounting for 17.3% of all deaths.[60]

Diabetes Mellitus

The International Diabetes Foundation (IDF) estimated there were 451 million people living with DM in 2017. It is expected this statistic will increase to 693 million cases by 2045.[61] Globally, half of all diabetic cases are undiagnosed, and the majority occur in LMICs.[61, 62] Within South Africa, the prevalence of DM among adults at least 30 years of age has risen from 5.5% in 2000 to 9% (2 million people) in 2009.[63, 64]

Furthermore, DM increases the risk of CVD, specifically stroke and CAD, even if controlled. The risk multiplies if there are other risk factors present. The leading cause of mortality amongst diabetics is stroke and heart disease.[65] It is estimated that 68% of people with DM over 65 years of age die of some form of heart disease; and of those, 16% are from stroke.[66] Due to its microvascular complications (e.g.; blindness, lower limb amputations from lack of circulation, and renal failure), DM contributes towards substantial morbidity, as well.[67]

2.2.1 DETERMINANTS OF NON-COMMUNICABLE DISEASES

There are underlying socioeconomic, cultural, political and environmental determinants of NCDs, which increase the likelihood of both modifiable and inherent risk factors for such diseases. These complex, underlying determinants (i.e.; causes of the causes) attributing to

NCDs are globalization, urbanization, population ageing, and the political/policy environment.[68] Figure 2-4 depicts the determinants and risk factors attributing to the advancement of NCDs, which are also described in detail.

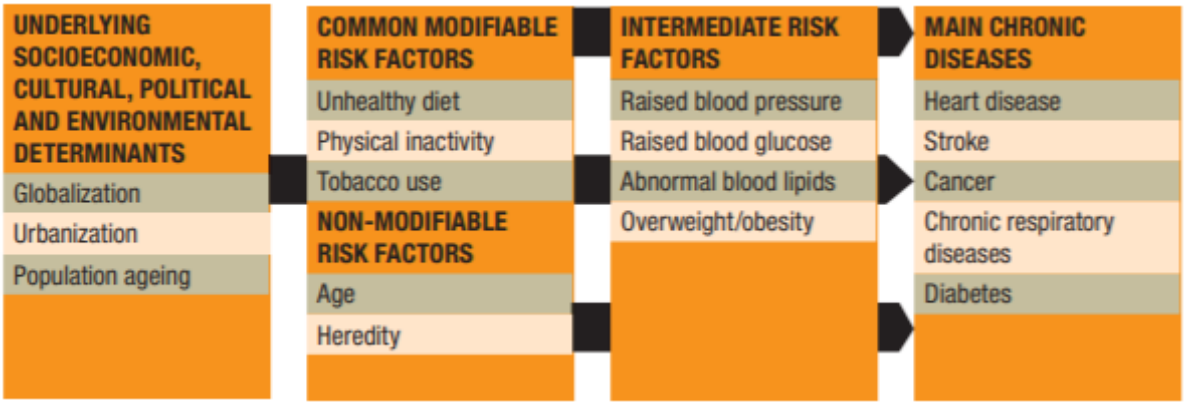


Figure 2-4. Causes of Chronic Non-Communicable Diseases[68]

The WHO defines globalization as, '*the increasing interconnectedness of countries and the openness of borders to ideas, people, commerce and financial capital'*.[68] It is known that globalization drives population risk of chronic disease both directly and indirectly. While the sharing of information, communication and technologies does improve healthcare systems, globalization has assisted with a *nutrition transition* among LMICs. Increased global production, promotion and marketing of unhealthy products, such as fast-foods chains, underlie the transition towards unhealthy behaviours and lifestyles. Specifically, a nutritional transition depicts a transferral from customary diets largely derived from plant-based food sources, which are high in fibre and low in fat, to high-energy dense foods also high in fats, salt and sugar.[69, 70] Although healthier, the production of plant-based foods is demanding of labour; while the contemporary, high-energy dense foods are often processed and mass produced, requiring less labour. This nutritional transition drives the global obesity epidemic and has aided with the epidemiologic transition towards NCDs among LMICs.[71-74]

Rapid urbanization and migration of impoverished people from rural areas contribute to the socioeconomic disparities, attributing to poor diet.[58] Food systems in urban areas have limited availability of affordable, healthier food choices, which encourage the poorer populations to eat cheaper, processed foods.[69, 70] To cater for the impoverished population, low-cost and quick meal options have become readily available for families via street food

vendors and fast food restaurant chains - predominantly McDonald's and Kentucky Fried Chicken.[74-76] Globally branded carbonated soft drinks, such as Coca-Cola, are high in sugar, and typically offered in conjunction with street foods and fast foods.[77]

Urbanization and socioeconomic change amplify the negative aspects of globalization and the nutritional transition. In Africa, Asia and Latin America, the proportion of people in Africa, Asia and Latin America living in urban areas rose from 16% to 50% since the 1950s.[68] The shift from rural to urban living is attractive, as it provides greater opportunities for employment and higher-paying jobs. Urbanization is often accompanied with improvements in infrastructure (e.g.; roads, electricity, water and sanitation); accessibility to additional resources of communication (e.g.; availability of computers and internet); and modern technologies, such as the ability to refrigerate and freeze food stuffs.[78] Urbanization acclimatises communities to the effects of globalization - new, exciting products and technologies, as well as marketing of unhealthy goods (e.g.; processed and fast foods and cigarettes). As compared to rural populations, who conduct more manual labour; urban populations more frequently acquire less physically active and/or sedentary types of employment. Unplanned urban sprawl may be a less pedestrian-friendly environment and further reduce habitual physical activity, such as walking or cycling.[78, 79]

Rapid population ageing is also transpiring globally and is a driving force towards NCDs. The global elderly population, defined as aged 70+ years, is estimated to increase from 269 million in 2000 to 1 billion by 2050. While higher-income countries will double their elderly population, in that timeframe the same aged population among LMICs will quadruple (from 174 million to 813 million).[68]

Generally, health-related policies are crucial determinants of population health. National and local government policies relating to food and agriculture, trade, media advertising and marketing, transport, and urban design shape the available opportunities for healthy choices. It is more difficult for populations living within an unsupportive policy environment to benefit from the existing knowledge-base on risk factors and prevention of NCDs.[68] For example, environmental factors, such as air pollution, contribute to a variety of chronic diseases including asthma and other respiratory diseases.[68] A non-smoker who sits among smokers at a restaurant is still exposed to second-hand tobacco smoke.

2.2.2 MODIFIABLE AND NON-MODIFIABLE RISK FACTORS FOR NON-COMMUNICABLE DISEASES

CVD and DM have risk factors which may be monitored and/or controlled prior to the development of the NCD. Some of the risk factors are inherent and therefore not preventable, but most are indeed modifiable. The more risk factors an individual acquires, the greater their overall risk.[66]

2.2.2.1 Modifiable Risk Factors

A cause for concern is the increased prevalence of modifiable NCD risk factors in South Africa: tobacco and excessive alcohol use, physical inactivity, and unhealthy diet.[15]

Not only is cigarette smoking a strong independent factor for developing CVD, but it is associated with sudden cardiac arrest in people with coronary heart disease.[66] DM also accelerates the damage caused by smoking.[65] In 2009 it was reported that 23.7% of South African adults smoked cigarettes, and while this is a decrease of around 7% of smokers from 1995, the continued reduction has plateaued.[80] The mean age of initiating smoking in South Africa is 17.4 years.[81]

Drinking too much alcohol can raise your BP, contribute to obesity, and increase your risk for cardiomyopathy, stroke, and other diseases. South Africa is ranked as having one of the highest consumption rates of absolute alcohol per drinker per year.[82] Conversely, there is literature from studies to suggest that a very low alcohol consumption may protect against the development of CVD in middle-aged and elderly individuals.[68] The adverse effects of alcohol use outweigh this protective benefit amongst younger age populations.

Diets which are high in fat, salt and/or sugar and conversely, low in protein and fibre, especially if paired with physical inactivity, put individuals at risk of many illnesses.[66] Insufficient physical activity is defined as '*less than 5 x 30 minutes of moderate activity per week or less than 3 x 20 minutes of vigorous activity per week'*. Inactivity is currently the fourth leading risk factor for mortality, worldwide.[57] It is estimated that over 30% of people aged 15 years or older (28.2% of men and 34.4% of women) are insufficiently physically active, globally.[57]

2.2.2.2 Non-Modifiable Risk Factors

Age, sex, family history, and genetic predisposition may affect one's risk of CVD and DM.[83, 84]

Increasing age is known to be one of the highest risk factors for CVD, with a tripling of risk per additional decade of life.[85] The risk of stroke doubles every decade after reaching 55 years of age.[86] The American Heart Association (AHA) estimates that 82% of coronary heart disease-related deaths are of people aged 65 years or older.[66] However, among LMICs, CVD is now occurring in younger individuals than in the developed countries.[7]
Age as a risk factor for DM, differs depending on the type of disease. An individual is more at risk of Type 2 diabetes if over 45 years of age.

Men have greater risk of CVD than women, specifically for heart attacks which often occur earlier in life for men than for (pre-menopausal) women.[66, 85] However, women are more at risk of dying from heart attacks than men.[66] A recent study in Scotland reported that men are biologically more susceptible than women for developing Type 2 diabetes, gaining far less weight than women of similar age upon diagnosis.[87] A theory is that men may be less sensitive to insulin than women, or that their type of visceral fat (adipose tissue encircling abdominal organs, see section 2.2.3 Obesity) is more harmful.[87] However, there are female-only conditions which may increase a woman's susceptibility of developing DM. For example, if a woman develops gestational diabetes while pregnant or has polycystic ovary syndrome (PCOS), she is more at risk.[65, 84]

There are also heredity factors which play a role in risk of CVD and DM. Race, specifically being of African, Asian, Latino, Native American, or Pacific Islander descent increases one's risk of heart disease and DM. Caucasians are at lower risk.[65, 66, 84] Individuals with a family history of heart disease and DM, often have at least one risk factor for those diseases, themselves.[65, 66] Specifically, if an individual's biological parents have CVD, that triples the person's risk.[88]

2.2.3 PRECURSORY CONDITIONS OF NON-COMMUNICABLE DISEASES

Over time, poor lifestyle choices (e.g.; modifiable risk factors), which may be compounded by inherent risk factors, give way to obesity, raised BP, elevated blood glucose, and abnormal levels of blood lipids/fats, which can lead to the development of NCDs.[89, 90]

Obesity

Being overweight and obese are conditions defined by abnormal or excessive fat accumulation over time. Specifically, excessive visceral fat – weight developed around the centre of the body

and its organs (i.e.; liver, stomach, intestines) - may impair health and is linked with chronic disease, especially CVD and Type 2 DM.[65] Most adults with Type 2 DM are overweight with a high waist-to-hip ratio (WHR).[65] People who have excess body fat are more likely to develop chronic disease, even if those same people have no other risk factors.

Trends from a recent meta-analysis shows greater obesity in Southern Africa within the past three decades.[91] South Africa's reported obesity prevalence has risen from 56% in 2002 to 65% in 2012.[81, 92] The South African National Health and Nutrition Examination Survey (SANHANES), 2012, reports black African women living in urban townships and some rural communities are most at risk of becoming obese.[81]

Hypertension

HT, also known as high or raised BP, is a condition in which the blood vessels have persistently raised pressure and is created by force of the blood pushing against the artery wall as it is pumped by the heart. Often it is accompanied by no symptoms, and if left untreated it may cause heart disease and stroke, kidney disease and eye disease.[93] Causes of HT are as follows, but not limited to: obesity; DM, which accelerates the damage of HT; stress; inactivity; chronic alcohol consumption; and insufficient intake of key vitamins and minerals, such as potassium, calcium and magnesium.[65, 93] Risk factors for HT are increased age, male sex before the age of 55 years and female sex after the age of 55 years, black African race, and family history of HT. Obesity is a risk factor, as a higher volume of blood circulates through blood vessels in order to supply the body's cells with oxygen and nutrients, causing greater pressure against vessel walls. Lifestyle habits, specifically smoking tobacco and consuming too much dietary sodium, may also increase the risk.[94]

HT has been depicted as the leading risk factor for mortality and the third ranked cause of disability-adjusted life-years (DALY).[95] Globally, HT is attributable for an estimated 13% of CVD deaths, followed by tobacco use (9%), DM (6%), sedentary lifestyle/lack of exercise (6%), and obesity (5%).[57] In 2000, 26.4% of the global adult population (972 million) had HT, with double the amount of individuals affected living in LMICs as compared to high income countries (639 million people vs 333 million). The prevalence is estimated to rise to 29.2% (1.56 billion people; an absolute increase of 60%) by 2025, which equates to a raise of 9% in men and 13% in women.[96] Of this projected increase in disease, over three-quarters of the world's hypertensive population will be in LMICs.[96]

The HSFSA reports that South Africa is a country with one of the highest rates of HT globally, with 6.3 million South Africans living with high BP.[97] The South African Demographics and Health Survey (SADHS) 2016 reported the prevalence of HT in South Africa's Gauteng Province in men and women aged 15 years or older to be 39.5% and 42.3%, respectively. Black Africans have a slighter higher prevalence of HT, which increases even more for urbanised populations (46.5% for women and 45.4% men).[98]

Hyperglycaemia

As described earlier, hyperglycaemia is a condition in which an individual's serum glucose levels are consistently elevated, and is the leading symptom of having DM. Diabetics have high blood glucose as their bodies do not produce or use enough insulin to metabolise the glucose, but both overeating and physical inactivity can also lead to sustained high blood glucose levels.[99] Overtime, this may reduce the efficiency of insulin within a previously healthy individual, by giving the body more glucose than it can process. This condition is called insulin sensitivity or insulin resistance, and is often a pre-diabetic condition. Stress in a person's life, inclusive of illness, also triggers the release of hormones which cause disorder within the body's glucose metabolic process.[100]

A study conducted in Brazil, a LMIC comparable to South Africa, found that the prevalence of individuals with intermediate hyperglycaemia (i.e.; elevated blood glucose levels but not yet reaching the cut-off for diagnosis for DM) ranged between 16.1% and 52.6% depending on the screening method utilised.[101]

Hypercholesterolemia

Hypercholesterolemia is defined as having an elevation of the lipid or fat in the blood.[15] The body needs lipids to function, and there are different types of lipids in your body. The main two classes of lipids are triglycerides, which are primarily used as stored fat; and lipoproteins, which are complex particles transporting fat molecules around the body. Low-density lipoproteins (LDL) are known as '*bad cholesterol'* as elevated levels lead to a build-up of cholesterol within arteries. High-density lipoproteins (HDL), known as '*good cholesterol'*, assists with removing other forms of cholesterol from the bloodstream.[102] Elevated levels of triglycerides and LDL may limit blood flow, especially amongst smokers, increasing the chance of clogged arteries and one's risk of CVD. Elevated levels of HDL are associated with

lower risk of CVD. DM is known to increase blood triglycerides and decrease levels of HDL.[65]

Atherosclerosis is the build-up of fats and cholesterol plaque on the arterial walls, which may eventually cause obstruction of blood flow. Often atherosclerosis has no symptoms until a plaque ruptures or the build-up is severe enough to cause acute occlusion of the artery via blood clot.[103] Having DM accelerates this process, putting diabetics at increased risk of atherosclerosis and blood clots.[65] There are no symptoms of hypercholesterolemia prior to experiencing a heart attack or stroke, and a person must undergo diagnostic testing for diagnosis.

There is evidence across most populations that blood cholesterol levels increase with age, putting older people at greater risk of CVD. A prospective follow-up study of nearly 15,000 middle-aged people in Finland reported serum TC levels continued to increase among men until levelling off around 45 to 50 years of age, while TC blood levels continued to increase sharply for women until between 60 and 65 years of age.[104]

2.3 HIV/AIDS AND HIV-NON-COMMUNICABLE DISEASE COMORBIDITY

2.3.1 OVERVIEW OF THE HIV/AIDS EPIDEMIC

Despite the epidemiologic transitions towards chronic disease, communicable disease still contributes significantly to the burden within LMICs, which also exacerbates the local NCD epidemic.

Since the discovery of one or two isolated cases of HIV in-country in the late 1980s,[105] South Africa has become the epicentre of the HIV/AIDS epidemic with the highest prevalence of HIV-1, globally.[8] It is largely a subtype clade C epidemic.[106] Of the approximate 36.7 million PLHIV across the globe,[9] over 20% (7.9 million) reside in South Africa as of 2017.[8, 10-12]. Figure 2-5 depicts the historical timeline and policy implementation surrounding HIV/AIDS both globally and within South Africa.

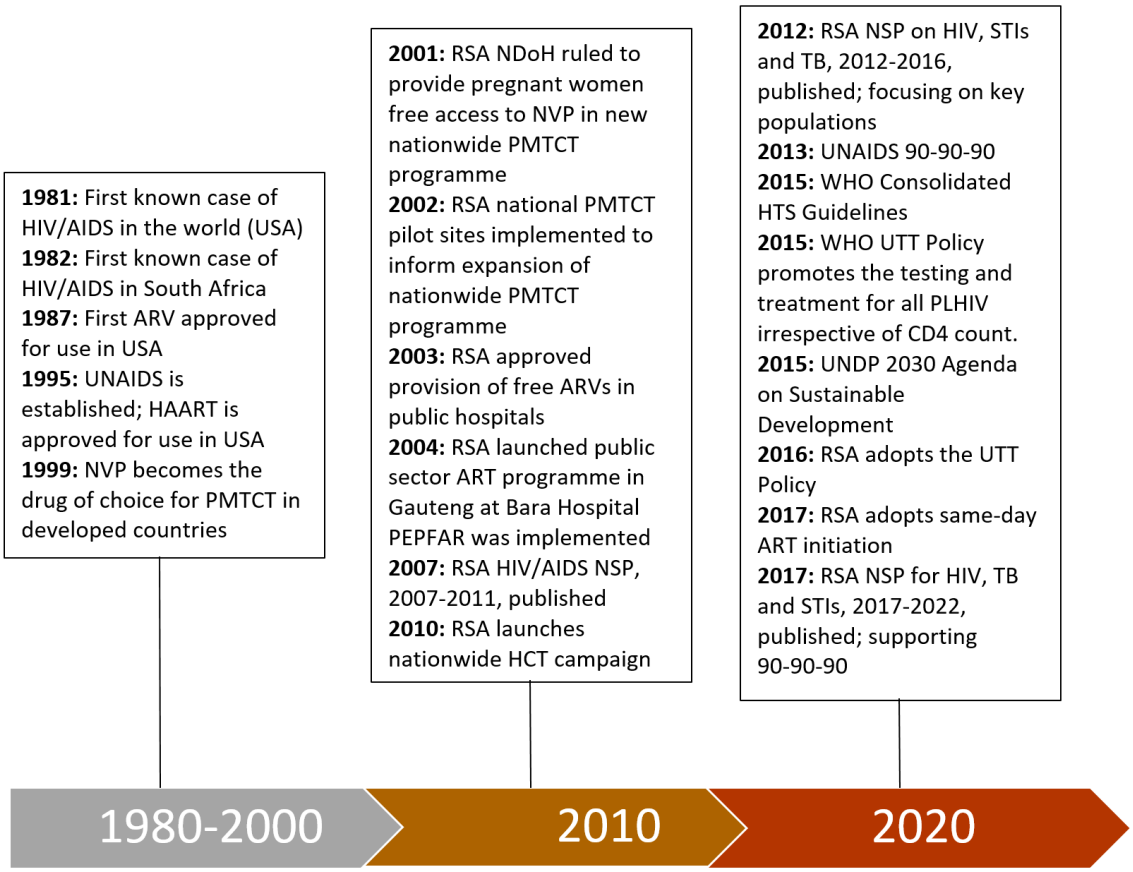


Figure 2-5. Historical Timeline and Policy Implementation around HIV/AIDS [107]

Human immunodeficiency virus, HIV; Acquired immune deficiency syndrome, AIDS; United States of America, USA; Antiretrovirals, ARVs; United Nationals Joint Programme on HIV/AIDS, UNAIDS; Highly active antiretroviral therapy, HAART; Nevirapine, NVP; Prevention of mother-to-child transmission, PMTCT; Republic of South Africa, RSA; National Department of Health, NDoH; Antiretroviral therapy, ART; President's Emergency Plan for AIDS Relief, PEPFAR; National strategic plan, NSP; HIV counselling and testing, HCT; Sexually transmitted infections, STIs; Tuberculosis, TB; HIV testing services, HTS; World Health Organization, WHO; Universal test and treat, UTT; People living with HIV, PLHIV; United Nations Development Programme, UNDP.

The HIV-1 subtype C epidemic within South Africa originated around 1960.[106] There were large genetic variants of subtype C in-country, reflecting the diversity of southern Africa and its migration into the country of South Africa. A massive number of viral strains and infections were introduced into South Africa by foreign immigrants – largely employed as migrant labourers for the mining sector - in the 1970s and 1980s, increasing the viral diversity from <20% in 1980 to >90% by 1990.[106] The increased HIV prevalence only started to be noticed in the 1990s, decades after the epidemic began.

Today, the HIV prevalence among the general population is 18.9%,[8] however, the prevalence among the general population aged 15-49 years is 20.6%.[12] The prevalence in adults aged 15-49 years varies greatly by province, with rates ranging from 12.6% in the Western Cape to 27.0% in KwaZulu-Natal. Five of the nine provinces have an HIV prevalence of over 20% (Eastern Cape, Free State, KwaZulu-Natal, Mpumalanga, and North West).[108]

The mode of transmission is primarily heterosexual, with epidemic disparities by both race and sex. Black Africans have substantially greater risk than any other racial group within the country.[12] Poverty is predominant factor increasing the disproportioned HIV prevalence between sexes and among racial groups.[109] Literature has shown this disparity has been created by historical and current disparate cultural, social and economic status in South Africa.[109-112]

Male-to-female transmission is more biologically efficient than female-to-male transmission.[113-115] Overall, HIV peak prevalence occurs in 35-39 year olds at 31.5%. However, male HIV prevalence peaks at a later age (45-49 years, 24.8%) as compared to females (35-39 years, 39.4%) (see Figure 2-6).[12] Peak infections occur in young women aged 15-24 years,[105] comprising 37% of new infections documented in 2016.[2] The disparity in HIV prevalence by sex is most pronounced in those aged 20-24 years, with females having an HIV prevalence three times greater than their male counterparts (15.6% vs 4.8%, respectively) (see Figure 2-6).[12] The Fifth South African National HIV Prevalence, Incidence, Behaviour and Communication Survey (SABSSM V), a population-based, cross-sectional survey of households in South Africa, reported the annual incidence of young women aged 15-24 years to be over three times greater than that of young men (1.51% vs 0.49%, respectively).[12]

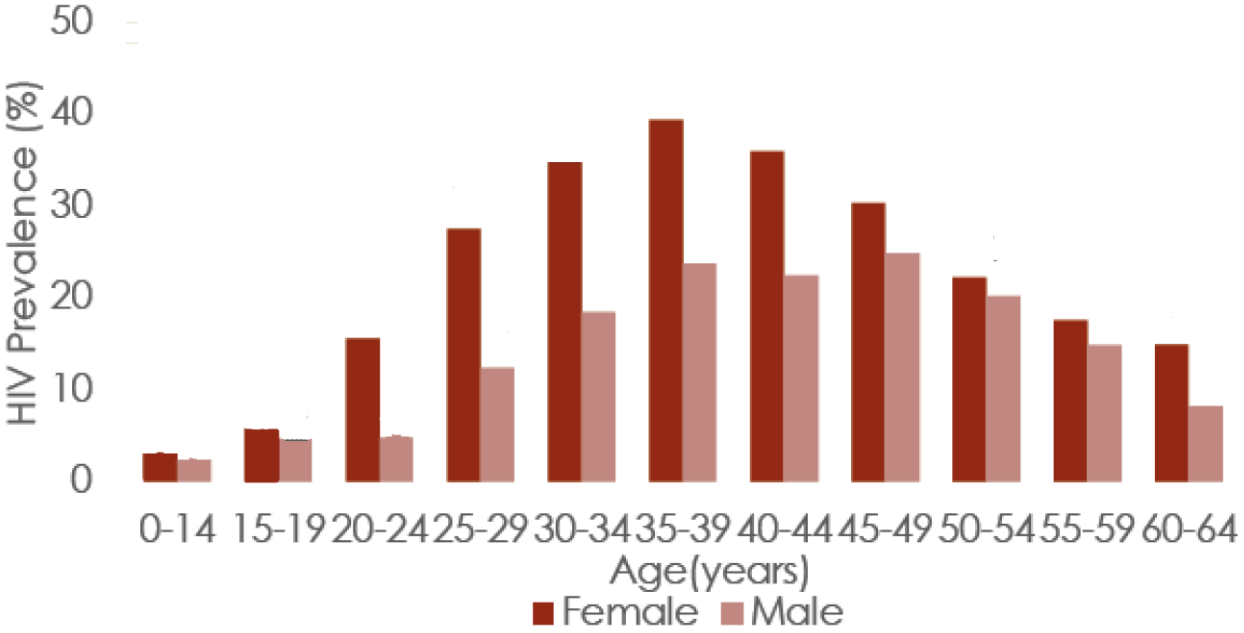


Figure 2-6. HIV Prevalence by Age and Sex, 2017[12]

Some factors attributing to such disparity in HIV prevalence between the sexes are the lower socioeconomic position of women,[116-118] and cultural and social norms such as intergenerational sex, transactional sex and gender-based violence (GBV).[118-120] Analysis from the South African National HIV Surveys 2002–2012 show younger women (aged 15–24 years) with age-disparate partners (5+ years senior) have an increased risk of acquiring HIV, with the odds of HIV infection increasing for each year increase in the male partner's age.[121] These infected young women then have same-age relationships with and infect male partners, who in turn infect younger women.[122] South Africa has a high prevalence of GBV, with one in five partnered women and 40% of divorced or separated women having experienced physical violence.[98]

Aside from young women, key populations (as defined in Table 2-1) affected by South Africa's epidemic are MSM and female sex workers (FSWs). Both MSM and FSWs bear a disproportionately high HIV burden. The HIV prevalence among MSM vary depending on geographical setting in South Africa, ranging from 13.2% in Soweto to 25.5% in Cape Town to as high as 49.5% in the greater Johannesburg area.[123-125] Sexual transmission among men can be attributed to the high per-act risk of transmission of anal intercourse, as well as the low uptake of HIV prevention and care services in this population due to experiences of stigma

and discrimination in the health sector.[126] Recent studies surveying the HIV prevalence among FSWs within the South African metropolitan cities of Cape Town, Durban, and Johannesburg suggest it to be between 39.7% and 71.8% (Johannesburg).[127] An even higher HIV prevalence of 88.4% was found among FSWs recruited along a major trucking route within South Africa – the N3 Route.[128]

Table 2-1. Defining Key Populations for HIV

Key Population	Definition
Sex Workers (SWs)	Adults who voluntarily receive money or goods in exchange for sexual services either regularly or occasionally.[129] SWs can be female, male or transgender adults.
Transgender people	The umbrella term for persons whose gender identity or expression (masculine, feminine, other) is different from their sex at birth (male, female).[130]
Men who have sex with men (MSM)	Gay, bisexual, and other men who have sex with men. This community is disproportionately affected HIV, syphilis, and other sexually transmitted infections (STIs).[131]
Persons who inject drugs (PWID)	Intravenous drug users are more at-risk of bloodborne pathogens, such as HIV and Hepatitis B and C.[132]
Inmates	Incarcerated men and women are more susceptible to HIV-infection through sharing needles for drug use, the unavailability of condoms, and higher risk of rape associated with prison environments.[133]

Human immunodeficiency virus, HIV.

Approximately one-fifth of women of reproductive age are HIV-infected,[134] which highlights the critical need for ART initiation for the prevention of mother-to-child transmission (PMTCT). In 2016, among pregnant, HIV-infected mothers, more than 95% were enrolled in PMTCT services and on antiretrovirals (ARVs) to prevent transmission to their children.[135] However, an estimated 12,000 children were still infected through vertical transmission, only 58% of children living with HIV have been initiated on treatment, and there were 8,600 deaths in children aged 0 to 14 years attributed to HIV and AIDS illnesses.[135] Within the general population, behavioural factors associated with HIV infection include early sexual debut, inconsistent condom use, and multiple concurrent partnerships.[122, 136-138] The earlier age of sexual debut and low condom use may have reduced the success of prevention efforts. The 2016 SADHS found that only 58% of women and 65% of men with multiple sexual partners within the past year reported using a condom during their last sexual intercourse. The number of sexually active men aged 15–49 years with multiple sexual partners has increased, with the mean number of lifetime partners reported as 14.7.[98]

Initially, the South African government's response to the HIV/AIDS epidemic was denialist. This approach during the Mbeki presidency led to an estimated 330,000 deaths, between the

years 2000 and 2005, due to the failed provision of lifesaving ART.[105, 139] Following Mbeki's (forced) resignation from presidency in 2008, an unprecedented nationwide rollout of ART commenced in the fight against HIV/AIDS.[105, 140]

The WHO introduced its Universal Test and Treat (UTT) Policy, which implemented the strategy of offering all persons diagnosed with HIV-infection to be initiated on treatment irrespective of CD4+ count.[141] South Africa was among the first countries in Africa to adopt the UTT policy, and its ART services underwent a massive expansion in recent years, to keep aligned with the WHO's changing guidelines. The policy was introduced in-country and implemented on 1 September 2016.[142] Furthermore, same-day initiation (SDI), advocating for ART initiation on the day of HIV diagnosis, followed exactly one year later. Previously, South Africa only initiated treatment for those with a CD4 < 200 cell/mm^3, and had 3.39 million people on treatment in mid-2015.[11, 143] UTT launched in-country in 2016, which initially more than doubled the numbers of people eligible for ART (7.1 million).[144] By December 2016, South Africa had 3.9 million PLHIV initiated on ART, and had the largest ART programme, globally.[2, 144] Mathematical modelling on the new UTT guidelines has shown that UTT could lead to substantial reductions in HIV incidence, potentially eliminating it as a public health problem over a period of 15–20 years.[48, 145]

In 2018 and with the largest ART programme in the world, South Africa could boast that 4.4 million people are receiving ART, equating to 61% of PLHIV in the country.[146] Largely attributable to the rollout of lifesaving treatment, the life expectancy in South Africa has risen from 56 to 64.2 years between 2009 and 2018 (61.1 years for males, 67.3 years for females).[105, 134]

Within eastern and southern Africa, progress in the prevention, treatment and control of HIV falls below the 90-90-90 target.[147] Figure 2-7 depicts current progress.

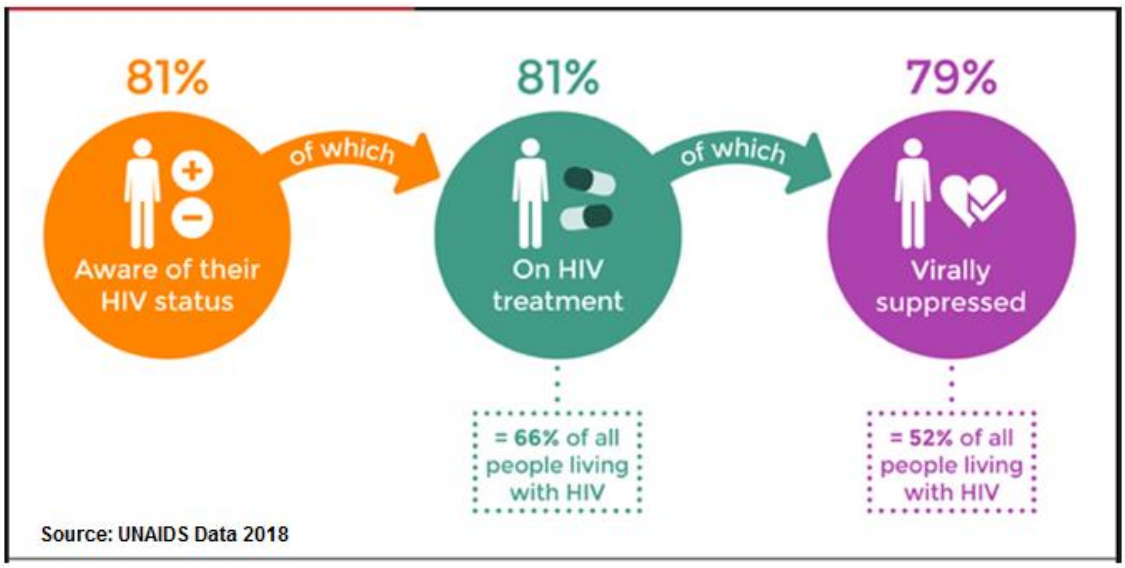


Figure 2-7. East and Southern Africa: Progress towards 90-90-90

Human immunodeficiency virus, HIV.

2.3.2 HIV-NON-COMMUNICABLE DISEASE COMORBIDITIES

There is evidence that HIV-infection, itself, and ART use might be risk factors for NCDs. The virus is known to cause a persistent inflammatory state and immune dysfunction mechanisms, which are linked to metabolic syndrome diseases such as DM or hypercholesterolemia.[148, 149] HIV-infected individuals stable on ART are at higher-risk of NCD comorbidities due to metabolic consequences, such as body fat redistribution and cardio-metabolic abnormalities associated with HIV treatment.[148] With the scale-up of ART, HIV is becoming a chronic disease with people living with HIV (PLHIV) reaching nearly the same life expectancy as healthy individuals.[122] Historically, NCDs are thought of as 'aging diseases'.[150] Not only is HIV-infection seemingly associated with an accelerated 'aging' process, but PLHIV, now living longer while on treatment, are becoming increasingly at-risk for non-HIV-related chronic conditions of aging similar to the HIV-uninfected population.[151]

A systematic review and meta-analysis of 57 studies reported the prevalence of HIV comorbidity with either CVD, cervical cancer, depression or DM. Regarding CVD risk factors among PLHIV, the analysis reported the prevalence of HT (21.2%), hypercholesterolemia (22.2%), obesity (7.8%), and metabolic syndrome (16-31% depending on the criteria used).[15, 149] Another facility-based study conducted in Swaziland screened 1826 ART patients at least 40 years of age for CVD risk factors. About 39% had at least one CVD risk factor and 8% with

at least two CVD risk factors.[152] There is a paucity of literature of HIV-CVD comorbidities in LMICs, however PLHIV develop CVD at a higher frequency than their uninfected counterparts. Furthermore, HIV has been shown to be an independent risk factor of stroke.[15, 153]

A systematic review of DM among PLHIV shows a wide prevalence range (1.3-18%) largely determined by the lack of standardised criteria used for the screening and diagnosis of DM. PLHIV are exposed to additional DM risk factors, such as inflammation, which may affect hormones regulating insulin sensitivity. Additionally, some ARVs have been identified as being associated with DM.[15]

2.4 COMBATTING NCDS: RECOMMENDED GUIDELINES VS WHAT IS IN PRACTICE

2.4.1 GLOBAL AND LOCAL CALLS FOR ACTION

The 2030 Agenda is a compilation of 17 Sustainable Development Goals (SDG), 169 targets and 231 indicators building upon the successes of the Millennium Development Goals (MDGs), which were benchmarks to meet towards ending poverty by 2015.[154-156] The third SDG (SDG3) calls for all countries to '*ensure healthy lives and promote well-being for all at all ages'*, making a bold commitment to end the epidemics of HIV/AIDS, TB, malaria, other communicable diseases, as well as NCDs by 2030.[157] Three years into the implementation of this goal, the 2018 progress report shared that while the global HIV incidence has decreased from 0.40 to 0.26 per 1,000 uninfected people between 2005 and 2016, the rate for women of reproductive age in SSA is a staggering 2.58 per 1,000 uninfected persons.[158] In 2016, 32 million people died from CVD, cancer, DM, or chronic respiratory disease, globally; with the mortality rate of those aged 30 to 70 years being 18%.[158]

The primary focus of the majority of global prevention and treatment policies still surround communicable disease. However, they have begun to incorporate chronic disease into their scope due to the noted epidemiologic transition towards NCDs.

As mentioned within this thesis introduction, in December 2013 the UNAIDS set ambitious, new targets to drive the progress toward HIV treatment scale up beyond 2015. Previous AIDS targets set incremental steps to monitor progress by the 2015 deadline, whereas those set for post-2015 were to fast-track the elimination of HIV by 2030. Stakeholder consultations on

these new targets have been held in all regions of the world.[159] Additional goals are for there to only be 500,000 new HIV infections among adults (a 75% reduction compared to 2010) and zero discrimination by 2020. The UNAIDS 95-95-95 target is a step up from 90-90-90, with only 200,000 new infections among adults by 2030.[160]

To support the UNAIDS fast-tracked targets, the WHO issued global, evidence-based guidelines for HIV prevention, testing, treatment and care services and promoted policy changes within fast-tracked countries.[161] The guidance delivers a mix of HTS approaches which countries may tailor dependent on the context of its epidemic. Among the many strategies included, the guidelines encourage the integration of screening efforts for HIV, TB, STIs and NCDs to increase access to and uptake of HIV testing to curb the HIV epidemic while also addressing the threat of NCDs and other HIV-related comorbidities.[42]

Countries, such as South Africa, have been and are attempting to align their National Development Plans (NDPs) and national department of health (NDoH) strategies with the aforementioned global prevention and treatment guidelines and policies. South Africa's NDP aims to eliminate income poverty and reduce inequalities. Regarding public health, the NDP calls for public sector health system reform with the goal of access to quality health care for all, regardless of financial status. Objectives are to address the social determinants that affect health (i.e.; physical [in]activity, diet, tobacco use and alcohol consumption), strengthen the health system inclusive of decentralised health care models, prevent and reduce the communicable and NCD disease burden, implement a national health insurance system, and increase the number of well-trained human resources available in the health sector.[20]

The SANDoH has created two, separate NSPs to further assist in outlining strategies and setting targets towards the elimination of disease. The SANDoH NSP for the Prevention and Control of NCDs, 2013-2017, set ten targets to be reached by the year 2020, with the main goal of reducing relative premature mortality (under 60 years of age) from NCDs by 25%.[21] The NSP called for early identification of NCDs and their main risk factors through screening for them within HTS. Through the monitoring of risk factors, there will be earlier detection and potentially prevented morbidity and mortality relating to NCDs. Metabolic risk factors to measure include obesity, HT, hypercholesterolemia, and poor glucose control; while lifestyle factors to monitor are diet, alcohol and tobacco use and lack of exercise. The NSP also aims to

reduce mortality related to HT, DM and asthma through the integration of NCD screenings within routine primary health care (PHC). [21]

The NSP for HIV, TB, and STIs, 2017–2022, has put forth eight goals, of which include breaking the cycle of transmission; reaching the 90-90-90 targets in every district; having targeted interventions reaching all key and vulnerable populations; mobilising resources and maximising efficiencies for a sustainable response; and taking data-driven action.[2]

Despite initiatives in recent years, there is evidence that the strategies proposed within the NSPs have not been standardised and there is still massive fallout along the continuum of care for HIV – and also presumably for NCDs and co-morbidities - within the country. As of December 2017, only 84.9% of PLHIV aged 15-64 years knew of their HIV status; 70.6% of PLHIV who knew their status were on ART, and 87.5% of PLHIV on ART were virally suppressed.[108] Table 2-2 shows this data stratified by sex.

Table 2-2. South Africa's Progress towards UNAIDS 90-90-90, by Sex, 2017

UNAIDS 90-90-90 Target	Total % of 15-64 yr olds	% Females	% Males
Target 1: PLHIV knowing status	84.9%	88.9%	78.0%
Target 2: PLHIV with known status on ART	70.6%	72.2%	67.4%
Target 3: PLHIV on ART with Viral Suppression	87.5%	89.9%	82.1%

Joint United Nations Programme of HIV/AIDS, UNAIDS; People living with HIV, PLHIV; Antiretroviral therapy, ART.

2.4.2 CURRENT NATIONAL SCREENING AND MANAGEMENT GUIDELINES

It is presumed the fallout in the cascade for NCDs would be larger than for HIV, as while there are explicit national guidelines for the screening and management of HIV, there are no such national guidelines for NCDs and/or NCD risk factors of obesity, HT, hyperglycaemia and hypercholesterolemia. Rather healthcare providers are to use the recommendations of local, regional, and global clinical societies. The lack of explicit national guidelines for NCDs creates unstandardised practice within the public sector. Guidelines are simply not sufficient enough to improve clinical practice unless they are indeed implemented, monitored and evaluated.

The current policy for Adult Primary Care (APC) in South Africa requires that all patients should have their weight, BP, pulse and temperature routinely checked.[162, 163] This is in conflict with the South African National HTS: Policy and Guidelines, 2015, [23] which states all PHC clinics should offer HIV rapid testing, syndromic screening for TB and STIs, and BP readings and utilise the following integrated referral systems: family planning (FP) for all clients, isoniazid preventive therapy (IPT) evaluation for TB patients, PMTCT and ART for clients identified as HIV-infected, and medical male circumcision (MMC) for HIV-uninfected male clients.[23]

Screening of blood glucose and cholesterol for DM and hypercholesterolemia is not currently routine practice in either PHC or within the HTS programme. The following outlines the current screening and management guidelines for NCDs and NCD risk factors among both the general population and PLHIV within South Africa.

2.4.2.1 Obesity

While national APC guidelines call for monitoring of a patient's weight,[163] it is not specified as to *how* weight is to be monitored and used as an indicator for obesity. There are, however, four simple methods for assessing if an adult is overweight or obese – through waist measurements, the calculation of WHR, the calculation of a waist-to-height ratio (WtHR), and/or BMI.

To fall within a healthy, normal waist circumference range, women should measure 88cm or less, while men should measure 102cm or less.[164] If a patient's hip line is also measured, a WHR can be calculated. The WHO states a female would be at elevated risk of CVD through abdominal obesity if her WHR is above 0.85, while a man would be if his WHR is above 0.90 or greater.[165] BMI calculations classify a patient's weight as underweight, normal, overweight, or obese. Table 2-3 provides the WHO classification definitions of disease risk by BMI and waist circumference for men and women.

Table 2-3. WHO Classification of Disease Risk by BMI and Waist Circumference Thresholds[164]

	BMI (kg/m²)	Obesity Class	Disease Risk* Relative to Normal Weight and Waist Circumference	
			Men 102 cm (40 in.) or less	Men >102 cm (40 in.)
			Women 88 cm (35 in.) or less	Women >88 cm (35 in.)
Underweight	<18.5		–	–
Normal	18.5 – 24.9		–	–
Overweight	25.0 – 29.9		Increased	High
Obesity	30.0 – 34.9	I	High	Very high
	35.0 – 39.9	II	Very high	Very high
Extreme obesity	40.0†	III	Extremely high	Extremely high

*Disease risk for type 2 diabetes, hypertension, and CVD.
†Increased waist circumference can also be a marker for increased risk, even in persons of normal weight.

World Health Organization, WHO; Body mass index, BMI.

Additionally, the WtHR has been shown to be a simple and effective obesity screening tool for CVD risk,[166] and deemed even more predictive than BMI or a waist circumference. The benchmark of WtHR >0.5 has been vetted an indicator of 'early health risk'.[167]

These measurements and classifications are not mandated as part of routine clinical care. However, if a BMI is calculated and the patient is found to be obese, the national APC guidelines suggest the patient also be screened for HT, DM, and hypercholesterolemia and be managed accordingly.[168]

2.4.2.2 Hypertension

There are conflicting HT screening and treatment guidelines available for use in South Africa, with the primary ones being the 2018 National PHC Guidelines and the published guidelines as recommended by the Southern African Hypertension Society (SAHS).[168, 169] These national and regional recommendations are also at odds with international guidelines published jointly by the AHA/American College of Cardiology (ACC).[170] Table 2-4 outlines the differences in classifications of HT and treatment initiation among the aforementioned guidelines.

Table 2-4. Classifications of Hypertension by Guidelines (in mmHg)

Guidelines:	National Primary		SAHS		AHA/ACC	
BP Categories:	SBP	DBP	SBP	DBP	SBP	DBP
Normal			<120	<80	<120	<80
Optimal			120-129	<80		
Elevated					120-129	<80
High Normal			130-139	80-89		
Hypertension						
Stage 1	*140-159	*90-99	140-159	90-99	*130-139	*80-89
Stage 2	160-179	100-109	*160-179	*100-109	≥140	≥90
Stage 3	≥180	≥110	≥180	≥110		

National and SAHS: All hypertensive patients are prescribed lifestyle modification
****Treatment should be initiated; National Primary Care Guidelines recommend treatment initiation at Stage 1 HPT if lifestyle modification failed after three months***
Southern African Hypertension Society, SAHS; American Heart Association, AHA; American College of Cardiology, ACC; Blood pressure, BP; Systolic BP, SBP; Diastolic BP, DBP; Hypertension, HPT.

The 2018 National PHC Guidelines states that a patient must have their BP read three times, a minimum of two days apart, prior to diagnosis with elevated BP (barring that the BP is not severely elevated for which immediate action is taken).[168] Whereas, the SAHS states there may be two readings taken one to two minutes apart, and a consecutive third reading is taken only if there is >5mmHg difference between the first two readings.[169] However, the SAHS does feel repeat measurements should be performed on at least three separate occasions within four weeks unless BP is ≥ 180/110 mmHg (e.g.; stage 3 severe HT).

Both national and regional guidelines state that HT is defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg, and the universal goal of antihypertensive treatment is a BP < 140/90 mmHg regardless of CVD risk and underlying comorbidity.[168, 169, 171] Sparking controversy, the AHA/ACC guidelines recently redefined HT as a BP ≥ 130 systolic and/or diastolic ≥ 80 mmHg on at least two occasions with the resultant target BP being < 130/80 mmHg.[170] While there is published literature identifying a clear relationship between increasing BP and cardiovascular events starting from 115/75 mmHg,[170, 172] there is currently no evidence to support treatment for systolic BP between 130 and 140 mmHg in patients without additional cardiovascular risk factors to justify the revised AHA/ACC BP target < 130/80 mmHg.[170] Historically the pragmatic definition of HT has been >140/90 mmHg where diagnosis and treatment do more good than harm.[170, 173]

As initially backed by the International Society of Hypertension (ISH),[173] the SAHS felt the revised AHA/ACC definition of HT and BP target was not relevant globally, specifically for LMICs where adopting it would significantly increase the prevalence of HT.[170, 174] If implementing the change within South Africa, the prevalence was projected to rise from 35.1% to 50.2%. This increased burden of disease would constitute greater use of health resources for the increased number of patient monitoring visits, use of antihypertensive medication, as well as laboratory services to monitor for therapy side effects, such as acute kidney injury and electrolyte abnormalities.[170, 175, 176] However, subsequently, the ISH updated its guidelines for treating hypertension in line with the lower thresholds for treatment in many LMICs, including South Africa.[177]

Regarding prescribed treatment, the National PHC Guidelines and the SAHS state all patients with HT should undergo lifestyle modification. The National PHC Guidelines declare if a patient with mild HT (i.e.; stage 1 HT; 140 mmHg ≤ systolic BP ≤ 159 mmHg; and/or 90 mmHg ≤ diastolic BP ≤ 99 mmHg) and without CVD risk factors responds poorly to lifestyle modification after three months, treatment is initiated. If the patient has mild HT and has CVD risk factors, therapy is initiated immediately.[168] However, the SAHS state that treatment initiation should only begin once a client without any other CVD risk factors reaches moderate HT (i.e.; stage 2 HT; 160 mmHg ≤ systolic BP ≤ 179 mmHg; and/or 100 mmHg ≤ diastolic BP ≤ 109 mmHg).[169] Hypertensive patients who have initiated therapy should be monitored monthly to adjust medication, if required. Once stable, monitoring may be every three to six months. For elderly patients without any comorbidity, treatment should only be initiated if BP is > 160/90 mmHg.[168, 169]

2.4.2.3 Hyperglycaemia and Type 1 and 2 Diabetes Mellitus

There is currently no clear policy for the screening of blood glucose for either Type 1 or Type 2 DM within the public PHC sector. However, guidelines do state if patients present with specific symptoms (e.g.; for Type 1 DM: hunger, polyuria, ketoacidosis, thirst, unexplained weight loss, tiredness; for Type 2 DM: thirst, polyuria, tiredness, changes in vision, susceptibility to infections – urinary and respiratory tract and skin), screening for blood glucose should take place.[168] Within the public sector, such screening is conducted through testing for RPG (*random* is defined as any time of day without regard to time since last meal) or fasting plasma (blood) glucose (FPG; *fasting* is defined as no caloric intake for at least eight hours).

Both Type 1 and Type 2 DM are diagnosed when a patient presents with symptoms (specifically the classic polyuria and polydipsia for Type 2 DM) and has hyperglycaemia (RPG ≥ 11.1 mmol/L or FPG ≥ 7.0 mmol/L).

If a patient is asymptomatic but found to be obese, the patient should be screened for DM, as per the National PHC Guidelines. If the patient screens hyperglycaemic on two tests conducted on two separate days, they are diagnosed with Type 2 DM.

Diabetic patients undergo monthly monitoring of blood glucose levels, weight and BP; and have HbA1c testing one month prior to the patient's annual hospital visit. Diabetes-related glycaemic targets for low-risk populations (young, newly diagnosed, no cardiovascular risk factors) are HbAa1c < 6.5% and FPG 4.0-7.0 mmol/L; whereas the majority population's HbA1c target is < 7% and the high-risk group (elderly, poor-prognosis) is < 7.5%. As obesity, HT and hypercholesterolemia in diabetic patients are common, creating further complications;[65] weight, BP and blood lipids are monitored at visits and lifestyle modification is encouraged.[168]

2.4.2.4 Hypercholesterolemia and Assessing Cardiovascular Risk

While not explicitly outlining screening for hypercholesterolemia, the 2018 National PHC Guidelines provides an algorithm for the screening and prevention of ischaemic heart disease and atherosclerosis,[168] which has a cholesterol-based component. Patients at risk of CVD may benefit from lifestyle modification and lipid-lowering medicine therapy. Patients should be managed according to their level of risk, and medicines should be given to those with high-CVD risk, even if their cholesterol is within the normal range.

A patient is of high CVD risk and should receive lipid-lowering medicine if they have any of the following: established atherosclerosis disease, and/or Type 2 DM and over 40 years of age, and/or has had DM for over 10 years, and/or has DM with chronic kidney disease (CKD). Otherwise, a person who has any of the following may potentially be at risk for CVD and should be managed according to their 10-year risk of experiencing a CVD event: DM, HT, central obesity (waist circumference ≥ 94 cm [men] and ≥ 80 cm [women]), smoking, and older age (men > 55 years of age, women > 65 years of age).

The 10-year risk may be calculated in two ways, by either a) BMI-based risk assessment, or b) Framingham risk score (a cholesterol-based assessment). Both models uses the predictors of age, DM, smoking, treated and untreated systolic BP as predictors within the risk assessment.[178] The BMI-based calculation also incorporates the patient's BMI, while the Framingham risk score incorporates lipids (both TC and HDL) to determine the 10-year risk of a cardiovascular event,[168] and requires the addition of points per risk factor to determine the overall patient-centred risk score.

If a patient receives a 10-year risk score up to 19%, they are to adhere to prescribed lifestyle modifications and be reassessed between one and five years, depending. The patient is to start statin treatment along with a lifestyle modification if receiving a risk score of ≥ 20% risk. When lipid-lowering medications are prescribed, it is always done so in tandem with lifestyle modification.

Patients are explicitly prompted to have their random TC assessed if they have any family history of familial or other heritable hypercholesterolemia, regardless of their CVD risk assessment. If the test results are > 7.5 mmol/L, patients are referred for further examination for genetic disorders after excluding secondary causes such as uncontrolled DM and/or hypothyroidism.[168]

2.4.2.5 Screening of Non-Communicable Diseases amongst People Living with HIV

While weight and BP are both checked at each ART clinic visit, along with an STI and TB symptoms screening, there is no routine monitoring for both blood glucose and cholesterol amongst HIV-infected persons, regardless of treatment initiation, either within the PHC or HTS setting.

Within South Africa, the APC recommends that an HIV-infected patient be assessed for CVD risk at diagnosis, and at every visit the patient's weight be monitored, with further investigation if the patient loses ≥ 5% of their body weight within four weeks. The public sector does not recommend blood glucose screening routinely at ART initiation, but rather that HIV-infected people over ten years of age, including pregnant women, should screen for glycosuria via a urine dipstix test prior to ART initiation.[179] However, glycosuria, a condition in which a person's urine contains more glucose than usual, is typically evident only during late-stage diabetes and/or kidney damage.[180] In contrast, within the US, the 2016 American Diabetes

Association (ADA) guidelines for the diagnosis and management of DM states that fasting glucose and lipid levels should be measured in HIV patients prior to initiating ART, with additional screening three months post-ART initiation or when changing highly active ART (HAART), and then annually thereafter. If a patient is found to have pre-diabetes, they should have their glucose levels monitored every three to six months.[181]
While the 2018 National PHC Guidelines makes no mention of HT-HIV comorbidities, the SAHS has acknowledged that long-term HAART is associated with a higher prevalence of systolic HT.[182] There is also evidence that certain classes of ARVs may cause hypercholesterolemia.[169, 183]

Two of the three main classes of ARVs are protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NRTIs). They inhibit or induce key functions of HIV enzymes, and therefore assist in the prevention of HIV from multiplying.[37] However, they may also affect calcium channel blockers (CCBs) - the main class of antihypertensives - through drug interactions also affecting drug metabolism.[184, 185] This results in either an enhancement or loss of antihypertensive efficacy.[169] Due to these contraindications, it is critical for PLHIV receiving HAART to have their BP monitored at each monitoring clinic visit.

Some of the protease inhibitors put patients at higher risk for hypercholesterolemia than others. For example, lopinavir/ritonavir are associated with a higher risk of hypercholesterolemia, specifically hypertriglyceraemia, than atazanavir/ritonavir.[186] A challenge with controlling high cholesterol among PLHIV, is that many statins (e.g.; simvastatin) cannot be taken with protease inhibitors, as they affect the metabolism of the lipid-lowering therapy which results in extremely high blood levels. Therefore, it is currently recommended that PLHIV should have their fasting lipid levels assessed three months after being initiated on ART. PLHIV on ART with a 10-year CVD risk score of >20% should switch to atazamavir/ritonavir and have their fasting lipid profile repeated in three months. If there is persistent hypercholesterolemia, the patient qualifies for lipid-lowering therapy, with the criteria for treatment initiation the same as for HIV-uninfected patients.[186]

PIs and NRTIs also put HIV patients at an increased risk of hyperglycaemia and DM. It has been reported that the incidence of newly onset hyperglycaemia among PLHIV on ART is on average about 5%. Additionally, while the ADA has set the diagnosis of DM at an HbA1c

reading of 6.5% or higher,[187] a lower HbA1c threshold of 5.8% has been suggested for ART patients due to its association with better sensitivity and specificity.[188] However, the ADA does not recommend using HbA1c as a diagnostic tool for DM among PLHIV.[189] There is evidence that HbA1c is not reliable in patients with iron-deficient anaemia, and therefore some guidelines conflict on whether to use it for screening.[190] HbA1c is also more expensive than measuring fasting plasma glucose levels, the oral glucose tolerance test, or random plasma level measures.[191]

2.5 HEALTH SYSTEMS BARRIERS AND STRATEGIES

Even though South Africa has aligned its NDP, NSPs and National HTS Guidelines to support the UNAIDS, WHO, and UNDP global targets, evidence of expanded strategies are required to facilitate reaching the targets of increased uptake and identification of newly-identified individuals with disease and their linkage to care for both NCDs and communicable diseases. There is compelling evidence of at least six, critical challenges creating barriers towards these targets, and they are as follows: 1) health systems fragmentation, 2) service delivery and supply chain management, 3) shortage of human resources, 4) syndromic management of disease, 5) long wait time for health screening results, and 6) passive linkage to care and treatment. Innovative strategies within HTS and the PHC system are needed to overcome each of these obstacles. There is evidence of acceptable strategies to help combat these barriers, and each are further detailed.

2.5.1 HEALTH SYSTEM FRAGMENTATION vs INTEGRATION OF SERVICES

Despite the global call for health service integration, many LMIC countries, including South Africa, have traditionally responded to complex health problems through the vertical healthcare system approach. As mentioned within this thesis' introduction, verticalised healthcare systems occur through the creation of disease-specific programmes, which specialise in allocating resources towards attacking a singular issue. Countries may have adopted this method due to the pressures of meeting global disease prevention and treatment targets, as well as donor funding being restricted to single-diseases - such as HIV and TB – and being reluctant to fund costs for other conditions, which may increase the cost of service provision.[47] Furthermore, combining disease-related services has also been perceived as a threat to gains made in one or both programmes.[46]

The separation of disease-related services may cause differentiation within the healthcare system, which may be functional and/or structural in nature. Functional differentiation is often through dedicated staff with selected skillsets and/or expertise focused on one disease or intervention.[22, 192] Structural differentiation is typically through the establishment of separate units or departments with different health practitioners in order to deliver single, disease-related services (i.e.; HIV or TB or CVD or DM).[193] While the goal of differentiation is indeed to enhance the efficiency and performance of disease prevention, care and treatment programmes,[194, 195] the likelihood of fragmentation is high, due to the nature of its completely divergent operations.[194]

With uncoordinated, service fragmentation for interdependent programmes, such as for HIV and NCDs, there is often service and resource duplications, distortions, disruptions, and distractions; all which have downstream effects.[196] This has been well documented among LMICs.[197-205]

Duplications occur when both programme-specific and health system-wide entities conduct the same functions, creating not only financial implications through the replication of resources, but inefficiencies towards achieving desired patient-related health outcomes.[47, 196, 206, 207] Distortions exist when there are perceived differences between health systems. For example, healthcare providers may leave their current positions within the general public health sector seeking jobs within higher-paying verticalised service programmes.[208] Not only does this exacerbate staff shortages within the public sector, but the remaining staff may become unmotivated within their jobs.[196, 206, 209-212] Multiple, unsynchronised disease-specific training curricula or campaigns take healthcare providers away for longer periods of time than necessary, disrupting routine health service delivery.[196, 206] Additionally, the poor coordination of multiple disease programmes can be distracting. For example, each verticalised practice has its own health reporting system which needs attention, distracting staff from performing their overall scope of work.[196, 201]

Most importantly, fragmentation negatively impacts at the patient level. Although all desired services may exist within one health facility, the routine offer of integrated services is not normalised and/or standardised. Patients typically need to attend multiple clinics or visit various healthcare providers within the same clinic to acquire the assistance they need. This acts as a deterrent to patients seeking healthcare services, limiting the reach of preventative

screening efforts and/or referral to care and treatment services, as they are not provided at the same time, in the same place, by the same person.[23]

A more successful healthcare system would build on synergies amongst its differentiated units, integrating resources and services where able, to minimise fragmentation.[194] This reflects more of a horizontal health care system, where generalist staff manage multiple conditions.

2.5.1.1 Ideal Clinics and Integrated Chronic Disease Management

Recognising the increasing demands within the PHC system due to both acute and chronic conditions, the SANDoH launched an initiative - the *Ideal Clinics Programme* - in July 2013. Its target was to systematically improve upon the identified deficiencies in the quality of care provided in public PHC facilities.[213, 214] The NDoH defined the Ideal Clinic as, '*a clinic with good infrastructure, adequate staff, adequate medicine and supplies, good administrative processes, and sufficient adequate bulk supplies… us[ing] applicable clinical policies, protocols and guidelines… harness[ing] partner and stakeholder support…. collaborat[ing] with other government departments, the private sector and non-governmental organisations to address the social determinants of health.*'[213] To become an Ideal Clinic, a facility is graded upon 211 elements and must meet a minimum weighted overall score.[214]

A key focus within an Ideal Clinic is the concept of the Integrated Clinical Services Management (ICSM). Building upon the strengths of the HIV programme, ICSM provides patients seeking preventative services integrated care for both chronic and acute diseases.[214] This provides a more patient-centred PHC system and the same continuum of care for multiple diseases, which is a step towards health systems strengthening. The APC Guide (2016/2017), as referenced earlier within this thesis, is the ICSM's integrated symptom-based approach for the screening and management of the following diseases for adults in South Africa: HIV, TB, asthma/COPD, CVD, DM, mental health conditions, epilepsy, musculoskeletal disorders, and women's health.[179] Aligning itself with various NDoH policies and clinical protocols (primarily for HIV, TB, STIs and maternal care), uniform checklists and algorithms are presented to assist in standardising the approach of clinical care for adults who attend PHC facilities with symptoms or who are being seen at chronic monitoring visits.[179]

Theoretically, once a patient is identified with any chronic condition, needing long-term management, they should enter the Integrated Chronic Disease Management system (ICDM),

which differentiates between chronic and acute care needs. The triggering of a separate service for chronic care patients was a strategy to combat health system deficiencies through improved operational efficiency and patient clinical outcomes.[162, 215] The ICDM operates at the facility level, as well as within the community with assisted self-management of disease.

A pilot of the ICDM model was implemented across 42 PHC clinics in South Africa.[162, 215] An assessment of the facility reorganisation and clinical support components of the ICDM 18-months after initiation uncovered some barriers to its sustainability and scale-up. While facility reorganisation and the clinical support provided to professional nurses in patient management supported the implementation of the ICDM; suboptimal clinical leadership oversight, resistance of healthcare providers towards adoption of the ICDM, adaptability and infrastructure limitations may negatively affect its longevity.[215]

A modification of the Innovative Care for Chronic Conditions (ICCC) Framework developed by the WHO, which was the cornerstone of the ICDM model in South Africa, highlighted additional complexities relating to integrated care for chronic conditions which must be understood for its success. Healthcare systems must recognise the dynamics between the effects of chronic disease morbidities (and comorbidities); provider workload and capacity; and related patient perspectives, specifically regarding beliefs and behaviours. These interactions should inform primary health care re-engineering and ICDM to optimize health outcomes.[216]

2.5.2 SUPPLY CHAIN MANAGEMENT

Identifying people living with chronic NCDs and HIV, as well as other disease, is only worthwhile if the health system can also successfully deliver the prevention, treatment and care services through a well-functioning supply chain. Unfortunately there is nationwide evidence of failure in these service deliveries and supply chain management.[217]

Within the Stop Stockouts Project (SSP) Stock Outs National Survey of nearly 1900 clinics, one in five health facilities reported a stock-out of adult ARVs within the last three months. Of these, 70% reported the stock-outs lasted longer than one month.[217] The stock-outs were mainly single medications, with few fixed-dose combination tablets;[38] and nearly 20% of the stock-outs of ARVs or TB medicines resulted in the patient forced to leave the health facility without medication in-hand.[37] The provinces reporting the highest frequency of

stock-outs longer than one month were the Free State, Gauteng and Mpumalanga, highlighting the deficiencies in the provincial supply chain and emergency response mechanisms.[37]

To combat this failure in the health system, the NDoH created a supply chain task force with the aim to initiate supply chain reforms which should have a positive impact on reducing stock-outs of essential medications in South Africa.[48] About R300 million was granted to the SSP for the development of a national electronic medicine stock management system.[217] This system could assist in reducing stock-outs through real-time tracking of the use of supplies and implementing an early warning system to identify impending shortages.[218] The Central Chronic Medicine Dispensing and Distribution Programme was created to deliver chronic disease medication directly to health facilities, assuring availability of stock.[2]
Additional strategies are required to address the root causes of stock-outs in the supply chain, improve and implement monitoring tools to track existing and potential issues in essential medication supply, and work closely with stakeholders, including the NDoH, to develop and implement a national supply chain strategic plan.[48, 217, 218]

2.5.3 SHORTAGE OF HUMAN RESOURCES AND TASK-SHIFTING

SSA has a deficit of 4.2 million health care workers, and this is estimated to increase to 6.1 million by 2030.[24] In relation to higher-income countries, such as the United States, there are 69.2 vs. 230 doctors and 388 vs. 1212 nurses per 100,000 population in South Africa.[25] South Africa has substantially less doctors than most income-comparable (low- and middle-income) countries.[26] The South African NDP and both NSPs require a substantial growth and diversification in human resources and commits to invest greater resources towards the training and mobilisation of these personnel.[48] However, it avoids addressing any reasons for the current shortages of healthcare workers – both political and budgetary in nature – which may serve as barriers to its goals.[219] The severe shortage in human resources is compounded by personnel hiring limitations put in place across the NDoH because of fiscal constraints in the 2016 budget.[220] Among other line items requiring attention, the health sector budget needs to manage the increase in current health personnel costs resulting from the 2015 wage agreement, which is expected to result in a 7.4% annual growth in wages across government.[221] Simply put, there is not enough manpower or funds to increase the human resources needed to implement both communicable and NCD NSPs.[219, 220] South Africa must work with what resources the country already has.

With limited healthcare providers nationwide serving a population with a high burden of both communicable and NCDs, comes a high level of occupational *burnout*. Burnout is characterized as, '*physical and emotional exhaustion from long-term exposure to* [both physically and emotionally] *demanding work'*; and it affects interpersonal skills, job performance, career satisfaction, and psychological health.[222, 223] Studies have shown that clinicians and nurses with burnout are more likely to report career dissatisfaction and intention to leave the medical profession.[224]. Not only does this attrition of staff add to the crisis of minimal human resources, but it raises a constant need for the shifting of dynamics and (re-)training among retained staff. Lastly, burnout among healthcare providers has been associated with a decrease in quality of service delivery relating to increased self-reported errors, reduction in provided clinical care time, and higher mortality rates.[225-227] In SSA, where burnout prevalence among healthcare workers is between 40-80%, factors relating to burnout are unfavourable work conditions, and high job-related demands paired with low job-related satisfaction. Burnout is more prevalent among women,[228-230] people of younger age,[231] and among workers with less support and/or resources to manage their workloads.[222, 232, 233]

The WHO Consolidated HTS Guidelines reported a strategy to cope with the shortages of trained healthcare workers (and associated burnout). *Task-shifting* (also referred to as task-sharing), defined as, *'the rational redistribution of tasks between cadres of healthcare providers with longer training, and those with shorter training, such as trained lay providers'*.[42] This method increases the effectiveness and efficiency of available personnel, expanding the role of trained lay providers, to empower the currently available workforce to employ services to more people.[42, 50, 51]

In response to such healthcare workforce shortages, adaptations and innovations, such as task-shifting and the use of multidisciplinary teams, have been utilised.[234] Since 2010, the South African National HTS Guidelines have permitted the implementation of non-health care workers – or lay providers - to conduct HIV testing by means of a finger prick method.[235] The country has employed additional strategies to address the human resources shortfall. The National Health Insurance (NHI) Policy was birthed as part of South Africa's major health reform process. This policy, which includes contracting with private general health practitioners and public clinics, has the potential to assist with skilled staffing shortages, provided favourable contracting conditions.[236] Community health workers (CHWs) are

being scaled up as part of ward-based outreach teams. These workers are responsible for contact tracing and counselling, but the National Policy on CHWs is still not finalised, and there are large provincial differences in contracting methods and salary. The current ratio of CHWs is far too small per population for impact, given their large and increasing scope of work.[237] While these aforementioned strategies are a step in the right direction, they are not enough to meet the scope of work outlined in the NDP or NSPs.

Task-shifting has been conducted in SSA for over a decade.[238] Multiple systematic reviews crossing many healthcare domains conclude that positive outcomes may be achieved by diverting tasks to nurses and lay or CHWs.[238-240] Additionally, substantial cost-savings have been reached through shifts towards nurse-based care and treatment and further task-shifting of POCT to non-healthcare workers.[220, 235, 241] Healthcare providers with less training often have a lower salary than those providers with longer training. However, cost-effectiveness may vary by settings.

There are opportunities available for trained lay providers to deliver a wide range of healthcare services beyond HIV prevention, treatment and care. For example, the WHO has reported lay providers may perform vaccinations, TB and STI screening and testing and bed net distribution for malaria prevention.[42] Furthermore, the following clinical services may be conducted by lay providers in addition to the provision of counselling and referrals: mother, newborn and child health services; promotion of HIV testing in pregnancy; and prescription of ART by nurses.[242]

A study in rural Malawi which delegated HTS from health workers with longer training to health workers with shorter training reported a five-fold increase in uptake of monthly HIV testing.[243] A study in the Sisonke District in South Africa concluded HIV testing conducted by trained lay providers is just as accurate as the testing provided by laboratory staff and healthcare providers with longer training.[244] Of 3986 samples tested by both cadres of healthcare workers, all but 23 results matched, of which only two were deemed *critical errors* (discordant results between laboratory staff and lay provider).[244] A similar study in Malawi found only four of 2911 samples tested yielded different results.[245] Furthermore, HTS clients in Botswana who received their services from lay providers and participated in an exit survey expressed their high-level of satisfaction with the services received, sharing they were comfortable with returning for additional service in the future.[246] Perhaps the level of client

comfortability was reflective of the social and cultural sensitivity lay providers often have to the culture of the community, as so many of them are actual members of the community, and are culturally competent whilst speaking with their peers.[247, 248] In an analysis of 25 WHO African region countries, 60% allowed trained lay providers to conduct HTS with RDTs, while 80% allowed the same cadre to provide pre- and post-test counseling.[249]

Specifically within the WHO Consolidated Guidelines, the WHO has endorsed and strongly recommends the provision of HTS by lay providers using RDTs.[42] However there are considerations that have to be made whilst utilising this recommendation. Lay providers need training, mentoring and supervision by on-site supervisors, which ideally include someone trained in laboratory procedures. National competency standards must be met to ensure high quality HTS. Modules must depict how to cover the full HTS procedure, inclusive of specimen collection, the conduct of the RDTs following the validated national testing algorithm and testing strategy, providing results and counselling, and reporting of results. Both external and internal quality assurance (QA) must be conducted.

The NSP for NCDs did recognise the lack of human resources required to meet current health-related targets and the critical need to train additional health workers. The plan recommends for all healthcare workers – professional and non-professional, alike – to be trained on the prevention and control of NCDs, and in the care of diagnosed persons (inclusive of palliative care).[21] Presumably, if a lay provider may conduct HIV fingerprick RDT, then they may equally conduct other fingerprick RDT, such as for blood cholesterol and blood glucose. Furthermore, a validation study of community-based lay providers resulted in empirical evidence to support BP measurement by non-health workers using electronic devices. Non-health workers recorded BP that differed from qualified health workers by no more than 10 mmHg.[250] An assessment of screening for CVD risk using a non-lab-based screening tool derived from the Framingham risk score as implemented by CHWs in LMICs was shown to be a cost-effective and acceptable for use, and hence a feasible strategy for integration into task-shifting.[251]

The WHO encourages countries to review and revise their national policies to permit trained lay providers to conduct full HTS using RDTs; acknowledge and remunerate trained lay counsellors appropriately, in keeping with their newly specialised skills; and address these expanded roles within national policies and regulatory frameworks.[42]

2.5.4 SYNDROMIC MANAGEMENT OF DISEASE vs DIAGNOSTIC TESTING

The national NSPs require the prevention, treatment and control of various diseases and/or risk factors of disease. However, the syndromic management of disease – the identification of consistent groups of symptoms and easily recognised signs - is typically utilised by South Africa. Syndromic management of disease is largely conducted for STIs and TB.

Subsequent to the identification of STI symptoms without diagnostic laboratory testing, the presumptive provision of treatment covers the majority of pathogens responsible.[252] Patients with identified TB symptoms are referred for diagnostic testing following the national testing algorithm for TB case confirmation. Further diagnostic testing (for TB patients) and treatment referral (for both TB and STI patients) rely on accurate reporting of symptoms by the patient, and those who are asymptomatic (i.e.; without the production of symptoms) or who do not feel comfortable disclosing their symptoms are missed. Additionally, asymptomatic patients would most likely not seek health care services at facility, unless for additional reasons, leaving them open to disease-related morbidity and mortality. Many common STIs, such as *Chlamydia trachomatis* (CT), are asymptomatic but still transmissible; can cause permanent damage to a woman's reproductive system – potentially leading to infertility if left undetected and untreated; and create additional risk for contracting HIV.[253] Asymptomatic STIs are difficult to be identified, as they need diagnostic testing, and are therefore difficult to be completely controlled.[253] Moving from syndromic management of disease among LMICs, towards diagnostic testing would assist in correctly identifying patients who are asymptomatic.

An objective of the current NSP for HIV, TB, and STIs, is to increase the detection and treatment of highly prevalent and largely asymptomatic STIs by 50%;[2] however, there is no fleshed-out strategy to achieve this. The WHO Global Health Sector Strategy on STIs 2016–2021 has outlined the goals and targets for global STI prevention and control. The first strategic direction is to collect information on STI prevalence and incidence across representative populations.[254] Understanding regional and national STI epidemics is essential to advocate, fund, plan, and implement interventions for STI prevention and control. In order for this to be executed, countries first must shift from syndromic to aetiologic surveillance of STIs.

As described earlier within this thesis regarding NCDs, many risk factors such as HT, hyperglycaemia and hypercholesterolemia are asymptomatic until actual disease has

progressed. People with weak immune systems, such as HIV-infected individuals, are more at-risk of comorbidity. They may be less able to control NCDs or fight off other communicable diseases, if they are not properly screened for conditions and monitored.[255]

2.5.5 RAPID DIAGNOSTIC TESTING

In South Africa, the standard practice is to send blood samples to the laboratory for tests like CD4 count, and blood cholesterol and/or glucose levels. The samples are processed and results are then returned to the clinic to be communicated to the patient at a follow-up appointment. A study conducted at a public-sector HIV/AIDS treatment facility in Johannesburg, South Africa, demonstrated that 65% of HIV-infected walk-in patients to the HTS program did not return for their CD4 test results within 12 weeks, if at all.[30] It could be assumed that similar delays could occur for the collection of other non-rapid NCD risk factor screening test results; which in turn, is associated with further delays or fallout in linkage to prevention, care and treatment services.[8, 30] The identification of newly diagnosed and/or infected patients and their continued care and treatment is solely dependent upon the patient returning for their follow-up appointment to receive their diagnosis. Therefore, where feasible, RDT should be employed.

In resource-poor settings, validated rapid, point-of-care (POC) technology can offer inexpensive, large-scale screening programmes for both NCDs and communicable disease, as well as other emerging infections, through the expansion of critical laboratory testing to both facilities and rural areas and provision of real-time results.[256, 257] Furthermore, laboratory-diagnosis of certain diseases, such as STIs, is unaffordable and inaccessible for most LMICs; and rapid, accurate, and affordable POCT can bridge this gap.[258] For example, an additional benefit of the rapid GeneXpert technology for the diagnosis of TB are reduced staff time needed for testing and the potential to increase volume of testing.[259] A study found that a CT rapid test with a sensitivity of 65% can lead to a greater proportion of infected individuals identified and treated compared to a nucleic acid amplified test (NAAT, the gold standard) with a 90% sensitivity, when the return rate for test results and treatment is low.[260] Rapid STI diagnostics also help to identify asymptomatic cases.

Not only do POCT machines provide same-day results, continuity of care, and help to increase the uptake of testing, but they also provide a cost-benefit, as depicted in Table 2-5.

Table 2-5. Comparison of Point-of-Care vs. Laboratory Benefits

Screening Test	Point-of-Care Benefits	Laboratory Costing

HIV RDT vs. HIV Antibody ELISA test (laboratory)	USD$5 per test Provided by the South African Department of Health *Results in 15 minutes*	USD$15.15 per test *Results in 1+ week*
HbA1c	USD$8.32 per test *Results in 5 minutes*	USD$15.26 per test *Next-day results*
Full Lipid Profile (TC, TG, HDL, LDL) vs. individual laboratory tests	USD$7.36 per 4-in-1 test *Results in 5 minutes*	TC: USD$5.78 TG: USD$8.84 HDL: USD$7.36 LDL: USD$7.36 TOTAL: USD$29.36 *Next-day results*
Rapid CT testing vs. CT PCR Laboratory testing	USD$3.61 per test *Results in 30 minutes*	USD$63.15 per test *Results in 1+ week*
TOTAL COST PER CLIENT	USD$30.52 *(USD$92.42 saved in total)*	USD$122.94

Human immunodeficiency virus, HIV; Rapid diagnostic testing, RDT; Enzyme-linked immunosorbent assay, ELISA; Glycated haemoglobin, HbA1c; Total cholesterol, TC; Triglycerides, TG; High-density lipoprotein, HDL; Low-density lipoprotein, LDL; Chlamydia Trachomatis, CT; Polymerase chain reaction, PCR.

For some POCT, the unit cost per test may be larger through the loss of bulk testing in laboratories, but it offers potentially substantial savings through enabling rapid delivery of results and reduction of facility, client and personnel costs.[261] For example, with public sector pricing in South Africa, the rapid GeneXpert technology for TB screening costs $14.93 per sample, compared to $16.88 per sample using conventional automated liquid culture-based methods in the laboratory.

The NSP does call for increased laboratory support and use of POCT methods, specifically for common STIs,[2] but it does not explicitly state which testing kits should be used as the gold standard. However, there is no standardised use of such technology to facilitate a quick turn-around of screening results.

2.5.5.1 Available Rapid Diagnostic Testing Technologies for Blood Glucose and Cholesterol

In 1970, the first POC instrument – the Ames Reflectance Meter - was developed to produce quantitative blood glucose results for clinician-use only, weighing 1.2kg and costing USD$495.[262] Over the next four decades, this POCT technology evolved into more lightweight (as light as 9 grams), portable and affordable models (a.k.a; glucometers) for use by both patients and healthcare providers, alike.[263] Results become available within five minutes from minimal volumes of blood required for analysis (0.3-1 µL).[264]

Blood glucose tests are either fasting or non-fasting, with fasting being the most common method as it provides more accurate and more easily interpreted results.[265] In 2009, the WHO Consultation recognised that HbA1c could be used as a RDT for DM. HbA1c may be measured to signify the average blood glucose concentration over a three month period – no fasting is necessary. The higher the concentration of HbA1c, the greater the indication of poorer control of blood glucose levels, indicative of DM and CVD.[266] An evaluation of the costs and quality of care related to the introduction of HbA1c POCT for Type 2 diabetic patients was conducted at community health centres in Cape Town, South Africa. The resulting evidence reports that HbA1c POCT is feasible, easy to integrate into the organization of care, and results in the immediate feedback to patients and thus higher patient satisfaction. However, it has not significantly improved test coverage, treatment intensification, counselling, or glycaemic control.[267]

In the same manner that handheld glucometers were created; there are also validated, rapid POC technology available to screen for blood cholesterol. There are lipidometers screening simply for TC, and there are other machines which may screen for complete lipid profiles - TC, triglycerides, HDL and LDL. Each of these are typically conducted while fasting.

2.5.6 PASSIVE LINKAGE TO CARE AND TREATMENT

The most crucial piece of the care cascade is its linkage of individuals diagnosed with disease to care and treatment services. Within HTS it is also critical to link HIV-uninfected clients who are at-risk of HIV acquisition to prevention services. The CDC defines *successful linkage to care* as, *a 'newly-identified HIV-infected person engaging with a healthcare provider within 30 days of diagnosis'*.[38] Timely provision of ART is known to reduce mortality in PLHIV and within TB/HIV co-infected adults,[268] and linkage to HIV prevention services is critical for HIV-uninfected persons with ongoing risk (e.g.; sero-discordant couples).[63] People who are diagnosed late with HIV and have delayed treatment initiation typically have disease progression, with CD4 counts below 200 cells/µL.[269] Over the past decade, late initiation has not decreased.[269] For example, the National HTS Policy and Guidelines reported that the large-scale HCT drive in 2010, which tested 13 million South Africans in 18-months, did not increase the number of people in HIV care or on treatment.[23] In resource-limited settings, such as SSA, it is reported that as much as 40% of PLHIV who are diagnosed are not linked to treatment services.[32-34] The majority of those who do initiate ART do so very late in the advanced stages of infection,[270, 271] which results in high mortality shortly after starting

therapy.[34, 272] It is common for PLHIV who are linked to care to cycle in and out of care with varying levels of adherence.[33]

Efficient linkage to care and treatment is also crucial for other chronic conditions. Studies have found hypertensive patients with poor medical management and treatment follow-up are at greater risk of an acute cardiovascular event or death.[273] Earlier initiation of metformin after diagnosis for Type 2 DM patients is associated with more optimal health outcomes than delayed treatment - better glycemic control, greater weight reduction, and a lower risk for therapy intensification.[274] Other studies utilising predictive modelling also support earlier treatment to combat DM-related morbidity, especially for the prevention of microvascular disease.[275] Compared to no treatment, a treatment target of HbA1c < 7% (<53mmol/mol) within six months of diagnosis with DM may reduce the risk of end-stage renal disease by 44% and blindness by 73%.[274, 275]

A challenge towards achieving timely linkage to care and initiation of treatment is passive referral (e.g.; only providing names and contact information for care and treatment services), which is widely implemented in South Africa, across all health domains.[31] Known barriers that also delay linkage to care are individual patient factors (e.g.; unacceptance of the result, perceived health status, depression and/or lack of coping skills, fear of disclosure), social or cultural factors (e.g.; stigma and discrimination, risk of IPV, and lack of social and/or family support), structural and economic factors (e.g.; distance to the facility, lack of transportation or money for transportation, legal issues for minors testing without parental consent), and health system barriers (e.g.; incorrect or missed referrals, staff shortages, stigmatizing or unfriendly services, and long wait times in facilities).[33, 35, 36, 276, 277] Potentially a more active approach, such as assisting patients with their referrals, would increase timely linkage to care and treatment, as would strategies addressing the aforementioned real and/or perceived barriers to healthcare-seeking behaviour.[36]

The current NSP for HIV, TB, and STIs calls for improvement in linkage to care to ensure expedited initiation of ART for all people diagnosed with HIV, as soon as they are ready for treatment and preferably same day. However, it doesn't explicitly offer innovative ways to link people to services, outside of using '*PLHIV to enhance linkage to care'*.[2] Additional guidance is needed.

2.5.6.1 Examples of Active Linkage to Care and Treatment Strategies in Literature

The WHO Consolidated HTS Guidelines published recommended, evidence-based practices to actively assist with increasing patient linkage to care and treatment services.[42] A systematic review and meta-analysis of both community and facility-based HTS and linkage to care gaps in SSA reported that facilitated or '*active*' linkage services achieved both higher linkage to care and ART initiation than passive referral.[278] The same outcomes could be described for NCD linkage to care and treatment. Additionally, a systematic review of literature aiming to increase linkage of PLHIV among urban areas of SSA to care and treatment reported four common, active approaches: 1) health system interventions, 2) patient convenience and accessibility, 3) behaviour-related interventions and peer support, and 4) incentives.[279] These approaches are supported by the WHO, and each of these strategies can be facilitated by healthcare workers and implemented within either a health facility or the community.

While the effectiveness of active referral vary greatly depending on the model of HTS (e.g.; facility-based vs community-based), high rates of linkage to care and treatment are possible with intensive, proactive interventions. The success of such strategies can only be confirmed through a patient tracking system, and different approaches must be monitored and evaluated, as a combination approach may be best. A study among referred hypertensive patients in rural Uganda that included an intervention package consisting of a short counselling session after diagnosis, a referral appointment within 30 days, and a transportation voucher, resulted in 83% linkage to care.[277] The scale-up of best strategies should evaluate its financial cost against its health outcomes.[23]

Health System Interventions

Health system interventions, such as integrating HIV services into routine care or other relevant health services (e.g.; STI and TB) at a single facility (horizontal healthcare system); task-shifting; and comprehensive care, including improved referrals, education and communication [280] have been found to improve patient retention in care. It has been reported that a combination of post-diagnosis, active referral strategies, specifically for comprehensive care, have the potential to improve linkage to care.[279] This strategy has been discussed prior within this thesis.

Patient Convenience and Accessibility

Patient convenience and accessibility strategies include immediate testing with same-day results[33, 281-285] and/or immediate treatment initiation,[281, 286-288] and community testing including home-based HTS and treatment initiation or decentralised treatment provision and/or community-based distribution.[280, 289-292] Accelerated ART initiation did significantly improve linkage to care at both one month and three months post-diagnosis, and significant improvement was seen both as a solitary strategy and as a combination intervention.[293-295] This strategy could potentially improve NCD patient retention within the care cascade.

Behaviour-Related Interventions and Peer-Support

There are many behaviour-related interventions and peer-support strategies that may assist patients with engaging in care. Such strategies are assisted peer services and care facilitation (i.e.; using trained lay providers or community outreach workers serving as peer-navigators or case managers to support PLHIV); mobile phone appointment reminders and/or actively searching for patients who have missed appointments; and health education.[290, 291, 296-298]

Peer-navigators are defined as, '*trained personnel* (e.g.; nurses, lay counsellors, peers) *who help patients overcome modifiable barriers to care and achieve their care goals by providing a tailored approach to addressing individual needs'*.[299-301] These staff provide practical assistance (e.g.; transportation and coordination of dependents), care facilitation (e.g.; communicate with providers, coordinate care appointments), health literary and psychosocial support, and addressed patient attitudes and beliefs.[299] Peer-navigators maintain an active relationship with the patients, assisting patients to reach care while providing care case management, and they may also provide support and identify those with disease who are lost to follow-up.[289, 302-304] A systematic review of 67 randomised controlled trials largely conducted in the United States, utilising peer-navigators to help patients with various chronic diseases (e.g.; cancer, DM, HIV, CVD, etc.) navigate the healthcare system, concluded peer-navigators do improve processes of care.[299] A study in Kenya reported that over four times as many patients were enrolled in care when they utilised assisted peer-services.[305] Literatures does show a strong social support system - whether from family, friends and/or the greater community - can allow for disclosure, coping and resilience required to mitigate challenges associated with linking to care and initiating treatment. A support system provides a sense of humanity and belonging, and is known to decrease stigmatised beliefs.[306, 307] A

study amongst 559 HIV-infected adolescents and youth in Kenya, showed significant improvements in linkage to and early retention in care after the implementation of peer-navigated services and psychosocial support were offered.[308]

Furthermore, intensified post-test counselling by CHWs;[309] using communication technologies (e.g.; mobile phones and text messaging) to assist with disclosure of patient health status, adherence of treatment and retention in care;[310, 311] and promoting intimate partner notification and partner testing may also increase patient linkage to care.[312-314] While there is evidence that multiple counselling sessions as a care facilitation strategy did not seem to assist with linkage to care, and therefore additional counselling sessions post-diagnosis may not be needed to improve ART initiation,[315] studies utilising both health education paired with mobile phone appointment reminders had varying effects on linkage to care.[293, 294] These combination strategies could have a positive effect on linkage to and retention in care and would need to be further investigated.

Incentives

Lastly, non-cash financial incentives, such as providing transportation vouchers from testing site to care facility[33, 316] or mobile telephone airtime, have been explored to assist with linking patients to care.[290, 291, 317] Studies conducted in Swaziland (providing airtime) and in South Africa (providing transport reimbursement) concluded that these strategies did not link significantly more patients to care within one month.[293, 315]

2.6 BUILDING UPON THE ESTABLISHED HIV TESTING SERVICES PROGRAMME

2.6.1 DEFINING HIV TESTING SERVICES

HTS is blanket terminology for all services offered that are packaged together with HIV testing. These services include counselling – both pre-test information and post-test counselling, the coordination with laboratory services to support QA and the delivery of reliable test results; and the linkage of clients to the required HIV prevention, treatment and care services, as well as other clinical and support services.[318]

Historically, HTS is conducted in a session of approximately 45 minutes – ten minutes for pre-test counselling, 15-20 minutes to conduct the HIV RDT, and 15 minutes for post-test counselling.[319] The South African National HTS Guidelines state that intensive and lengthy

individual risk assessments during the pre-test counselling session is no longer needed or recommended.[23] When pre-test counselling has not been supplied, there have not been any documented, unintended adverse events or consequences. Many providers in government health facilities simply do not have the time to perform detailed risk assessments due to the large number of clients. Pre-test information can be simplified and shared through either individual or group educational outreach sessions, as long as they are presented in an age-appropriate manner.[23, 320] Though group sessions could decrease the HTS pre-test counselling time, group dynamics remain a challenge.[319] Post-test counselling may include individual risk assessments and risk reduction plans dependent on HIV-status.[319]

HTS has increased in South Africa, with more than 4500 public healthcare facilities offering provider-initiated counselling and testing (PICT), following the launch of the national HCT campaign in 2010.[23, 321]

2.6.2 THE RATIONALE FOR INTEGRATING NON-COMMUNICABLE DISEASE SERVICES INTO HTS

In recognizing the impact of NCDs within the general population and the anticipated impact among PLHIV, it is critical to engage in models of integrated screening, prevention and care for both NCDs and HIV. As a chronic communicable disease, HIV has much in common with NCDs. The principles of 'epidemiologic synergy' between NCDs and HIV strongly suggest that NCD control must be addressed if HIV is to be brought under effective control.[322] Chronic diseases require long-term engagement within the healthcare system; sustainable and robust drug procurement processes and effective laboratory monitoring systems; a interdisciplinary workforce, and outreach within communities. Effective diagnosis and management of NCDs, much like HIV, also hinge on successfully addressing behavioural risk factors, supporting self-management and treatment adherence by recipients in care, as well as garnering support from community groups that can complement the services provided at healthcare facilities.

An integrated healthcare system could capitalise on the programme already established for HIV through the adoption of a public health approach to tackle NCDs, heeding the lessons learned from HIV and building on the systems and partnerships already established in many countries in SSA.[4] Ensuring integration of NCD screening and treatment into facility-based HTS, as put forth by NDoH NSPs, National HTS Policy and Guidelines, and WHO Consolidated

Guidelines on HTS, would increase the uptake of both HIV and NCD testing and potentially treatment of individuals with disease and comorbid disease.[48]

2.6.3 EXAMPLES OF INTEGRATED HIV TESTING SERVICES IN LITERATURE

It is important to note that where South Africa has managed to integrate HTS into some services (mainly within antenatal care [ANC], STI and TB clinics), there has been success.[63]

Introducing HTS into ANC was the first example of integrated HTS, and was widely accepted, boosted women's HIV-knowledge, and allowed for more expedited entry into both HIV prevention (e.g.; PMTCT) and treatment (e.g.; ART) services.[90] The current NSP for HIV, TB, and STIs encourages the integration of HTS within ANC, delivery and well-child care settings to ensure PICT of mothers, conduct 100% birth testing of newborns exposed to HIV, and test all children up to 18 months of age to identify those who have acquired HIV through breastfeeding.[13]

Diagnosing STI patients with HIV co-infection is a crucial HIV prevention strategy, and also improves the quality of care for PLHIV. STI care and treatment services are one of the key entry points into HIV prevention and treatment services.[63] The WHO recommended - and South Africa complied - that all TB-control programmes initiate HIV testing for both confirmed and presumptive TB patients.[91] Conversely, standalone HTS provides an opportunity for screening for and early detection of TB and potentially HIV-TB co-infection. The WHO strongly recommends that '*systematic TB screening should be integrated into HTS and offered wherever HIV testing is carried out and to all populations receiving HIV testing, irrespective of their test results*'.[63] All identified persons with TB symptoms should then be referred for confirmatory diagnostic testing according to country guidelines.[92]

Regarding the integration of NCDs within HTS, there have also been successes. As aforementioned, the ICDM pilot yielded positive outcomes. The intention was for the 'ideal clinic' to infiltrate every clinic in South Africa, but the majority of South Africa's healthcare facilities never made the transformation.[43] Five studies within LMICs which integrated an additional health service component into an existing service have indicated that adding on services probably increases service utilisation and outputs of healthcare delivery.[85] These studies depicted at least five models of HIV-NCD integrated care: 1) integrated community-based screening, 2) integration of NCD screening within HIV care facilities, 3) decentralised

HIV-NCD integrated clinic models, 4) differentiated care, and 5) integrated comprehensive healthcare for all. These models will now be described.

Integrated community-based screening has provided a multi-disease screening package for HIV and NCDs in the general population. Human resources and RDT are required for this model. A case study in three rural districts in Uganda evaluated the feasibility and rapid diagnostic yield of testing for HIV, HT, and DM using the integrated community-based screening approach. Healthcare workers trained in HTS conducted the integrated screenings, and individuals who screened as having any disease were then referred to their nearest local clinic. The study found a high yield of newly-diagnosed individuals using this high-coverage approach, though patients spent a median time of 95 minutes being interviewed, screened and counselled.[323] Between 2013-2014 and within 32 communities in Uganda and Kenya, a community health campaign targeting HIV testing paired with door-to-door multi-disease testing campaign (inclusive of screening for malaria, HT, DM and CD4) achieved 89% adult HIV testing coverage.[324] A study utilising mobile HTS units conducting rapid POC screening for HIV, TB symptoms and HT in South Africa obtained a high yield of newly-identified HIV-infected individuals.[325]

There is evidence of PLHIV enrolled in care also being screened for NCDs and NCD risk-factors. A study in Tanzania screened PLHIV for DM, HT, and various NCD risk-factors (e.g.; BMI, waist circumference, physical activity, etc.) within 12 HTS centres in both rural and urban settings. Comorbidity was high, however, linkage to care rates and follow-up clinical outcomes were unavailable.[326]

Decentralised HIV-NCD integrated clinic models have been deemed successful in leveraging the already established HIV infrastructure and health service streams. Existing HIV-trained healthcare providers essentially serve as ICDM providers. An intuitive and clear patient clinic flow is key to ensure efficiency and avoiding the creating of increased workload for providers within this model.[327]

Another model incorporated differentiated care for patients with HIV and/or NCDs. Differentiated care is essentially a client-centred approach; customising care delivery to the individual's needs. It has been found this allows for longer periods between follow-up for stable

patients, which leads to a reduced workload burden for providers and time-related burden for patients.

The integration of HTS and multi-disease screening and health services, such as screening for cardiovascular risk factors have the potential to be beneficial, but need to be evaluated further. The long-term cost-effective impact of these interventions and their associated linkage to care and treatment have not been adequately assessed.[63] Currently, there is no evidence to support integration improves healthcare delivery or health outcomes of patients.[55]

2.7 SUMMARY

The review of literature has highlighted the extent, globally, to which the epidemiologic transition from communicable disease to chronic NCDs has taken place, especially among LMICs, driven by globalization, urbanization and an aging population. The result is an increase in unhealthy behaviours in lifestyle – unhealthy diets, physical inactivity, tobacco use, and excessive alcohol consumption, leading to health conditions – obesity, hypertension, hyperglycaemia, and hypercholesterolemia, which then develop into NCDs, such as CVD and DM, overtime.

The epidemiologic synergy between NCDs and HIV creates a concern for countries with a high burden of HIV, such as South Africa, and there are both global and national policies and guidelines calling for the strengthening and integration of prevention, care and treatment services for both cadres of disease. While there are well-developed, national screening and treatment guidelines for HIV in South Africa, there are no such explicit national guidelines for NCDs and/or NCD risk factors of obesity, HT, hyperglycaemia and hypercholesterolemia, for the general population or for PLHIV.

There are also well-documented health systems failures which create barriers for strengthened prevention, care and treatment services – health system fragmentation, poor supply chain management, lack of trained healthcare professionals, syndromic management, long wait time for results, and passive linkage to care and treatment. Health system strengthening strategies must be employed to combat these barriers. There is some limited evidence that integrated services (a horizontal healthcare system approach), task-shifting, RDT, and active linkage to care strategies may assist in more efficiently identifying people with disease and subsequently

linking them to care and treatment services. Additional studies are needed to support or negate the effects and patient health-health related outcomes of these strategies.

The epidemiologic synergy between NCDs and HIV has ignited the idea of building upon the current resources, partnerships, and programmes which have already been well-established for HIV to tackle NCDs, as well. Both global and local policies, guidelines, and strategic plans call for the integration of NCD screening and treatment into facility-based HTS to increase the uptake of both HIV and NCD testing and potentially of treatment initiation for individuals with both singular and comorbid disease. However, the standardised implementation of integrated NCD-HTS has not yet occurred.

This literature review has identified gaps in research towards which this PhD thesis will contribute evidence-based data. As screening for precursory NCD conditions is not routine care in the general population or among PLHIV in South Africa, this study provides the prevalence of NCD risk factors, HIV and associated comorbid disease among adults in an urban setting within an LMIC. Additionally, this study has implemented and evaluated the health systems strengthening strategies of integrated NCD and HIV screening and referral services, task-shifting of RDT from nurses to lay counsellors, and peer-navigated linkage to care services, all within an HTS programme. In presenting the evidence-based data, policymakers may be informed of critical population health statistics, the success or failure of various health system strengthening strategies, and re-evaluate national health screening and management guidelines, accordingly.

2.8 CONCEPTUAL FRAMEWORK

The strategies employed within the chosen integrated NCD-HTS model for this PhD study drew from three separate health provision strategies: 1) the verticalised healthcare system,[328] 2) the horizontal healthcare system,[328] and 3) the (HIV) care continuum cascade.[329] All three strategies have already been described in depth within this thesis.

The framework created for this thesis can be found in Figure 2-8. It starts with a depiction of what is currently existing in the public healthcare sector: the various continuums of care (the independent, inverse triangular cascades from patient diagnosis to reaching the point of controlled disease) within separate health programmes of a verticalised healthcare system (e.g.;

HIV, STIs, TB, NCDs, cancer). Now, facing the problem of colliding epidemics, patients with comorbidities are disadvantaged within vertical systems, which create process duplication and lead to inefficient health service and delivery.

To assist in the provision of comprehensive health service coverage for those most in need, the framework introduces four strategies (as depicted by the green arrows): integration of services, task-shifting, point of care testing, and active linkage to care. The integration of services creates a horizontal healthcare system, by which all health programmes once separated are now fully assimilated within a single programme and have a more streamlined continuum of care. This is a more community-oriented and/or comprehensive, patient-centred primary healthcare approach.

This thesis hypothesised that the continuum of care would be reshaped by the three latter strategies (task-shifting, point-of-care testing and active linkage to care), catching some of the patient attrition within the cascade. Task-shifting allows for additional healthcare personnel to assist clients, which increases the amount of services provided – in this case, health screening. POC testing, providing same-day results, increases the volume of clients who are informed of their screening results and obtain referrals. Active referral and linkage to care increases the likelihood that a patient has successfully reached his/her referral clinic, been initiated on treatment, and has the disease controlled. Each of these pieces of the framework assist in the creation of an improved healthcare continuum within a stronger, horizontal healthcare system.

It is unrealistic to believe that every PLHIV will voluntarily enter a facility-based integrated NCD-HTS clinic for testing, however, it is thought that through offering integrated health services, more PLHIV will be identified than through standard of care HTS, contributing to the first UNAIDS 90-90-90 target. Through task-shifting of RDT to counsellors rather than relying on clinicians or nurses, 100% of those screened will know their status, and a greater proportion of referred HTS clients with abnormal health screening results – both HIV and NCDs - will be linked to care using the study's active linkage to care strategy as compared to passive referral.

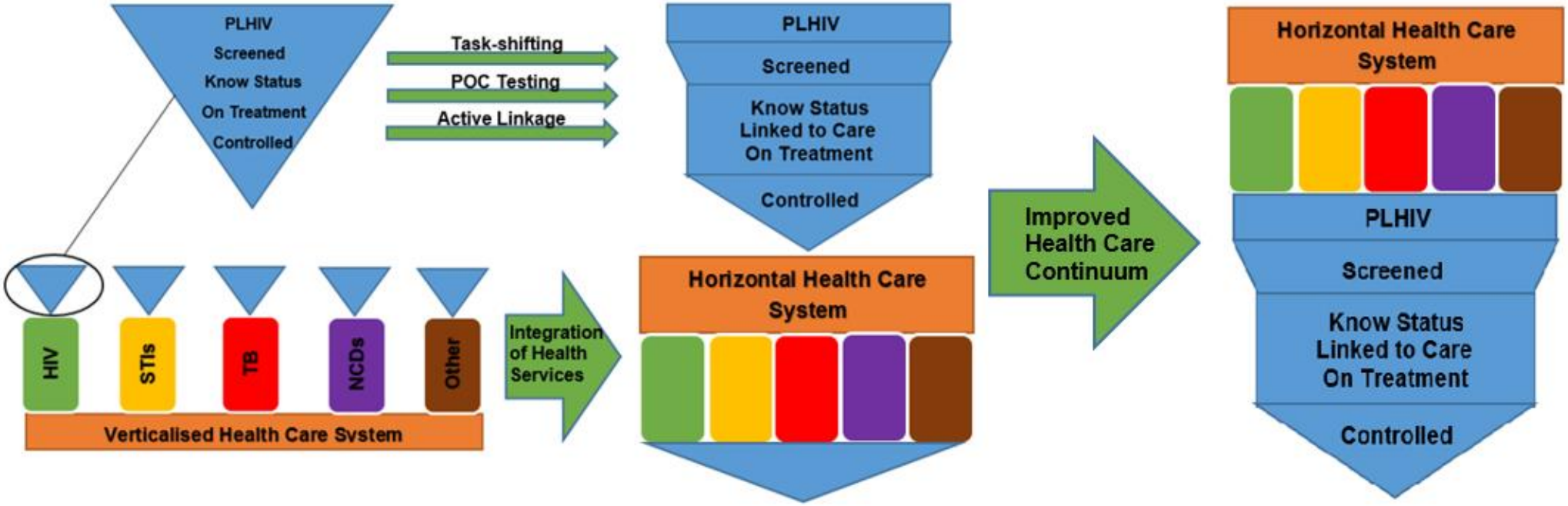


Figure 2-8. Theoretical Framework Illustrating the Effects of Implementing an Integrated NCD-HTS with Task-shifting, Point of Care Testing, and Active Linkage to Care Strategies on the Care Continuum Cascade

3.0 METHODOLOGY

This chapter describes the overall methodological approach for the four inter-linked papers of this PhD Thesis. Details regarding the specific methods for each paper are provided as an appendix (see: Appendix A, Original Papers, II through V).

3.1 OVERVIEW

This PhD study was a prospective evaluation of an integrated NCD-HTS centre incorporating both task-shifting RDT of NCD risk factors to lay counsellors and optional peer-navigated linkage to care and treatment for a convenience sample of walk-in adults within Soweto, South Africa. The integrated NCD-HTS was embedded within a standard of care HTS centre. The overall evaluation consisted of two phase longitudinal study design to compare targeted study measures between the three-month standard of care HTS phase utilising passive referral (19 February to 14 June, 2018) against a subsequent nine-month integrated NCD-HTS phase with active referral (18 June 2018 to 28 March 2019). Due to standard of care HTS being more of a routine, established programme, a shorter timeframe was established for Phase 1. The interventions introduced during the integrated NCD-HTS were new, and being evaluated as part of a pilot study. Therefore, the longer timeframe was decided upon.

The data collection method chosen were structured surveys. There were various data collection tools pertaining to the aforementioned investigations, such as the HTS client demographics form, HTS client health screening results sheet, HTS client clinic exit form, and HTS client linkage to care follow-up form. The data collection tools contained both close-ended and open-ended questions.

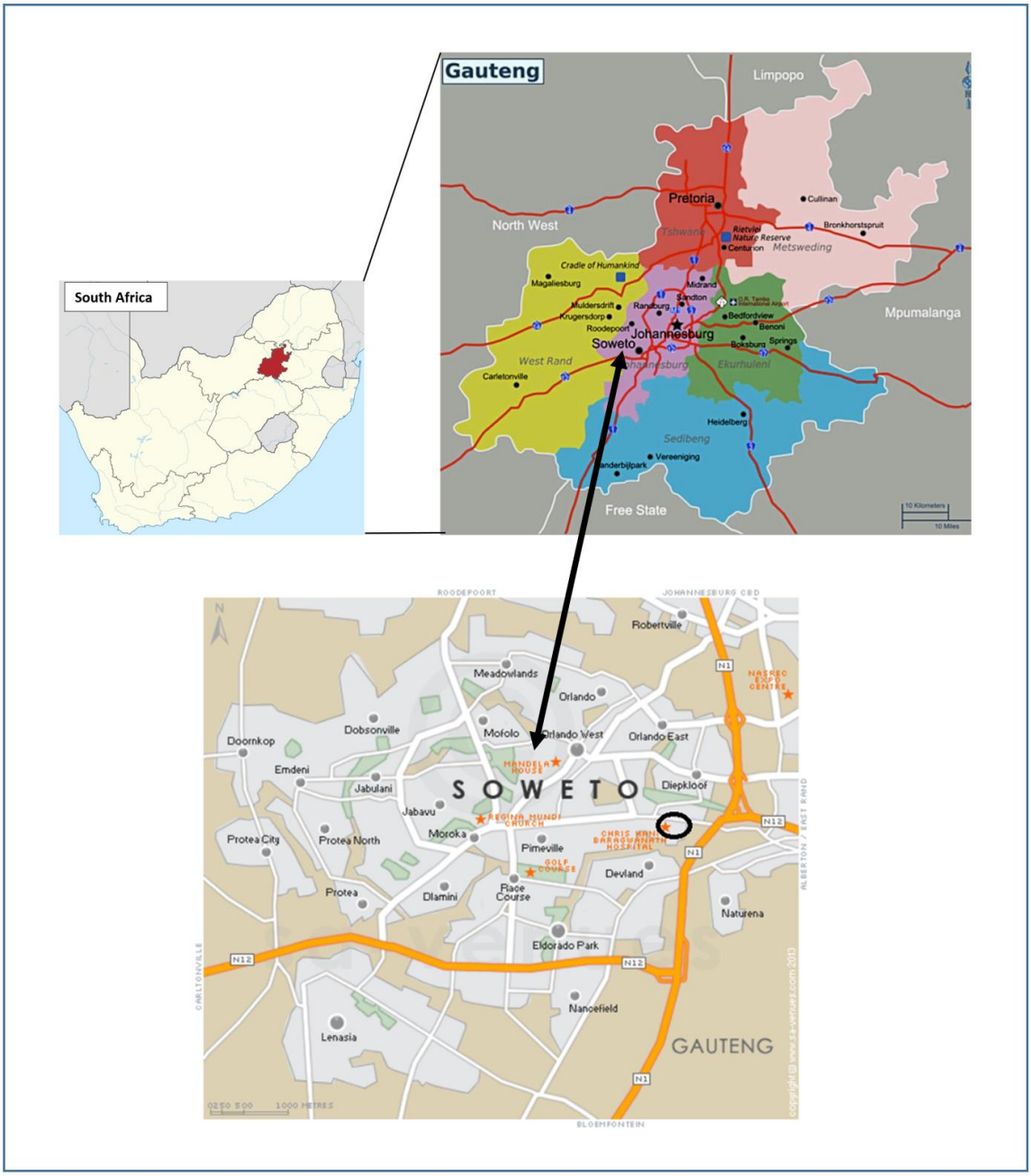
3.2 STUDY SETTING AND SURROUNDING POPULATION

3.2.1 STUDY SETTING

Soweto, the study setting, is the largest group of urban African townships in South Africa, located in the City of Johannesburg Metropolitan Municipality in Gauteng Province, bordering the city's mining belt in the south.[332] By 2003, the Greater Soweto area consisted of 87 townships grouped together into zones.[333] Measuring 200 km^2 and located 15km south west of Johannesburg, it holds a population of about 1.3 million people, which has increased by 48.1% in the last 10 years.[332, 334]

Soweto, an urban township, could be one of the most vulnerable populations to NCD-HIV comorbidities in South Africa. The SADHS has reported that South African townships are known to have a higher HIV prevalence, and urban populations have a higher prevalence of NCD risk factors than the overall national prevalence.[98, 335]

This study was implemented within a facility-based HTS centre operating within the Perinatal HIV Research Unit (PHRU) in Soweto, South Africa. PHRU, one of Africa's leading research centres, is situated at the New Nurses Home of Chris Hani Baragwanath Academic Hospital (Bara Hospital), the largest hospital in Africa and the southern hemisphere and the third largest hospital, globally.[336] . PHRU conducts HIV treatment and prevention, TB and other HIV co-infections research amongst adult, paediatric and adolescent populations of Soweto. PHRU is a research unit of the University of the Witwatersrand and a division of the Wits Health Consortium (WHC).[337] Figure 3-1 shows a map of the study setting.



Sources: www.gautengonline.gov.za; https://www.south-africa-tours-and-travel.com/map-of-johannesburg-south-africa.html; **Soweto Map, SA-Venues.com, with the PHRU circled.**

Perinatal HIV Research Unit, PHRU; HIV testing services, HTS.

Figure 3-1. Map of Soweto and the PHRU Zazi HIV Testing Services Centre

PHRU was chosen as the study site over other facilities, as it has a walk-in, free-of-charge HTS centre located on its ground floor – the Zazi HTS Centre (Zazi). This HTS centre is a well-established provider of voluntary counselling and testing (VCT) and well known within the underprivileged community, which contains key and vulnerable populations. As Zazi is a walk-in facility serving the general population of Soweto, target populations seen within the clinic

have included older adolescents, young women, pregnant and postpartum women, MSM, and couples and partners.

The Zazi (loosely translating from isiZulu to English as '*Know Yourself*') HTS Centre has provided on-site HCT for adults in Soweto since 2001. It also facilitates CD4 count testing for HTS clients not yet initiated on treatment, through the collection of blood samples transported to a referral laboratory for analysis. Zazi initially conducted CD4 count screening as >350 cells/mm^3 was formerly required to start treatment. Now with UTT implemented in-country, Zazi still offers this screening as an indicator of health for HIV-infected clients not yet on treatment. Although government clinics within Soweto should also provide free HTS, at the time of writing, Zazi remains the only service provider of walk-in, free, accessible HTS within the Bara Hospital. HIV treatment is not provided on-site, but HTS clients are given referral letters to local clinics. The existing referral system ensures comprehensive clinical care, treatment and support services, including access to HAART and PMTCT for those who are living with HIV in Soweto and the surrounding areas. There is a network of local clinics which offer free treatment for STIs and NCDs.

3.2.2 SURROUNDING POPULATION: DEMOGRAPHICS AND INFRASTRUCTURE

Black Africans comprise 98.5% of the population in Soweto, while those of mixed-race (a.k.a.; coloureds) and other racial groups (e.g.; Indians/Asians, Whites, etc.) account for 1% and 0.4%, respectively. The population is roughly split evenly by sex – 49.6% are male and 50.4% are female. Eleven of the recognised national languages are spoken, with a large majority of residents conversing in IsiZulu (37.1%), followed by Sesotho (15.5%).[338]

Today, it remains the most populous black African, urban residential area in South Africa.[339] Soweto is mostly composed of old matchbox houses - four-room, low-cost brick houses built by the former government to provide cheap accommodation for black African workers during apartheid. Additionally, hostels were built to house male migrant workers and have since been improved upon, currently existing as flats for couples and families.[340] Informal settlements, created with corrugated iron, also accommodate the rapidly growing population.[339]

The economic development of Soweto was severely stunted by the apartheid government limiting infrastructure and restricting residents to low-income self-employment categories, such as managing general shops and butcheries or hawking goods.[341] Although South Africa

has made strides in reducing this poverty since the lift of apartheid in 1994, the trajectory of poverty reduction has recently reversed (from 2011), threatening to destroy any progress made.[342] Research has shown that as high as 62% of residents within some of the poorest zones in Soweto, such as Orlando East and Pimville, are either unemployed or pensioners.[343] Today, many parts of Soweto, specifically the northwest and southeast areas, still rank among the lowest income households in Johannesburg.[340] Overall, roughly 19% of Soweto's population does not earn an income, while the majority of income earners bring home between R19,601 and R38,200 per year (~USD$1,600-3,110).[338]

The largest proportional majority of households are rented in Soweto (28.6%), with an equal amount of households being owned and either having been fully paid-off or currently being paid-off. Informal settlements or government-provided housing, which are free of charge, equate to 14.3% of the household dwellings.[338] Of these households, 55% reported having piped water, 91% had access to a flush toilet connected to a sewage system, and 93% used electricity for lighting. Nearly every household reported to own a mobile phone (93.4%), 89.9% of families owned either an electric or gas stove for cooking, and televisions were owned by 85.5% of residences. Between one-fifth and one-quarter of houses contained a computer, motor car, and/or satellite television (20.2%, 23.6%, and 24.4%, respectively). Of residents who are at least 20 years of age, only 9.3% have received a higher education.[339]

Soweto is mainly served by the large-spread Bara Hospital.[336] It is spread across 0.7km^2 and contains 3,200 beds,[336] which is nearly three times the World Health Organisation's recommendation for successful hospital management (1,200 beds), and 30 operating theatres.[344, 345] The hospital assists 148,000 ward patients and conducts 42,000 operations, per annum.[344]

In 2014, the former Health Minister opened the Zola-Jabulani District Hospital in Soweto in hopes the facility would help to ease the patient burden on the Bara Hospital. In contrast, it only has 300 beds and three theatres for minor operations such as caesarean sections and appendectomies.[345] The hospital serves non-emergencies presenting from the northern and western communities of Soweto, including Dobsonville, Emdeni, Meadowlands, Moletsane, Mofolo, Zola and Jabulani.[345]

Due to the population of Soweto growing rapidly and the associated healthcare burden, the NDoH has reported that additional hospitals are needed.[345] There are 19 (public) satellite clinics in Soweto, and only a few private hospitals and clinics.[344]

3.2.3 SURROUNDING POPULATION: HEALTH PROFILE

Prior to this PhD study, the most recent unpublished data from Zazi reported that over the calendar year of 2017, 1,130 HIV rapid tests were conducted. While the data collected does not identify the number of unique individuals tested as compared to repeat testers, 52.1% of the rapid tests were conducted on women and 47.9% were on men (n=589 and n=541, respectively). Within the final quarter of 2017, data were collected on age groups. In those three months, 250 HIV rapid tests were conducted; and of those tests, 47 (18.8%) were for persons aged 18-24 years with 33 being young women, a key population. Those HTS clients aged 25-34 years and 50+ years comprised 30.8% (n=77) and 13.2% (n=13.2) of the tests, respectively. The majority of the clients were aged 35-49 years (n=93, 37.2%).[346]

Of the 1,130 HIV rapid tests conducted at Zazi in 2017, 227 (20.1%) screened HIV-infected. Therefore, one could presume the HIV prevalence is higher than 20.1%, since data did not differentiate by repeat testers. Of those who screened as HIV-infected, 66.5% (n=151) were women and the remaining 33.5% (n=76) were men.[346] Zazi had last reported reliable data on client CD4 count in 2013. Out of 900 clients presenting for CD4 screening, 27.4% (n=247) received CD4 results of under 350 cells, which at the time signified eligibility for treatment.[347]

There has not been any previous data collection on the prevalence or incidence of HT, DM, or hypercholesterolemia at Zazi. However, the Women's Initiative in Sexual Health (WISH) study conducted between November 2013 and February 2015, enrolled and screened 143 young women (16–22 years old) from Soweto through the PHRU for various STIs.[348] Of those enrolled, 45% were found to have *bacterial vaginosis* (BV), 65% had human papilloma virus (HPV) (53% being high-risk strains linked to cervical cancer), and 18% had CT.[348] Another study tested 352 youths aged 16-24 years from Durban and Soweto for various genital tract infections (GTIs).[349] The female prevalence for both sites for CT was 18.2%, *Mycoplasma genitalium* (MG) 9.6%, *Trichomonas vaginalis* (TV) 8.1%, *Neisseria gonorrhoeae* (NG) 7.1%.[349] BV prevalence was 53.0% and candidiasis 9.6%. Male CT prevalence was 7.8%, MG 3.3%, TV <1%, and NG 1.3%.[349] By site, the prevalence of non-ulcerative STIs was

higher among females in Soweto compared with Durban (44.1% and 25.0% respectively, p=0.008).[349] Other STI data for men in Soweto is predominantly related to MSM.

Outside of Zazi/PHRU data, the Heart of Soweto Study established a prospective registry of men and women from Soweto presenting with heart disease to Bara Hospital.[350] Preliminary results published in 2006 from information collected on 12,000+ men and women identified CVD in 35% of the individuals, with almost one-quarter of those affected aged below 40 years. Two of the five most common diagnoses overall were HT (54%) and DM (10%).[350] The prevalence of CVD risk factors was very high; only 13% of patients had no risk factors, while 47% of patients were diagnosed with HT and were obese.[350] The SADHS 2016 reported about one in five residents of Gauteng Province are severely obese (BMI ≥ 35).[98]

3.3 DATA SOURCES, SAMPLING AND SAMPLE SIZE

All data is owned by the PHRU, part of the WHC, which is a wholly owned Company of the University of the Witwatersrand, Johannesburg (South Africa) under its Faculty of Health Sciences. The PhD candidate conceptualized, implemented and managed both sets of operations (PHRU Zazi HTS health screening programme and its embedded PHRU Evaluation of Zazi Study) relating to each of the data sources utilised for the PhD, as detailed in this thesis section.

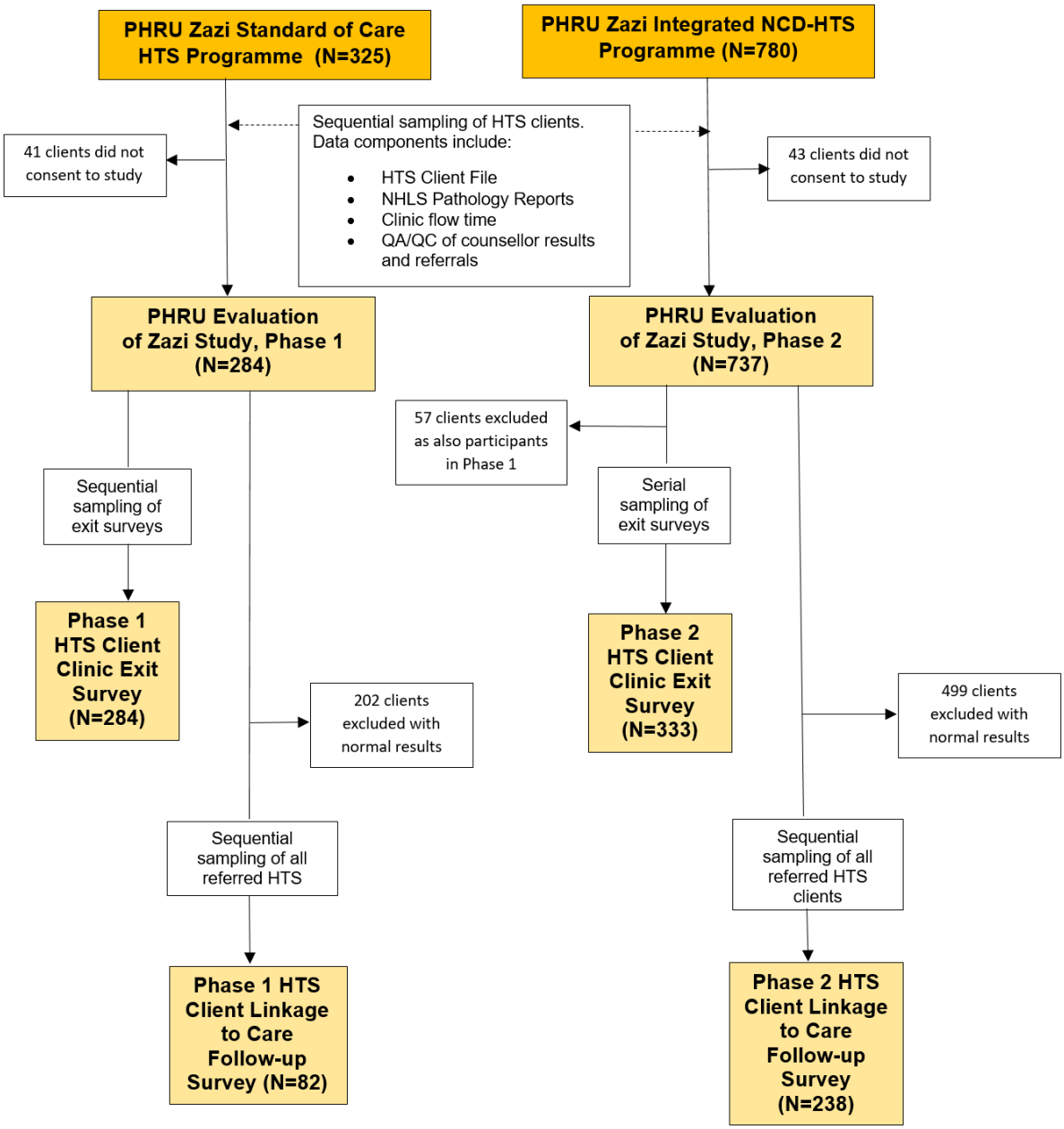
3.3.1 DATA SOURCES AND SAMPLING

The study uses data from the following two main sources (see Figure 3-2):

- *PHRU Zazi HTS health screening programmatic data* (standard of care HTS from 19 February to 14 June, 2018; integrated NCD-HTS from 18 June 2018 to 28 March 2019). This involved the sequential data sampling of walk-in, adult, Zazi HTS clients, aged 18+ years, who consented to the HTS health screening programme and for their data to be used in research. The HTS health screening programme data included all data collected within the Zazi HTS client file during the HTS clinic visit within the following, five paper forms: 1) HTS client demographics, 2) HTS counselling guide, 3) family (health) history and client behavioural, 4) HTS client health screenings results report, and 5) HTS client referral sheet. The HTS client file also included processed electronic pathology results (for CD4 count) delivered and printed from an electronic database managed by NDoH – the National Health Laboratory Services (NHLS) InterSystems' TrakCare Laboratory information System

(LIS). The data collected within this data source enabled the investigation of the following PhD study objectives – disease prevalence patterns by age and sex, quality of task-shifting of RDT of NCD risk factors to lay counsellors, and feasibility of integrating RDT of NCD risk factors within standard of care HTS clinic flow.

- *PHRU Evaluation of Zazi study data.* This data source included two subsets of the HTS clients identified within the PHRU Zazi HTS health screening programme who subsequently consented to and enrolled within the PHRU Evaluation of Zazi study. This data source contained both the HTS client clinic exit form data and HTS client linkage to care follow-up form data. All study participants completed HTS client clinic exit forms after their HTS clinic visit (therefore the same data collection dates as the PHRU Zazi HTS health screening programmatic data source for each HTS phase). All study participants who were referred to care or treatment services for at least one abnormal health screening result completed HTS client linkage to care follow-up forms (standard of care HTS from 19 May to 14 September 2018; integrated NCD-HTS from 18 June 2018 to 28 June 2019). This data source involved the sequential sampling of standard of care HTS and the serial sampling of integrated NCD-HTS client clinic exit forms, and the sequential sampling of all HTS client linkage to care follow-up forms. The data collected within this data source enabled the investigation of the following PhD study aims – HTS client level of satisfaction with each HTS model's HTS services and clinic flow time, proportion of HTS clients linked to care by mode of referral (i.e.; passive vs active), barriers to HTS client linkage to care and initiation of treatment across all chronic diseases.



Perinatal HIV Research Unit, PHRU, HIV testing services, HTS; Non-communicable disease, NCD; National Health and Laboratory Service, NHLS; Quality assurance/quality control; QA/QC

Figure 3-2. Flow Chart of the Two Data Sources Used and Their Linkages

3.3.2 DATA SAMPLING AND SAMPLE SIZE

Figure 3-2 shows the different data samples for this study.

3.3.2.1 PHRU ZAZI HTS Health Screening Progamme Data

This programmatic sample comprised all male and female adults, aged 18 years or older, who walked-in voluntarily to the Zazi HTS Centre for free health screening services, and who consented to the HTS health screening programme and for their data to be used in research. There were separate informed consent forms for standard of care HTS and integrated NCD-HTS screening measures. HTS clients who refused to consent to their data being captured were still able to access the health screening services they desired and were eligible for through National Guidelines. HTS clients who presented to the clinic in a very ill state, needing immediate emergency medical attention, were immediately referred to the relevant clinic/hospital for the appropriate assessment and treatment (e.g.; there is capacity at PHRU to refer infants, children, and younger adolescents for specialized HIV testing services).

The purpose of this programmatic sample was to review HTS client files and health outcomes for an entire HTS client population. Therefore, the maximum sample size was the full 100% of eligible, consenting HTS clients.

While a sample size was not required for programmatic data review, a sample size estimate was still conducted. As Zazi serves walk-in HTS clients from the population of Soweto, the sample size was determined using a one-sample approach and estimates derived from prevalence data from the South African general population. STI and TB prevalence were not included in this sample calculation, as the programme did not conduct diagnostic screening for these diseases. Estimates were determined using the following formula without finite population correction: $n=Z^2P(1-P)/d^2$; where n=sample size, Z=z-statistic at 5% level of significance, P=prevalence of disease, and d=margin of error (or difference). Table 3-1 provides the sample size estimates for the various diseases screened for and data included in the Zazi HTS health screening programme, using the estimated population of Soweto at the time the sample size calculation was conducted (1.2 million; currently, the population is around 1.3 million).

Table 3-1. Sample Size Estimates for ZAZI HTS Programmatic Data

Prevalence	Margin of Error (or Difference)			
	3%	5%	8%	10%
HIV **M: 9.9%** **F: 14.4%**	M: 381 F: 527	M: 138 F: 190	M: 54 F: 74	M: 35* F: 48
HT **M: 11%**	M: 418	M: 151	M: 59	M: 38*

F: 14%	F: 514	F: 186	F: 73	F: 47
Overweight/Obese BMI **M: 29.2%** **F: 56.6%**	M: 883 F: 1049	**M: 318** **F: 378**	M: 125 F: 148	M: 80 F: 95
High Blood Glucose/DM **M: 4.5%** **F: 4.5%**	M: 184 F: 184	M: 67* F: 67*	M: 26* F: 26*	M: 17* F: 17*
Hypercholesterolemia **M: 23.8%** **F: 30.9%**	M: 775 F: 912	M: 279 F: 329	M: 109 F: 129	M: 70 F: 83

***Assumption normality is not suitable at proposed population**
Male, M; Female, F; Human immunodeficiency virus, HIV; Hypertension, HT; Body mass index, BMI; Diabetes mellitus, DM.

The largest estimated sample size calculated was 696 individuals (318 males and 378 females), with a 5% margin of error. For planning purposes, we assumed 60% of HTS clients would be female and 40% male.[347] Our resulting study sample exceeded this estimated sample size benchmark.

3.3.2.2 PHRU Evaluation of ZAZI Study Data

Zazi HTS Client Clinic Exit Forms

As per the Zazi HTS health screening programmatic sample size, all 1,105 HTS clients (325 for standard of care HTS and 780 for integrated NCD-HTS) were approached for consent into the embedded PHRU Evaluation of Zazi study. Enrolment hinged on the HTS client meeting the inclusion criteria as per Table 3-2, listed within a Study Criteria Checklist, and consenting to the study elements (HTS client clinic exit form and HTS client linkage to care follow-up forms) through a study informed consent form.

Table 3-2. Inclusion Criteria for ZAZI HTS Clients

Inclusion Criteria
Willing to have contact information collected and used for linkage to care follow-up (i.e., telephone number, address of residence, place of employment and other locator information)
Have an activated mobile or landline telephone, or access to a mobile or landline telephone
Agree to complete an HTS client clinic exit form in-person after the clinic visit and prior to leaving the Zazi HTS Centre
Agree to complete client linkage to care follow-up form either in-person after being peer-navigated to care and treatment services or telephonically at follow-up time points
Agree to have their data collected and used in aggregate data analysis for research purposes
Able to communicate in English, Sesotho, and/or isiZulu
Capable and willing to provide written informed consent to participate in the Zazi Evaluation Study

***Perinatal HIV Research Unit, PHRU; HIV testing services, HTS**

Only those HTS clients who consented to the subsequent study filled out the HTS client clinic exit form during each HTS phase. As data stemming from both open- and close-ended questions is not suited to a pre-determined sample size, HTS client clinic exit forms were collected for the full duration of each HTS model. The sampling approach for analysis ended up being sequential sampling within standard of care HTS, including all data collected. For integrated NCD-HTS, serial sampling was implemented, allowing for data to be reviewed and analysed monthly, using chronologically collected data. The sample was deemed complete once data analysis showed consistent results deeming the data endpoint could be closed-out. The final HTS client clinic exit form sample size was 284 surveys for standard of care HTS there were 333 forms for integrated NCD-HTS (N=617).

Zazi HTS Client Linkage to Care Follow-Up Surveys

The sample size for the HTS client linkage to care follow-up form depended on study participants having at least one abnormal screening result. Therefore, only those participants with at least one referral for care and treatment completed HTS client linkage to care follow-up forms. Follow-up continued for a maximum of three months post-clinic visit (standard of care HTS follow-up was conducted between 19 March and 14 September 2018; integrated NCD-HTS follow-up occurred between 18 June 2018 and 28 June 2019). The final HTS client linkage to care follow-up form sequential sample size was 82 and 238 surveys (N=320) for standard of care and integrated NCD-HTS, respectively.

3.4 PHD STUDY MEASURES AND DATA COLLECTION FROM BOTH DATA SOURCES

A summary of the name and content of all source documents used to collect data for both data sources utilised within this PhD is in Table 3-3.

Final source documents were developed over a 12-month period in consultation with both doctoral supervisors, the CDC (as the sponsor), and the University of the Witwatersrand Human Research Ethics Committee (Medical) (Wits HREC). It was ensured through multiple mock data collection runs that all questions were worded properly and that the time it took to gather the information was reasonable. The HTS Client Contact Information Sheet, HTS Client Demographics Form, and HTS Client Health Screening Results Report were adapted from standard PHRU study-related templates. The Zazi HTS Counselling Guide was structured to contain all required topics for pre-test, post-test and risk-reduction counselling (inclusive of

HIV risk-reduction modalities, such as provision of condoms and discussion of voluntary MMC), as recommended by the National HTS Guidelines.[2]

After receiving both CDC and Wits HREC approval of all source documents (see Appendix C), specific documents which could be given to and/or read by an HTS client (e.g.; HTS Health Screening Programme and Study Consent Forms, HTS Client Contact Information Sheet and HTS Client Demographics Form, and HTS Client Clinic Exit Form) were sent to Dilicom, a local languages and communications company, for translation and back-translation into Sesotho and isiZulu.

Prior to the HTS health screening programme and study implementation, the clinic team was introduced to and trained on the use of all data source documents by the doctoral candidate. As counsellors, the enrolled nurse, and peer-navigators were to collect data in real-time; data capturing/collection training entailed going through each tool, question by question, and discussing possible HTS client responses, including current terms in common usage, and how to properly capture data using Good Clinical Practice (GCP).
The following subsections detail the PhD study measures for which data was collected within each source document and how data collection was conducted.

Table 3-3. Data Points per Data Source, by Source Document

SOURCE DOCUMENT	SOURCE DOCUMENT CONTENTS	APPENDIX
FIRST DATA SOURCE: ZAZI HTS HEALTH SCREENING PROGRAMME		
HTS Client Demographics Form*	HTS client demographics	D
HTS Client Counselling Guide*	HTS phase-specific; includes pre-test, post-test and risk-reduction counselling	D
HTS Data Collection Form*	Includes HTS client family health history and behaviour, and STI and TB symptoms screening	D
HTS Client Health Screening Results Report*	HTS phase-specific HTS client health screening results	D
HTS Counsellor Recommended Referral Sheet	HTS phase-specific; contains counsellor-recorded recommended HTS-client referrals, including if the client (female) wants Chlamydia rapid testing, if in integrated NCD-HTS. Sheet also contains nurse's QA/QC of recommended referrals against the Results Report.	D
CD4 Count Laboratory Results	HTS client CD4 count results, as delivered by NHLS	Not Applicable
SECOND DATA SOURCE: EVALUATION OF ZAZI STUDY		

HTS Client Clinic Exit Form	Phase-specific; collected data on HTS client acceptability and satisfaction with HTS model	D
HTS Client Linkage to Care Follow-Up Form	Phase-specific; collected data on HTS linkage to care and initiation of treatment; and preference regarding passive or navigated linkage to care, if in Phase 2	D

***Includes start and stop times within HTS clinic flow**
HIV immunodeficiency virus, HIV; Sexually transmitted infections, STIs; Tuberculosis, TB; Non-communicable diseases, NCDs; Quality assurance/quality control, QA/QC; National Health Laboratory Service, NHLS.

3.4.1 PHRU HIV TESTING SERVICES HEALTH SCREENING PROGRAMME DATA

The PHRU HTS Health Screening Programme data source collected study measures relating to HTS client demographics, behavioural risk factors, HTS client health screening history, HTS health screening results, quality of task-shifting RDT of NCD risk factors and provision of referrals to care and treatment services to lay counsellors, and feasibility of integrating RDT of NCD risk factors into standard of care HTS. All data was initially collected on paper source documents; or if a laboratory result, it was extracted from the associated laboratory results reporting system, printed and filed as a paper source document once received. The data was subsequently captured into the study database – research electronic data capture (REDCap).

The doctoral candidate held five, mock client visits prior to the launch of each HTS phase. During these mock visits, the doctoral candidate served as the faux HTS client with a pre-determined predisposition (e.g.; pregnant female, to test HIV-infected with high BP, and present with one TB symptom and two STI symptoms). The clinical staff member assigned to interact with the faux HTS client rotated, but all clinical staff members were present and collected their own data on their own set of paper forms. After each mock visit, the doctoral candidate reviewed all data collected from staff, identified any misunderstandings/errors, and retrained the study team on salient points.

3.4.1.1 HTS Client Demographics

HTS client demographic study measures for which data were collected are listed within Appendix A, papers II and III, under *Study Measures*. HTS client demographics data were either self-collected by literate clients in the HTS reception area or if illiterate, data was collected with the help of the HTS counsellors once in the counselling room (during standard of care HTS) or peer-navigators within reception (during integrated NCD-HTS).

3.4.1.2 HTS Client Health Screening History

Once within the HTS counsellors' room, the counsellors asked and then recorded answers to health screening history question using the Zazi HTS Family History and Client Behaviour Form. Questions included, had the client ever been diagnosed any condition (i.e.; high blood pressure/hypertension, high blood sugar/diabetes, high cholesterol, HIV); and of so, had they ever been on treatment for any of those conditions. From this data and the subsequently taken health screening results, the following categories of HTS clients were determined (and defined within Appendix A, paper III, under *Study Measures*): *Newly diagnosed, previously diagnosed, controlled disease, and uncontrolled disease.*

3.4.1.3 HTS Client Health Screening Results

Clinical data was collected by the study counsellors and enrolled nurse or consulting clinician. The counsellors collected all of the HTS client health screening results for those screenings they conducted (i.e.; height, weight and BP measurements; HIV RDT; and symptoms screening for STIs and TB within standard of care HTS; with the addition of BMI categorization and blood glucose and TC RDT within integrated NCD-HTS). The nurse or consulting clinician accessed the CD4 count results received from the laboratory.

Height, Weight, BMI Calculations, and BP Measurements

The counsellor measured the HTS client's weight in kilograms (kgs) and height in centimetres (cms), using an electronic scale and a wall-mounted stadiometer located within the corridor directly outside of the counsellors' private office space. If within integrated NCD-HTS and once back within the counsellor's office, the counsellor also discussed the HTS client's BMI classification using a BMI chart (Figure 3-3). (The actual BMI result was auto-calculated within the database once HTS client height and weight data were entered at a later time).

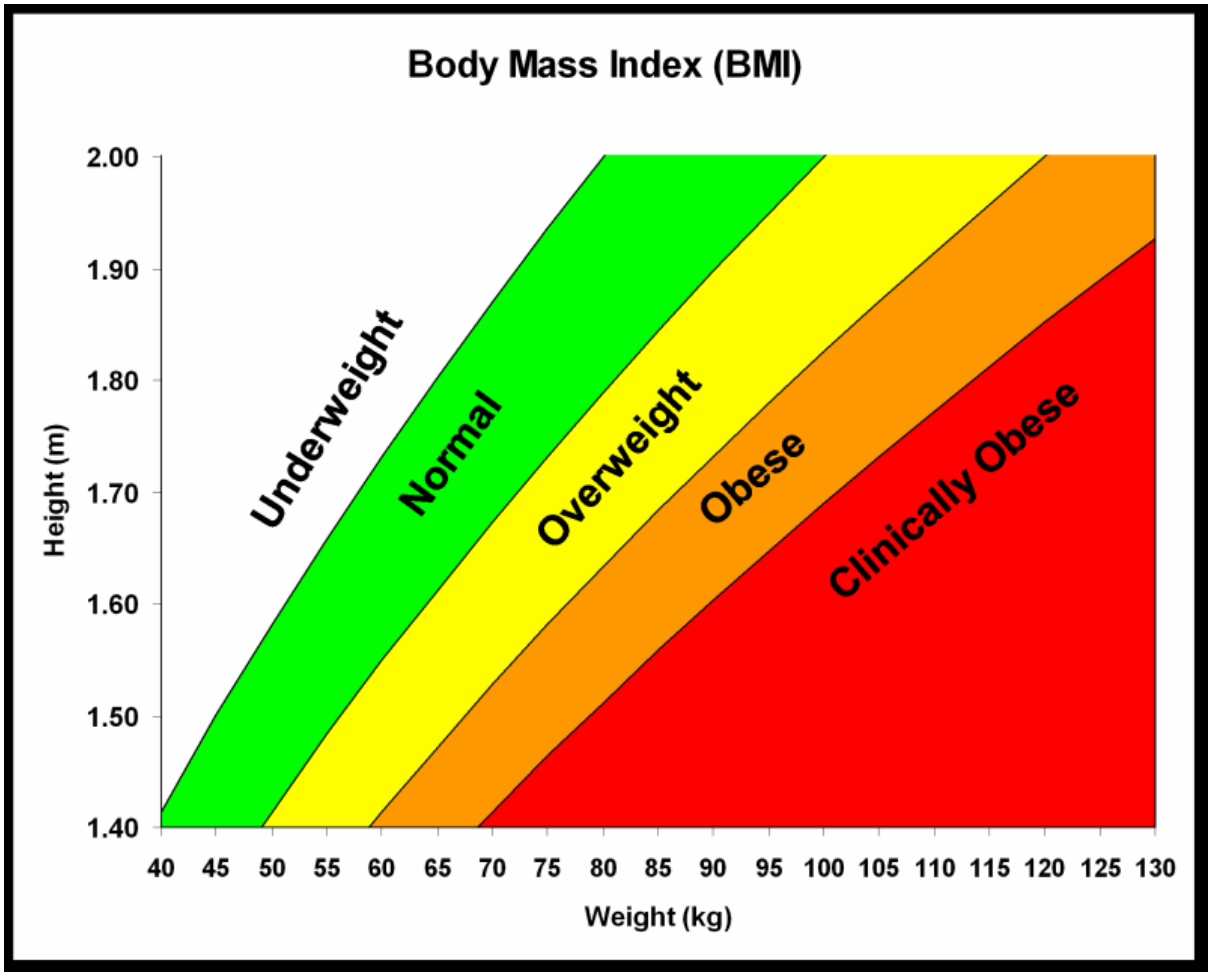


Figure 3-3. Body Mass Index Categories by Height and Weight

BP readings were taken by the counsellors using automated BP cuffs and monitor. If an abnormal reading was obtained (see Table 3-4), the counsellor waited five minutes before repeating the reading to confirm the abnormal result. Both results were recorded.

Rapid Diagnostic Testing of HIV, Blood Glucose and Cholesterol

The counsellors then conducted all fingerprick RDT (HIV rapid testing only, if standard of care HTS; and HIV, both RPG and average HbA1c, and TC, if within integrated NCD-HTS). Only one finger prick was necessary to conduct all preliminary fingerprick RDTs. If a confirmatory HIV test was required, a second fingerprick was performed.

Screening for HIV was initially conducted using the ABON^{TM} Biopharm HIV 1/2/0 Tri-Line HIV RDT kit (Hangzhou, Co., Ltd.). Confirmatory HIV testing was conducted using the First Response® HIV 1-2-0 Card Test (Premier Medical Corporation Ltd.).

The HbA1c testing was performed using a POC machine, the *Hemocue HbA1c 501 Analyzer*, which is certified according to the International Federation of Clinical Chemistry & Laboratory Medicine (IFCC) and the National Glycohaemoglobin Standardisation Programme (NGSP) and approved for use in South Africa.[351] It ensures that the system has a measuring range of 20-130 mmol/mol (IFCC) or 4.0-14.0% (NGSP) to ensure the quality of the tests.[351]

Two, separate handheld POC machines were used to test random glucose and TC using testing strips. The random glucose RDT machine was the *Multicare IN*, and full lipid profiles were screened by the *LUX Multiparameter Device*, both procured from *LABSTIX Diagnostics*. Both machines are CE approved (a certification mark indicating conformity with health, safety, and environmental protection standards for products sold within the European Economic Area [EEA])[352] and were approved for use in South Africa by the NDoH.

Screening for STIs and TB Symptoms and NCD Risk Behaviour

Within the private counselling room while waiting for the RDT screening results, the counsellors conducted the Zazi HTS Family History and Client Behaviour Form, which incorporated the standardised NDoH symptoms screening for STIs and TB, and contained questions surrounding alcohol and tobacco use. The questions surrounding alcohol and tobacco use were taken from the validated 2003 SADHS.[27] The questionnaire also asked questions about HIV, STI and TB testing and treatment history. The HTS client was then probed about personal and family-related diagnosis and treatment history of HT, DM, hypercholesterolemia, and CVD (see section 3.4.1.2 HTS Client Health Screening History).

CD4 Count

For HTS clients who received a result of HIV-infection and self-reported that they had not yet been initiated on treatment, CD4 count analysis was made available. The nurse conducted phlebotomy for CD4 count analysis (sample sent to the NHLS for processing using the PanLeucogating [PLG] technology for CD4 enumeration) for HIV-infected clients not yet initiated on ART. All CD4 count results from the NHLS had to be extracted from the electronic NDoH NHLS InterSystems' TrakCare LIS. The nurse was granted password-protected access into the online system to check upon the receipt of results. All results contained client name, date of specimen arrival at NHLS, and date results were made available on TrakCare. Typically CD4 count results were posted within the system one business day after phlebotomy was conducted and specimen couriered. Upon logging into the system, the nurse printed the

available results and filed them in the HTS client file as a source document, to be entered directly into the study database at a later time.

3.4.1.4 Quality of Task-Shifting Rapid Diagnostic Testing and Referrals to Lay Counsellors

To assess the quality of the task-shifting of RDT and provision of referrals to treatment and care for NCD risk factors to lay counsellors, the nurse performed a QA/quality control (QC) audit on 100% of the HTS client health screening results and recommended referrals to care and treatment that were collected and recorded by the counsellors. The criteria for referring an HTS client to care and treatment services for abnormal health screening results are outlined within Table 3-4. Abnormal results were defined and referrals conducted as per national guidelines.

Table 3-4. Treatment and Care Services and Referral Criteria

Health Screening	Abnormal Result	Referred?
BMI	BMI ≤ 18 or 25 ≤ BMI	None
BP	More than 140/90 Less than 90/60	Yes, to local clinic of choice
Total Cholesterol (TC)	TC > 5 mmol/L TC = 'Low'*	Yes, to local clinic of choice
Blood Glucose	IF random blood glucose > 11.0 mmol/L, AND/OR IF average blood glucose ≥ 6.5 mmol/L, OR 'Low'*	Yes, to local clinic of choice
Syndromic STI	Identify 1+ symptom	Yes, to local clinic of choice
Syndromic TB	Identify 1+ symptom	Yes, to local clinic of choice
HIV	Positive test result	Yes, to local clinic of choice

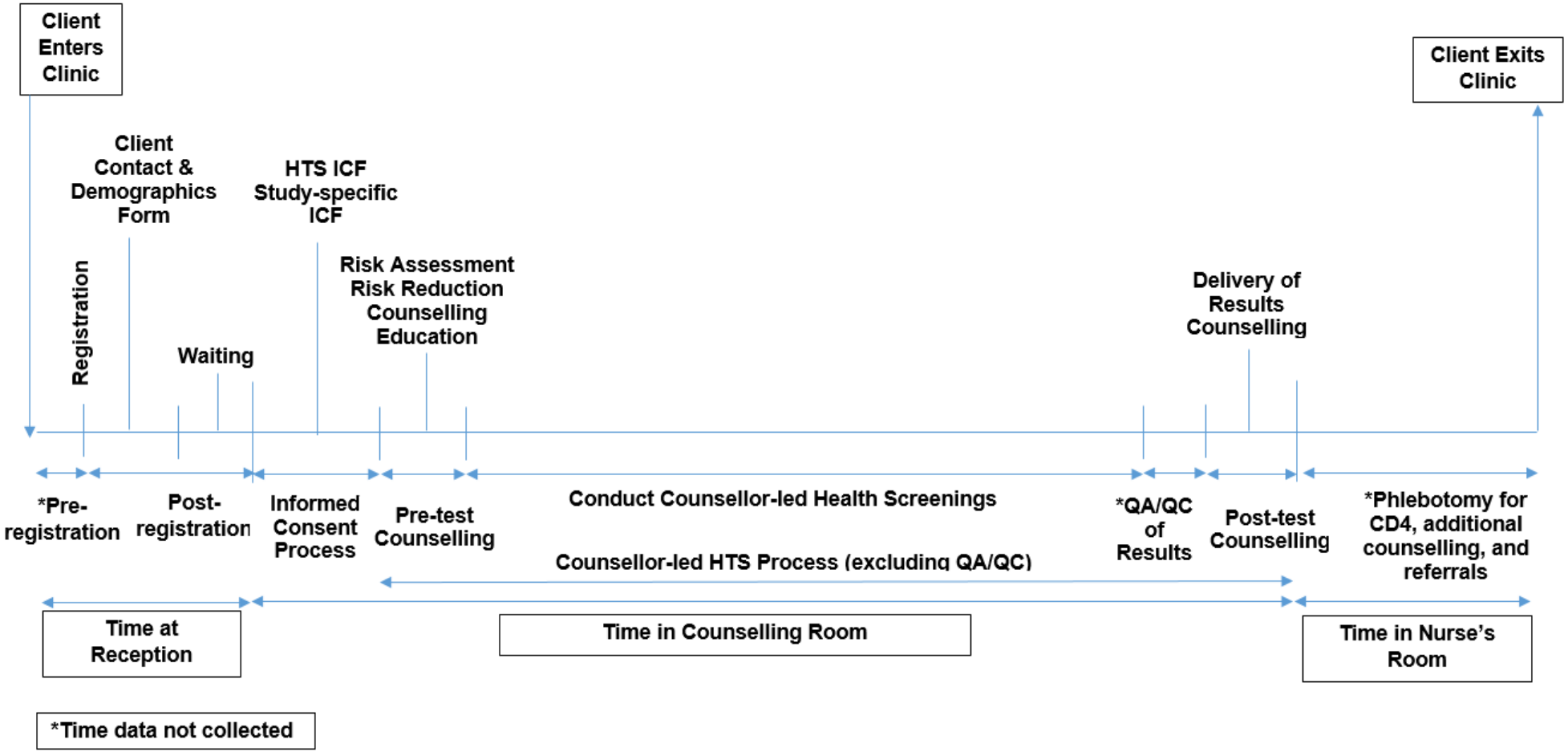
***As read by POC RDT**
Body Mass Index, BMI; Blood Pressure, BP; Sexually Transmitted Infections, STIs; Tuberculosis, TB; Human Immunodeficiency Virus, HIV.

The nurse tick-marked 'Correct' or 'Incorrect' on the HTS Recommended Referral Sheet for each screening result and paired referral, indicating the quality of counsellor-led screenings/referrals. If required, the nurse made corrections on both forms (the HTS Client Health Screening Results Report and the HTS Counsellor Recommended Referral Sheet). Once to satisfaction, the nurse signed off on each form, and filled in, printed and signed the HTS

client referral letter, which indicated the counsellor was able to disclose results to the HTS client.

3.4.1.5 Feasibility of Integrating RDT of NCDs into Standard of Care HTS Clinic Flow

The feasibility of integrating RDT of NCD risk factors into standard of care HTS was investigated through measuring its impact on clinic flow time. Clinic flow start and stop time measures (in minutes) were recorded by clinic staff (receptionist for post-registration timeframe, and counsellors for time spent in counselling room) in real-time on HTS client file source documents after direct observation of a computer's clock. Clinic flow is depicted within Figure 3-4. Pre-registration time, time taken for QA/QC of results, and time spent within the nurse's room (for phlebotomy for CD4 count, provision of referral letters and additional counselling within both HTS phases) was not reported. Independent sections of the clinic flow for which time was collected were defined as follows (and defined within Appendix A, paper IV): *time spent at reception, post-registration; for pre-test counselling*; *conducting health screenings; for post-test counselling; and total time for counsellor-led HTS process*.



HIV testing services, HTS; Informed consent Form, ICF; Quality assurance / quality control, QA/QC

Figure 3-4. HTS Client Clinic Flow

3.4.2 PHRU EVALUATION OF ZAZI STUDY DATA

This data source centred around study measures on HTS client satisfaction of HTS-phase services provided and clinic flow time, and on linkage to care and treatment initiation. Similar to the first data source, the Evaluation of Zazi Study data was also initially collected on paper source documents. The data was subsequently captured into REDCap.

Prior to the launch of each HTS phase, both counsellors and peer-navigators underwent a mock telephonic follow-up call data collection training procedure for the HTS client clinic exit surveys and linkage to care follow-up surveys. After each mock visit, the doctoral candidate reviewed all data collected from staff, identified any misunderstandings/errors, and retrained the study team on salient points.

3.4.2.1 HTS Client Clinic Exit Form Data

The purpose of the HTS Client Clinic Exit Form was to collect data on HTS client level of satisfaction study measures. In responding to this survey, HTS clients provided their perspectives regarding quality of counselling, screenings and referrals; reasons for their choice in type of linkage to care and treatment services (passive vs. active referral), if in integrated NCD-HTS; rate their emotional and physical discomfort during procedures; and provide overall impressions and satisfaction of the HTS Centre. The structured HTS Client Clinic Exit Form was developed to consist of both close-ended questions and open-ended questions for free response to assess client satisfaction with each clinic model. The close-ended questions included a five-point Likert format with differing responses for various questions. The Likert responses were designed to assess client satisfaction with each clinic model's HTS process (i.e.; pre- and post-test counselling, and preparedness for and level of comfort/discomfort during screening procedures), the helpfulness of speaking with the nurse, and overall satisfaction of each clinic model. Time satisfaction was also assessed throughout the clinic flow. The responses to the open-ended questions helped us to further understand the responses to the close-ended questions. Where able, the same questions were asked in both standard of care HTS and integrated NCD-HTS Client Clinic Exit Forms. Given that additional services were provided during integrated NCD-HTS, the associated survey contained additional questions. Both close-ended and open-ended questions can be found within Appendix D, which contains the HTS Client Clinic Exit Form.

The form was provided to HTS client study participants after they had received their HTS screening results and referral letters, which concluded the HTS client's clinic visit. Data was

collected prior to the HTS client leaving the HTS Centre in both HTS phases. The forms were given to the HTS client by either the counsellors or the nurse – whomever was the last staff member to receive the HTS client. If the HTS client was literate, as assessed during the informed consent process, the survey was self-administered in the waiting room. If the HTS client needed assistance, either a counsellor (during standard of care HTS) or peer-navigator (during integrated NCD-HTS) sat with the HTS client to administer the form and record HTS client responses. Once completed, the form was handed to the clinic receptionist, who inserted the form into the HTS client file as a source document. The HTS client was then free to leave the HTS clinic.

3.4.2.2 HTS Client Linkage to Care Follow-Up Data

The purpose of the HTS Client Linkage to Care Follow-up Forms was to collect data on the HTS client linkage to care and treatment initiation study measures. Data was collected and captured by either the study counsellors (during standard of care HTS) or the peer-navigators (during integrated NCD-HTS).

Within standard of care HTS, once HTS clients received their post-test counselling and referral letters, the HTS clients were left to attend their care and treatment referral clinics on their own, as per standard of care passive referral. During integrated NCD-HTS, the nurse shared two options with all referred HTS clients: 1) choose passive, self-linkage to care, as per standard of care HTS, or 2) utilise the offered service of active, navigated linkage to care. Peer-navigators were paid, clinic-based staff who, if requested, physically accompanied the HTS client from the HTS clinic to their local referral clinic of choice within the unbranded HTS study vehicle, which had an assigned study driver. This active linkage to care service was a standing offer to the HTS client for uptake at any time between the HTS client clinic visit and three months after the clinic visit. If the HTS client preferred active linkage to care, the nurse first determined if the HTS client preferred a male or female peer-navigator and then introduced the HTS client to his/her assigned staff member.

The assigned peer-navigator probed for when the HTS client would like to attend their referral clinic, noting preferred date and time within their diary. On the agreed upon date and time, the peer-navigator accompanied the HTS client either from the HTS clinic (typically if same-day) or from their home (typically if set for another day) to the referral clinic. If able to, the peer-navigator remained with the HTS client in the referral clinic reception area until seeing that a

client file had been opened. However, due to confidentiality purposes, the peer-navigator was never able to accompany the HTS client into the actual referral consultation.

The structure of the HTS Client Linkage to Care Follow-up Forms was similar to the HTS Client Exit Forms. These forms were HTS phase-specific, structured, and consisted of both close-ended questions with five-point Likert response format, and open-ended questions for free response. Clients were asked if they attended any of their referral appointments and initiated on any treatment, and if not, why not; and to provide their perspectives regarding preferences and reasons for their choice in type of linkage to care and treatment (passive vs. active).

For standard of care HTS, all follow-up forms were conducted by the counsellor telephonically, from the privacy of their office. The first follow-up call was conducted one month after the HTS client's HTS clinic visit. If there were any outstanding referral appointments identified as yet to be reached, the follow-up call was repeated for those specific referrals at month two, and then at month three, if needed.

Peer-navigators conducted the HTS Client Linkage to Care Follow-Up Form during integrated NCD-HTS telephonically from the privacy of the nurse's office. If after the HTS clinic visit, an HTS client chose active linkage to care, the peer-navigator made the first follow-up call at the end of that day (i.e.; same day as clinic visit). If there were still outstanding referral appointments identified as yet to be reached, the HTS client was asked if they wanted the help of a peer-navigator for the remaining referrals. If so, an appointment was scheduled. With any outstanding referral appointments, the survey was repeated at two weeks, one month, two months and three months, if needed.

All telephonic calls served to actively engage or re-engage clients into care and treatment services to help with retention in the care cascade. *Successful linkage to care* and *successful initiation of treatment* were defined as HTS client self-reported attendance of referral appointment and treatment initiation within one month of HTS clinic visit. *Delayed linkage to care* and *delayed initiation of treatment* were defined as between one and three months post-clinic visit. A HTS client for which follow-up contact was not successful (i.e.; the HTS client did not answer their mobile phone) or who had not yet reached his or her referral appointment within three months was defined as *lost to follow-up*.

Where possible (when government data allowed), linkage to care for HIV-infected HTS clients and ART initiation was confirmed by the TIER.Net system (previously known as the HIV eRegister). TIER.net captures data elements and indicators required to monitor HIV and ART services.[353] If government clinics entered timely data, the HTS clinic staff could use HTS client full legal names to confirm or collect the dates of HTS client linkage to public ART referral clinics.

Appendix D contains the HTS Client Linkage to Care Follow-up Form.

3.5 DATA MANAGEMENT

3.5.1 DATA CAPTURE AND QUALITY CONTROL

PHRU is a REDCap consortium partner, and therefore REDCAP software version 6.2.5 © (2015, Vanderbilt University) was selected as the electronic database system for this study. REDCap, a free-of-charge, metadata-driven software application, allows for password-protected, role-based real-time data collection into intuitive electronic case report forms. To ensure data quality integrity from paper to electronic, REDCap application settings were utilized to allow for primary data entry validation checks to flag and filter erroneous data; quality assurance/controls; and secure, role-based, remote audit capabilities. This allowed for built-in algorithms, skip patterns and prompts to further improve the quality of the data captured.

All staff were delegated to perform electronic data entry and underwent a three-day training on data entry into the electronic database, as facilitated by the creators of the database – the study statistician and the doctoral candidate. Both quantitative and open-ended response data were captured within the database exactly as it appeared within the paper data source documents.
Rigorous data cleaning and quality check procedures were undertaken daily on the data entry/capture from paper forms as part of quality control practice. Upon the launch of each HTS phase, the doctoral candidate performed a daily review of completed HTS client source document files up to the first 100 HTS clients enrolled. All errors in data collection were flagged and returned to the data collector for correction on paper in real-time prior to data capture. Error trends were discussed in team meetings where re-training then occurred. All staff performed a self-check on data collected, and the study statistician verified the completeness of source documents captured. For each HTS phase, the doctoral candidate captured the data

from the first 50 HTS client files to ensure the database was working properly. Any erroneous values against the source documents were immediately discussed with the study statistician, rectified, and re-checked. From that point, staff began electronic data capture from the paper forms. The doctoral candidate or statistician performed a 100% cross-check of all the entered data against the HTS client files for verification purposes. Errors were sent back to the respective data collector/capturer for correction. This ensured consistency, accuracy and completeness of the data.

The statistician and doctoral candidate performed continuous QA checks on both paper collection and data capture to ensure that the database was clean and there were no illogical entries. Any query was resolved immediately in conjunction with the enrolled nurse and/or doctoral candidate and/or statistician.

3.5.2 DATA ANALYSIS

A quantitative approach to data analysis was chosen for this study. The quantitative data included closed-end information that is presented in a numerical representation; while the open-ended response data is more subjective, allowing for the HTS clients/study participants to have a 'voice' to be interpreted.[354] The open-ended response components have been used to compliment the quantitative data in explanation of results in order to apply a broader perspective. The combination of both inductive and deductive reasoning helps to provide additional evidence and support for study findings, as well as often reduces any potential for personal biases of the study investigator.[354]

There are many types of study designs, and this study was of a concurrent nested (embedded) study design. With the quantitative and open-ended response data collected concurrently (simultaneously), the data sets are independent of one another, but analysed concurrently.[355, 356] The study's priority was given to the close-ended data collection and analysis, which largely guided the study's aims and objectives, and the open-ended survey response data components (both client surveys) were embedded into the study providing a supportive – or complimentary - role.[357] Therefore, the chosen method for data integration was that the smaller set of narrative responses from participants was embedded into the primary quantitative data source and used to supplement the results.[356]

Surveys were the data collection method, using various data collection tools (paper forms), as they historically provide a high level of structure and standardization, and investigator

involvement with participants is low, reducing bias.[355] Additionally, surveys are ideal when collecting data from a large sample size is desired, such as within this study; whereas interviews and focus groups are more geared towards smaller sample populations.[355]

Data analysis descriptions for this PhD study can be found within the Appendix A, Original Papers, Papers II through V Methods sections of this thesis. However the following sub-sections further detail the choice in variables and reasons behind the choice in analysis approaches for the close- and open-ended survey response components.

3.5.2.1 Study Measures and Variables

Appendix E contains the study variables – both independent and dependent - and their respective data sources.

Explanatory Factors

Demographic measures, some of which were used to stratify the study population, were a mix of continuous (e.g.; age) and categorical variables (i.e.; sex). A wealth quintile was developed using the socioeconomic measures and determined using Principal Component Analysis (PCA). The socioeconomic measures included the following variables: type of house, source of water, type of toilet facility; type of fuel used for cooking; type of fuel used for lighting; possession of household items and other ownership items. Prior to calculating the wealth quintile, variables with more than two levels were recoded into binary (0 or 1) for each level of response. Frequencies were run on all the binary variables and only those with responses between 5% and 95% were retained. The retained variables were evaluated by the PCA method using the varimax rotation to identify those contributing largely to the wealth construct. Variables meeting a pre-specified cut-off and loading in at least two factors were excluded. The remaining variables were retained and scored to create the socioeconomic index. Five wealth quintiles were estimated on the scored measure using 20 percentile intervals.[358]

Outcome Measures

For HTS health screening results, outcome measures included the following: BMI, BP reading, STI symptoms, TB symptoms, Chlamydia results, HIV results, CD4 count, HbA1c result, random glucose result, and TC result. BMI was calculated by dividing HTS client weight (in kg) by the square of height (in m^2) and classified as underweight, normal, overweight and obese using the WHO classification.[359] Overweight and obese categories were merged resulting in

three categories for analysis. Regarding BP, if the first measurement was high or low, according the the South African HT Practice Guidelines as per standard of care,[169] then a second BP reading was conducted. An average BP was used for the classification. The confirmatory HIV test result was what was recorded as the final HIV result. For all other health screening result outcome measures, they have already been defined.

Quality of task-shifting outcome measures were simply categorical variables denoting if the health screening results was recorded correctly (yes or no). The outcome measures relating to the feasibility of task-shifting the RDT of NCD risk factors into clinic flow were all dependent variables. They were derived from taking the difference between various start and stop times recorded within the clinic flow. These time differences were then presented in minutes for time spent at reception, within pre-test counselling, for health screenings, within post-test counselling, for the conduct of the HTS Data Collection Form, and for the time spent within the total HTS process (e.g.; reception time, pre-test counselling time, screenings time, etc.).

HTS client satisfaction outcome measures relating to each section of clinic flow time and HTS services were entirely independent, categorical variables, (i.e.; very satisfied, somewhat satisfied, neutral, somewhat unsatisfied, very unsatisfied).

Linkage to care and treatment initiation outcome measures were the basic count of HTS clients linked to care and initiated on treatment were derived from the categorical, independent variables (e.g.; HIV-positive client linked to care (yes or no), ART treatment initiation (yes or no), etc). The time to linkage to care and treatment initiation outcome variables were calculated as the difference between the date of HTS clinic visit and the reported date of being linked to care and having initiated treatment (e.g.; date from HIV diagnosis to the date the patient arrived at the ART referral clinic and date from HIV diagnosis to the date the patient initiated ART). This was presented as a continuous variable with the unit of measure being days. This continuous variable was then transformed into a categorical outcome measure through cut-offs to determine if the linkage to care/treatment initiation was *successful* (within 30 days), *delayed* (between 30 and 90 days), or if the HTS client was *lost to follow-up* (e.g.; for either linkage to care for ART and/or for ART treatment initiation).

3.5.2.2 Statistical Analysis

All statistical analysis was conducted in SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC) using SAS/STAT procedures.

Close-Ended Data

Descriptive statistics, such as medians, interquartile ranges (IQR), minimum and maximum values, were presented for continuous variables (e.g.; BMI, CD4 count, etc). Data was presented in frequencies and percentages for categorical variables. The stratification variables (i.e.; age category – 18-24 years, 25-34 years, 35-44 years, 45+ years; sex; HIV-status; etc.) were chosen based upon scientific literature. For any analysis of referral, the analysis was conducted based on condition. There were patients having comorbidity and multiple referrals, but each condition was analysed separately.

To investigate the relationships identified within the data (and therefore within the study population), we tested the data for statistical significance, calculating a p-value and 95% confidence intervals (CIs).[360] Depending on sample size and type of variables compared, investigators strategically chose among Chi Square analysis, Fisher's Exact Test, or Kruskal-Wallis Test. Data analysis and interpretation of research findings included a review of both the statistical significance (if the observed significance level was less than or equal to 0.05, the width and overlap of CIs), as well as whether the relationship made meaningful epidemiological sense.

Associations between categorical variables were tested by either Chi-square or Fishers exact test, as appropriate.[360] Fishers exact test is a more precise test for utilisation when sample sizes are small (used when at least one quarter of the samples within the contingency table had a frequency of less than five).[361]

Continuous data were compared parametrically using the two-sample t-test or non-parametrically using the Kruskal-Wallis test. While the Kruskal-Wallis test could also compare continuous variables against an independent variable with three or more groups (e.g.; age categories), it is not advisable as the results become difficult to interpret. The weakness is that it cannot specify which specific group within the independent variable is statistically significantly different than the others, if there are more than two groups; only that at least two

groups were different.[362] Therefore, it was decided to simply describe the stratification of data by independent variables with three or more groups, rather than test for statistical significance.

Open-Ended Data

Content analysis is the process of categorizing verbal (or behavioural) data to classify, summarize and present the data.[363] Specifically, it allowed for the tabulation of frequencies of the identified words and/or phrases (i.e.; codes) found within the data prior to interpretation and then helping to identify implicit and explicit themes.[364] This method of analysis is known to be very useful in encapsulating the intricacies of meaning within a data set, as it compares theme frequencies, distinguishes theme co-occurrence, and can demonstrate relationships among themes.[365]

Pre-determined themes were based around quantitative survey questions. Investigators used both open coding and axial coding as a way to initially organise the raw data and interconnect categories of coding.[363] Through scanning the primary data, word and phrase repetitions were used to identify common themes.[363] If a code did not fit appropriately into a pre-determined category or theme, a new category was created.

There were primary and secondary data comparisons prior to finalising the analysis of the open-ended data and tabulating the number of codes within each theme category. The doctoral candidate and a second investigator performed the data analysis separately, and then met to review the analysis and discuss any differences, agreeing upon the final results.

3.6 ETHICAL CONSIDERATIONS

3.6.1 ETHICS COMMITTEE CLEARANCE

Prior to this PhD study being implemented, both the HTS health screening programme and embedded study serving as data sources for this PhD were approved by the University of the Wits HREC (Medical) under a single protocol (ethical clearance number: Zazi Evaluation Study – 170307) (Appendix C). The same protocol was reviewed and approved in accordance with the CDC human research protection procedures and was determined to be research, but investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes.

3.6.2 STAKEHOLDER ENDORSEMENT

The study team invited representatives from the provincial department of health (DoH) on-site for a proposed protocol debrief and to invite discussion surrounding study aims. The investigators received endorsement from the SANDoH for both HTS health screening programme and study implementation. The doctoral candidate also presented a protocol debrief to the PHRU Adult HIV Prevention and Treatment Community Advisory Board (CAB), made up of key members of the surrounding community, which was met with support.

3.6.3 HTS STAFF CERTIFICATIONS AND TRAINING

Zazi HTS staff, which included the clinic receptionist, counsellors, nurse, and peer-navigators, statistician and consulting clinician; were trained on the HTS health screening programme and embedded study activities by the doctoral candidate using formal protocols and standard operating procedures (SOPs). Topics covered were the following: aims and objectives, methodology and procedures, data management and security, research ethics, safety, human subject's protection (HSP) and confidentiality, including informed consent.

Each counsellor, nurse and consulting clinician hired already had certification in HTS, and all applicable certificates were on file in the PHRU Zazi HTS Centre. All staff interacting with PHRU Zazi HTS clients and/or handling client data were carefully trained and received a refresher certification on GCP and the ethical considerations guiding research on human subjects. These principles were fully respected during the study process. All clinical staff performing health screening services for PHRU Zazi HTS clients (i.e.; counsellors, nurse, and consulting clinician) received a day-long training and certification on Good Clinical Laboratory Practice (GCLP) and a day-long re-certification on GCLP-related fingerprick testing methods, as provided by the Bio Analytical Research Corporation South Africa (BARC SA), the clinical trial division for Lancet Laboratories.[366]

Before the launch of the standard of care HTS phase, the Zazi's consulting clinician and nurse conducted in-house training for the counsellors on the proper conduct of automated BP readings and measuring a client's height and weight using a wall-mounted stadiometer and scale. Prior to the integrated NCD-HTS phase, the consulting clinician and nurse trained the counsellors on interpretation of BMI results (REDCap automatically calculated BMI from recorded height and weight measurements). The counsellors, nurse and consulting clinician were also thoroughly trained and certified on the use of the handheld POC blood glucose and

cholesterol testing machines, interpretation of associated results, and correct counselling methods by accredited trainers. Representatives from Hemocue (supplier of the POC HbA1c machine) and LabStix Diagnostics (supplier of the POC random glucometer and lipidometer) conducted on-site training on the use of their devices and on the daily QA/QC process required. Each counsellor delegated to perform each type of RDT was observed in the practice of screening procedures by the trainers and potential QA problems were identified, discussed, and corrected.

3.6.4 PROTECTION OF HUMAN SUBJECTS

3.6.4.1 Confidentiality

All HTS staff members received training in confidentiality, and signed an Employee Confidentiality Agreement upon being delegated to the study. Confidentiality was maintained by not divulging information to other personnel, except for those directly involved in the HTS health screening programme and/or study. HTS client names were avoided on data source documents, and instead numeric codes were used. There were three exceptions to this rule and they were as follows: 1) HTS client names remained on the HTS Client Contact Information Sheet to facilitate contacting the client at a later time-point for any follow-up purposes; 2) the HTS Health Screenings Results Report given to the HTS client contained his/her name, as unnamed results reports were not accepted in a referral to local clinics; and 3) any NHLS laboratory results received and printed from the InterSystems' TrakCare LIS contained the HTS client name. HTS client files were labelled with their assigned numeric codes. The HTS Centre screening and enrolment log, linking the HTS client's initials with the assigned numeric codes was maintained by the enrolled nurse and kept in a locked filing cabinet in a locked office separate from where HTS client counselling and RDT took place. The clinic has a separate corridor for consultations to maximise privacy.

At the completion of an HTS clinic visit, HTS client files were temporarily housed in the enrolled nurse's locked filing cabinet within her locked office for QA/QC procedures. After which, files of clients consenting to the PHRU Zazi HTS programme, only, were stored in an access-controlled, gated and locked filing room built inside of the HTS Centre. Files of HTS clients who consented for the study's HTS survey procedures remained locked in the enrolled nurse's filing cabinet. All data from HTS client files entered into the secure password-protected database did not have any names, only numeric codes.

3.6.4.2 Written HTS Programme and Study Informed Consent

PHRU Zazi HTS staff conducting the informed consent process followed the PHRU SOP on obtaining informed consent and the requirements of the University of the Witwatersrand Institutional Review Board (IRB). Participation in both the HTS health screening programme and study was only by those HTS clients who voluntarily agreed to participate and provided written consent to participate after the procedures were fully explained. HTS counsellors administered the informed consent process to the HTS clients within the privacy of their offices prior to pre-test counselling and screening.

Two separate, written informed consents were obtained from any eligible HTS client volunteer for each HTS phase: 1) for HTS clients who wished to be screened and referred (HTS programme informed consent), and 2) for clients who also wished to provide clinic exit surveys and be contacted for follow-up (study informed consent). All HTS clients had to determine whether they would allow the collection and entry of their data spanning from the point of demographics form data collection through to the referral form into the database, and for their data to be used in aggregate data analysis. If n HTS client consented to the HTS programme, but not to the use of their data, then their HTS client file was filled out, but data was not entered into the database or included in the aggregate data analysis.

To overcome communication, cultural and literacy barriers in the process of informed consent, all HTS client consent forms were translated into the local languages of Sotho and IsiZulu and approved for use by Wits HREC (Medical). HTS clients who were unable to read were either provided with an impartial witness (e.g.; another willing and literate HTS client waiting at clinic reception) or given the choice to leave and return to the clinic with a friend or family member who could assist in verifying that the information described to the HTS client was in accordance with the informed consent document.

During each informed consent process, each potential HTS client was given a copy of the informed consent form in the client's preferred language to read along with the administrator. After the end of each section within the informed consent form, there was ample time for potential HTS clients to ask any questions and summarise the content to ensure understanding. Major sections of each informed consent form provided information on the procedures

involved including any potential risks, voluntary participation and the right to withdraw, and confidentiality. No waiver of any element of the Informed Consent was sought.

After reading through the informed consent form, both the eligible HTS client and administrator signed off on the consent form. Prior to signing off on the informed consent form, the counsellors used and signed off on an Inclusion/Exclusion Criteria Checklist to confirm all criteria for the enrolment of the HTS client was met. A copy of the signed informed consent form was given to each consenting HTS client, and the original copy was filed within the HTS client file.

3.6.4.3 Minimizing Risks and Maximizing Benefits

The PhD study was designed to minimize risk and maximize benefit to both HTS clients and their local communities. For example, it provided enhancements of client knowledge of HIV/DM/HT and disease prevention, as well as counselling and guidance. The investigators ensured adequate training so that staff members protected the privacy of HTS clients, and obtained meaningful informed consent. HTS clients retained the right to decline tests without prejudice and their well-being was prioritised at all times.

In both HTS phases, HTS clients identified during counselling as being newly at-risk (e.g; HTS clients identified with an STI) were counselled by the counsellors and encouraged to return for retesting in six weeks. Other high-risk clients (e.g.; FSW and MSM), were counselled to return for re-testing every three months.

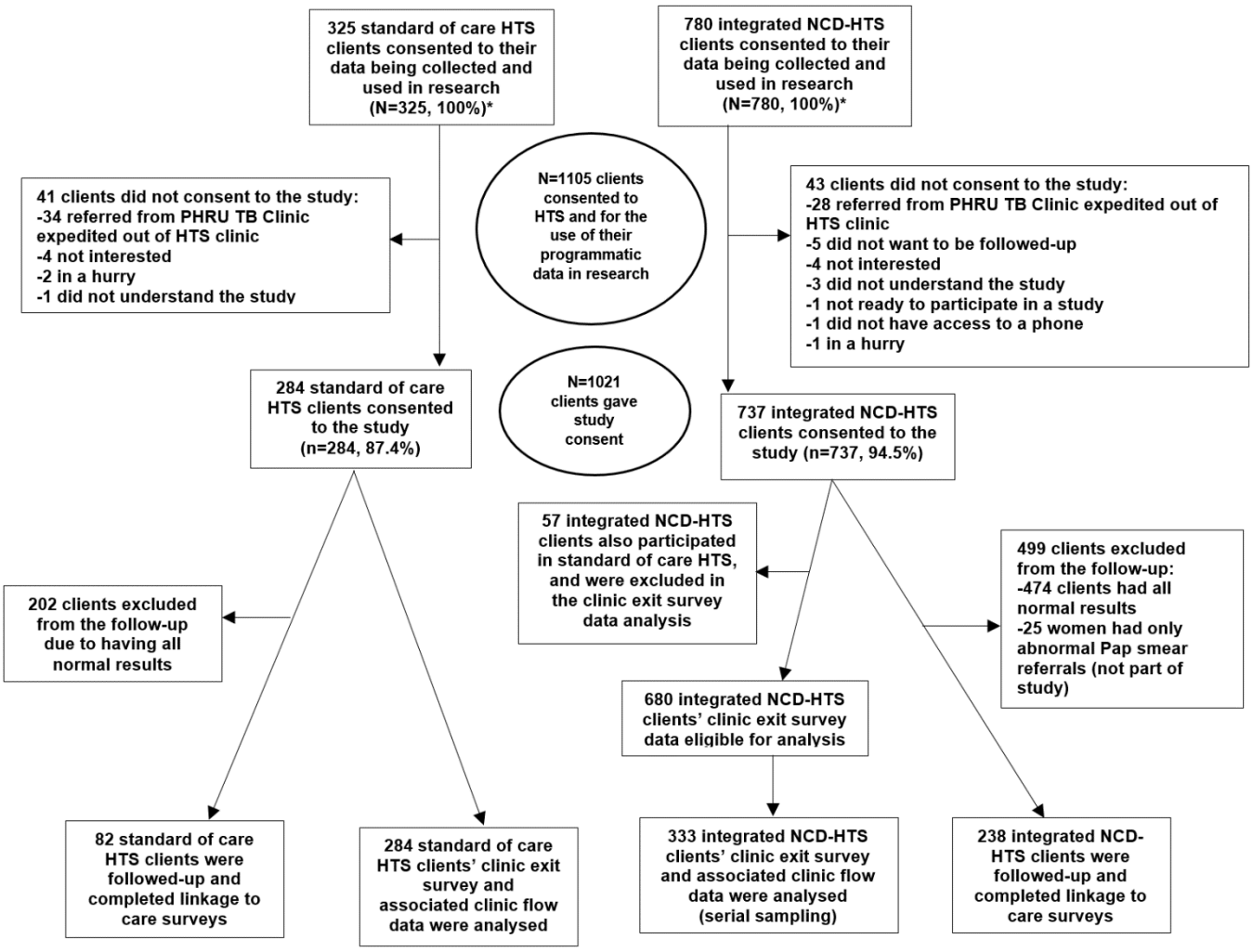
4.0 RESULTS

This chapter presents key findings of the study in accordance with the four thesis themes and referring to the four thesis papers. To begin with, HTS client participant sampling and general background characteristics of the HTS programme participants are presented.

4.1 SAMPLING AND SOCIODEMOGRAPHICS OF STUDY PARTICIPANTS

4.1.1 HTS CLIENTS OVERALL, BY HTS PHASE

Figure 4-1 depicts the overall HTS participant flow for inclusion into the HTS health screening programme and subsequent studies – inclusive of HTS client clinic exit surveys and HTS client linkage to care follow-up surveys, by HTS phase. HTS client and study participant flow charts for the individual studies comprising this thesis may be found within Paper II, Figure 1 (standard of care HTS client flow through screening);[358] Paper III, Figure 1 (integrated NCD-HTS client flow through screening); Paper IV, Figure 1 (HTS client participant flow through client clinic exit surveys);[367] and Paper V, Figure 1 (HTS client participant flow through linkage to care follow-up).



HIV Testing Services, HTS; Non-communicable diseases, NCDs; Perinatal HIV Research Unit, PHRU; Tuberculosis, TB. Consent for HTS and for programmatic data to be used in research related to the collection of the following data: HTS client file, NHLS pathology reports and other health screening results and referrals. Study consent related to the completion of HTS client clinic exit surveys and follow-up linkage to care surveys

Figure 4-1. Overall HTS Participant Flow, by HTS Phase

Standard of Care HTS Clients

Nearly all of the adults entering the Zazi HTS Centre consented to the HTS health screening programme and allowed their data to be used in aggregate data analysis (97.6%, n=325/333). Of the eight non-participants, five clients left the clinic prior to the informed consent process and three clients refused having their data be used in research.

Of the 325 standard of care HTS clients, the largest proportion of clients were female (51.1%, n=166/325), black African (98.5%, n=320/325), single (71.5%, n=231/323), had completed

high school (31.5%, n=102/324), and belonged to the lower three wealth quintiles (75.7%, n=246/325). Males were significantly older than females (median [IQR] age 37.5 [31.0–45.0] years vs 33.0 [26.0–41.0] years, respectively; p=0.001).

The younger age groups of 18-24 and 25-35 years reported drinking alcohol more frequently (13.3%, n=19/143 on a weekly basis; and 41.3%, n=59/143 on a monthly basis) compared to the older age groups. About three-quarters of clients from both age groups 18-24 and 25-35 years who reported they do drink, reported they drink >4 standard-size drinks per sitting (75%, n=24/32 and 72%, n=49/68; respectively). Almost all of clients who reported they had ever smoked cigarettes, still smoke (99.0%, n=77/78); and of these clients, the highest proportion were aged 25-34 (53%, n=16/30) and 35–44 years (52%, n=11/21).

The distribution of standard of care HTS client demographics by age group is shown within Paper II, Table 1.[358]

Integrated NCD-HTS Clients

Nearly all of the adults entering the Zazi HTS Centre consented to the HTS health screening programme and allowed their data to be used in aggregate data analysis (99.4%, n=780/785). Of the five non-participants, three clients left the clinic prior to being seen by a counsellor and two clients refused having their data be used in research.

Of the 780 integrated NCD-HTS clients, the largest proportion of clients were female (65.8%, n=513/780), black African (98.3%, n=767/780), single (70.7%, n=551/779), had tertiary education (43.1%, n=336/780), and belonged to the lower three wealth quintiles (69.9%, n=545/780). The median age was 32.0 years (IQR: 25.0-42.0). Males were significantly older than females (median [IQR] age 37.0 [29.0–47.0] years vs 31.0 [25.0–39.0] years, respectively; p=0.0001). Only 33.4% were formally employed (n=259/776), of which the vast majority were in the older age groups. Of those not in formal employment, sources of income included informal trading, social grants and pensions.

The younger age groups of 18-24 and 25-35 years reported drinking alcohol more frequently (17.1% [n=73/428] on a weekly basis; and 37.9% [n=162/428] on a monthly basis) compared to the older age groups. Over half of clients aged 18-24 and about three-quarters of clients aged 25-35 years who reported they do drink, reported they drink >4 standard-size drinks per sitting

(56.5% [n=64/113] and 70.1% [n=150/214], respectively). Almost all of clients who reported they had ever smoked cigarettes, still smoke (98.4%, n=188/191); and of these clients, the highest proportion were aged 25-34 (33.3%, n=92/276).

The distribution of integrated NCD-HTS client demographics by age group is shown within Paper III, Table 1.

Comparison between HTS Phase Clients

To create two, independent study populations for comparing the demographics, only, between standard of care HTS and integrated NCD-HTS study participants, we excluded the 77 participants from integrated NCD-HTS who were also standard of care HTS participants.

The standard of care HTS study participants had a significantly older median age in years as compared to the integrated NCD-HTS study participants (35.0 [IQR:28.0-42.0] vs 32.0 [IQR:25.0-41/0]; p-value=0.0009). There were significantly more male study participants in standard of care HTS as compared to integrated NCD-HTS (48.9% [n=159/325] vs 32.1% [n=226/703]; p-value<0.0001). The global p-value comparing the wealth quintiles was p<0.0451, signifying there was a statistically significant difference between each HTS phase's proportions of wealth quintiles. However, when comparing HTS phases by each quintile, there were no statistically significant differences. There were no other significantly different demographics between the two HTS phase clients (see Table 4-1).

Table 4-1. Comparison of Standard of Care HTS and Integrated NCD-HTS Clients

Variable	Overall	Standard HTS	Integrated NCD-HTS	P-Value
No. of enrolment	1028	325	703	
Age (In years)				
18-24 (%)	196/1028 (19.1)	52/325 (16.0)	144/703 (20.5)	0.0776
25-34 (%)	375/1028 (36.5)	110/325 (33.8)	265/703 (37.7)	
35-44 (%)	259/1028 (25.2)	94/325 (28.9)	165/703 (23.5)	
≥45 (%)	198/1028 (19.3)	69/325 (21.2)	129/703 (18.3)	
Median (IQR)	33.0 (26.0-41)	35.0 (28.0-42)	32.0 (25.0-41)	**0.0009**
Min, Max	(18-73)	(18-73)	(18-70)	
Sex				
Female (%)	643/1028 (62.5)	166/325 (51.1)	477/703 (67.9)	**<.0001**
Male (%)	385/1028 (37.5)	159/325 (48.9)	226/703 (32.1)	
Race				
Black African (%)	1011/1028 (98.3)	320/325 (98.5)	691/703 (98.3)	0.8438
Coloured/mixed race (%)	17/1028 (1.7)	5/325 (1.5)	12/703 (1.7)	
Nationality				
South African (%)	35/1024 (3.4)	16/321 (5.0)	19/703 (2.7)	0.0623
Other (%)	989/1024 (96.6)	305/321 (95.0)	684/703 (97.3)	
Ethnic group				
Zulu (%)	443/1026 (43.2)	135/324 (41.7)	308/702 (43.9)	0.8257
Sotho (%)	173/1026 (16.9)	60/324 (18.5)	113/702 (16.1)	
Tsonga (%)	99/1026 (9.6)	31/324 (9.6)	68/702 (9.7)	
Tswana (%)	79/1026 (7.7)	24/324 (7.4)	55/702 (7.8)	
Xhosa (%)	96/1026 (9.4)	27/324 (8.3)	69/702 (9.8)	
Other (%)	136/1026 (13.3)	47/324 (14.5)	89/702 (12.7)	
Marital status				
Divorced/Widowed (%)	42/1025 (4.1)	19/323 (5.9)	23/702 (3.3)	0.1416
Living together/Married (%)	242/1025 (23.6)	73/323 (22.6)	169/702 (24.1)	
Single (%)	741/1025 (72.3)	231/323 (71.5)	510/702 (72.6)	
Highest education				
Up To High School (%)	436/1027 (42.5)	138/324 (42.6)	298/703 (42.4)	0.0953
Matriculated (%)	362/1027 (35.2)	102/324 (31.5)	260/703 (37.0)	
Tertiary education (%)	229/1027 (22.3)	84/324 (25.9)	145/703 (20.6)	
Wealth quintile				
Quintile 1 (%)	270/1028 (26.3)	78/325 (24.0)	192/703 (27.3)	**0.0451**
Quintile 2 (%)	244/1028 (23.7)	87/325 (26.8)	157/703 (22.3)	
Quintile 3 (%)	280/1028 (27.2)	81/325 (24.9)	199/703 (28.3)	
Quintile 4 (%)	196/1028 (19.1)	60/325 (18.5)	136/703 (19.3)	
Quintile 5 (%)	38/1028 (3.7)	19/325 (5.8)	19/703 (2.7)	

Variable	Overall	Standard HTS	Integrated NCD-HTS	P-Value
In the last year, how often would you usually drink alcohol?				
Weekly (%)	130/961 (13.5)	32/290 (11.0)	98/671 (14.6)	0.3507
Monthly (%)	317/961 (33.0)	93/290 (32.1)	224/671 (33.4)	
Sometimes (%)	168/961 (17.5)	51/290 (17.6)	117/671 (17.4)	
Never drank alcohol in the last year (%)	346/961 (36.0)	114/290 (39.3)	232/671 (34.6)	
About how many standard-size drinks do you usually have in one day?				
1-2 (%)	69/613 (11.3)	25/175 (14.3)	44/438 (10.0)	0.1745
3-4 (%)	142/613 (23.2)	34/175 (19.4)	108/438 (24.7)	
>4 (%)	402/613 (65.6)	116/175 (66.3)	286/438 (65.3)	
Do you use drugs?				
Yes often (weekly) (%)	78/1027 (7.6)	24/325 (7.4)	54/702 (7.7)	0.9797
Sometimes (%)	26/1027 (2.5)	8/325 (2.5)	18/702 (2.6)	
No (%)	923/1027 (89.9)	293/325 (90.2)	630/702 (89.7)	
Have you ever smoked cigarettes?				
No (%)	710/961 (73.9)	212/290 (73.1)	498/671 (74.2)	0.7182
Yes (%)	251/961 (26.1)	78/290 (26.9)	173/671 (25.8)	
Do you still smoke cigarettes now?				
No (%)	4/251 (1.6)	1/78 (1.3)	3/173 (1.7)	0.7913
Yes (%)	247/251 (98.4)	77/78 (98.7)	170/173 (98.3)	
About how many cigarettes do you or did you usually smoke in one day?				
1-2 (%)	38/250 (15.2)	12/77 (15.6)	26/173 (15.0)	0.8704
Less than 5 (%)	87/250 (34.8)	27/77 (35.1)	60/173 (34.7)	
10 (%)	102/250 (40.8)	33/77 (42.9)	69/173 (39.9)	
20 (%)	22/250 (8.8)	5/77 (6.5)	17/173 (9.8)	
30 (%)	1/250 (0.4)	0/77 (0.0)	1/173 (0.6)	

Note: 77 participants from integrated NCD-HTS were excluded from the analysis, as they also participated in standard of care HTS. HIV Testing Services, HTS; Non-Communicable Diseases, NCD; Interquartile Range, IQR

4.1.2 HTS CLIENTS PARTICIPATING IN STUDY CLINIC EXIT SURVEY, BY HTS PHASE

Standard of Care HTS Client Participants

Of the 325 standard of care HTS clients who consented to the screening process and allowed the use of their data, 41 (12.6%) did not consent to the HTS study. The majority of these clients (n=34/41, 82.9%) were referred TB clients from the PHRU TB clinic, who needed to be expedited through the Zazi HTS clinic. The remaining six non-consenting clients were not interested (n=4), in a hurry (n=1), or didn't understand the study (n=1), and therefore were not enrolled. The remaining 284 clients did consent to the HTS study and undertook the HTS client clinic exit survey. As the HTS client clinic exit survey data was matched with the HTS clinic flow time data, the clinic flow timeframes were only analysed for the same 284 HTS client participants. (Figure 4-1)

The distribution of demographics of the sub-sample of standard of care HTS client participants who completed client clinic exit surveys is shown within Paper IV, Table 1.

Integrated NCD-HTS Client Participants

Of the 780 integrated NCD-HTS clients who consented to the screening process and allowed the use of their data, 43 (5.5%) did not consent to the HTS study. The majority of these clients (n=28/43, 65.1%) were referred TB clients, who were automatically excluded from the study. Of the remaining 15 non-consenting clients, five did not want to be followed-up, five were not interested in participating or not ready to participate, three did not understand the study, one did not have a phone and was excluded from the study, and the last client was in a hurry. A further 57 clients (7.3%) were excluded from the study utilising the client clinic exit surveys, as these clients also participated within the standard of care HTS phase. The remaining 680 clients were eligible for the study and completed HTS client clinic exit surveys. Using the serial sampling method, the first 333 collected HTS client clinic exit surveys were analysed before content saturation was reached. Therefore, the clinic flow timeframes were only analysed for the same 333 HTS client participants. (Figure 4-1)

The distribution of demographics of the sub-sample of integrated NCD-HTS client participants who completed client clinic exit surveys is shown within Paper IV, Table 1.

Comparison between HTS Phase Client Participants

Of the study participants completing the HTS client clinic exit survey, standard of care HTS participants were significantly older (median age [IQR] was 35.0 [28.0–43.0] years vs. 31.0 [25.0–40.0] years; p=0.0003), likely to be divorced (6.7% [n=19/282] vs. 2.4% [n=8/332]; p=0.0091) and be tertiary educated (27.9% [n=79/283] vs. 20.1% [n=67/333]; p=0.0234) compared to NCD-HTS participants. Standard of care HTS had significantly less proportions of females (53.9% [n=153/285] vs. 67.6% [n=225/333]; p=0.0005), Zulu speakers (41.0% [n=116/283] vs. 49.0% [n=163/333]; p=0.0480) and clients reporting their parents as their source of income (13.0% [n=37/284] vs. 20.5% [n=68/331]; p=0.0135) as compared to integrated NCD-HTS.

The comparison between HTS phase study participants who completed the HTS client clinic exit survey can be seen within Paper IV, Table 1.

4.1.3 HTS CLIENTS PARTICIPATING IN STUDY FOLLOW-UP SURVEY, BY HTS PHASE

Standard of Care HTS Client Participants

Of the 284 standard of care HTS clients consenting to the study, 202 (71.1%) were excluded from the follow-up linkage to care study, as they all received normal screening results. The remaining 82 standard of care HTS client participants were enrolled for follow-up. (Figure 4-1.)

The distribution of demographics of the sub-sample of standard of care HTS client participants who were followed-up to confirm linkage to care and treatment initiation is shown within Paper V, Table 1.

Integrated NCD-HTS Client Participants

Of the 737 integrated NCD-HTS clients consenting to the study, 499 (67.7%) were excluded from the follow-up linkage to care study. The majority of these clients (n=474/499) had received normal screening results, while the remaining 25 clients were women who had received abnormal pap smear results, only, which was not within the scope of this study. The remaining 238 integrated NCD-HTS client participants were enrolled for follow-up. (Figure 4-1).

The distribution of demographics of the sub-sample of integrated NCD-HTS client participants who were followed-up to confirm linkage to care and treatment initiation is shown within Paper V, Table 1.

Comparison between HTS Phase Client Participants

There were significantly more followed-up standard of care HTS client participants who were from outside of South Africa (8.8% [n=7/80] vs 1.7% [n=4/232]; p=0.0033), divorced/widowed (12.2% [n=10/82] vs 3.4% [n=8/232]; p=0.0034), and who had high BP (50.0% [n=41/82] vs 27.6% [n=64/232]; p<0.0001) as compared to integrated NCD-HTS. However, integrated NCD-HTS had significantly more participants who were living together/married than standard of care HTS (27.6% [n=64/232] vs 15.9% [n=13/82]; p=0.0338). Integrated NCD-HTS had more females (70.3% [n=163/232]) and those with some high school education (43.5% [n=101/232]).

The comparison between HTS phase study participants who were followed-up to confirm linkage to care and treatment initiation can be seen within Paper V, Table 1.

4.2 HEALTH TRANSITION

Results linked to the theme of *Health Transition* were the health screening results within both HTS phases, which show prevalence of disease amongst both HTS client populations.

4.2.1 STANDARD OF CARE HTS HEALTH SCREENING RESULTS

Overall Health Screening Results, by Age Group and Sex

Of the standard of care HTS clients screened, 33.5% (n=109/325) had an overweight/obese BMI, 27.5% (n=89/324) had elevated BP, 20.9% (n=68/325) were HIV-infected, 3.5% (n=11/318) had at least one STI symptom, 1.4% (n=4/289) had at least one TB symptom. Of the 34 laboratory-confirmed TB patients who entered Zazi for expedited HIV screening, 19 (56%) were HIV-infected. Of the 68 clients who were HIV-infected, 39 were eligible to have had their CD4 count measured (median CD4: 327 cells/mm^3, IQR: 157–569). The remaining 29 HIV-infected clients were ineligible for CD4 count monitoring at Zazi, as they were already in care.

In comparing screening results by age groups, clients aged ≥45 years had the highest proportion of overweight/obese BMI of all the age groups (46.4%, n=32/69). Clients in age

groups 35–44 and ≥45 years were more likely to be overweight/obese compared with the group aged 25–34 years (37.2% [n=35/94] vs 22.7% [n=25/110]; p=0.0234) and (46.4% [n=32/69] vs 22.7% [n=25/110]; p=0.0009). The older age groups (25–34, 35–44 and ≥44 years) had significantly higher proportions of high BP (22.7% [n=25/110] vs 5.8% [n=3/52], p=0.0077; 33.0% [n=31/94] vs 5.8% [n=3/52], p=0.0002; and 44.1% [n=30/68] vs 5.8% [n=3/52], p<0.0001; respectively) relative to the youngest age group (18–24 years).

HIV infections were most prevalent amongst 35–44 year olds (26%, n=24/94) followed by those ≥45 years (20%, n=14/69) and 25–34 years (20.0%, n=22/110). STI symptoms were highest in the group of people aged 18–24 years (10%, n=5/51).

Females were significantly more likely to be overweight/obese than males (45.8% [n=76/166] vs 20.8% [n=33/159]; p<0.001). A significantly higher number of males were diagnosed with high BP compared with females (32.9% [n=52/158] vs 22.3% [n=37/166]; p=0.032). Females obtained a significantly higher rate of HIV diagnosis than males (26.5% [n=44/166] vs 15.1% [n=24/159]; p=0.012).

These screening results are further detailed within Paper II, Table 2.[358]

Non-Communicable Disease Health Screening Results, by HIV-Status

Results stratifying the distribution of BP and BMI by age group and sex for both HIV-uninfected and HIV-infected clients can be seen within Paper II, Figure 2 and Table 3.[358] All HIV-infected clients aged 18-24 years (n=8) had normal BP readings regardless of BMI. High BP readings increased with age, with the largest proportion of high BP being among those clients aged ≥45 years (28.6%).

Though not significant, HIV-infected females had higher BP readings relative to HIV-infected males (25.0% vs 12.5%; p=0.22). For HIV-uninfected clients, a similar BP trend was seen by age, while the opposite was seen by sex. In the HIV-infected group, high BP was most common among those who were overweight/obese as opposed to normal weight (57.1% [n=8/14] vs 24.5% [n=13/53]; p=0.0193). Whereas, in the HIV-uninfected group, clients who were underweight were more likely to have a normal BP than to have high BP (24.3% [n=43/177] vs 10.7% [n=8/75]; p=0.0138). In addition, a high proportion of males who were

overweight/obese had high BP compared with normal BP (34.7% [n=17/49] vs 15.7% [n=13/83]; p=0.0117).

4.2.2 INTEGRATED NCD-HTS HEALTH SCREENING RESULTS

Overall Health Screening Results, by Age Group and Sex

Overall integrated NCD-HTS health screening results for each age group and sex can be found within Table 4-2, while these screening results by age group with a sex comparison can be found within Table 4-3.

Table 4-2. Overall Integrated NCD-HTS Screening Results by Age Group and Sex

Variable	Overall	18-24	25-34	35-44	≥45	Female	Male	P-Value
HIV Results								
Positive (%)	149/775 (19.2)	10/153 (6.5)	53/285 (18.6)	50/182 (27.5)	36/155 (23.2)	108/511 (21.1)	41/264 (15.5)	0.0606
Negative (%)	626/775 (80.8)	143/153 (93.5)	232/285 (81.4)	132/182 (72.5)	119/155 (76.8)	403/511 (78.9)	223/264 (84.5)	
CD4 Count (Cells/mm3								
Median (IQR)	86, 341 (246-500)	367 (198-492)	332 (232-412)	339 (231-490)	502 (363-536)	65, 347 (262-507)	21, 315 (182-412)	0.1796
Body Mass Index (BMI)								
Underweight (%)	133/770 (17.3)	32/153 (20.9)	58/279 (20.8)	25/184 (13.6)	18/154 (11.7)	59/506 (11.7)	74/264 (28.0)	**<.0001**
Normal (%)	348/770 (45.2)	77/153 (50.3)	127/279 (45.5)	86/184 (46.7)	58/154 (37.7)	210/506 (41.5)	138/264 (52.3)	**0.0044**
Overweight/Obese (%)	289/770 (37.5)	44/153 (28.8)	94/279 (33.7)	73/184 (39.7)	78/154 (50.6)	237/506 (46.8)	52/264 (19.7)	**<.0001**
Median (IQR)	770,23.2 (19.4-27.3)	21.9 (18.8-25.6)	23.1 (19.0-26.6)	23.3 (20.0-29.3)	25.2 (20.7-29.4)	506,24.3 (21.1-29.4)	264,20.4 (18.1-24.2)	**<.0001**
Blood Pressure								
Low (%)	7/772 (0.9)	4/153 (2.6)	2/283 (0.7)	0/182 (0.0)	1/154 (0.6)	5/508 (1.0)	2/264 (0.8)	**0.7526**
Normal (%)	626/772 (81.1)	143/153 (93.5)	248/283 (87.6)	136/182 (74.7)	99/154 (64.3)	427/508 (84.1)	199/264 (75.4)	**0.0035**
High (%)	139/772 (18.0)	6/153 (3.9)	33/283 (11.7)	46/182 (25.3)	54/154 (35.1)	76/508 (15.0)	63/264 (23.9)	**0.0023**
Blood glucose								
Average (HbAa1c)								
Normal (%)	683/766 (89.2)	140/153 (91.5)	262/280 (93.6)	159/180 (88.3)	122/153 (79.7)	449/505 (88.9)	234/261 (89.7)	0.7534
High (%)	83/766 (10.8)	13/153 (8.5)	18/280 (6.4)	21/180 (11.7)	31/153 (20.3)	56/505 (11.1)	27/261 (10.3)	
Random glucose								
Normal (%)	765/769 (99.5)	152/153 (99.3)	280/281 (99.6)	179/181 (98.9)	154/154 (100.0)	502/506 (99.2)	263/263 (100.0)	-
High (%)	4/769 (0.5)	1/153 (0.7)	1/281 (0.4)	2/181 (1.1)	0/154 (0.0)	4/506 (0.8)	0/263 (0.0)	
Total Cholesterol (TC)								
Low (%)	88/768 (11.5)	25/153 (16.3)	39/280 (13.9)	11/181 (6.1)	13/154 (8.4)	53/505 (10.5)	35/263 (13.3)	0.2455
Normal (%)	618/768 (80.5)	123/153 (80.4)	233/280 (83.2)	146/181 (80.7)	116/154 (75.3)	407/505 (80.6)	211/263 (80.2)	0.9034
High (%)	62/768 (8.1)	5/153 (3.3)	8/280 (2.9)	24/181 (13.3)	25/154 (16.2)	45/505 (8.9)	17/263 (6.5)	0.2375

Variable	Overall	18-24	25-34	35-44	≥45	Female	Male	P-Value
Syndromic STI								
1+ symptoms (%)	24/776 (3.1)	7/153 (4.6)	9/285 (3.2)	5/183 (2.7)	3/155 (1.9)	20/511 (3.9)	4/265 (1.5)	0.0665
No symptoms (%)	752/776 (96.9)	146/153 (95.4)	276/285 (96.8)	178/183 (97.3)	152/155 (98.1)	491/511 (96.1)	261/265 (98.5)	
Syndromic TB								
1+ symptoms (%)	19/748 (2.5)	3/153 (2.0)	6/273 (2.2)	5/179 (2.8)	5/143 (3.5)	8/505 (1.6)	11/243 (4.5)	**0.0166**
No symptoms (%)	729/748 (97.5)	150/153 (98.0)	267/273 (97.8)	174/179 (97.2)	138/143 (96.5)	497/505 (98.4)	232/243 (95.5)	

Human Immunodeficiency Virus, HIV; Sexually Transmitted Infection, STI; Tuberculosis, TB.

Table 4-3. Integrated NCD-HTS Screening Results by Age Group with a Sex Comparison

		18-24			25-34			35-44			≥45		
Variable	**Overall**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**
HIV Results													
Positive (%)	149/775 (19.2)	6/127 (4.7)	4/26 (15.4)	**0.0451**	43/197 (21.8)	10/88 (11.4)	**0.0359**	36/110 (32.7)	14/72 (19.4)	**0.0496**	23/77 (29.9)	13/78 (16.7)	0.0516
Negative (%)	626/775 (80.8)	121/127 (95.3)	22/26 (84.6)		154/197 (78.2)	78/88 (88.6)		74/110 (67.3)	58/72 (80.6)		54/77 (70.1)	65/78 (83.3)	
Are you currently taking or have ever taken antiretroviral?													
No (%)	103/149 (69.1)	6/6 (100.0)	4/4 (100.0)		36/43 (83.7)	9/10 (90.0)	0.6174	25/36 (69.4)	11/14 (78.6)	0.5187	8/23 (34.8)	4/13 (30.8)	0.8062
Yes (%)	46/149 (30.9)	-	-		7/43 (16.3)	1/10 (10.0)		11/36 (30.6)	3/14 (21.4)		15/23 (65.2)	9/13 (69.2)	
CD4 Count (Cells/mm^3)													
n, Median (IQR)	86, 341 (246-500)	5, 420 (313-463)	3, 279 (116-524)	0.8815	30, 330 (246-500)	7, 338 (156-412)	0.7860	24, 363 (240-569)	9, 315 (182-347)	0.2663	6, 513 (408-540)	2, 393 (276-510)	0.3173
Body Mass Index (BMI)													
Underweight (%)	133/770 (17.3)	22/127 (17.3)	10/26 (38.5)	**0.0158**	27/192 (14.1)	31/87 (35.6)	**<.0001**	6/111 (5.4)	19/73 (26.0)	**0.0001**	4/76 (5.3)	14/78 (18.0)	**0.0143**
Normal (%)	348/770 (45.2)	61/127 (48.0)	16/26 (61.5)	**0.2095**	82/192 (42.7)	45/87 (51.7)	0.1613	45/111 (40.5)	41/73 (56.2)	**0.0377**	22/76 (29.0)	36/78 (46.2)	**0.0276**
Overweight/Obese (%)	289/770 (37.5)	44/127 (34.7)	0/26 (0.0)	-	83/192 (43.2)	11/87 (12.6)	**<.0001**	60/111 (54.1)	13/73 (17.8)	**<.0001**	50/76 (65.7)	28/78 (35.9)	**0.0002**
n, Median (IQR)	770, 23.2 (19.4-27.3)	127, 22.7 (19.4-26.5)	26,18.8 (17.6-20.4)	**<.0001**	192, 24.0 (21.2-28.7)	87,19.4 (17.0-22.5)	**<.0001**	111,25.6 (22.1-31.5)	73,20.4 (18.3-24.1)	**<.0001**	76,27.5 (23.0-31.5)	78,22.0 (19.4-27)	**<.0001**

		18-24			25-34			35-44			≥45		
Variable	**Overall**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**
Blood Pressure													
High (%)	139/772 (18.0)	4/127 (3.2)	2/26 (7.7)	0.4963	22/195 (11.3)	11/88 (12.5)	0.8049	26/110 (23.6)	20/72 (27.8)	0.5296	24/76 (31.6)	30/78 (38.5)	0.4207
Low (%)	7/772 (0.9)	3/127 (2.4)	1/26 (3.9)		1/195 (0.5)	1/88 (1.1)		-	-		1/76 (1.3)	0/78 (0.0)	
Normal (%)	626/772 (81.1)	120/127 (94.5)	23/26 (88.5)		172/195 (87.2)	76/88 (86.4)		84/110 (76.4)	52/72 (72.2)		51/76 (67.1)	48/78 (61.5)	
Blood glucose Average (HbA1c)													
High (%)	83/766 (10.8)	11/127 (8.7)	2/26 (7.7)	0.8717	16/193 (8.3)	2/87 (2.3)	0.0585	15/109 (13.8)	6/71 (8.5)	0.2780	14/76 (18.4)	17/77 (22.1)	0.5737
Normal (%)	683/766 (89.2)	116/127 (91.3)	24/26 (92.3)		177/193 (91.7)	85/87 (97.7)		94/109 (86.2)	65/71 (91.5)		62/76 (81.6)	60/77 (77.9)	
Random glucose													
High (%)	4/769 (0.6)	1/127 (0.79)	0/26 (0.00)	-	1/193 (0.52)	0/88 (0.00)	-	2/110 (1.82)	0/71 (0.00)	-	0/76 (0.0)	0/78 (0.0)	-
Normal (%)	765/769 (99.4)	126/127 (99.21)	26/26 (100.0)		192/193 (99.48)	88/88 (100.0)		108/110 (98.18)	71/71 (100.0)		76/76 (100.0)	78/78 (100.0)	
Total Cholesterol (TC)													
High (%)	62/768 (8.1)	5/127 (3.9)	0/26 (0.0)	0.5739	6/192 (3.1)	2/88 (2.3)	0.6911	20/110 (18.2)	4/71 (5.6)	**0.0151**	14/76 (18.4)	11/78 (14.1)	0.7600
Low (%)	88/768 (11.5)	21/127 (16.5)	4/26 (15.4)	-	20/192 (10.4)	19/88 (21.6)	**0.0122**	6/110 (5.5)	5/71 (7.0)	0.6625	6/76 (7.9)	7/78 (9.0)	-
Normal (%)	618/768 (80.5)	101/127 (79.5)	22/26 (84.6)	-	166/192 (86.5)	67/88 (76.1)	**0.0319**	84/110 (76.4)	62/71 (87.3)	0.0683	56/76 (73.7)	60/78 (76.9)	-

Variable	Overall	18-24			25-34			35-44			≥45		
		Female	Male	P-Value	Female	Male	P-Value	Female	Male	P-Value	Female	Male	P-Value
Syndromic STI													
1+ symptoms (%)	24/776 (3.1)	6/127 (4.72)	1/26 (3.85)	0.8452	8/197 (4.06)	1/88 (1.14)	0.1921	3/110 (2.73)	2/73 (2.74)	0.9960	3/77 (3.90)	0/78 (0.00)	-
No symptoms (%)	752/776 (96.9)	121/127 (95.28)	25/26 (96.15)		189/197 (95.94)	87/88 (98.86)		107/110 (97.27)	71/73 (97.26)		74/77 (96.10)	78/78 (100.0)	
Syndromic TB													
1+ symptoms (%)	19/748 (2.5)	1/127 (0.79)	2/26 (7.69)	**0.0207**	3/194 (1.55)	3/79 (3.80)	0.2500	1/110 (0.91)	4/69 (5.80)	0.0534	3/74 (4.05)	2/69 (2.90)	0.7070
No symptoms (%)	729/748 (97.5)	126/127 (99.21)	24/26 (92.31)		191/194 (98.45)	76/79 (96.20)		109/110 (99.09)	65/69 (94.20)		71/74 (95.95)	67/69 (97.10)	

Human Immunodeficiency Virus, HIV; Sexually Transmitted Infection, STI; Tuberculosis, TB.
Overall, men have significantly more underweight BMI as compared to women (28.0% [n=74/264] vs 11.7% [n=59/506]; p<0.0001), and women have significantly more overweight/obese BMI than men (46.8% [n=237/506] vs 19.7% [n=52/264]; p<0.0001).
Overall, women have significantly more low BP than men (1.0% [n=5/508] vs 0.8% [n=2/264]; p=0.0041) and significantly more normal BP than men (84.1% [n=427/508] vs 75.4% [n=199/264]; p=0.0027).

Over one-third of the participants (37.5%, n=289/770) were overweight/obese, and BMI increased by age for both sexes. Women had significantly more overweight/obese BMI than men, both overall (46.8% [n=237/506] vs 19.7% [n=52/264]; p<0.0001) and within each age group. Over one-third of women aged 18-24 years and 25-34 years were overweight/obese (34.7% [n=44/127] and 43.2% [n=83/192]), respectively. Men, inversely, had significantly more underweight BMI than women, both overall (29.2% [n=77/264] vs 11.7% [n=59/506]; p<0.0001) and by age group. Younger males (18-24 and 25-34 year olds) had the highest proportion of being underweight (38.5% [n=10/26] and 34.9% [n=30/86], respectively).
Overall, 18.0% (n=139/772) of participants had high blood pressure. The prevalence of elevated BP increased by age for both sexes, peaking at 31.6% (n=24/76) in women and 38.5% (n=30/78) in men aged 45+ years. Females had significantly more normal blood pressure than men (84.1% [n=427/508] vs. 75.4% [n=199/264]; p=0.0027).

Overall, 10.8% (n=83/766] of clients had high HbA1c, and the prevalence was similar between sexes. Only four participants screened with high random blood glucose. Prevalence of high HbA1c peaked amongst 45+ year olds (18.4% [n=14/76] of women and 22.1% [n=17/77] of men). Of the 18-34 year olds, 7.2% (n=31/433) had high HbA1c (8.5% [n=13/153] of 18-24 year olds and 6.4% [n=18/280] of 25-34 year olds).

A total of 62 participants (8.1% [n=62/768) screened with high cholesterol, of which the majority were women aged 35+ years (54.8% [n=34/62]). There were over three times as many women aged 25-34 years with high TC as compared to men of the same age group (18.2% [n=20/110] vs 5.6% [n=4/71]; p=0.0151).

A total of 775 participants tested for HIV, with 19.2% (n=149/775) screening as HIV-infected of which the majority were female (72.5%, n=108). Overall, HIV prevalence peaked amongst 35-44 year olds (27.5%, n=50/182), as well as for both sexes (32.7% [n=36/110] of women and 19.4% [n=14/72] of men). Six out of ten HIV-infections amongst 18-24 years olds were among women. The median CD4 count (n=86) for HIV-infected clients was 341 cells/mm^3 (IQR: 246-500); but of those with a CD4 count below 200 cells/mm^3, the majority proportion were female (60.0%, n=9/15) and 35-44 years of age (46.7%, n=7/15). Those clients with the lowest median CD4 count were 18-24 year old men (279 cells/mm^3, IQR: 116-524). Of the 149 HIV-infected participants, 30.9% (n=46/149) were on ART, with peak use amongst those aged

45+ years (65.2% [n=15/23] females and 69.2% [n=9/13] males). None of the 18-24 year olds had been initiated on treatment.

NCD-HIV Comorbidity by Sex and ART Use

NCD screening results amongst HIV-infected participants by sex can be found within Paper III, Table 3. A comparison of overall NCD screening results by HIV-status can be found within Paper III, Supplementary Table 2.

HIV-uninfected clients had significantly more overweight/obese BMI than HIV-infected clients (39.5% [n=244/618] vs 29.5% [n=44/149]; p=0.0243). Overall, the majority proportion of participants with overweight/obese BMI were women (82.0%, n=237/289), aged 25-34 years (32.5%, n=94/289). There were high rates of overweight/obesity among women regardless of HIV status (HIV-uninfected women: 80.3% [n=196/244]; and HIV-infected women: 90.9% [n=40/44]). HIV-infected women had significantly more overweight/obese BMI than HIV-infected men (37.0% [n=40/108] vs 9.8% [n=4/41]; p=0.0011), and this was inversely true for underweight BMI (males vs females: 43.9% [n=18/41] vs 13.0% [n=14/108]; p<0.0001).
Of all participants who had elevated BP, 18.0% (n=25/139) were also HIV-infected. There were no significant differences in prevalence of high BP by HIV status or by sex among those with HIV.

HIV-infected clients had significantly more high HbA1c than HIV-uninfected clients (16.1% [n=24/149] vs 9.6% [n=59/614]; p=0.0223). The majority proportion of both HIV-infected and HIV-uninfected clients with high HbA1c were women (79.2% [n=19/24] and 62.7% [n=37/59]). However, the PLHIV with high HbA1c were mostly aged 35-44 years (41.7%, n=10/24), while the majority of their HIV-uninfected counterparts were aged 45+ years (42.4%, n=25/59). Only four (16.7%, n=4/24) of the HIV-infected clients with high HbA1c were on ART, and we could find no association between ART use and high HbA1c.

Ten percent (n=15/149) of the HIV-infected participants also had high TC. While there was not a significant difference in prevalence of high or low TC by HIV status, HIV-infected men had significantly more low TC than HIV-infected women (22.0% [n=9/41] vs 9.3% [n=10/108]; p=0.0380). Of all comorbidities, HIV-infected individuals on ART had

significantly more high total cholesterol than HIV-infected clients not on ART (21.7% [n=10/46] vs. 4.9% [n=5/103]; p=0.0016)

4.3 HEALTH SYSTEMS STRENGTHENING

Health system strengthening strategies were evaluated through an assessment of the quality of task-shifting NCD risk factor screening to counsellors and feasibility of integrating NCD risk factor screening into standard of care HTS, using both the QA/QC of counsellor-led screening results and recommended referrals and median clinic flow time for each HTS phase.

4.3.1 QUALITY OF TASK-SHIFTING

Table 4-4 provides results for the counsellor-led screening results and recommended referrals, which were QA/QC'ed by the study nurse.

Out of 772 clients screened for BP, seven (0.9%) were found to have low BP and 139 (18.0%) high BP. After these 146 clients were rechecked by the nurse, three (2.1%) and 59 (40.4%) client referrals were given for low and high BP, respectively. There was one (33.3%, n=1/3) and five (8.5%, n=5/5) incorrect referrals made by counsellors for low and high BP, respectively. There were 2.4% (n=2/83) incorrect referrals for high blood glucose, whereas 97.6% (n=81/83) were correctly given. Blood cholesterol testing resulted in 62 (8.1%, n=62/768) referrals for high blood cholesterol, with 58 (93.6%, n=58/62) and 4 (6.5%, n=4/62) referrals correctly and incorrectly given, respectively. Across STI and TB symptoms screenings, all (24 STI and 17 TB referrals) were correctly referred. More than 10% of referrals were given for HIV (12.6%, n=97/773) with one (1.0%, n=1/97) referral incorrectly given.

Table 4-4. Correct and Incorrect Counsellor Referrals

Variable	Overall Screening results	Proportion referred	Counsellors: Correct referrals	Counsellors: Missed opportunities
Blood pressure (BP)				
Low BP (%)	7/772 (0.9)	3/7 (42.9)	2/3 (66.7)	1/3 (33.3)
High BP (%)	139/772 (18.0)	59/139 (42.5)	54/59 (91.5)	5/59 (8.5)
Normal (%)	626772 (81.1)	-	-	-
Blood glucose				
High blood glucose (%)	83/766 (10.8)	83/83 (100.0)	81/83 (97.6)	2/83 (2.4)
Normal (%)	683/766 (89.2)	-	-	-
Blood cholesterol				
High blood cholesterol (%)	62/768 (8.1)	62/62 (100.0)	58/62 (93.6)	4/62 (6.5)
Low/Normal (%)	706/768 (91.9)	-	-	-
STI Screening				
1+STI symptom (%)	24/776 (3.1)	24/24 (100.0)	24/24 (100.0)	0/24 (0.0)
No symptoms (%)	752/776 (96.9)	-	-	-
TB screening				
1+ TB symptom (%)	19/748 (2.5)	17/19 (89.5)	17/17 (100.0)	0/17 (0.0)
No symptoms (%)	730/748 (97.5)	-	-	-
HIV				
Positive (%)	149/775 (19.2)	97/149 (65.1)	96/97 (99.0)	1/97 (1.0)
Negative (%)	626/775 (80.8)	-	-	-

Sexually Transmitted Infections, STI; Tuberculosis, TB; Human Immunodeficiency Virus, HIV.
Note: Of the 146 clients with abnormal BP measured by counsellors, 83 were not referred as their BP resolved when re-checked by the nurse prior to referral. Of the 19 clients with 1+ TB symptom, 2 were not referred because they currently had TB and were already on treatment. Of the 149 HIV-infected clients, 52 were not referred because 46 were on treatment, 1 had to be referred by TB clinic and 5 did not come back for referral.

4.3.2 FEASIBILITY OF INTEGRATING NCD SCREENINGS INTO CLINIC FLOW

The median time spent in minutes within each point of HTS phase clinic flow (time at reception, for pre-test counselling, for counsellor-led screenings, for Family History and Behaviour Form, for post-test counselling, total time for counsellor HTS process, and total time spent within the HTS centre), as well as a comparison of the time spent between the standard

of care and integrated NCD-HTS models is found within Paper IV, Table 2. A visual depiction of the clinic flow and the difference in time can be seen within Paper IV, Figure 3.

The median time spent at reception in minutes was significantly shorter during standard of care HTS relative to integrated NCD-HTS (15.0, IQR: 9.0–21.0, [n=265/284] vs. 19.0, IQR: 12.0-28.0, [n=331/333]; p<0.0001). There was no statistically significant difference in time spent for pre-test counselling between HTS models. While the median time in minutes spent for all counsellor-led screenings was significantly shorter for standard of care HTS as compared to integrated NCD-HTS (17.0, IQR: 13.0–22.0, [n=281/284] vs. 21.0, IQR: 17.0-27.0, [n=332/333]; p<0.0001), the time spent on the Family History and Behavioural Survey (part of the screening process) was shorter during integrated NCD-HTS (6.0, IQR: 5.0-8.0, [n=330/333] vs 8.0, IQR: 6.0-11.0, [n=281/284]; p < 0.0001). Post-test counselling time was significantly shorter during standard of care HTS relative to integrated NCD-HTS (7.0, IQR: 5.0–8.0, [n=284/284] vs. 8.0, IQR: 6.0-10.0, [n=332/333]; p<0.0001)

Standard of care HTS clients took a significantly shorter median time (in minutes) for the overall counsellor-led HTS process (i.e.; pre-test counselling, counsellor-led health screenings, and post-test counselling) relative to those in integrated NCD-HTS (36.5, IQR: 31.0–45.0, [n=284/284] vs. 41.5, IQR: 35.0–51.0, [n=332/333]; p<0.0001). Regarding the total amount of time a client spends in the clinic from starting to finish, standard of care HTS clients spent significantly shorter time in minutes as compared to integrated NCD-HTS clients (86.0, IQR: 72.0-108.0, [n=283/284] vs 102.0, IQR: 87.0-136.0, [n=331/333]; p<0.0001).

4.4 SCREENING AND TREATMENT POLICIES/GUIDELINES AND PRACTICE

The results pertaining to screening and treatment policies and practice are the proportions of integrated NCD-HTS clients with newly and previously diagnosed chronic disease, proportions of those previously diagnosed who had ever initiated treatment and remained with uncontrolled as compared to controlled chronic disease, and the care cascades from client referral through linkage to care and initiation of treatment for clients within both HTS phases. This subsection also presents HTS client responses depicting barriers to linkage to care and initiation of treatment, some of which are also supportive results for other themes (e.g.; *Health Systems Strengthening* and *Transferability*), but fit best within this subsection.

4.4.1 INTEGRATED NCD-HTS CLIENTS WITH NEWLY DIAGNOSED, CONTROLLED AND UNCONTROLLED DISEASE

The proportions of integrated NCD-HTS clients who were newly and previously diagnosed with hypertension, high blood glucose and cholesterol; as well as the proportions of those previously diagnosed clients who had ever taken treatment who were found to have either controlled or uncontrolled disease; can be found within Paper III, Table 4 and Supplementary Table 2. Table 4-5 and table 4-6 detail the same types of proportions for integrated NCD-HTS clients who were diagnosed with HIV-infection *and* comorbid with NCD risk factors. Table 4-5 shows the associated data singularly for each condition (e.g.; the proportion of clients comorbid with HIV and high BP who were newly diagnosed with HIV, followed by the proportion of the same clients who were newly diagnosed with high BP). Table 4-6 reports the overall comorbid data (e.g.; how many clients comorbid with HIV and high BP were newly diagnosed for *both* conditions).

Table 4-5. Integrated NCD-HTS Comorbid Clients: Newly vs Previously Diagnosed and Controlled vs Uncontrolled Disease, by Condition

		Newly diagnosed		Previously diagnosed		Ever been on treatment		Controlled		Uncontrolled	
Variable	**Prevalence**	**HIV**	**NCD**	**HIV**	**NCD**	**HIV**	**NCD**	**HIV**	**NCD**	**HIV**	**NCD**
HIV	149/775 (19.2)	77/149 (51.7)	-	72/149 (48.3)	-	46/72 (63.9)	-	46/72 (63.9)	-	26/72 (36.1)	-
HIV-High BP comorbidity	25/769 (3.3)	9/25 (36.0)	15/22 (68.2)	16/25 (64.0)	7/22 (31.8)	10/16 (62.5)	7/7 (100.0)	10/16 (62.5)	-	6/16 (37.5)	7/7 (100.0)
HIV-High HbA1c comorbidity	24/614 (3.2)	13/24 (54.2)	20/20 (100.0)	11/24 (45.8)	-	4/11 (36.4)	-	4/11 (36.4)	-	7/11 (63.6)	-
HIV-High TC comorbidity	15/765 (2.0)	3/15 (20.0)	13/13 (100.0)	12/15 (80.0)	-	10/12 (83.3)	-	10/12 (83.3)	-	2/12 (16.7)	-

Human Immunodeficiency Virus, HIV; Non-communicable Disease, NCD; Blood Pressure, BP; Average Glycated Haemoglobin, HbA1c; Total Cholesterol, TC. *Newly diagnosed* was defined as HTS client self-reporting normal results at last screening and subsequently screening with abnormal results. *Previously diagnosed* was defined as HTS client self-reporting abnormal results at last screening and also screening with abnormal results. *Controlled* was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with normal results. *Uncontrolled* was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with abnormal results.

Note: TB patients were not asked questions on history of blood pressure, glucose and cholesterol resulting in missing data. If the first blood pressure reading was high, then a second reading was taken. The average reading of the two blood pressure readings was then categorized to determine prevalence of high blood pressure. Those HTS clients referred for high blood pressure were clients whose second BP reading was high and who had consented for follow-up.

Table 4-6. Integrated NCD-HTS Comorbid Clients: Newly vs Previously Diagnosed and Controlled vs Uncontrolled Disease, for Both Conditions

Variable	Prevalence	Newly diagnosed	Previously diagnosed	Ever been on treatment	Controlled	Uncontrolled
HIV	149/775 (19.2)	77/149 (51.7)	72/149 (48.3)	46/72 (63.9)	46/72 (63.9)	26/72 (36.1)
HIV-High BP comorbidity	25/769 (3.3)	6/22 (27.8)	5/22 (22.7)	5/5 (100.0)	-	5/5 (100.0)
HIV-High HbA1c comorbidity	24/614 (3.2)	10/20 (50.0)	0/20 (0.0)	-	-	-
HIV-High TC comorbidity	15/765 (2.0)	3/13 (23.1)	0/13 (0.0)	-	-	-

Human Immunodeficiency Virus, HIV; Non-communicable Disease, NCD; Blood Pressure, BP; Average Glycated Haemoglobin, HbA1c; Total Cholesterol, TC. *Newly diagnosed* was defined as HTS client self-reporting normal results at last screening and subsequently screening with abnormal results. *Previously diagnosed* was defined as HTS client self-reporting abnormal results at last screening and also screening with abnormal results. *Controlled* was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with normal results. *Uncontrolled* was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with abnormal results.
Note: TB patients were not asked questions on history of blood pressure, glucose and cholesterol resulting in missing data. If the first blood pressure reading was high, then a second reading was taken. The average reading of the two blood pressure readings was then categorized to determine prevalence of high blood pressure. Those HTS clients referred for high blood pressure were clients whose second BP reading was high and who had consented for follow-up.

Of the integrated NCD-HTS clients with self-reported health screening history data available, 72.4% (n=97/134) with elevated BP, 96.1% (n=73/76) with high blood glucose, and 93.3% (n=56/60) with high TC were newly diagnosed. Of those who had self-reported they previously knew their condition, 83.8% (n=31/37) self-reported they had already initiated antihypertensive medications, 66.6% (n=2/3) on medication to control high blood glucose, and 25.0% (n=1/4) on lipid-lowering therapy. All clients who self-reported they had initiated treatment for these conditions remained with uncontrolled disease when screening at the integrated NCD-HTS centre. Of the 149 HIV-infected participants, 48.3% (n=72) already knew their HIV-status; and of these clients, 63.9% (n=46/72) were on ART.

Of the HIV-infected clients with high BP, 36.0% (n=9/25) were newly diagnosed with HIV; of which the majority were female (66.7%, n=6/9) and aged 25-34 years (44.4%, n=4/9). Of the participants screened as having both HIV and high BP with screening history data available, 27.8% (n=6/22) were newly diagnosed for both conditions; half of which were females and aged 35-44 years (50.0%, n=3/6; each).

Of the 24 HIV-infected participants with high HbA1c, 54.2% (n=13/24) were newly diagnosed with HIV, of which the majority were female (69.2%, n=9/13) and aged 35-44 years (53.9%, n=7/13). None of the HIV-infected participants with high HbA1c were on medication for high blood glucose; and half were newly diagnosed for both conditions (50.0%, n=10/20), of which the majority were female (80.0%, n=8/10) and aged 35-44 years (70.0%, n=7/10).

One-fifth (20.0%, n=3/15) of clients with both HIV-infections and high TC were newly diagnosed with both conditions, of which all were female and two-thirds were aged 35-44 years.

4.4.2 PROPORTIONS OF AND TIME TAKEN UNTIL CLIENTS LINKED TO CARE AND INITIATED ON TREATMENT

Paper V, Tables 2&3 contain the results of the proportions of clients referred for each condition who were linked to care (Table 2), and initiated on treatment (Table 3). The tables also report the median time in days taken for clients to be linked to care and initiated on treatment. This data is further described in the following sub-sections.

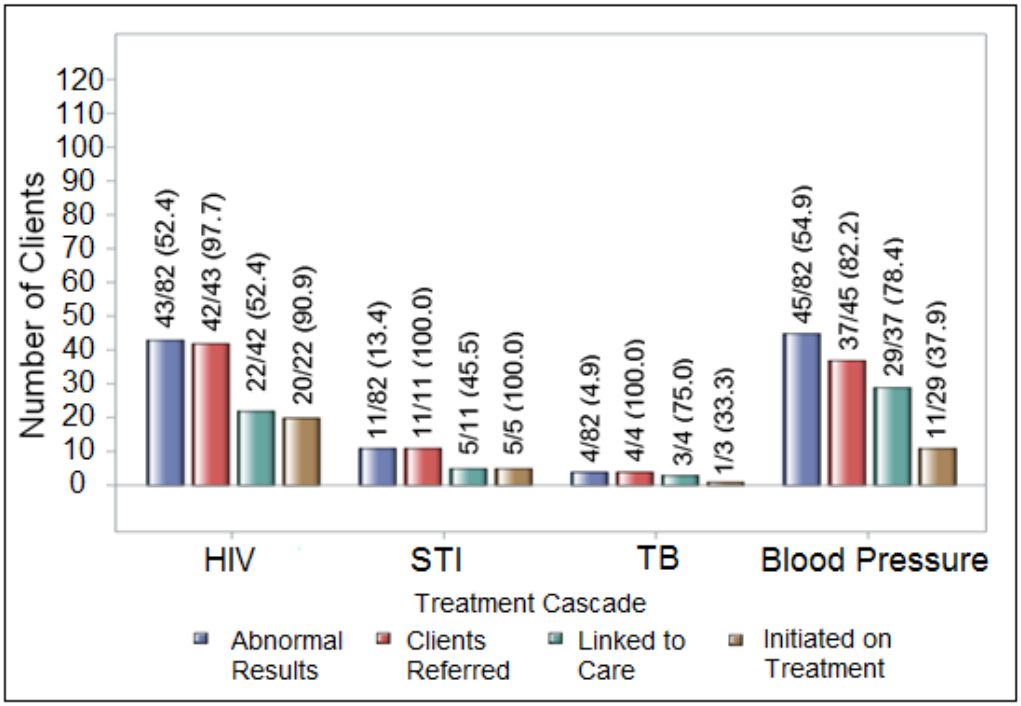
4.4.2.1 Overall, Standard of Care Referrals from Both Standard of Care and Integrated NCD-HTS

Of 320 client referrals across both standard of care and integrated NCD-HTS, 40.0% (n=128) were referred for HIV-infection, 11.9% (n=38) for STI symptoms, 6.6% (n=21) for TB symptoms, and 28.8% (n=92) for either high or low BP. The majority of these referred clients were linked to care within three months for ART (68.8%, n=88/128), STIs (73.7%, n=28/38), TB (71.4%, n=15/21), and high/low BP (84.8%, n=78/92) (please see Paper V, Supplementary Table 1).

It took a median time of 6.5 days (IQR:2.0-19.0), 8.0 days (IQR:3.0-23.0) and 10.0 days (IQR:2.0-20.0) for clients referred for STIs, abnormal BP, and TB, respectively, to link to care for these conditions, across both HTS phases. Of these participants who did link to care, 88.6% (n=78/88) were initiated on ART, 78.6% (n=22/28) were initiated on treatment for STIs, 6.7% (n=1/15) began TB treatment, and 37.2% (n=29/78) were initiated on anti-hypertensive medications (please see Paper V, Supplementary Table 1). Therefore, of all referred clients, 60.9% (n=78/128) were initiated on ART, and 57.9% (n=22/38) were treated for STIs, 4.8% (n=1/21) for TB, and 31.5% (n=29/92) for high BP. It took between an average of 2.0 days (IQR: 2.0-2.0; for TB) and 9.0 days (IQR: 5.0-21.0; for ART) for clients to initiate treatment for standard of care referrals. Treatment was not needed for a high proportion of those linked to care for high/low BP in either HTS Phase (standard of care HTS: 58.6%, n=17/29; integrated NCD-HTS: 61.2%, n=30/49). None of the participants referred for low BP were initiated on treatment across HTS phases.

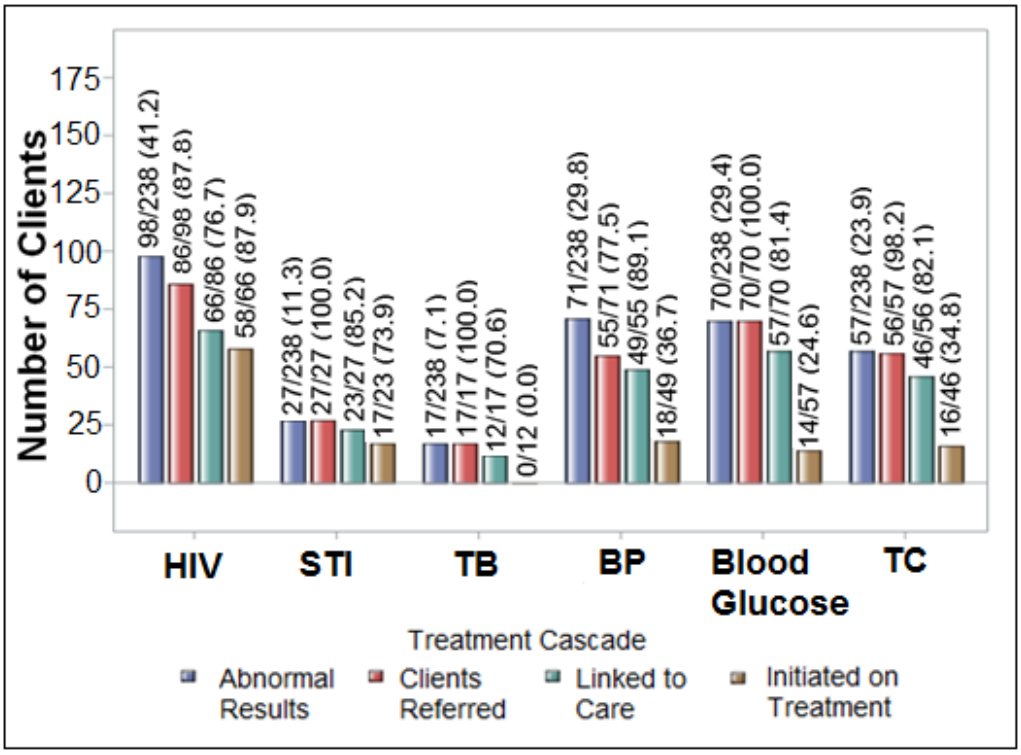
4.4.2.2 Comparison of Standard of Care HTS vs Overall Integrated NCD-HTS Linkage to Care and Treatment Initiation

Paper V, Figures 2a & 2b – also being shared here as Figures 4-2 & 4-3 – visually depict the standard of care and integrated NCD-HTS care cascades, which are described in this sub-section.



Human Immunodeficiency Virus (HIV), Sexually Transmitted Infections (STIs), Tuberculosis (TB), Blood Pressure (BP). Only HIV-infected clients who had not already been initiated on ART were referred. Abnormal results for BP take the average of two readings, while referrals were given to clients with two abnormal readings.

Figure 4-2. Standard of Care HTS Cascade, with Passive Linkage to Care



Human Immunodeficiency Virus (HIV), Sexually Transmitted Infections (STIs), Tuberculosis (TB), Blood Pressure (BP), Total Cholesterol (TC). Only HIV-infected clients who had not already been initiated on ART were referred. Abnormal results for BP take the average of two readings, while referrals were given to clients with two abnormal readings. One integrated NCD-HTS client with high cholesterol was not referred.

Figure 4-3. Integrated NCD-HTS Cascade, with Optional Navigated Linkage to Care

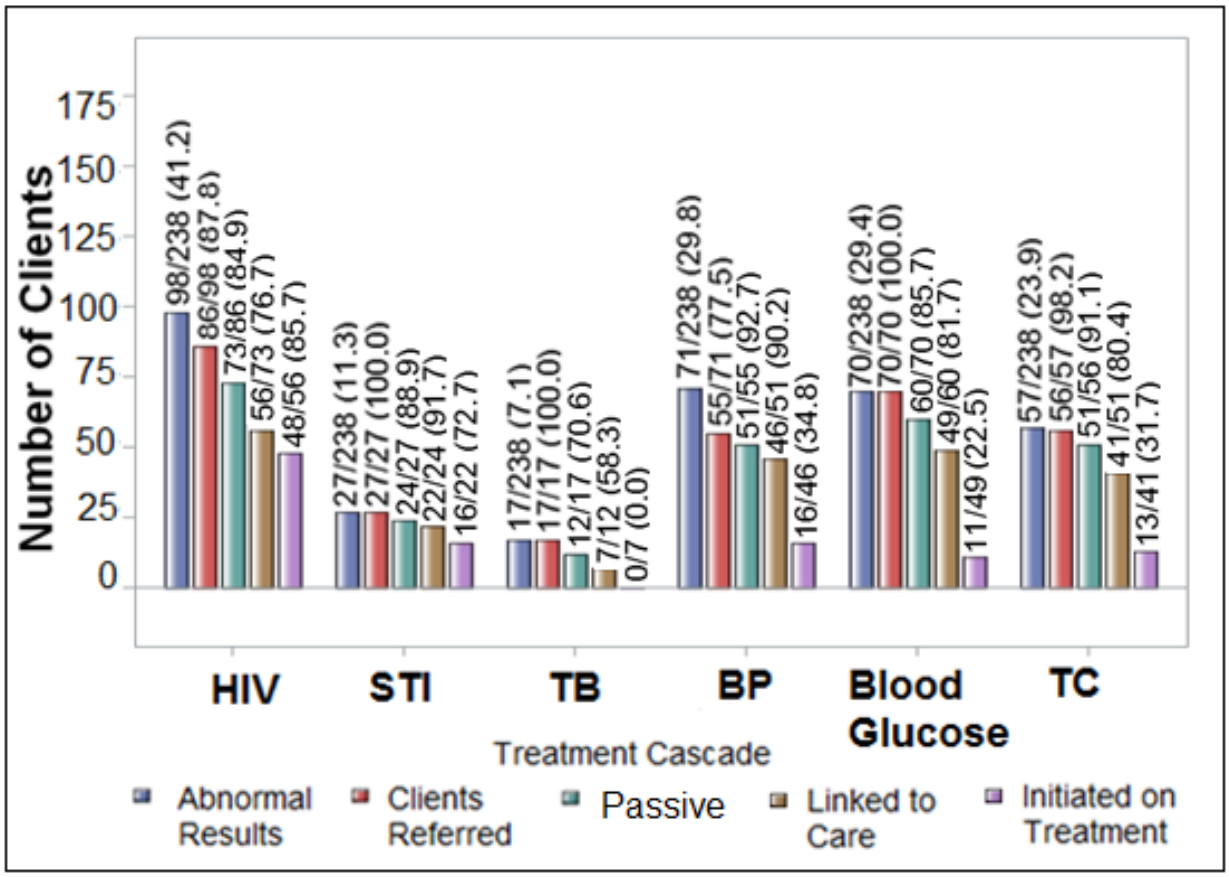
Overall, integrated NCD-HTS – with its optional active referral - had a larger proportion of clients linked to care for HIV, STIs, and high/low BP; with significantly more referred clients linked to care for ART and STIs as compared to standard of care HTS (76.7% [n=66/86] vs. 52.4% [n=22/42], p=0.0052; and 85.2% [n=23/27] vs. 45.5% [n=5/11], p=0.0117; respectively). Overall, integrated NCD-HTS also linked clients to care within a shorter time on average, across all conditions, as compared to standard of care HTS (the shortest being 6.0 days for STIs [IQR:1.0-17.0] with the longest being both 8.0 days for TB [IQR:1.5-18.5] and 8.0 days for high/low BP [IQR:2.0-14.0] vs the shortest being 8.0 days for HIV [IQR:2.0-22.0] and the longest being 13.0 days for high/low BP [IQR:6.0-32.0]).

Not excluding those clients who linked to care but were not initiated on treatment, standard of care HTS – with passive referral, only - had higher proportions of clients who were linked to care subsequently initiated on treatment for each condition, as compared to integrated NCD-HTS. However, integrated NCD-HTS initiated its clients on treatment in a shorter amount of time for HIV, STIs, and BP compared to standard of care HTS - the shortest time being 5.0 days for STIs (IQR:1.0-21.0) and the longest time being both 8.0 days for ART (IQR:5.0-17.0) and 8.0 days for high BP (IQR:2.0-13.0) vs the shortest time being 8.0 days for high BP (IQR:2.0-29.0) and the longest time being 19.5 days for ART (IQR:6.5-26.5).

For the referrals specific to integrated NCD-HTS, 81.4% (n=57/70) and 82.1% (n=46/56) of clients referred for hyperglycaemia and high cholesterol were linked to care; and of those, 24.6% (n=14/57) and 34.8% (n=16/46) were initiated on treatment, respectively. It took 14.5 days on average (IQR: 7.0-24.0) for clients to initiate treatment for hyperglycaemia and 11.5 days on average (IQR: 1.5-21.0) for high cholesterol. A high proportion of clients did not need treatment once re-assessed at the referral clinic for each condition – 70.2% (n=40/57) of referred clients for high glucose and 63.0% (n=29/46) of referred clients for high cholesterol, respectively.

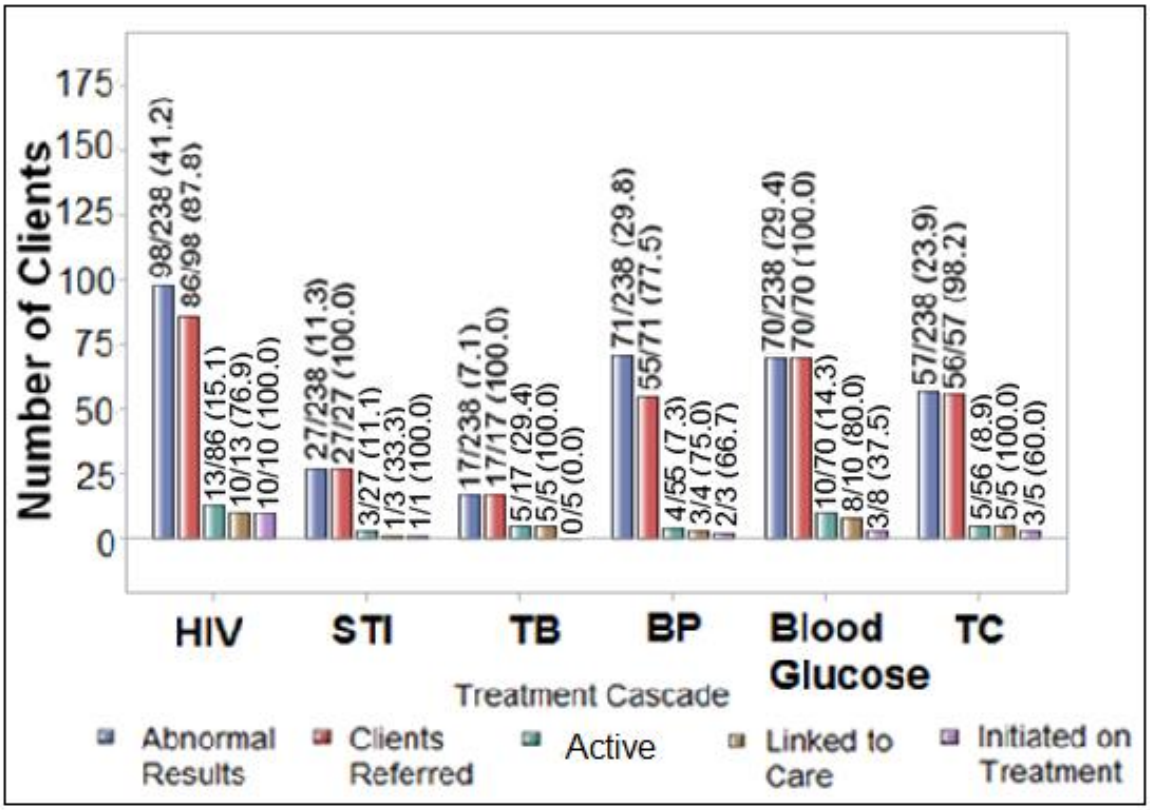
4.4.2.3 Integrated NCD-HTS Passive vs Active Linkage to Care and Treatment

Paper V, Figures 2c & 2d – also being shared here as Figures 4-4 & 4-5 – visually depict the integrated NCD-HTS care cascades for referred clients electing either passive or active linkage to care. These results are further described in this sub-section.



Human Immunodeficiency Virus (HIV), Sexually Transmitted Infections (STIs), Tuberculosis (TB), Blood Pressure (BP), Total Cholesterol (TC). Only HIV-infected clients who had not already been initiated on ART were referred. Abnormal results for BP take the average of two readings, while referrals were given to clients with two abnormal readings. One integrated NCD-HTS client with high cholesterol was not referred. Significantly more Phase 2 participants chose passive referral over active referral (89.1% [n=212/238] vs. 10.9% n=26/238]; p<0.0001). Of the participants who were referred for STIs, significantly more were linked to care who chose passive referral as compared to active linkage to care (91.7% [n=22/24] vs. 33.3% [n=1/3]; p=0.0073) compared to active linkage to care.

Figure 4-4. Integrated NCD-HTS Care Cascade, Passive Referral Only



Human Immunodeficiency Virus (HIV), Sexually Transmitted Infections (STIs), Tuberculosis (TB), Blood Pressure (BP), Total Cholesterol (TC). Only HIV-infected clients who had not already been initiated on ART were referred. Abnormal results for BP take the average of two readings, while referrals were given to clients with two abnormal readings. One integrated NCD-HTS client with high cholesterol was not referred.

Figure 4-5. Integrated NCD-HTS Care Cascade, Active Referral Only

Significantly more participants chose passive referral over active referral (89.1% [n=212/238] vs. 10.9% [n=26/238]; p<0.0001). Of the participants referred for STIs who were linked to care, significantly more chose passive referral as compared to active referral (91.7% [n=22/24] vs. 33.3% [n=1/3]; p=0.0073). There were no other statistically significant differences between passive and active linkage to care and treatment initiation (please see Paper V, Supplementary Table 2 for these comparisons).

Across conditions, a high proportion of integrated NCD-HTS participants were passively linked to care, ranging from 91.7% (n=22/24) for STIs to 58.3% (n=7/12) for TB. Those linked to care for STI were linked within the lowest average number of days of 6.5 (IQR: 2.0-17.0), whereas those reaching care for TB did so within the highest average number of days (17.0, IQR: 2.0-20.0).

The majority of integrated NCD-HTS clients who were passively linked to care for ART and did reach care were initiated on treatment successfully (75.0%, n=42/56) within an average

number of days of 9.0 (IQR: 6.0-17.5). STI passive referrals also had a high number of participants successfully initiated on treatment (63.6%, n=14/22). A large proportion of passively referred clients within integrated NCD-HTS did not need to initiate treatment after further assessment: 63.0% (n=29/46) for BP clients, 71.4% (n=35/46) and 68.3% (n=28/41) of clients with hyperglycaemia and high blood cholesterol, respectively. Of the ten participants who were actively linked to care for ART within integrated NCD-HTS, 90.0% were successfully initiated on treatment in an average of 2.5 (IQR: 0.0-8.0) days.

4.4.3 BARRIERS TO LINKAGE TO CARE AND INITIATION OF TREATMENT

This sub-section reports the HTS client responses to the following questions, if applicable: 1) why did you choose passive referral over active referral?, 2) why did you not go to your referral clinic?, and 3) if you did attend your referral clinic, why were you not initiated on treatment? Table 4-7, summarises these data points, and they are also further described.

Table 4-7. HTS Client Responses Surrounding Barriers to Linkage to Care and Initiation of Treatment

Themes	Sub-themes	Frequency	Examples of HTS Client Responses
Reasons for choosing passive referral over active referral (N=70)	Prefer to go alone	55.7% (n=39/70)	'I can manage on my own.'
	Close proximity/familiar with referral clinic	11.4% (n=8/70)	'Clinic is nearby and I am familiar with it.'
	Chose to self-support	8.6% (n=6/70)	'I believe I have to take responsibility and go alone.' 'I will [have to] go to the clinic [alone] anyway for my treatment.'
	Have own transport	7.1% (n=5/70)	'I will use my car to my referral clinic.'
	Already have a support system	5.7% (n=4/70)	'I have my sister.'
	Did not like the idea of navigated linkage to care	5.7% (n=4/70)	'I don't like it.'
	Want privacy	2.9% (n=2/70)	'I need my privacy.'
	Have a referral letter	2.9% (n=2/70)	'I am comfortable because I have a referral letter.'
Reasons for referred HTS clients not linking to care (N=95)	Too busy	41.1% (n=39/95)	'I was busy with a part time job, but when I have time, I will go.'
	Not ready for treatment	23.2% (n=22/95)	'I still want to digest the whole thing, then I will go.' 'I am not ready to take treatment.'
	Unable to attend clinic	14.7% (n=14/95)	'I have not gone to my referral due to personal and family reasons.' '[I do not] have money to go to the clinic…'
	Treatment refuser	8.4% (n=8/95)	'[I] never went to the clinic and [I] will not go. [I am] not ready to start treatment at the clinic, they'd want to [initiate me].'
	Waiting for partner	4.2% (n=4/95)	'I am still busy discussing it with my boyfriend.'

			'[I] didn't go, waiting for [my] boyfriend to go with [me].'
	Health system barriers	3.2% (n=3/95)	'[I] gave the nurse the referral letter, but they only focused on the BP and Cholesterol [referrals and] didn't check [my] STI symptoms'. '[I] didn't have enough time to be checked for TB when [I] went to the clinic for [my] STI [referral] as [I] had to go to work'
	Chose muti	2.1% 9n=2/95)	'[I] didn't go to the local clinic [for high cholesterol], [my] partner prepared muti for [us] to drink.'
	Not comfortable in going to referral clinic	1.1% (n=1/95)	'…and [I am] not comfortable… because there is family member [there] and [the] clinic is [in my] hood…'
	No more symptoms	1.1% (n=1/95)	'[I] will not be going to the referral clinic as [I do] not see what [I] suspected as an STI [anymore].'
	Forgot	1.1% (n=1/95)	'[I] had forgotten about [my] high blood referral but [I] will go before the end of the week.'
Reasons for HTS clients who linked to care not initiating on treatment (N=196)	Normalised condition/negative results upon reassessment	49.7% (n=97/196)	'The doctor checked [my] cholesterol and it was found to be within normal levels.'
	Prescribed healthy lifestyle modification	16.2% (n=32/196)	'[I] went to the clinic, but they didn't initiate [me]. They said [I] must boost [me] iron by changing [my] diet and eat[ing] more of the food that boosts iron.'
	Continued monitoring	14.7% (n=29/196)	'[I am] being advised to change diet and come back to clinic regularly.'
	Already on medication	6.1% (n=12/196	'[I am] already on treatment, so [my] medication was not changed…'
	Follow-up laboratory results/counselling needed	6.1% (n=12/196)	'I was given a date to come back after blood was collected, but [I haven't gone back due to hectic work schedule'. '...[I am] still attending adherence classes and still [need] to go back when free at work…'].
	Not helped	4.6% (n=6/196)	'I couldn't open file, because the clinic was full.' 'They said they won't give me treatment, because it is caused by stress - even when it was 168 over 110.'
	Initial pill given, no prescription	1.0% (n=2/196)	'The tests were not high enough for [me] to be initiated on treatment, but they gave [me] a pill to help stabilize the sugar and will continue monitoring.'
	Pregnant	0.5% (n=1/196)	'They advised me to give birth first [before addressing her STI symptom referral].'

4.4.3.1 Integrated NCD-HTS Client Reasons for Choosing Passive over Active Linkage to Care

There were 67 integrated NCD-HTS client responders who reported 70 total reasons as to why they chose passive referral over active referral (n=67/212, 31.6%). The main reason stated was that the client preferred to go alone (55.7%). Other reasons described were the close proximity and/or familiarity of the referral clinic (11.4%) and choosing to self-support (8.6%) (e.g.; '*I*

believe I have to take responsibility and go alone' and *'I will [have to] go to the clinic [alone] anyway for my treatment'*). Having one's own transport (7.1%) and/or support system (5.7%) (e.g.; the support of a partner, family member, friend, or work colleague), and wanting privacy or having a referral letter to present to the clinic (2.9%, each) were other reasons for choosing passive linkage to care. Overall, 5.7% expressed they did not like the idea of navigated linkage to care.

4.4.3.2 Reasons for Not Linking to Care

There were 75 responses received by clients across both HTS phases yielding 95 reasons for not successfully linking to care across all referrals. Of the 95 reasons, 41.1% were due to being too busy to attend the referral but were still planning on going and 23.2% were not yet ready or needed to absorb their results prior to seeking care and/or treatment services. Other clients were unable to attend their referrals due to various reasons (i.e.; having been sick or hurt, having relocated or been travelling, not having enough money for transport to the clinic, or due to personal and/or family issues; 14.7%). There were blunt refusals towards obtaining treatment from clients referred for HIV-infection and/or high BP, (8.4%). One client referred for high BP shared: *'[I] never went to the clinic and [I] will not go. [I am] not ready to start treatment at the clinic, they'd want to [initiate me]*'. Some clients wished to wait for their partner to participate in couples' HIV counselling and testing before seeking treatment (4.2%).

There were a few barriers (3.2% in total) encountered at the point of entry into the health system (i.e.; not receiving help due to results not being looked at by the provider, having run out of time at the clinic, and the nurse not understanding the referral letter).For example, one client shared: '*[I] gave the nurse the referral letter, but they only focused on the BP and Cholesterol [referrals and] didn't check [my] STI symptoms'.* Another client shared: '*[I] didn't have enough time to be checked for TB when [I] went to the clinic for [my] STI [referral] as [I] had to go to work'.*

Two responses from clients referred for hyperglycaemia and high blood cholesterol shared that they chose to drink traditional African medicine (i.e.; *muti*), instead. Other responses regarded (STI) symptoms having cleared up, forgetting about their referral, and stigma-related reasons serving as a deterrent for linking to care (1.1%, each). For example, one client referred for ART shared: '*[I do not] have money to go to the clinic and [I am] not*

comfortable… because there is family member [there] and [the] clinic is [in my] hood so [I am] uncomfortable but [I am] making a plan'.

4.4.3.3 Reasons for Linking to Care but Not Being Initiated on Treatment

There were 160 responses received by clients across both HTS phases yielding 196 reasons for not initiating treatment across all referrals. Of the 196 reasons, 49.7% were due to BP, blood glucose and/or blood cholesterol having normalised and/or receiving a negative STI and/or TB test result upon being re-checked at the referral clinic. For NCD risk factor referrals (i.e.; BP, blood glucose and cholesterol), 16.2% were prescribed a healthy lifestyle modification rather than medication, ['*Client went to the clinic, but they didn't initiate her. They said she must boost her iron by changing her diet and eat[ing] more of the food that* boosts *iron*.']; 14.7% were to undergo continued monitoring; and 6.1% were already initiated on treatment prior to their diagnosis.

Other reasons for non-initiation were that laboratory tests were conducted (e.g.; blood and/or sputum analysis), administrative tasks had to be completed (e.g.; ART adherence classes), and follow-up appointments were required prior to initiation of treatment (6.1%). For example, three of these clients who had been referred for ART shared similar reasons as follows: ['*She was given a date to come back after blood was collected, but [she] hasn't [gone] back due to hectic work schedule']*. A fourth HIV-infected client shared: ['*...[I am] still attending adherence classes and still [need] to go back when free at work…*'].

Additionally, 4.6% were either not helped due to the clinic being full or just not having their condition checked, ['*I couldn't open file, because the clinic was full.*'] and ['*They said they won't give me treatment, because it is caused by stress - even when it was 168 over 110*.']; 1.0% were given an initial pill to control their high BP and/or hyperglycaemia, not a prescription, ['*The tests were not high enough for him to be initiated on treatment, but they gave him a pill to help stabilize the sugar and will continue monitoring*.']; and one client (0.5%) self-reported that she could not receive STI treatment as she was found to be pregnant.

4.5 TRANSFERABILITY

Likelihood of transferability of the strategies implemented (i.e.; integrating counsellor-led NCD screenings into standard of care HTS) was measured within the study through assessing client satisfaction among both HTS phases. The study specifically analysed HTS client

satisfaction with the HTS services provided, clinic flow time, and any likes, dislikes and suggestions shared by HTS model.

4.5.1 CLIENT SATISFACTION WITH SERVICES

Paper IV, Figure 2, provides a visual representation of client satisfaction with various HTS services and compares the data by HTS phase.

4.5.1.1 Client Satisfaction with Pre-Test and Post-Test Counselling by HTS Model

The majority of participants were very satisfied with the pre-test and post-test counselling they received in standard of care HTS (97.5% [n=276/283] and 95.0% [n=268/282]) and integrated NCD-HTS (97.3% [n=322/331] and 96.7% [n=320/331]).

There were four main suggestions from seven standard of care HTS responders on how to improve pre-test counselling: minimise the paperwork (n=3/7), provide in-depth information on health and/or disease (n=2/7), explain the rapid testing technology and screening machines used (HIV test kits and BP cuff and monitor) (n=1/7), and strengthen communication (n=1/7), presumably around the rapid testing process and instruments used. Four responders in integrated NCD-HTS suggested different improvements for pre-test counselling. They were providing further health information, inclusive of '*relationship goals and health practice*'; creating set appointment times between '8–15hrs'; providing additional screenings, such as '*prostate cancer*'; and explaining the new rapid testing machines (glucometer and lipidometer). Only one standard of care HTS client shared a suggestion to improve post-test counselling, which was for the counsellor to provide '*tips on what the client should work towards*'.

4.5.1.2 Client Satisfaction with Health Screening Procedures by HTS Model

Most participants were very prepared for the health screening procedures in standard of care HTS (90.8%, n=256/282) and integrated NCD-HTS (90.6%, n=300/331); and very comfortable with the level of comfort/discomfort while being tested in standard of care HTS (90.7%, n=254/280) and integrated NCD-HTS (94.0%, n=311/331). In standard of care HTS, of those who saw the nurse, 96.5% (n=82/85) found speaking with the nurse very helpful, while 98.3% (n=172/175) did in integrated NCD-HTS. Overall, the majority of participants were very satisfied with the experience they had at Zazi HTS centre in both standard of care HTS (97.8%, n=272/278) and integrated NCD-HTS (97.9%, n=320/327).

Only ten standard of care HTS responders (3.5% of clients, n=10/284) made suggestions to improve health screening procedures. Three responders desired additional health screenings

such as '*STI test and blood sugar test'* and also requested there to be less paperwork/administrative tasks; and one individual suggested each of the following: offer circumcision, improve the current testing procedure, explain the data collection process, and provide home visits. Integrated NCD-HTS contained only four responders (n=4/333), of which three suggested additional integrated HTS to include breast cancer and eye screening; and one client requested standardised appointments for certain screenings for which one might be unprepared.

4.5.2 CLIENT SATISFACTION WITH CLINIC FLOW TIME

Paper IV, Table 2, contains the level of HTS client satisfaction with different sections of the HTS clinic flow within both HTS phases.

Overall, the large majority of participants within both standard of care HTS and integrated NCD-HTS were very/somewhat satisfied with the time spent at reception, within pre-test counselling, providing screenings and test results, and within post-test counselling. There were no statistically significant differences in levels of HTS client satisfaction of counsellor-led HTS between the two HTS phases.

Specifically, when comparing the proportions of HTS client satisfaction within standard of care vs integrated NCD-HTS: 93.2% [n=262/281] vs 94.9% [n=313/330] of HTS clients were very/somewhat satisfied with the amount of time spent at reception, 96.4% [n=270/280] vs 98.5% [n=326/331] with time spent in pre-test counselling, 97.1% [n=272/280] vs 97.3% [n=322/331] with time conducting screening, and 98.2% [n=273/278] vs 97.6% [n=321/331] with time spent on post-test counselling.

4.5.3 HTS CLIENTS LIKES, DISLIKES, AND RECOMMENDATIONS BY HTS MODEL

This sub-section reports the HTS client responses to the following questions: 1) what did you like at the Zazi HTS centre?; 2) what did you dislike at the Zazi HTS centre?; and for integrated NCD-HTS clients, 3) what would you have wished the Zazi HTS centre would have provided you? Table 4-8, summarises the data points relating to the first and last question, and all data are also further described.

Table 4-8. HTS Client Responses Surrounding Likes, Dislikes, and Recommendations to the Zazi HTS Centre by HTS Phase

Themes	Sub-themes	Frequency		Examples of HTS Client Responses
		SOC HTS	Integrated NCD-HTS	
What was liked by HTS clients	Enjoyed services/customer care	49.6% (n=132/266)	35.5% (n=124/349)	'Exceptional service, satisfied [with] the whole procedure.'
	Friendly and supportive staff	12.8% (n=34/266)	22.3% (n=78/349)	'I liked the counsellor, very friendly and funny.'
	Provider communication style	9.4% (n=25/266)	8.6% (n=30/349)	'They explained to me everything and answered all my questions satisfactorily.'
	Felt comfortable	6.4% (n=17/266)	4.3% (n=15/349)	'They made me feel comfortable and relaxed.'
	Everything	4.5% (n=12/266)	8.0% (n=28/349)	'[I liked] everything, from reception to the end.'
	Counselling session	4.1% (n=11/266)	6.6% (n=23/349)	'I like the way they handle their counselling and the process of testing.'
	How clients were treated	--	4.3% (n=15/349)	'I was treated with respect.'
	Other	13.2% (n=35/266)	10.4% (n=36/349)	--
***Other* comprised responses falling under 4.0% of the total responses, and related to: professional environment, clinic flow time, how clients were treated, warm reception, feeling satisfied or safe, services were good for the community, the nurse, gaining knowledge, able to understand results, attention given, privacy, integrated services, and provision of tea.**				
What integrated NCD-HTS clients recommended	Provide medications	45.6% (n=36/79)		'I wish the clinic could provide the treatment (meds) for [those] diagnosed.'
	Additional services	20.3% (n=16/79)		'Home visit for patient who are terminal ill.'
	Refreshments	16.5% (n=13/79)		'Something like a sandwiches or cookies.'
	Minimise wait time	7.6% (n=6/79)		'Should try to reduce time one spend waiting.'
	Other	10.0% (n=8/79)		--
***Other* comprised responses falling under 4.0% of the total responses, and related to: providing more information, having additional staff and supplies, provide PrEP and PEP, have staff name tags, provide travel reimbursement, and minimise paperwork.**				

Standard of Care (SOC), HIV Testing Services (HTS), Non-communicable diseases (NCDs), Pre-exposure prophylaxis (PrEP), Post exposure prophylaxis (PEP)

4.5.3.1 What HTS Clients Liked by HTS Model

There were 246 (86.6%, n=246/284) responders depicting what clients liked about the clinic in standard of care HTS. Of these, 49.6% (n=132/266) reported that they enjoyed the services and/or customer care they received. Two responders stated, '*Good services, as I am a regular participant*' and '*Good service I got from reception to end'*. Additionally, 12.8% (n=34/266) stated they liked the friendly and supportive staff they interacted with, and 9.4% (n=25/266) shared they appreciated the clinic provider communication style. For example, one client shared, '*I was treated with respect and the staff was very friendly and kind. They explained to*

me everything and answered all my questions satisfactorily.' Other responses depicted clients liked feeling comfortable (6.4%, n=17/266), the in-depth and professional counselling session (4.1%, n=11/266), and the warm and welcoming clinic environment (3.4%, n=9/266).

In integrated NCD-HTS, 307 (92.2%, n=307/333) clients shared what they liked about Zazi. The majority of responses reported that of Phase 1 responses – 35.5% (n=124/349) appreciated the service, specifically the new screenings; 22.3% (n=78/349) enjoyed the welcoming, professional and supportive staff; and 8.6% (n=30/349) liked the effective communication of and information shared by the health care providers. One client responded, '*The staff member are very patient and explain things very well.'*

4.5.3.2 What HTS Clients Disliked by HTS Model

Of the 206 (72.5%, [n=206/284]) responders for standard of care HTS, 91.3% (n=190/208) shared they did not dislike anything about Zazi. Of the remaining responders, the most common reasons for dissatisfaction were with the amount of time spent waiting in the clinic (2.9%, n=6/208) and administration time spent during the clinic visit (i.e.; client registration systems and paperwork; 2.4%, n=5/208).

Of the 300 (90.1%, n=300/333) responders for integrated NCD-HTS, 88.7% (n=268/302) disliked nothing. Of the remaining responses (n=34/302), the top two reasons for dissatisfaction were duration of the clinic visit (55.9%, n=19/34), with responses being '*I spent more time than expected*' and *'[I] waited for too long at reception'*; and the amount of administrative paperwork conducted (17.7%, [n=6/34]).

4.5.3.3 What Integrated NCD-HTS Clients Wish Zazi HTS Would Have Provided

When integrated NCD-HTS clients were asked to share if they wished the clinic would have provided them anything else, 23.7% (n=79/333) made suggestions. Of these responders, 45.6% (n=36/79) wished medications – ART, and for both chronic conditions and over-the-counter – were available onsite. Additionally, 20.3% (n=16/79) requested additional services (e.g.; prostate and breast cancer screening, regular follow-up calls, and home visits for terminally ill patients); and 16.5% (n=13/79) would have liked refreshments served. Only 7.6% (n=6/79) clients wished the clinic could minimise time spent waiting.

5.0 DISCUSSION

This thesis explored the burden of NCD risk factors, HIV, and comorbidity among adults who attended an HTS centre within an HIV endemic urban-township setting in a LMIC; and also evaluated strategies implemented within the HTS programme aiming to improve the healthcare continuum. This section discusses the results in relation to national and international findings. It is organised into four thematic areas: health transition, health systems strengthening, health screening and treatment policies/guidelines and practice, and transferability of strategies into the public health system. This chapter concludes with contemplating how thesis findings relate to the conceptual framework and describes both strengths and limitations of the thesis, overall.

5.1 EPIDEMIOLOGIC TRANSITION IN PUBLIC HEALTH

Key Findings

- **High rates of overweight and obese South African young adults;**
- **High prevalence of elevated BP and HbA1c, and HIV amongst adult South Africans;**
- **NCD risk factors-HIV comorbitiy identified in adults in an urban, African township of Soweto, South Africa;**
- **The younger populations, aged 18-24 and 25-34 years, also carried a high prevalence of HIV and NCD risk factors; and**

Results from both HTS phases showed there is a high prevalence of both HIV and NCD risk factors; and the HIV-NCD risk factor comorbidity amongst an African urban, adult population in Johannesburg, South Africa. Both standard of care HTS and integrated NCD-HTS health screening results depicted high levels of overweight/obese BMI, elevated BP, and HIV; while integrated NCD-HTS health screening results also reported high rates of diabetic-level HbA1c and high TC. Of concern is that these chronic conditions also affected the younger populations (18-24 and 25-35 year olds), and the integrated NCD-HTS data showed women presented with disease earlier than men. Males had significantly more elevated BP than women, despite that women were significantly more overweight/obese than men. Women had more HIV-infection than men (standard of care HTS found this difference to be significant). HIV-infected clients had significantly higher HbA1c than HIV-uninfected clients, while those clients without HIV-infection were significantly more overweight/obese. This study also found integrated NCD-HTS clients on ART had significantly higher TC than HIV-infected clients not on treatment.

5.1.1 NON-COMMUNICABLE DISEASE RISK FACTOR PREVALENCE

This data supports existing research showing South Africa as having the highest rate of overweight/obese people in SSA.[368] The prevalence of high BP amongst the participants was far greater than previously reported by a national household survey conducted by Statistics South Africa (10.4%) – nearly three times more amongst standard of care HTS clients and nearly double the amount amongst integrated NCD-HTS clients.[369] One-in-ten integrated NCD-HTS clients had diabetic-level HbA1c, which was a similar prevalence to that found within formal urban settings as reported by the SADHS.[98] Eight percent of clients had high TC.

An important finding was that while a high percentage of integrated NCD-HTS clients screened with high HbA1c, only four of these participants had high random blood glucose, suggesting that for our population HbA1c is a better measure for abnormal glucose metabolism. Clients with abnormal HbA1c levels should be referred for further evaluation for DM. Iron-deficiency anaemia has been associated with elevated HbA1c levels, which resolve upon iron therapy.[370-375] This should always be a consideration when evaluating a client for DM. While the exact mechanism underlying the effects of iron deficiency anaemia on HbA1c levels is not fully known, it is potentially due to the modifications to the structure of haemoglobin (Hb) and levels of HbA1c in both old and new red blood cells.[190, 376] A national survey reported an overall prevalence of anaemia of 17.5% amongst South Africans aged 15 years and older, and women had nearly double the prevalence (22%) as compared to men (12.2%). Persons aged 65 years and older had the highest prevalence of anaemia (25.9%). Black Africans had an overall anaemia prevalence of 12.9% and combined moderate to severe anaemia prevalence of 1.7%; and participants from informal urban areas exhibited the lowest mean Hb levels (14.2 g/dL).[81]

5.1.2 HIV PREVALENCE AND NCD RISK FACTOR COMORBIDITY BY ART USE

Each HTS phase within the study found a higher HIV prevalence than reported by the latest National HIV Prevalence, Incidence, Behaviour and Communication Survey. The standard of care HTS population's HIV prevalence was slightly higher than the reported overall national prevalence, while the HIV prevalence for each sex amongst the integrated NCD-HTS client population was higher than previously reported for black Africans.[12] However, integrated NCD-HTS client HIV prevalence was similar to that found within the latest SADHS for Gauteng.[98] Both HTS phase HIV-infected clients had similar median CD4 counts (standard

of care HTS: 327 cells/mm^3; integrated NCD-HTS: 341 cells/mm^3), indicating HIV-infected populations with weakened immune systems.

The HIV-infected participants had high rates of comorbidity with all NCD risk factors screened for across both HTS phases. When compared to the HIV-uninfected group, HIV-infected clients only had significantly higher HbA1c levels. This finding supports a systematic review which found the prevalence of DM amongst TB patients in SSA to be significantly high, with an even higher prevalence amongst those co-infected with HIV.[377] In addition, participants on ART had significantly higher TC than those HIV-infected participants not on ART. This finding was not unique to only hypercholesterolemia. Metabolic consequences of PIs and NRTIs – two of the three main classes of ART - create an increased risk of hypertension and hyperglycaemia amongst PLHIV on treatment, as already described within this thesis' literature review.[37][149, 169, 183]

5.1.3 DISEASE PREVALENCE TRENDS BY AGE GROUP AND SEX

This study data highlighted chronic disease trends amongst the younger age groups, which differ from previous reports. While the data largely corroborates various national surveys regarding the prevalence of overweight/obese BMI, elevated BP, high HbA1c and cholesterol increasing with age,[81, 98, 378] this study found exceptions to this trend. The 18-24 year old standard of care HTS clients had more overweight/obese BMI than their 25-34 year old counterparts, and 18-24 year old integrated NCD-HTS clients had higher HbA1c and TC than the 25-34 year old group.

In general, there was a high prevalence of NCD risk factors amongst all age groups, even the youth. Irrespective of sex, data showed a high prevalence of overweight/obese BMI and diabetic-level HbA1c amongst the 18-24 year olds. Between one-quarter and one-third of the youngest clients had overweight/obese BMI across HTS phases. Nearly one in ten of the young adults within integrated NCD-HTS had high HbA1c; and compared to the SADHS, this study reported the 18-24 year olds had nearly nine times the prevalence of diabetic-level HbA1c for women and nearly four times the level for men.[98] While only about five percent of 18-24 year olds had elevated BP, fourteen percent of clients from the two youngest age groups (18-35 years olds) had the same condition, across HTS phases.

Adding to this age-group trend, was the finding that women seemed to present with chronic disease earlier than men. Across HTS phases, these study results are compatible with national data regarding females having significantly more HIV-infection[46, 108] and being significantly more overweight/obese[81, 98] than men across all age groups. This thesis also found over twice the prevalence of high TC amongst women than previously reported.[98] This trend towards the earlier development of NCD risk factors, especially among women, is worrisome as it has also been well documented that women have a higher HIV prevalence across all age groups. Peak HIV-infections occur among young women aged 15-24 years.[12, 98] Across HTS phases, HIV-infected women had between four and five times the rates of overweight/obese BMI than HIV-infected men.

The exception to the trend by sex and age was elevated BP. These study findings contradicted the Statistics South Africa national household survey in which prevalence of high BP increased with age in both sexes and was higher in women for all age groups.[369] There is a large literature outlining the relationship between overweight/obese BMI and chronic diseases such as hypertension.[6, 70, 379] However, while the female participants were significantly more overweight/obese than male participants, they did not have more hypertension in either HTS phase – men had significantly more high BP. Across HTS phases, about one in four men and one in six women had high BP. Integrated NCD-HTS male clients aged 18-24 years, none of which were overweight/obese, had over twice the prevalence of elevated BP than women of the same age. One in five men 18-35 years of age exhibited elevated BP.

5.2 HEALTH SYSTEM STRENGTHENING STRATEGIES

Key Findings

- **Incorrect screening referrals for high BP were more common than incorrect screening referrals for blood glucose or TC results;**
- **Including three additional counsellor-led NCD risk factor screening services only increased the time of counsellor-led HTS by five minutes, on average;**
- **Overall average time to conduct counsellor-led integrated NCD-HTS remained within the historical standard of care HTS timeframe of 45 minutes;**
- **Significantly more integrated NCD-HTS clients chose passive referral over peer-navigators linkage to care;**
- **Optional peer-navigated referral linked clients to care for all chronic conditions and facilitated treatment initiation for HIV and STIs in a shorter average time as compared to standard of care HTS passive referral; and**
- **Optional peer-navigated referral did not lead to significantly more clients initiated on treatment.**

This study showed task-shifting of rapid fingerprick testing for blood glucose and TC and provision of related referrals by lay counsellors; integrating NCD risk factor screening into standard of care HTS; and optional peer-navigated linkage to care are potential strategies to assist with health system strengthening efforts towards improving diagnosis and linkage to care for NCDs. Integrated NCD-HTS clients responded with strong satisfaction with the HTS services rendered and the clinic flow time. Counsellors were able to provide quality NCD risk factor rapid testing and interpretation of results for provision of referrals. There were less incorrect referrals noted by the supervising nurse for high glucose and TC as compared to high BP, which is already a standard of care HTS practice. The integration of screening for obesity via BMI categorization and rapid testing for blood glucose and TC into standard of care HTS was deemed feasible. The screening integration only increased the counsellor-led HTS clinic flow time by five minutes, on average, and it still remained within the traditional standard of care HTS timeframe of 45 minutes. While significantly more integrated NCD-HTS clients chose passive referral as opposed to peer-navigated referral, having peer-navigated referral as an option within integrated NCD-HTS did link significantly more clients to care for HIV referrals than did the solely passive referral offered by standard of care HTS. While not significant, optional peer-navigated referral did link clients to care for all chronic conditions and facilitated treatment initiation for HIV and STIs in a shorter average time than compared with standard of care passive referral. However, there was no significant difference in clients initiating treatment by mode of referral.

5.2.1 QUALITY TASK-SHIFTING OF NCD RISK FACTOR RAPID TESTING

Throughout the implementation of integrated NCD-HTS, the percentage of counsellor-led incorrect screening referrals for the newly added rapid blood glucose and cholesterol testing ranged from 2.4% (blood glucose) to 6.5% (blood cholesterol), which is low overall. Referrals for blood glucose and TC were conducted more correctly than referrals for abnormal BP, which is a standard of care HTS screening procedure. With national guidelines stating bloods must be rechecked at a referral clinic prior to prescription and initiation of medication (for HT, DM, and/or hypercholesterolemia),[169, 380, 381] the benefits of lay counsellors performing additional fingerprick rapid testing and providing referrals outweigh the risks of a potential incorrect screening referral equating to missed opportunities for disease management or unnecessary referrals.

Within this study, about four-in-five clients referred for high blood glucose or cholesterol were successfully linked to care for reassessment. Of those confirmed as having been linked to care, about one-quarter were initiated on treatment for high blood glucose and one-third for high blood cholesterol. These clients would have been completely missed opportunities for chronic disease diagnosis and management within standard of care HTS. While three-quarters and two-thirds of clients referred for high blood glucose and cholesterol, respectively, were not initiated on treatment, this does not necessarily mean the integrated NCD-HTS referral was incorrect upon client reassessment. There has been a shift towards the prescription of holistic management and lifestyle modification of NCD precursors given concerns of the economic sustainability of lifelong drug therapy.[380] In resource-limited settings, drug treatment may be delayed if the added CVD risk is low or moderate.[380] These patients may have been told to modify their lifestyles to lower their CVD risk, rather than prescribed treatment, and put on a health monitoring plan for six to twelve months.[380]

It was encouraging to find the level of integrated NCD-HTS training the counsellors received prior to implementing integrated screenings appeared to be adequate for the provision of quality task-shifting. Aside from the outsourced GCLP and rapid fingerprick testing method day-courses, training of the counsellors was conducted in-house over the course of one week. Key pieces of the training were practicals – the two days hands-on trainings with the lipidometers and glucometers by the accredited trainers and the two days of mock client visits within the clinic space. These practicals were crucial for learning how to manipulate the POC machines in order to read the results and therefore correctly interpret them for the purpose of referrals.

When organising trainings, management strived to adhere to the considerations listed within the WHO Consolidated Guidelines regarding provision of HTS by lay providers using RDTs.[42] The WHO recommends lay providers obtain training, mentoring and supervision by on-site supervisors, ideally including someone trained in laboratory procedures.[42] This was achieved through having the clinic model be counsellor-led, but nurse/clinician managed. Staff liaised with BARC SA and the POC testing machine trainers, as needed. The WHO also states national competency standards must be met to ensure high quality HTS. Modules must depict how to cover the full HTS procedure, inclusive of specimen collection, the conduct of the RDTs following the validated national testing algorithm and testing strategy, providing results and counselling, and reporting of results. Both external and internal QA must be

conducted.[42] Each of the aforementioned was covered within training, which perhaps contributed to the quality healthcare output.

5.2.2 FEASIBILITY OF INTEGRATED SCREENING WITHIN STANDARD OF CARE HTS CLINIC FLOW

As described within the thesis' literature review, standard of care HTS is historically conducted in about 45 minutes – ten minutes for pre-test counselling, 15–20 minutes to conduct the HIV RDT, and 15 minutes for post-test counselling.[319] Within both HTS phases of this study, individual - not group - pre-test counselling was conducted, and counsellors incorporated individual risk assessments and risk reduction plans into its post-test counselling as per national guidelines.[23] While it took the counsellors a significantly longer time to conduct the rapid health screenings and post-test counselling within integrated NCD-HTS as compared to standard of care HTS, both HTS models of the counsellor-led HTS process were completed in a faster median time than the typical 45 minute HTS timeframe. This was largely due to the faster than average post-test counselling timeframes. The shorter post-test counselling sessions could have reflected the eventual triage to the nurse for clients needing referrals and further counselling, which unfortunately was not included in the timeframe.

Given the relatively small difference in time spent between the counsellor-led standard of care HTS and integrated NCD-HTS models, despite introducing three new screening measures for NCD risk factors, it is important to consider investigating if the same quality of care standard is actually met – in both screening conduct and information-sharing. While study findings showed there is indeed quality screening conducted, the assessment of the quality of integrated counselling was not an objective of this thesis.

Further discussion on the feasibility of implementing integrated NCD-HTS into the public sector is within section 5.4, *Transferability*.

5.2.3 CLIENT SATISFACTION OF INTEGRATED NCD-HTS SERVICES AND CLINIC FLOW TIME

The integrated NCD-HTS model showed a high level of client satisfaction with healthcare delivery system factors, such as the warm and welcoming environment, inclusive of professional and non-judgemental healthcare providers; screenings offered; communication of health information; and clinic flow time. Over one in ten of our study participants were repeat clients in the short-term, which constitutes positive user experience. Furthermore, the great majority of all clients opted in to each NCD screening integrated within our HTS programme.

A study has shown that high-reported patient satisfaction likely overstates the quality of health services due to positively framing statements, which induces bias. Evaluations including patient satisfaction surveys also need to complement patient satisfaction measures with more objective measures of quality.[382] While the client survey utilised in this thesis did contain objective measures, using a 5-point Likert scale, it is important to consider investigating if the same quality of care standard was actually met – in both screening conduct and information-sharing, as aforementioned. Despite the high level of client satisfaction, perhaps the quality of counselling did suffer. There were shorter than average counselling sessions and clients did suggest more robust information sharing, such as explaining the new rapid testing machines and providing further health practice information.

Integrated NCD-HTS clients shared their dislike for the amount of time it took to complete paperwork. The study site was embedded within a research unit, and therefore, there were extensive data collection procedures for other research-related purposes. For example, the demographics form and client contact information sheet were broader in nature and would not typically be distributed as such in the public sector for completion at reception. Screening procedures would not typically include such a lengthy family history and behavioural survey (median time of 8 and 6 minutes, for standard of care HTS and integrated NCD-HTS, respectively). The extra time spent within the clinic on this paperwork would not occur within public sector HTS procedures, and therefore the integrated NCD-HTS timeframe from reception through counsellor-led HTS would become shorter and even more feasible.

5.2.4 PEER-NAVIGATED LINKAGE TO CARE

This thesis presents a comparison between standard of care HTS with passive referral and integrated NCD-HTS with optional peer-navigated (active) referral. While significantly more referred clients preferred the passive referral method as compared to active referral, having peer-navigated referral as an option did aid in linking significantly more HIV-infected clients to care than solely offering passive referral. While not significant, optional active referral also both linked clients to care for all standard of care screening referrals and assisted with initiating HIV and STI patients on treatment in a shorter average time than standard of care HTS passive referral. However, this strategy did not translate to significantly more clients referred for NCD risk factors linked to care or initiated on treatment or significantly more HIV-infected clients initiated on ART. Through further investigation, multi-level barriers affecting linkage to care and initiation of treatment across chronic diseases were identified.

While a known challenge towards achieving timely linkage to care and initiation of treatment is passive referral,[31] this study identified yet another challenge – significantly more referred participants actually prefer passive as compared to peer-navigated linkage to care and treatment. To sufficiently assess the success or failure of this health systems strengthening strategy, it is critical to understand *why* –why was peer-navigated referral not as popular with integrated NCD-HTS clients; what barriers exist towards choosing this option?

Ultimately, understanding why a patient seeks or refuses entry into care and treatment services requires the understanding of complex health-risk and treatment-seeking behaviours which are influenced by factors at multiple levels.[383-386] After an extensive review of multi-level theories within literature and comparison with findings from this thesis, a complex model – the Transdisciplinary Model of Health Decision-Making (TMHD) (see Figure 5-1) - was selected as the best explanatory paradigm for the decision of an HIV-infected person to initiate ART. While this model explicitly pertains to patient barriers and facilitators towards accessing HIV care and ART initiation, these study results found it is applicable to accessing NCD-related healthcare, as well.

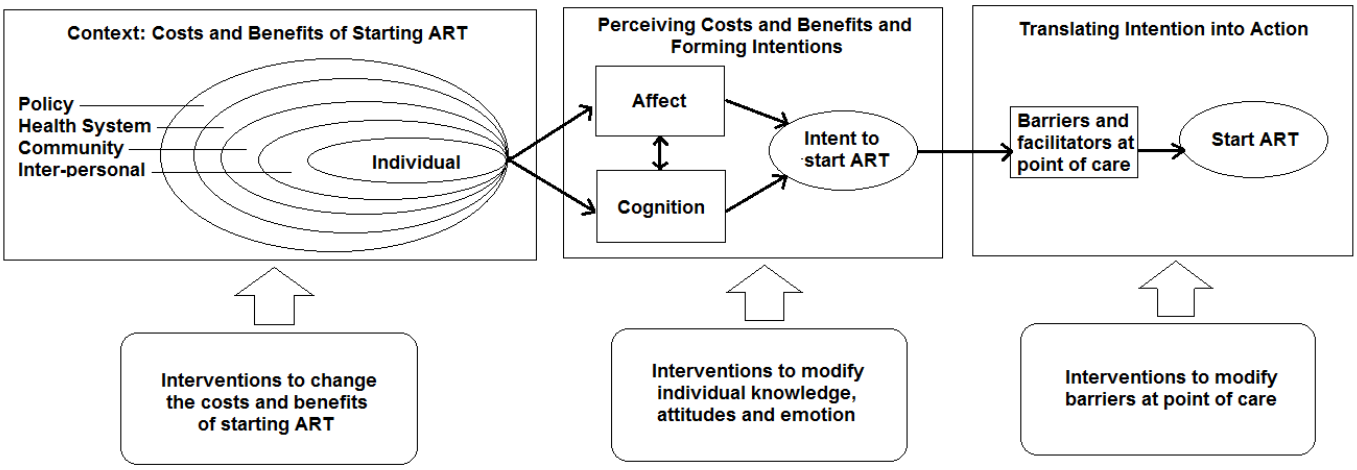


Figure 5-1. Transdisciplinary Model of Health Decision-Making (TMHD)[383]

The TMHD was created after a systematic review of qualitative studies conducted within LMICs on reasons for ART non-initiation between January 2000 and April 2017.[383] The model integrates individual-, community-, and structural-level contexts, the formation of individual beliefs surrounding those contexts, and the behavioural action implemented based on those beliefs.[383] This thesis identified barriers towards accessing care and treatment across all TMHD model contexts, for both HIV and NCDs: individual, inter-personal, community, health systems, and policy-levels. This section will address the individual, inter-

personal, and community-level barriers. Sections 5.3 and 5.4 will describe the health systems and policy-level challenges, respectively.

Health behaviour change is based on an individual's current emotional or cognitive state, limited personal resources, and socio-demographics or socioeconomic status; which assist in conscious decision-making processes.[383] Most participants who refused peer-navigated referral shared they simply preferred to go to their referral clinic alone. Perhaps the reasoning was more truly be related to experienced internal stigma and fear of external stigma, which drives the desire to be alone. Studies have found internalised shame felt by people living with disease can create self-defeating beliefs, leading to demoralization and the desire to conceal one's status for fear of social isolation.[307] Half of the study participants who didn't link to care across chronic diseases either actively or passively refused treatment (e.g.; refused their referral letter vs stating they had been too busy to attend clinic for various reasons). One-quarter of participants were not ready to engage with treatment at diagnosis and needed time to absorb their results first before deciding if they would access care. The decision to not link to care for these types of clients had less to do with a negative perception towards peer-navigated referral and more to do with an individual sentiment towards the idea of treatment.

While this study did not collect further information as to why clients were not treatment-ready, a patients' perceived health and the perception that one does not need to start treatment without the presence of symptoms has been a long contributing reason for ART treatment refusal amongst various HIV-infected populations (i.e.; women, men who have sex with men, etc.).[387-391] Fear of losing one's health and/or beauty due to medication, and through that, unwanted disclosure of status have also been documented reasons for treatment refusal.[307, 383] The perceived visual and psychological side-effects of ART (e.g.; body dysmorphic syndromes, feeling of lethargy) may outweigh the perceived benefits of treatment for an HIV-infected individual.[307] A model based on the cross-fertilization of HIV/AIDS and diabetes care depicts an individual's perception surrounding self-management of medications, required lifestyle modifications, and the level of psychological and physical suffering stemming from chronic disease may impact their choice to access health services and/or initiate treatment.[392]

PLHIV may have a subjective feeling of health and wellness that is not innately related to their actual clinical status, which therefore affects their engagement with care.[307, 393-398]

Literature suggests that among both couples and individuals, patients who have a higher CD4 count are more likely to either delay ART initiation or refuse treatment.[395, 399, 400] Perceived health could also be a deterring factor towards NCD patients accessing care, as many conditions do not present any symptoms (i.e.; HT, hyperglycaemia, hypercholesterolemia);[65, 93, 103] chronic diseases (both HIV and NCDs, alike) require daily adherence of medication; and perceived treatment regimen demands and side effects are known deterrents within populations of lower income with poor health literacy.[401] However, this study's rates of linkage to care for NCDs were high.

Further individual-level factors affecting access to care may be an individual's knowledge base and beliefs, including religious beliefs, which are guiding forces informing decision-making.[307] Limited personal resources (e.g.; transportation costs, ability to leave work and/or household duties),[402] as seen within this study population, and lack of mental resilience of patients from impoverished communities already combatting much hardship (e.g.; food insecurity, unstable housing, and limited access to affordable transportation to the clinic)[307] affect health-seeking behaviour. Prior quantitative reviews have identified predictive demographic risk factors for treatment refusers in generalized HIV epidemics among LMICs, inclusive of male gender, younger age, lower socioeconomic status, higher transport costs and distance, as well as perceived stigma.[270, 276]

Within the inter-personal context, there are social-motivational aspects which also affect entry into care. Attitudes regarding privacy, confidentiality, and interactions with healthcare providers all play a role. Furthermore, an emerging theme of a scoping literature review depicted negative patient perceptions of healthcare providers – largely the fear of being mistreated due to stigma[403] - within HIV programmes may also have a negative impact on the engagement with NCD care, either located within or outside of HIV programmes, and therefore effect the NCD-care continuum.[404] In particular, this study highlighted the importance of being received in a compassionate and caring manner to clients. When asked what they enjoyed about their experience within the study clinic, participants repeatedly shared they enjoyed the welcoming, professional and supportive staff; appreciated being treated with respect from the health care providers; and liked the effective communication of and information shared by the health care providers. If entering an impersonal environment and being handled by judgemental staff, it may contribute to a patient's sense of isolation and feeling stigmatised.[307]

Within the community-level context, the externalised stigma associated with the public nature of unwanted disclosure experienced within communities, lack of social support, and preference for traditional healers are known barriers to engaging into care and treatment for PLHIV.[307, 383] These study findings corroborated with each of these points. Some of the participants feared going to their referral due to external stigma – the clinic was in their neighbourhood or they knew people working there, and many preferred to simply have their CD4 count monitored within the privacy of our clinic, instead. Some participants desired social support, and wanted to wait for their partners to also be tested, so that they could be tested and obtain treatment together. Both treatment acceptors and refusers are known to seek out the counsel of traditional healers for 'immuno-boosters' for either treatment enhancement or substitute.[307] Among both high blood glucose and cholesterol-referred clients, there were participants who opted to take *muti*, the name for traditional medicine within South Africa, instead.

Regardless of passive linkage to care being favoured and individual, inter-personal, and community-level barriers towards choosing active referral and/or accessing care; this thesis showed optional peer-navigated referral did achieve its goal. Significantly more HIV-infected patients were linked to care, and clients with chronic disease reached care in a shorter amount of time on average than those utilising passive referral, only. The use of this strategy as part of an intervention package should not be discounted. However, these results could be attributable to other study-related aspects. Integrated NCD-HTS offered additional screenings which could have resulted in more HIV-infected clients referred with more than one condition. Patients with multiple chronic conditions tend to use services more frequently.[405]

5.3 SCREENING AND TREATMENT POLICIES/GUIDELINES AND PRACTICE

Key Findings

- **The majority of the integrated NCD-HTS clients were newly diagnosed with NCD risk factors;**
- **There were high rates of newly diagnosed NCD risk factor-HIV comorbidity;**
- **All previously diagnosed clients with HT, high blood glucose and TC who had been on treatment remained with uncontrolled disease at screening;**
- **There continues to be health system and policy-level barriers at point of entry to care; and**
- **Current national guidelines use a gated-approach for screening of chronic disease, largely excluding the at-risk populations of young adults, PLHIV who do not know their status, and HIV-infected persons not on treatment.**

The majority of the integrated NCD-HTS clients found to have chronic disease risk factors were newly diagnosed. There were also high rates of newly diagnosed NCD risk factor-HIV comorbidity. Furthermore, all of the clients who had been previously diagnosed with HT, high blood glucose and cholesterol and had already initiated treatment were found to have uncontrolled disease once screened during integrated NCD-HTS. Health systems and policy-level barriers were identified at the point of entry into care which barred efficient initiation of treatment across chronic diseases. Current South African national guidelines do not adequately allow for the most effective screening for and management of NCDs or their risk factors amongst both the general population and PLHIV. A review of the current chronic disease screening and management guidelines is needed.

5.3.1 PROPORTIONS OF NEWLY DIAGNOSED AND CONTROLLED VS UNCONTROLLED DISEASE

Between three-quarters and nearly all participants with various NCD risk factors and almost one-in-ten clients living with HIV were previously not aware of their status. Of those participants screened to have comorbidity with HIV, about one-quarter were newly diagnosed with both HIV and high BP and/or high TC and half were newly diagnosed with both HIV and high glucose. This predominance of previously unknown disease is higher than what was reported by the SADHS, which reported 29% of females and 34% of males had not been previously diagnosed with HT by a HCW; and 64% of women and 66% of men screened as pre-diabetic (adjusted HbA1c level: 5.7-6.4%). This indicates a large proportion of South African adults are not aware of either their health condition or that they are at-risk.[98]

Although this study only had a small sample size of participants reporting they had taken treatment for NCD conditions, all of these clients subsequently screened with uncontrolled disease at the study site. This proportion is far larger than the already high rates of uncontrolled disease reported by the SADHS – of those on antihypertensive drugs and medication for DM, 23% of females and 9% of men did not exhibit controlled BP and about 85% still had uncontrolled blood glucose levels.[98] The Southern African Hypertension Society has reported that more than 90% of hypertensive patients are not controlled due to multiple factors: lack of awareness or education, failure to access treatment due to failure to screen, screened but not diagnosed, diagnosed but untreated, and treated but not controlled through ineffectual medication regimens or nonadherence.[170, 173] Less than two-thirds of the HIV-infected integrated NCD-HTS clients who already knew their HIV status had initiated ART, and those

who had not yet initiated treatment had a low median CD4 count (under 350 cells/mm^3). The HIV-infected participants were at risk of transmitting the virus to other people.

The high rates of previously unknown chronic disease and known, uncontrolled chronic disease amongst South Africans point towards missed opportunities for critical screening and inadequate patient management within the public sector. Contributing to these gaps is the lack of explicit national screening guidelines for NCDs - healthcare providers have been left to use the recommendations of local, regional, and global clinical societies. This creates non-standardised practice.

5.3.2 HEALTH SYSTEMS BARRIERS TOWARDS LINKAGE TO CARE AND INITIATION OF TREATMENT

This thesis has identified that there is still immense fallout within the care and treatment cascade from diagnosis of disease to entry into care and initiation of treatment across chronic diseases. This fallout exists regardless of the mode of referral (passive vs optional peer-navigated linkage to care). Despite policies propagating same day ART initiation, the time from referral to treatment initiation was found to span an average of nine days; and for other chronic disease conditions, time to initiation of medications ranged from an average of two to 14.5 days. Identified challenges at the health systems point of entry to care, relating to the incorrect implementation of health policies/guidelines, contributed towards inefficient or lost initiation of treatment across chronic diseases.

Out of all HIV-infected participants, three-quarters were linked to care and two-thirds were initiated on ART. In resource-limited settings, such as SSA, it is reported that as much as 40% of PLHIV who are diagnosed are not linked to treatment services,[32-34] and late initiation has not decreased over the past decade.[269] With the most crucial piece of HTS being its linkage to care and treatment services for the timely provision of treatment/therapy, the NDoH has passed various policies and guidelines to expedite treatment initiation. In addition to the launch of the WHO's UTT policy within South Africa in September 2016;[142] SDI, advocating for ART initiation on the day of HIV diagnosis, followed exactly one year later. Three years in, despite these initiatives, still less than two-thirds of PLHIV have entered care and started ART.[12, 145] This thesis corroborates this data. While some HIV-infected participants did achieve SDI of ART, the overwhelming majority did not. While this may be attributable to the clinic not providing treatment on-site (SDI typically applies to treatment facilities also

administering rapid testing), participants who did link to care with the intention of initiating treatment still experienced barriers towards treatment initiation treatment initiation.

Despite the UTT and SDI policies, this study provides evidence of PLHIV having additional blood testing conducted (including CD4 count) and/or being required to complete three ART adherence counselling modules prior to initiating treatment at a scheduled follow-up appointment. Stage 2 hypertensive patients were identified as having not been initiated on medication, and patients with uncontrolled NCD risk factors did not have their current treatment regimens re-assessed and/or adjusted for optimal health outcomes, as per national guidelines.[168]

A large proportion of clients who linked to care with NCD risk factors self-reported they were told they '*did not need treatment* [with pharmaceuticals]' after being re-assessed at the referral clinic. Overall, three-in-five referred clients were told they did not need to initiate treatment for abnormal BP or high cholesterol. Seven-in-ten referred clients did not need to initiate treatment for high glucose. It is possible that the confirmatory testing methods used at referral clinics differed from those used at the integrated NCD-HTS centre, yielding different results (e.g.; FPG vs HbA1c testing). Additional research would be needed to determine if this was true, and if so, a reassessment of standard of care protocols within the public health sector is critical. It is also possible that the current national guidelines for case management were just not followed. For example, most patients with NCD risk factors were correctly prescribed lifestyle modification measures; however, it is also recommended such measures be prescribed in tandem with medication.[168]

5.3.3 AT-RISK POPULATIONS MISSED WITHIN CURRENT CHRONIC DISEASE SCREENING AND MANAGEMENT GUIDELINES

While screening for HT and checking a patient's weight is part of the standard of care within the public sector, both in PHC clinics and HTS, additional screening for chronic disease follows a gated-approach (i.e; is risk-factor dependent). For example, only patients with symptoms of hyperglycaemia are screened for blood glucose and typically only those with additional risk factors (e.g.; older age, overweight/obese BMI, CVD risk) are screened for blood lipids. There are specific populations which fall through the cracks within this type of approach for health screenings.

Screening for DM within the general population hinges on either being overweight with risk factors for hyperglycaemia or metabolic decompensation or being at least 45 years of age.[381] Hypercholesterolemia screening criteria is being of older age and having DM. Problematically, symptoms of diabetes are often either less severe or absent, with a significant percentage of cases (30–80%) remaining undiagnosed.[381, 406] With over one-quarter of the 18-25 year old and over one-third of the 18-44 years old participants being overweight/obese, if asymptomatic, these individuals would be missed in the screening process for DM. Three-fifths of the clients with high cholesterol were under 45 years of age. Over half of the HIV-infected clients did not previously know their status, and this population had significantly lower median BMI and significantly higher average blood glucose than HIV-infected individuals, with the majority under 45 years of age. These sub-populations would be missed opportunities for screening for disease within the public health system. With screening for DM and hypercholesterolemia amongst PLHIV based around the initiation of ART, one-third of the HIV-infected participants who knew their status and chose not to initiate ART would have been unscreened. Furthermore, HIV-infected participants on ART still had significantly higher TC than those not on treatment.

Furthermore, while HbA1c testing is deemed a better screening method for DM, as it reports the average blood glucose level over the past three months, RPG screening – not HbA1c – is used in the public health sector in South Africa to screen for diabetes.[381] Both RPG and HbA1c testing do not involve fasting. As aforementioned, it is troubling that the study's HbA1c and RPG screening results among the same clients were poorly correlated, suggesting the population was not at-risk for DM. Additionally, HIV-infected clients were significantly more at risk for high HbA1c, but not for high RPG. While there are other methods of screening for blood glucose, such as the urine test, they are not as accurate as a blood test and only used when blood tests are not available.[407]

5.4 TRANSFERABILITY TO THE PUBLIC HEALTH SECTOR: HOW GENERALISABLE ARE THESE FINDINGS?

These integrated NCD-HTS health screening results add evidenced-based support towards a critical matter: it is no longer a question of *should* we be integrating routine NCD screenings into our healthcare system, but *how*? Currently there is a gated-approach towards screening for NCD risk factors in the public health sector. The evidence presented within this thesis supports

the argument to screen for NCDs using a pragmatic approach – universal screening for adults, regardless of age or other CVD risk factors (e.g.; BMI), HIV-status or ART use. However, the main beneficial health outcome goal of such routine screening for disease hinges on if the patient is subsequently linked to care and treatment services, and the patient either modifies their lifestyle and behaviours or the disease is clinically managed accordingly. Therefore, a critical question remains: *Will integrating routine NCD risk factor screening enhance disease management?*

Enhancing care for the population through the promotion of health screening – and at an earlier age – will create both an additional workload and financial burden on the healthcare system regarding patient case management. It then becomes more a matter of determining what strategies are cost-effective for and how much the public healthcare system can handle. It might not be able to cope with the increased demands, creating unintended negative effects on other areas of the system; and these are the realistic dangers of expanding services within an under-resourced healthcare system. This section compares thesis findings with what is currently known about South Africa's public healthcare system and discusses which evidence-based strategies could potentially be transferred successfully.

5.4.1 GENERALISABLIITY OF CLIENT POPULATION AND STUDY SITE

This study's population largely reflects that of the general population of Soweto - a nearly all Zulu-speaking, Black Africans of lower socio-economic status.[338, 343] The integrated NCD-HTS client population was comprised of mostly women, which mimics typical attendance by sex within HTS centres. Within SSA and globally, men are historically underrepresented in HIV testing and treatment services.[408, 409] When stratifying the integrated NCD-HTS client population by age group and sex, the two youngest age groups (18-24 and 25-34 year olds) presented with the lowest male attendance (one-fifth and one-third, respectively) in comparison to their female counterparts. According to a study utilising three national HIV population-based household surveys (2005, 2008, 2012), black African males of younger age, who are single and unemployed, residing in urban or rural informal areas are more likely to have poor uptake of HTS services.[409] Despite 18-24 year olds and adults 45 years and older comprising the two largest adult age demographics among the general population of Soweto (23.1% and 20.3%, respectively),[410] the largest proportion of integrated NCD-HTS clients were 25-34 year olds. However, this age group has the highest HTS attendance, also correlating with peak HIV prevalence.[12]

With the study population reflecting the same demographics as the general population of Soweto typically attending HTS centres, the client health burden outcomes could be generalizable to the greater Soweto area and populations of similar geo-economics amongst LMICs. However, the study site was not as generalizable to HTS clinics within the public sector.

The integrated NCD-HTS centre serving as the study site operated within and was staffed by a research unit, the PHRU. While it is the only walk-in HTS site on the grounds of the Chris Hani Baragwanath Academic Hospital, it is still a slightly different setting as it is not a government health centre and its staff were not government healthcare workers (HCWs). This impacts the generalisability and/or transferability of the investigated health system strengthening strategies to typical community HTS settings. Aspects of this limitation are described further in the sub-sections.

5.4.2 TRANSFERABILITY OF FEASIBLE AND QUALITY INTEGRATED NCD-HTS SERVICES WITH TASK-SHIFTING

While the implementation of integrated NCD-HTS within the study site was found to be feasible and clients also deemed the clinic flow time and services provided to be highly satisfactory, it may not be possible for the public sector to scale up the same model as successfully. The study site differs to the public sector in the level of health systems resources available – human resources, facility space and supplies, leadership, etc. - in a way which may affect the same outcome of feasibility and quality of task-shifted integrated services and positive user experience. Key factors identified in literature which contribute towards successful service integration are structural infrastructure and reorganisation of location of services, staff ratios, and capacity building.[411] This section delves into those key factors and addresses the debate regarding the feasibility and cost-effectiveness of the gated-approach to health promotion versus universal healthcare. It concludes with a brief discussion on other potential integrated screening strategies to consider.

5.4.2.1 Infrastructure, Staffing, and Capacity Building

Infrastructural challenges may inhibit the transferability of implementing feasible integrated NCD-HTS. With limited facility space, compounded by inadequate staffing, an integrated services model may maintain the current health systems structural challenges similarly seen within fragmented service delivery. Long clinic wait times due to a heavy influx of patients

promote patient attrition in care and patient dissatisfaction.[411, 412] The study site was small in size, requiring only a reception area and one office per staff member for the conduct of all health screenings within the same healthcare provider room. Within limited space, this study proved it is still possible to execute efficient integrated NCD-HTS services. However, one may still doubt that the public sector has the capacity to increase its workload with integrated services.

A South African qualitative study reported as long as nurses are expected to habitually manage a large number of patients, integrating HIV services into primary care – or presumably chronic care into HTS – is unlikely to be successful, as it will negatively impact service delivery.[413] This could be especially true in LMICs like South Africa, which implement UTT and SDI policies, greatly increasing the number of patients serviced. While task-shifting could potentially alleviate some of this workload burden, there are still other staff-related barriers affecting the successful transferability of integrated services into the public sector. These challenges need to be addressed.

While this thesis did not investigate the levels of HTS counsellor motivation, job satisfaction, and perception of ability to meet patient needs, given the nature of this research clinic, study staff may not have experienced the stresses that public service health workers experience. Salaries were above the public sector pay-grade, and all counsellors were long-term contract hires. Each counsellor received a new skillset by virtue of implementing integrated services, and were provided their own private offices with fully stocked supplies in which to screen clients. Furthermore, the study site was small, with only three counsellors, allowing for close supervision by the study nurse. Ad hoc meetings were held – at a minimum, weekly – for training/re-training purposes and to discuss any difficulties experienced by staff relating to work conditions, tasks required, and even emotional needs. Solutions to such challenges were brainstormed and achieved as a team. While they did experience heavy client volume at times, with only three HTS counsellors attending, all staff seemed dedicated to the success of the project and were retained hires throughout the study. Therefore, the study staff work environment and morale were vastly different from that of public sector healthcare workers.

Perhaps a more pertinent question to be asked is, *what is the best way to add additional services within PHC clinics?* This thesis found task-shifting of RDT of NCDs to counsellors, after essentially one week of initial training, to be both feasible and of quality. Alleviating the

workload burden and associated burnout of certain cadres of staff (i.e.; nurses) by empowering the skillsets of others through task-shifting (i.e.; counsellors) could improve work-related motivation and job satisfaction over time. Cultivating HTS counsellors' skillsets could serve as motivation for further career growth and experience. Through relief in their workload, professionally trained HCWs of senior-level could experience increased work satisfaction, and in turn may then focus efforts towards stronger supervision and support of staff with lower qualification levels.

Downstream effects would be positive impacts on health workforce retention, quality of service provision and healthcare outcomes.[414-416] A qualitative study investigating the successfulness of integrating new practices within a hospital workflow through interviewing hospital staff, found that successful integration was linked to interventions that proved fundamentally fulfilling to HCWs (i.e.; through rendering their jobs easier or more satisfying). This occurred through positive shifts in attitudes (e.g.; staff acceptance of the innovation) and/or social norms (e.g.; workplace climate) over substantial time – as long as one year.[417] Therefore, ideally skills training and capacity building need to be sustained over time.

In 2012, the NDoH adopted the WHO policy on collaborative HIV-TB activities[418] and released a practical guide for full TB-HIV service integration at PHC facilities.[419] The guide promoted continual training to HCWs, task-sharing amongst different levels of staff, integration of HIV and TB data registers and of TB–HIV services within the community to increase the demand for integrated services at all levels of care.[411, 419] A joint review of the programme two years after implementation deemed efforts as suboptimal. While successful at the PHC level, the functional integration of these services was not homogeneously distributed across all areas.[411, 420] A more recent appraisal of the programme within the eThekwini District containing over one hundred clinics determined that only twenty percent of the PHC clinics reached full integration of services. The capacity building for integrated HIV-TB programme was deemed inadequate for nurse-initiated management of ART (NIMART) and TB infection and TB management, which aids in preventing the desired task-shifting to lower levels of staff as mandated by national guidelines.[2, 411, 412] Similar failures in capacity building have been experienced within NIMART integration in South African PHC clinics.[412, 421] These studies, however, relate largely to failed capacity building relating to integrated patient treatment. This thesis deemed capacity building for task-shifting of RDT of NCDs to counsellors as feasible.

5.4.2.2 Feasibility and Cost-Effectiveness of Universal Healthcare

A key argument between gated and universal approaches to healthcare is one of feasibility and health economics, as well as resource availability (which has already been addressed within section 5.4.2.1). At both clinical and policy levels, the cost of implementing healthcare interventions need to be weighed against desired health outcomes.[422, 423] At what point - or threshold – does an intervention become cost-effective?

Screening each patient for all conditions is not typically thought of as a cost-effective approach, as a person with chronic disease would then need lifelong treatment. However, the World Obesity Federation Report estimated the cost of obesity, alone, within South Africa to be USD$3.5 billion.[424] Historically, there have been low levels of lifestyle/behaviour modification due to the provision of health information. This is most notable when looking at the high rates of HIV and obesity which still persist despite far-reaching educational campaigns regarding safe-sex practices and healthy lifestyles. The health sector must now consider affecting change through broader screening practices and subsequent initiation of treatment.

There are pragmatic side-effects of tailoring healthcare for sub-populations. Having to follow risk-factor algorithms to determine the application of screening for chronic disease could lead to HCWs largely defaulting on screening. Universal screening would make practice easier and more routine for providers. Not only has this thesis found integrated universal screening to be feasible within HTS, but evidence from high income countries – where the NCD epidemic originated – shows it is possible to delay NCD-related morbidity and mortality by several decades and thus avoiding mortality amongst the aging population, if screening is initiated earlier in life.**[68]**

There is risk accumulation for NCDs over the course of an individual's life, especially when focusing on modifiable risk factors and precursory conditions (see Figure 5-2). While interventions targeting the middle and older age-groups will indeed reap major short-term benefits, in the longer term, strategies targeting younger populations could potentially and substantially reduce the chronic disease pandemic, while also providing cost-savings.[68]

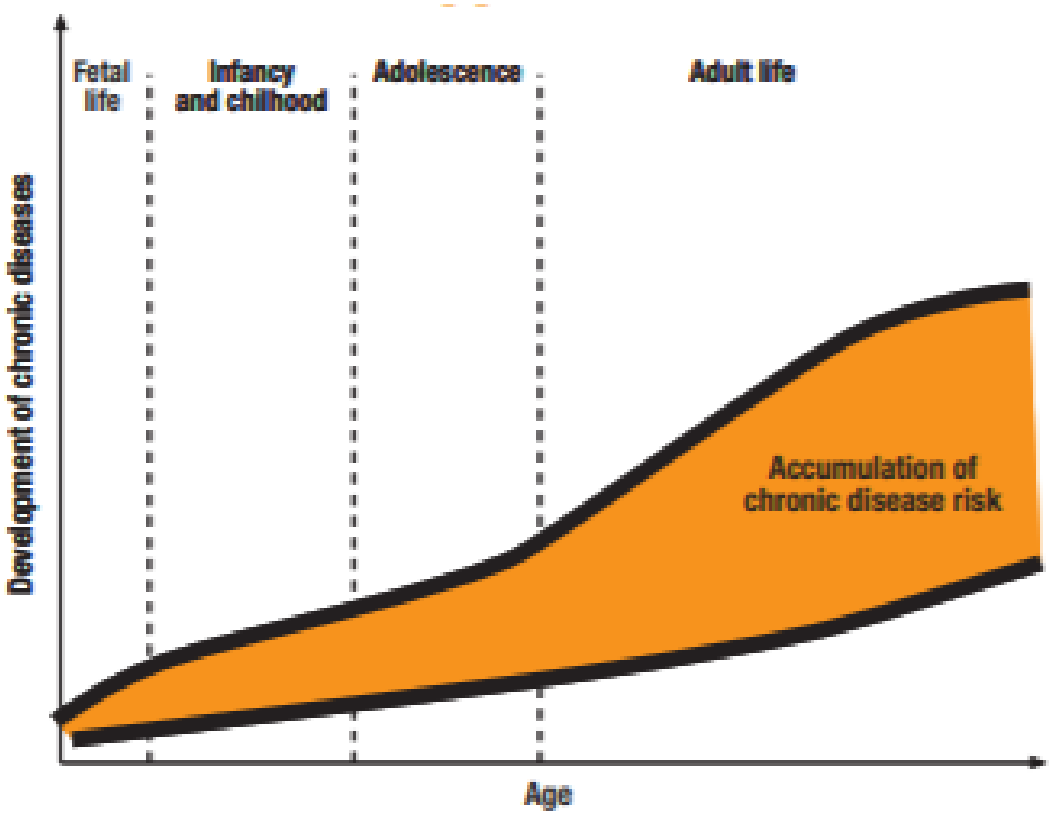


Figure 5-2. Accumulation of NCD Risk over Lifespan[68]

Numerous specialist committees on chronic disease management support the earlier screening and treatment of disease, as timely initiation of treatment optimises long-term health outcomes.[402] The ADA and the European Association for the Study of Diabetes (EASD) recommend early pharmacotherapy for the management of hyperglycaemia in type 2 diabetes.[181] Longitudinal, randomized clinical trials, such as the landmark United Kingdom Diabetes Prevention Study (UKDPS), have outlined the benefits of earlier rather than delayed glycaemic control with pharmacotherapy. Patients with incident DM who received intensive pharmacotherapy had significantly larger decreases in HbA1c and reduced risk of diabetes-related complications as compared to patients who received conventional dietary management.[425, 426] Other studies utilising predictive modelling also support earlier treatment to combat diabetes-related morbidity, especially for the prevention of microvascular disease.[275] Compared to no treatment, a treatment target of HbA1c < 7% (<53mmol/mol) within six months of diagnosis with DM may reduce the risk of end-stage renal disease by 44% and blindness by 73% compared with no treatment.[274, 275] Screening for high TC early on in life could help prevent chronic inflammation, especially amongst PLHIV. Therefore, earlier

universal screening and initiation of treatment is cost-effective in the long-term, saving on future costs relating to chronic disease-related morbidity and mortality.

5.4.2.3 Other Integrated Screening Strategies to Consider

Further cost-effective and feasibility studies are urgently needed to evaluate integrating universal NCD screening into the public health sector. Other methods for increasing the screening of NCDs are required. Given the high burden of NCDs in SA, healthcare facilities need to reconfigure their structure to implement the management of NCDs. PHC clinics are ideal avenues for the screening and management of NCDs. Diagnostic capabilities should be strengthened minimising the need for referral. Community screening and broad-based education outreach could also improve the identification of NCDs at community-level. The SADHS screened participants for weight, height, waist circumference, BP, Hb levels, and then collected blood samples for HbA1c and HIV testing.[98] However, such surveys are not implemented annually. There has been some success with the Integrated School Health Policy (ISHP), which screens school-aged children for BMI, oral and eye health on school grounds.[427] Perhaps similar opportunities for adults to be screened for NCDs – at pension/grant distribution points, at community events, etc. – should be investigated.

There is a growing call for community-based outreach to relieve the impact of high patient volume on public healthcare services.[428] There may be a greater role for PHC ward-based outreach teams, including CHWs, to conduct community-level health screening programmes, given the growing evidence base on the feasibility of task-shifting of NCD screening tio lay providers and successful peer-navigated linkage to care, especially if embedded within a nurse/clinician managed model. CHW models of care for Type 2 diabetes self-management work best when coordinated by a facility linked nurse (Gary et al, 2009;, which could also apply to other models of community-based risk screening (e.g.; CVD risk), under a revised scope of practice for CHWs.[429, 430]

5.4.3 TRANSFERABILITY OF INTEGRATED SCREENING AND ACTIVE LINKAGE TO CARE YIELDING INCREASED UPTAKE OF CARE AND TREATMENT

Historically, South Africa has a poor track record of screening integration leading to successful programmes of increased care and treatment. There have been several community-based

surveys conducted in South Africa which have found that while diagnosed, HT is poorly treated.[431-435] Other studies have reported similar findings regarding inadequate care for most of the other chronic diseases among adults, including DM and hyperlipidaemia.[98, 436, 437] This study corroborates this evidence in that all previously diagnosed clients on treatment for NCD risk factors remained with uncontrolled disease. Despite some positive impacts of offering the option of peer-navigated linkage to care, it did not translate to increased initiation of treatment. *Why?* As previously mentioned, there are multi-level contextual barriers towards patients accessing care and initiating treatment (see Figure 5-1, TMHD). As individual, inter-personal, community, and policy-level challenges have already been discussed in relation to this thesis, this section will continue to discuss the health systems barriers; and concludes with the relevance of peer-navigation findings for the existing public health sector.

5.4.3.1 Health System Building Blocks

Health system factors or programmatic barriers to initiation of treatment, have been well documented using the WHO health system building blocks.[48] In addition to limited health workforce which was already discussed, other notable health system building blocks relative to this thesis are service delivery, supply chain management, and health information systems.
As discussed previously, the overburdened health care system is still a deterrent to treatment initiation. Government clinics already have a heavy influx of patients and long queues, which are often paired with inadequate staffing and healthcare facility space, negatively impacting service delivery.[201, 202, 413] Many participants cited they were not helped due to the clinic being too full, or if they were seen by a healthcare provider for comorbidities, some conditions deemed less critical (i.e; cholesterol) were not checked or addressed as the provider did not have enough time. Not only are each of these cases missed opportunities for intervention, which would decrease the likelihood of morbidity and mortality, but the patient must have continued mental resilience to re-engaged with the healthcare system that failed them.[438, 439]

While this study did not contain evidence towards supply chain management challenges, stock-outs of chronic medication will affect the desired healthcare outcomes of a universal screening policy. A South African case study in 2011 reported ART and TB treatment stock-outs existed within 80% and 30% of clinics, respectively, inhibiting the integration of HIV–TB management.[411] The literature review within this thesis further described this issue.

Health information systems drive action and rely on M&E of programmatic service delivery to identify service utilisation gaps and outcomes. However, there is little M&E relating to tracking linkage to prevention, care and treatment services or retention in care. A limitation of this study was that HTS client linkage to care and treatment initiation could not be confirmed through TIER.net, the accessible electronic database managed by government ART clinic staff to capture data elements and indicators required to monitor HIV and ART services. Although the portal was available, data was not entered for any of the study participants. Where resources are available, an electronic data capturing system is required to promote the timely submission and analysis of clinical data required for health service delivery improvements, including long term retention in care.[48]

However, despite the challenges experienced within this study, and the additional health systems barrier described, there have been examples of successful implementation of integrated screening services leading to improved patient care. A case study conducted in rural Malawi on integrated NCD screening and care services within an existing HIV programme – similar to this thesis' model - reported an improvement in access to NCD care for HIV-infected patients. The healthcare model's success was largely attributable to aforementioned facilitators - strong leadership, allowing for real-time discussions about challenges encountered and allowing for process improvement, staff ownership of their specific duties, and a well-defined and uniform patient flow process. Furthermore, four studies examining the effects of various integrated models of care on HIV stigma have concluded some level of integration could potentially result in HIV-stigma reduction for PLHIV through successful achievement of combined care for HIV-uninfected NCD clients and PLHIV within the same facility.[367, 440-443]

Perhaps to achieve the desired endpoint of increased uptake of treatment and control of chronic disease, there should be a phased-in approach of the investigated health systems strengthening strategies while also working towards the improvement of generic issues, such as infrastructure, resource availability, and drug supply.[444] This could achieve sustained coverage of multiple interventions through their incremental scale-up as the overall health system capacity builds.[445]

5.4.3.2 Relevance of Peer-Navigation Findings for the Existing Public Healthcare Sector

In contrast to the study site, public healthcare facilities offer treatment on-site, typically initiating HIV-infected patients on ART using NIMART. Unless there is a medication stock-out, it would be rare for a patient to be tested in a public sector facility that does not also initiate

treatment. However, as previously described, treatment initiation often does not occur on the same day as screening. Therefore, while a new cadre of peer-navigator may not be needed to help guide a patient from a stand-alone testing centre to a separate treatment centre, this study's findings have shown that there is value in a pro-active approach towards retention in care for patients opting out of same-day initiation.

5.5 Telephonic and physical tracing of patients who have not yet initiated treatment or defaulted on treatment should become a routine service provided by existing public sector cadres, such as lay counsellors or PHC ward-based outreach teams (WBOTs). Preliminary studies have shown this combined tracing approach by CHWs effective.[428, 446] Community-based outreach has also proven to improve maternal and infant health, as well as youth and adolescents health, in high HIV-prevalence settings (increase in antenatal triple ART initiation and lower risk of stillbirth, more timely ART initiation, and substantially longer-term retention in care)[447-449] Community-based outreach is a low-cost intervention towards aiding progress towards several health-related goals.[448] However, there are limited data on its impact on other chronic diseases.[428]LINKAGE BETWEEN FINDINGS AND CONCEPTUAL FRAMEWORK

This thesis investigated the impact of a horizontal approach towards the integration of screening services for NCD risk factors within an HTS programme, task-shifting of POC RDT to counsellors, and peer-navigated linkage to care on the healthcare and treatment continuum as portrayed within the conceptual framework (Figure 1-2). In doing so, it has documented different categories of factors affecting retention of the adult population within the care cascade from screening through treatment initiation, across chronic diseases. Integration of screening services and task-shifting of POC RDT did successfully diagnose more people living with chronic disease, and optional peer-navigated referral did successfully link more HIV-comorbid clients to care facilities as compared to standard of care passive referral. However, these combined strategies did not successfully link all referred clients to care or have them initiate treatment significantly more – or within a significantly shorter time – than standard of care clients. Engagement with and retention in care could be enhanced through the improvement of individual, inter-personal, community-based, health systems-related and policy-level interventions. Attention must be given specifically to interventions positively affecting psychosocial and treatment-seeking behaviour and to rectify improper implementation of

health screening and management guidelines. Figure 5-3 represents the adapted conceptual framework, including thesis findings.

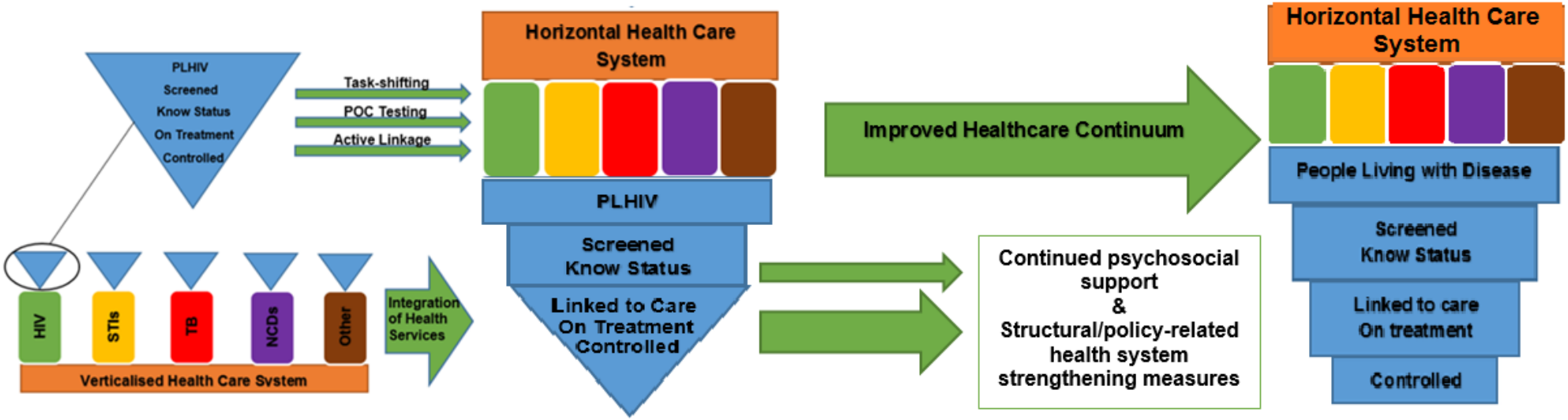


Figure 5-3. Adapted Thesis Conceptual Framework

5.6 STUDY LIMITATIONS

This study has several limitations worth noting, which can be categorised into four broad domains: study design and sampling method, study site, and data collection.

5.6.1 STUDY DESIGN AND SAMPLING METHODS

Being a cross-sectional study, there may have been difficulty in interpreting associations, as the chosen study design does not help determine cause-and-effect since the data collected was simply a 'snapshot in time'. This study also had a convenience sample of participants self-selecting to attend a single HTS centre in Soweto, South Africa. There is potential for a sampling bias as these participants were not randomly sampled from multiple facilities.

In order to investigate the study aims and objectives, there were direct comparisons between standard of care HTS and integrated NCD-HTS data. Therefore, being descriptive in nature, there was no control for any parameters. The standard of care HTS and integrated NCD-HTS client populations had slightly different characteristics, which may have limited the ability to compare them fully without any confounding factors. For example, during integrated NCD-HTS, the HTS clinic was assisting with HIV rapid test screening for the enrolment of women into HIV prevention (pre-exposure prophylaxis [PrEP]) trials conducted at PHRU, as well as conducting screenings for cervical cancer and HPV for female clients. Although there was not a statistically significant difference in proportions of clients by sex between the two HTS phases, this may have encouraged the higher volumes of women attending the clinic during the integrated NCD-HTS phase, as the sex ratio presented within the standard of care phase is a more typical representation.[358] Also, while only a difference of three years, the integrated NCD-HTS contained a statistically significant younger median aged population (32 years) as compared to standard of care HTS (median age of 35 years). While the demographic results did largely reflect that of the 2016 SADHS, the integrated NCD-HTS results and comparison of HTS phase results would have been different if more of the older aged population would have been sampled. Additionally, some of the sub-group sample sizes for comparisons were small (e.g., the sample size for those who opted for active linkage to care), which may have affected statistical precision.

5.6.2 STUDY SITE

Limitations surrounding the study site impacting the generalisability of study results to typical community health clinic settings has already been heavily discussed within this thesis.

Regarding study health screening procedures and comparisons to the public health sector, there were differences in available resources, which affects generalisability to the government clinic populations. The public health sector may only use the resources available, which might not always be rapid diagnostic methods but laboratory-based analysis of samples with reagents. While the rapid diagnostic testing technology used within the study at the study site (e.g.; HbA1c and random blood glucose testing machines) have different sensitivities and specificities, which affect patient results, laboratory analysis could differ, as well.

5.6.3 DATA COLLECTION

Client questionnaires and surveys also inherently contained some limitations by design. Firstly, the HTS client clinic exit surveys were not administered uniformly. Literate HTS clients could complete them independently, while HTS clients needing assistance were asked the questions by either counsellors during standard of care HTS or by peer-navigators during integrated NCD-HTS. HTS client self-administration of the survey limits bias, whereas study staff-assisted administration may create acquiescence bias (i.e., the HTS client tending to respond favourably/positively) or social desirability bias (i.e., the HTS client responding in ways will lead towards them being accepted by the administrator). Other questions within different questionnaires collecting personal and clinical data, which were always administered by study staff, were left to the interpretation and disclosure of the client. For example, questions surrounding drug use did not specify a timeframe (i.e., within the last six months). Conversely, the study staff administrating the questions could have mistakenly used leading questions or created a wording bias when conversing with the HTS client in trying to elicit responses. The study team did, however, hold training discussions on potential reflexivity to help raise awareness of and decrease self-imposed biases during data collection and analysis.

The survey data was at risk of other biases. The five-point Likert response format was subjective rather than objective, in that the responses ‘Very satisfied’, ‘Somewhat satisfied’, etc., were not defined. There was risk of misclassification due to recall bias, as some questions asked HTS clients to recollect past experiences – sometimes as long as three months prior - and provide their thoughts. Additionally, the sample size of HTS client responses – specifically for the free-response questions – was limited to how many HTS clients chose to answer a particular question, rather than leave the question blank. Whereas not all variables had complete responses, the majority of participants responded with more than 98% response rate, which was reassuring for our study. There was some subjective interpretation of the HTS client

free-responses through investigator's own understanding paired with thematic context, but this was limited by having two investigators agree on the analysis.

There were also some limitations regarding the clinic flow time data collection and analysis. Most of the data captured in the Demographics Form, Client Contact forms, and Family History and Behavioural Questionnaire is affiliated with the PHRU Zazi HTS programme/study and not part of routine public healthcare. For HTS clients either self-administering or being assisted with the completion of the Demographics and Client Contact Forms at reception, the time spent at reception was lengthened. While the Family History and Behavioural Questionnaire did include the STI TB symptoms screening, the majority of it was HTS programme/study-related, increasing the time it took for the counsellors to conduct the HTS screenings. Additionally, the study did not collect clinic flow time in a standardised manner for the pre-registration time at reception, the time it took the counsellors to QA/QC all counsellor-led screening results with the nurse, or the time the clients spent with the nurse, and therefore, this data was not included within this thesis. Therefore, a timeframe is not provided for the phlebotomy for CD4 count, writing of referral letters and any further counselling conducted by the nurse. Furthermore, there may be a social desirability bias effect on clinic flow times between HTS models due to the Hawthorne effect (i.e.; clinic staff knowing they are being timed).

Lastly, certain data – specifically linkage to care and treatment initiation data, previous diagnosis of disease and previous treatment of conditions - were self-reported by HTS clients and could not be confirmed through other sources. A large proportion of clients linking to care self-reported that they were told they did not need treatment, and this also remains unconfirmed. While it was attempted, investigators were unable to confirm linkage to ART clinics using TIER.net, an accessible electronic database managed by government ART clinic staff to capture data elements and indicators required to monitor HIV and ART services. Additionally, a proportion of clients were lost to follow-up, which may have caused an underestimation of reported linkage to care and treatment initiation.

5.7 STUDY STRENGTHS

Despite the study limitations mentioned, this thesis had several strengths, which are worth highlighting.

This thesis contains formative research which makes a worthwhile contribution to the understanding of the burden of chronic disease in the adult population of Soweto, South Africa. It was the first study to integrate screening for obesity, blood pressure, blood glucose (HbA1c) and TC into a facility-based HTS setting within a LMIC known to have high rates of HIV. Given the limited published evidence-base that exists for integrated HTS models in South Africa and among LMICs, this evaluation offers unique insight into the burden of NCDs amongst both the general population and amongst PLHIV. Through the enrolment of voluntary, walk-in HTS clients from the community, the disease prevalence results from this evaluation are likely to be generaliseable to the general population of Soweto, South Africa, and similar geographical settings.

There is a gap in literature for studies providing robust, current evidence of the range of hypertension, hyperglycaemia, and hypercholesterolemia prevalence amongst different groups by sex, age group and populations at-risk (i.e.; PLHIV, young adults), as well as the extent of unmet healthcare services (e.g.; the proportion of patients with undiagnosed, untreated and uncontrolled chronic disease).[450] This thesis adds to the knowledge base to fill this gap, while also investigating the population-level management of disease through the examination of the care cascade across diseases. The identification of points of attrition within the care continuum helps to provide insight to prevention and treatment programmes, guiding future policies and interventions.

This thesis also evaluated the quality and feasibility of multiple health system strengthening strategies (e.g.; integrated screening and referral, task-shifting, and peer-navigated linkage to care and treatment) aimed to alleviate the attrition within the care continuum, while also providing end-user perspectives (i.e.; HTS client) on the selected strategies. While there have been many studies focusing on the multi-level factors which reduce successful linkage to care and treatment initiation, there is a paucity of evidence-based research on strategies that may be utilised to address these challenges to improve linkage rates, especially in urban sub-Saharan Africa.[279] This thesis addresses these aspects.

The evidence provided within this thesis may be synthesised to provide recommendations for health programme managers and service providers, as well as health policy-makers.

6.0 CONCLUSIONS, IMPLICATIONS, AND FUTURE RESEARCH

This thesis set out to further understand the epidemiologic health transition through an investigation into the burden of NCD risk factors, HIV and related comorbidity amongst adults in a resource-limited, urban setting in South Africa. The aim was to assess the quality and feasibility of and client satisfaction with the implementation of three health systems strengthening strategies – integrated screening services, task-shifting of RDT of NCD risk factors to counsellors, and peer-navigated linkage to care – within a standard of care HTS centre, and their impact on the healthcare continuum across several chronic diseases. This thesis compared study findings with current healthcare screening and management policies and practice, identifying gaps within each attributing to fallout in the care cascade for sub-populations of adults. Lastly, it considered the transferability of each health systems strengthening strategy into the public healthcare sector.

6.1 SUMMARY OF KEY FINDINGS

The first NCD Countdown 2030 Report has shown that South Africa is on a failing trajectory to reach the United Nation's (UN) SDG to reduce NCDs by 2030, specifically to minimise premature deaths by CVD and DM. Currently, South African men and women, 30 to 70 years of age, have a 32.3% and 21.2% likelihood of NCD-related mortality, respectively.[451] This study adds to this knowledge, highlighting the health transition of an emerging NCD epidemic within the younger adult populations (18-24 and 25-34 years of age), with women presenting with chronic disease earlier than men. This study highlights the high rates of chronic disease (obesity, hypertension, hyperglycaemia and hypercholesterolemia) and comorbidity amongst PLHIV; previously unknown chronic disease largely due to gaps identified within our currently recommended national screening protocols; and known, uncontrolled chronic disease, which unveils suboptimal patient management.

Contributing to these gaps is the lack of explicit national screening guidelines and policies for NCDs, creating non-standardised practice, and the risk-factor based gated approach of screening methods. Largely, younger populations (under 45 years of age) and PLHIV who do not know their status do not meet the criteria for NCD health screening unless they also present with additional risk factors for DM or CVD. Screening for HIV-infected persons centres principally around ART initiation or change in regimen, and the majority of PLHIV are not yet on treatment.

This thesis provides evidence for quality and feasible health systems strengthening strategies, which also were met with user-satisfaction, to assist with combatting the attrition within the healthcare continuum. It is feasible to integrate quality counsellor task-shifted NCD risk factor rapid testing into a standard of care HTS facility, yielding client satisfaction. With adequate organisational integration and supervision, trained HTS counsellors can provide high quality rapid testing of blood glucose and cholesterol and associated referrals to clients. While counsellor-led integrated NCD-HTS does significantly increase time to the clinic flow, as compared to standard of care HTS, it is still within historical HTS timeframes.[367] HTS clients were highly satisfied with both integrated NCD-HTS services provided and the time in which it took to provide them.

Optional peer-navigated referral, another health systems strengthening strategy investigated, did link significantly more HIV-infected and comorbid clients to care and link clients referred for all conditions to care in less time as compared to standard of care passive referral. However, peer-navigated referral was not as popular a choice amongst HTS clients as standard of care passive referral, nor did it equate to significantly increased treatment uptake. This thesis identified both psychosocial- and health systems-related barriers towards linkage to care and treatment uptake across conditions.

Psychosocial barriers experienced by referred clients affecting their access of care related to both internally and externally experienced stigma, as well as perceptions associated with treatment-seeking behaviours (i.e.; not ready for treatment). The identified health systems barriers were both structural (e.g.; overburdened referral clinic) and policy-related in nature (i.e.; healthcare management policies were not correctly implemented), which either delayed or denied initiation of treatment.

The transferability of the investigated health systems strengthening strategies into the public health sector may be possible with the required level of clinical integration (NCD and HIV screening, treatment, and health education activities occurring concurrently), organisational integration (human resources, supervision, infrastructure, etc), and structural processes (clinic flow). While examples of integrated healthcare (e.g.; HIV and TB) have not always been successful – largely due to organisation factors – the barriers are not insurmountable. Along with task-shifting to alleviate some of the healthcare burden and burnout felt by other highly trained healthcare professionals, additional strategies are needed. Lastly, psychosocial and

health systems strengthening barriers affecting access to care and treatment still remain a hindrance and must be addressed.

Figure 6-1 summarises the key findings of this thesis.

HEALTH TRANSITION

Patterns of chronic NCDs amongst adults aged 18+ years in Soweto, South Africa

High rates of overweight or obesity, elevated BP, high HbA1c and TC, HIV and comorbidity

Heavy burden of chronic disease amongst younger adults (18-24 and 25-34 years old); Women present with disease earlier than men

DM: If overweight + 1 risk factor for DM; **CVD**: If having DM; **otherwise** from 45+ years of age.

PLHIV screened prior to and 3-months post ART initiation, 3-months post HAART initiation, and every 3-6 months if pre-diabetic.

CHRONIC DISEASE SCREENING POLICY AND PRACTICE

POLICY-LEVEL BARRIERS: Screening Gaps

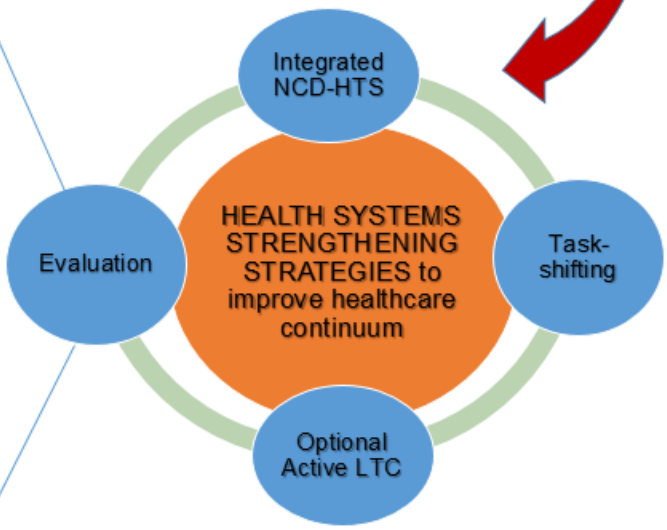
Young adults who do not have additional risk factors for DM

RPG tests used rather than screening for HbA1c

HIV-infected young adults who do not know their status and do not have additional risk factors for DM; PLHIV who are not on ART

EVALUATION

- Feasible integration of NCD screenings into HTS: Including BMI categorisation and RDT for blood glucose and TC into standard of care HTS only increased counsellor-led HTS by 5 minutes, on average
- Quality task-shifting: Counsellors were able to provide correct blood glucose and TC RDT results and referrals to clients
- Client satisfaction of task-shifting integrated NCD-HTS and clinic flow time was high
- Clients preferred passive referral over peer-navigated referral
- Significantly more PLHIV were linked to care with optional peer-navigated referral
- Clients were linked to care faster across all disease platforms with optional peer-navigated referral, but it did not equate to significantly more treatment initiation.



TRANSFERABILITY OF STRATEGIES TO PUBLIC SECTOR
despite relatively successful evaluation

GENERALISABILITY

- Integrated NCD-HTS client population demographics are generalizable to the population of Soweto, South Africa, attending HTS centres, and can reflect an accurate burden of disease.
- Generalisability of study site to public health sector HTS remains to be seen. Differences in levels of staff motivation and job satisfaction, supervision, and capacity building.

INDIVIDUAL-, INTER-PERSONAL-, AND COMMUNITY-LEVEL BARRIERS towards patient treatment-seeking behaviour: Psychosocial in nature

HEALTH SYSTEMS-LEVEL BARRIERS AT POINT OF ENTRY TO CARE: Structural in nature

POLICY-LEVEL BARRIERS AFFECTING CARE AND MANAGEMENT OF PATIENTS: Improper implementation of current guidelines and policies, barring patients from initiating or obtaining better treatment

Figure 6-1. Key Findings of Thesis

6.2 EVIDENCE-BASED RECOMMENDATIONS FOR FEASIBLE AND COST-EFFECTIVE UNIVERSAL NCD SCREENING AND MANAGEMENT

The evidence presented within this thesis supports the argument to integrate hyperglycaemia and hypercholesterolemia screening for adults aged 18+ years into standard of care HTS and PHC using a pragmatic approach – universal screening, regardless of age, other CVD risk factors (e.g.; BMI), or even HIV-status and ART use. HbA1c screening should become the preliminary screening for abnormal glucose metabolism, as opposed to RPG, in order to expedite further evaluation for DM.

Furthermore, it is recommended that the SANDoH re-evaluate the national APC guidelines for the screening and treatment of HT, given the high burden of HT in our communities. Earlier interventions (initiation of treatment at a lower threshold) may mitigate morbidity and mortality. Given the low cost of antihypertensive medications and the ease of management, revised guidelines may impact DALYs.

A more pro-active patient case management approach - including both telephonic and physical patient tracing and strategies to address psychosocial barriers to health seeking behaviour and retain diagnosed patients within the care continuum - is also recommended. Lastly, health systems barriers at the point of entry to care must be addressed – chronic disease management guidelines must be a standardised practice and correctly implemented within the public sector. This study has shown that having the option of peer-navigated linkage to care does connect significantly more patients to the point of entry to care and more efficiently than standard of care passive referral, however it does not necessarily translate to increased treatment. While prompt linkage to care and treatment is ideal and should be encouraged, strategies need to also address various, complex levels of psychosocial and health systems barriers at the point of entry into care and treatment.[452] Peer-navigated linkage to care has shown that telephonic and physical patient tracing has promise. Additional research is required to identify best strategies to integrate such patient tracing into the existing public health sector for timely treatment initiation.

An economic evaluation investigating the cost-effectiveness of implementing these recommendations is required to identify whether universal screening is cost effective for the public health system and whether longer term cost savings could be achieved.

In summary, the findings of this thesis indicates that urban South Africa, like other LMICs, is undertaking a health transition towards chronic disease, which is greatly affecting the adult population, starting at an earlier age. The findings present a complex, multifaceted health systems and policy challenge which calls for further evidence and research. This thesis recommends a revision of current health screening and management guidelines and the implementation of multi-level interventions to assist in identifying individuals with unknown disease and both engaging and retaining patients in care.

6.3 FUTURE RESEARCH

While adding to local, national, and regional knowledge-base surrounding its aims and objectives, this thesis has also enabled additional research questions to evolve. Supplementary needs for research to build upon these thesis findings, as well as to account for its limitations, are listed below:

- Investigating integrated NCD-HTS with task-shifted RDT of NCD risk factors to lay counsellors within a multi-site study design conducted within public health sector HTS clinics across South Africa. A more robust, nation-wide study on the same thesis aims and objectives will assist in determining the generalisability of thesis results and properly assessing the transferability of such health systems strengthening strategies.
- Understanding HTS counsellor levels of job-related motivation, satisfaction, stress and perceived ability to meet patient needs and what factors assist with improvement; which would all affect the ability to both take on and sustain additional workload required by an integrated NCD-HTS model. These indicators would need to be measured both before and during – at multiple time points - the implementation of the proposed interventions.
- Investigating healthcare provider feedback on proposed health system strengthening strategies through an in-depth qualitative study. This thesis did not investigate healthcare provider feedback on the interventions, due to the limited sample size of three, integrated NCD-HTS counsellors at the one study site. However, it is important to incorporate healthcare provider feedback into strategy implementation evaluations

to assist in understanding how interventions are received and their true implications, as well as to obtain information on how to optimise these strategies in practice. To obtain broader perspectives from both healthcare providers, a qualitative study method is required. The evidence-base would be far richer with in-depth interviews or focus group discussions to compliment the data collected within quantitative surveys with free response questions.

- Examining the quality of integrated NCD-HTS counselling sessions, in order to compliment the findings related to quality task-shifting of NCD risk factor screenings to HTS counsellors.
- Understanding active linkage to care strategies which would best address the identified psychosocial barriers towards chronic disease patients accessing care and treatment, which delay same-day treatment initiation at test and treat clinics.
- Examining additional active linkage to care strategies – either offered singularly or as a combined intervention package with telephonic and physical patient tracing – which may further improve patient re-engagement with the healthcare system, and increase treatment uptake and control of chronic disease. Potential options to increase linkages to care could be strengthening patient case management, community-based follow up by CHWs (e.g.; home-based support), or ongoing adherence counselling. Implementation research and evaluation is required to determine how best to offer such interventions in a manner that is both efficient for healthcare service providers and effective for patients without endangering treatment outcomes.
- Scrutinising the current patient management practice existing within the public sector to determine if the present national chronic disease screening and management guidelines and policies are being truly implemented and in a standardised manner.
- Piloting a phased-in approach – or incremental scale-up - of the best identified psychosocial and health systems strengthening strategies while also simultaneously conducting quality improvement assessments to ensure sustainability of such strategies.
- Evaluating and comparing the cost-effectiveness of universal NCD screening to determine cost of treatment and healthcare outcomes. Health economics is a critical piece towards the transferability of this thesis' findings. Such an analysis may determine that universal NCD screening is not feasible economically, and future studies would need to assess other approaches towards integrated screening and improvement of population health (e.g., community-based strategies).

- Investigate risk factors for hypertension to better understand why males have significantly more hypertension than females, despite females being significantly more overweight/obese than males.

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APPENDICES

APPENDIX A. ORIGINAL PAPERS

PAPER I

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AOSIS

Page 1 of 6 Opinion Paper

Will the current National Strategic Plan enable South Africa to end AIDS, Tuberculosis and Sexually Transmitted Infections by 2022?

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Background: In May 2017, the South African National AIDS Council released the fourth National Strategic Plan (NSP) for HIV, tuberculosis and sexually transmitted infections. This five-year plan (2017–2022), which aims to track the progress towards transitioning these

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Will the current National Strategic Plan enable South Africa to end AIDS, Tuberculosis and Sexually Transmitted Infections by 2022?

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Abstract

Background: In May 2017, the South African National AIDS Council released the fourth National Strategic Plan (NSP) for HIV, tuberculosis and sexually transmitted infections. This five-year plan (2017–2022), which aims to track the progress towards transitioning these epidemics to no longer being public health threats by the year 2030, is built on the successes and barriers of the previous NSP (2012–2016). However, the NSP does not address some critical components, which may contribute to a future failure in achieving its hefty goals.

Objectives: This article outlines the gaps within the new NSP, as well as highlighting aspects requiring careful focus, which are critical to address in order for South Africa to make progress towards the set targets.

Method: This commentary included an in depth review of the NSP, other South African National Strategic Plans and documents, and scientific literature.

Results: The NSP does not address gaps in funding, oversights in prevention and treatment strategies, human resource shortages and lacking health system requirements.

Conclusion: To realistically achieve the NSP targets and goals, a robust, client-centred strategy addressing the NSP gaps needs to be implemented. The strategy must be cost-effective; provide active linkage to care; and address health system weaknesses that inhibit its successful implementation, including human resources, service delivery and supply chain management, accountability and monitoring and evaluation (M&E).

Fourth National Strategic Plan

In May 2017, the South African National AIDS Council released the fourth National Strategic Plan (NSP) for HIV, tuberculosis (TB) and sexually transmitted infections (STIs). This five-year plan (2017–2022), which aims to track the progress towards transitioning these epidemics to no longer being public health threats by the year 2030, is built on the successes and barriers of the previous NSP (2012–2016).1,2 However, the NSP does not address some critical components, which may contribute to a future failure in achieving its hefty goals. This article outlines the gaps within the new NSP (Table 1), as well as highlighting aspects requiring careful focus, in order for South Africa to make progress towards the set targets.

Today's epidemics: Where are we now?

South Africa's successes since the previous NSP include a 34% and 15% decrease in new HIV infections and TB incidence, respectively.[1] By December 2016, South Africa had 3.9 million people initiated on antiretroviral treatment (ART) – the largest HIV treatment programme globally.[1,3] Increased coverage of ART and combination prevention strategies, such as nationwide campaigns to scale up voluntary medical male circumcision (VMMC) (2.4 million procedures conducted) and the distribution of male and female condoms, has led to a decline in new HIV infections.[1,4] Mathematical modelling on the new Universal Test and Treat (UTT) guidelines, which allow for initiation of treatment irrespective of CD4+ count, has shown that UTT could lead to substantial reductions in HIV incidence, potentially eliminating it as a public health problem over a period of 15–20 years.[5] The decreased TB incidence could be attributed to the national treatment success rate rising to 83% by 2016 – with some districts exceeding the End TB Strategy target of 90%.[6] New diagnostic tests, including the rapid GeneXpert technology, have led to more efficient diagnosis and initiation of treatment of new smear-positive and drug-resistant TB cases, which are responsible for the majority of TB transmissions.[1,6,7] This rapid diagnosis and increased treatment success rate has contributed to the decline in numbers of new TB cases nationwide.[6]

TABLE 1: Summary of gaps within the National Strategic Plan.

NSP topic and proposal	Identified gaps and issues
Prevention and treatment	
• Reduce STIs: *Treponema pallidum, Neisseria gonorrhoeae, Chlamydia trachomatis.* • Eliminate congenital syphilis. • 90% national coverage of HPV immunisation programme. • Increase detection/treatment of highly prevalent and asymptomatic STIs.	• Key prevention interventions still remain at low coverage. • PrEP is not available nationwide. • Partner-notification strategies are lacking. • No baseline STI service coverage data. • Low cervical cancer screening coverage. • HPV screening is not policy.
Testing modalities	
• PICT for ANC settings. • Increase laboratory support and POC testing, specifically for common STIs.	• PICT should be standardised across other services within health facilities. • within health facilities. • Gold standard POC testing kits for STIs are not yet specified.
Linkage to care	
Improve linkage to care to expedite ART initiation • Focus on same-day initiation. • Use PLWH to help link diagnosed patients to care	• Standard of care is passive linkage to care. • Active linkage to care strategies is not defined.
Service delivery and supply chain management	
Strengthen and enhance efforts to reduce stock-outs • Create a national supply chain task force. • Support a centralised medicine distribution system.	• A national supply chain strategic plan is needed. • Current deficiencies in provincial supply chains and emergency management response. • Root causes of poor supply chain management have not been pinpointed.
Human resources	
Calls for growth and diversification of trained healthcare professionals.	Does not address reasons for current shortage in human resources: • Personnel hiring limitations because of fiscal constraints. • National policy of CHWs not yet finalised. • Increased health personnel costs resulting from 2015 Wage Agreement.
Health information systems	
Calls for data-driven action.	Lacks a strong M&E framework • No M&E indicators for linkage to prevention, care and treatment, or retention in care. • No guidance on how patients should be tracked through continuum of care. • No standardised national data capturing system.
Financing	
Total cost of NSP over 5 years is R207 billion.	Does not account for the projected gap of a few billion rand, annually: • Domestic fiscal spending ceiling. • Unreliable foreign aid contributions. • Cost-saving strategies need to be implemented.

NSP, National Strategic Plan; STIs, sexually transmitted infections; HPV, human papilloma virus; PrEP, pre-exposure prophylaxis; PICT, provider-initiated counselling and testing; ANC, Antenatal Care; CHW, Community Health Worker; POC, point-of-care; PLWH, people living with HIV and/or AIDS; M&E, monitoring and evaluation.

Although TB incidence and number of new HIV infections have declined, they have fallen short of the 50% reduction target.[1,2] The number of new HIV, TB and STI infections remains unacceptably high (270 000 new cases of HIV in 2016; 450 000 new cases of TB in 2015; and 1.4 million STIs treated annually in public health facilities).[1] South Africa remains the country with the largest number of HIV/AIDS infections globally, with 18% of adults aged 15–49 years HIVinfected.[1,8,9] While HIV incidence is decreasing, the prevalence is increasing because of a recovering life expectancy (from 58.3 to 62.4 years between 2011 and 2015), as 50% of people living with HIV/AIDS (PLWH) are on life-saving therapy.[1]

TB is currently the leading cause of death within South Africa, with 63% of TB incidence occurring in PLWH, the largest number of HIV-associated TB cases globally.[1,10] Eclipsing the (modest) decline in TB incidence since 2012 is an increased prevalence of multidrug-resistant TB – the number of cases have doubled between 2007 and 2012.[1] Less data are available on South Africa's STI epidemic; however, it remains a serious public health problem and risk factor for HIV infection.

The earlier age of sexual debut and low condom use may have reduced the success of prevention efforts. The 2016 Demographic and Health Survey found that only 58% of women and 65% of men with multiple sexual partners within the past year reported using a condom during their last sexual intercourse. The number of sexually active men aged 15–49 years with multiple sexual partners has increased, with the mean number of lifetime partners reported as 14.7. South Africa has a high prevalence of gender-based violence, with one in five partnered women and 40% of divorced or separated women having experienced physical violence.[11] HIV transmission dynamics in South Africa include cyclical intergenerational sex.[12] Analysis from the South African National HIV Surveys 2002–2012 show younger women (aged 15–24 years) with age-disparate partners (5 + years senior) have an increased risk of acquiring HIV, with the odds of HIV infection increasing for each year increase in the male partner's age.[13] These infected young women then have same-age relationships with and infect male partners, who in turn infect younger women.[14] In 2014, South Africa launched a VMMC campaign targeting the circumcision of 4.3 million men by 2016.[15] Uptake fell short, especially in traditionally non-circumcising regions,[16] because of pain, the six-week healing period requiring abstinence and perceptions regarding traditional circumcision versus medical circumcision.[17,18]

Setting South Africa up to fail?

The NSP 2017–2022 has put forth eight goals, which include breaking the cycle of transmission; reaching the 90-90-90 targets in every district; having targeted interventions reaching all key and vulnerable populations; utilising a multidepartment and multisectoral approach; implementing equal treatment and social justice; promoting leadership and shared accountability; mobilising resources and maximising efficiencies for a sustainable response; and taking data-driven action.[1] We argue that there are major gaps in the prevention and treatment goals, as well as glaring health system constraints to achieving these goals, that deserve closer scrutiny. Human immunodeficiency virus lobbyists and healthcare organisations have challenged the government publicly because of its failure in considering these aforementioned gaps.[19]

Gaps in prevention and treatment goals

The NSP focuses on five STIs and holds the following primary objectives: the reduction of *Treponema pallidum*, *Neisseria gonorrhoeae* and *Chlamydia trachomatis*; elimination of congenital syphilis; and 90% national coverage of the human papilloma virus (HPV) immunisation programme (of Grade 4 learners in South Africa).[1] The South Africa HIV Investment Case states that the most cost-effective intervention options, which are also applicable to combating the spread of STIs, are those that prevent new infections and thus translate into treatment savings costs (e.g. condom availability and VMMC).[20] However, these key prevention interventions still remain at low coverage; with expansion efforts – the scaling up of these prevention interventions – only having recently begun.[20] Furthermore, pre-exposure prophylaxis is not yet available nationally but is only provided through demonstration projects targeting young women, sex workers and men who have sex with men.[21,22] Details of proposed implementation for partner-notification strategies for HIV and TB infections and STIs are lacking.1 HIV and STI partner notification in South Africa largely depends on the patients diagnosed with infections notifying their own sex partners, as opposed to provider-assisted partner notification.[23,24] Studies in South Africa show that up to 50% of persons diagnosed with STIs have no intention of notifying their partner.[25]

An objective of the NSP is to increase the detection and treatment of highly prevalent and largely asymptomatic STIs such as chlamydia and HPV (prevalence of 17% – 42% and

71% in young women, respectively)[26] by 50%;1 however, there is no fleshed-out strategy to achieve this. Additionally, no baseline STI service coverage data currently exist in South

Africa.[1] Women need increased access to screening for HPV and cervical cancer in order to obtain referrals to care and treatment, if required. While not policy, given HPV's association with cervical cancer, screening women for HPV would help identify those at risk. These women could then be screened for cervical cancer in government facilities more frequently than current guidelines allow – up to three times in a lifetime (if HIV-uninfected).[27] Routine facility data from the District Health Information System show that cervical screening coverage among women aged 30 + years was 56%.[28] This coverage rate may be an overestimate, as smears done more than once in 10 years in the same women, smears done for women under the age of 30 years and repeat smears done because of poor sample quality could inflate the numerator. Even once diagnosed, passive referral is widely implemented in South Africa, across all health domains.

A wider range of testing modalities must be used to reach NSP and global targets for increased disease detection for HIV, TB and STIs.[20] The South Africa HIV Investment Case communicated that various sub-options may be developed to help reach targets – provider-initiated counselling and testing (PICT) in key populations (e.g. young women) with cost-effective point-of-care (POC) rapid screening technology could be proposed.[20]

The NSP encourages PICT in the antenatal care setting to ensure 100% birth testing of newborns exposed to HIV, as well as PICT of mothers and testing of all children up to 18 months to identify those who have acquired HIV through breastfeeding.[1] However, PICT is not standardised across other services within health facilities[29] where the standard of care is usually client-initiated counselling and testing. The World Health Organization (WHO) recommends PICT as an effective public health intervention to increase access to counselling and reduce missed opportunities for testing.[30]

In resource-poor settings, POC technology can offer inexpensive, large-scale screening programmes for HIV, TB, STIs and other emerging infections by expanding critical laboratory testing to rural areas and providing real-time results.[31,32] For some POC testing, the unit cost per test may be larger through the loss of bulk testing in laboratories, but it offers potentially substantial savings through enabling rapid delivery of results and reduction of facility and personnel costs.[33] The NSP does call for increased laboratory support and use of POC testing methods, specifically for common STIs,[1] but it does not explicitly state which testing kits should be used as the gold standard. It is not yet standard of care. For example, with public sector pricing in South Africa, the rapid GeneXpert technology for TB screening costs $14.93

per sample, compared to $16.88 per sample using conventional automated liquid culture-based methods in the laboratory. Additional benefits of the GeneXpert are reduced staff time needed for testing and the potential to increase volume of testing.[34]

The NSP calls for improvement in linkage to care to ensure expedited initiation of ART for all people diagnosed with HIV, as soon as they are ready for treatment and preferably same day. However, it doesn't explicitly offer innovative ways to link people to services, outside of using 'PLWH to enhance linkage to care'.[1] Additional guidance is needed. A systematic review and meta-analysis of community and facility-based HIV testing and linkage to care gaps in sub-Saharan Africa reported that facilitated linkage (e.g. clinic staff actively scheduling a referral visit or accompanying the patient to that visit) achieved both higher linkage to care and ART initiation than passive referral (e.g. providing clients with phone numbers and referral information).[35]

Lacking health system requirements

Achieving the NSP goals requires attention to critical health system requirements. We have used the WHO health system building blocks[36] to frame the discussion around these requirements, which include service delivery and supply chain management; health workforce; health information systems; financing and leadership or governance.

Service delivery and supply chain management

Delivering the services outlined in the NSP requires a well-functioning supply chain. In the Stop Stockouts Project (SSP) Stock Outs National Survey (June 2016), implemented in the last quarter of 2015, health facilities nationwide reported the following when queried about the last three months prior to contact: one in five facilities reported a stock-out of adult antiretrovirals (ARVs) (472/1875), and 70% of facilities reported the stock-out lasting longer than one month (529/760).[37] Nearly one in five stock-outs of ARVs or TB medicines resulted in the patient leaving the health facility without medication.[37] The three provinces with the highest frequency of stock-outs (Mpumalanga, Gauteng and the Free State) reported stock-outs lasting for longer than one month, depicting deficiencies in the provincial supply chain and a failure in emergency response mechanisms.[37] Stock-outs included few fixed-dose combination tablets and consisted of mainly single medications.[38]

In the aftermath of the SSP National Survey, the National Department of Health (NDoH) created a national supply chain task force to initiate supply chain reforms. In partnership, the SSP was granted R300 million to develop a national electronic medicine stock management system.[39] The NSP declares that steps will be taken to strengthen and enhance efforts to reduce stock-outs, such as an early warning system to identify impending shortages and a distribution system for delivery of medicines for chronic diseases to health facilities – the Central Chronic Medicine Dispensing and Distribution Programme.[1] While these efforts should have a positive impact on reducing stock-outs of essential medications in South Africa, additional strategies are required to address the root causes of stock-outs in the supply chain, improve and implement monitoring tools to track existing and potential issues in essential medication supply, and work closely with stakeholders, including the NDoH, to develop and implement a national supply chain strategic plan.[37,39]

Health workforce

The NSP requires a substantial growth and diversification in human resources and commits to invest greater resources towards the training and mobilisation of these personnel. However, it avoids addressing any reasons for the current shortages of healthcare workers – both political and budgetary in nature – which may serve as barriers to its goals.[19] South Africa has significantly lower numbers of doctors than most income-comparable (upper middle income) countries.[40] The severe shortage in human resources is compounded by personnel hiring limitations put in place across the NDoH because of fiscal constraints in the 2016 budget;[20] simply put, there is not enough manpower to implement the NSP.[19,20]

The NSP implementation period coincides with a major health reform process in South Africa, namely the implementation of the National Health Insurance Policy. This policy, which includes contracting with private general practitioners and public clinics, has the potential to assist with skilled staffing shortages provided favourable contracting conditions.[41] Substantial cost-savings have been reached through shifts towards nurse-based care and treatment and further task-shifting of POC testing to non-healthcare workers (lay counsellors).[20,42,43]

A further cadre requiring greater legislative security are Community Health Workers (CHWs), who are being scaled up as part of ward-based outreach teams. These workers are responsible for contact tracing and counselling, but the national policy on CHWs is still not finalised and

there are large provincial differences in contracting methods and salary. The current ratio of CHWs is far too small per population for impact, given their large and increasing scope of work.[44] South Africa's health sector budget also needs to manage the increase in health personnel costs resulting from the 2015 wage agreement, which is expected to result in a 7.4% annual growth in wages across government.[45]

Health information systems

Data-driven action relies on monitoring and evaluation (M&E) of programmatic service delivery to identify service utilisation gaps and outcomes. However, there is little to no mention of NSP M&E indicators tracking linkage to prevention, care and treatment services or retention in care. Within the NSP's M&E framework indicators, there is no definition for 'lost to follow-up' or guidance on how patients should be tracked and data collected throughout the continuum of care.

Where resources are available, an electronic data capturing system can promote the timely submission and analysis of clinical data required for health service delivery improvements, as has been implemented in the Western Cape. The province introduced an award-winning offline electronic version of the typically used paper register system in many healthcare facilities: the Primary Health Care Information System (PHCIS). The PHCIS is now the most widely used patient-based system in South Africa and on the continent, with the patient master index having records for over 80% of patients in the Western Cape. Patient information can be shared across clinics irrespective of location.[46,47] It incorporates a three-tiered monitoring approach, allowing the Ministries of Health to strategically implement one of the tiers in each facility offering ART services. Each tier has the ability to produce the same nationally required monthly enrolment and quarterly cohort reports to assist in aggregating all tier outputs into a single database at any level of the health system. Implementing such a system at country level for pre-antiretroviral wellness, ART, TB and so on can be an efficient approach to ensuring system-wide synchronisation and accurate M&E of services, including long term retention in care.[47]

Financing

In 2016, the health sector's share of the national budget sat at only 13.1% (R159.4 billion).[20] Of that share, the HIV and AIDS programme allocations made by the NDoH were R17.5

billion.[20] Health spending is highly dependent on economic growth, with which South Africa is struggling. The current national gross domestic product (GDP) and existing ratios of expenditure estimate that a 1% growth in GDP equates to a R1.5 billion real increase in public health spending annually. Unfortunately, actual health budget increases are less, as a result of the revenue growth being used to decrease national deficits and pay higher interest rates.[20] It is expected there will only be an annual growth of between 0.4% and 1.3% over the medium term (covering the three financial years from 2016 and 2017 through 2018 and 2019), equating to R913 million per annum for the HIV and AIDS programme.[20]

The total cost of implementing the proposed NSP over the five-year period is a staggering R207 billion, which constitutes a major funding gap. Annual cost estimates rise from R35.1 billion to R45.7 billion, with two goals (prevention and treatment) accounting for 86.5% of the projected budget.[1]

NSP costing does not fully account for the lack of available government funding and foreign development assistance. While South Africa has increased national spending, the government has also declared adherence to a fiscal spending ceiling, as previously budgeted.[20] Mobilisation of additional domestic resources is limited by the country's low economic growth, the weakened rand, and high levels of government debt and low credit ratings, which have both increased the cost of national borrowing.[1,20] Foreign development assistance is uncertain at best. Historically, South Africa received significant contributions from two main funders – the President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria, both of which are now simultaneously decreasing monetary support.[1,20] The bilateral Partnership Framework Implementation Plan with PEPFAR projected a funding decline from $450 million to $250 million over five years.

The broad NSP has vague strategies (such as the language surrounding the need for provision of condoms within schools and the decriminalisation of sex work while lacking concrete plans on how to do so) with unknown associated costs.[48,49] The South African HIV and TB Investment Case conducted by the NDoH depicts the gap of a few billion rand, annually, between required funding and projected available amounts.[50] Cost-savings strategies should focus on improving return on investments by refining the efficiency of current services to deliver high-value, high-impact interventions.[1,51]

Summary

To realistically achieve the NSP targets and goals, a robust, client-centred strategy addressing the NSP gaps needs to be implemented. The strategy must be cost-effective; provide active linkage to care; and address health system weaknesses that inhibit its successful implementation, including human resources, service delivery and supply chain management, accountability and M&E.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

K.L.H. conceptualised the manuscript and was the primary author. G.G. and T.D. provided conceptual contributions and review of the manuscript.

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Demographics and health profile on precursors of non-communicable diseases in adults testing for HIV in Soweto, South Africa: a cross-sectional study

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Demographics and health profile on precursors of non-communicable diseases in adults testing for HIV in Soweto, South Africa: a cross-sectional study

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Abstract

Objectives: This cross-sectional study investigated the burden of HIV-non-communicable disease (NCD) precursor comorbidity by age and sex. Policies stress integrated HIV-NCD screenings; however, NCD screening is poorly implemented in South African HIV testing services (HTS).

Setting: Walk-in HTS Centre in Soweto, South Africa.

Participants: 325 voluntary adults, aged 18+ years, who provided written or verbal informed consent (with impartial witness) for screening procedures were enrolled.

Primary and secondary outcomes: Data on sociodemographics, tuberculosis and sexually transmitted infection symptoms, blood pressure (BP) (≥140/90=elevated) and body mass index (<18.5 underweight; 18.5–25.0 normal; >25 overweight/obese) were stratified by age-group, sex and HIV status.

Results: Of the 325 participants, the largest proportions were female (51.1%; n=166/325), single (71.5%; n=231/323) and 25–34 years (33.8%; n=110/325). Overall, 20.9% (n=68/325) were HIV infected, 27.5% (n=89/324) had high BP and 33.5% (n=109/325) were overweight/obese. Among HIV-infected participants, 20.6% (14/68) had high BP and 30.9% (21/68) were overweight/obese, as compared with 29.3% (75/256) and 12.1% (31/256) of the HIV-uninfected participants, respectively. Females were more likely HIV-infected compared with males (26.5% (44/166) vs 15.1% (24/159); p=0.012). In both HIV-infected and uninfected groups, high BP was most prevalent in those aged 35–44 years (25% (6/24) vs 36% (25/70); p=0.3353) and >44 years (29% (4/14) vs 48% (26/54); p=0.1886). Males had higher BP than females (32.9% (52/158) vs 22.3% (37/166); p=0.0323); more females were overweight/obese relative to males (45.8% (76/166) vs 20.8% (33/159); p<0.0001). Females were more likely to be HIV infected and overweight/obese.

Conclusion: Among HTS clients, NCD precursors rates and co-morbidities were high. Elevated BP occurred more in older participants. Targeted integrated interventions for HIV-

infected females and HIV-infected people aged 18–24 and 35–44 years could improve HIV public health outcomes. Additional studies on whether integrated HTS will improve the uptake of NCD treatment and improve health outcomes are required.

Strengths and limitations of this study

- This study established the previously unknown level of comorbidity of non-communicable disease (NCD) precursors among adults presenting to a standard of care HIV testing services (HTS) centre in Soweto, South Africa.
- This study investigates NCD precursor and HIV comorbidity by sex and age group (18–24 years, 25–34 years, 35–44 years and ≥45 years) to determine demographics of higher risk.
- This study has a convenience sample of participants self-selecting to attend a single HTS clinic in Soweto. There is potential for bias as these participants were not randomly sampled from multiple facilities.
- As standard of care HTS includes syndromic screening for sexually transmitted infections (STIs) and tuberculosis (TB), this study was not able to confirm suspected STIs and TB with diagnostic testing in clinic.

Introduction

The epicentre of the HIV epidemic is South Africa which is estimated to have 7.9 million people living with HIV (PLHIV) and has a high HIV prevalence among the general population aged 15–49 years (20.6%).[1] South Africa's colliding epidemics of HIV/AIDS, and other communicable and chronic non-communicable diseases (NCDs), specifically HIV-NCD comorbidities, may complicate HIV treatment and impact survival.[2 3] To combat this, the South African National HIV Testing Services (HTS) Policy and Guidelines 2015[4] stresses the importance of integrating screening efforts for HIV, tuberculosis (TB), sexually transmitted infections (STIs) and NCDs.[4] Globally, South Africa has the highest estimated TB incidence among PLHIV with nearly 200 000 TB/HIV cases in 2017.[5 6] In South Africa, 3.4% of new TB cases and 7.1% of previously treated TB cases are multidrug resistant/rifampicin resistant.[6] The STI prevalence in South Africa is high,[7] though there is no baseline epidemiological data that exists.[8] Additionally, the prevalence of chronic NCDs is predicted to cause almost three-

quarters as many deaths as communicable, maternal, perinatal and nutritional disease combined by 2020, exceeding them as the most common causes of death by 2030 in Africa.[9]

While the KwaZulu-Natal Province has the highest HIV prevalence (27.0%) out of South Africa's nine provinces,[1] the Gauteng Province has the highest number of new HIV infections.[10] Another cause for concern is the rise of precursors of NCDs, such as obesity and high blood pressure (BP) within this province. The South African Demographics and Health Survey (SADHS) in 2016 reported about one-in-five Gauteng residents are severely obese (body mass index (BMI) ≥35), and the province's prevalence of hypertension in women and men aged 15 years or older to be 42.3% and 39.5%, respectively. The prevalence of hypertension is slightly higher for the black/African ethnic group, and increased even more for women and men in urban areas of residence (46.5% and 45.4%).[11]

Soweto, the largest group of urban African townships in South Africa, falls within the City of Johannesburg Metropolitan Municipality (JHB) district, Gauteng Province.[12] By 2003, the Greater Soweto area consisted of 87 townships grouped together into zones.[7] Measuring 200 km^2, it holds a population of about 1.3 million people which has increased by 48.1% in the last 10 years.[6 8] With South African townships known to have a higher HIV prevalence and the SADHS reporting urban populations have a higher prevalence of NCD precursors than the overall national prevalence,[11 13] the community of Soweto could be one of the most vulnerable populations to HIV-NCD comorbidities.[12] Collecting data on the health status of the general population of Soweto could prove useful in understanding the true burden of comorbid disease and provide insight to prevention and treatment programmes.

Black Africans comprise 98.1% of the population in Soweto.[14] While there has been a large collection of data depicting the health profile of Gauteng province and the JHB district, there is a paucity of literature on the burden of disease affecting the general population of Soweto. Existing data are largely from studies targeting key populations, and/or age or sex groups. For example, there is no systematically collected and reported baseline STI prevalence data for Soweto, however studies have clearly explained the STI health profile of men who have sex with men and for adolescents residing in Soweto.[15 16] The Heart of Soweto Study established a prospective registry of men and women from Soweto presenting with heart disease to the Chris Hani Baragwanath Academic (Bara) Hospital.[17] Preliminary results published in 2006 from information collected on 12 000+ men and women identified cardiovascular disease in 35% of

the individuals, with almost a quarter affected aged below 40 years. Two of the five most common diagnoses overall were hypertension (54%) and diabetes (10%).[17]

The South African National HTS: Policy and Guidelines[4] call for integrated screenings was adopted from the WHO Consolidated Guidelines on HIV Counselling and Testing (HCT),[18] a collation of evidence-based best practices for effective delivery of HTS and subsequent linkage to HIV prevention, care and treatment services. The global guidance, as well as the national policy, also focus on supporting the Joint United Nations Programme on HIV/AIDS 90-90-90 global HIV targets.[19] The aim of 90-90-90 is to diagnose 90% of all HIV-infected persons, provide antiretroviral therapy (ART) for 90% of those diagnosed and achieve viral suppression for 90% of those treated by 2020.[19]

The aim of this paper was to establish the level of comorbidity of NCD precursors among adults presenting to a standard of care HTS in Soweto, South Africa. Here we present baseline demographic and health profile data. National and global policies stress integrated screening to address NCD precursors (eg, BP and BMI). However, screening is poorly implemented in many South African HTS, and programmes need data for health planning.

Methods

Study design and setting

This was a cross-sectional study which evaluated a health screening programme within the Zazi' HTS clinic at the Perinatal HIV Research Unit (PHRU), a leading research centre situated at the Bara Hospital in Soweto.

The PHRU Zazi HCT Clinic, which loosely translates from Zulu to English as 'Know Yourself', has provided on-site HIV testing and counselling for adults in Soweto since 2001. It also facilitates CD4 count testing for clients not yet initiated on treatment. Zazi initially conducted CD4 count screening as >350 cells/mm3 was formerly required to start treatment. Now that a CD4 count threshold is no longer required to initiate treatment, Zazi still offers the test as an indicator of health for HIV-infected clients not yet on treatment. Zazi is currently the only service provider of walk-in, free, accessible HTS service supplied to Bara Hospital, the largest hospital in the southern hemisphere. HIV treatment is not provided on-site, but clients are given referral letters to local clinics.

To align itself with the global and national policies, the Zazi clinic expanded its health service provision in 2018, and began offering height and weight measurements, BP readings and symptom screenings for STIs and TB within its HTS. If required, clients were given referral letters for additional testing and treatment at their local government clinics; treatment was not provided on-site for any illness. In this manner, the Zazi clinic reflected the South African National Department of Health's (NDoH) newly proposed HTS standard of care.

Sampling and sample size

The study sample was comprised of all eligible walk-in PHRU Zazi HTS clients, who consented for both the health screening programme and for their data to be captured and used in research, between 19 February 2018 and 14 June 2018. Any client who allowed the use of his/her health screening results and data via study consent were included in the aggregate data capture. If consent was not given, the client was still able to undergo health screening without data capture. All clients who consented to the programme and to data capture were then asked if they would like to partake in a clinic exit survey prior to leaving the clinic and consent was obtained. Figure 1 depicts the participant flow chart in Zazi.

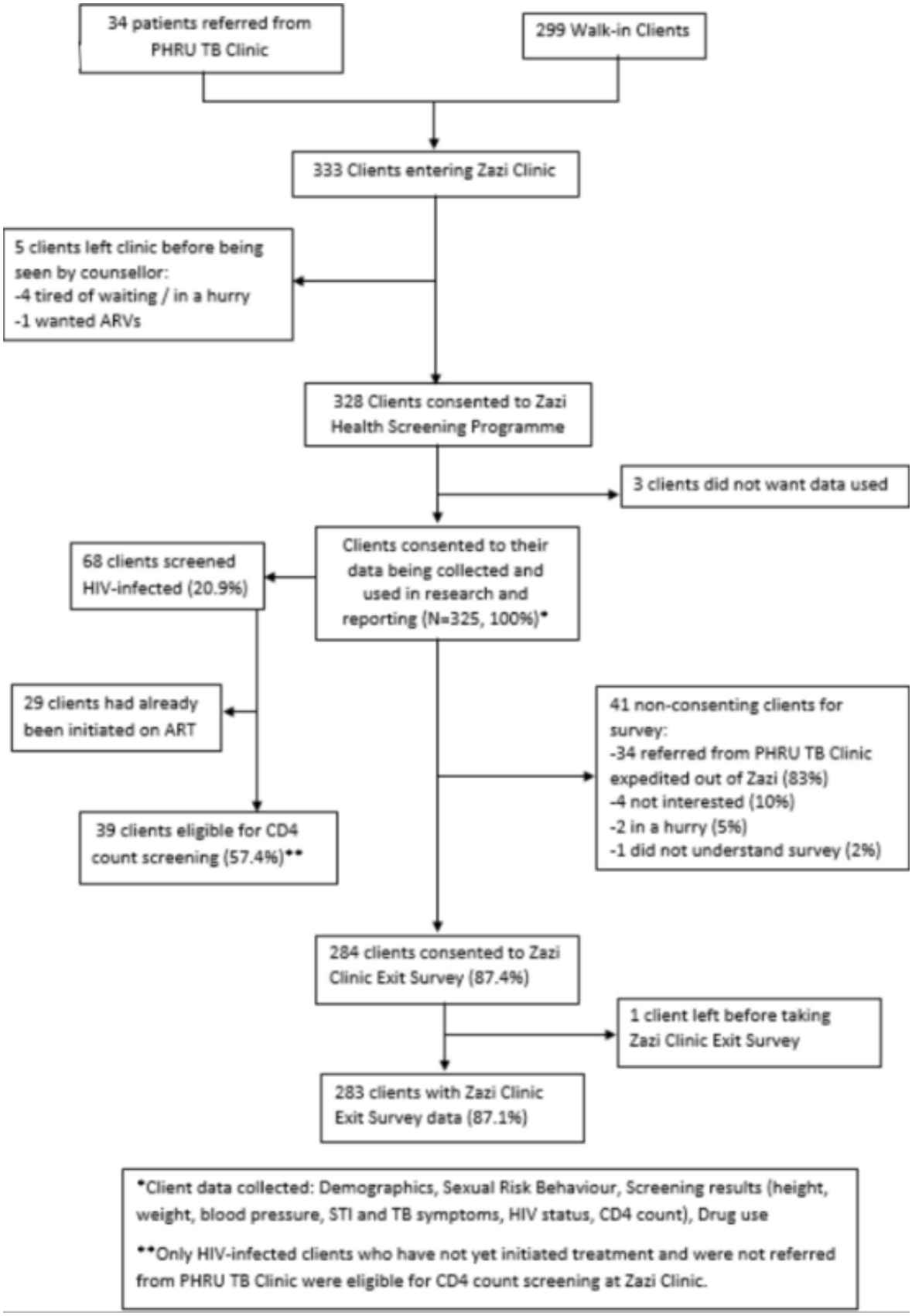

Figure 1. Participant flow chart for the Zazi clinic. PHRU, Perinatal HIV Research Unit; STI, sexually transmitted disease; TB, tuberculosis.

Inclusion and exclusion criteria

Eligibility criteria for participation in the integrated screenings were the following: at least 18 years of age; able to communicate in either English, IsiZulu and/or Sotho; and able and willing to provide written or verbal informed consent (with impartial witness) for health screening procedures. If a client presented to the clinic and there was immediate cause for concern, they were excluded from the programme and redirected to the Bara casualty ward.

Data collection and management

Client demographic and clinic exit survey data were either self-collected by literate clients in the reception area, or collected with help of the clinic receptionist or lay counsellors for clients unable to read or write. Clinical data were collected by the study lay counsellors and enrolled nurse while in private rooms through consultation with the client. Demographic, behavioural and clinical data were collected through screenings and questionnaires and recorded onto paper forms comprising PHRU Zazi HTS client file. Clinical data collected included health profile and screening results (see Study measures: Health profile and screening results section below) and client interest in pre-exposure prophylaxis (PrEP). Source documents were the client file and CD4 count pathology reports as accessed and printed by the enrolled nurse from the electronic National Health Laboratory Services InterSystems' TrakCare Laboratory Information System.

The Programme Manager and statistician led data cleaning checks prior to clinical staff entering data into the electronic database (REDCap), performing a 100% cross-check of all captured data against the client files for verification purposes.

Study measures

Demographic and substance use information

Data were collected on sex, age, race, nationality, ethnic group, marital status, highest level of education, employment, details regarding home residence—type of housing, source of water and fuel for cooking and lighting, type of toilet facility, as well as possession of household and ownership items.

A wealth quintile was developed using the socioeconomic measures and determined using Principal Component Analysis (PCA).[20-22] The socioeconomic measures included the following variables: type of house, source of water, type of toilet facility; type of fuel used for

cooking; type of fuel used for lighting; possession of household items and other ownership items. Prior to calculating the wealth quintile, variables with more than two levels were recoded into binary (0 or 1) for each level of response. Frequencies were run on all the binary variables and only those with responses between 5% and 95% were retained. The retained variables were evaluated by the PCA method using the varimax rotation to identify those contributing largely to the wealth construct. Variables meeting a prespecified cut-off and loading in at least two factors were excluded. The remaining variables were retained and scored to create the socioeconomic index. Five wealth quintiles were estimated on the scored measure using 20 percentile intervals.

Additional information was collected on substance use including how often clients drank alcohol in the last year and number of drinks per occasion, usage of illicit drugs and type of illicit drugs, current cigarette smoking status and number of cigarettes smoked per day. Questions surrounding alcohol, tobacco and drug use were taken from the validated 2003 SADHS.[23]

Health profile and screening results

Client health profile and screening results include BMI, BP readings, STI and TB symptoms, HIV results and CD4 count.

BMI was calculated by dividing client weight (in kg) by the square of height (in m2) and classified as underweight, normal, overweight and obese using the WHO classification.[24] Overweight and obese categories were merged resulting in three categories.

BP was classified as high, normal or low using systolic and diastolic BP. High BP was defined as >140/90 mm Hg, normal BP was considered ≤140/90 and ≥90/60 mm Hg, and low BP was classified as <90/60 mm Hg. If the first measurement was high or low then a second BP reading was conducted, and an average BP was used for the classification. BP cut-offs used were from the South African Hypertension Practice Guidelines, as per standard of care.[25]

STI symptoms were defined as having at least one of the following symptoms: (1) abnormal, bad-smelling or itchy discharge from the vagina/penis/anus; (2) any blood coming from the vagina/penis/anus; (3) current sores on/in vagina/penis/anus; (4) burning sensation while passing urine and/or (5) any lower abdominal pain (if female).

TB symptoms were defined as having one or more of the following symptoms: (1) cough for more than 2 weeks, (2) blood in the sputum, (3) persistent fever and/or night sweats for more than 2 weeks, (4) weight loss of ≥1.5 kg in the last month and/or (5) lived with someone who has/had TB in the last month.26 TB symptoms were assessed for clients who were not already diagnosed with TB on entering the clinic.

The STI and TB symptom screening utilised standardised questions provided by the NDoH.

Data analysis

Descriptive statistics (eg,; medians and IQRs) were determined for continuous variables (eg, age, BMI and CD4 count). Frequencies and their percentages were determined for categorical variables and stratified by age group (18–24, 25–34, 35–44 and ≥45 years), sex and HIV status where appropriate.

To test statistical significance for categorical measures stratified by sex, Fisher's exact test or $\chi 2$ analysis as appropriate was used. Continuous variables were compared by sex using the Kruskal-Wallis test. The distribution of precursors of NCDs (BMI and BP) were presented graphically by age-group and sex.

All statistical analysis was conducted in SAS Enterprise Guide V.7.1 (SAS Institute) using SAS/STAT procedures PROC FREQ, PROC NPAR1WAY and PROC FACTOR.

Patient and public involvement

This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. We have invited our research community advisory board to help us disseminate our findings.

Ethical considerations

This study was reviewed in accordance with the Centers for Disease Control and Prevention human research protection procedures and was determined to be a research, but investigators did not interact with human subjects or had access to identifiable data or specimens for research purposes.

Results

Demographic, substance use and health profile data were collected on 325 eligible walk-in Zazi clients.

Demographics and substance use

Males were significantly older than females (median (IQR) age 37.5 (31.0–45.0) years vs 33.0 (26.0–41.0) years, respectively; p=0.001) (table 1). The largest proportion of clients were female (51.1%, (n=166/325)), predominantly black Africans (98.5% (n=320/325)), South African (95.0% (n=305/321)), Zulu-speaking (41.7% (n=135/324)) and single (71.5% (n=231/323)). About one-third had completed high school (31.5% (n=102/324)), and the majority had initially come to Zazi for HIV testing (96.3% (n=313/325)). Most clients belonged to the lower wealth quintiles: first quintile (24.0% (78/325)), second quintile (26.8% (n=87/325)) and third quintile (24.9% (n=81/325)). Clients aged 25–34 and 35–44 years mostly fell within the first quintile (28.2% (n=31/110) and 28% (n=26/94), respectively), whereas the younger age group (18–24 years) mostly reflected the second quintile (40% (n=21/52)). The oldest clients (≥45 years) did not contribute towards the highest wealth quintile. Of clients with substance use data available, 11.0% (n=32/290), 7.4% (n=24/325) and 26.9% (n=78/290) reported drinking alcohol, using drugs weekly and ever smoked cigarettes, respectively. People aged 18–24 years reported drinking alcohol on a monthly basis (49% (n=22/45)) and drank >4 standard-size drinks per sitting (75% (n=24/32)). Clients aged 25–34 years reported drinking weekly (14% (n=14/98)) and monthly (38% (n=37/98), and among those who do drink, the majority drank >4 standard-size drinks per sitting (72% (n=49/68)). The majority of clients who reported having ever smoked cigarettes, still smoke (99% (n=77/78)) about 10 cigarettes per day (43% (33/77)). Of these, the highest proportion were aged 25–34 (53% (n=16/30)) and 35–44 years (52% (n=11/21)) (table 1).

Table 1 Demographic characteristics and substance use by age group

Variable	Overall	Age in years 18–24	25–34	35–44	≥ 45
Sex					
Female (%)	166/325 (51.1)	39/52 (75.0)	56/110 (50.9)	44/94 (46.8)	27/69 (39.1)
Male (%)	159/325 (48.9)	13/52 (25.0)	54/110 (49.1)	50/94 (53.2)	42/69 (60.9)
Race					
Black (%)	320/325 (98.5)	51/52 (98.1)	108/110 (98.2)	92/94 (97.9)	69/69 (100.0)
Coloured/mixed race (%)	5/325 (1.5)	1/52 (1.9)	2/110 (1.8)	2/94 (2.1)	0/69 (0.0)
Nationality					
South African (%)	305/321 (95.0)	51/52 (98.1)	103/109 (94.5)	86/91 (94.5)	65/69 (94.2)
Other (%)	16/321 (5.0)	1/52 (1.9)	6/109 (5.5)	5/91 (5.5)	4/69 (5.8)
Ethnic group					
Zulu (%)	135/324 (41.7)	26/52 (50.0)	49/109 (45.0)	29/94 (30.9)	31/69 (44.9)
Sotho (%)	60/324 (18.5)	10/52 (19.2)	17/109 (15.6)	21/94 (22.3)	12/69 (17.4)
Tsonga (%)	31/324 (9.6)	5/52 (9.6)	12/109 (11.0)	10/94 (10.6)	4/69 (5.8)
Tswana (%)	24/324 (7.4)	1/52 (1.9)	10/109 (9.2)	7/94 (7.4)	6/69 (8.7)
Xhosa (%)	27/324 (8.3)	5/52 (9.6)	7/109 (6.4)	10/94 (10.6)	5/69 (7.2)
Other (%)	47/324 (14.5)	5/52 (9.6)	14/109 (12.8)	17/94 (18.1)	11/69 (15.9)
Marital status					
Divorced/widowed (%)	19/323 (5.9)	0/52 (0.0)	2/110 (1.8)	7/92 (7.6)	10/69 (14.5)
Living together/married (%)	73/323 (22.6)	3/52 (5.8)	21/110 (19.1)	17/92 (18.5)	32/69 (46.4)
Single (%)	231/323 (71.5)	49/52 (94.2)	87/110 (79.1)	68/92 (73.9)	27/69 (39.1)
Highest education					
Up to high school (%)	138/324 (42.6)	19/52 (36.5)	41/110 (37.3)	37/93 (39.8)	41/69 (59.4)
Matriculated (%)	102/324 (31.5)	21/52 (40.4)	35/110 (31.8)	30/93 (32.3)	16/69 (23.2)
Tertiary education (%)	84/324 (25.9)	12/52 (23.1)	34/110 (30.9)	26/93 (28.0)	12/69 (17.4)
Why did you decide to come to the clinic today?					
HIV testing (%)	313/325 (96.3)	52/52 (100.0)	106/110 (96.4)	92/94 (97.9)	63/69 (91.3)
CD4 count retest (%)	18/325 (5.5)	1/52 (1.9)	6/110 (5.5)	4/94 (4.3)	7/69 (10.1)
TB screening (%)	14/325 (4.3)	4/52 (7.7)	4/110 (3.6)	6/94 (6.4)	0/69 (0.0)
General STI screening (%)	15/325 (4.6)	5/52 (9.6)	3/110 (2.7)	7/94 (7.4)	0/69 (0.0)
Check blood pressure (%)	15/325 (4.6)	4/52 (7.7)	4/110 (3.6)	5/94 (5.3)	2/69 (2.9)
Wealth quintile					
Quintile 1 (%)	78/325 (24.0)	13/52 (25.0)	31/110 (28.2)	26/94 (27.7)	8/69 (11.6)
Quintile 2 (%)	87/325 (26.8)	21/52 (40.4)	21/110 (19.1)	20/94 (21.3)	25/69 (36.2)
Quintile 3 (%)	81/325 (24.9)	9/52 (17.3)	25/110 (22.7)	24/94 (25.5)	23/69 (33.3)
Quintile 4 (%)	60/325 (18.5)	7/52 (13.5)	25/110 (22.7)	15/94 (16.0)	13/69 (18.8)
Quintile 5 (%)	19/325 (5.8)	2/52 (3.8)	8/110 (7.3)	9/94 (9.6)	0/69 (0.0)
In the last year, how often would you usually drink alcohol?					
Weekly (%)	32/290 (11.0)	5/45 (11.1)	14/98 (14.3)	9/84 (10.7)	4/63 (6.3)
Monthly (%)	93/290 (32.1)	22/45 (48.9)	37/98 (37.8)	23/84 (27.4)	11/63 (17.5)
Sometimes (%)	51/290 (17.6)	5/45 (11.1)	17/98 (17.3)	20/84 (23.8)	9/63 (14.3)
Never drank alcohol in the last year (%)	114/290 (39.3)	13/45 (28.9)	30/98 (30.6)	32/84 (38.1)	39/63 (61.9)

About how many standard-size drinks do you usually have in 1 day?					
1–2 (%)	25/175 (14.3)	5/32 (15.6)	7/68 (10.3)	8/52 (15.4)	5/23 (21.7)
3–4 (%)	34/175 (19.4)	3/32 (9.4)	12/68 (17.6)	12/52 (23.1)	7/23 (30.4)
>4 (%)	116/175 (66.3)	24/32 (75.0)	49/68 (72.1)	32/52 (61.5)	11/23 (47.8)
Do you use drugs?					
Yes often (weekly) (%)	24/325 (7.4)	3/52 (5.8)	15/110 (13.6)	2/94 (2.1)	4/69 (5.8)
Sometimes (%)	8/325 (2.5)	2/52 (3.8)	3/110 (2.7)	3/94 (3.2)	0/69
No (%)	293/325 (90.2)	47/52 (90.4)	92/110 (83.6)	89/94 (94.7)	65/69 (94.2)
Have you ever smoked cigarettes?					
No (%)	212/290 (73.1)	29/45 (64.4)	68/98 (69.4)	63/84 (75.0)	52/63 (82.5)
Yes (%)	78/290 (26.9)	16/45 (35.6)	30/98 (30.6)	21/84 (25.0)	11/63 (17.5)
Do you still smoke cigarettes now?					
No (%)	1/78 (1.3)	1/16 (6.3)	0/30 (0.0)	0/21 (0.0)	0/11 (0.0)
Yes (%)	77/78 (98.7)	15/16 (93.8)	30/30 (100.0)	21/21 (100.0)	11/11 (100.0)
About how many cigarettes do you or did you usually smoke in 1 day?					
1–2 (%)	12/77 (15.6)	2/15 (13.3)	2/30 (6.7)	4/21 (19.0)	4/11 (36.4)
<5 (%)	27/77 (35.1)	6/15 (40.0)	12/30 (40.0)	4/21 (19.0)	5/11 (45.5)
10 (%)	33/77 (42.9)	5/15 (33.3)	16/30 (53.3)	11/21 (52.4)	1/11 (9.1)
20 (%)	5/77 (6.5)	2/15 (13.3)	0/30 (0.0)	2/21 (9.5)	1/11 (9.1)

The total frequencies for each variable do not necessarily equal the total sample size due to missing responses.
STI, sexually transmitted disease; TB, tuberculosis.

Communicable disease screening results

Overall, 3.5% (n=11/318) had STI symptoms, 1.4% (n=4/289) had TB symptoms and 20.9% (n=68/325) were HIV infected. There were 34 laboratory-confirmed TB clients who entered Zazi, and of those, 19 (56%) were among the HIV infected. STI symptoms were highest in the group of people aged 18–24 years (10% (n=5/51)). HIV infections were most prevalent in the group of aged 35–44 years (26% (n=24/94)) followed by those ≥45 years (20% (n=14/69)) and 25–34 years (20.0% (n=22/110)). Of the 68 HIV-infected clients, 39 had their CD4 count measured (median CD4: 327 cells/mm3, IQR: 157–569). The remaining 29 HIV-infected clients were already in care, monitored regularly. A higher proportion of clients aged ≥45 years were overweight/obese (46% (n=32/69)) (table 2).

In comparing screening results by age groups, clients in age groups 35–44 and ≥45 years were more likely to be overweight/obese compared with the group aged 25–34 years (37.2% (n=35/94) vs 22.7% (n=25/110); p=0.0234) and (46.4% (n=32/69) vs 22.7% (n=25/110); p=0.0009). The older age groups (25–34, 35–44 and ≥44 years) had significantly high proportions of high BP (22.7% (n=25/110) vs 5.8% (n=3/52; p=0.0077)), (33.0 (n=31/94) vs 5.8% (n=3/52; p=0.0002) and (44.1% (n=30/68) vs 5.8% (n=3/52; p<0.0001) relative to the younger age group (18–24 years). In addition, clients who were ≥45 years were more likely to

be obese compared with the group aged 25–34 years (44.1% (n=30/68) vs 22.7% (n=25/110); p=0.0027).

Females obtained a significantly higher rate of HIV diagnosis than males (26.5% (n=44/166) vs 15.1% (n=24/159); p=0.012) (table 2). The proportion of males and females reporting no interest in learning about PrEP (95.6% (n=129/135) vs 91.8% (n=112/122); p=0.21) was similar between sex. Females were significantly more likely to be overweight/obese than males (45.8% (n=76/166) vs 20.8% (n=33/159); p<0.001). A significantly higher number of males were diagnosed with high BP compared with females (32.9% (n=52/158) vs 22.3% (n=37/166); p=0.032). Overall, 33.5% (n=109/325) were overweight/obese, 27.5% (n=89/324) and 1.5% (n=5/324) had high and low BP, respectively (table 2).

Table 2 Screening results by age group and sex

		Age in years				Sex		
Variable	**Overall**	**18–24**	**25–34**	**35–44**	**≥45**	**Female**	**Male**	**P value**
Body mass index (BMI)								
Underweight (%)	69/325 (21.2)	13/52 (25.0)	26/110 (23.6)	17/94 (18.1)	13/69 (18.8)	24/166 (14.5)	45/159 (28.3)	0.002
Normal (%)	147/325 (45.2)	22/52 (42.3)	59/110 (53.6)	42/94 (44.7)	24/69 (34.8)	66/166 (39.8)	81/159 (50.9)	0.043
Overweight/obese (%)	109/325 (33.5)	17/52 (32.7)	25/110 (22.7)	35/94 (37.2)	32/69 (46.4)	76/166 (45.8)	33/159 (20.8)	<0.001
Median number of BMI (IQR)	n=325, 220.1 (19.1–27)	n=52, 210.4 (18.4–26.5)	n=110, 210.0 (18.5–24.7)	n=94, 220.8 (19.4–27.7)	n=69, 230.9 (19.4–28.9)	n=166, 240.0 (20.1–29.6)	n=159, 200.4 (18.0–23.8)	<0.001
Min–max number of BMI	n=325 (13–43)	n=52 (14–35)	n=110 (14–40)	n=94 (14–43)	n=69 (13–35)	n=166 (14–43)	n=159 (13–33)	
Blood pressure								
High (%)	89/324 (27.5)	3/52 (5.8)	25/110 (22.7)	31/94 (33.0)	30/68 (44.1)	37/166 (22.3)	52/158 (32.9)	0.032
Low (%)	5/324 (1.5)	0/52 (0.0)	2/110 (1.8)	1/94 (1.1)	2/68 (2.9)	2/166 (1.2)	3/158 (1.9)	0.61
Normal (%)	230/324 (71.0)	49/52 (94.2)	83/110 (75.5)	62/94 (66.0)	36/68 (52.9)	127/166 (76.5)	103/158 (65.2)	0.025
Syndromic STI								
1+ symptoms (%)	11/318 (3.5)	5/51 (9.8)	2/109 (1.8)	4/94 (4.3)	0/64 (0.0)	10/163 (6.1)	1/155 (0.6)	0.007
No symptoms (%)	307/318 (96.5)	46/51 (90.2)	107/109 (98.2)	90/94 (95.7)	64/64 (100.0)	153/163 (93.9)	154/155 (99.4)	
Syndromic TB								
1+ symptoms (%)	4/289 (1.4)	0/46 (0.0)	1/97 (1.0)	2/84 (2.4)	1/62 (1.6)	2/155 (1.3)	2/134 (1.5)	0.88
No symptoms (%)	285/289 (98.6)	46/46 (100.0)	96/97 (99.0)	82/84 (97.6)	61/62 (98.4)	153/155 (98.7)	132/134 (98.5)	
HIV result								
Positive (%)	68/325 (20.9)	8/52 (15.4)	22/110 (20.0)	24/94 (25.5)	14/69 (20.3)	44/166 (26.5)	24/159 (15.1)	0.012
Negative (%)	257/325 (79.1)	44/52 (84.6)	88/110 (80.0)	70/94 (74.5)	55/69 (79.7)	122/166 (73.5)	135/159 (84.9)	
Was CD4 count (cells/mm^3) measured for all HIV-infected clients?								
No (%)	29/68 (42.6)	4/8 (50.0)	7/22 (31.8)	9/24 (37.5)	9/14 (64.3)	17/44 (38.6)	12/24 (50.0)	0.37
Yes (%)	39/68 (57.4)	4/8 (50.0)	15/22 (68.2)	15/24 (62.5)	5/14 (35.7)	27/44 (61.4)	12/24 (50.0)	
CD4 count (cells/mm^3)								
Median (IQR)	n=39, 327 (157-569)	n=4, 310 (209-452)	n=15, 259 (144-468)	n=15, 335 (94.0–653)	n=5, 591 (463-615)	n=44, 365 (190-511)	n=24, 244 (124-622)	0.69
Min–max	n=39 (27–1000)	n=4 (190–511)	n=15 (91–845)	n=15 (27–1000)	n=5 (313–953)	n=44 (27–1000)	n=24 (72–845)	

The total frequencies for each variable do not necessarily equal the total sample size due to missing responses. Participants were able to opt out of any screening, and specifically syndromic TB screening was only conducted for clients not already presenting with diagnosed TB.
P values (overweight/obese): 25–34 vs 35–44 years=0.0234, 25–34 vs ≥45 years=0.0009; p values (high blood pressure): 18–24 vs 25–34=0.0077, 18–24 vs 35–44 years=0.0002, 18–24 vs ≥45 years=<0.0001, 25–34 vs ≥45 years=0.0027.
STI, sexually transmitted disease; TB, tuberculosis.

NCD screening results, stratified by HIV status

Both figure 2 and table 3 present the distribution of BP and BMI, stratified by age-group and sex for HIV-infected and HIV-uninfected clients. All HIV-infected clients aged 18–24 years (n=8) had normal BP readings, regardless of BMI (figure 2A, table 3). High BP readings increased with age with the highest readings being among the oldest age group (≥45 years, 28.6%). Though not significant, HIV-infected females had higher BP readings relative to HIV-infected males (25.0% vs 12.5%; p=0.22) (figure 2B, table 3). For HIV-uninfected clients, a similar BP trend was seen by age (figure 2C, table 3), while the opposite was seen by sex (figure 2D, table 3).

In the HIV-infected group, high BP was most common among those who were overweight/obese as opposed to normal weight (57.1% (n=8/14) vs 24.5% (n=13/53); p=0.0193). Whereas, in the HIV-uninfected group, clients who were underweight had normal BP relative to high BP (24.3% (n=43/177) vs 10.7% (n=8/75); p=0.0138). In addition, a high proportion of males who were overweight/obese had high BP compared with normal BP (34.7% (n=17/49) vs 15.7% (13/83); p=0.0117) (table 3).

Figure 2. Distribution of BMI and BP by HIV status: (A) BMI and BP for HIV-infected people by age group (B) BMI and BP for HIV-infected people by sex. (C) BMI and BP for HIV-uninfected people by age group. (D) BMI and BP for HIV-uninfected people by age group. BMI, body mass index; BP, blood pressure.

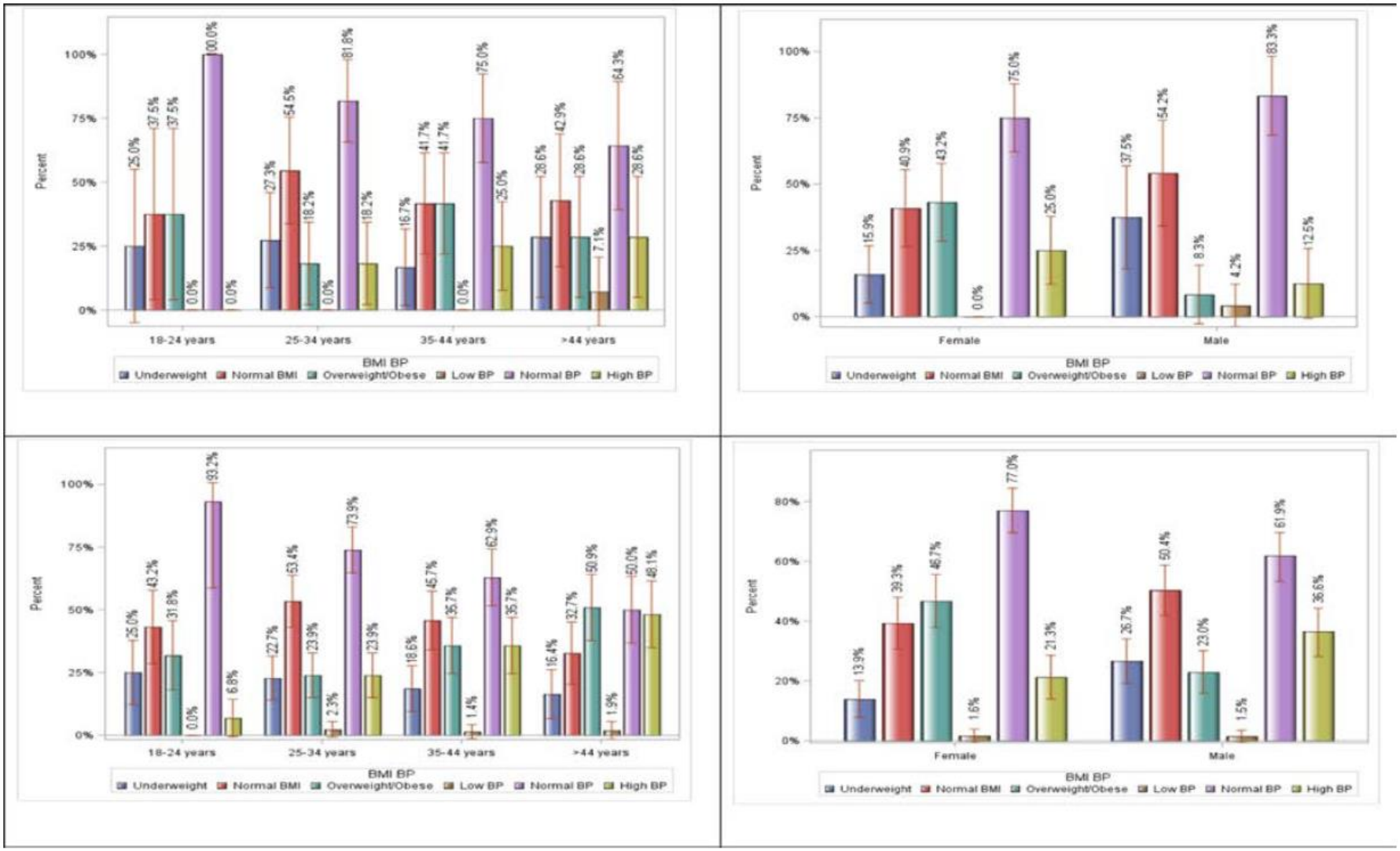

Table 3. BMI and blood pressure by age group and sex for HIV-infected and uninfected clients

	HIV infected				HIV uninfected			
Variable	Overall	Low BP	Normal BP	High BP	Overall	Low BP	Normal BP	High BP
Body mass index (BMI)								
Age group								
18–24 years								
Underweight (%)	2/8 (25.0)	0/0	2/8 (25.0)	0/0	11/44 (25.0)	0/0	11/41 (26.8)	0/3 (0.0)
Normal (%)	3/8 (37.5)	0/0	3/8 (37.5)	0/0	19/44 (43.2)	0/0	17/41 (41.5)	2/3 (66.7)
Overweight/obese (%)	3/8 (37.5)	0/0	3/8 (37.5)	0/0	14/44 (31.8)	0/0	13/41 (31.7)	1/3 (33.3)
25–34 years								
Underweight (%)	6/22 (27.3)	0/0	5/18 (27.8)	1/4 (25.0)	20/88 (22.7)	1/2 (50.0)	17/65 (26.2)	2/21 (9.5)
Normal (%)	12/22 (54.5)	0/0	11/18 (61.1)	1/4 (25.0)	47/88 (53.4)	1/2 (50.0)	32/65 (49.2)	14/21 (66.7)
Overweight/obese (%)	4/22 (18.2)	0/0	2/18 (11.1)	2/4 (50.0)	21/88 (23.9)	0/2 (0.0)	16/65 (24.6)	5/21 (23.8)
35–44 years								
Underweight (%)	4/24 (16.7)	0/0	4/18 (22.2)	0/6 (0.0)	13/70 (18.6)	0/1 (0.0)	8/44 (18.2)	5/25 (20.0)
Normal (%)	10/24 (41.7)	0/0	8/18 (44.4)	2/6 (33.3)	32/70 (45.7)	1/1 (100.0)	20/44 (45.5)	11/25 (44.0)
Overweight/obese (%)	10/24 (41.7)	0/0	6/18 (33.3)	4/6 (66.7)	25/70 (35.7)	0/1 (0.0)	16/44 (36.4)	9/25 (36.0)
>44 years								
Underweight (%)	4/14 (28.6)	1/1 (100.0)	3/9 (33.3)	0/4 (0.0)	9/54 (16.7)	1/1 (100.0)	7/27 (25.9)	1/26 (3.8)
Normal (%)	6/14 (42.9)	0/1 (0.0)	4/9 (44.4)	2/4 (50.0)	18/54 (33.3)	0/1 (0.0)	9/27 (33.3)	9/26 (34.6)
Overweight/obese (%)	4/14 (28.6)	0/1 (0.0)	2/9 (22.2)	2/4 (50.0)	27/54 (50.0)	0/1 (0.0)	11/27 (40.7)	16/26 (61.5)
Sex								
Female								
Underweight (%)	7/44 (15.9)	0/0	7/33 (21.2)	0/11 (0.0)	17/122 (13.9)	1/2 (50.0)	13/94 (13.8)	3/26 (11.5)
Normal (%)	18/44 (40.9)	0/0	14/33 (42.4)	4/11 (36.4)	48/122 (39.3)	1/2 (50.0)	38/94 (40.4)	9/26 (34.6)
Overweight/obese (%)	19/44 (43.2)	0/0	12/33 (36.4)	7/11 (63.6)	57/122 (46.7)	0/2 (0.0)	43/94 (45.7)	14/26 (53.8)
Male								
Underweight (%)	9/24 (37.5)	1/1 (100.0)	7/20 (35.0)	1/3 (33.3)	36/134 (26.9)	1/2 (50.0)	30/83 (36.1)	5/49 (10.2)
Normal (%)	13/24 (54.2)	0/1 (0.0)	12/20 (60.0)	1/3 (33.3)	68/134 (50.7)	1/2 (50.0)	40/83 (48.2)	27/49 (55.1)
Overweight/obese (%)	2/24 (8.3)	0/1 (0.0)	1/20 (5.0)	1/3 (33.3)	30/134 (22.4)	0/2 (0.0)	13/83 (15.7)	17/49 (34.7)

P values (HIV infected): normal BP vs high BP (underweight)=0.1239, normal BP vs high BP (normal)=0.3732, normal BP vs high BP (overweight/obese)=0.0193.
P values (HIV uninfected): normal BP vs high BP (underweight)=0.0138, normal BP vs high BP (normal)=0.5664, normal BP vs high BP (overweight/obese)=0.1389.
P values (HIV-uninfected males): normal BP vs high BP (overweight/obese)=0.0117.
BP, blood pressure.

Discussion

This study has shown that there is a high prevalence of HIV, NCD precursors and HIV-NCD precursor comorbidity among an urban, adult population in Johannesburg, South Africa; and could depict similar health burden outcomes within analogous geographical locations in South Africa. Men have significantly higher BP than women, even though females are significantly more overweight/obese than males. Women have significantly more HIV-infection than men, and there is an association between high BMI and hypertension among HIV-infected women. Overall, HIV-uninfected persons have higher BP compared with their HIV-infected counterparts among all age groups, and HIV-uninfected males have higher BP compared with HIV-infected males. Our study reports a higher HIV prevalence than the national prevalence.[1] Over one-third of clients were overweight/obese, representing a higher prevalence of this BMI among black Africans as compared with the SADHS.[11] The prevalence of high BP among our study participants is nearly three times that of a recent national general household survey conducted by Statistics South Africa, which reported an overall 10.4% prevalence of hypertension, as diagnosed by a medical professional.[27]

Our study results are compatible with national data regarding females having significantly more HIV-infections as compared with men[28 29]; a high prevalence of overweight/obesity among all age-groups which increased with age[11]; significantly more overweight/obesity among women[11 30]; and prevalence of hypertension increasing with age.[31] However, our study's overall HIV prevalence was slightly higher than the national prevalence,[5] with the majority of infections being clients 35+ years of age. One-third of all Zazi clients being overweight/obese represented a lower prevalence than reported by the SADHS for the black African population (67.4% of women and 27.4% of men).[11] We found all age-groups to exhibit a high prevalence of elevated BP, even the youth; and men had significantly higher BP than women. This contradicts the Statistics South Africa national household survey in which prevalence of high BP increased with age in both sexes and was higher in women for all age groups.[27] Additionally, it is possible that clinical practice guidelines used in South Africa are underdiagnosing elevated BP and hypertension, as they are more liberal than other scales utilised globally. While South Africa defines hypertension as >140/90 mm Hg, the USA defines stage 1 hypertension being either systolic 130–139 mm Hg or diastolic 80–89 mm Hg.[32]

When stratifying data by HIV-status, HIV-infected women have higher BP than HIV-infected men. The opposite is true for the HIV-uninfected group which is more reflective of the overall population. Previous studies suggest that hypertension in HIV-positive individuals is associated

primarily with traditional risk factors such as being of older age, overweight and having other NCDs, such as diabetes and dyslipidaemia.[33] Investigations have suggested a lower CD4 count as a strong independent predictor of hypertension in HIV-infected individuals through processes of persistent immune activation, chronic inflammation, endothelial dysfunction and microbial translocation associated with inadequate immune recovery.[34–37] Of the 39 clients who had their CD4 count taken at Zazi, males had a lower median CD4 count than women (244 vs 365 cells/mm3, respectively). While this does not support the hypothesis that lower CD4 count is linked with increased BP in HIV-infected individuals, it does follow the trend that men present to healthcare facilities later—and therefore often more sickly—than women. A systematic literature review yielded conflicting and inconclusive evidence to determine prevalence of hypertension in PLHIV and its association with ART and HIV-related and traditional risk factors—including sex.[33 38] Evidence has shown binge drinking and tobacco use increase the risk of NCDs.[39 40] A study using data from the WHO Study on global AGEing and adult Health Wave 1 showed smoking and hypertension were both risk factors of stroke among older South African adults.[41] South Africa is ranked as having one of the highest consumption rates of absolute alcohol per drinker per year.[42] In 2009, it was reported that 23.7% of South African adults smoked cigarettes, and while this is a 7% decrease since 1995, the reduction has plateaued.[43] Zazi men were more likely than women to consume alcohol and to smoke cigarettes which may account for their increased likelihood of elevated BP.[44 45]

Both longitudinal and cross-sectional study data have shown obesity to be a known independent risk factor for hypertension.[46–48] This is shown within our study, as we found that elevated BP was associated with overweight/obesity in women and not men. The majority of men with higher BP had a normal BMI. Studies have shown for every 1 kg/m^2 increase in BMI, there were between 1.3–1.7 and 1.2–1.4 mm Hg increases in BP for men and women, respectively.[49] Furthermore, antihypertensive treatment mitigates the association of BMI with systolic BP by two-thirds.[50] There is less data known on the relationship of body composition and BP in black African men.[31]

Our study demographics largely reflect that of the general population of Soweto—a nearly all black African, gender-balanced population of lower socioeconomic status, with the great majority speaking Zulu, followed by Sesotho.[14 51] The Zazi clinic, however, seems to draw more clients who have received higher education than that of the general population.[52] Therefore, aside from having clients with an overall higher education, the Zazi study population

does reflect the same demographics as the general population of Soweto and could be generalizable to similar geographical populations.

While the gender-balanced Zazi population is representative of the general population, there is conflicting literature to determine if it mimics typical attendance by sex within HTS centres. Literature historically shows men tend to be under-represented in HIV testing and treatment services in sub-Saharan Africa and globally.[53 54] However, the latest SADHS reports that 69% of men had ever tested and 45% did so within the previous 12 months; not radically different from what our study has found. When stratifying our data by age-group and sex, only one age category (18–24 years) contained low male attendance (one-quarter) in comparison to their female counterparts. A study using data from three national HIV population-based household surveys (2005, 2008, 2012) reported sociodemographic factors linked to poor HIV testing uptake in men: being aged 15–24 years, of black African race group, being single and unemployed, and residing in urban informal and rural informal areas.[54] Within the Zazi clinic, the two age-groups with the lowest attendance were 18–24 years and 45+ years, despite these age-groups comprising the two largest of the adult age demographics among the general population of Soweto (23.1% and 20.3%, respectively).[55] Unfortunately, these are also the age groups largely related to the HIV transmission cycles in South Africa. HIV transmission dynamics in South Africa include cyclical intergenerational sex.[56] Younger women (aged 15–24 years) tend to have age-disparate partners (5+ years senior), with the odds of HIV infection increasing for each year increase in the male partner's age.[57] Once older, these infected women have same-age relationships, infecting their male partners, who in turn infect younger women.[58 59] Furthermore, global data depict older women sharing many of the same risk factors for HIV as younger women, including lack of HIV prevention knowledge, having multiple sex partners (if divorced or widowed) and less likely to practice safer sex due to being postmenopausal and not of reproductive age.[60] Unfortunately within South Africa, ageing women are not the target of HIV risk reduction programmes which focus on men and young women,61 and they are less likely to go for testing.[60]

Currently, South Africa and other low-income and middle-income countries (LMICs) largely provide government healthcare through vertical programmes of dedicated staff operating within separate physical spaces among facilities offering these services (ie, HIV, TB, NCDs). Large funders focus on specific diseases and are reluctant to fund costs for other conditions, which may increase the cost of service provision.[62] Furthermore, combining HIV with other platforms, such as NCDs, has also been perceived as a threat to gains made in HIV control

programmes.[16] Disadvantages of vertical models are service duplication, inefficiency and service fragmentation.[62]

The WHO promotes integration as a solution. Intended outcomes are improved efficiency and quality of health services, and increased access and utilisation of health services between geographical and socioeconomic groups, leading to greater equity.[62] Integrated care cascades require clinical space and skilled personnel, and it is necessary to leverage the existing infrastructure and build integrated care capacity of staff who have supported unilateral HIV programmes.[16] While integration of HIV with other programmes, such as reproductive health and TB, has occurred through the establishment of inclusive national policies, evidence of HIV-NCD integration in clinical practice is scarce.[63–65] Five studies within LMICs which integrated an additional health service component into an existing service (eg, adding family planning or HTS to routine services) indicated that adding on services probably increases service utilisation and outputs of healthcare delivery. However, there is no evidence that a fuller form of integration improves healthcare delivery or health status.[62]

The top cause of death and disability worldwide are chronic NCDs, which attribute to more than three in five deaths,[66] with LMICs, such as South Africa, being disproportionately impacted.[67] Successful ART programmes enable PLHIV to reach a near-normal life expectancy,[20] and HIV infection is now considered a chronic condition requiring long-term management, just like NCDs.[16] PLHIV are also at increased risk of NCDs,[21] and comorbidities of disease can be particularly devastating as they are compounded by the metabolic consequences of the roll out of ART medications.[68] Our study population exhibited high rates of HIV, overweight/obese BMI and elevated BP across all age groups. HIV-infected females had higher BP than HIV-uninfected females, and HIV-infected people aged 18–24 and 35–44 years were more overweight/obese than their HIV-uninfected counterparts. These precursors to NCDs increased the risk for HIV-NCDs comorbidities in these populations. Now, more than ever, healthcare must be integrated, and targeted interventions among these groups at HIV clinics could help reduce the risk of disease.

Limitations

Zazi only conducted STI symptoms screening and was unable to refer for asymptomatic STIs. One could assume the STI prevalence is higher in actuality. The clinic only screened for TB symptoms which is only the very beginning of the TB diagnostic algorithm and may not accurately describe the TB prevalence as other pathogens can cause TB symptoms. Without

any other means of confirming TB, it could be confirmed if the clients identified with TB symptoms actually had TB, needing to start treatment. The clinic did, however, have 34 clients who presented to Zazi with laboratory-confirmed TB (10.5%). Unfortunately, the clinic was not able to collect CD4 count for all identified HIV-infected individuals; only for those who had not already initiated treatment and were not referred by the PHRU TB Clinic. Additionally, viral loads were not available, and therefore there were no ART referrals based on this biomarker. Responses to specific clinical questions were left to the interpretation and disclosure of the client. For example, questions surrounding drug use did not specify a timeframe (ie, within the last 6 months).

This study has a convenience sample of participants self-selecting to attend a single HTS clinic in Soweto. There is potential for bias as these participants have not been randomly sampled from multiple facilities. Some of our sub-group sample sizes for comparison are small which therefore affects statistical precision.

Conclusion

This study has shown a high prevalence of HIV-NCD comorbidity among an urban, adult population in Johannesburg, South Africa, which can be generalisable to similar settings. There is a need for an HIV-NCD integrated approach when considering health screening and interventions. A more holistic, patient-centred approach would benefit HIV-infected patients specifically, as NCD comorbidity can cause worsened conditions. Integrating screening for NCDs into HTS may increase service uptake. Targeted integrated interventions for HIV-infected females and HIV-infected people aged 18–24 and 35–44 years could improve HIV public health outcomes. More studies on whether integrated healthcare screenings will improve the uptake of NCD treatment and improve health outcomes are required. There is also a critical need to revise the current national hypertension result category cut-offs in order to improve the prevention and treatment of this NCD precursor for both the general population and PLHIV.

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PAPER III

Hopkins KL, Hlongwane K, Otwombe K, Dietrich J, Cheyip M, Olivier J, van Rooyen H, Doherty T, Gray GE. *The Horrific Burden of Non-Communicable Diseases and HIV-Comorbidity amongst Adults: Screening Results from an Integrated HIV Testing Services Clinic for Adults in Soweto*. As of 15 February 2021, at CDC Headquarters in Atlanta obtaining official CDC Eclearance for submission to *JAMA*.

The Horrific Burden of Non-Communicable Diseases and HIIV-Comorbidity amongst Adults: Screening Results from an Integrated HIV Testing Services Clinic for Adults in Soweto

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Abstract

Background: The main cause of death/disability worldwide are chronic non-communicable diseases (NCDs), with low and middle-income countries disproportionately impacted. South Africa is also the epicentre of the HIV/AIDS epidemic, and HIV-infection and antiretroviral therapy (ART) use might be risk factors for NCDs. The public healthcare sector utilises a risk-factor gated-approach (e.g.; age, ART use) towards screening for NCDs. Sounder models of integrated services that effectively diagnose, treat, and control NCDs for both HIV-infected and uninfected persons are required. We investigated the burden of NCD, HIV, and comorbidity; as well as the levels of unknown disease and previously-known, uncontrolled disease within an HIV testing services (HTS) centre in South Africa.

Methods: This was a cross-sectional study of walk-in adults attending an integrated NCD-HTS centre in Soweto, South Africa from June 2018-March 2019. Screenings conducted were: body mass index (BMI) categorizations, blood pressure (BP) readings, rapid blood glucose (both random and glycated haemoglobin [HbA1c]) and total blood cholesterol (TC) testing, and HIV rapid testing. Surveys collected data on socio-demographics, health risk behaviour (alcohol and tobacco use), previous health screening history and treatment use for hypertension (HT), diabetes mellitus (DM), hypercholesterolemia, and HIV. Screening results were stratified by age group (18-24, 25-34, 35-44 and ≥45 years), sex, HIV status and ART use. Analysis included Fisher's exact, chi-squared, Kruskal Wallis, and Student's T-tests.

Results: Of 780 enrolled participants, most were black African (98.3%[n=767/780]) women (65.8%[n=513/780]), with a median age of 32.0 years (interquartile range [IQR]: 25.0-42.0). Of clients screened, 19.2% (n=149/775) were HIV-infected, 37.5% (n=289/770) were overweight/obese, 18.0% (n=139/772) had high BP, 10.8% (n=83/766) had high HbA1c (four clients had high random glucose), and 8.1% (n=62/768) had high TC. Women had significantly more overweight/obese BMI than men (46.8% [n=237/506] vs 19.7% [n=52/264]; p<0.0001); and 39.8% (n=127/319) of 18-34 year old women were overweight/obese. Males had significantly higher BP than women (23.9% [n=63/264] vs. 15.0% [n=76/508]; p=0.0023). Of 18-34 year olds, 7.2% (n=31/433) had high blood glucose; and there were over three times as many women aged 25-34 years with high TC as compared to men of the same age group (18.2% [n=20/110] vs 5.6% [n=4/71]; p=0.0151). The majority of HIV-infected clients were female (72.5%[n=108/149]). Overall, HIV-uninfected clients had significantly more overweight/obese BMI than HIV-infected clients (39.5% [n=244/618] vs 29.5% [n=44/149]; p=0.0243); but HIV-infected clients had significantly more high HbA1c than HIV-uninfected clients (16.1%

[n=24/149] vs 9.6% [n=59/614]; p=0.0223). HIV-infected individuals on ART had significantly higher TC than those not on ART (21.7% [n=10/46] vs. 4.9% [n=5/103]; p=0.0016). Of the HIV-infected participants, 48.3% (n=72/149) already knew their HIV-status, and of those, 63.9% (n=46/72) were on ART. Of all participants screened with elevated BP, high HbA1c and high TC, 72.4% (n=97/134), 96.1% (n=73/76), and 93.3% (n=56/60) were newly diagnosed for each condition, respectively. Of the clients who self-reported as being previously diagnosed, 83.8% (n=31/37) of hypertensive clients, two (n=2/3) clients with high HbA1c, and one (n=1/4) client with high TC self-reported they had already been initiated on treatment. All clients were found to have uncontrolled disease after screening.

Conclusion: There is a chronic NCD catastrophe plaguing South Africa, and amongst relatively young adults (18-34 years), especially women. Current South African national guidelines do not adequately allow for the most effective screening for and prevention of diabetes or hypercholesterolemia, or their pre-cursors amongst the general population or PLHIV. Rapid HbA1c and rapid TC screening should be integrated into standard of care practice for adults within the public health sector, regardless of BMI categorization, HIV status or ART use. There are severe needs for the integrative management of adherence to chronic medications, especially in the monitoring of ART patients due to the metabolic side effects of treatment for PLHIV.

Introduction

The main cause of death and disability worldwide are chronic non-communicable diseases (NCDs), such as cardiovascular disease (CVD) and diabetes mellitus (DM), attributing to more than three in five deaths.[1] With low and middle-income countries (LMICs), such as South Africa, being disproportionately impacted,[2] the World Health Organization (WHO) estimates that 90% of people who die from NCDs before the age of 60 are from LMICs.[1] South Africa is also the epicentre of the HIV/AIDS epidemic, containing the world's highest prevalence of HIV-1.[3] There are an estimated 36.7 million people living with HIV (PLHIV), globally,[4] of which over 20% (7.9 million) reside in South Africa as of 2017.[3, 5-7]

There is evidence that HIV-infection itself, and antiretroviral therapy (ART) use might be risk factors for NCDs. The virus is known to cause a persistent inflammatory state and immune dysfunction mechanisms, which are linked to metabolic syndrome diseases such as DM or dyslipidaemia.[8, 9] HIV-infected individuals stable on ART are at higher-risk of NCD

comorbidities due to metabolic consequences, such as body fat redistribution and cardio-metabolic abnormalities associated with HIV treatment.[8] With the scale-up of ART, HIV is becoming a chronic disease with PLHIV reaching nearly the same life expectancy as healthy individuals.[10] Historically, NCDs are thought of as 'aging diseases'.[11] Not only is HIV-infection seemingly associated with an accelerated 'aging' process, but PLHIV, now living longer while on treatment, are becoming increasingly at-risk for non-HIV-related chronic conditions of aging similar to the HIV-uninfected population.[12]

Studies have reported the two main NCDs affecting PLHIV residing within LMICs are CVD and DM.[13] CVD, alone, has multiple pre-cursors which should be monitored within individuals to prevent the onset of disease. Chief risk factors for CVD are hypertension and elevated blood cholesterol.[13] Obesity is a risk factor for both CVD and DM,[12, 14] and LMICs are exhibiting greater increases in both childhood and adult overweight and obesity rates relative to high-income countries.[15-17] A systematic review and meta-analysis of 57 studies in both high income and LMICs reported the prevalence of HIV comorbidity with CVD risk factors (CVDRF). The prevalence of hypertension was found to be 21.2%, hypercholesterolemia 22.2%, obesity 7.8%, and metabolic syndrome 16-31%, depending on the criteria used.[9] In Swaziland, a facility-based study (N=1826) screening ART patients at least 40 years of age for CVDRF found 39% to have at least one CVDRF, while 8% exhibited at least two CVDRFs.[18]

While screening for hypertension and checking a patient's weight is part of routine standard of care within the public sector, both within primary health care clinics and HIV testing and care clinics, there is currently a risk-factor based gated-approach towards screening for other NCDs.[19, 20] Only overweight individuals – of any age - are screened for DM if also exhibiting at least one other risk factor for hyperglycaemia or metabolic decompensation.[21] For adults of normal weight, screening for DM only starts at 45 years of age.[21] The criteria for cholesterol screening and initiation of lipid-lowering therapy centres largely around being of older age and having DM. Due to the contraindications of ART, screening for blood glucose and lipids amongst PLHIV is recommended prior to and three months post-ART initiation, or three months after initiating HAART and then annually thereafter. PLHIV on treatment who are found to be pre-diabetic should be monitored every three to six months.[22] The criteria for blood glucose and lipid-lowering treatment initiation for PLHIV is the same as for HIV-uninfected patients.[23]

In recognizing the anticipated impact of NCDs on both the general population and amongst PLHIV, it becomes critically important to pursue sounder models of integrated services that effectively prevent, diagnose, treat, and control NCDs for both HIV-infected and uninfected persons. The most logical and economical approach is to capitalize on the service platforms already established for HIV, which include facility-based HIV Testing Services (HTS).[24]

An HTS Centre in Soweto, South Africa, expanded its standard of care HTS services for walk-in adult clients to also include NCD risk factor screenings: body mass index (BMI) calculations; and rapid total blood cholesterol and blood glucose (both random and average HbA1c) screenings. The primary aim of this study was to investigate the prevalence of both previously diagnosed and undiagnosed HIV and NCD risk factors (elevated BP, and high blood glucose [random and average HbA1c] and total cholesterol [TC]) and HIV-NCD risk factor comorbidity (including overweight/obese BMI) among adults attending an integrated NCD-HTS. A secondary aim was to determine the rates of both controlled and uncontrolled disease among those clients who were previously diagnosed and had ever been initiated on treatment.

To our knowledge, this study investigates the first integrated screening service for HIV, obesity, elevated blood pressure, and both random and average blood glucose and cholesterol using rapid testing technology within a facility-based HTS setting in a LMIC known to have high rates of HIV. Findings from this study could potentially generate the crucial attention required towards improving HIV and NCD screening, prevention and management systems to curb the epidemics of related morbidity and mortality seen globally.

Methods

Study Design and Setting

This is a cross-sectional study describing the health screening results of walk-in adults attending an integrated NCD-HTS centre, at the Perinatal HIV Research Unit (PHRU), a leading research centre within the Wits Health Consortium – affiliated with the University of the Witwatersrand Faculty of Clinical Medicine, and situated at the Chris Hani Baragwanath Academic (Bara) Hospital in Soweto, South Africa. The HTS centre has previously reported a high client prevalence of HIV (20.9%).[25]

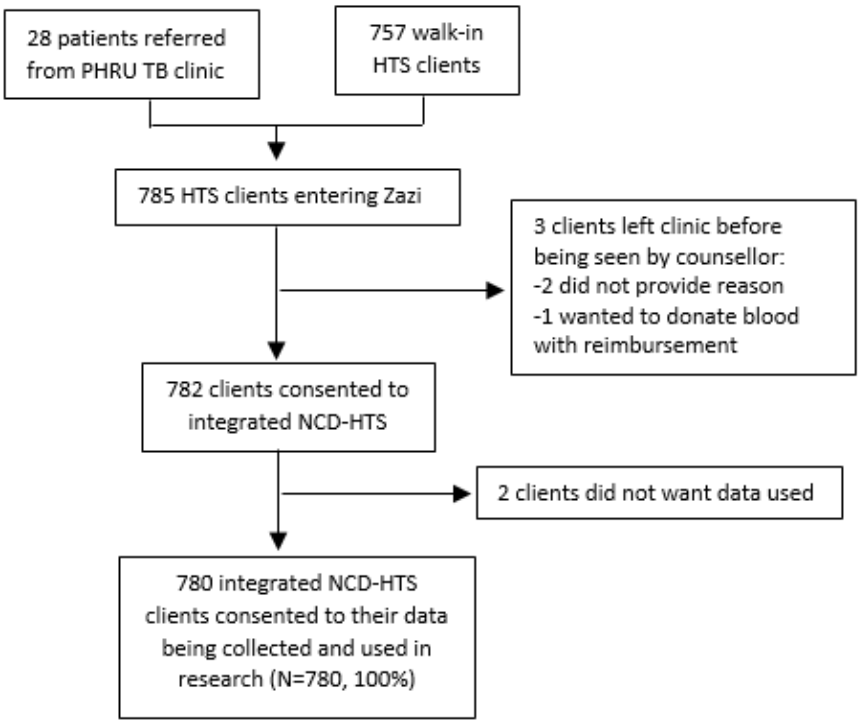
Sampling

The study sample comprised all eligible walk-in clients, who consented for both the health screening programme and for their data to be captured and used in research between 18 June 2018 and 28 March 2019. If consent was not given, the client was still able to undergo health screening without data capture.

Demographics and health profile data; including health risk behaviour (alcohol and tobacco use), previous health screening history and treatment use, health screening results, and ART status for HIV-infected clients (i.e.; currently taking ART or not), were collected from eligible HTS clients.

Figure 1 depicts the participant flow for this study.

Figure 1. Integrated NCD-HTS client flow from screening through treatment initiation in Soweto, South Africa, 18 June 2018 – 28 March 2019



PHRU, Perinatal HIV Research Unit; TB, Tuberculosis; HTS, HIV Testing Services; NCD, Non-communicable Diseases.

Inclusion and Exclusion Criteria

To be eligible for participation in the study, participants had to be at least 18 years old; fluent in either English, IsiZulu and/or Sesotho; and provide either written or verbal informed consent (with an impartial witness) for health screening procedures. A client was excluded from the

programme and redirected to the Bara casualty ward if he/she presented to the clinic and there was immediate cause for concern regarding their health.

Data Collection and Management

Client demographics were either self-collected by literate clients in the reception area or collected with help of study staff for clients unable to read or write. Clinical data, including information on alcohol and tobacco use, was collected by the study staff. All data were collected through questionnaires and health screenings and recorded directly onto paper forms comprising the PHRU HTS client file. Source documents included the client file and the CD4 count pathology reports, which were printed and filed within the client file. The pathology reports were accessed and printed by the enrolled nurse from the electronic National Health Laboratory Services (NHLS) InterSystems' TrakCare Laboratory Information System (LIS).[26]

Study Measures

Demographic and Risk Behaviour Information

Data were collected on sex, age, race, nationality, ethnic group, marital status, highest level of education, source of income, and details regarding home residence – type of housing, source of water and fuel for cooking and lighting, type of toilet facility, as well as possession of household and ownership items. Clients were asked about their alcohol and tobacco use, with the questions taken from the validated 2003 South African Demographic and Health Survey (SADHS).[27]

Health Screening Results

Client health screening results included BMI, BP readings, HIV results and CD4 count. These parameters have been previously described.[25] The integrated NCD-HTS also contained additional screening results for the following:

Average blood glucose (HbA1c) and *random blood glucose* were both classified as high, normal or low. HbA1c and average glucose were considered high if ≥ 6.5 mmol/L and ≥ 11 mmol/L, respectively; and low if either machine read 'low'. All other readings were classified as normal.

Total cholesterol (TC) was also classified as high (≥5 mmol/L) or low, if the point-of-care diagnostic machine read 'low'. Otherwise, TC was classified as normal.

For HIV-infected clients, all self-reported ART use ('on ART' or 'not on ART') was documented.

Health Screening History

Health screening history questions included: have you ever been diagnosed with high blood pressure/hypertension, high blood sugar/diabetes, or high cholesterol; and if yes, have you ever been on treatment for any of those conditions. From this data and the health screening results, the following categories of HTS clients were defined:

Newly diagnosed: HTS clients who did not self-report having a previous condition, but were screened to have abnormal results for that condition at Zazi.

Previously diagnosed: HTS clients who self-reported as having a previous condition and were screened to have abnormal results for that condition at Zazi.

Controlled: HTS clients who self-reported they were previously diagnosed with and had ever taken treatment for a condition and were screened to have normal results for that condition at Zazi.

Uncontrolled: HTS clients who self-reported they were previously diagnosed with and had ever taken treatment for a condition and were screened to have abnormal results for that condition at Zazi.

Ethical Considerations

The health programme was approved by the University of Witwatersrand, Human Research Ethics Committee (Wits HREC). This study was also reviewed in accordance with the Centers for Disease Control and Prevention human research protection procedures and was determined to be research, but investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes.

Data Analysis

Frequencies and percentages were determined for categorical variables that were stratified by age group (18-24, 25-34, 35-44 and ≥45 years), sex, HIV status, and ART use.

To test statistical significance for categorical measures stratified by HIV status and sex, Chi-square analysis or Fisher's exact test was used as appropriate. Descriptive statistics including means (standard deviations) and medians (interquartile ranges [IQR]) were determined for

continuous measures that were stratified by sex and HIV status. These were compared parametrically and non-parametrically using both the two-group student t and Kruskal-Wallis tests.

A wealth quintile was developed using the socio-economic measures and the Principal Component Analysis (PCA) variable reduction, as previously described.[25, 28-30]. Five wealth quintiles with 20 percentile intervals were determined.

All statistical analysis was conducted in SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC) using SAS/STAT procedures PROC FREQ, PROC NPAR1WAY and PROC FACTOR.

Results

Demographics of Participants by Age Group

We enrolled 780 participants in the study, of which the largest proportions of clients were women (65.8%, n=513/780), black African (98.3%, n=767/780) and of single relationship status (70.7%, n=551/779) with median age of 32.0 years (IQR: 25.0-42.0). Just over half had completed either high school or had some tertiary education (64.0%, n=499/780). Only 33.4% were formally employed (n=259/776), of which the vast majority were in the older age groups. Of those not in formal employment, sources of income ranged from informal trading, social grants and pensions. Over sixty percent of participants reported drinking alcohol (65.1%, n=507/779) with about one in ten drinking excessively (10.3%, n=52/507); and one-quarter had ever smoked cigarettes (25.5%, n=191/748).(Table 1)

Table 1. Client Characteristics by Age Group, 18 June 2018 – 28 March 2019

		Age in years			
Variable	**Overall**	**18-24**	**25-34**	**35-44**	**≥45**
Median age (IQR)	32.0 (25.0-42)	22.0 (20.0-23)	29.0 (26.0-32)	38.0 (37.0-41)	52.0 (48.0-58)
Gender					
Female (%)	513/780 (65.8)	127/153 (83.0)	198/287 (69.0)	111/185 (60.0)	77/155 (49.7)
Male (%)	267/780 (34.2)	26/153 (17.0)	89/287 (31.0)	74/185 (40.0)	78/155 (50.3)
Race					
Black African (%)	767/780 (98.3)	150/153 (98.0)	282/287 (98.3)	182/185 (98.4)	153/155 (98.7)
Coloured/White (%)	13/780 (1.7)	3/153 (2.0)	5/287 (1.7)	3/185 (1.6)	2/155 (1.3)

Variable	Overall	Age in years 18-24	25-34	35-44	≥45
Nationality					
Other (%)	21/780 (2.7)	3/153 (2.0)	8/287 (2.8)	4/185 (2.2)	6/155 (3.9)
South African (%)	759/780 (97.3)	150/153 (98.0)	279/287 (97.2)	181/185 (97.8)	149/155 (96.1)
Ethnic group					
Other (%)	98/776 (12.6)	17/153 (11.1)	35/285 (12.3)	33/185 (17.8)	13/153 (8.5)
Sotho (%)	127/776 (16.4)	29/153 (19.0)	34/285 (11.9)	33/185 (17.8)	31/153 (20.3)
Tsonga (%)	74/776 (9.5)	12/153 (7.8)	22/285 (7.7)	28/185 (15.1)	12/153 (7.8)
Tswana (%)	60/776 (7.7)	11/153 (7.1)	20/285 (7.0)	14/185 (7.6)	15/153 (9.8)
Xhosa (%)	79/776 (10.2)	16/153 (10.5)	34/285 (11.9)	17/185 (9.2)	12/153 (7.8)
Zulu (%)	338/776 (43.6)	68/153 (44.4)	140/285 (49.1)	60/185 (32.4)	70/153 (45.8)
Marital status					
Divorced\widowed (%)	35/779 (4.5)	0/153 (0.00)	1/287 (0.4)	10/185 (5.4)	24/154 (15.6)
Living Together\married (%)	193/779 (24.9)	12/153 (7.8)	54/287 (18.8)	60/185 (32.4)	67/154 (43.5)
Single (%)	551/779 (70.7)	141/153 (92.2)	232/287 (80.8)	115/185 (62.2)	63/154 (40.9)
Highest education					
Up To High School (%)	281/780 (36.0)	75/153 (49.0)	108/287 (37.6)	59/185 (31.9)	39/155 (25.2)
Matriculated (%)	163/780 (20.9)	37/153 (24.2)	71/287 (24.7)	39/185 (21.1)	16/155 (10.3)
Tertiary (%)	336/780 (43.1)	41/153 (26.8)	108/287 (37.6)	87/185 (47.0)	100/155 (64.5)
Source of money to live on?					
Employed (%)	259/776 (33.4)	20/153 (13.1)	105/286 (36.7)	80/183 (43.7)	54/154 (35.1)
Self-employed (%)	143/776 (18.4)	23/153 (15.0)	48/286 (16.8)	41/183 (22.4)	31/154 (20.1)
Social/Disability grant (%)	110/776 (14.2)	22/153 (14.4)	50/286 (17.5)	25/183 (13.7)	13/154 (8.4)
Parents (%)	153/776 (19.7)	80/153 (52.3)	52/286 (18.2)	15/183 (8.2)	6/154 (3.9)
Pension (%)	23/776 (3.0)	1/153 (0.7)	2/286 (0.7)	2/183 (1.1)	18/154 (11.7)
Unemployed (%)	88/776 (11.3)	7/153 (4.)	29/286 (10.1)	20/183 (10.9)	32/154 (20.8)
Wealth quintile					
Quintile 1 (%)	208/780 (26.7)	49/153 (32.0)	76/287 (26.5)	48/185 (24.0)	35/155 (22.6)
Quintile 2 (%)	177/780 (22.7)	33/153 (21.6)	63/287 (22.0)	37/185 (20.0)	44/155 (28.4)
Quintile 3 (%)	220/780 (28.2)	42/153 (27.5)	75/287 (26.1)	56/185 (30.3)	47/155 (30.3)
Quintile 4 (%)	152/780 (19.5)	24/153 (15.7)	60/287 (20.9)	41/185 (22.2)	27/155 (17.4)
Quintile 5 (%)	23/780 (3.0)	5/153 (3.3)	13/287 (4.5)	3/185 (1.6)	2/155 (1.3)
Do you drink alcohol?					
No (%)	272/779 (34.9)	39/153 (25.5)	68/286 (23.8)	77/185 (41.6)	88/155 (56.8)
Yes (%)	507/779 (65.1)	114/153 (74.5)	218/286 (76.2)	108/185 (58.4)	67/155 (43.2)

Variable	Overall	Age in years 18-24	25-34	35-44	≥45
How do you use alcohol?					
Socially	451/507 (89.0)	106/114 (93.0)	188/218 (86.2)	97/108 (89.8)	60/67 (89.5)
Excessively	52/507 (10.3)	7/114 (6.1)	28/218 (12.8)	11/108 (10.2)	6/67 (9.0)
Never	4/507 (0.7)	1/114 (0.9)	2/218 (0.9)	0/108 (0.00)	1/67 (1.5)
Have you ever smoked cigarettes?					
No (%)	557/748 (74.5)	121/152 (79.6)	184/276 (66.7)	137/178 (77.0)	115/142 (81.0)
Yes (%)	191/748 (25.5)	31/152 (20.4)	92/276 (33.3)	41/178 (23.0)	27/142 (19.0)
Do you still smoke cigarettes now?					
No (%)	3/191 (1.6)	1/31 (3.2)	2/92 (2.2)	0/41 (0.0)	0/27 (0.0)
Yes (%)	188/191 (98.4)	30/31 (96.8)	90/92 (97.8)	41/41 (100.0)	27/27 (100.0)

IQR, Interquartile range

Screening Results of Participants by Age Group and Sex

HIV and NCD risk factor screening results may be found within Table 2 and Supplementary Table 1.

Table 2. Client Screening Results by Sex for each Age Group, 18 June 2018 – 28 March 2019

		18-24			25-34			35-44			≥45		
Variable	**Overall**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**	**Female**	**Male**	**P-Value**
HIV Results													
Positive (%)	149/775 (19.2)	6/127 (4.7)	4/26 (15.4)	**0.0451**	43/197 (21.8)	10/88 (11.4)	**0.0359**	36/110 (32.7)	14/72 (19.4)	**0.0496**	23/77 (29.9)	13/78 (16.7)	0.0516
Negative (%)	626/775 (80.8)	121/127 (95.3)	22/26 (84.6)		154/197 (78.2)	78/88 (88.6)		74/110 (67.3)	58/72 (80.6)		54/77 (70.1)	65/78 (83.3)	
Are you currently taking or have ever taken antiretroviral?*													
No (%)	26/72 (36.1)	-	1/1 (100.0)		7/14 (50.0)	2/3 (66.7)	0.9999	6/17 (35.3)	3/6 (50.0)	0.6430	5/20 (25.0)	2/11 (18.2)	0.9999
Yes (%)	46/72 (63.9)	-	-		7/14 (50.0)	1/3 (33.3)		11/17 (64.7)	3/6 (50.0)		15/20 (75.0)	9/11 (81.8)	
CD4 Count (Cells/mm^3)													
n, Median (IQR)	86, 341 (246-500)	5, 420 (313-463)	3, 279 (116-524)	0.8815	30, 330 (246-500)	7, 338 (156-412)	0.7860	24, 363 (240-569)	9, 315 (182-347)	0.2663	6, 513 (408-540)	2, 393 (276-510)	0.3173
Body Mass Index (BMI)													
Underweight (%)	133/770 (17.3)	22/127 (17.3)	10/26 (38.5)	**0.0158**	27/192 (14.1)	31/87 (35.6)	**<.0001**	6/111 (5.4)	19/73 (26.0)	**0.0001**	4/76 (5.3)	14/78 (18.0)	**0.0143**
Normal (%)	348/770 (45.2)	61/127 (48.0)	16/26 (61.5)	**0.2095**	82/192 (42.7)	45/87 (51.7)	0.1613	45/111 (40.5)	41/73 (56.2)	**0.0377**	22/76 (29.0)	36/78 (46.2)	**0.0276**
Overweight/Obese (%)	289/770 (37.5)	44/127 (34.7)	0/26 (0.0)	-	83/192 (43.2)	11/87 (12.6)	**<.0001**	60/111 (54.1)	13/73 (17.8)	**<.0001**	50/76 (65.7)	28/78 (35.9)	**0.0002**
n, Median (IQR)	770, 23.2 (19.4-27.3)	127, 22.7 (19.4-26.5)	26,18.8 (17.6-20.4)	**<.0001**	192, 24.0 (21.2-28.7)	87,19.4 (17.0-22.5)	**<.0001**	111,25.6 (22.1-31.5)	73,20.4 (18.3-24.1)	**<.0001**	76,27.5 (23.0-31.5)	78,22.0 (19.4-27)	**<.0001**
Blood Pressure													
High (%)	139/772 (18.0)	4/127 (3.2)	2/26 (7.7)	0.4963	22/195 (11.3)	11/88 (12.5)	0.8049	26/110 (23.6)	20/72 (27.8)	0.5296	24/76 (31.6)	30/78 (38.5)	0.4207
Low (%)	7/772 (0.9)	3/127 (2.4)	1/26 (3.9)		1/195 (0.5)	1/88 (1.1)		-	-		1/76 (1.3)	0/78 (0.0)	
Normal (%)	626/772 (81.1)	120/127 (94.5)	23/26 (88.5)		172/195 (87.2)	76/88 (86.4)		84/110 (76.4)	52/72 (72.2)		51/76 (67.1)	48/78 (61.5)	

Variable	Overall	18-24			25-34			35-44			≥45		
		Female	Male	P-Value	Female	Male	P-Value	Female	Male	P-Value	Female	Male	P-Value
Blood glucose													
Average (HbA1c)													
High (%)	83/766 (10.8)	11/127 (8.7)	2/26 (7.7)	0.8717	16/193 (8.3)	2/87 (2.3)	0.0585	15/109 (13.8)	6/71 (8.5)	0.2780	14/76 (18.4)	17/77 (22.1)	0.5737
Normal (%)	683/766 (89.2)	116/127 (91.3)	24/26 (92.3)		177/193 (91.7)	85/87 (97.7)		94/109 (86.2)	65/71 (91.5)		62/76 (81.6)	60/77 (77.9)	
Random glucose													
High (%)	4/769 (0.6)	1/127 (0.79)	0/26 (0.00)	-	1/193 (0.52)	0/88 (0.00)	-	2/110 (1.82)	0/71 (0.00)	-	0/76 (0.0)	0/78 (0.0)	-
Normal (%)	765/769 (99.4)	126/127 (99.21)	26/26 (100.0)		192/193 (99.48)	88/88 (100.0)		108/110 (98.18)	71/71 (100.0)		76/76 (100.0)	78/78 (100.0)	
Total Cholesterol (TC)													
High (%)	62/768 (8.1)	5/127 (3.9)	0/26 (0.0)	0.5739	6/192 (3.1)	2/88 (2.3)	0.6911	20/110 (18.2)	4/71 (5.6)	**0.0151**	14/76 (18.4)	11/78 (14.1)	0.7600
Low (%)	88/768 (11.5)	21/127 (16.5)	4/26 (15.4)	-	20/192 (10.4)	19/88 (21.6)	**0.0122**	6/110 (5.5)	5/71 (7.0)	0.6625	6/76 (7.9)	7/78 (9.0)	-
Normal (%)	618/768 (80.5)	101/127 (79.5)	22/26 (84.6)	-	166/192 (86.5)	67/88 (76.1)	**0.0319**	84/110 (76.4)	62/71 (87.3)	0.0683	56/76 (73.7)	60/78 (76.9)	-

***ART use reported only for HIV-infected clients who were previously diagnosed.**
All 4 participants with high random glucose also had high HbA1c.
Overall, men have significantly more underweight BMI as compared to women (28.0% [n=74/264] vs 11.7% [n=59/506]; p<0.0001), and women have significantly more overweight/obese BMI than men (46.8% [n=237/506] vs 19.7% [n=52/264]; p<0.0001).
Overall, women have significantly more low BP than men (1.0% [n=5/508] vs 0.8% [n=2/264]; p=0.0041) and significantly more normal BP than men (84.1% [n=427/508] vs 75.4% [n=199/264]; p=0.0027).

Supplementary Table 1. Screening results by age group and sex

Variable	Overall	18-24	25-34	35-44	≥45	Female	Male	P-Value
HIV Results								
Positive (%)	149/775 (19.2)	10/153 (6.5)	53/285 (18.6)	50/182 (27.5)	36/155 (23.2)	108/511 (21.1)	41/264 (15.5)	0.0606
Negative (%)	626/775 (80.8)	143/153 (93.5)	232/285 (81.4)	132/182 (72.5)	119/155 (76.8)	403/511 (78.9)	223/264 (84.5)	
CD4 Count (Cells/mm3								
Median (IQR)	86, 341 (246-500)	367 (198-492)	332 (232-412)	339 (231-490)	502 (363-536)	65, 347 (262-507)	21, 315 (182-412)	0.1796
Body Mass Index (BMI)								
Underweight (%)	133/770 (17.3)	32/153 (20.9)	58/279 (20.8)	25/184 (13.6)	18/154 (11.7)	59/506 (11.7)	74/264 (28.0)	**<.0001**
Normal (%)	348/770 (45.2)	77/153 (50.3)	127/279 (45.5)	86/184 (46.7)	58/154 (37.7)	210/506 (41.5)	138/264 (52.3)	**0.0044**
Overweight/Obese (%)	289/770 (37.5)	44/153 (28.8)	94/279 (33.7)	73/184 (39.7)	78/154 (50.6)	237/506 (46.8)	52/264 (19.7)	**<.0001**
Median (IQR)	770,23.2 (19.4-27.3)	21.9 (18.8-25.6)	23.1 (19.0-26.6)	23.3 (20.0-29.3)	25.2 (20.7-29.4)	506,24.3 (21.1-29.4)	264,20.4 (18.1-24.2)	**<.0001**
Blood Pressure								
Low (%)	7/772 (0.9)	4/153 (2.6)	2/283 (0.7)	0/182 (0.0)	1/154 (0.6)	5/508 (1.0)	2/264 (0.8)	**0.7526**
Normal (%)	626/772 (81.1)	143/153 (93.5)	248/283 (87.6)	136/182 (74.7)	99/154 (64.3)	427/508 (84.1)	199/264 (75.4)	**0.0035**
High (%)	139/772 (18.0)	6/153 (3.9)	33/283 (11.7)	46/182 (25.3)	54/154 (35.1)	76/508 (15.0)	63/264 (23.9)	0.0023
Blood glucose								
Average (HbAa1c)								
Normal (%)	683/766 (89.2)	140/153 (91.5)	262/280 (93.6)	159/180 (88.3)	122/153 (79.7)	449/505 (88.9)	234/261 (89.7)	0.7534
High (%)	83/766 (10.8)	13/153 (8.5)	18/280 (6.4)	21/180 (11.7)	31/153 (20.3)	56/505 (11.1)	27/261 (10.3)	
Random glucose								
Normal (%)	765/769 (99.5)	152/153 (99.3)	280/281 (99.6)	179/181 (98.9)	154/154 (100.0)	502/506 (99.2)	263/263 (100.0)	-
High (%)	4/769 (0.5)	1/153 (0.7)	1/281 (0.4)	2/181 (1.1)	0/154 (0.0)	4/506 (0.8)	0/263 (0.0)	
Total Cholesterol (TC)								
Low (%)	88/768 (11.5)	25/153 (16.3)	39/280 (13.9)	11/181 (6.1)	13/154 (8.4)	53/505 (10.5)	35/263 (13.3)	0.2455
Normal (%)	618/768 (80.5)	123/153 (80.4)	233/280 (83.2)	146/181 (80.7)	116/154 (75.3)	407/505 (80.6)	211/263 (80.2)	0.9034
High (%)	62/768 (8.1)	5/153 (3.3)	8/280 (2.9)	24/181 (13.3)	25/154 (16.2)	45/505 (8.9)	17/263 (6.5)	0.2375

HIV Results and ART Use

Of the 775 participants who opted to test for HIV, 19.2% (n=149/775) were HIV-infected; and of those, most were female (72.5%, n=108/149) (Supplementary Table 1). Of those HIV-infected participants who were previously diagnosed (48.3%, n=72/149), 63.9% (n=46) were on ART. Overall, 86 HIV-infected participants had a median CD4 count of 341 cells/mm3 (IQR: 246-500). Of those with CD4 count below 200 cells/mm3, 60% (n=9/15) were females; and 13.3% (n=2/15) were 18-24 years, 40.0% (n=6/15) were 25-34 years, and 46.7% (n=7/15) were 35-44 years.

HIV prevalence peaked amongst 35-44 year olds (27.5%, n=50/182) for both sexes (32.7%, n=36/110, among women; 19.4%, n=14/72, among men). Amongst 18-24 year olds, 60.0% (n=6/10) HIV-infections were among women. Only one of the HIV-infected 18-24 year olds were previously diagnosed, and he was not on ART; and 18-24 year old men had the lowest median CD4 count (279, IQR: 116-524) of all participants.

NCD Risk Factor Screening Results

Regarding BMI, 37.5% (n=289/770) of participants were overweight/obese with BMI increasing by age group for both sexes. Overall and by age group, women have significantly more overweight/obese BMI than men - just under half of all the women were overweight/obese compared to only 20% of men (46.8% [n=237/506] vs 19.7% [n=52/264]; p<0.0001). More than one-third of women in the younger age groups were overweight/obese – 34.7% (n=44/127) of 18-24 year olds and 43.2% (n=83/192) of 25-34 year olds. Inversely, men were significantly more underweight in comparison to women (29.2% [n=77/264] vs 11.7% [n=59/506]; p<0.0001), and this trend remained for each age group. Younger males (18-24 and 25-34 year olds) had the highest proportion of being underweight (38.5%, n=10/26) and (35.6%, n=31/87) respectively.

Overall, 18.0% (n=139/772) of participants, had high blood pressure. Relative to females, males were significantly more likely to be diagnosed with high blood pressure (23.9% [n=63/264] vs. 15.0% [n=76/508]; p=0.0023). The prevalence of high BP increased by age group for both sexes, rising from 3.2% (n=4/127) to 31.6% (n=24/76) among women and from 7.7% (n=2/26) to 38.5% (n=30/78) among men.

About one in ten adults (10.8%, n=83/766) had high HbA1c, with a similar prevalence amongst the sexes. Of the 83 participants with high HbA1c, only four also had high random blood

glucose. Of the younger age groups, 7.2% (n=31/433) had high blood glucose (8.5%, n=13/153, of 18-24 year olds; and 6.4%, n=18/280, of 25-34 year olds).

Overall, 62 (8.1%, n=62/768) participants screened with high TC, of which 54.8% (n=34/62) were women aged 35 years and older compared to 24.2% (n=15/62) of their male counterparts. There were over three times as many women aged 25-34 years with high TC as compared to men of the same age group (18.2% [n=20/110] vs 5.6% [n=4/71]; p=0.0151).

The oldest age group (≥45 years) had the highest proportion of overweight/obesity (50.7%, n=78/154), high blood pressure (35.1%, n=54/154), high blood glucose (20.3%, n=31/153) and high TC (16.2%, n=25/154).

NCD Risk Factor – HIV Comorbidity

Prevalence of comorbidity by sex may be found within Table 3 and Supplementary Table 2.

Table 3. Screening Results by Sex for HIV-Infected Clients, 18 June 2018-28 March 2019

Variable	Overall	Female	Male	P-Value
Are you currently taking or have ever taken antiretroviral?*				
No (%)	26/72 (36.1)	18/51 (35.3)	8/21 (38.1)	0.9999
Yes (%)	46/72 (63.9)	33/51 (64.7)	13/21 (61.9)	
CD4 Count (Cells/mm3				
n, Median (IQR)	86, 341 (246-500)	65, 347 (262-507)	21, 315 (182-412)	0.1796
Body Mass Index (BMI)				
Underweight (%)	32/149 (21.5)	14/108 (13.0)	18/41 (43.9)	**<.0001**
Normal (%)	73/149 (49.0)	54/108 (50.0)	19/41 (46.3)	0.6899
Overweight/Obese (%)	44/149 (29.5)	40/108 (37.0)	4/41 (9.8)	**0.0011**
n, Median (IQR)	149, 21.6 (18.8-27)	108, 23.0 (19.9-29.8)	41, 19.1 (17.2-21.3)	**<.0001**
Blood Pressure				
Low (%)	2/148 (1.4)	1/107 (0.9)	1/41 (2.4)	0.5031
Normal (%)	121/148 (81.8)	89/107 (83.2)	32/41 (78.1)	
High (%)	25/148 (16.9)	17/107 (15.9)	8/41 (19.5)	
Blood glucose				
Average (HbA1c)				
Normal (%)	125/149 (83.9)	89/108 (82.4)	36/41 (87.8)	0.6181
High (%)	24/149 (16.1)	19/108 (17.6)	5/41 (12.2)	
Random glucose				
Normal (%)	147/149 (98.6)	106/108 (98.1)	41/41 (100.0)	-
High (%)	2/149 (1.34)	2/108 (1.9)	0/41 (0.0)	
Total Cholesterol (TC)				
Low (%)	19/149 (12.8)	10/108 (9.3)	9/41 (22.0)	**0.0380**
Normal (%)	115/149 (77.2)	85/108 (78.7)	30/41 (73.1)	0.4723
High (%)	15/149 (10.0)	13/108 (12.0)	2/41 (4.9)	0.1946

*** ART use reported only for HIV-infected clients who were previously diagnosed**
Both participants with high random glucose also had high HbA1c.
Overall, HIV-uninfected clients had significantly more overweight/obese BMI than HIV-infected clients (39.5% [n=244/618] vs 29.5% [n=44/149]; p=0.0243), HIV-infected clients had significantly more high HbA1c than HIV-uninfected clients (16.1% [n=24/149] vs 9.6% [n=59/614]; p=0.0223).

Supplementary Table 2. Screening Results by HIV Status

Variable	Overall	Positive	Negative	P-Value
Body Mass Index (BMI)				
Underweight (%)	133/767 (17.3)	32/149 (21.5)	101/618 (16.3)	0.1374
Normal (%)	346/767 (45.1)	73/149 (49.0)	273/618 (44.2)	0.2887
Overweight/Obese (%)	288/767 (37.5)	44/149 (29.5)	244/618 (39.5)	**0.0243**
Median number of BMI(IQR)	770,23.2 (19.4-27.3)	149,21.6 (18.8-27)	618,23.5 (19.8-27.3)	**0.0314**
Blood Pressure				
Low (%)	7/769 (0.9)	2/148 (1.4)	5/621 (0.8)	0.5295
Normal (%)	623/769 (81.0)	121/148 (81.8)	502/621 (80.8)	0.7977
High (%)	139/769 (18.1)	25/148 (16.9)	114/621 (18.4)	0.6771
Blood glucose Average (HbAa1c)				
Normal (%)	680/763 (89.1)	125/149 (83.9)	555/614 (90.4)	**0.0223**
High (%)	83/763 (10.9)	24/149 (16.1)	59/614 (9.6)	
Random glucose				
Normal (%)	762/768 (99.5)	147/149 (98.7)	615/617 (99.7)	0.1217
High (%)	4/768 (0.5)	2/149 (1.3)	2/617 (0.3)	
Total Cholesterol (TC)				
Low (%)	88/765 (11.5)	19/149 (12.8)	69/616 (11.2)	0.5946
Normal (%)	616/765 (80.5)	115/149 (77.2)	501/616 (81.3)	0.2510
High (%)	61/765 (8.0)	15/149 (10.1)	46/616 (7.5)	0.2932

Note: Total frequencies for each screening do not necessarily equal the total sample size, as participants were able to opt out of any screening.

Overall, HIV-uninfected clients had significantly more overweight/obese BMI than HIV-infected clients (39.5% [n=244/618] vs 29.5% [n=44/149]; p=0.0243), with a significantly higher median BMI (23.5 [IQR: 19.8-27.3] vs. 21.6 [IQR: 18.8-27]; p=0.0314). Both the HIV-uninfected and infected groups with overweight/obese BMI were comprised mostly of women (80.3% [n=196/244] vs 90.9% [n=40/44]). About one-third of both the HIV-uninfected and HIV-infected groups with high BMI were aged 25-34 years (32.8% [n=80/244] vs 31.8% [n=14/44], respectively). HIV-infected women had significantly more overweight/obese BMI than HIV-infected men (37.0% [n=40/108] vs 9.8% [n=4/41]; p=0.0011), and this was inversely true for underweight BMI (43.9% [n=18/41] vs 13.0% [n=14/108]; p<0.0001).

Of the 139 participants who screened with high BP, 18.0% (n=25) were PLHIV. There were no significant differences in prevalence of high BP by HIV status or by sex among those with HIV.

HIV-infected clients had significantly more high HbA1c than HIV-uninfected clients (16.1% [n=24/149] vs 9.6% [n=59/614]; p=0.0223). The largest proportions of the HIV-infected clients were female (79.2%, n=19/24), aged 35-44 years (41.7% [n=10/24]), and none of them were on medication for high blood glucose. Of the 59 HIV-uninfected clients, the majority were female (62.7%, n=37/59), aged ≥45 years (42.4%, n=25/59), and two of them self-reported they had been on treatment.

There was not a significant difference in prevalence of high TC by HIV status; however, HIV-infected individuals on ART had significantly higher TC than HIV-infected not on ART (21.7% [n=10/46] vs. 4.9% [n=5/103]; p=0.0016).

Clinical Characteristics, Linkage to Care and Treatment Initiation

Table 4 contains the clinical characteristics of diagnosed participants across screened for conditions.

Table 4. Clinical Characteristics, Linkage to Care and Treatment Initiation of Referred Integrated NCD-HTS clients, 18 June 2018 – 28 March 2019

Variable	Prevalence	Newly diagnosed	Previously diagnosed	Ever been on treatment	Controlled	Uncontrolled
HIV	149/775 (19.2)	77/149 (51.7)	72/149 (48.3)	46/72 (63.9)	46/72 (63.9)	26/72 (36.1)
High Blood Pressure	139/772 (18.0)	97/134 (72.4)	37/134 (27.6)	31/37 (83.8)	-	31/31 (100.0)
High Blood glucose (HbA1c)	83/766 (10.84)	73/76 (96.05)	3/76 (3.95)	2/3 (66.7)	-	2/2 (100.0)
High Total Cholesterol (TC)	62/768 (8.07)	56/60 (93.33)	4/60 (6.67)	1/4 (25.0)	-	1/1 (100.0)

Newly diagnosed **was defined as HTS client self-reporting normal results at last screening and subsequently screening with abnormal results at Zazi HTS.**
Previously diagnosed **was defined as HTS client self-reporting abnormal results at last screening and also screening with abnormal results at Zazi HTS.**
Controlled **was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with normal results at Zazi HTS. For HIV-infected clients, this simply means, on ART.**
Uncontrolled **was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with abnormal results at Zazi HTS.**

Note: TB patients were not asked questions on history of blood pressure, glucose and cholesterol resulting in missing data. If the first blood pressure reading was high, then a second reading was taken. The average reading of the two blood pressure readings was then categorized to determine prevalence of high blood pressure. Those HTS clients referred for high blood pressure were clients whose second BP reading was high and who had consented for follow-up.

Of the HIV-infected participants, 48.3% (n=72/149) already knew their HIV-status, and of those, 63.9% (n=46/72) had already been initiated on treatment.

Of all participants screened with elevated BP, high HbA1c and high TC, 72.4% (n=97/134), 96.1% (n=73/76), and 93.3% (n=56/60) were newly diagnosed at screening for each condition, respectively. Of the clients who self-reported as being previously diagnosed, 83.8% (n=31/37) of hypertensive clients, two (n=2/3) clients with high HbA1c, and one (n=1/4) client with high TC self-reported they had already been initiated on treatment. All clients were found to have uncontrolled disease after screening.

Discussion

This was the first study to integrate screening for obesity, blood pressure, blood glucose (HbA1c) and TC into a facility-based HTS setting within a LMIC known to have high rates of HIV. Our data highlights the high rates of NCD risk factors, HIV, and comorbidity affecting the adult population of Soweto, South Africa; and amongst relatively young adults aged 18-34 years. This study shows women are presenting with chronic disease at an earlier age than men. The majority of these health conditions were newly diagnosed, and all clients who had been previously diagnosed with hypertension, high blood glucose and cholesterol and had already initiated treatment remained with uncontrolled disease. Current South African national guidelines do not adequately allow for the most effective screening for and management of these NCDs or their risk factors amongst the general population or PLHIV. We urge a review of the current national health screening and management guidelines for NCDs, and any opportunity for integrative screening should be seized upon.

Overall, there was a high prevalence of each chronic disease for which there was screening (overweight/obese BMI, elevated BP, high HbA1c and TC, and HIV) amongst participants. Over one-third of all clients were overweight/obese – representing a higher prevalence of this BMI among black Africans as compared to the SADHS.[31] One-fifth of adults had elevated BP, one-in-ten participants had diabetic levels of HbA1c, and eight percent of clients had high TC. Nearly one-in-five adults had HIV-infection. Our data supports existing research showing

South Africa as having the highest rate of overweight/obese people in sub-Saharan Africa[1] and corroborates with various national surveys in that both the prevalence of overweight/obese BMI and elevated BP increase with age.[31, 32] While our study's prevalence of high HbA1c was similar to that reported within formal urban settings within the SADHS,[31] we found over twice the prevalence of high TC among women than previously reported.[31] Our study population had a higher overall HIV prevalence and for each sex than was reported for black Africans in the Fifth South African HIV Prevalence, Incidence, Behaviour and Communication Survey, 2017.[7] However, our study's HIV statistics were similar to those found within the latest SADHS for Gauteng.[31]

We found our HIV-infected study participants to have high rates of comorbidity with all NCD risk factors for which we screened, and with significantly higher HbA1c than their HIV-uninfected counterparts. This finding supports a systematic review which found the prevalence of DM among TB patients in sub-Saharan Africa to be significantly high, with an even higher prevalence among those co-infected with HIV.[33] Additionally, our participants on ART had significantly higher TC than those HIV-infected participants not on ART. This finding is not unique to only hypercholesterolemia. Metabolic consequences of two of the three main classes of ART - protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NRTIs) – are known to put HIV patients at an increased risk of hypertension, hyperglycaemia and hypercholesterolemia.[37][9, 34, 35] The Southern African Hypertension Society has acknowledged that long-term, highly active ART (HAART) is associated with a higher prevalence of systolic HT,[36] and PIs and NRTIs may affect both calcium channel blockers (CCBs) - the main class of antihypertensive medications – and statins (e.g.; simvastatin; the main lipid-lowering therapy) through drug interactions also affecting drug metabolism.[37, 38] This results in either an enhancement or loss of drug efficacy leading to extremely high blood glucose and/or cholesterol levels.[23, 35] It has also been reported that the incidence of newly onset hyperglycaemia among PLHIV on ART is on average about 5%.[39]

Of grave concern is our study data highlights disturbing chronic disease trends amongst the younger age groups, which differ from previous reports. Irrespective of sex, there are worrying levels of overweight/obese BMI and diabetic-level HbA1c among the 18-24 year olds. Over one-third of women aged 18-24 years had overweight/obese BMI, and nearly one-in-ten of these young adults had high HbA1c. While only four percent of 18-24 year olds had elevated BP, about ten percent of 18-35 years old had the same condition. In contrast to data from national surveys showing the prevalence of diabetic level HbA1c to increase with age,[31, 32]

our study showed 18-24 year olds had higher rates of elevated HbA1c than 25-34 year olds. As compared to the SADHS, our study reported our 18-24 year olds to have nearly nine times the prevalence of diabetic-level HbA1c for women and nearly four times the level for men.[31] Our 18-24 year olds also exhibited a higher prevalence of elevated TC than 25-34 year olds.

Furthermore, women seem to present with chronic disease earlier than men. Women were found to have significantly more HIV-infection - six out of ten HIV-infections amongst 18-24 years olds were among women - and overweight/obese BMI than men across all age groups. Although it wasn't statistically significant, 18-24 year old women had a higher prevalence of high HbA1c and high TC than 18-24 year old men or either sex amongst the 25-34 year olds. This trend towards the earlier development of NCD risk factors, especially among women, is worrisome as it has also been well documented that women have a higher HIV prevalence across all age groups, and peak HIV-infections occur among young women aged 15-24 years.[7, 31] Our HIV-infected women had about four times the rates of overweight/obese BMI than HIV-infected men.

The exception to the trend by sex and age was elevated BP. Despite copious literature outlining the relationship between overweight/obese BMI and chronic diseases such as hypertension,[40-42] our male participants aged 18-24 years, none of which were overweight/obese, had over twice the prevalence of elevated BP than women of the same age. Studies have shown an association between tobacco use, alcohol consumption and hypertension.[43-45] One-quarter of our participants had smoked cigarettes and over sixty percent reported drinking alcohol – one-in-ten admitted to excessive alcohol use. Previous studies in the same setting report males are more likely than females to smoke tobacco and drink alcohol, which may account for their increased likelihood of elevated BP.[25, 45]

The majority of our participants with chronic disease were newly diagnosed. Just over half of HIV-infected clients, about three-quarters of hypertensive clients, and nearly all clients with high blood glucose and cholesterol were previously not aware of their condition. Of the participants screened to have comorbidity with HIV, about one-quarter were newly diagnosed with both HIV and high BP and/or high TC and half were newly diagnosed with both HIV and high glucose. We report higher levels of unknown disease compared to the SADHS, which reported 29% of females and 34% of males had not been previously diagnosed with HT by a healthcare provider; and 64% of women and 66% of men screened as pre-diabetic (adjusted

HbA1c level: 5.7-6.4%), indicating a large proportion of South African adults are either not aware of their condition or not aware they are at-risk.[31]

Although our study only had a small sample size of participants reporting they had taken treatment for NCD conditions, all subsequently screened with uncontrolled disease at our HTS centre. This proportion is far higher than what was reported in the SADHS – of those on antihypertensive drugs and medication for DM, 23% of females and 9% of men did not exhibit controlled BP and about 85% still had uncontrolled blood glucoses levels.[31] Less than two-thirds of our previously diagnosed HIV-infected participants had initiated ART – which excludes all of the 18-24 year olds, and those who had not yet initiated treatment had a low median CD4 count (under 350 cells/mm3) – with the 18-24 year old men having the lowest CD4 count.

The high rates of chronic disease; previously unknown chronic disease; and known, uncontrolled chronic disease amongst our participants point towards missed opportunities for critical screening and suboptimal patient management within South Africa's public sector.

While HbA1c testing is a superior screening method for DM, reporting the average blood glucose level over the past three months, random plasma glucose (RPG) screening – not HbA1c – is used in the public health sector.[21] Our study's HbA1c and RPG screening results among the same clients were poorly correlated. Over one in ten clients had elevated HbA1c, however only four clients had elevated RPG levels, suggesting our population was not at-risk for DM. Iron deficiency anaemia could have been the cause of such discrepancy. Studies have shown that it influences HbA1c levels independent of glycaemia among non-diabetic and diabetic patients, alike,[46-49] which resolves following iron therapy.[50, 51] While the exact mechanism underlying the effects of iron deficiency anaemia on HbA1c levels is not fully known, it is potentially due to the modifications to the structure of haemoglobin and levels of HbA1c in both old and new red blood cells.[52, 53] While we did not screen for this condition, a national survey reported an overall prevalence of anaemia of 17.5% among South Africans aged 15 years and older, with women having almost double the prevalence (22%) as compared to males (12.2%). [32]

Screening for DM within the general population hinges on either being overweight with risk factor for hyperglycaemia or metabolic decompensation or being at least 45 years of age.[21] Hypercholesterolemia screening criteria is being of older age and having DM. Problematically, symptoms of diabetes are often either less severe or absent, with a significant percentage of

cases (30–80%) remaining undiagnosed.[21, 54] With over one-quarter of our 18-25 year olds and over one-third of our 18-44 years olds being overweight/obese, if asymptomatic, these individuals would be missed in the screening process for DM. Three-fifths of our clients with high cholesterol were under 45 years of age. Over half of our HIV-infected clients did not previously know their status, and this population had significantly lower median BMI and significantly higher average blood glucose than HIV-infected individuals, with the majority under 45 years of age. These sub-populations would be missed opportunities for screening for disease within the general population. With screening for DM and hypercholesterolemia amongst PLHIV based around the initiation of ART, one-third of our HIV-infected participants who knew their status and chose not to initiate ART would have been unscreened. Furthermore, our HIV-infected participants on ART still had significantly higher TC than those not on treatment.

We recommend that rapid blood glucose and cholesterol screening become routinely monitored within the public health sector, regardless of BMI classification, HIV-status or ART use, for adults aged 18+ years. Despite the confounding by iron deficiency anaemia, we recommend HbA1c screening become the preliminary screening for diabetes, as opposed to RPG, in order to avoid misdiagnosing patients as having normal glucose levels. Adherence to chronic medications for those initiated on treatment is critical to improve health outcomes.

Limitations

This study has a convenience sample of participants self-selecting to attend a single HTS clinic in Soweto. There is potential for bias as these participants have not been randomly sampled from multiple facilities.

This study was a cross-sectional study and may not explain causality. Some of our sub-group sample sizes for comparison are small which may have affected statistical precision.

During the time of the study, the integrated NCD-HTS clinic was assisting with HIV rapid test screening for the enrolment of women into HIV prevention (pre-exposure prophylaxis) trials conducted at PHRU, as well as conducting screenings for cervical cancer and human papilloma virus (HPV) for female clients. This may have encouraged the higher volumes of women attending the clinic, as the balanced sex ratio presented within the standard of care phase is a more typical representation.[25]

The integrated NCD-HTS clinic also operated within a research unit, and while it is the only HTS site within Chris Hani Baragwanath Academic Hospital and not receiving in-patients from the hospital, it is still not a government health centre. This impacts generalisability to typical community health clinic settings. Furthermore, the public health sector may only use the resources available, which might not always be rapid diagnostic methods but laboratory-based analysis of samples with reagents. While the rapid diagnostic testing technology used within the study (e.g.; HbA1c and random blood glucose testing machines) have different sensitivities and specificities, which affect patient results, laboratory analysis could differ, as well.

Conclusion

Our study describes the chronic NCD catastrophe plaguing South Africa, and amongst relatively young adults (18-34 years), especially women. Current South African national guidelines do not adequately allow for the most effective screening for and prevention of diabetes or hypercholesterolemia, or their pre-cursors amongst the general population or PLHIV. Any opportunity for integrative screening should be seized upon, and rapid HbA1c and rapid blood cholesterol screening methods should be integrated into standard of care practice for adults within the public health sector, regardless of BMI categorization, HIV status or ART use. There are severe needs for the integrative management of adherence to chronic medications, especially in the monitoring of ART patients due to the metabolic side effects of treatment for PLHIV.

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PAPER IV

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Level of adult client satisfaction with clinic flow time and services of an integrated non-communicable disease-HIV testing services clinic in Soweto, South Africa: a cross-sectional study

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Level of Adult Client Satisfaction with Clinic Flow Time and Services of an Integrated Non-Communicable Disease-HIV Testing Services Clinic in Soweto, South Africa: A Cross-Sectional Study

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Abstract

Background: While HIV Testing Services (HTS) have increased, many South Africans have not been tested. Non-communicable diseases (NCDs) are the top cause of death worldwide. Integrated NCD-HTS could be a strategy to control both epidemics. Healthcare service strategies depends partially on positive user experience. We investigated client satisfaction of services and clinic flow time of an integrated NCD-HTS clinic.

Methods: This prospective, cross-sectional study evaluated HTS client satisfaction with an HTS clinic at two phases. Phase 1 (February–June 2018) utilised standard HTS services: counsellor-led height/weight/BP measurements, HIV rapid testing, and symptoms screening for sexually transmitted infections/Tuberculosis. Phase 2 (June 2018–March 2019) further integrated counsellor-led obesity screening (BMI/abdominal measurements), rapid cholesterol/glucose testing; and nurse-led Chlamydia and HPV/cervical cancer screening. Socio-demographics, proportion of repeat clients, clinic flow time, and client survey data (open/closed-ended questions using five-point Likert scale) are reported. Fisher's exact test, chi-square analysis, Kruskal Wallis test conducted comparisons. Multiple linear regression determined predictors associated with clinic time. Content thematic analysis was conducted for free response data.

Results: 284 and 333 participants were from Phase 1 and 2, respectively (N=617). Phase 1 participants were significantly older (median age 36.5 (28.0–43.0) years vs. 31.0 (25.0–40.0) years; p=0.0003), divorced/widowed (6.7%, [n=19/282] vs. 2.4%, [n=8/332]; p=0.0091); had tertiary education (27.9%, [n=79/283] vs. 20.1%, [n=67/333]; p=0.0234); and less female (53.9%, [n=153/284] vs 67.6%, [n=225/333]; p=0.0005), compared to Phase 2. Phase 2 had 10.2% repeat clients (n=34/333), and 97.9% (n=320/327) were 'very satisfied' with integrated NCD-HTS, despite standard HTS having significantly shorter median time for counsellor-led HTS (36.5, interquartile range [IQR]: 31.0-45.0 vs. 41.5, IQR: 35.0-51.0; p<0.0001). Phase 2 associations with longer clinic time were clients living together/married (est=6.548; p=0.0467), more tests conducted (est=3.922; p<0.0001), higher overall satisfaction score (est=1.210; p=0.0201). Those who matriculated experienced less clinic time (est=-7.250; p=0.0253).

Conclusions: It is possible to integrate counsellor-led NCD rapid testing into standard HTS within historical HTS timeframes, yielding client satisfaction. Rapid cholesterol/glucose testing should be integrated into standard HTS. Research is required on the impact of cervical

cancer/HPV screenings to HTS clinic flow to determine if it could be scaled up within the public sector.

Keywords: HIV/AIDS, HIV prevention, non-communicable diseases, HIV testing services, client satisfaction, healthcare, comorbidities

Background

HIV Testing Services (HTS) (i.e.; pre- and post-test counselling, laboratory services, delivery of results, and the linkage of clients to the required HIV prevention, treatment and care services) has increased in South Africa, with more than 4500 public health facilities offering provider-initiated counselling and testing (PICT) following the launch of the national HTS campaign in 2010[1, 2]. However, the country is still falling short of the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90–90–90 target, where by 2020, 90% of all people living with HIV (PLHIV) will know their HIV status; 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy (ART); and 90% of all people receiving ART will have viral suppression[3]. As of December 2017, only 84.9% of PLHIV aged 15–64 years knew their HIV status (88.9% of HIV-infected females, 78.0% of HIV-infected males), 70.6% of PLHIV were on ART, and 87.5% of PLHIV on ART were virally suppressed (89.9% of females and 82.1% of males)[4]. Although there has been an increase in the uptake in HIV testing (a 19.4% increase since 2012)[5], a significant number of South Africans have not yet been tested.

Furthermore, the top cause of death and disability worldwide are chronic non-communicable diseases (NCDs), such as cardiovascular disease (CVD) and diabetes mellitus (DM), attributing to more than three in five deaths[6]. In South Africa, cervical cancer, largely caused by the sexually transmitted Human Papilloma Virus (HPV), is the second most prevalent form of (preventable) cancer[7-9]. Lower and middle income countries (LMICs), such as South Africa, are being disproportionately impacted by these diseases[10]. The recent South African Demographics and Health Survey (SADHS) reports alarming levels of unknown NCDs within the population[11]. With the scale-up of ART, HIV is becoming a chronic disease with PLHIV reaching nearly the same life expectancy as healthy individuals[12]. Historically, NCDs are thought of as ‘aging diseases’[13]. Not only is HIV-infection seemingly associated with an accelerated ‘aging’ process, but PLHIV, now living longer while on treatment, are becoming

increasingly at-risk for non-HIV-related chronic conditions of aging similar to the HIV-uninfected population[14].

There are varying models of HTS service provision under investigation to determine the effect on uptake of HIV and/or NCD testing (e.g.; home-based or work-place testing, client-initiated or provider-initiated testing, provision of integrated services, etc.)[15-21]. National and global policies stress integrated screening to address NCD pre-cursors (e.g. blood pressure [BP] and body mass index [BMI])[22-24]. However, integrated screening is implemented infrequently and/or in a non-standardised manner in many South African HTS, and health programmes require evidence to inform widespread adoption. While integration of HIV with other programmes, such as reproductive health and tuberculosis (TB), has occurred through the establishment of inclusive national policies, both research and evidence-based data on the acceptability, effectiveness, feasibility and sustainability of HIV-NCD integration in clinical practice is scarce[25-27].

While integration of screening, prevention and referral services may be an intuitive solution for combating the morbidity and mortality associated with HIV and NCDs, there is minimal evidence regarding the patient- and service-level effect of such a strategy[28]. Competent care and health systems are necessary for achieving high-quality care. However, it is believed that health systems – and its interventions - be evaluated in part by the confidence of people in their health system and the processes of care, inclusive of assessing user experience[29]. Not only is such measurement critical for accountability and improvement, but a positive user experience has a fundamental value which can improve retention in care, adherence to treatments, and confidence in health systems[29]. Additionally, some studies have found that positive user experience is linked to better technical quality[29], and although patients cannot force the provision of better care, they can improve their health by actively choosing to seek better providers and/or remain in care[30]. The integration of new services could have substantial impacts on clinic operations, provider responsibilities, and the quality of care delivered, causing dissatisfaction among clients[28]. For example, the integration of HIV services with sexual and reproductive health services could result in an increased patient burden and therefore inadequate staffing to support this shift, yielding patient dissatisfaction[31].

The utility of assessing patient/client satisfaction measures, specifically when paired with open-ended responses, is that it gives the recipients of healthcare a voice, which may reveal elements of the quality of the processes of care shaping the user experience[29]. Client ratings

and recommendations are critical for accountability and improvement[29], helping to shape service delivery in real-time. There is currently a gap in literature surrounding health system user experience among LMIC[29].

Acceptance of any service – or model of service - is partially dependent on client satisfaction with the service provided. This model focuses on whether client expectations are 'confirmed' (i.e.; satisfied) or 'disconfirmed' (i.e.; dissatisfied)[32]. Health care is no different[33]. Client-related factors linked to satisfaction in relation to health care may be related to the distance and expense incurred in traveling to the clinic, level of confidentiality maintained, types of services offered and clients' decision to accept specific services, duration of services and/or wait time, human relations and/or facility environment, and availability of treatment[32, 34, 35]. Client satisfaction, when included as part of a more holistic evaluation, inclusive of complimentary components such as healthcare provider satisfaction and quality of care, is a critical piece to evaluate a healthcare delivery strategy's feasibility and acceptability.

The Perinatal HIV Research Unit (PHRU) Zazi HTS Clinic, has provided on-site HIV testing and counselling for adults in Soweto, South Africa, since 2001. Zazi also draws blood for CD4 count testing at a contracted laboratory for HIV-infected clients not yet initiated on treatment, as an indicator of stage of disease. Zazi is currently the only service provider of walk-in, free, accessible HTS supplied to the Chris Hani Baragwanath Academic Hospital (Bara Hospital), the largest hospital in the southern hemisphere. HIV treatment is not provided on-site, but clients are given referral letters to local clinics[36].

To reflect the South African National Department of Health's (NDoH) newly proposed HTS standard of care[22], the Zazi clinic expanded its health service provision in February 2018, and began offering counsellor-led height and weight measurements, BP readings, and symptom screenings for sexually transmitted infections (STIs) and TB within its HIV rapid testing service[36]. As part of a larger feasibility and acceptability study, this standard of care HTS clinic (Phase 1) introduced additional health screening services in June 2018, transforming itself into an integrated NCD-HTS clinic model (Phase 2). The integrated NCD-HTS model included the following services in addition to the standard of care HTS: counsellor-led waist circumference measurements and BMI calculations; rapid blood cholesterol and blood glucose (both random and average [HbA1c]); and for female clients, nurse-led rapid Chlamydia testing, Human Papilloma Virus (HPV) genotyping, and cervical cancer screening via Pap smear.

There is a paucity of client satisfaction research for different integrated service models within scientific literature. The aim of our study was to describe client satisfaction with the services of and clinic flow time within an integrated NCD-HTS clinic in Soweto, South Africa. This paper presents the client clinic exit survey data and clinic flow time collected on each clinic model – standard of care HTS versus integrated NCD-HTS – along with the respective client demographics. We also report the proportion of repeat clients. Understanding client opinions and level of satisfaction regarding each model of health service will provide a deeper understanding of whether or not a particular model is meeting the community's needs and expectations. Feedback may improve healthcare service and the overall client experience. This study is but one piece of an overall evaluation being conducted on this integrated NCD-HTS model to determine its feasibility and acceptability. Other complimentary components being investigated with results presented elsewhere are HTS provider satisfaction, quality of task-shifting NCD-precursor rapid testing to lay counsellors, and health outcomes (i.e.; referrals, linkage to care and treatment initiation) for HTS clients.

Methods

Study Design and Setting

This is a prospective, mixed-methods study using cross-sectional data evaluating client satisfaction of two phases of a health screening programme within the Zazi HTS centre at PHRU, a leading research centre situated at Bara Hospital in Soweto, South Africa. In Phase 1, the clinic operated under the standard of care HTS guidelines for three months (from 19 February and 14 June, 2018). In Phase 2 (between 18 June 2018 and 28 March 2019), the clinic conducted integrated NCD-HTS screening for nine months. Each phase had its own, independent walk-in client population (i.e.; data were not longitudinal).

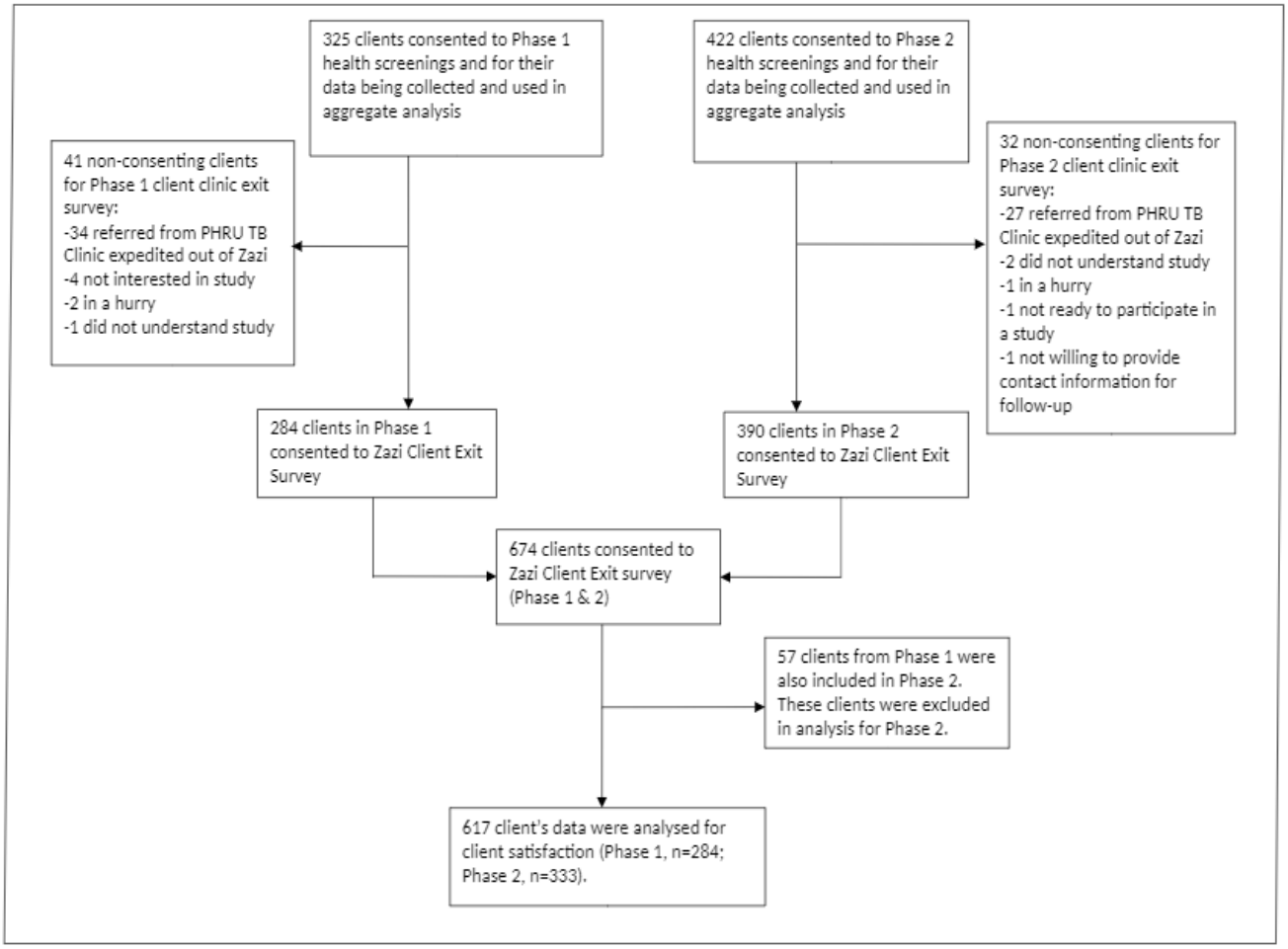
Clinic Staffing

The Zazi clinic is unique from government clinics in that it is driven by three counsellors and supported by one nurse, with clients only being triaged to the nurse for specialised endocervical screening procedures requested and/or for any prevention, treatment and/or care referrals required. The staff also catered to a client's emotional needs and did not limit the time of a counselling session.

Sampling

Our sampling approach was serial sampling, allowing for all eligible walk-in PHRU Zazi HTS clients who consented to the health screening programme to be approached to partake in a clinic visit exit survey prior to leaving the clinic (a specific informed consent form and survey was used for each Phase) and for their data to be captured and used in research. Consenting clients were enrolled as study participants. Survey data was reviewed and analysed monthly, using chronologically collected surveys, and the sample was deemed complete once content saturation was reached. Further details on recruitment and sampling can be seen in Supplementary Figure 1.

Supplementary Figure 1. Participant Flow Chart



Inclusion and Exclusion Criteria

Eligibility criteria for participation in the study were the following: at least 18 years of age; able to communicate in either English, IsiZulu and/or Sotho; and able and willing to provide written or verbal informed consent (with an impartial witness) for health screening procedures

and completion of client exit survey. If a client presented to the clinic critically ill, they were not enrolled but referred to the Bara Hospital casualty ward.

Data Collection and Management

Client demographic and clinic exit survey data were self-reported and collected either by self-completion of a survey by English-literate clients in the reception area, or collected with the help of the clinic receptionist or lay counsellors for clients unable to read or write. Each survey was checked by clinic staff for logical completion. Clinic flow timeframes from registration through the counsellor-led HTS session were noted and logged on paper forms by either the clinic receptionist, lay counsellors, or the nurse. All surveys and forms comprised part of the PHRU Zazi HTS client file. Data from patient files were cleaned and verified prior to entry into the Research Electronic Data Capture (REDCap) database.

Study Measures

Demographic Information and Repeat Clients

Data were collected on sex, age, race, nationality, ethnic group, marital status, highest level of education, employment, and details regarding socio-economic status (type of housing, source of water and fuel for cooking and lighting, type of toilet facility, as well as possession of household and ownership items).

We determined the proportion of Phase 2 clients who were repeat clients within Phase 2.

Clinic Flow Time

Clinic flow time start and stop time measures (in minutes) were recorded by clinic staff (receptionist for post-registration timeframe, and counsellors for time spent in counselling room) providers in real-time on clinic records (not study-specific records) after direct observation of a computer's clock Clinic flow is depicted within Figure 1. Pre-registration time, time taken for QA/QC of results, and time spent within the nurses room (for Phase 2 female-only screenings and provision of referral letters and additional counselling) was not reported. Independent sections of the clinic flow for which time was reported are defined as follows:

Time spent at reception, post-registration: From when a client was registered with the receptionist until the client was received by the counsellor. The time was spent in the waiting room, where the Demographics and Client Contact forms were also completed.

For pre-test counselling: From when the counsellor initiated pre-test counselling until it was concluded.

Conducting health screenings: From when the pre-test counselling concluded until both health screenings and the Family History and Behavioural Questionnaire were completed. The following health screenings were conducted by the counsellor – height/weight measurements, BP readings, STI and TB symptoms screening and HIV rapid testing (for standard of care HTS); and standard of care HTS combined with abdominal girth measurements, BMI categorizations, blood sugar rapid tests (both HbA1c and random), blood cholesterol rapid test (for integrated NCD-HTS). The questionnaire, which was administered while waiting for the finger prick rapid testing results, included symptom screening questions, among others.

For post-test counselling: From when the counsellor initiated post-test counselling until it was concluded. This also included risk-reduction counselling and delivery of all aforementioned counsellor-led health screening results.

Total time for counsellor-led HTS process: From when the pre-test counselling started until post-test counselling ended, excluding the QA/QC of results.

Figure 1. Client Clinic Flow Diagram

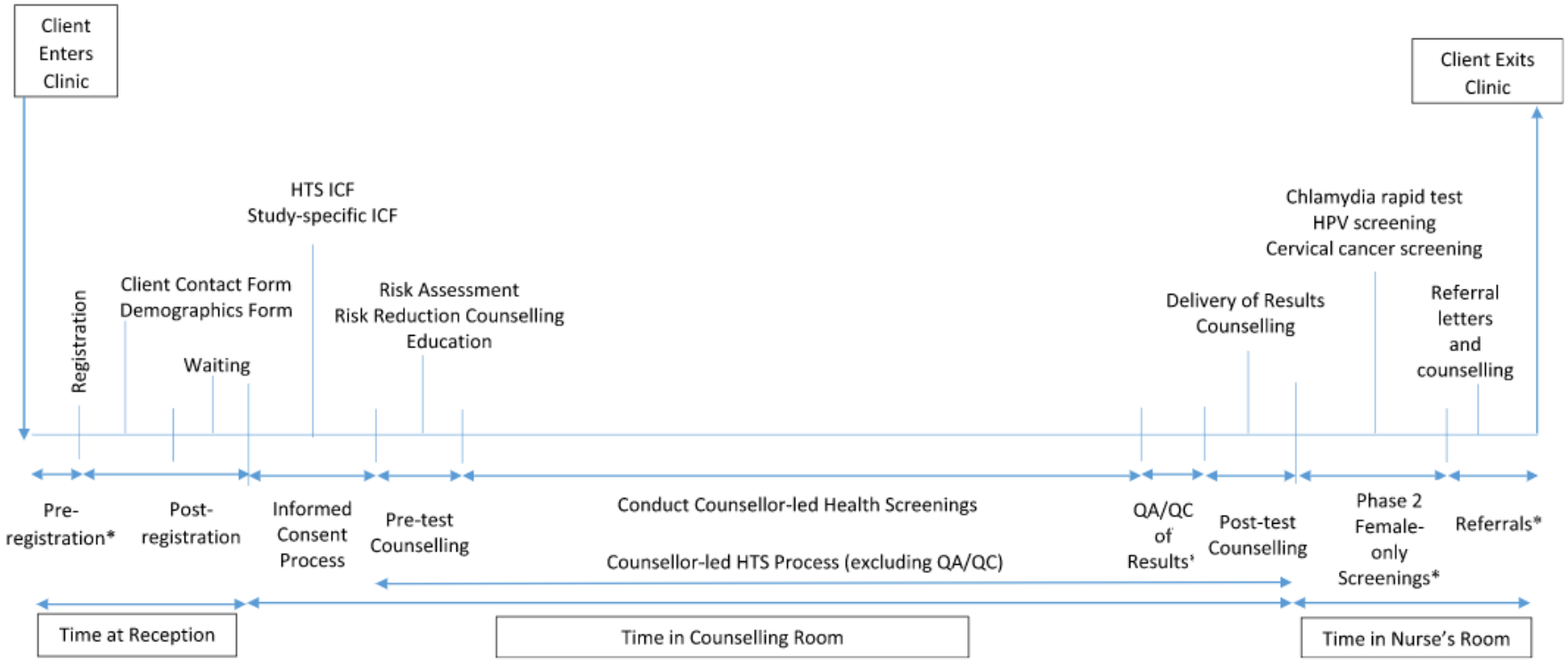


Fig. 1 Client clinic flow diagram. Original diagram. Hopkins KL 2020. *Time data not collected

Client Exit Survey

We developed a structured client exit survey which consisted of both close-ended and open-ended questions for free responses to assess client satisfaction with each clinic model. This survey was solely created for the purposes of this study and has not been previously published. The close-ended questions included a five-point Likert format with differing responses for various questions (e.g.; *I feel very satisfied, I feel somewhat satisfied, I feel neither satisfied nor dissatisfied/neutral, I feel somewhat dissatisfied, I feel very dissatisfied*). The Likert responses were designed to assess client satisfaction with each clinic model's HTS processes (i.e.; pre- and post-test counselling, and preparedness for and level of comfort/discomfort during screening procedures), the helpfulness of speaking with the nurse, and overall satisfaction of each clinic model. Time satisfaction was also assessed throughout the clinic flow.

The responses to the open-ended questions helped us to further understand the responses to the close-ended questions. The open-ended questions included: *Please explain why you opted out of any offered services?; In your own opinion, what improvement(s) should be made for pre-test counselling / for the health screening testing procedure(s)?; In your own words, please describe what you liked / disliked about Zazi today; In your own words, please share if there is anything else you wished the Clinic would have provided you.*

Overall satisfaction score was defined as the sum of scores from the Likert scale with values ranging from 1-5 and higher values signifying more satisfaction. The questions included rating the amount of time it took before seeing a counsellor; the amount of time it took the counsellor to provide pre-test counselling, health screenings, and provide results and conduct post-test counselling; and the amount of time spent with the nurse for further consultation and referrals.

Quantitative Data Analysis

Frequencies and their percentages were determined for categorical variables and stratified by model of HTS.

To test statistical significance for categorical measures stratified by phase, Fisher's exact test or chi-square analysis was used, where appropriate. Descriptive statistics, such as medians and interquartile ranges, were determined for continuous measures (e.g.; age) and compared by HTS model non-parametrically using the Kruskal Wallis test. Multiple linear regression was

used to determine predictors associated with time spent (in minutes) in the clinic. Regression residuals, including plots, were used to assess model fit.

A wealth quintile was developed using the socio-economic measures and determined using Principal Component Analysis (PCA)[37-39]. The socio-economic measures included *type of house* (shack/zozo [a common isiZulu term meaning *tin-roofed shack*], flat/cottage, room/garage, hostel, shared house, standalone brick house or other); *source of water* (tap water indoors, only outside tap water, well/borehole, stream/river/pond or other); *type of toilet facility* (flush toilet inside [connected to sewage], outside pit latrine/toilet, flush toilet inside [septic tank], no toilet facility or other); *type of fuel used for cooking* (electricity, gas, paraffin, coal, candle, firewood/straw or other); *type of fuel used for lighting* (electricity, gas, paraffin, coal, candle, firewood/straw or other); *possession of household items* such as radio, computer, landline telephone, TV, refrigerator, mobile phone; and ownership of bicycle, car/truck, sheep/goat/cattle, motorcycle/scooter or donkey/horse. Prior to calculating the wealth quintile, variables with more than two levels were recoded into binary (0 or 1) for each level of response. Frequencies were run on all the binary variables, and only those with responses between 5% and 95% were retained. The retained variables were evaluated by the PCA method using the varimax rotation to identify those contributing largely to the wealth construct. Variables meeting a pre-specified cut-off and loading in at least two factors were excluded. The remaining variables were retained and scored to create the socio-economic index. Five wealth quintiles were estimated on the scored measure using 20 percentile intervals, increasing in levels of wealth (i.e.; first quintile was lowest level of wealth and fifth quintile was highest). Client satisfaction results were presented graphically for health screenings.

All statistical analysis was conducted in SAS Enterprise Guide 7.1 (SAS Institute, Cary NC) using the SAS/STAT procedures PROC FREQ, MEANS, NPAR1WAY, FACTOR, SGPANEL, and PROC GLM.

Qualitative Data Analysis

Using SAS Enterprise Guide 7.1 (SAS Institute, Cary NC), a print out of all open-ended responses per question was obtained. The first author read through each text response (codes) to gain an overall understanding of the data. All codes were collated in an excel spreadsheet under the pre-determined themes, which were based around quantitative questions. Thereafter the first author developed a codebook by assigning defined categories of grouped codes. Most

categories were also pre-determined. However, if a code did not fit nicely, a new category was created. Categories were then analysed further to create more detailed sub-categories.

Content thematic data analysis was utilised by counting the number of codes per category, using SAS. A response to a particular question could be assigned to multiple categories, which may have increase the sample size of certain variables. All non-responses to a particular question (free responses left blank by participants) and responses agreed upon as non-logical were not included in the analysis, thus decreasing the sample size for that question.

Inductive coding was used to deduce meaning from the qualitative data[40]. Concepts from research literature served as deductive codes. Validity of initial codes was checked by identifying whether it is repeated across different responses to the same survey question within the study, highlighted by participants themselves as an important issue[41].

Agreement on the data analysis was achieved through a second review by a co-author.

Results

Characteristics of participants and repeat clients

A total of 617 participants of median age 33.0 (IQR: 26.0–41.0) years, were included in the analysis from both HTS models (284 and 333 participants for standard of care HTS and integrated NCD-HTS, respectively), and the largest proportion of participants were females (61.3%, [n=378/617]), black African (99.2%, [n=612/617]), South African (96.6%, [n=592/613]), Zulu speaking (45.3%, [n=279/616]), single (70.7%, [n=434/614]), educated up to high school (40.1%, [n=247/616]), and employed (36.9%, [n=227/615]). More than one quarter were within the third wealth quintile category (i.e.; middle class; 26.6%, [n=164/617]). Participants of standard of care HTS were significantly older (median age was 35.0 (28.0–43.0) years vs. 31.0 (25.0–40.0) years; p=0.0003), likely to be divorced (6.7%, [n=19/282] vs. 2.4%, [n=8/332]; p=0.0091) and be tertiary educated (27.9%, [n=79/283] vs. 20.1%, [n=67/333]; p=0.0234) compared to those of integrated NCD-HTS. Standard of care HTS had significantly less proportions of females (53.9%, [n=153/285] vs. 67.6%, [n=225/333]; p=0.0005), Zulu speakers (41.0%, [n=116/283] vs. 49.0%, [n=163/333]; p=0.0480) and clients reporting their parents as their source of income (13.0%, [n=37/284] vs. 20.5%, [n=68/331]; p=0.0135) as compared to integrated NCD-HTS.(Table 1)

Of the 333 Phase 2 clients who completed a survey, 10.2% (n=34/333) went on to become repeat clients within Phase 2.

Table 1. PHRU Zazi Evaluation Study Participant Demographics by Phase (Phase 1, Feb-June 2018; Phase 2, June 2018–March 2019

Variable	Overall	Phase 1	Phase 2	*P*-Value
No. of enrolment	617	284	333	
Age (in years)				
18–24 (%)	113 (18.4)	44 (15.5)	69 (20.7)	0.0680
25–34 (%)	223 (36.1)	95 (33.5)	128 (38.4)	
35–44 (%)	16 (26.7)	83 (29.2)	82 (24.6)	
≥45 (%)	116 (18.8)	62/ (21.8)	54 (16.3)	
Median (IQR)	33.0 (26.0–41)	35.0 (28.0–43)	31.0 (25.0–40)	0.0003
Mean (SD)	34.9 (10.8)	36.5 (10.9)	33.6 (10.5)	0.0008
Min, Max	(18–73)	(18–73)	(18–64)	
Sex				
Female (%)	378 (61.3)	153 (53.9)	225 (67.6)	0.0005
Male (%)	239 (38.7)	131 (46.1)	108 (32.4)	
Race				
Black (%)	612 (99.2)	281 (98.9)	331 (99.4)	0.6657
Coloured/mixed race (%)	5 (0.8)	3 (1.1)	2 (0.6)	
Nationality[a]				
South African (%)	592 (96.6)	268 (95.7)	324 (97.3)	0.2831
Other (%)	21 (3.4)	12 (4.3)	9 (2.7)	
Ethnic group[a]				
Zulu (%)	27 (45.3)	116 (41.0)	163 (48.9)	0.3544
Sotho (%)	101 (16.4)	50 (17.7)	51 (15.3)	
Tsonga (%)	70 (11.4)	31 (11.0)	39 (11.7)	
Tswana (%)	39 (6.2)	22 (7.7)	17 (5.2)	
Xhosa (%)	49 (8.0)	24 (8.5)	25 (7.5)	
Other (%)	78 (12.7)	40 (14.1)	38 (11.4)	
Marital status[a]				
Divorced/Widowed (%)	27 (4.4)	19 (6.7)	8 (2.4)	0.0298
Living together/Married (%)	153 (24.9)	66 (23.4)	87 (26.2)	
Single (%)	434 (70.7)	197 (69.9)	237 (71.4)	
Highest education[a]				
Up To High School (%)	247 (40.1)	111 (39.2)	136 (40.8)	0.0598
Matriculated (%)	223 (36.2)	93 (32.9)	130 (39.0)	
Tertiary education (%)	146 (23.7)	79 (27.9)	67 (20.2)	

Source of money to live on?[a]				
Employed (%)	227 (36.9)	111 (39.1)	116 (35.0)	0.0395
Parents (%)	105 (17.1)	37 (13.0)	68 (20.5)	
Pension (%)	18 (2.9)	12 (4.2)	6 (1.9)	
Self-employed (%)	118 (19.2)	61 (21.5)	57 (17.2)	
Social/Disability grant (%)	74 (12.0)	29 (10.2)	45 (13.6)	
Unemployed (%)	73 (11.9)	34 (12.0)	39 (11.8)	
Wealth quintile				
Quintile 1 (%)	163 (26.4)	69 (24.3)	94 (28.2)	0.2145
Quintile 2 (%)	138 (22.4)	73 (25.7)	65 (19.5)	
Quintile 3 (%)	164 (26.6)	74 (26.1)	90 (27.0)	
Quintile 4 (%)	124 (20.1)	52 (18.3)	72 (21.6)	
Quintile 5 (%)	28 (4.5)	16 (5.6)	12 (3.7)	

IQR interquartile range, *SD* standard deviation
[a]Overall may not be equal to the sample size as a result of missing responses

Reasons for declining HTS services for each HTS model

Only two clients opted out of HTS services in standard of care HTS, with one client dismissing CD4 count testing as she preferred to have it conducted at her ART referral clinic and another client declining being screened for STI symptoms as she responded that she was currently abstinent. A total of 36 survey responders (10.8% of clients) reported opting out of services in integrated NCD-HTS. Among these, 40% (n=16/40, all women) refused cervical cancer screening for reasons related to reproductive health (i.e.; menstruation [n=13/40, 32.5%]; having had a hysterectomy and therefore no cervix present [n=2/40, 5.0%]; and sharing, '[I am] No longer interested in having babies' [n=1/40, 2.5%], which also represents a misunderstanding surrounding the purpose of the Pap smear procedure). Other reasons included the desire to reschedule their clinic visit (n=10/40, 25.0%); being unprepared for or unsure of the new screenings (n=6/40, 15.0%) (specifically for the pelvic exam); lack of time (n=4/40, 10.0%), including either needing to return to work or needing to leave due to family obligations; worried about potential results (n=2/40, 5.0%); having recently had a Pap smear or currently having an STI (n=1/40, 2.5%, each).

Client satisfaction with pre-test and post-test counselling by HTS model

Figure 2 presents the distribution of client satisfaction by HTS model. The majority of participants were very satisfied with the pre-test and post-test counselling they received in standard of care HTS (97.5%,[n=276/283] and 95.0%, [n=268/282]) and integrated NCD-HTS (97.3%, [n=322/331] and 96.7%, [n=320/331]).

Figure 2. PHRU Zazi Evaluation Study Client Satisfaction by Phase (Phase 1, Feb-June 2018; Phase 2, June 2018–March 2019).

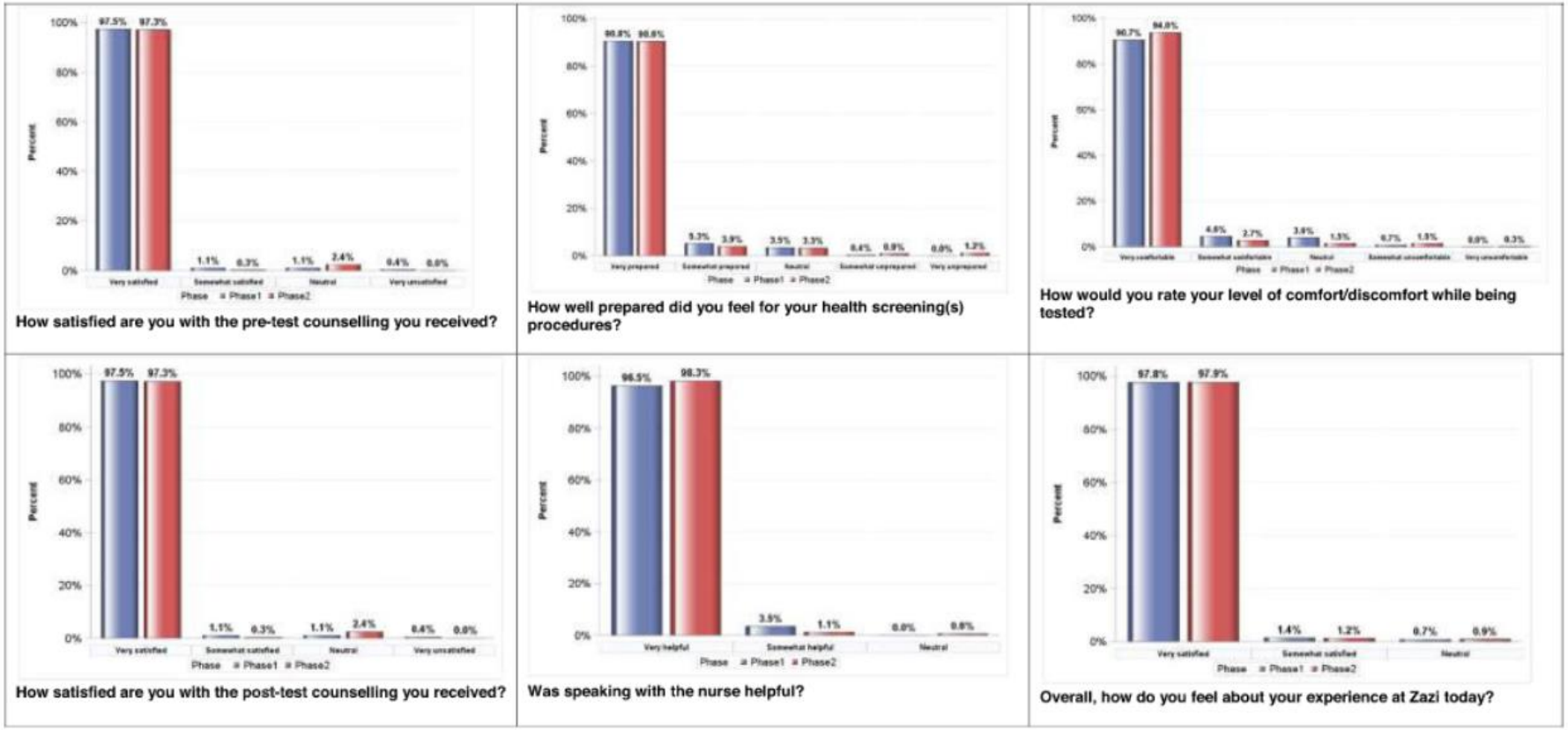


Fig. 2 PHRU Zazi Evaluation Study Client Satisfaction by Phase (Phase 1, Feb-June 2018; Phase 2, June 2018–March 2019). **a** (top left): How satisfied are you with the pre-test counselling you received?. **b** (top middle): How well prepared did you feel for your health screening(s) procedures?. **c** (top right): How would you rate your level of comfort/discomfort while being tested?. **d** (bottom left): How satisfied are you with the post-test counselling you received?. **e** (bottom middle): Was speaking with the nurse helpful?. **f** (bottom right): Overall, how do you feel about your experience at Zazi today?

There were four main suggestions from seven standard of care HTS responders on how to improve pre-test counselling: minimise the paperwork (n=3/7), provide in-depth information on health and/or disease (n=2/7), explain the rapid testing technology and screening machines used (HIV test kits and BP cuff and monitor) (n=1/7), and strengthen communication (n=1/7), presumably around the rapid testing process and instruments used. Four responders in integrated NCD-HTS suggested different improvements for pre-test counselling. They were providing further health information, inclusive of 'relationship goals and health practice'; creating set appointments times between '8–15hrs'; providing additional screenings, such as 'prostate cancer'; and explaining the new rapid testing machines (glucometer and lipidometer).

Only one standard of care HTS client shared a suggestion to improve post-test counselling, which was for the counsellor to provide 'tips on what the client should work towards'. Presumably this relates to strengthening risk reduction counselling.

Client satisfaction with health screening procedures by HTS model

Most participants were very prepared for the health screening procedures in standard of care HTS (90.8%, [n=256/282]) and integrated NCD-HTS (90.6%, [n=300/331]); and very comfortable with the level of comfort/discomfort while being tested in standard of care HTS (90.7%, [n=254/280]) and integrated NCD-HTS (94.0%, [n=311/331]). In standard of care HTS, of those who saw the nurse, 96.5% (n=82/85) found speaking with the nurse very helpful, while 98.3% (n=172/175) did in integrated NCD-HTS. Overall, the majority of participants were very satisfied with the experience they had at Zazi in both standard of care HTS (97.8%, [n=272/278]) and integrated NCD-HTS (97.9%, [n=320/327]). (Figure 2)

Only ten standard of care HTS responders (3.5% of clients, [n=10/284]) made suggestions to improve health screening procedures. Three responders desired additional health screenings such as 'STI test and blood sugar test' and also requested there to be less paperwork/administrative tasks; and one individual suggested each of the following: offer circumcision, improve the current testing procedure, explain the data collection process, and provide home visits. Integrated NCD-HTS contained only four responders (n=4/333), of which three suggested additional integrated HTS to include breast cancer and eye screening; and one client requested standardised appointments for certain screenings for which one might be unprepared (e.g.; Pap smear).

Clinic flow time and time-related client satisfaction by HTS model

Participants in standard of care HTS took a significantly shorter median time (in minutes) in the counsellor-led HTS process relative to those in integrated NCD-HTS (36.5, IQR: 31.0–45.0, [n=284/284] vs. 41.5, IQR: 35.0–51.0, [n=332/333]; p<0.0001) minutes (Table 2, Figure 3). The majority of participants in standard of care HTS (93.2%, [n=262/281]) and integrated NCD-HTS (94.9%, [n=313/330]) were very/somewhat satisfied with the time spent at reception; though the median time in minutes was significantly shorter in standard of care HTS relative to integrated NCD-HTS (15.0, IQR: 9.0–21.0, [n=265/284] vs. 19.0, IQR: 12.0-28.0, [n=331/333]; p<0.0001). Overall, participants felt very/somewhat satisfied by the amount of time spent on pre-test counselling (97.6% [n=596/611]). The median time taken to conduct screenings (17.0, IQR: 13.0–22.0, [n=281/284] vs. 21.0, IQR: 17.0-27.0, [n=332/333]; p<0.0001) and for post-test counselling (7.0, IQR: 5.0–8.0, [n=284/284] vs. 8.0, IQR: 6.0-10.0, [n=332/333]; p<0.0001) was significantly shorter in standard of care HTS relative to integrated NCD-HTS. (Figure 3)

Table 2. PHRU Zazi Evaluation Study Client Satisfaction with Clinic Flow Time by Phase (Phase 1, Feb-June 2018; Phase 2, June 2018–March 2019)

Variable	Overall	Phase 1	Phase 2	*P*-Value
Total time (in minutes) in clinic[a]				
Median (IQR)	*n* = 614, 96.0 (79.0–121)	*n* = 283, 86.0 (72.0–108)	*n* = 331, 102 (87.0–136)	< 0.0001
Time (in minutes) spent in Reception[a]				
Median (IQR)	*n* = 596, 17.0 (11.0–25)	*n* = 265, 15.0 (9.00–21)	*n* = 331, 19.0 (12.0–28)	< 0.0001
Time (in minutes) for pre-test counselling[a]				
Median (IQR)	*n* = 615, 9.00 (7.0–13.0)	*n* = 283, 10.0 (7.0–14.0)	*n* = 332, 9.0 (6.5–13.0)	0.0755
Min, Max	2, 83	2, 74	2,83	
Total time (in minutes) for counsellor-led screenings[a]				
Median (IQR)	*n* = 613, 19.0 (15.0–24.00)	*n* = 281, 17.0 (13.0–22.00)	*n* = 332, 21.0 (17.0–27)	<.0001
Time (in minutes) for Family History and Behaviour Survey[a]				
Median number of time (IQR)	*n* = 611, 7.0 (5.0–10)	*n* = 281, 8.0 (6.0–11)	*n* = 330, 6.0 (5.0–8)	<.0001
Mean number of time (SD)	*n* = 611, 8.1 (4.54)	*n* = 281, 9.4 (5.3)	*n* = 330, 7.1 (3.4)	<.0001
Min, Max number of time	*n* = 611, (2–65)	*n* = 281, (3–65)	*n* = 330, (2–22)	
Time (in minutes) for post-test counselling[a]				
Median (IQR)	*n* = 616, 7.0 (5.0–9)	*n* = 284, 7.0 (5.0–8)	*n* = 332, 8.00 (6.0–10)	<.0001
Min, Max	1, 41	1, 17	1,41	
Total time (in minutes) for counsellor HTS process[a]				
Median number of time (IQR)	*n* = 616, 39.0 (32.0–48.5)	*n* = 284, 36.5 (31.0–45)	*n* = 332, 41.5 (35.0–51)	<.0001
Mean number of time (SD)	*n* = 616, 43.1 (15.9)	*n* = 284, 39.2 (12.2)	*n* = 332, 46.4 (17.8)	<.0001
Min, Max number of time	*n* = 616, (18–138)	*n* = 284, (18–111)	*n* = 332, (21–138)	
How would you rate the amount of time it took from when you entered the clinic until you were seen by a counsellor?[a]				
I feel very/somewhat satisfied (%)	575 (94.1)	262 (93.2)	313 (94.8)	0.6820
I feel very/somewhat unsatisfied (%)	12 (2.0)	6 (2.1)	6 (1.8)	
Neutral (%)	24 (3.9)	13 (4.6)	11 (3.3)	
How would you rate the amount of time it took the counsellor to provide the pre-test counselling you received?[a]				
I feel very/somewhat satisfied (%)	596 (97.5)	270 (96.4)	326 (98.5)	–
I feel very/somewhat unsatisfied (%)	3 (0.5)	3 (1.1)	0 (0.0)	
Neutral (%)	12 (2.0)	7 (2.5)	5 (1.5)	
How would you rate the amount of time it took the counsellor to provide the health screening tests and test results to you?[a]				
I feel very/somewhat satisfied (%)	594 (97.2)	272 (97.1)	322 (97.3)	0.9264
I feel very/somewhat unsatisfied (%)	5 (0.8)	2 (0.7)	3 (0.9)	
Neutral (%)	12 (2.0)	6 (2.1)	6 (1.8)	
How would you rate the amount of time it took the counsellor to provide the test results and post-test counselling you received?[a]				
I feel very/somewhat satisfied (%)	594 (97.9)	273 (98.2)	321 (97.6)	–
I feel very unsatisfied (%)	1 (0.2)	1 (0.4)	0 (0.0)	
Neutral (%)	12 (2.0)	4 (1.4)	8 (2.4)	
How would you rate the amount of time you spent with the nurse for further consultation and referrals?[a]				
I didn't see the nurse (%)	201 (43.7)	195 (69.9)	6 (3.3)	<.0001
I feel very/somewhat satisfied (%)	257 (55.9)	83 (29.7)	174 (96.1)	
Neutral (%)	2 (0.4)	1 (0.4)	1 (0.6)	

IQR interquartile range, *SD* standard deviation
[a]Overall may not be equal to the sample size as a result of missing responses
Counsellor-led HTS per phase is inclusive of pre-test counselling, phase-inclusive screenings, and post-test counselli

Figure 3. PHRU Zazi Evaluation Study HTS Clinic Time Flow Chart by Phase (Phase 1, Feb-June 2018; Phase 2, June 2018–March 2019)

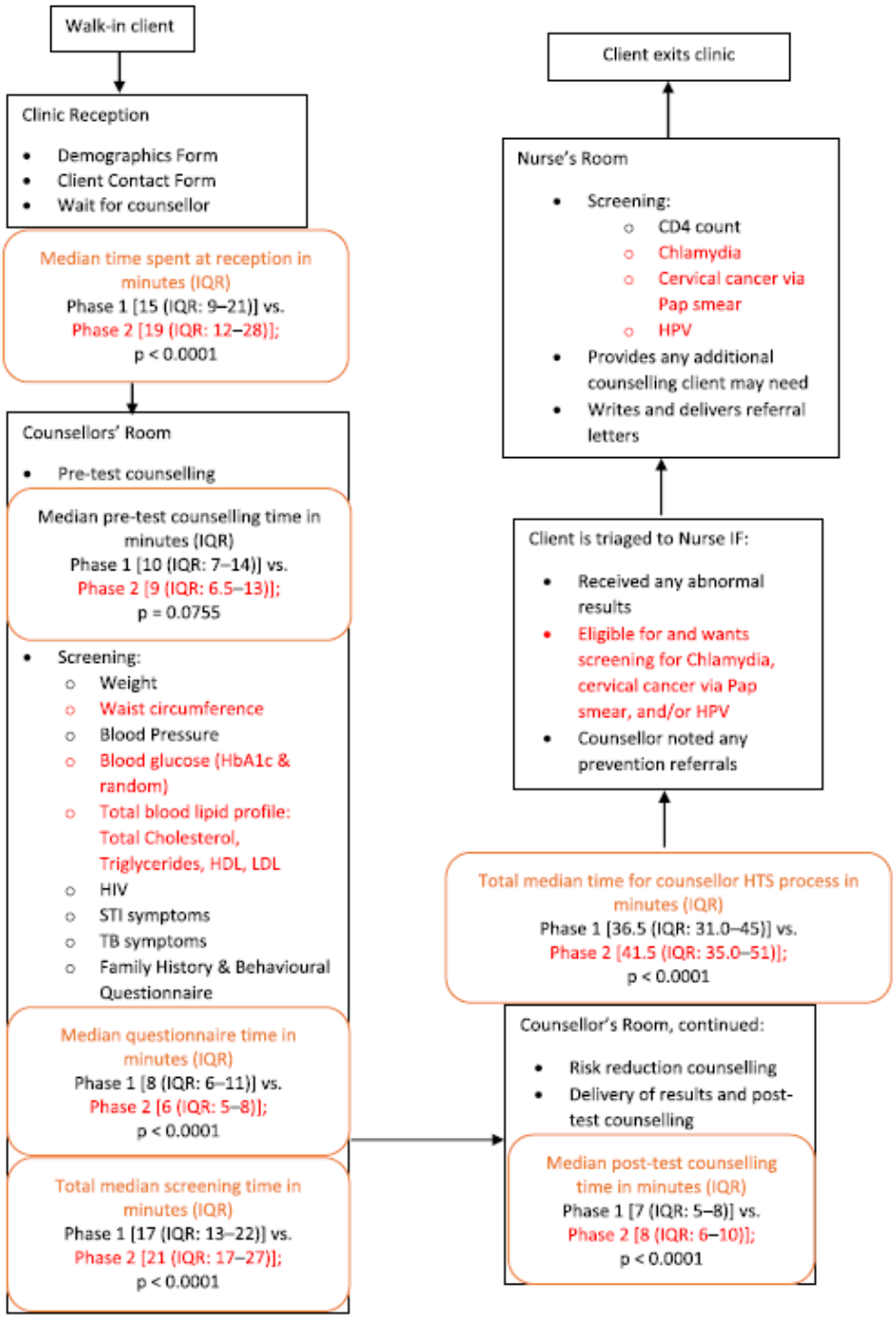


Fig. 3 PHRU Zazi Evaluation Study HTS Clinic Time Flow Chart by Phase (Phase 1, Feb-June 2018; Phase 2, June 2018–March 2019). IQR, interquartile range; HbA1c, glycated haemoglobin/average blood glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; STI, sexually transmitted infections; TB, tuberculosis; HPV, human papilloma virus. Black text denotes Phase 1 activities; black and red text denote Phase 2 activities. Orange text reports median clinic flow time in minutes

Factors associated with total time (in minutes) spent in the clinic

Controlling for sex, living together/married (est=6.548; p=0.0467), number of tests a client underwent (est=3.922; p<0.0001), and higher overall satisfaction score (est=1.210; p=0.0201) were associated with longer time spent in the clinic. Those who matriculated spent less time in the clinic (est=-7.250; p=0.0253) (Supplementary Table 1).

Supplementary Table 1. Factors Associated with Total Time (in Minutes) Spent in Zazi Clinic

	Univariate		Multivariate	
Variable	**Est (SE)**	**P-Value**	**Est (SE)**	**P-Value**
Age (in years)	-0.026 (0.134)	0.8492	-	-
Gender				
Female vs. Male	3.910 (2.958)	0.1867	-0.633 (3.081)	0.8373
Marital Status				
Divorced/widowed vs. Single	-3.775 (7.080)	0.5941	-2.728 (6.814)	0.6901
Living together/married vs. Single	7.809 (3.373)	0.0210	6.548 (3.285)	**0.0467**
Highest education				
Matriculated vs. Up To High School	-5.279 (3.304)	0.1106	-7.250 (3.233)	**0.0253**
Tertiary education vs. Up To High School	-6.974 (3.737)	0.0625	-4.591 (3.645)	0.2083
Number of tests done	4.497 (0.602)	<.0001	3.922 (0.686)	**<.0001**
Overall satisfaction score	2.060 (0.453)	<.0001	1.210 (0.519)	**0.0201**

Est (SE)= Estimates (Standard Error)

What clients liked by HTS model

There were 246 (86.6%, [n=246/284]) responders depicting what clients liked about the clinic in standard of care HTS. Of these, 49.6% (n=132/266) reported that they enjoyed the services and/or customer care they received. Two responders stated, 'Good services, as I am a regular participant' and 'Good service I got from reception to end'. Additionally, 12.8% (n=34/266) stated they liked the friendly and supportive staff they interacted with, and 9.4% (n=25/266)

shared they appreciated the clinic provider communication style. For example, one client shared, 'I was treated with respect and the staff was very friendly and kind. They explained to me everything and answered all my questions satisfactorily.' Other responses depicted clients liked feeling comfortable (6.4%, [n=17/266]), the in-depth and professional counselling session (4.1%, [n=11/266]), and the warm and welcoming clinic environment (3.4%, [n=9/266]).

In integrated NCD-HTS, 307 (92.2%, [n=307/333]) clients shared what they liked about ZAZI. The majority of responses reported that of Phase 1 responses – 35.5% (n=124/349) appreciated the service, specifically the new screenings; 22.3% (n=78/349) enjoyed the welcoming, professional and supportive staff; and 8.6% (n=30/349) liked the effective communication of and information shared by the health care providers. One client responded, 'The staff member are very patient and explain things very well.'

What clients disliked by HTS model

Of the 206 (72.5%, [n=206/284]) responders for standard of care HTS, 91.3% (n=190/208) shared they did not dislike anything about Zazi. Of the remaining responders, the most common reasons for dissatisfaction were with the amount of time spent waiting in the clinic (2.9%, [n=6/208]) and administration time spent during the clinic visit (i.e.; client registration systems and paperwork; 2.4%, [n=5/208]). Other reasons for dissatisfaction were that treatment (1%, n=2/208]), contraceptives (0.5%, [n=1/208]), and snacks (0.5%, n=1/208]) were not offered onsite; and outcome of results (unacceptance of one's HIV diagnosis), wanting additional screenings, and untidiness of the reception area (0.5%, [n=1/208] each).

Of the 300 (90.1%, [n=300/333]) responders for integrated NCD-HTS, 88.7% (n=268/302) disliked nothing. Of the remaining responses (n=34/302), the top two reasons for dissatisfaction were duration of the clinic visit (55.9%, [n=19/34]), with responses being 'I spent more time than expected' and '[I] waited for too long at reception'; and the amount of administrative paperwork conducted (17.7%, [n=6/34]).

What clients wish ZAZI would have provided

When integrated NCD-HTS clients were asked to share if they wished the clinic would have provided them anything else, 23.7% (n=79/333) made suggestions. Of these responders, 45.6% (n=36/79) wished medications – ART, and for both chronic conditions and over-the-counter – were available onsite. Additionally, 20.3% (n=16/79) requested additional services (e.g.;

prostate and breast cancer screening, regular follow-up calls, and home visits for terminally ill patients); and 16.5% (n=13/79) would have liked refreshments served. Only 7.6% (n=6/79) clients wished the clinic could minimise time spent waiting.

Discussion

This study reports a response of strong satisfaction from adult clients attending an integrated NCD-HTS clinic in Soweto, South Africa, regarding the counsellor-led HTS process and overall HTS experience, and with the time spent in clinic. Clients were appreciative of the newly integrated screenings and associated communication, and the welcoming clinic environment. Compared to standard of care HTS, including four additional counsellor-led NCD screening services (abdominal girth measurements, BMI categorizations, and blood cholesterol and glucose rapid testing) only increased the time of counsellor-led HTS by five minutes, on average. Clients who were married/living together, underwent more screenings, and had a higher overall satisfaction score spent significantly longer time within the clinic, while those who completed high school spent significantly less time in the clinic as compared to those who did not. While our study population demographics are similar to the general population of Soweto, increasing the likelihood of generalisability, the transferability of such an integrated HTS model, especially inclusive of nurse-led endocervical screenings, into the public sector would need further investigation.

Our study's integrated NCD-HTS model has shown a high level of client satisfaction with healthcare delivery system factors, such as the warm and welcoming environment, inclusive of professional and non-judgemental healthcare providers; screenings offered; communication of health information; and clinic flow time. This conflicts with other studies' findings that at the systems level, there are major gaps in safety, prevention, integration and continuity of care[29]. One in three patients across LMICs cited negative experiences with their health system in relation to attention, respect, communication, and length of visit – often shorter than five minutes; and less than one-quarter of people in LMICs believe their health system works well[29]. Specifically, as healthcare systems evolve to meet the growing demands associated with the NCD epidemic, there is potential for HIV-related stigma to influence where and how NCD care is provided for PLHIV and HIV-uninfected individuals[42, 43]. An emerging theme of a scoping literature review was that negative perceptions of healthcare providers – or fear of being mistreated due to stigma[44] - within HIV platforms may have a negative impact on the

engagement with NCD care, either located within or outside of HIV platforms, and therefore effect the NCD-care continuum[42]. Stigma is reported as being an increasing barrier to woman accessing cervical cancer screening, due to fear of the diagnoses' association with HIV[45]. While our results did corroborate with the other study's conclusion of overall satisfaction being associated with longer length of visit, over one in ten of our study participants were repeat clients in the short-term, which constitutes positive user experience. Furthermore, the great majority of all clients opted in to each NCD screening integrated within our HTS platform, including cervical cancer screening for women.

Regarding clinic flow time, historically HTS is conducted in about 45 minutes – ten minutes for pre-test counselling, 15–20 minutes to conduct the HIV rapid testing, and 15 minutes for post-test counselling[46]. The South African National HTS guidelines state that intensive and lengthy individual risk assessments during the pre-test counselling session is no longer needed or recommended[22]. Many providers in government health facilities simply do not have the time to perform detailed risk assessments due to the large number of clients. With the objective of PICT being timely detection of HIV and subsequent initiation of treatment, pre-test information can be simplified and shared through either individual or group educational outreach sessions, as long as they are presented in an age-appropriate manner[22, 47]. Though group sessions could decrease the HTS pre-test counselling time, group dynamics remain a challenge[46]. Post-test counselling may include individual risk assessments and risk reduction plans dependent on HIV status[47].

Zazi conducted individual - not group - pre-test counselling, and incorporated individual risk assessments and risk reduction plans into its post-test counselling as per national guidelines. While it took the counsellors a significantly longer time to conduct the rapid health screenings and post-test counselling in integrated NCD-HTS as compared to standard of care HTS, both HTS models of the counsellor-led HTS process were completed in a faster median time than the typical 45 minute HTS timeframe. This was largely due to the faster than average post-test counselling timeframes. The shorter post-test counselling sessions could reflect the eventual triage to the nurse for clients needing referrals and further counselling. More than 96% of clients in each HTS model responded they were 'very/somewhat satisfied' with the time it took to pass through the HTS process, and the large majority were 'very satisfied' with the entire way it was conducted.

Given the relatively small difference in time spent between the counsellor-led standard of care HTS and integrated NCD-HTS models, despite introducing four new NCD-precursor screening measures, it is important to consider investigating if the same quality of care standard is actually met – in both screening conduct and information-sharing. Some studies have shown there is high satisfaction with healthcare among LMICs, despite widespread quality deficits, potentially due to low expectations and users either lacking knowledge about what constitutes good quality or being resigned about the quality of available services[48]. A study has shown that high-reported patient satisfaction likely overstates the quality of health services due to positively framing statements, which induces bias. Evaluations including patient satisfaction surveys need to complement patient satisfaction measures with more objective measures of quality[49]. Perhaps our quality of counselling did suffer, as there were shorter than average counselling sessions and clients suggested more robust information sharing, such as explaining the new rapid testing machines and providing further health practice information. However, our clients' overall satisfaction score and increased number of screenings was associated with spending significantly more time in the clinic. This could potentially be attributable to the additional time spent providing client requested health information. Our clients of lesser education (i.e.; who had not yet matriculated) spent significantly more time in the clinic potentially due to longer discussions around health education.

With the addition of three, nurse-led endocervical screenings and increased client triage to the nurse to include NCD-referrals, the total median clinic time would increase even further and would likely push the integrated NCD-HTS clinic flow beyond the average HTS timeframe of 45 minutes. However, being an HTS clinic embedded within a research unit, there were also data collection aspects of Zazi that would not be implemented in government clinics, thus decreasing time spent. Clients shared their dislike for the time it took to complete such forms. For example, an extensive demographics form and client contact information sheet would not be distributed and completed in the waiting room, and screening would not include a lengthy family history and behavioural survey (median time of 8 and 6 minutes, for standard of care HTS and integrated NCD-HTS, respectively).

While the total integrated clinic time for integrated NCD-HTS was manageable for Zazi clients, it may not be possible for the public sector to scale up the same model of integrated services in a way that ensures the same level of positive user experience without additional human resources (i.e.; lay counsellors). Government clinics already have a heavy influx of patients and long queues. A qualitative study in South Africa reported as long as nurses are expected to

manage large number of patients each day in primary care, HIV and AIDS services are unlikely to be successfully integrated into PHC, as inadequate staffing and healthcare facility space will negatively impact service delivery[50]. This is especially true in countries like South Africa, which are implementing Universal Test and Treat and same-day initiation policies. However, a case study that integrated NCD screening and care services within an existing HIV programme – similar to Zazi's model - conducted in rural Malawi reported an improvement in access to NCD care for HIV-infected patients. The healthcare model's success was largely attributable to strong leadership, allowing for real-time discussions about challenges encountered and allowing for process improvement, staff ownership of their specific duties, and a well-defined and uniform patient flow process. However, it was stated a missing element was a patient satisfaction survey to track the impact of the clinic's redesign[51]. Furthermore, four studies examining the effects of various integrated models of care on HIV stigma have concluded some level of integration could potentially result in HIV-stigma reduction for PLHIV through combining care for HIV-uninfected NCD clients and PLHIV within the same facility[52-55].

In order to be scaled up within the public sector, the integrated NCD-HTS clinic model would have to utilise minimal paperwork/questionnaires in its clinic visit process, and employ enough clinic staff to support the client burden. Additionally, there would need to be clinic and staffing adjustments to accommodate women who desire cervical cancer screening, but through a scheduled appointment. Ideally, the healthcare staff conducting the rapid screenings would be well trained and confidently relied upon to conduct the testing, interpret findings, disseminate the results, and provide referrals without micromanagement. This would eliminate the need for and additional time spent to cross-check results and recommended referrals with a nurse or clinician, as was the process at Zazi. Due to the human resource shortfalls of health care practitioners, the public sector could replicate Zazi's counsellor-led integrated NCD-HTS model. At the very least, the integration of rapid blood glucose and cholesterol testing into standard of care HTS would be feasible, as the time ranged between an acceptable 35 and 51 minutes. If Pap smears and HPV screening are to be integrated for female patients to reap the health benefits, additional data on added time spent would need to be analysed.

Limitations

Most of the data captured in the Demographics Form, Client Contact forms, and Family History and Behavioural Questionnaire is affiliated with the PHRU Zazi HTS programme/study and

not part of routine public healthcare. For clients either self-administering or being assisted with the completion of the Demographics and Client Contact Forms at reception, the time spent at reception was lengthened. The completion of the Family History and Behavioural Questionnaire increased the time it took for the counsellors to conduct the HTS screenings.

The study unfortunately did not collect clinic flow time in a standardised manner for the pre-registration time, the time it took the counsellors to QA/QC all counsellor-led screening results with the nurse, or the time the clients spent with the nurse, and therefore, did not include it within this paper. Therefore, a timeframe is not provided for the endocervical screenings for women (Chlamydia rapid test, and HPV and cervical cancer screenings), writing of referral letters and any further counselling conducted by the nurse. Furthermore, there may be a social desirability bias affect clinic flow times between HTS models due to the Hawthorne effect (i.e.; clinic staff knowing they are being timed).

A limitation of the Client Clinic Exit Survey and its content thematic analysis is the interpretativism - the researchers' interpretation of the client response through their own understanding pair with thematic context. We tried to limit this by having multiple investigators agree on the analysis. The sample size of client responses per free-response question was also limited to how many clients actually chose to answer the question, rather than leave it blank. The five-point Likert response format was also subjective, in that the responses 'Very satisfied', 'Somewhat satisfied', etc. were not defined. Whereas not all variables had complete responses, the majority of participants responded with more than 98% response rate.

Additionally within integrated NCD-HTS, the Zazi clinic was assisting with HIV rapid test screening for the enrolment of women into HIV prevention trials conducted at PHRU. The higher volumes of females seen could be more of an intervention than by chance.

Despite the limitations, our data were reassuring, as we had limited missing data.

Conclusions

This study has shown that it is possible to integrate counsellor-led NCD rapid testing into standard of care HTS, yielding client satisfaction. While counsellor-led integrated NCD-HTS significantly increases time to the clinic flow, as compared to standard of care HTS, it is still within historical HTS timeframes. It is suggested that rapid blood cholesterol and blood glucose testing be integrated into the standard of care HTS within the public sector to extend prevention efforts and quickly identify otherwise undiagnosed pre-cursors of NCD, as well as HIV-

comorbidities. Studies regarding the transferability of these screenings into the public sector are required. While cervical cancer and HPV screenings were greatly appreciated by integrated NCD-HTS clients, further evidence on the impact to HTS clinic flow is needed to determine if such a robust integrated screening could be scaled up within the public sector.

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PAPER V

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Does peer-navigated linkage to care work? A cross-sectional study of active linkage to care within an integrated non-communicable disease-HIV testing centre for adults in Soweto, South Africa

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Does peer-navigated linkage to care work? A cross-sectional study of active linkage to care within an integrated non-communicable disease-HIV testing centre for adults in Soweto, South Africa.

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Abstract

Introduction: South Africa is the HIV epidemic epicentre; however, non-communicable diseases (NCDs) will be the most common cause of death by 2030. To improve identification and initiation of care for HIV and NCDs, we assessed linkage to care (LTC) in a HIV Testing Services (HTS) Centre before and after integrated testing for NCDs with optional peer-navigated linkage to care.

Materials Methods: This two-phase prospective, cross-sectional study was conducted at an adult HTS Centre in Soweto, South Africa. Phase 1 (February-June 2018) utilised standard of care (SOC) HTS services (blood pressure [BP], rapid HIV testing, sexually transmitted infections [STI]/Tuberculosis [TB] symptom screening) with passive referral for abnormal/positive results. Phase 2 (June 2018-March 2019) further integrated blood glucose/cholesterol/chlamydia rapid testing, with optional peer-navigated referral. Enrolled referred clients completed a telephonic follow-up survey confirming LTC/treatment initiation ≤3 months post-screening. Socio-demographics, screening results, time to LTC/treatment initiation peer-navigated referral uptake were reported. Analysis included Fisher's exact, chi-squared, Kruskal Wallis, and Student's T-tests. Thematic analysis was conducted for open-ended survey responses.

Results: Of 320 referrals, 40.0% were HIV-infections, 11.9% STIs, 6.6% TB, and 28.8% high/low BP. Of referred Phase 2 participants, 29.4% were for glucose and 23.5% cholesterol. Integrated NCD-HTS had significantly more client LTC for HIV (76.7%[n=66/86] vs 52.4%[n=22/42], p=0.0052) and clients LTC within a shorter average time (6-8 days [Interquartile range (IQR):1–18.5] vs 8–13 days [IQR:2–32]) as compared to SOC HTS. Integrated NCD-HTS clients initiated HIV/STIs/BP treatment on average more quickly as compared to SOC HTS (5 days for STIs [IQR:1-21], 8 days for HIV/BP [IQR:5-17 and 2-13, respectively] vs 10 days for STIs [IQR: 4-32], 19.5 days for HIV [IQR:6.5-26.5], 8 days for BP [IQR:2–29)]. Participants chose passive over active referral (89.1% vs 10.9%; p<0.0001). Participants rejecting peer-navigated referral preferred to go alone (55.7% [n=39/70]). Non-LTC was due to being busy (41.1% [n=39/95]) and not being ready/refusing treatment (31.6% [n=30/95]). Non-initiation of treatment post-LTC was due to normalised results assessed at clinic (49.7% [n=98/196]), prescribed lifestyle modification/monitoring (30.9% [n=61/196]), and poor clinic flow/congestion and/or further testing required (10.7% [n=21/196]).

Conclusions: Ensuring LTC and treatment initiation is critical to reduce disease-specific morbidity/mortality. Same-day treatment initiation is not achieved across disease platforms, despite peer-navigated referral. There are health systems barriers at entry to care. Additional research may identify best strategies for timely treatment initiation.

Keywords: HIV; non-communicable diseases; HIV Testing Services; integrated HIV Testing Services; health systems strengthening

Background

Since 2015, the Joint United Nations Programme on HIV/AIDS (UNAIDS) has been driving the elimination of the HIV pandemic by 2030 as a threat to global health. UNAIDS's fast-tracked strategy was to implement the 90-90-90 targets so that by 2020, 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and that 90% of all people receiving antiretroviral therapy will have viral suppression.[1] The epicentre of the HIV pandemic is in South Africa, which contains over 20% of the global burden.[2] As of 2017, South Africa's progress in the prevention, treatment and control of HIV falls below the 90-90-90 targets. Encouragingly, 84.9% of all PLHIV within South Africa know their status, yet only 70.6% of PLHIV who know their status are on ART, and of those, 87.5% are virally supressed. This equates to 59.9%

of all PLHIV in South Africa having initiated ART and 52.4% of all PLHIV being virally suppressed.[2] These data highlight the ongoing challenges within the HIV Care Cascade of severe patient attrition from HIV-diagnosis to treatment initiation. Downstream effects of low treatment coverage, including delayed treatment, comprise increases in morbidity and mortality, with additional, preventable onward transmission of HIV.[3]

Psychosocial barriers to seeking healthcare are known to cause patient attrition in the HIV care cascade.[4-6] Patient healthcare-seeking behaviour may be positively or negatively influenced at multiple levels: individual (e.g., acceptance of result, coping ability), relationship (e.g. social support, risk of intimate partner violence [IPV]),[7] community (e.g. stigma) and health systems (e.g. prior negative experiences with the health system which lead to lack of trust).[8] These challenges, leading to subsequent failed retention in care, are not unique to HIV management. Many of the barriers towards retention in the treatment cascade are consistently reported across both chronic communicable and non-communicable disease (NCDs) platforms.[9] Due to the typically weak healthcare systems in low and middle-income countries (LMICs), such as South Africa, chronic NCDs are presenting new and substantial challenges to both patients and healthcare providers.[9] For example, the routine, primary focus on treating acute diseases is creating fallout in the NCD cascade.[9-12] Currently, NCDs are predicted to cause almost three-quarters as many deaths as communicable, maternal, perinatal, and nutritional diseases combined, making them the most common causes of death in Africa by 2030.[13]

There is a critical need for evidence-based strategies to improve patient retention within the care cascade across all health domains. Innovative strategies addressing the aforementioned barriers to patient retention from diagnosis to care may increase linkage to care and treatment.[8] Passive referral (e.g.; only providing names and contact information for care and treatment services) is widely implemented in South Africa's public health sector across all platforms.[14] Passive referral leaves patients to overcome psychosocial barriers on their own. Active referral is a more facilitated approach, assisting the patient to remain engaged within the healthcare system, and in this context, reach care and initiate treatment. Various active referral methods, such as transport reimbursement to the referral clinic or telephonic follow-up with patients for continued health education, combat different patient retention barriers (i.e.; both individual-level barriers – resource-based and cognitive barriers, respectively).[15-17] Physically assisting patients with reaching their referrals could potentially address multiple

psychosocial-level barriers through the provision of an emotional support system, reducing internal stigma and helping the patient cope with their diagnosis.[18]

We present a cross-sectional study from the Zazi standard of care HIV testing services (HTS) clinic providing services for adult clients in Soweto, South Africa. Here, further integrated screenings for NCD risk factors were performed while also implementing optional assisted linkage to care – accompanied referral to the client's referral clinic of choice. In this manner, the integrated NCD-HTS model identified both HIV-infection and NCD precursors in its clients, and sought to decrease the fallout in the care cascade across disease platforms through its active linkage to care. The aim of this study was to compare the client linkage to care and treatment initiation between the two, independent clinic phases within the same facility: standard of care HTS with passive referral vs integrated NCD-HTS with optional active referral; as well as obtain HTS client feedback surrounding the active referral strategy.

Methods

Study Design

This is a prospective study utilising both cross-sectional and client follow-up survey data of a health screening programme at the Zazi HTS Centre. The programme implemented two different approaches of health screening (standard of care HTS vs integrated NCD-HTS), each with their own mode of patient referral (passive only vs a choice between passive or active referral). Standard of care HTS with passive linkage to care operated from 19 February 2018 through 14 June 2018. Counsellors conducted height, weight, and blood pressure (BP) measurements, sexually transmitted infection (STI) and tuberculosis (TB) symptoms screenings, and HIV rapid testing. Integrated NCD-HTS with optional navigated linkage to care immediately followed, from 18 June 2018 through 28 March 2019, within the same clinic space operated by the same healthcare providers. In addition to the standard of care HTS screenings, integrated NCD-HTS also provided BMI classifications, rapid testing for both blood glucose (both random and average HbA1c) and cholesterol (via full lipid profile) for all HTS clients; and rapid Chlamydia testing for women. Within integrated NCD-HTS, clients had the option of a clinic staff member accompanying them to their referral clinic of choice, with the help of a driver, if needed.

Setting

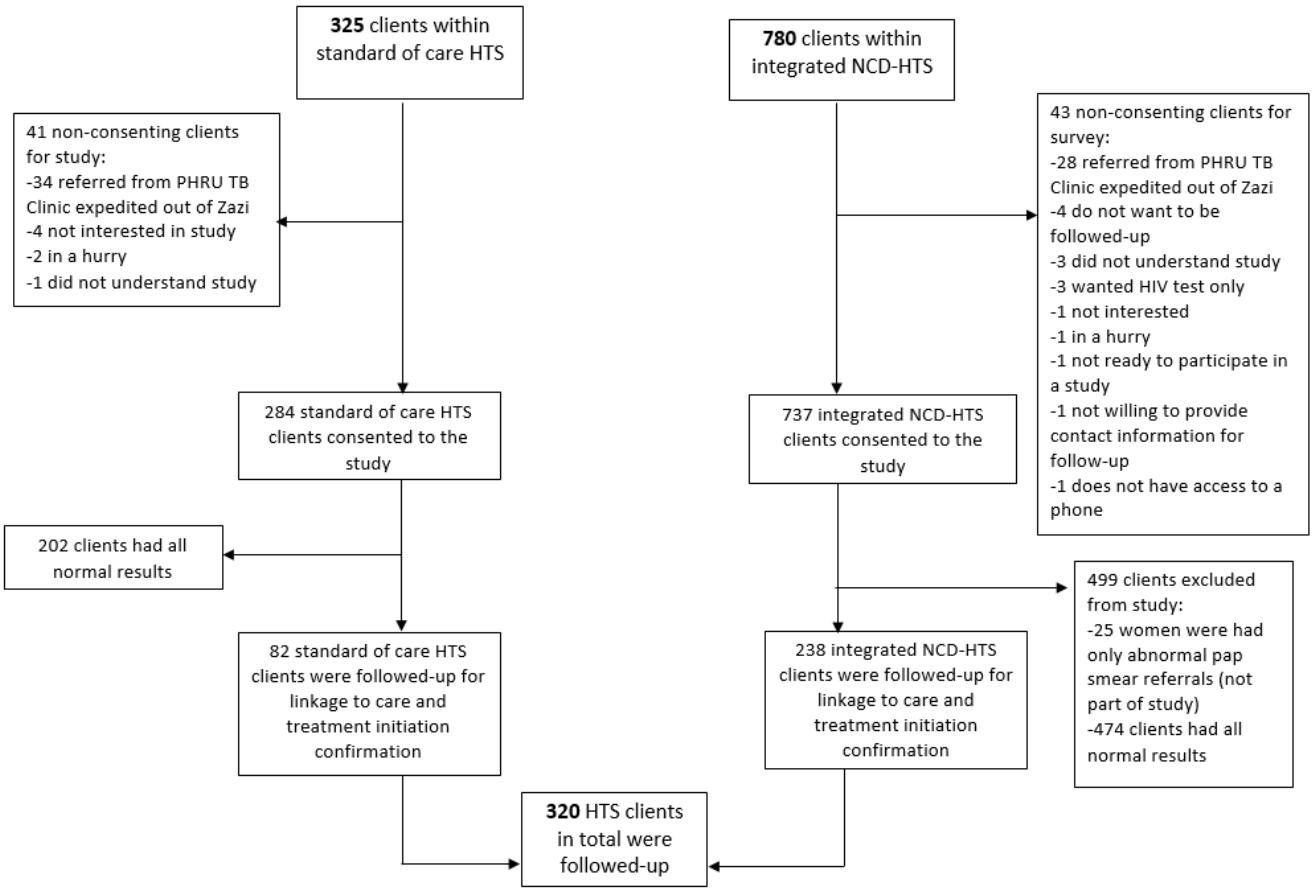
The Zazi HTS centre at the Perinatal HIV Research Unit (PHRU) is a leading research centre within the Wits Health Consortium, affiliated with the University of the Witwatersrand Faculty of Clinical Medicine, situated at Chris Hani Baragwanath Academic Hospital within Soweto, South Africa.

Sampling and Sample Size

The study sample was a convenience sample comprised of all eligible (see: Inclusion and Exclusion Criteria below) walk-in standard of care HTS and integrated NCD-HTS clients presenting to the clinic during the aforementioned timeframe of operation.

Figure 1 depicts the participant flow from eligible walk-in clients through to enrolled study participants for each phase.

Figure 1 Standard of Care HTS (19 February – 14 June 2018) vs Integrated NCD-HTS (18 June 2018 – 28 March 2019) Participant Flow Chart, Zazi HTS Centre in Soweto, South Africa



HIV Testing Services, HTS; Non-communicable diseases, NCDs; Perinatal HIV Research Unit, PHRU; Tuberculosis, TB.

Inclusion and Exclusion Criteria

Eligibility criteria: at least 18 years of age; able to communicate in either English, IsiZulu and/or Sesotho; able and willing to provide written or verbal informed consent (with impartial witness if failed literacy assessment) for both the HTS health screening procedures and for participation in the study-related Linkage to Care Follow-up surveys, and have been referred to the client's local clinic of choice for at least one abnormal or positive screening result (see: Study Measures: Abnormal Results / Referrals). Each participant had to either own or have access to a mobile or landline telephone and be willing to share that telephonic contact number with study staff for use in study follow-ups.

Any HTS phase-specific consenting client was included in the aggregate data capture.

Exclusion criteria: Immediate need for higher level of care; confirmed TB.

Data Collection and Management

Client literacy was assessed through asking each client to read the first paragraph of the HTS programme informed consent. Client demographical questionnaires were either self-collected by literate clients in the reception area or collected with the assistance of clinic staff for illiterate clients. Clinical data were collected by the three study counsellors and one nurse. All referral letters were given to clients by the study nurse, and all client linkage to care follow-up data was collected by counsellors and Linkage Navigators (paid clinic staff managing active linkage to care). All data were collected through questionnaires/surveys and screenings and recorded directly onto paper forms comprising the PHRU HTS client file. Data from client files were cleaned and verified prior to entry into the Research Electronic Data Capture (REDCap) database.

Study Measures

Demographics

Data were collected on sex, age, race, nationality, ethnic group, marital status, highest level of education, source of income, and details regarding home residence – type of housing, source of water and fuel for cooking and lighting, type of toilet facility, as well as possession of household and ownership items.

Abnormal or Positive Screening Results / Referrals

Standard of care HTS clients were given a referral for care and treatment if they had any of the following: high (>140/90 mmHg) or low (<90/60 mmHg) BP, one or more STI and/or TB

symptom(s) according to national syndromic management guidelines,[19] and/or HIV-infection.

The referrals for integrated NCD-HTS included standard of care HTS referrals, as well as the following: hyperglycaemia (HbA1c ≥ 6.5 mmol/L and/or random blood glucose ≥ 11 mmol/L), high total cholesterol (≥5 mmol/L), and positive rapid Chlamydia test (STI referral).

Client Linkage to Care Follow-up Survey

We developed a structured HTS client linkage to care follow-up survey consisting of both closed-ended questions, assessing if the client had made it to their referral(s) and if so, were initiated on treatment; and open-ended questions for free response. The responses to the open-ended questions helped us to further understand the responses to the closed-ended questions (e.g.; why the client refused active linkage to care (if integrated NCD-HTS), the date of linkage to care and treatment initiation, and/or reasons behind not reaching referrals and/or being initiated on treatment).

For standard of care HTS, the first follow-up call was conducted one month after the client obtained his/her referral(s). If there were any outstanding referrals identified as remaining, the follow-up call was repeated for those specific referrals at month two, and then at month three, if needed.

In the case of integrated NCD-HTS, if after the clinic visit, a client chose active linkage to care, the Linkage Navigator made the first follow-up call at the end of that day (i.e.; same day as clinic visit). If at the time of follow-up, there were still outstanding referrals identified as remaining, the HTS client was asked if they would like the help of a Linkage Navigator for the remaining referrals. If so, an appointment for navigated referral was scheduled. With any referrals not having been attended by the client, the survey was repeated at two weeks, one month, two months, and three months, if needed.

Client Linkage to Care and Treatment Initiation

For the purposes of the study, successful linkage to care followed the CDC definition of, *a newly-identified HIV-infected person engaging with a health care provider within 30 days of diagnosis* (at the Zazi HTS centre).[16] This definition was adopted for linkage to care for all conditions – communicable and NCDs, alike – and for successful treatment initiation, which was additionally defined as an initiation of pharmacological treatment. If a client reported linkage to care and/or treatment initiation between one and three months after referral, they

were considered to have *delayed linkage to care and/or delayed treatment initiation*. A client for which follow-up contact was not successful (i.e. the HTS client did not answer their mobile phone) or who had not yet reached his or her referral appointment within three months was defined as *lost to follow-up*.

Quantitative Data Analysis

Descriptive statistics (e.g. medians and interquartile ranges as well as means and standard deviation) were determined for continuous variables. Frequencies and their percentages were determined for categorical variables and stratified by phase (Phase1 and Phase2) where appropriate.

To test statistical significance for categorical measures stratified by phase, Fisher's exact or chi-square tests were used. Comparisons for descriptive statistics, such as medians (interquartile ranges) and means (standard deviations) for continuous variables by HTS phase were determined using the Kruskal-Wallis test and Student's T-Test. The standard of care and integrated NCD HTS (overall, passive, and active) care cascades from client health screenings through initiation of treatment were presented graphically.

All statistical analyses were conducted in SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC) using SAS/STAT procedures.

Data Analysis of Open-ended Questions

Using SAS Enterprise Guide 7.1 (SAS Institute, Cary NC), a print out of all open-ended responses per survey question was obtained. The first author read through each text response to gain an overall understanding of the data and identify thematic codes. All codes were collated in an excel spreadsheet under the pre-determined themes. If a code did not fit under a pre-determined theme, new themes were created. Categories were then analysed further to create more detailed sub-categories.

The responses in each category were counted using SAS. A response to a particular question could be assigned to multiple categories, which may increase the sample size of certain variables. All non-responses to a particular question (free responses left blank by participants) and responses agreed upon as non-logical were not included in the analysis, thus decreasing the sample size for that question. Agreement on the data analysis was achieved through a second review by a co-author.

Ethical Considerations

The ZAZI health programme and embedded study were both approved by the University of Witwatersrand, Human Research Ethics Committee (Wits HREC). The study was reviewed in accordance with the Centers for Disease Control and Prevention (CDC) human research protection procedures and was determined to be programmatic research, but CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes (CGH 2018-017). All voluntary participants provided written informed consent prior to any study procedures being conducted.

Results

Although 1,021 participants consented for follow-up, only 314 individuals were eligible for this study as they had abnormal or positive results that required referral. Of these clients, six participated in both HTS phases, and therefore there were 82 sets of client referrals from the standard of care HTS and 238 client referrals from NCD-HTS for follow-up (N=320 client referrals). Figure 1 depicts the participant flow.

Demographics

Of the 314 individual participants, the median age was 37.0 years (IQR:29.0-44.0), most were female (67.8%, n=213/314), single (69.7%, n=219/314), with incomplete high school education (42.2%, n=132/313), and were neither employed or self-employed (i.e. income came from social/disability grants, parents, and pensions) (43.2%, n=135/312). HIV prevalence was high (44.4%, n=139/313), one third of participants had high BP readings (33.4%, n=105/313), and 2.2% (n=7/313) had low BP readings. Standard of care HTS had significantly more participants who were from outside of South Africa (8.8%[n=7/80] vs 1.7%[n=4/232]; p=0.0033), divorced/widowed (12.2%[n=10/82] vs 3.4%[n=8/232]; p=0.0034), and who had high BP (50.0%[n=41/82] vs 27.6%[n=64/232]; p<0.0001) as compared to integrated NCD-HTS. However, integrated NCD-HTS had significantly more participants who were living together/married than standard of care HTS (27.6%[n=64/232] vs 15.9%[n=13/82]; p=0.0338).

Integrated NCD-HTS had more females (70.3%, n=163/232) and those with incomplete high school education (43.5%, n=101/232).(Table 1).

Table 1 Baseline Characteristics of Participants by HTS Phase at Zazi HTS Centre: Standard of Care HTS, 19 Feb-14 June 2018; Integrated NCD-HTS, 18 June 2018-28 March 2019

Variable	Total	Standard HTS &Passive LTC	NCD-HTS & Optional Active LTC	P-Value
Age (in years)				
18-24 (%)	43/314 (13.7)	10/82 (12.2)	33/232 (14.2)	0.9642
25-34 (%)	92/314 (29.3)	24/82 (29.3)	68/232 (29.3)	
35-44 (%)	102/314 (32.5)	28/82 (34.1)	74/232 (31.9)	
≥45 (%)	77/314 (24.5)	20/82 (24.4)	57/232 (24.6)	
Median age (IQR)	37.0 (29.0-44.0)	37.0 (31.0-43.0)	37.0 (28.0-44.0)	0.5818
Sex				
Female (%)	213/314 (67.8)	50/82 (61.0)	163/232 (70.3)	0.1219
Male (%)	101/314 (32.2)	32/82 (39.0)	69/232 (29.7)	
Race				
Black African (%)	311/314 (99.0)	80/82 (97.6)	231/232 (99.6)	0.1081
Coloured/White (%)	3/314 (1.0)	2/82 (2.4)	1/232 (0.4)	
Nationality				
Other (%)	11/312 (3.5)	7/80 (8.8)	4/232 (1.7)	**0.0033**
South African (%)	301/312 (96.5)	73/80 (91.3)	228/232 (98.3)	
Ethnic group				
Other (%)	43/311 (13.8)	13/81 (16.0)	30/230 (13.0)	0.4587
Sotho (%)	55/311 (17.7)	15/81 (18.5)	40/230 (17.4)	
Tsonga (%)	28/311 (9.0)	6/81 (7.4)	22/230 (9.6)	
Tswana (%)	27/311 (8.7)	11/81 (13.6)	16/230 (7.0)	
Xhosa (%)	32/311 (10.3)	7/81 (8.6)	25/230 (10.9)	
Zulu (%)	126/311 (40.5)	29/81 (35.8)	97/230 (42.2)	
Marital status				
Divorced\widowed (%)	18/314 (5.7)	10/82 (12.2)	8/232 (3.4)	**0.0034**
Living Together\married (%)	77/314 (24.5)	13/82 (15.9)	64/232 (27.6)	**0.0338**
Single (%)	219/314 (69.7)	59/82 (72.0)	160/232 (69.0)	0.6129

Variable	Total	Standard HTS &Passive LTC	NCD-HTS & Optional Active LTC	P-Value
Highest education				
No formal education (%)	5/313 (1.6)	1/81 (1.2)	4/232 (1.7)	0.2669
Primary school (%)	14/313 (4.5)	2/81 (2.5)	12/232 (5.2)	
High school (%)	132/313 (42.2)	31/81 (38.3)	101/232 (43.5)	
Matriculated (%)	102/313 (32.6)	25/81 (30.9)	77/232 (33.2)	
Tertiary education (%)	60/313 (19.2)	22/81 (27.2)	38/232 (16.4)	
Source of money to live on?				
Employed (%)	115/312 (36.9)	31/82 (37.8)	84/230 (36.5)	0.8070
Self-employed (%)	62/312 (19.9)	15/82 (18.3)	47/230 (20.4)	
Social/Disability grant (%)	45/312 (14.4)	11/82 (13.4)	34/230 (14.8)	
Parents (%)	40/312 (12.8)	10/82 (12.2)	30/230 (13.0)	
Pension (%)	14/312 (4.5)	6/82 (7.3)	8/230 (3.5)	
Unemployed (%)	36/312 (11.5)	9/82 (11.0)	27/230 (11.7)	
HIV Result				
Positive (%)	139/313 (44.4)	43/82 (52.4)	96/231 (41.6)	0.0885
Negative (%)	174/313 (55.6)	39/82 (47.6)	135/231 (58.4)	
Syndromic STI				
1+ symptoms (%)	38/314 (12.1)	11/82 (13.4)	27/232 (11.6)	0.6716
No symptoms (%)	280/314 (89.2)	71/82 (86.6)	209/232 (90.1)	
Syndromic TB				
1+ symptoms (%)	21/314 (6.7)	4/82 (4.9)	17/232 (7.3)	0.4453
No symptoms (%)	293/314 (93.3)	78/82 (95.1)	215/232 (92.7)	
Blood Pressure				
High (%)	105/313 (33.4)	41/82 (50.0)	64/232 (27.6)	**<0.0001**
Low (%)	7/313 (2.2)	4/82 (4.9)	3/232 (1.3)	
Normal (%)	202/313 (64.3)	37/82 (45.1)	165/232 (71.1)	
Blood glucose				
High (%)	66/230 (28.7)	-	66/230 (28.7)	-
Normal (%)	164/230 (71.3)	-	164/230 (71.3)	
Total Cholesterol (TC)				
High (%)	57/232 (24.6)	-	57/232 (24.6)	-
Low (%)	22/232 (9.5)	-	22/232 (9.5)	
Normal (%)	153/232 (65.9)	-	153/232 (65.9)	

Six Integrated NCD-HTS participants were excluded, as they were also within standard of care HTS.

NB: Of the HIV-infected participants, 9 were not followed up because they were already on treatment, and 2 were of those excluded from the table. Abnormal blood pressure within this table was reported as an average of the two blood pressure readings during screening and not entirely a reflection of true referrals. Of those with high blood glucose, 4 were of those excluded from the table. There was 1 participant with high blood cholesterol who was not followed up.
Human Immunodeficiency Virus (HIV), HIV Testing Services (HTS), Linkage to Care (LTC), Non-communicable disease (NCD), Interquartile range (IQR), Sexually Transmitted Infections (STIs), Tuberculosis (TB)

Care Cascades with Time to Care and Treatment Initiation by HTS Phase and Referral

Overall, Standard of Care Referrals from both standard of care and integrated NCD-HTS

Of 320 client referrals across both standard of care and integrated NCD-HTS, 40.0% were referred for HIV-infection, 11.9% for STIs, 6.6% for TB symptoms, and 28.8% for either high or low BP. The majority of these referred clients were linked to care within three months for ART (68.8%, n=88/128), STIs (73.7%, n=28/38), TB (71.4%, n=15/21), and high/low BP (84.8%, n=78/92) (Supplementary Table 1). It took a median time of 6.5 days (IQR:2.0-19.0), 8.0 days (IQR:3.0-23.0) and 10.0 days (IQR:2.0-20.0) for clients referred for STIs, abnormal BP, and TB, respectively, to link to care for these conditions, overall (Table 2).

Supplementary Table 1 Standard of Care HTS (19 Feb-14 June 2018) vs Integrated NCD-HTS (18 June 2018 – 28 March 2019): Linkage to Care and Treatment Initiation in Soweto, South Africa

	Linkage to Care				Treatment Initiation			
Variable	**Total**	**Standard HTS & passive LTC**	**NCD-HTS & optional active LTC**	**P-Value**	**Total**	**Standard HTS & passive LTC**	**NCD-HTS & optional active LTC**	**P-Value**
HIV/ART (%)	88/128 (68.8)	22/42 (52.4)	66/86 (76.7)	**0.0052**	78/88 (88.6)	20/22 (90.9)	58/66 (87.9)	0.6981
STI (%)	28/38 (73.7)	5/11 (45.5)	23/27 (85.2)	**0.0117**	22/28 (78.6)	5/5 (100.0)	17/23 (73.9)	0.1976
TB (%)	15/21 (71.4)	3/4 (75.0)	12/17 (70.6)	0.8605	1/15 (6.7)	1/3 (33.3)	0/12 (0.0)	-
BP (%)	78/92 (84.8)	29/37 (78.4)	49/55 (89.1)	0.1607	29/78 (37.2)	11/29 (37.9)	18/49 (36.7)	0.9159

HIV Testing Services (HTS), Linkage to Care (LTC), Human Immunodeficiency Virus (HIV), Antiretroviral Therapy (ART), Sexually Transmitted Infections (STI), Tuberculosis (TB), Blood Pressure (BP), Non-communicable disease (NCD)

Table 2 Successful vs Delayed Linkage to Care and Time from Referral to Care by HTS Phase in Soweto, South Africa: Standard of Care HTS Passive Referral, 19 Feb-14 June 2018 vs Integrated NCD-HTS Optional Active Referral, 18 June 2018-28 March 2019

Variable	HIV/ART	TB	STI	BP	Blood glucose	Blood cholesterol
Total HTS Linkage						
Successful (%)	75/127 (59.1)	14/21 (66.7)	24/38 (63.2)	65/92 (70.7)	48/70 (68.6)	39/56 (69.6)
Delayed (%)	12/127 (9.5)	1/21 (4.8)	4/38 (10.5)	13/92 (14.1)	9/70 (12.9)	7/56 (12.5)
Lost to follow-up (%)	40/127 (31.5)	6/21 (28.6)	10/38 (26.3)	14/92 (15.2)	13/70 (18.6)	10/56 (17.9)
Median (IQR)	7.0 (2.0-18.0)	10.0 (2.0-20.0)	6.5 (2.0-19.0)	8.0 (3.0-23.0)	7.0 (1.0-21.0)	11.5 (3.0-19.0)
Min, Max	(0-59)	(0-34)	(0-76)	(0-73)	(0-73)	(0-73)
Standard of Care HTS						
Successful (%)	19/42 (45.2)	2/4 (50.0)	3/11 (27.3)	21/37 (56.8)	-	-
Delayed (%)	3/42 (7.1)	1/4 (25.0)	2/11 (18.2)	8/37 (21.6)	-	-
Lost to follow-up (%)	20/42 (47.6)	1/4 (25.0)	6/11 (54.6)	8/37 (21.6)	-	-
Median number of days (IQR)	8.0 (2.0-22.0)	10.0 (2.0-34.0)	10.0 (4.0-32.0)	13.0 (6.0-32.0)	-	-
Min, Max	(0-58)	(2-34)	(2-35)	(1-65)	-	-
Overall Integrated NDC-HTS						
Successful (%)	56/85 (65.9)	12/17 (70.6)	21/27 (77.8)	44/55 (80.0)	48/70 (68.6)	39/56 (69.6)
Delayed (%)	9/85 (10.6)	-	2/27 (7.4)	5/55 (9.1)	9/70 (12.9)	7/56 (12.5)
Lost to follow-up (%)	20/85 (23.5)	5/17 (29.4)	4/27 (14.8)	6/55 (10.9)	13/70 (18.6)	10/56 (17.9)
Median (IQR)	7.0 (2.0-17.0)	8.0 (1.5-18.5)	6.0 (1.0-17.0)	8.0 (2.0-14.0)	7.0 (1.0-21.0)	11.5 (3.0-19.0)
Min, Max	(0-59)	(0-27)	(0-76)	(0-73)	(0-73)	(0-73)
Integrated NCD-HTS Passive Linkage						
Successful (%)	47/72 (65.3)	7/12 (58.3)	20/24 (83.3)	41/51 (80.4)	41/60 (68.3)	34/51 (66.7)
Delayed (%)	8/72 (11.1)	-	2/24 (8.3)	5/51 (9.8)	8/60 (13.3)	7/51 (13.7)

Variable	HIV/ART	TB	STI	BP	Blood glucose	Blood cholesterol
Lost to follow-up (%)	17/72 (23.6)	5/12 (41.7)	2/24 (8.3)	5/51 (9.8)	11/60 (18.3)	10/51 (19.6)
Median number of days (IQR)	8.0 (3.0-19.0)	17.0 (2.0-20.0)	6.5 (2.0-17.0)	8.0 (2.0-14.0)	7.0 (1.0-21.0)	11.0 (3.0-19.0)
Min, Max	(1-59)	(1-24)	(0-76)	(0-73)	(0-73)	(1-73)
Integrated NCD HTS Active Linkage						
Successful (%)	9/13 (69.2)	5/5 (100.0)	1/3 (33.3)	3/4 (75.0)	7/10 (70.0)	5 /5(100.0)
Delayed (%)	1/13 (7.7)	-	-	-	1/10 (10.0)	-
Lost to follow-up (%)	3/13 (23.1)	-	2/3 (66.7)	1/4 (25.0)	2/10 (20.0)	-
Median number of days (IQR)	0.0 (0.0-6.0)	6.0 (0.0-10.0)	0.0 (0.0)	6.0 (0.0-15.0)	3.5 (0.0-23.5)	12.0 (10.0-15.0)
Min, Max	(0-49)	(0-27)	(0)	(0-15)	(0-49)	(0-27)

NB: One referred participant was excluded from HIV/ART due to missing date of linkage to care.

Successful linkage to care **was defined as have been linked to care within 30 days (one month);** ***Delayed linkage to care*** **was defined as having been linked to care between one and three months;** ***Lost to follow-up*** **is defined as not having confirmed linkage to care by three months. There were no significant differences in time from referral to linkage to care for any referral type between HTS phases, overall. There were significantly more NCD-HTS participants who chose passive linkage who achieved successful linkage to care as compared to those who chose passive linkage (83.3%[n=20/24] vs 33.3%[n=1/3]; p=0.0495.**

Human Immunodeficiency Virus (HIV), Antiretroviral Therapy (ART), Tuberculosis (TB), Sexually Transmitted Infections (STIs), Blood Pressure (BP), Interquartile Range (IQR), Non-communicable Disease (NCD), HIV Testing Services (HTS)

Of all eligible participants who did link to care across both HTS phases, 88.6% (n=78/88) were initiated on ART, 78.6% (n=22/28) were initiated on treatment for STIs, 6.7% (n=1/15) began TB treatment, and 37.2% (n=29/78) were initiated on anti-hypertensive medications (Supplementary Table 1). Of all referred clients, 60.9% (n=78/128) were initiated on ART, and 57.9% (n=22/38) were treated for STIs, 4.8% (n=1/21) for TB, and 31.5% (n=29/92) for high BP (Supplementary Table 1).

Across HTS phases, it took an average of 2.0 days (IQR:2.0-2.0; for TB) and 9.0 days (IQR:5.0-21.0; for ART) for clients to initiate treatment (Table 3). Treatment was not needed for a high proportion of those linked to care for high/low BP in either HTS Phase (standard of care HTS: 58.6%[n=17/29]; integrated NCD-HTS:61.2%[n=30/49]).(Table 3) None of the participants referred for low BP were initiated on treatment across HTS phases.

Table 3 Successful vs Delayed Treatment Initiation and Time from Referral to Treatment Initiation by HTS Phase in Soweto, South Africa: Standard of Care HTS Passive Referral, 19 Feb-14 June 2018 vs Integrated NCD-HTS Optional Active Referral, 18 June 2018-28 March 2019

Variable	HIV/ART	TB	STI	BP	Blood glucose	Blood cholesterol
Total HTS Linkage						
Successful (%)	68/88 (77.3)	1/3 (33.3)	18/28 (64.3)	13/78 (16.7)	13/57 (22.8)	14/46 (30.4)
Delayed (%)	10/88 (11.4)	-	4/28 (14.3)	16/78 (20.5)	1/57 (1.8)	2/46 (4.4)
Treatment not needed (%)		-	6//28 (21.4)	47/78 (60.3)	40/57 (70.2)	29/46 (63.0)
Lost to follow-up (%)	10/88 (11.4)	2/3 (66.7)	-	2/78 (2.6)	3/57 (5.3)	1/46 (2.2)
Median (IQR)	9.0 (5.0-21.0)	2.0 (2.0-2.0)	6.5 (2.0-28.0)	8.0 (2.0-18.0)	14.5 (7.0-24.0)	11.5 (1.5-21)
Min, Max	(0-70)	(2-2)	(0-76)	(0-63)	(1-35)	(0-46)
Standard of Care HTS						
Successful (%)	17/22 (77.3)	1/3 (33.3)	3/5 (60.0)	9/29 (31.0)	-	-
Delayed (%)	3/22 (13.6)	-	2/5 (40.0)	2/29 (6.9)	-	-
Treatment not needed (%)	-	1/3 (33.3)	-	17/29 (58.6)	-	-
Lost to follow-up (%)	2/22 (9.1)	1/3 (33.3)	-	1/29 (3.5)	-	-
Median number of days (IQR)	19.5 (6.5-26.5)	2.0 (2.0-2.0)	10.0 (4.0-32.0)	8.0 (2.0-29.0)	-	-
Min, Max	(1-57)	(2-2)	(2-35)	(1-63)	-	-
Overall Integrated NCD-HTS Linkage						
Successful (%)	51/66 (77.3)	-	15/23 (65.2)	17/49 (34.7)	13/57 (22.8)	14/46 (30.4)
Delayed (%)	7/66 (10.6)	-	2/23 (8.7)	1/49 (2.0)	1/57 (1.8)	2/46 (4.4)
Treatment not needed (%)	-	-	6/23 (26.1)	30/49 (61.2)	40/57 (70.2)	29/46 (63.0)
Lost to follow-up (%)	8/66 (12.1)	-	-	1/49 (2.0)	3/57 (5.3)	1/46 (2.2)
Median (IQR)	8.0 (5.0-17.0)	-	5.0 (1.0-21.0)	8.0 (2.0-13.0)	14.5 (7.0-24.0)	11.5 (1.5-21.0)
Min, Max	(0-70)	-	(0-76)	(0-33)	(1-35)	(0-46)

Variable	HIV/ART	TB	STI	BP	Blood glucose	Blood cholesterol
Integrated NCD-HTS Passive Linkage						
Successful (%)	42/56 (75.0)	-	14/22 (63.6)	15/46 (32.6)	10/49 (20.4)	11/41 (26.8)
Delayed (%)	6/56 (10.7)	-	2/22 (9.1)	1/46 (2.2)	1/49 (2.0)	2/41 (4.9)
Treatment not needed (%)	-	-	6/22 (27.3)	29/46 (63.0)	35/49 (71.4)	28/41 (68.3)
Lost to follow-up (%)	8/56 (14.3)	-	-	1/46 (2.2)	3/49 (6.1)	-
Median number of days (IQR)	9.0 (6.0-17.5)	-	6.5 (1.5-24.5)	8.5 (3.0-16.0)	13.0 (5.0-21.0)	11.0 (2.0-19.0)
Min, Max	(1-70)	-	(1-76)	(0-33)	(1-35)	(1-46)
Integrated NCD-HTS Active Linkage						
Successful (%)	9/10 (90.0)	-	1/1 (100.0)	2/3 (66.7)	3/8 (37.5)	3/5 (60.0)
Delayed (%)	1/10 (10.0)	-	-	-	-	-
Treatment not needed (%)	-	-		1/3 (33.3)	5/8 (62.5)	1/5 (20.0)
Lost to follow-up (%)	-	-	-	-	-	1/5 (20.0)
Median number of days (IQR)	2.5 (0.0-8.0)	-	0.0 (0.0)	3.0 (0.0-6.0)	24.0 (11.0-27.0)	12.0 (0.0-27.0)
Min, Max	(0-49)	-	(0)	(0-6)	(11-27)	(0-27)

NB: One referred participant was excluded from HIV/ART due to missing date of linkage to care.
***Successful treatment initiation* was defined as having initiated treatment within 30 days (one month); *Delayed initiation of treatment* was defined as having initiated treatment between one and three months; *Lost to follow-up* was defined as not having confirmed treatment initiation by three months. *Treatment not needed* did not exclude prescribed lifestyle modification.**
The time in days from referral to treatment initiation was shorter in integrated NCD-HTS relative to standard of care HTS for ART [12.8 (SD=13.9) vs. 17.8 (SD=13.9); p=0.1762] and BP [9.5 (SD=9.7) vs. 18.1 (SD=22.6); p=0.2543]. It took significantly less number of days for participants who were linked to care for ART to be initiated on treatment in integrated NCD-HTS as compared to standard of care HTS [0.98 (SD=2.5) vs. 5.84 (SD=9.0); p=0.0319]. Human Immunodeficiency Virus (HIV), Antiretroviral Therapy (ART), Sexually Transmitted Infections (STI), Tuberculosis (TB), Blood Pressure (BP), Interquartile Range (IQR), Non-communicable disease (NCD), HIV Testing Services (HTS)

Standard of Care HTS vs Overall Integrated NCD-HTS

Overall, integrated NCD-HTS – with its optional active referral - had a larger proportion of clients linked to care for HIV, STIs, and high/low BP; with significantly more referred clients linked to care for ART and STIs as compared to standard of care HTS (76.7%[n=66/86] vs. 52.4%[n=22/42], p=0.0052; and 85.2%[n=23/27] vs. 45.5%[n=5/11], p=0.0117; respectively; Figures 2a&2b). Overall, integrated NCD-HTS also linked clients to care within a shorter time on average, across all conditions, as compared to standard of care HTS (the shortest being 6.0 days for STIs [IQR:1.0-17.0] with the longest being both 8.0 days for TB [IQR:1.5-18.5] and 8.0 days for high/low BP [IQR:2.0-14.0] vs the shortest being 8.0 days for HIV [IQR:2.0-22.0] and the longest being 13.0 days for high/low BP [IQR:6.0-32.0]).(Table 2)

Not excluding those clients who linked to care but were not initiated on treatment, standard of care HTS – with passive referral, only - had higher proportions of clients who were linked to care subsequently initiated on treatment for each condition as compared to integrated NCD-HTS (Figures 2a & 2b). However, integrated NCD-HTS initiated its clients on treatment in a shorter amount of time for HIV, STIs, and BP compared to standard of care HTS - the shortest time being 5.0 days for STIs [IQR:1.0-21.0] and the longest time being both 8.0 days for ART [IQR:5.0-17.0] and 8.0 days for high BP [IQR:2.0-13.0] vs the shortest time being 8.0 days for high BP [IQR:2.0-29.0] and the longest time being 19.5 days for ART [IQR:6.5-26.5].

For the referrals specific to integrated NCD-HTS, 81.4% (n=57/70) and 82.1% (n=46/56) of clients referred for hyperglycaemia and cholesterol were linked to care; and of those, 24.6% (n=14/57) and 34.8% (n=16/46) were initiated on treatment, respectively (Figure 2b). It took 14.5 days on average (IQR:7.0-24.0) for clients to initiate treatment for hyperglycaemia and 11.5 days on average (IQR:1.5-21.0) for high cholesterol. A high proportion of clients did not need treatment once re-assessed at the referral clinic for each condition – 70.2% (n=40/57) of referred clients for high glucose and 63.0% (n=29/46) of referred clients for high cholesterol, respectively (Tables 2&3).

Figure 2 Standard of Care (19 Feb-14 June 2018) & Integrated NCD-HTS (18 June 2018-28 March 2019) Care and Treatment Cascades in Soweto, South Africa

Only HIV-infected clients who had not already been initiated on ART were referred. Abnormal results for BP take the average of two readings, while referrals were given to clients with two abnormal readings. One integrated NCD-HTS client with high cholesterol was not referred. Significantly more clients referred for ART and STIs were linked to care in NCD-HTS as compared to standard of care HTS (76.7%[n=66/86] vs. 52.4%[n=22/42], p=0.0052; and 85.2%[n=23/27] vs. 45.5%[n=5/11], p=0.0117; respectively). Significantly more Phase 2 participants chose passive referral over active referral (89.1% [n=212/238] vs. 10.9% n=26/238]; p<0.0001). Of the participants who were referred for STIs, significantly more were linked to care who chose passive referral as compared to active linkage to care (91.7% [n=22/24] vs. 33.3% [n=1/3]; p=0.0073) compared to active linkage to care. Sexually Transmitted Infections (STIs), Tuberculosis (TB), Human Immunodeficiency Virus (HIV), Antiretroviral Therapy (ART)

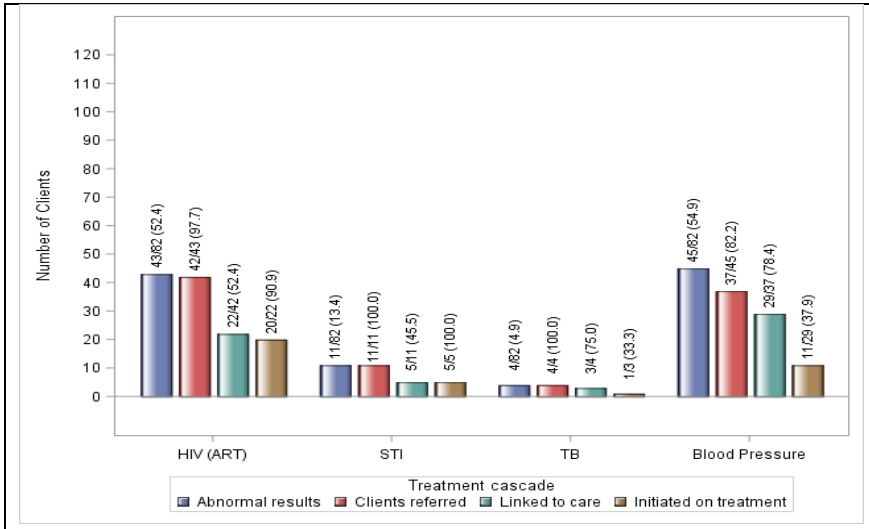


Figure 2a: Standard of Care HTS Cascade with Passive Linkage to Care

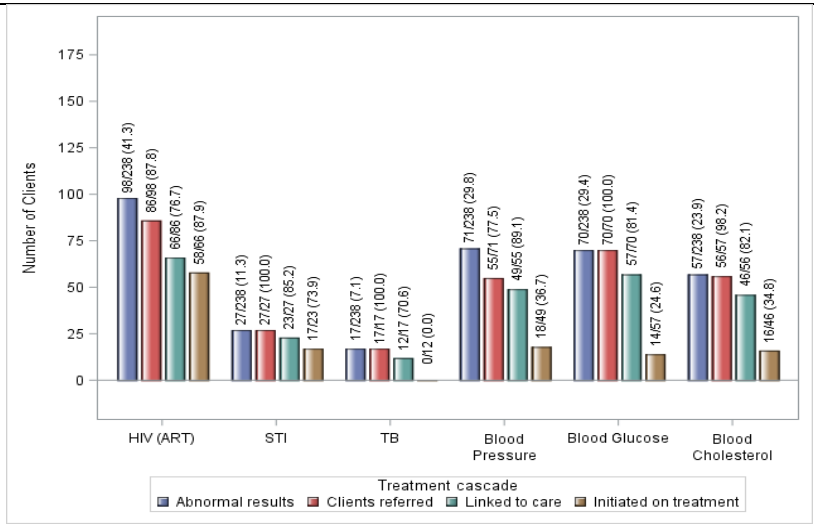


Figure 1b: Overall Integrated NCD-HTS Cascade

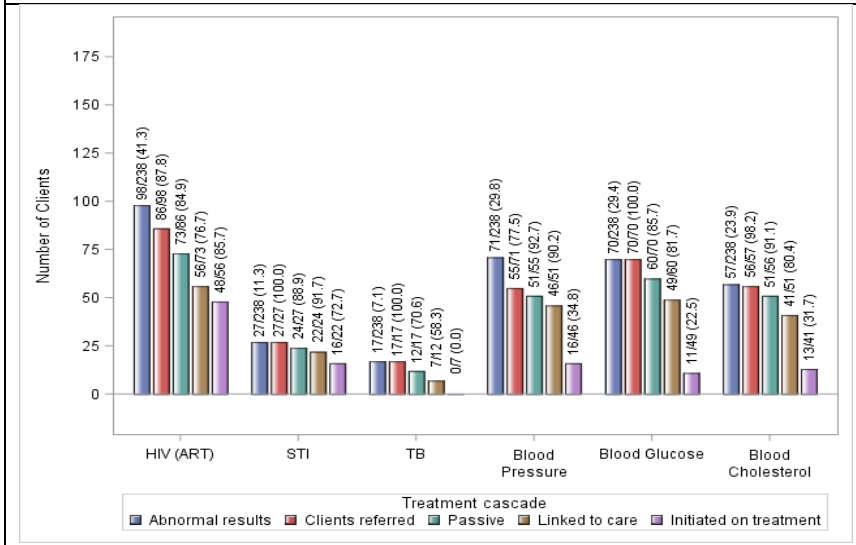


Figure 2c: Integrated NCD-HTS Cascade with Passive Linkage to Care

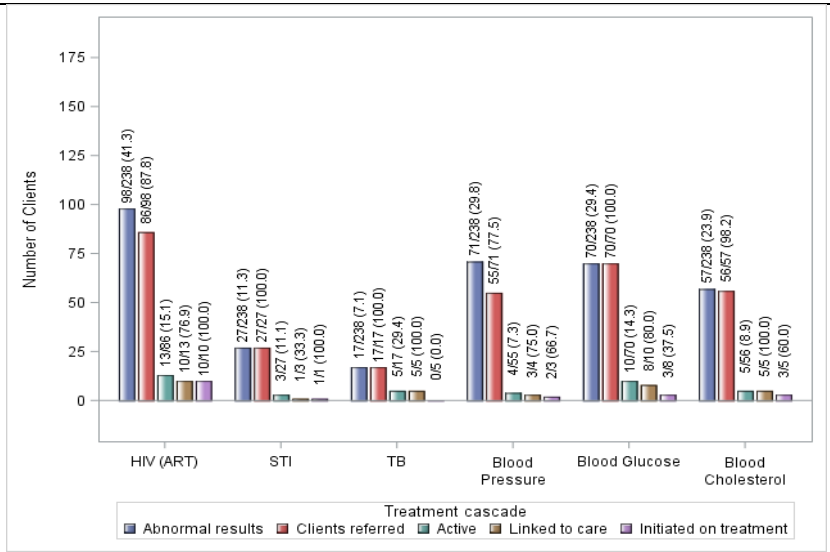


Figure 2d: Integrated NCD-HTS Cascade with Active Linkage to Care

Integrated NCD-HTS Passive vs Active Linkage to Care and Treatment

Figures 2c & 2d show the integrated NCD-HTS care and treatment cascade for referred clients electing either passive or active linkage to care and treatment.

Significantly more participants chose passive referral over active referral (89.1% [n=212/238] vs. 10.9% [n=26/238]; p<0.0001). Of the participants referred for STIs who were linked to care, significantly more chose passive referral as compared to active referral (91.7% [n=22/24] vs. 33.3% [n=1/3]; p=0.0073). There were no other statistically significant differences between passive and active linkage to care and treatment initiation (Supplementary Table 2).

Across conditions, a high proportion of integrated NCD-HTS participants were passively linked to care, ranging from 91.7% (n=22/24) for STIs to 58.3% (n=7/12) for TB. Those linked to care for STI were linked within the lowest average number of days of 6.5 (IQR: 2.0-17.0), whereas those reaching care for TB did so within the highest average number of days (17.0, IQR: 2.0-20.0) (Table 2).

The majority of integrated NCD-HTS clients who were passively linked to care for ART and did reach care were initiated on treatment successfully (75.0%, n=42/56) within an average number of days of 9.0 (IQR:6.0-17.5). STI passive referrals also had a high number of participants successfully initiated on treatment (63.6%, n=14/22). A large proportion of passively referred clients within integrated NCD-HTS did not need to initiate treatment after further assessment: 63.0% (n=29/46) for BP clients, 71.4% (n=35/46) and 68.3% (n=28/41) of clients with hyperglycaemia and high blood cholesterol, respectively. Of the 10 participants who were actively linked to care for ART within integrated NCD-HTS, 90.0% were successfully initiated on treatment in an average of 2.5 (IQR:0.0-8.0) days. (Table 3)

Supplementary Table 2 Comparing Passive and Active Linkage to Care and Treatment Initiation within Integrated NCD-HTS in Soweto, South Africa; 18 June 2018-28 March 2019

		Confirmed Linkage to Care			Confirmed Initiation of Treatment		
Variable	**Referred**	**Passive**	**Active**	**P-Value**	**Passive**	**Active**	**P-Value**
Care & Treatment							
HIV/ART (%)	86/238 (36.1)	56/73 (76.7)	10/13 (76.9)	0.9868	48/56 (85.7)	10/10 (100.0)	0.2057
STI (%)	27/238 (11.3)	22/24 (91.7)	1/3 (33.3)	0.0073	16/22 (72.7)	1/1 (100.0)	0.5436
TB (%)	17/238 (7.1)	7/12 (58.3)	5/5 (100.0)	0.1316	-	-	-
BP (%)	55/238 (23.1)	46/51 (90.2)	3/4 (75.0)	0.3479	16/46 (34.8)	2/3 (66.7)	0.2670
Blood Glucose (%)	70/238 (29.4)	49/60 (81.7)	8/10 (80.0)	0.9001	11/49 (22.5)	3/8 (37.5)	0.3592
Cholesterol (%)	56/238 (23.5)	41/51 (80.4)	5/5 (100.)	0.2789	13/41 (31.7)	3/5 (60.0)	0.2098

Significantly more clients chose passive referral over active referral (89.1% [n=212/238] vs. 10.9% n=26/238]; p<0.0001)
Non-communicable diseases (NCDs), HIV Testing Services (HTS), Human Immunodeficiency Virus (HIV), Sexually Transmitted Infections (STI), Tuberculosis (TB), Blood Pressure (BP)

Reasons for Choosing Passive over Active Linkage to Care

There were 67 responders who shared 70 total reasons as to why they chose passive referral over active referral (n=67/212, 31.6%). The main reason stated was that the client preferred to go alone (55.7%). Other reasons described were the close proximity and/or familiarity of the referral clinic (11.4%) and choosing to self-support (8.6%) (e.g.; '*I believe I have to take responsibility and go alone*' and '*I will [have to] go to the clinic [alone] anyway for my treatment*'). Having one's own transport (7.1%) and/or support system (5.7%) (e.g.; the support of a partner, family member, friend, or work colleague), and wanting privacy or having a referral letter to present to the clinic (2.9%, each) were other reasons for choosing passive linkage to care. Overall, 5.7% expressed they did not like the idea of navigated linkage to care.

Reasons for Not Successfully Linking to Care

There were 75 responses received by clients across both HTS phases yielding 95 reasons for not successfully linking to care across all referrals. Of the 95 reasons, 41.1% were due to being too busy to attend the referral but were still planning on going and 23.2% were not yet ready or needed to absorb their results prior to seeking care and/or treatment services. Other clients were unable to attend their referrals due to various reasons (i.e.; having been sick or hurt, having relocated or been travelling, not having enough money for transport to the clinic, or due to personal and/or family issues; 14.7%). There were blunt refusals towards obtaining treatment from clients referred for HIV-infection and/or high BP, (8.4%). One client referred for high BP shared: *'[I] never went to the clinic and [I] will not go. [I am] not ready to start treatment at the clinic, they'd want to [initiate me]*'. Some clients wished to wait for their partner to participate in couples' HIV counselling and testing before seeking treatment (4.2%).

There were a few barriers (3.2% in total) encountered at the point of entry into the health system (i.e.; not receiving help due to results not being looked at by the provider, having run out of time at the clinic, and the nurse not understanding the referral letter).For example, one client shared: *'[I] gave the nurse the referral letter, but they only focused on the BP and Cholesterol [referrals and] didn't check [my] STI symptoms'*. Another client shared: *'[I] didn't have enough time to be checked for TB when [I] went to the clinic for [my] STI [referral] as [I] had to go to work'*.

Two responses from clients referred for hyperglycaemia and high blood cholesterol shared that they chose to drink traditional African medicine (i.e.; *muti*), instead. Other responses regarded (STI) symptoms having cleared up, forgetting about their referral, and stigma-related reasons

serving as a deterrent for linking to care (1.1%, each). For example, one client referred for ART shared: *'[I do not] have money to go to the clinic and [I am] not comfortable… because there is family member [there] and [the] clinic is [in my] hood so [I am] comfortable but [I am] making a plan'.*

Reasons for Not Being Initiated on Treatment

There were 160 responses received by clients across both HTS phases yielding 196 reasons for not initiating treatment across all referrals. Of the 196 reasons, 49.7% were due to BP, blood glucose and/or blood cholesterol having normalised and/or receiving a negative STI and/or TB test result upon being re-checked at the referral clinic. For NCD risk factor referrals (i.e.; BP, blood glucose and cholesterol), 16.2% were prescribed a healthy lifestyle modification rather than medication, ['*Client went to the clinic, but they didn't initiate her. They said she must boost her iron by changing her diet and eat[ing] more of the food that boosts iron.*']; 14.7% were to undergo continued monitoring; and 6.1% were already initiated on treatment prior to their diagnosis.

Other reasons for non-initiation were that laboratory tests were conducted (e.g.; blood and/or sputum analysis), administrative tasks had to be completed (e.g.; ART adherence classes), and follow-up appointments were required prior to initiation of treatment (6.1%). For example, three of these clients who had been referred for ART shared similar reasons as follows: ['*She was given a date to come back after blood was collected, but [she] hasn't [gone] back due to hectic work schedule'*]. A fourth HIV-infected client shared: *['...[I am] still attending adherence classes and still [need] to go back when free at work…'*].

Additionally, 4.6% were either not helped due to the clinic being full or just not having their condition checked, ['*I couldn't open file, because the clinic was full.*'] and ['*They said they won't give me treatment, because it is caused by stress - even when it was 168 over 110.*']; 1.0% were given an initial pill to control their high BP and/or hyperglycaemia, not a prescription, ['*The tests were not high enough for him to be initiated on treatment, but they gave him a pill to help stabilize the sugar and will continue monitoring.*']; and one client (0.5%) self-reported that she could not receive STI treatment as she was found to be pregnant.

Discussion

Our study presents a comparison between standard of care HTS with passive referral and integrated NCD-HTS with optional navigated (active) referral. We have identified that there is

still immense fallout within the treatment cascade from referral to care and treatment across disease platforms, regardless of the referral mode. Despite policies propagating same day ART initiation, the time from referral to treatment initiation was found to span an average of nine days; and for other conditions, time to initiation ranged from an average of two to 14.5 days. Significantly more referred patients preferred the standard of care passive referral method as compared to assisted referral. Regardless, having active referral as an option did aid in linking significantly more HIV-infected clients to care than solely offering passive referral. However, this strategy did not translate to significantly more referred PLHIV initiated on ART. We identified individual-level barriers and failures at the health systems point of entry which barred efficient initiation of treatment across disease platforms, inclusive of the public healthcare sector improperly implementing its healthcare policies and/or guidelines.

Out of all HIV-infected study participants, three-quarters were linked to care and two-thirds were initiated on ART. In resource-limited settings, such as sub-Saharan Africa, it is reported that as much as 40% of PLHIV who are diagnosed are not linked to treatment services,[20-22] and late initiation has not decreased over the past decade.[23] With the most crucial piece of HTS being its linkage to care and treatment services for the timely provision of treatment/therapy, the NDoH has passed various policies and guidelines to expedite treatment initiation. South Africa was among the first countries in Africa to adopt the WHO's Universal Test and Treat policy, introducing the policy in-country in September 2016.[24] Having previously only initiated treatment for those with a CD4 < 200 cell/mm3.[25, 26] ART services underwent a massive expansion to implement the strategy of offering all persons diagnosed with HIV-infection initiation of treatment irrespective of CD4+ count.[27] Furthermore, same-day initiation (SDI), advocating for ART initiation on the day of HIV diagnosis, followed exactly one year later. Three years later, despite these initiatives, still less than two-thirds of PLHIV have entered care and started ART.[2, 28] Our study corroborates this data.

While some HIV-infected participants did achieve SDI of ART, the overwhelming majority did not. While this may be attributable to the clinic not providing treatment on-site (SDI typically applies to treating facilities also administering rapid testing), understanding why a patient achieves or fails in timely treatment initiation requires understanding treatment-seeking behaviours which are influenced by factors at multiple, complex levels (e.g.; individual, community-based, systems/structural-levels).[4, 5, 29, 30]. This study identified individual and health systems barriers towards treatment initiation for both HIV and NCD risk factors, contributing to attrition within both the HIV and NCD care cascades.

Half of our study participants who didn't link to care across disease platforms either actively or passively refused treatment (e.g.; refusing their referral letter vs sharing they had been too busy to attend clinic for various, supposed reasons); while one-quarter were not ready to engage with treatment at diagnosis, needing time to absorb their results. While our study did not collect further information as to why clients were not treatment-ready, a previous cross-sectional study conducted between December 2008 and December 2009 within our same study site - the Zazi HTS Centre in Soweto, South Africa - showed that of over 2,500 adults testing HIV-infected and eligible for treatment, 20% refused ART. The leading reason for treatment refusal was that the patient felt 'healthy' (37%), despite refusers having a median CD4+ cell count of 110 cells/mm3 and triple the rate of active tuberculosis as seen in non-refusers.[6] Patients' perceived health and the perception that one does not need to start treatment without the presence of symptoms has been a long contributing reason for ART treatment refusal amongst various HIV-infected populations (i.e.; women, men who have sex with men, etc.).[31-34] Fear of losing one's health and/or beauty due to medication, and through that, unwanted disclosure of status have also been documented reasons for treatment refusal.[4, 35] The perceived visual and psychological side-effects of ART (e.g.; body dysmorphic syndromes, feeling of lethargy) may outweigh the benefits of treatment for an HIV-infected individual.[35] This finding, along with additional studies on various HIV-infected populations (i.e. serodiscordant couples, pregnant women, individuals), support the idea that PLHIV may have a subjective feeling of health and wellness that is not innately related to their actual clinical status, which therefore affects their engagement with care.[35-39] This may also be true for patients with referred NCD risk factors, as many conditions do not present any symptoms (i.e.; hypertension, hyperglycaemia, hypercholesterolemia).[40-42] Chronic diseases (both HIV and NCDs, alike) require daily adherence of medication, and perceived treatment regimen demands and side effects are known deterrents within populations of lower income with poor health literacy.[43]

Our study participants who did link to care with the intention of initiating treatment still experienced health system barriers towards treatment initiation at the point of care: non-adherence of healthcare providers to current treatment policies/guidelines and an overburdened health care system.

Despite the UTT and SDI policies, our study provides evidence of PLHIV having additional blood testing conducted (including CD4 count) and/or being required to complete three ART adherence counselling modules prior to initiating treatment at a scheduled follow-up appointment. We also identified stage 2 hypertensive patients who were not initiated on

medication as per national guidelines,[44] and/or patients with uncontrolled NCD risk factors (i.e.; had already initiated treatment, but remained with abnormal screening results) who did not have their current treatment regimens re-assessed and/or adjusted for optimal health outcomes. A large proportion of our clients with NCD risk factors self-reported they were told they 'did not need treatment [with pharmaceuticals]' after being re-assessed at the referral clinic after successfully linking to care. Overall, three in five referred clients were told they did not need to initiate treatment for abnormal BP or high cholesterol, with none of the participants referred for low BP initiated on treatment across HTS phases; and seven in ten referred clients did not need to initiate treatment for high glucose. It is possible that the confirmatory testing methods used at referral clinics differed from those used at the Zazi HTS Centre, yielding different results (e.g.; fasting plasma glucose testing vs our average blood glucose testing). Additional research would be needed to determine if this was true, and if so, a reassessment of standard of care protocols within the public health sector is critical. It is also possible that the current national guidelines for case management were just not followed. For example, most patients with NCD risk factors were correctly prescribed lifestyle modification measures; however, it is also recommended such measures be prescribed in tandem with medication.[44]

Additionally, our clients' self-reported reasons eluded to the overburdened health care system as still being a deterrent to treatment initiation. Many of our study participants cited they were not helped due to the clinic being too full, or if they were seen by a healthcare provider for comorbidities, some conditions deemed less critical (i.e.; cholesterol) were not checked or addressed as the provider did not have enough time. Government clinics already have a heavy influx of patients and long queues, which are often paired with inadequate staffing and healthcare facility space, negatively impacting service delivery.[45-47] Not only are each of these cases missed opportunities for intervention, which would decrease the likelihood of morbidity and mortality, but the patient must have continued mental resilience to re-engaged with the healthcare system that failed them.[48, 49] While a known challenge towards achieving timely linkage to care and initiation of treatment is passive referral,[14] our study identified yet another challenge – significantly more referred study participants actually prefer passive as compared to assisted linkage to care, with most participants sharing they simply preferred to go alone. Perhaps the reasoning could more truly be related to experienced internal and fear of external stigma, which drives the desire to be alone. Studies have found internalised shame felt by people living with disease can create self-defeating beliefs, leading to demoralization and the desire to conceal one's status for fear of social isolation.[35] Within the

inter-personal context, there are social-motivational aspects which also affect entry into care. Attitudes regarding privacy, confidentiality, and interactions with healthcare providers all play a role. Furthermore, an emerging theme of a scoping literature review depicted negative patient perceptions of healthcare providers – largely the fear of being mistreated due to stigma[50] - within HIV platforms may also have a negative impact on the engagement with NCD care, either located within or outside of HIV platforms, and therefore effect the NCD-care continuum.[51] Even though passive linkage to care was preferred, our study shows active linkage to care achieved its goal – an HTS model offering active linkage to care as an option did link significantly more HIV-infected patients to care and in a shorter amount of time on average. However, these results could be attributable to other study-related aspects. Integrated NCD-HTS offered additional screenings which could have resulted in more HIV-infected clients referred with more than one condition. Patients with multiple chronic conditions tend to use services more frequently.[52] Though not statistically significant, integrated NCD-HTS also had more female clients; and ART uptake is higher among women than men.[53]

Regardless, the literatures does show a strong social support system—whether from family, friends and/or the greater community—can allow for disclosure, coping, and resilience required to mitigate challenges associated with initiating treatment. Our active referral provided such a support system, which creates a sense of humanity and belonging, and is known to decrease stigmatised beliefs.[35, 54] A study amongst 559 HIV-infected adolescents and youth in Kenya, showed significant improvements in linkage to and early retention in care after the implementation of peer-navigated services and psychosocial support were offered.[55] A systematic review and meta-analysis of community and facility-based HIV testing and linkage to care gaps in sub- Saharan Africa reported that facilitated or ‘active’ linkage services achieved both higher linkage to care and ART initiation than passive referral.[56] The same could be described for NCD linkage to care. A study among referred hypertensive patients in rural Uganda that included an intervention package consisting of a short counselling session after diagnosis, a referral appointment within 30 days, and a transportation voucher, resulted in 83% linkage to care.[57]

Our study stresses that active linkage to care does indeed work. It then becomes important for the public healthcare sector to emphasise a case managing approach through community health workers or case managers. These dedicated staff members can forge close relationships with their patients, supporting and following the patient’s journey from diagnosis of disease through initiation of treatment and treatment adherence (even to achievement of viral load suppression

for HIV-infected patients). With this strategy in place, there will no longer be a need to offer passive referral, as case management is an active approach.

Limitations

This study was a cross-sectional study and may not explain causality. This study was a direct comparison, which is descriptive, and therefore, there was no control for any parameters. The standard of care HTS and integrated NCD-HTS populations had slightly different characteristics, which may have limited the ability to compare them. For example, during integrated NCD-HTS, the HTS clinic was assisting with HIV rapid test screening for the enrolment of women into HIV prevention (pre-exposure prophylaxis) trials conducted at PHRU, as well as conducting screenings for cervical cancer and human papilloma virus (HPV) for female clients. Although there was not a statistically significant difference in proportions of clients by sex between the two HTS phases, this may have encouraged the higher volumes of women attending the clinic during the integrated NCD-HTS phase, as the sex ratio presented within the standard of care phase is a more typical representation.

Some sample sizes for comparisons were small, specifically the sample size for those opting for active linkage to care, which may have affected statistical impact. The sample size of client responses per free-response question was also limited to how many clients actually chose to answer the question; responses left blank were not included in the analysis.

Our reports of linkage to care and treatment initiation were self-reported by the clients and not able to be confirmed through other sources. A large proportion of clients linking to care self-reported that they were told they did not need treatment, and this also remains unconfirmed. We were unable to confirm linkage to ART clinics using TIER.net, an accessible electronic database managed by government ART clinic staff to capture data elements and indicators required to monitor HIV and ART services. Additionally, a proportion of clients were lost to follow-up, which may have caused an underestimation or overestimation of reported linkage to care and treatment initiation.

Conclusions

In resource-limited settings, such as sub-Saharan Africa, it is reported that as much as 40% of PLHIV who are diagnosed are not linked to treatment services,[20-22] and late initiation has not decreased over the past decade.[23] This is not unique to HIV programmes, but also for other chronic diseases. Patients who are linked to care, cycle in and out of care with varying

levels of adherence.[21] Cost-effective strategies are required to improve linkage to and retention in care and treatment services for people diagnosed with all chronic disease. While prompt linkage to treatment and care is ideal and should be encouraged, strategies need to also address various, complex levels of psychosocial and health systems barriers at the point of entry into care and treatment.[58] We believe assisted linkage to care has promise, but only within a package of other active linkage to care strategies. Additional research is required to identify best strategies for timely treatment initiation, and perhaps healthcare provider case management approaches should be emphasised.

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Disclaimer

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APPENDIX B. TURNITIN REPORT

The PhD candidate would like to report that of the top seven listings, numbers 1, 2, 3, 6 and 7 (11%) were referencing the PhD candidate's own work.

Turnitin Originality Report

Processed on: 15-Jul-2020 2:33 PM SAST
ID: 1357802127
Word Count: 63382
Submitted: 1

1021544:PhD_Thesis_FINAL_Kathryn_L_Hopkins_15... By Kathryn Hopkins

Similarity Index	Similarity by Source	
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https://www.researchsquare.com/article/c7e45a80-30b2-4689-b2a9-679bde4bfbb6/v1

3% match (publications)
Kathryn L Hopkins, Khuthadzo Hlongwane, Kennedy Otwombe, Janan Dietrich et al. "Demographics and health profile on precursors of non-communicable diseases in adults testing for HIV in Soweto, South Africa: a cross-sectional study", BMJ Open, 2019

1% match (Internet from 17-Jul-2019)
https://sajhivmed.org.za/index.php/hivmed/article/view/796/1255

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http://ecuo.org

1% match (Internet from 15-Jul-2020)
https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-020-05256-9

<1% match (publications)
Kathryn L. Hopkins, Khuthadzo E. Hlongwane, Kennedy Otwombe, Janan Dietrich et al. "Level of adult client satisfaction with clinic flow time and services of an integrated non-communicable disease-HIV testing services clinic in Soweto, South Africa: a cross-sectional study", BMC Health Services Research, 2020

APPENDIX C. ETHICS CLEARANCE APPROVALS

APPENDIX C1. Original Wits Human Research Ethics Committee (Medical) Clearance Certificate

12-06-17;09:10PM; ; # 1/ 7

University of the Witwatersrand, Johannesburg

Human Research Ethics Committee: (Medical)
FWA Registered No IRB 00001223

SECRETARIAT: Suite 189, Private Bag x2600, Houghton 2041, South Africa Tel: +27-11-274 9200 Fax: +27-11-274 9281

09 June 2017 **FAXED & COURIERED**

Dr K Hopkins,
Perinatal HIV Research Unit
PO Box 114
Soweto
Diepkloof
1034

Fax: 011 989 9762

Dear Dr Hopkins,

PROTOCOL: ZAZI EVALUATION STUDY - EVALUATION OF THE FEASIBILITY AND ACCEPTABILITY OF INTEGRATING SCREENING FOR CHLAMYDIA, HUMAN PAPILLOMA VIRUS, METABOLIC SYNDROME, DISEASE AND CERVICAL CANCER, WITH ACTIVE LINKAGE TO CARE, INTO A STANDARD OF CARE HIV TESTING SERVICES CENTRE FOR ADULTS IN SOWETO, SOUTH AFRICA

ETHICS REFERENCE NO: 170307

RE : FINAL ETHICS APPROVAL

This is to certify that the above-mentioned trial has been approved by the University of the Witwatersrand, Human Research Ethics Committee (HREC), and the Protocol/Expert Reviewer. Date of Meeting where trial was reviewed: 31 March 2017.

The University of the Witwatersrand, Human Research Ethics Committee Approval Granted for the above mentioned study is valid for five years. Where required by Sponsor to have approval on a more frequent basis it remains the responsibility of the Sponsor and Investigator to apply for continuing review and approval, or for the duration of the Trial.

1. It is the responsibility of the Sponsor and Principal Investigator to ensure, where required, that relevant approvals are in place and compliance with the following is adhered to before a trial may begin:

- If trial is being conducted in Provincial Health facilities: Approval from the Hospital CEO / Clinic Manager / District Research Committee (whichever is applicable) be obtained.
- The study is submitted onto The National Health Research Database (NHRD).
- The relevant approvals are uploaded onto the NHRD system: Ethics Approval, MCC Approval, Hospital CEO / Clinic Manager / District Research Committee Approval.

* A copy of the MCC Approval and/or MCC Notification letter must be submitted to the Ethics Secretariat Office for record purposes (IF MCC APPROVAL / NOTIFICATION IS APPLICABLE).

* The study is conducted according to the protocol submitted to the University of the Witwatersrand, Human Research Ethics Committee. Any amendments to the protocol must first be submitted to the Human Research Ethics Committee for approval.

* During the study, the University of the Witwatersrand, Human Research Ethics Committee is informed immediately of :

  - Any Unexpected Serious Adverse Events or Unexpected Adverse Drug Reactions, which, in the Investigator and/or the Sponsor's opinion are suspected to be related to the study drug. (Refer to POL-IEC-001 and SOP-IEC-005, Item 3.4).
  - Any data received during the trial which, may cast doubt on the validity of the continuation of the study.

* The University of the Witwatersrand, Human Research Ethics Committee is notified of any decision to discontinue the study and the reason stated.

* The Investigators authorised by this approval participate in this study. Additional Investigators shall be submitted to the University of the Witwatersrand, Human Research Ethics Committee for approval prior to their participation in the study.

* In the event of an authorised Investigator ceasing to participate in the study, the University of the Witwatersrand, Human Research Ethics Committee must be informed and the reason for such cessation given.

2. PRINCIPLES OF INFORMED CONSENT:
* The University of the Witwatersrand, Human Research Ethics Committee requires that in all studies, the Principles of Informed Consent are adhered to. This applies to volunteers as well as patients.

3. PROGRESS REPORTS:
* The University of the Witwatersrand, Human Research Ethics Committee requests that the MCC Progress Reports be submitted twice a year either in March and September or six monthly from start of study to the HREC Secretariat Office - 011 274 9281 and a report of the final results, at the conclusion of the study. (IF APPLICABLE)

4. REIMBURSEMENT TO PATIENTS FOR TRANSPORT:
* The Human Research Ethics Committee: (Medical) is in agreement that reimbursement per visit is according to the Medicines Control Council of SA and that reimbursement should be appropriate according to the situation.

5. TRANSPORT AND STORAGE OF BLOOD AND TISSUE SAMPLES IN SOUTH AFRICA:
* If blood specimens are to be stored for future analysis and is planned that such analysis will be done outside Wits, then the blood must be stored at a facility in South Africa agreed with the relevant IRB, with release of sub-samples only once projects have been approved by the local Research Ethics Committee applicable to where the analysis will be done as well as by the Wits Human Research Ethics Committee: (Medical).

6. GENETIC TESTING:
* The Human Research Ethics Committee: Medical; will not approve open-ended genetic testing as this does not fit the Human Research Ethics Committee criteria.

7. GOOD CLINICAL PRACTICE:
* The South African Department of Health, Medicines Control Council requires Good Clinical Practice (GCP) Training for all Investigators in Clinical Trials, and that GCP training be renewed every three (3) years.

As yet, there are no National Guidelines for the content of GCP courses. Until these are available the Wits Human Research Ethics Committee (Medical) will note courses completed by Investigators without approval of the content of the individual courses.

8. THE SUPPORTING APPROVAL DOCUMENTS ARE ATTACHED:

8.1 Ethics Approval Form signed by the Chairperson of the HREC - Kindly return the copy of the Approval Form signed by the Principal Investigator(s) per fax: 011 274 9281 for our records (this is applicable with the initial Approval).

8.2 List of members present at the HREC meeting held as per INDEPENDENT ETHICS COMMITTEE APPROVAL FORM

9. WE AWAIT YOUR RESPONSES AS REQUESTED: Ensure to have these documents forwarded at the earliest for the HREC records.

* MCC Approval letter and/or letter of Notification before the above study may commence / or where an Amendment may be implemented (IF MCC APPROVAL / NOTIFICATION IS APPLICABLE). It remains the responsibility of the Principal Investigator and/or Sponsor to ensure that the relevant approvals are in place.

* Copy of Independent Ethics Declaration Approval Form signed by the Principal Investigator. (this is applicable with the initial Approval).

* Kindly forward the above to the undersigned at fax: 011 274 9281 at your earliest convenience.

The above has been noted for the Ethics Committee information and records.

KINDLY FORWARD TO THE RELEVANT INVESTIGATORS / CRA / SPONSOR / STUDY CO-ORDINATORS - WHERE APPLICABLE

Regards,

PROF PETER CLEATON-JONES

For and on behalf of the Human Research Ethics Committee: (Medical)

INDEPENDENT ETHICS COMMITTEE APPROVAL FORM

Ethics Reference No.	170307	Date of Meeting	31 March 2017
		Recertification Due	23 February 2018 (If applicable)
Principal Investigators:	Dr K Hopkins	Investigators:	Prof GE Gray

Protocol Title:	Evaluation of the feasibility and acceptability of integrating screening for Chlamydia, Human Papilloma Virus, metabolic syndrome disease and cervical cancer, with active linkage to care, into a standard of care HIV Testing Services Centre for adults in Soweto, South Africa

DOCUMENTS REVIEWED			Tick As Appropriate	Yes	No
Protocol Number	Zazi Evaluation Study	Date:	12 May 2017		
Protocol	Zazi Protocol Version 1.0 - WITHDRAWN	Date:	01 March 2017	☑	☐
	Zazi Protocol Version 1.0	Date:	12 May 2017	☑	☐
Investigator's Brochure	N/A - Version: N/A - Dated:			☑	☐
Subject Information/Consent Form	Provider Information Leaflet and Informed Consent Form - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix C: Participant Information Leaflet and Informed Consent Form, Phase 2 - Version: 1.0 - Dated: 12 May 2017			☑	☐
	Appendix B: Participant Information Leaflet and Informed Consent Form, Phase 1 - Version: 1.0 - Dated: 12 May 2017			☑	☐
	Appendix A-2: Zazi VCT Centre Registry Information leaflet and Informed Consent Form, Phase 2 - Version: 5.0 - Dated: 12 Apr 2017			☑	☐
	Appendix A-1: Zazi VCT Centre Registry Information leaflet and Informed Consent Form, Phase 1 - Version: 5.0 - Dated: 12 Apr 2017			☑	☐
Advertisements	Appendix Q: Promotional materials: Healthy living educational brochure - Version: - - Dated:			☑	☐
	Appendix Q: Promotional materials: Zazi Integrated HTS centre flyer - Version: - - Dated:			☑	☐
	Appendix Q: Promotional materials: Zazi Integrated HTS centre poster - Version: - - Dated:			☑	☐
Questionnaires	Appendix M: Client Exit Survey in Clinic, Phase 2 - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix K: Client Exit Survey in Clinic, Phase 1 - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix J: Provider Survey 1-4 - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix I: Data collection form - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix H: ZAZI HTS Counsellor Recommended Referral Sheet - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix G: ZAZI HTS Results Report - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix F: Zazi Counselling Guide - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix E: Participant Demographics Form - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix D: Client Contact Information Sheet - Version: 1.0 - Dated: 01 Mar 2017			☑	☐
	Appendix O: Client Linkage to Care Follow-Up Survey, Phase 2 - Version: - - Dated:			☑	☐
	Appendix M: Client Linkage to Care Follow-Up Survey, Phase 1 - Version: - - Dated:			☑	☐
Insurance/Compensation	N/A	Valid From	To:	☐	☑
Synopsis of Study/Trial Summary	HIV Testing Services Centre for Adults			☑	☐
Other Documentation	Protocol Synopsis - Dated: 01 Mar 2017			☑	☐
	NHREC Trial Application ID#: 4684 - Dated: 07 Mar 2017			☑	☐
	Notice of Award - Dated: 30 Dec 2016			☑	☐
	HREC Application Form - Dated: 07 Mar 2017			☑	☐

Relevant Trial Hospital(s)	Chris Hani Baragwanath Hospital	☑	☐
Syndicate and/or Research Unit	Peri-Natal HIV Research Unit - PHRU	☑	☐

INDEPENDENT ETHICS COMMITTEE APPROVAL FORM

DETAILS OF COMMITTEE	
Name	University of the Witwatersrand Human Research Ethics Committee: (Medical)
Address	Research Office, Senate House University of the Witwatersrand, 1 Jan Smuts Avenue, BRAAMFONTEIN, Johannesburg, 2000

DETAILS OF MEETING	Yes	No
Is the Investigator a member of the committee ?	☐	☑
If "Yes" did he/she vote ?	☐	☑
Is the Committee organised and operated according to applicable laws and regulations together with ?	☑	☐
Local GCP requirements ?	☑	☐
ICH GCP requirements ?	☑	☐
FDA GCP requirements ? FWA Registered No. IRB00001223	☑	☐
Progress reports required either in March and September or six monthly from start of study ?	☑	☐

DECISION ON APPROVAL : is approval given to conduct the trial ?		Tick As Appropriate
Yes - with no conditions		☑
Remarks :	Our expectation is that our requirements are fulfulled once a company has submitted and uploaded relevant approvals onto NHRD.	
Yes - with conditions		☐
Specify conditions :		
No		☐
Specify reasons		

SIGNATURES		
I confirm that the details on this form are correct:		Date
Name: Prof PE Cleaton-Jones Chair / Deputy Chair of Committee	Signature:	09 June 2017

DECLARATION OF INVESTIGATOR/(S)

To be completed and ONE COPY returned to the Secretariat for the HREC at Wits Health Consortium, 8 Blackwood Avenue, Parktown, 2193 or Fax To: 011 274-9281

I/We fully understand the conditions under which I am/we are authorised to carry out and complete the above-mentioned research and I/we agree to ensure full compliance with these conditions. Should any amendment, alteration or departure be contemplated from the research procedure methodology or manner of execution, I/we will communicate with the Chairman of the Human Research Ethics Committee: (Medical) for approval prior to acting on any of the above mentioned proposed amendments, alterations or departures. I am/we are fully aware that any unauthorised amendment, alteration or departure as above will amount to misconduct and may lead to the institution of disciplinary procedures.

Any approval given by the HREC is conditional upon consent being obtained by the Investigator/s from the Superintendent (or equivalent official) of the Hospital, Clinic or Institution in which the research is, in part or full, to take place.

The Chairman may of course at his discretion place the matter before the full Committee.

DATE: 15 June 2017 SIGNATURE: R L Hopkins NAME: Kathryn Hopkins

PROTOCOL NUMBER Zazi Evaluation Study ETHICS REF.: 170307

Date Printed 09 June 2017

APPENDIX C2. WITS HREC Approval of Letter of Amendment for Zazi Evaluation Study

University of the Witwatersrand, Johannesburg

Human Research Ethics Committee: (Medical)
FWA Registered No IRB 00001223

SECRETARIAT: Suite 189, Private Bag x2600, Houghton 2041, South Africa Tel: +27-11-274 9200 Fax: +27-11-274 9281

Miss P Bhana

FAXED & COURIERED

Regulatory Consultant
Perinatal HIV Research Unit
PO Box 114
Diepkloof
1864

02 February 2018

Fax: 087 944 8082

Dear Miss Bhana,

PROTOCOL: ZAZI EVALUATION STUDY - EVALUATION OF THE FEASIBILITY AND ACCEPTABILITY OF INTEGRATING SCREENING FOR CHLAMYDIA, HUMAN PAPILLOMA VIRUS, METABOLIC SYNDROME DISEASE AND CERVICAL CANCER, WITH ACTIVE LINKAGE TO CARE, INTO A STANDARD OF CARE HIV TESTING SERVICES CENTRE FOR ADULTS IN SOWETO, SOUTH AFRICA

ETHICS REFERENCE NO: 170307

RE : APPROVAL - RESPONSE RE: LETTER OF AMENDMENT TO APPROVED PROTOCOL (THE ZAZI EVALUATION STUDY #170307)

We acknowledge receipt of your letter dated 25 January 2018 with the following documentation pertaining to the above-captioned trial.

Amendment Date:	08-Dec-2017	Amendment Version:	1.0
Amendment Number:		Received Date:	25-Jan-2018

The following has been approved by the Wits Human Research Ethics Committee: (Medical)

* Zazi Protocol Version 1.0 dated 08 December 2017 (Tracked and Clean)

* Appendix A-1: Programme Informed Consent Form, Phase 1, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix A-2: Programme Informed Consent Form, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix B: Study Participant Informed Consent Form, Phase 1, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix C: Study Participant Informed Consent Form, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix D-1: Provider Informed Consent Form, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix D-2: Employee Data Confidentially Agreement, Version 1.0 dated 08 December 2017 (Tracked and Clean)

* Appendix E: Client Contact Information Sheet, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix F-1: Participant Demographics Form, Phase 1, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix F-2: Participant Demographics Form, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix G-1 Zazi Counselling Guide, Phase 1, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix G-2 Zazi Counselling Guide, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix H-1: ZAZI HTS Results Report, Phase 1, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix H-2: ZAZI HTS Results Report, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix I-1: ZAZI HTS Counsellor Recommended Referral Sheet, Phase 1, Version 1.0 dated 08

December 2017 (Tracked and Clean)
* Appendix I-2: ZAZI HTS Counsellor Recommended Referral Sheet, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix J:Data collection form, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix K: Provider Survey 1-4, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix L: Client Exit Survey in Clinic, Phase 1, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix M: Client Linkage to Care Follow-Up Survey, Phase 1, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix N: Client Exit Survey in Clinic, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)
* Appendix O: Client Linkage to Care Follow-Up Survey, Phase 2, Version 1.0 dated 08 December 2017 (Tracked and Clean)

The contents mentioned in the cover letter has been noted.

Ethics Approval Date: 02 February 2018

The University of the Witwatersrand, Human Research Ethics Committee Approval Granted for the above mentioned study is valid for five years. Where required by Sponsor to have approval on a more frequent basis it remains the responsibility of the Sponsor and Investigator to apply for continuing review and approval, or for the duration of the Trial.

.

1. THIS APPROVAL IS SUBJECT TO THE FOLLOWING PROVISOS:

* A copy of the MCC Approval and/or MCC Notification letter must be submitted to the Ethics Regulatory Office Secretariat before the study commences / or where an Amendment may be implemented (IF MCC APPROVAL / NOTIFICATION IS APPLICABLE). It remains the responsibility of the Principal Investigator and/or Sponsor to ensure that the relevant approvals are in place.

.

* The study is conducted according to the protocol submitted to the University of the Witwatersrand, Human Research Ethics Committee. Any amendments to the protocol must first be submitted to the Human Research Ethics Committee for approval.

.

* During the study, the University of the Witwatersrand, Human Research Ethics Committee is informed immediately of :
  - Any Unexpected Serious Adverse Events or Unexpected Adverse Drug Reactions, which, in the Investigator and/or the Sponsor's opinion are suspected to be related to the study drug. (Refer to POL-IEC-001 and SOP-IEC-005, Item 3.4).
  - Any data received during the trial which, may cast doubt on the validity of the continuation of the study .

.

* The University of the Witwatersrand, Human Research Ethics Committee is notified of any decision to discontinue the study and the reason stated.

.

* The Investigators authorised by this approval participate in this study. Additional Investigators shall be submitted to the University of the Witwatersrand, Human Research Ethics Committee for approval prior to their participation in the study.

.

* In the event of an authorised Investigator ceasing to participate in the study, the University of the Witwatersrand, Human Research Ethics Committee must be informed and the reason for such cessation given.

.

2. PRINCIPLES OF INFORMED CONSENT:

* The University of the Witwatersrand, Human Research Ethics Committee requires that in all studies, the Principles of Informed Consent are adhered to. This applies to volunteers as well as patients.

.

3. PROGRESS REPORTS:

* The University of the Witwatersrand, Human Research Ethics Committee requests that the MCC Progress Reports be submitted twice a year either in March and September or six monthly from start of study to the HREC Secretariat Office - 011 274 9281 and a report of the final results, at the conclusion of the study. (IF APPLICABLE)

4. REIMBURSEMENT TO PATIENTS FOR TRANSPORT:

* The Human Research Ethics Committee: (Medical) is in agreement that reimbursement per visit is according to the Medicines Control Council of SA and that reimbursement should be appropriate according to the situation.

.

5. TRANSPORT AND STORAGE OF BLOOD AND TISSUE SAMPLES IN SOUTH AFRICA:

* If blood specimens are to be stored for future analysis and is planned that such analysis will be done outside Wits, then the blood must be stored at a facility in South Africa agreed with the relevant IRB, with release of sub-samples only once projects have been approved by the local Research Ethics Committee applicable to where the analysis will be done as well as by the Wits Human Research Ethics Committee: (Medical).

6. GENETIC TESTING

* The Human Research Ethics Committee: Medical; will not approve open-ended genetic testing as this does not fit the Human Research Ethics Committee criteria.

7. GOOD CLINICAL PRACTICE

The South African Department of Health, Medicines Control Council requires Good Clinical Practice (GCP) Training for all Investigators in Clinical Trials, and that GCP training be renewed every three (3) years.

As yet, there are no National Guidelines for the content of GCP courses. Until these are available the Wits Human Research Ethics Committee (Medical) will note courses completed by Investigators without approval of the content of the individual courses.

8. THE SUPPORTING APPROVAL DOCUMENTS ARE ATTACHED:

8.1 Ethics Approval Form signed by the Chairperson of the HREC - Kindly return the copy of the Approval Form signed by the Principal Investigator /(s) per fax: 011 274 9281 for our records (this is only applicable with the initial Approval).

The above has been noted for the Ethics Committee information and records.

KINDLY FORWARD TO THE RELEVANT INVESTIGATORS / CRA / STUDY CO-ORDINATORS

Regards,

PROF CLEMENT PENNY

For and on behalf of the Human Research Ethics Committee: (Medical)

APPENDIX C3. CENTERS FOR DISEASE CONTROL AND PREVENTION APPROVAL OF PROTOCOL

CGH HSR Tracking #: 2018-017

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

Use this form 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: Feasibility and acceptability of further integrated voluntary counselling and testing (VCT), with active	Project Location/Country(ies): South Africa
CDC Principal Investigator's name and SEV#: Nompumelelo Khanyile 8859	CDC Primary Contact's name and SEV# (Leave blank if same as PI):
Division: DGHT; CDC PI or PC Email: ycd1@cdc.gov	Telephone: 27124249010
Project start date (mm/dd/yyyy): 01/01/2018	Project end date (mm/dd/yyyy): 12/30/2020

Collaborating Institutions (List other collaborating institutions in the protocol or in a separate document)

☑ CoAg ☐ Grant ☐ contract #: GH001150	Original Award Year if CoAg: 2016	Current Budget Year if CoAg: 2017
Title (CoAg, Grant, or Contract): Strengthening Strategic Information, program implementation and a capacity building ...		
Supported Institution Name: Medical Research Council		
Supported Institution FWA# (if applicable): FWA00002753	FWA Exp. Date (if applicable): 09/01/2021	

Check appropriate category and subcategory

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

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

* Evaluation of a new intervention for effectiveness and comparison of different interventions are research under CDC policy.
Ω 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 all that apply)**

- ☐ **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 for certain animal research. Institution must also have assurance with the Office of Laboratory and Animal Welfare at NIH.

☑ **III. Activity is research involving human subjects but CDC involvement does not constitute "engagement in human subject research."** CDC employees or agents will not intervene or interact with living individuals or have access to identifiable information for research purposes. Appropriate IRB or ethics committee approval is required prior to approval. **(Check all that apply)**

- ☑ **A.** This project is funded under a grant/cooperative agreement/contract award mechanism.
- ☐ **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 CDC Support$^{\beta}$).
- ☐ **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 CDC Support).
- ☐ **D.** Activity is research involving linked data, but CDC non-disclosure form 0.1375B is signed.$^{\infty}$

β See definition of support on page 3.
∞ CDC form 0.1375B agreement is required for all subcategories (A-D) if CDC has access to linked data. This agreement prohibits the release of identifying key to CDC investigators under any circumstances. The purposes of the planned research do not contradict the terms of consent under which the information or specimens were collected, whether that consent was documented or not documented.

☐ **IV. Activity is research involving human subjects that requires submission to CDC Human Research Protection Office (Check one)**$^{\alpha}$

- ☐ 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)

α 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).

Public Access and Data Sharing

A. Type of data collected or generated: 2. By non-CDC staff, supported with CDC funding

Instructions: From the dropdown list, select the types of data that will be collected that best fits this project. Categories 1, 2, and 3 are data covered by CDC Policy (http://aops-mas-iis/Policy/Doc/policy385.pdf). Categories 4 and 5 are data covered by CDC Policy but release or sharing may be restricted or limited. Categories 6, 7 and 8 are data NOT covered by CDC Policy and no further information is needed under this section. Use the lowest number when the data falls under more than one type. **See Box below for more information on the categories.**

Provide a 2-3 sentences description of the data that will be collected in this project:

Data will be collected through medical records, data collection forms, and surveys

B. Data ownership: *Perinatal HIV Research Unit (PHRU), Medical Research Council, South Africa*

Instructions: Provide the name of the organization that will own the public health data for this project. If there are multiple organizations involved, provide the name of the organization that will retain and provide long-term control over the access and use of the data. Provide data steward's name and contact information if available.

C. Public access level: 1. Public – dataset or summary data tables will be available without restriction after data availability date

Instructions: From the drop-down list, select the data release category that will best fits how data will be available after data availability date.

Justifications:

Instructions: From the dropdown list, select the option that best fits the justification for restricted access or unavailability of data.

Provide a brief description (1-3 sentences) if "Other reason" is selected:

D. Anticipated data availability date (if applicable): 09/2021

Instructions: Provide the anticipated date (mm/yyyy) that the public health data will become available.

Box: Type of data collected or generated

1. *By CDC staff, supported with CDC funding* – CDC funds the activity and data are collected by CDC staff.
2. *By non-CDC staff, supported with CDC funding* – CDC funds or co-funds the data collection through mechanisms such as grants, cooperative agreements, contracts, or other funding mechanisms. Data is collected by non-CDC staff. When CDC funds another federal agency, an interagency agreement should indicate who would be responsible for the data.
3. *Provided to CDC and becomes part of a CDC data system* – Data is reported to CDC by another entity, e.g., by local health departments, that become a part of a CDC data collection system, e.g., CDC surveillance systems.
4. *Owned by partner and protected from release by laws or regulations* – CDC funds or co-funds the data collection. Data may be collected by CDC or non-CDC staff as in #1 and 2 above, but applicable US or country laws and regulations limit or restrict disclosure of data. Examples of US laws limiting disclosure include: the Privacy Act, Trade Secrets Act, or Section 308(d) of the US Public Health Service Act. When CDC funds activities in other countries, foreign laws and/or regulations may also apply.
5. *Not sharable due to potential dual-use research of concern* – Dual use research of concern is life sciences research that, based on current understanding, can reasonably be anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or material (http://intranet.cdc.gov/oadlss/manuals-and-policies/dual-use-research/). Data pertaining to DUR may not be sharable because of the potential threats.
6. *Owned by partner and shared with CDC, but no CDC funding* – CDC does not fund, collect, or own the data. Data may be shared with CDC.
7. *Owned by partner and has an agreement restricting data sharing* – CDC does not fund, collect, or own the data. Data may be shared with CDC under data sharing agreement.
8. *By another federal agency* – Another federal agency shares data with CDC under restricted terms agreement. The other federal agency is responsible for data release and sharing.

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 if one exists. If not, provide a separate project description (See suggested format below) in sufficient detail to justify the proposed category. Submit your request to your branch chief (or country director or designee for country staff).

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. Local IRB Exp. Date (if applicable):**

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

Comments/Rationale for Determination:

Approvals and Signatures

	Date:	**Remarks:**
Mary T. Glenshaw, PhD, MPH Digitally signed by Mary T. Glenshaw, PhD, MPH Date: 2017.12.08 15:54:50 +02'00' Investigator	09/01/2021	Signed for N.Khanyile
Mary T. Glenshaw, PhD, MPH Digitally signed by Mary T. Glenshaw, PhD, MPH Date: 2017.12.04 18:55:28 +02'00' Branch Chief/Country Director	12/04/2017	CDC SA ADS
Division Human Research Protection Coordinator Division ADS/ADLS or Director	1/11/2018	
Basia Tomczyk CGH Human Research Protection Coordinator CGH ADS/ADLS or Deputy ADS/ADLS	1/19/2018	

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 D. DATA COLLECTION TOOLS

APPENDIX D1. HTS CLIENT DEMOGRAPHICS FORM

Standard of care HTS (Phase 1) and integrated NCD-HTS (Phase 2) HTS Client Demographics Forms were very similar. Only the form for Phase 1 is presented as an appendix.

Zazi Client ID Number: _____ Study PTID: [__][__][__][__] or ☐ Not on study
Date [DD/MMM/YYYY]: [__][__]/[__][__][__]/20[__][__] Time [HH:MM]: [__][__]:[__][__]

We appreciate your time to fill this out. This form does not have your name because of confidentiality. You are welcome to ask us for help if something is not clear.

Date of birth	(e.g. 12 SEP 1980) [___][___] / [___][___][___] / [___][___][___][___]					
Gender (circle one)	Male Female		**If female, are you currently pregnant? (circle one)** Yes No			
Race (circle one)	Black	White	Coloured/ mixed race	Indian	Asian	Other (specify) _____
Nationality (circle one)	South African		Other (specify): _____			
Ethnic group (circle one)	Zulu	Sotho	Tsonga	Tswana	Venda	Xhosa
	North Sotho	Ndebele	Swazi	Other (specify) _____		
Marital status (circle one)	Single	Married, including traditional or marriage	Divorced	Widowed	Living together	Other (specify) _____
Do you have children? (circle one) Yes No			**If yes, how many children?** _____ **Please list their ages:** _____ **Have any died in the past 5 years?** Yes No			
Who do you live with? (circle all that apply)	Alone		Wife/ Husband/ Partner	Family	Friend(s)	Other (specify) _____
Highest education (circle one)	No formal education		Primary School		High School	
	Matriculated		Tertiary Education		Other (specify) _____	
Source of money to live on? (circle one)	Employed Occupation: _____		Social/Disability Grant		Parents	
	Self-employed		Pension		Other (specify) _____	

Type of house you live in (circle one)	Shack / Zozo	Flat / cottage	Room/ garage	Hostel
	Shared house	Stand alone brick house	Other (specify) _____	
Is this residence… (circle one)	Permanent	Rental	Informal	Other (specify) _____

Home water source (circle one)	Tap water indoors	Only outside tap water	Well / borehole
	Stream / River / Pond	Other water source (specify) _____	
Type of toilet facility (circle one)	Flush toilet inside (connected to sewage)	Outside pit latrine / toilet	Flush toilet inside (septic tank)
	No toilet facility	Other toilet facility (specify): _____	

Fuel for cooking (circle one)	Electricity	Gas	Paraffin	Coal
	Candles	Firewood / Straw	Other (specify) _____	
Fuel for lighting (circle one)	Electricity	Gas	Paraffin	Coal
	Candles	Firewood / Straw	Other (specify) _____	
Does your household have: (circle all that apply)	Radio	Computer	Landline telephone	None listed
	TV	Refrigerator	Mobile phone / cell phone	

Does anyone in your house own: (circle all that apply)	Bicycle	Car / Truck	Sheep / Goat / Cattle
	Motorcycle / Scooter	Donkey / Horse	None listed

How long have you continuously been living in/near Soweto?	Record in years (if under 1 year, write '00'): _____	**Have you ever lived elsewhere? (circle one)** Yes No	**If yes, where did you live earlier? (circle one)** City Town Rural/Farm

How did you get to the clinic? (Circle One)	Taxi	Bus	Own private transport	Other (specify) _____

Zazi HTS Programme Related Information

1. Who referred you to the Zazi Clinic? Please tick one

☐ Self-referral ☐ PHRU TB Clinic ☐ Other PHRU Clinics
☐Other local clinic ☐ Private Doctor ☐ Other, please specify: _____

2. Why did you decide to come to the clinic today? Please tick all that apply.

☐ HIV testing ☐ CD4 count retest
☐ TB screening ☐ general STI screening
Check blood pressure ☐

3. How did you find out about Zazi clinic? Please tick all that apply.

☐ From Zazi staff ☐ From staff at other clinics
☐ From other people who attended PHRU clinics
☐ From friends/family/community
☐ Other (specify): _____

For staff use only
If client was referred:
a. Name of referral clinic:
b. Were referral documents received? (circle one) Yes No
Initials of staff verifying that form is complete: _____
Today's date (dd/mmm/yyyy) [___][___]/[___][___][___]/20[___][___]
Time [HH:MM]: [__][__]:[__][__]

APPENDIX D2. HTS CLIENT COUNSELLING FORM

As the HTS Client Counselling Form utilised for Phase 2 is more robust than Phase 1, it is presented as an appendix.

Note: This guide is based on National HIV Counselling and Testing guidelines

Zazi Client ID Number: _____ Study PTID: [__][__][__][__] or ☐ Not on study
Date [DD/MMM/YYYY]: [__][__]/[__][__][__]/20[__][__]

PRE-TEST COUNSELLING Start time: [__][__]:[__][__]

1. **Reason for Testing**

- Ask the client why they have come to Zazi today.
  - All repeat CD4 testers are sent to the nurse first
  - TB clinic patients with active TB or currently on treatment referred to Zazi for HIV testing need to be counselled, tested and immediately released from the clinic
- Ask the client (and tick answer): Are you currently participating in, or have you ever participated in, an HIV Vaccine Trial?
  ☐ Yes --- call the Principal Investigator, client cannot receive a rapid HIV test until it is confirmed otherwise; in the meantime, skip to SCREENINGS
  ☐ No – client may continue with counselling

2. **Risk Assessment for HIV and STIs**

- **Counsellor:** ***To get to know you and to help you understand your health risks better, I will ask you some questions about yourself. This will also help us keep your records up-to-date for possible follow-up, if necessary. I am not here to judge you. I am here to support you. Everything you say is confidential, and no information collected will be used with your identification outside of this facility.***

Tell me about your sexual lifestyle:					
• *How many sexual partners do currently you have?*					
• *What types of partners are they? (circle all that apply)*	One night stand	Dating	Living together	Husband/ Wife	Other:
Frequency of new/different partners?	Daily	Weekly	Monthly	Yearly	Never
Do you typically use condoms with these partners?	Yes		No		
• *How often do you have sexual penetrative intercourse?*	Regularly	On occasion	Unusually	Never	Sexual Abuse
• *In instances where the client experiences rape or sexual abuse, ask them to tell you about it*					

Tell me about your last sexual encounter:						
• *When was it?* • *With whom? If group sex event, specify in 'Other'* • *How did you have sexual relations? (circle all that apply)* • *Did you use a condom with the last sexual encounter?*	Within 1 week	Within 1 month	Within 1-3 month	Within 3-6 month	Within 1 year	Within 3 years
	One night stand	Date	Partner	Living together	Husband / Wife	Other:
	Oral	Vaginal	Anal	Other:		
	Yes	No	If not, why not:			

Tell me about your other behaviour:					
• *Do you drink alcohol?* • *How often do you use alcohol?* • *How do you use alcohol?* • *Do you use drugs?* • *Which drugs do you use? (circle all that apply)*	Yes		No		
	Daily	Weekly	Sometimes	Never	
	Socially	Excessively	Never		
	Yes, often (weekly)	Sometimes	No		
	Dagga	Ecstasy	Mandrax	Other:	None
	Yes		No		

• *Do you usually have penetrative sexual intercourse with your partner(s) when you have been drinking or using drugs?*	Tell me more:	
Have you ever suffered from depression or stress?	Yes Tell me more:	No
Are you worried about getting / having HIV or AIDS?	Yes	No

3. Assessment of Risk Reduction of HIV/AIDS

Can you explain to me your understanding of HIV/AIDS? **Clients should be able to understand and explain the mode of transmission and exchange of fluids**	
What were your previous successes in attempting to reduce your risk of exposure to HIV?	
Can you tell me about some of your successes in practicing safer sex with a condom?	
Tell me about your challenges in reducing your risk of exposure to HIV?	
Can you demonstrate how to use a condom?(male or female) **Demonstrate for the client, afterwards**	
Can you tell me about the situations which increase your risk of exposure to HIV?	
Let us explore a number of options for reducing your risk to HIV. **Discuss HIV prevention measures, such as: partner reduction, condom use, VMMC, PrEP, etc.**	
Let us address your concerns about your feelings and behaviour clashing with your beliefs/culture when it comes to changing your sexual behaviour.	
Add any additional notes from your discussion with your client.	

4. Negotiating Risk Reduction Plan

Counsellor's Task	Client's Response	Comments
Identify priority risk reduction behaviour		
Explore behaviour(s) that the client will be most motivated about or capable of changing		

Identify a reasonable yet challenging incremental step toward changing the identified behaviour		
Break down the risk reduction action into specific and concrete steps		
Identify supports or barriers to the risk reduction step		
Identify problem solving mechanisms concerning the plan		
Role play the plan		
Confirm with the client that the plan is reasonable and acceptable		
Ask the client to be aware of strengths and weaknesses in the plan while trying it out		
Recognize the challenges of behaviour change		
Document the risk reduction plan with a copy to the counsellor		

5. **Education: HIV Testing**

Topic to cover	**Tick mark once done**
Benefits of HIV Testing and importance of knowing one's HIV status: Include the message that a diagnosis can give the person the power to look out for their own health by adopting positive living, a healthy lifestyle and starting treatment, if needed.	
Review the HIV Testing process: Test by fingerprick and the blood will be collected by pipettes and dropped into the test kit. Test results will be ready in 15-30 minutes. Remind that the test is voluntary, and if a person is not comfortable to take the test now, they may return at a later date.	
Clarify the meaning of *Confidentiality*	
Meaning of an HIV *negative* result	
Clarify the meaning of *Window Period*	
Meaning of an HIV *positive* result	
Meaning of an HIV *indeterminate* result: Include the explanation that the client may need to have blood drawn from the arm by the nurse and it will be sent to the lab for more testing before results may be given.	
Perception of risk to HIV exposure (does the client think they are at risk to HIV infection)	

6. **Client Support System**

Have you ever experienced a loss in your life? (circle one)	Yes No *If yes, who:* _____ *If yes, when:* _____
Have you ever thought about attempting suicide? (circle one)	Yes No

	If yes, how did this happen and how did you deal with this crisis?
How do you normally deal with stressful situations or a crisis?	
If the test is HIV positive, will you tell someone? (circle one)	Yes No Unsure *If yes, who:* _____ *If no or unsure, why:*
Who else would you tell if you are HIV positive? (circle one)	Family Partner Friend Other (specify): _____
How would you tell this person you trust?	
Do you think you will get support from that person? (circle one)	Yes No Unsure
Would you like us at Zazi to offer further support? (circle one)	Yes No Unsure

PRE-TEST COUNSELLING End time: [ ][ ]:[ ][ ]

SCREENINGS Start time: [ ][ ]:[ ][ ]

REMEMBER: clients who have been a participant in an HIV Vaccine Trial CANNOT be tested unless the Principal Investigator has confirmed they can.

Conduct ONE fingerprick to collect blood for HIV Testing, blood sugar (both average and random) and blood cholesterol (full lipid profile) testing. Conduct all rapid tests.

While waiting for HIV, blood sugar and cholesterol test results:

1. **Take height and weight measurements** and record on results report
2. **Calculate BMI** and record on results report
3. **Take blood pressure reading** and record on results report
4. **Complete the Client Data Collection Form.** Record STI and TB symptom screening results on the results report.
5. **HIV, blood sugar and cholesterol test results should be available.** Record on results report
6. **MAKE SURE RESULTS FORM IS FILLED OUT FOR ALL SCREENINGS.**
7. **IF APPLICABLE: Refer men wanting Chlamydia testing to the nurse. Refer any women who changed their mind and want screening for Chlamydia, HPV and/or cervical cancer to the nurse.**

NOTE: Deliver completed results and referral form to the nurse along with the client. While with the client, the nurse will cross-check all results/referrals and write referral letters.

SCREENINGS End time: [__][__]:[__][__]

REFERRALS Start time: [ ][ ]:[ ][ ]

[IF IT HAS NOT ALREADY BEEN DONE – SEE SCREENINGS #7, ABOVE] FILL OUT REFERRAL FORM. DELIVER BOTH RESULTS FORM AND REFERRAL FORM TO NURSE FOR CROSSCHECK.

RETURN TO THE CLIENT WITH WRITTEN REFERRAL LETTERS FROM NURSE. DO NOT SHARE REFERRALS UNTIL AFTER POST-TEST COUNSELLING.

REFERRALS end time: [__][__]:[__][__]

POST-TEST COUNSELLING Start time: [ ][ ]:[ ][ ]

1. Share BMI and Blood Pressure results with client
2. Share STI and TB symptom screening results with client
3. Share blood sugar and cholesterol results with client
4. Share HIV test results with client:

If client has an HIV Negative test result:

Counsellor's Key Tasks	Comments
Explain the implications of the negative test result	
Identify and prioritize the behaviours that correspond to the client's risk	
Motivate the client to stick with their risk reduction plan	
Encourage client to discuss their HIV status with current and future partners	

If client has an HIV Positive test result:

Counsellor's Key Tasks	Comments
Delivering the test results	
Inform client that the test results are available	
Provide results clearly and simply	
Review the meaning the of the result	
Allow the client time to absorb the meaning of the result	
Explore the client's understanding of the result	
Assess how the client is coping with the result	

Acknowledge the challenges of dealing with an initial positive result	
Discuss living positively. If the client is not prepared for this discussion, provide them with a pamphlet.	
Negotiating Disclosure and Partner Referral	
Explore client's feelings about telling partners about their HIV positive test results	
Remind client that the result does not indicate the partner's HIV status	
Identify partners that are at risk and need to be informed of their risk for HIV infection	
Discuss possible approaches to disclosure of HIV positive status to partners	
Anticipate potential partner(s) reaction(s)	
Support client to refer partner(s) for testing	
Practice and role play different approaches to disclosure	
Provide the client with support	
Identify Sources of Support	
Identify current health care resources	
Address the need for health care providers to know client's test result	
Explore client's access to medical services	
Identify needed medical referrals (ART, PMTCT, etc)	
Discuss situations in which the client may want to consider protecting their own confidentiality	
Discuss options of support groups (e.g.; post test club)	

POST-TEST COUNSELLING End time: [ ][ ]:[ ][ ]

SHARE REFERRAL LETTERS WITH CLIENT. CLIENT MAY FURTHER CONSULT WITH THE NURSE, IF NEEDED/REQUESTED

IF CLIENT IS A ZAZI STUDY PARTICIPANT, GIVE THEM A CLINIC EXIT SURVEY TO COMPLETE IN THE WAITING ROOM. THEY MAY GIVE IT TO THE RECEPTIONIST BEFORE LEAVING THE CLINIC.

Next Appointment Date: [__][__]/[__][__][__]/20[__][__]

NOTE:

- CD4 testers should be asked to return for their results in 2 days;
- Clients identified with STIs should be asked to return for HIV testing in 6 weeks;
- Other at-risk clients should be asked to return for HIV testing in 3 months; and
- Clients screened for cervical cancer and HPV should be asked to return to collect their results in 6 weeks.

APPENDIX D3. HTS CLIENT DATA COLLECTION FORM

The same HTS Client Data Collection Form was used for both HTS phases.

Form start time: [ ][ ]:[ ][ ]

HIV-Related Information

1. Would you like to be tested for HIV?
   ☐ Yes ☐ **No → skip to STI Section**
   a. If yes, is client here alone or for couples HTS: ☐ Alone ☐ Couples

2. When was your last HIV test done? (also check clinic file)
   ☐ within last 3 months ☐ 3-6 months ago ☐ 6 months to 1 year ago
   ☐ 1-5 years ago ☐ over 5 years ago ☐ **never→skip to STI section**

3. What was your last HIV test result?
   ☐ **negative→skip to STI section** ☐ **don't know→skip to STI section** ☐ positive

   a. If positive, date of first HIV diagnosis (mmm/yyyy):
   [ ][ ][ ]/[ ][ ][ ][ ]
   b. Date of last CD4 count (mmm/yyyy): [ ][ ][ ]/[ ][ ][ ][ ] OR
   ☐ **no CD4 count → skip to #4**
   c. Result of last CD4: [ ][ ][ ][ ] cells OR ☐ can't remember

4. **For clients who already know they are HIV-positive:**
   Are you currently taking or have ever taken antiretroviral treatment?
   ☐ no; specify reason:_____ →**Skip to #5**
   ☐ yes, **refer client to his/her treatment clinic for CD4**
   a. If yes, date of treatment initiation (mmm/yyyy):
   [ ][ ][ ]/[ ][ ][ ][ ]

   b. If yes, current type of treatment:
   ☐ one pill once a day (e.g. atripla, atroiza, odimune, tribus)

   ☐ Other, specify: _____

   If client does not know, tell them you will call them later asking them for the name of their medication.

   c. If yes, date of initiation of current treatment (mmm/yyyy):
   [ ][ ][ ]/[ ][ ][ ][ ]

5. **For clients who already know they are HIV-positive and have not initiated treatment:**
   Would you like to have blood drawn for your CD4 count?
   ☐ no; specify reason:_____ →**Skip to STI section**
   ☐ yes, note this on referral sheet →**Skip to STI section**

6. AFTER HIV TEST RESULTS ARE AVAILABLE AND POST-TEST COUNSELLING HAS OCCURRED:

If HIV test is negative or client didn't test for HIV	
For men: Interested in being referred for VMMC?	☐ Yes ☐ No ☐ Already circumcised
For all clients: Interested in learning more about PrEP?	☐ Yes ☐ No
If client answers 'Yes' to any part of #6, write the referral on the referral sheet. *If the client is a pregnant woman who tested HIV-infected, tick 'PMTCT referral' on the referral sheet.*	

STI Screening Questions (for sexually active individuals only)

1. Are you sexually active? ☐ Yes ☐ **No→Skip to TB section**

2. Have you ever been screened for any STI symptoms? ☐ Yes ☐ **No→skip to #4**

a. If yes, when were you last screened?
☐ within last 3 months ☐ 3-6 months ago
☐ 6 months to 1 year ago ☐ 1-5 years ago ☐ over 5 years ago
b. What was your last STI screening result?
☐ **negative→skip to #4** ☐ **don't know→skip to #4**
☐ positive
c. If positive, did you take treatment? ☐ Yes ☐ **No→skip to #3**
d. If yes, date of last treatment taken (mmm/yyyy): [___][___][___]/[___][___][___][___]

3. Do you currently have a diagnosed STI? ☐ Yes ☐ No
a. If yes, please specify: _____

STI symptoms screening:

4. Do you have an abnormal, bad-smelling or itchy discharge from the vagina/penis and/or anus?
☐ None ☐ Yes, from vagina/penis ☐ Yes, from anus ☐ Yes, from both vagina/penis and anus

5. Do you have any abnormal blood coming from your vagina/penis and/or anus?
☐ None ☐ Yes, from vagina/penis ☐ Yes, from anus ☐ Yes, from both vagina/penis and anus

6. Do you have sores on/in your vagina/penis at the moment? ☐ No ☐ Yes

7. Do you have sores on/in your anus at the moment? ☐ No ☐ Yes

8. Do you experience a burning sensation while passing urine? ☐ No ☐ Yes

9. Are you experiencing any lower abdominal pain?
☐ No ☐ Yes ☐ N/A, client is male

If client answers 'Yes' to any STI question #4-9, write the referral on the referral sheet.

10. **If in Phase 1:** If we had a rapid test for Chlamydia, a common STI that often does not have symptoms and can cause infertility, would you like to be screened for it? For women, our nurse would need to take a swab inside the vagina, and for men we can test from a urine sample.
☐ Yes ☐ No ☐ Unsure if she would accept a vaginal exam
☐ N/A, Project is in Phase 2
If in Phase 2: Would you like to be screened for Chlamydia, a common STI that often does not have symptoms and can cause infertility? For women, our nurse would need to take a swab inside the vagina, and for men we can test from a urine sample.
☐ Yes ☐ No ☐ Unsure if she would accept a vaginal exam
☐ N/A, Project is in Phase 1

If in Phase 2 and client answers 'Yes' to #10, write the referral on the referral sheet and send the client to the nurse at the end of the session.

HPV and Cervical Cancer (women only). If client is male, skip to Family Planning Section

1. What do you think a Pap smear is for?
   ☐ to check for cancer of the cervix ☐ other:_____

2. How many Pap smears have you had in your lifetime?
   ☐ None ☐ 1 ☐ 2 ☐ 3 ☐ More than 3

   a. If the client has had at least 1 Pap smear, what was the date of the last test (mmm/yyyy): [___][___][___]/[___][___][___][___]

3. Have you ever had (tick all that apply):
   ☐ cervical cancer ☐ abnormal cells on pap smear ☐ **no →skip to #4**
   a. If yes, when was the diagnosis (mmm/yyyy): [___][___][___]/[___][___][___][___]
   b. If yes, was the client treated? ☐ No ☐ Yes
   c. If no, why not: _____

4. **If in Phase 1:** If we offered a screening test for HPV, an STI associated with cervical cancer; and/or conducted Pap smears, the test to screen for abnormal cells on the cervix to identify cervical cancer, would you like to be screened? We would need to take a swab inside the vagina.
   ☐ Yes, HPV only ☐ Yes, Pap Smear only ☐ Yes, to both
   ☐ No, to both ☐ Unsure if she would accept a vaginal exam
   ☐ N/A, Project is in Phase 2

   If in Phase 2: Would you like to undergo a Pap Smear today? It is the test to screen for abnormal cells on the cervix to identify cervical cancer.
   ☐ Yes ☐ Unsure if she would accept a vaginal exam
   ☐ **No→skip to Family Planning section**
   ☐ **N/A, Project is in Phase 1→skip to Family Planning section**
   a. If yes, would you also like to be screened for HPV at the same time? HPV is an STI associated with cervical cancer.
   ☐ Yes ☐ No

If in Phase 2 and client answers 'Yes' to #4, write the referral on the referral sheet and send the client to the nurse at the end of the session.

Family Planning

1. Are you currently using a Family Planning method? ☐ Yes ☐ No
   a. If yes, which method(s) (tick all that apply):
      ☐ condoms ☐ oral contraceptives ☐ implant ☐ IUD ☐ injection
      ☐ Other: _____
   b. If no, would client like to be referred to Family Planning services?☐ Yes ☐ No
   If client answers 'Yes' to #1b, write the referral on the referral she

2. *Offer client condoms and lubricant.* Did client take some? ☐ Yes ☐ No

TB Screening Questions

1. Have you ever been screened for any TB symptoms? ☐ Yes ☐ **No→skip to #3**
   a. If yes, when were you last screened?
      ☐ within last 3 months ☐ 3-6 months ago
   ☐ 6 months to 1 year ago ☐ 1-5 years ago ☐ over 5 years ago
   b. What was your last TB screening result?
   ☐ **negative→skip to #3** ☐ **don't know→skip to #3**
   ☐ positive
   c. If positive, date of TB diagnosis (mmm/yyyy): [___][___][___]/[___][___][___][___]
   d. If positive, did you take treatment? ☐ Yes ☐ **No→skip to #2**
   e. If yes, date of treatment initiation (mmm/yyyy):
      [___][___][___]/[___][___][___][___]

2. Are you currently diagnosed with TB and/or taking TB treatment?
   ☐ **Yes, diagnosed only, record on referral sheet →skip to NCD section**
   ☐ Yes, diagnosed and on treatment **→skip to NCD section**
   ☐ No

TB symptoms screening:

3. Do you have any of the following:

TB Screening Questions	Yes	No
1. Cough for more than 2 weeks		
2. Blood in your sputum?		
3. Persistent fever and/or night sweats for more than 2 weeks		
4. Weight loss of ≥1.5 kg in the last month		
5. Live with someone who has/had TB in the last month		

If client answers 'Yes, diagnosed only' and/or 'Yes' to any TB Screening Questions, write the referral on the referral sheet.

NCD-Related Information

High Blood Pressure/Hypertension

1. Would you like your blood pressure read today? ☐ No ☐ Yes

2. Do your blood-related mother, father, sisters, brothers, or grandparents have a history of high blood pressure/hypertension?
   ☐ No ☐ Yes ☐ Unknown

3. Have you ever been diagnosed with hypertension (high blood pressure)?
   ☐ **No →skip to Blood Sugar section** ☐ Yes

   ☐ **Unknown → skip to Blood Sugar section**

   a. If yes, date of diagnosis (mmm/yyyy): [___][___][___]/[___][___][___][___]

4. **If client was previously diagnosed with hypertension:**
   Have you ever been on medication for high blood pressure? ☐ No ☐ Yes
   a. **If no, why not →then skip to Blood Sugar section:**
      ☐ Not necessary ☐ Declined
      ☐ Other (specify):_____
   b. If yes, which medications (specify): _____
   If client does not know, tell them you will call them later asking them for the name of their medication.

   c. If yes, list date of medication initiation (mmm/yyyy):
      [___][___][___]/[___][___][___][___]

High blood sugar/Diabetes

1. Have you ever been diagnosed as having sugar in the blood (diabetes)?
   ☐ **No→skip to #3** ☐ Yes ☐ **Unknown →skip to #3**

   a. If yes, date of diagnosis (mmm/yyyy): [___][___]/[___][___][___][___]

2. **If client was previously diagnosed with sugar in the blood (diabetes):**
   Did you start treatment for sugar in the blood (diabetes)?
   ☐ No ☐ Yes

   a. If no, why not: ☐ Not necessary ☐ Declined
      ☐ Other (specify)_____
   b. If yes, which medications (specify): _____
   If client does not know, tell them you will call them later asking them for the name of their medication.

   c. If yes, list date of medication initiation (mmm/yyyy): [__][__][__]/[__][__][__][__]

3. Do your blood-related mother, father, sisters, brothers, or grandparents have a history of sugar in the blood (diabetes)?
   ☐ No ☐ Yes ☐ Unknown

4. **If in Phase 1:** If we offered a rapid test to screen for sugar in the blood, a measurement that could determine if you had high sugar in the blood (diabetes), would you like to be screened for it? We would need to take a fingerprick blood sample.
   ☐ Yes ☐ No ☐ N/A, Project is in Phase 2
   If in Phase 2: Would you like your blood sugar screened today? This could help determine if you have high sugar in the blood (diabetes).
   ☐ Yes **☐ No→skip to Cholesterol section** ☐ N/A, Project is in Phase 1
   a. If yes, when was the last time you had something to eat or drink aside from water?
      ☐ within the hour ☐ 1-4 hours ago ☐ 4-8 hours ago ☐ 8+ hours ago

High Cholesterol/Hypercholesterolemia

1. Have you ever been diagnosed as having high cholesterol?
   ☐ No→skip to #3 ☐ Yes **☐ Unknown→skip to #3**

   a. If yes, date of diagnosis (mmm/yyyy): [__][__][__]/[__][__][__][__]

2. **If client was previously diagnosed with high cholesterol:**
   Have you ever been on treatment for high cholesterol?
   ☐ No ☐ **Yes →skip to 2b**
   a. **If no, why not, then skip to #3**:
      ☐ Not necessary ☐ Refused
   ☐ Other (specify):_____

   b. If yes, which medications (specify): _____

   If client does not know, tell them you will call them later asking them for the name of their medication.

   c. If yes, list date of medication initiation (mmm/yyyy):
   [__][__][__]/[__][__][__][__]

3. Do your blood-related mother, father, sisters, brothers, or grandparents have a history of high cholesterol?
   ☐ No ☐ Yes ☐ Unknown

4. **If in Phase 1:** If we offered a rapid test to screen for blood cholesterol, a measurement that could determine if you had high cholesterol and/or risk factors for stroke and heart disease, would you like to be screened for it? We would need to take a fingerprick blood sample.
   ☐ Yes ☐ No ☐ N/A, Project is in Phase 2
   If in Phase 2: Would you like your blood cholesterol screened today? It could help determine if you have high cholesterol and/or risk factors for things like stroke and heart disease.
   ☐ Yes **☐ No→skip to Cardiovascular section** **☐ N/A, Project is in Phase 1→skip to Cardiovascular section**
   a. If yes, when was the last time you had something to eat or drink aside from water?
   ☐ within the hour ☐ 1-4 hours ago ☐ 4-8 hours ago
   ☐ 8-14 hours ago ☐ 14+ hours ago

Cardiovascular Disease

1. Have your blood-related mother, father, sisters, brothers, or grandparents had a stroke? ☐ No ☐ Yes ☐ Unknown
2. Have your blood-related mother, father, sisters, brothers, or grandparents had a heart attack? ☐ No ☐ Yes ☐ Unknown
3. Have you ever had a stroke or heart attack? (Tick all that apply)
   ☐ **No →skip to Behavioural section** ☐ Stroke ☐ Heart attack

   ☐ **I don't know →skip to Behavioural section**

   a. If client has had a stroke, date of stroke (mmm/yyyy): [__][__][__]/[__][__][__][__]
   b. If client has had a heart attack, date of heart attack (mmm/yyyy)
      [__][__][__]/[__][__][__][__]

Behavioural Information

Alcohol Use

1. In the last year, how often would you usually drink alcohol?
   [__] days every week OR IF NOT EVERY WEEK

   [__][__] days every month OR IF NOT EVERY MONTH

   [__][__][__] days every year OR

   ☐ **never drank alcohol in the last year→skip to Smoking section**

2. Usually what type of alcohol do you drink? (Tick one)
   ☐ Beer ☐ Traditional beer ☐ Wine ☐ Spirits

3. About how many standard-size drinks do you usually have in one day?
   ☐ 1-2 ☐ 3-4 ☐ >4

Smoking

1. Have you ever smoked cigarettes? ☐ yes ☐ **no→skip to Physical Activity section**

2. For how many years have you smoked cigarettes? [__][__]

3. Do you still smoke cigarettes now? ☐ yes ☐ no

4. About how many cigarettes do you or did you usually smoke in one day?
   ☐ 1-2 ☐ Less than 5 ☐ 10 ☐ 20 ☐ 30 ☐ More than 30

Physical activity (Short IPAQ questionnaire)

I want to let you know what I mean with the words vigorous and moderate when you answer the next set of questions:
Vigorous physical activities *refer to activities that take hard physical effort and make you breathe much harder than normal.*
Moderate activities *refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.*

1a. During the last 7 days, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling? Think about *only* those physical activities that you did for at least 10 minutes at a time.
_____ **days per week**
1b. How much time in total did you usually spend on **one** of those days doing vigorous physical activities?
[__][__] **hours** [__][__] **minutes or** ☐ **none**

2a. Again, think *only* about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____ **days per week**

2b. How much time in total did you usually spend on **one** of those days doing moderate physical activities?

[__][__] hours [__][__] minutes or ☐ none

3a. During the last 7 days, on how many days did you **walk** for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did only for recreation, sport, exercise or leisure.
_____ **days per week**

3b. How much time in total did you usually spend walking on **one** of those days?

[__][__] hours [__][__] minutes or ☐ none

*This question is about the time you spent sitting on weekdays while at work, at home, while doing course work and during leisure time. This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television.*4. On average, over the last 7 days, how much time in total did you usually spend *sitting* on **one week day?**
[__][__] hours [__][__] minutes

Form End time: [ ][ ]:[ ][ ]

APPENDIX D4. HTS CLIENT HEALTH SCREENING RESULTS REPORT

Since the Phase 2 HTS Client Health Screening Results Report is more robust than the one used in Phase 1, only the report for Phase 2 is presented as an appendix.

NOTE: Pap Smear, HPV, and CD4 count results are provided by NHLS, and thus not on this report.
A copy of this report will be kept in the Zazi client file, and the original will be given to the client.

Client Name: _____
Zazi Client ID:_____ Study PTID: [__][__][__][__] or ☐Not on study
Date of Birth: [___][___] / [___][___][___] / [___][___][___][___] Male ☐ Female ☐
Date and time of testing: [___][___] / [___][___][___] / 20[___][___] [___][___]h[___][___]

Test	Not Done	Result	Results needing referral
Height and Weight and calculate Body Mass Index		Weight: [___][___][___] kg Height: [___][___][___] cm BMI: Height/(Weight)^2= [___][___]	Zazi does not refer for abnormal BMI. However less than 18 and greater than 25 is abnormal.
Abdominal girth		[___][___][___] cm	Zazi does not refer for abnormal waist circumference. However more than 102cm (men) and more than 88cm (women) is abnormal.
Blood Pressure A 2nd BP is not done when 1st is normal		BP 1: [___][___][___] / [___][___] BP 2: [___][___][___] / [___][___]	More than 140/90 Less than 90/60
Blood glucose: Average (HbAa1c) Random glucose	 ☐ ☐	 Average (HbA1c): [___][___].[___] Random glucose: [___][___].[___]	 Average: More than 6.5 Random: More than 11.1
Blood cholesterol: Triglycerides HDL LDL Total Cholesterol (TC)		 Triglycerides: [___][___].[___] HDL: [___][___].[___] LDL: [___][___].[___] Total Cholesterol: [___][___].[___]	 Triglycerides > 1.7 mmol/L HDL < 0.9 mmol/L LDL > 3 mmol/L TC > 5 mmol/L
Syndromic STI		☐ Discharge ☐ Blood ☐ Sores ☐ Lower abdominal pain ☐ Burning when urinating	If 1+ symptom is identified
Chlamydia		☐ Positive ☐ Negative ☐ Indeterminate	Any positive or indeterminate result
Syndromic TB		☐ Cough ☐ Blood in sputum ☐ Weight loss ☐ Sweats ☐ TB contact	If 1+ symptom is identified
HIV Rapid Test 1*		☐ Reactive ☐ Non-reactive ☐ Indeterminate	
HIV Rapid Test 2* A 2nd test is not done when 1st is non-reactive		☐ Reactive ☐ Non-reactive ☐ Indeterminate	
Final HIV Result		☐ Positive; indicates a positive HIV-1/2 antibody sample ☐ Negative; indicates a negative HIV-1/2 antibody sample ☐ Indeterminate; further testing required	Any positive or indeterminate result

*The HIV-1/2 Rapid Test Kits used are those provided by the South African Department of Health

Counsellor Name: _____ Counsellor Signature: _____

Date and Time: [___][___] / [___][___][___] / 20[___][___] [___][___]h[___][___]

Nurse Name: _____ Nurse Signature: _____

Date and Time: [___][___] / [___][___][___] / 20[___][___] [___][___]h[___][___]

Protocol Evaluation of ZAZI Study version 1.0 dated 8 December 2017
Zazi Results, Phase 2 version 1.0 dated 8 December 2017
Investigator: Kathryn Hopkins
Approved by Wits HREC
Date of Approval: 2 February 2018

Participant Initials: ___ ___
Participant Number: _____

APPENDIX D5. HTS COUNSELLOR RECOMMENDED REFERRAL SHEET

Since the Phase 2 HTS Counsellor Recommended Referral Sheet is more robust than the one used in Phase 1, only the sheet for Phase 2 is presented as an appendix.

Zazi Client ID:_____ Study PTID: _____ or ☐Not on study

Male ☐ Female ☐ Date: [___][___] / [___][___][___] / 20[___][___]

Test	Not Done	Referral (check all that apply)	NURSE USE ONLY Accuracy check
Blood Pressure		☐ High BP ☐ Low BP Client's preferred clinic: _____	☐ Correct ☐ Incorrect Comments: _____ _____ _____
Blood glucose		☐ High blood sugar ☐ Low Blood sugar Client's preferred clinic: _____	☐ Correct ☐ Incorrect _____ Comments: _____ _____
Blood Cholesterol		☐ High blood cholesterol Client's preferred clinic: _____	☐ Correct ☐ Incorrect Comments: _____ _____ _____
STI Screening		☐ 1+ STI symptom ☐ Currently has STI ☐ Wants Chlamydia screening ☐ Wants HPV screening Client's preferred clinic: _____	☐ Correct ☐ Incorrect _____ Comments: _____ _____ _____
Cervical Cancer Screening		☐ Wants Pap Smear Client's preferred clinic: _____	☐ Correct ☐ Incorrect Comments: _____ _____ _____
TB Screening		☐ 1+ TB symptom ☐ Currently has TB Client's preferred clinic: _____	☐ Correct ☐ Incorrect Client's preferred referral clinic: _____ Comments: _____ _____ _____
HIV		☐ Indeterminate result ☐ CD4 count ☐ ART ☐ PMTCT ☐ VMMC ☐ PrEP Client's preferred clinic: _____	☐ Correct ☐ Incorrect Comments: _____ _____ _____
Family Planning		☐ Wants injectable ☐ Wants oral contraception ☐ Wants other: _____ Client's preferred clinic: _____	☐ Correct ☐ Incorrect Comments: _____ _____ _____
Gender-based Violence		☐ Abused by partner ☐ Other: _____ Client's preferred clinic: _____	☐ Correct ☐ Incorrect Comments: _____ _____ _____

Counsellor's Name: _____ Counsellor's Signature: _____
Date and Time: [___][___] / [___][___][___] / 20[___][___] [___][___]h[___][___]

Nurse's Name: _____ Nurse's Signature: _____
Date and Time: [___][___] / [___][___][___] / 20[___][___] [___][___]h[___][___]

Protocol Evaluation of ZAZI Study version 1.0 dated 8 December 2017
Zazi Referrals, Phase 2 version 1.0 dated 8 December 2017
Investigator: Kathryn Hopkins
Approved by Wits HREC
Date of Approval: 2 February 2018

Participant Initials: ___ ___
Participant Number: _____

APPENDIX D6. HTS CLIENT CLINIC EXIT SURVEY

Since the Phase 2 HTS Client Clinic Exit Survey is more robust than the one used in Phase 1, only the survey for Phase 2 is presented as an appendix.

Zazi Client ID:_____ Study PTID: [___][___][___][___] Male ☐ Female ☐
Date and time: [___][___] / [___][___][___] / 20[___][___] [___][___]h[___][___]

"This brief survey asks questions about your experience within the clinic. It will ask about your opinions on counselling, health screenings and referrals you have received. You are not required to fill this out, but it would be greatly appreciated, helping us to make our clinic better for you and your community."

	Question	Responses
1.	Why did you first decide to come to the Zazi clinic today? **(circle all that apply)**	1 HIV testing for myself 2 HIV partner testing 3 CD4 4 TB screening 5 STI screening 6 Chlamydia rapid test 7 HPV screening 8 Get BMI calculation 9 Get waist circumference measurement 10 Check blood pressure 11 Check blood sugar 12 Check blood cholesterol 13 Cervical cancer screening 14 Counselling services 15 To get a referral letter 16 Worried about my health 17 Other; specify: _____ 97 Don't know 98 Decline to answer
2.	Once you got to the Zazi clinic and saw the services we offered, were there any additional services you chose to use that were different from what you answered in #1)? **(circle all that apply)**	0 No, my choice in services stayed the same 1 Yes, HIV testing 2 Yes, HIV partner testing 3 Yes, CD4 4 Yes, TB screening 5 Yes, STI screening 6 Yes, Chlamydia rapid test 7 Yes, HPV screening 8 Yes, BMI calculation 9 Yes, waist circumference measurement 10 Yes, Blood pressure 11 Yes, Blood sugar 12 Yes, Blood cholesterol 13 Yes, Cervical cancer screening 14 Yes, Counselling services 15 Yes, to get a referral letter 16 Yes, other; specify: _____ 97 Don't know 98 Decline to answer
3.	Did you opt out of any services?	1 Yes 2 No→**skip to #4** 97 Don't know 98 Decline to answer
3a.	Which services did you opt out of that you were eligible for? (circle all that apply)	1 HIV testing for myself 2 HIV partner testing 3 CD4 4 TB screening 5 STI screening 6 Chlamydia rapid test 7 HPV screening 8 Get BMI calculation 9 Get waist circumference measurement 10 Check blood pressure 11 Check blood sugar 12 Check blood cholesterol 13 Cervical cancer screening
3b.	Please explain why you opted out of any offered service.	_____
4.	Did you come to Zazi because you think you have a health problem?	1 Yes 2 No→**skip to #5** 97 Don't know 98 Decline to answer
4a.	Can you please explain what symptoms you are experiencing, or what your health problem is?	_____

5.	When you have a health problem, where do you usually go for help?	1 Hospital 2 Local government clinic 3 Counselling and testing clinics 4 Traditional healer 0 I don't go anywhere 97 Don't know 98 Decline to answer
6.	How would you rate the amount of time it took from when you entered the clinic until you were seen by a counsellor?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer

7.	How satisfied are you with the pre-test counselling you received?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
8.	Do you feel the quality of pre-test counselling should be improved?	1 Yes 0 No→ **skip to #9** 97 Don't know 98 Refuse to answer
8a.	In your own opinion, what improvement(s) should be made for pre-test counselling?	_____
9.	How would you rate the amount of time it took the counsellor to provide the pre-test counselling you received?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
10.	How well prepared did you feel for your health screening(s) procedures?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer
11.	How would you rate your level of comfort/discomfort while being tested?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
12.	How would you rate the amount of time it took the counsellor to provide the health screening tests and test results you received?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
13.	Do you feel the quality of the health screening test procedures should be improved?	1 Yes 0 No→ **skip to #14** 97 Don't know 98 Refuse to answer

13a.	In your own opinion, what improvement(s) should be made for the health screening test procedures?	_____
14.	Did you receive an abnormal result from the counsellor? **(circle all that apply)**	1 Yes, HIV 2 Yes, CD4 3 Yes, TB 4 Yes, STI 5 Yes, abnormal BMI 6 Yes, abnormal waist circumference measurement 7 Yes, high blood pressure 8 Yes, high blood sugar 9 Yes, high blood cholesterol 0 No, all results were normal 97 Don't know 98 Refuse to answer
15.	How did you feel immediately upon receiving your results?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer

16.	How did you feel after receiving both your results and post-test counselling?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer
17.	Is there anything else you felt after receiving your results and post-test counselling? If so, please explain.	_____
18.	How satisfied are you with the post-test counselling you received?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
19.	Do you feel the quality of post-test counselling should be improved?	1 Yes 0 No→ **skip to #20** 97 Don't know 98 Refuse to answer
19a.	In your own opinion, what improvement(s) should be made for post-test counselling?	_____

20.	How would you rate the amount of time it took the counsellor to provide the test results and post-test counselling you received?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
21.	Did you want to be screened for Chlamydia, HPV and/or cervical cancer? **(circle all that apply)**	1 Yes, Chlamydia 2 Yes, HPV 3 Yes, cervical cancer 0 No 97 Don't know 98 Refuse to answer
22.	Were you referred to the nurse for further consultation, tests, and/or referrals?	1 Yes 0 No→**skip to #32** 97 Don't know 98 Refuse to answer
23	Were you screened for Chlamydia?	1 Yes 0 No→**skip to #24** 97 Don't know 98 Refuse to answer
23a.	After speaking with the nurse, how well prepared did you feel for your Chlamydia screening procedure?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer
23b.	How would you rate your level of comfort/discomfort while being tested for Chlamydia?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
23c.	Did you receive an abnormal Chlamydia test result from the Nurse?	1 Yes 0 No 97 Don't know 98 Refuse to answer
23d.	How did you feel immediately upon receiving your Chlamydia test results?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer

23e.	How did you feel after receiving both your Chlamydia test results and post-test counselling from the Nurse?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer
24	Were you screened for HPV?	1 Yes 0 No→**skip to #25** 97 Don't know 98 Refuse to answer

24a	After speaking with the nurse, how well prepared did you feel for your HPV screening procedure?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer
24b	How would you rate your level of comfort/discomfort while being tested for HPV?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
24c.	How do you feel about having to wait a while and then return to the clinic for your HPV test result?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
25	Were you screened for cervical cancer?	1 Yes 0 No→**skip to #26** 97 Don't know 98 Refuse to answer
25a.	After speaking with the nurse, how well prepared did you feel for your cervical cancer screening procedure?	1 I feel very prepared 2 I feel somewhat prepared 3 Neutral 4 I feel somewhat unprepared 5 I feel very unprepared 97 Don't know 98 Refuse to answer
25b.	How would you rate your level of comfort/discomfort while being screened for cervical cancer?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
25c.	How do you feel about having to wait a while and then having to return to the clinic for your cervical cancer screening results?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
26	How satisfied are you with the additional testing and/or counselling you received from the Nurse?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
27	Do you feel the quality of additional testing and/or counselling provided by the Nurse should be improved?	1 Yes 0 No→ **skip to #28** 97 Don't know 98 Refuse to answer
27a.	In your own opinion, what improvement(s) should be made for post-test counselling?	_____
28	How would you rate the amount of time it took the Nurse to provide the additional screening tests and/or results and post-test counselling you received?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
29	Were you referred to any prevention, care or treatment services by the Nurse?	1 Yes 0 No→**skip to #30** 97 Don't know 98 Refuse to answer
29a.	Which referrals were you given by the Nurse? **(circle all that apply)**	1 ART clinic 2 STI clinic 3 TB clinic 4 High blood pressure 5 High blood sugar 6 High blood cholesterol 7 Circumcision 8 PMTCT 9 PrEP 10 Family Planning 97 Don't know 98 Refuse to answer

29b.	Do you plan on going to all of your referral service(s)?	1 Yes 0 No, please specify which ones you won't attend: _____ 97 Don't know 98 Refuse to answer
29c.	When do you think you will go to your referral services?	1 Today 2 This week 3 Within 2 weeks 4 Within 1 month 5 Within 2 months 6 Within 3 months 7 Longer than 3 months 0 Never 97 Don't know 98 Refuse to answer
30	Was speaking with the nurse helpful?	1 I feel it was very helpful 2 I feel it was somewhat helpful 3 Neutral 4 I feel it was somewhat unhelpful / waste of time 5 I feel it was very unhelpful / waste of time 6 I didn't see the nurse 97 Don't know 98 Refuse to answer
31	How would you rate the amount of time you spent with the nurse for further consultation and referrals?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 6 I didn't see the nurse 97 Don't know 98 Refuse to answer
32	Do you feel comfortable going to any referral services/clinics on your own?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
33	What could make you feel more comfortable about going to a referral service/clinic?	_____
34	Did you choose to use the help of a Zazi Linkage Navigator to help you reach your referrals?	1 Yes→**skip to #35** 0 No 97 Don't know 98 Refuse to answer
34a.	Why did you not want the help of a Linkage Navigator?	_____
35	How comfortable do you feel about the idea of a Zazi staff member going with you to your referral clinic?	1 I feel very comfortable 2 I feel somewhat comfortable 3 Neutral 4 I feel somewhat uncomfortable 5 I feel very uncomfortable 97 Don't know 98 Refuse to answer
36	In your own words can you explain why you would feel the way you do about Question #25?	_____
37	Overall, how do you feel about your experience at Zazi today?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
38	Overall, how do you feel about the amount of time you spent at Zazi today, from the moment you walked in until now?	1 I feel very satisfied 2 I feel somewhat satisfied 3 Neutral 4 I feel somewhat unsatisfied 5 I feel very unsatisfied 97 Don't know 98 Refuse to answer
39	In your own words, please describe what you liked about Zazi today.	_____
40	In your own words, please describe what you disliked about Zazi today.	_____
41	In your own words, please share if there is anything else you wished the Clinic would have provided you?	_____
42	Are there any other issues or concerns you experienced at the clinic that you would like to report?	_____
	Thank you. This concludes our Zazi Centre Client Exit Survey. Please give the survey to the Clinic Administrator at Reception.	

Participant Initials: ___ ___
Participant Number: _____

APPENDIX D7. HTS CLIENT LINKAGE TO CARE FOLLOW-UP SURVEY

Since the Phase 2 HTS Client Linkage to Care Follow-Up Survey is more robust than the one used in Phase 1, only the survey for Phase 2 is presented as an appendix.

Zazi Client ID:_____ Study PTID: [___][___][___][___] Male ☐ Female ☐
Original Screening Date: [___][___] / [___][___][___] / 20[___][___]
Actual Date: [___][___] / [___][___][___] / 20[___][___]

Follow-up call: ☐ Same day ☐ 2 weeks ☐ 1 month ☐ 2 months ☐ 3 months
Did client want help of Linkage Navigator: ☐ Yes ☐ No
Client was referred for (tick all that apply):
☐ ART clinic ☐ STI clinic ☐ TB clinic ☐ VMMC ☐ PMTCT ☐ PrEP
☐ FP ☐ High/low BP ☐ High Blood Sugar ☐ High Blood Cholesterol
☐ Gynecology ☐ GBV
Name of staff member calling: _____

	Part I. PHASE 2, CLIENT LINKAGE TO CARE FOLLOW-UP SURVEY: Same-day as screening	
If Linkage Navigator went with client to referral the same day as screening, Linkage Navigator fills this section out. If not, skip to next survey.		
1.	What referral appointment(s) did you take the client to today? **(tick all that apply)**	☐ ART clinic ☐ STI clinic ☐ TB clinic ☐ VMMC ☐ PMTCT ☐ PrEP ☐ FP ☐ High/low BP ☐ High Blood Sugar ☐ High Blood Cholesterol ☐ GBV
2.	Do you know if the client was initiated on treatment for anything? **(tick all that apply)**	☐ ART ☐ STI ☐ TB ☐ High/low BP ☐ High Blood Sugar ☐ High Blood Cholesterol
Questions 3 & 4 to be conducted by telephonic follow-up call by counsellors		
3.	Was using the service of a Linkage Navigator helpful?	☐Yes, why: _____ ☐ No, why not: _____ ☐ Don't know ☐ Decline to answer
4.	Would you have preferred to have gone to your referral appointments alone?	☐Yes, why: _____ ☐ No, why not: _____ ☐ Don't know ☐ Decline to answer
Question 5 to be answered by counsellors or nurse after checking TIER.NET, if client was referred to ART		
5.	Was client linkage to ART confirmed by TIER.NET?	☐Yes, date: [___][___] / [___][___][___] / 20[___][___] ☐ No
Part 2-5. PHASE 2, CLIENT LINKAGE TO CARE FOLLOW-UP TELEPHONE SURVEY: 2 weeks; and 1, 2, 3 months		
"Hello, I am calling for (*participant name)."[Confirm client identity with date of birth]. *"Hello, I am calling from the ZAZI HTS Centre to follow-up with you about your referral appointments. Do you have time for your* [2 week OR one month OR two month OR three month] *telephone survey now? This will take no more than 30 minutes. Let's begin…"		
1.	What referral appointment(s) have you been able to go to within the last 2 weeks	☐ ART clinic ☐ STI clinic ☐ TB clinic ☐ VMMC ☐ PMTCT ☐ PrEP ☐ FP

	[OR month OR two months OR three months]?	☐ High/low BP ☐ High Blood Sugar ☐ High Blood Cholesterol ☐ Gynecology ☐ GBV
2.	Could you please recall the date, to the best of your ability, of each referral appointment you attended, since you last spoke with us?	☐ ART clinic: [___][___] / [___][___][___] / 20[___][___] ☐ STI clinic: [___][___] / [___][___][___] / 20[___][___] ☐ TB clinic: [___][___] / [___][___][___] / 20[___][___] ☐ VMMC: [___][___] / [___][___][___] / 20[___][___] ☐ PMTCT: [___][___] / [___][___][___] / 20[___][___] ☐ PrEP: [___][___] / [___][___][___] / 20[___][___] ☐ FP: [___][___] / [___][___][___] / 20[___][___] ☐ High/low BP: [___][___] / [___][___][___] / 20[___][___] ☐ High Blood sugar: [___][___] / [___][___][___] / 20[___][___] ☐ High Cholesterol: [___][___] / [___][___][___] / 20[___][___] ☐ Gynecology: [___][___] / [___][___][___] / 20[___][___] ☐ GBV: [___][___] / [___][___][___] / 20[___][___]
3.	Did you use the assistance of a Linkage navigator for any of these referrals?	☐ Yes ☐ No
If client has NOT attended ALL referral appointments: (if client attended all referrals, skip to next section)		
4.	Could you please describe why you have not been able to reach all of your referral appointments?	
5.	Do you plan on going to any of the other referrals we suggested for you that you have not gone to yet?	☐Yes ☐ No →**SKIP to #4b** ☐ Don't know ☐ Decline to answer

5a.	If yes, when do you think you will go? *Let the client answer, and tick mark the answer that best fits.*	☐ This week ☐ Within 2 weeks ☐ Within the month ☐ Within 2 months ☐ Longer than 2 months ☐ Don't know ☐ Decline to answer
5b.	If no, why not?	
6.	Do you want the help of a Linkage Navigator for the remaining referrals?	☐Yes ☐ No ☐ Don't know ☐ Decline to answer
7.	Do you feel comfortable going to the remaining referral services/clinics on your own?	☐ I feel very comfortable ☐I feel somewhat comfortable ☐Neutral ☐ I feel somewhat uncomfortable ☐ I feel very uncomfortable

		☐Don't know ☐ Refuse to answer
8.	What do you think would have helped you reach the remaining referral services earlier?	
If client was referred to ART, STI, and/or TB clinics AND attended: (if client was not referred, skip to next section)		
9.	If client was referred to HIV clinic: were you initiated on ART?	☐ Yes, date of initiation: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Not referred to ART clinic ☐ Don't know ☐ Refuse to answer
10.	If client was referred to STI clinic: were you initiated on treatment?	☐ Yes, date of initiation: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Not referred to STI clinic ☐ Don't know ☐ Refuse to answer
11.	If client was referred to TB clinic: were you initiated on treatment?	☐ Yes, date of initiation: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Not referred to TB clinic ☐ Don't know ☐ Refuse to answer
If client was referred for high/low BP, blood sugar, and/or cholesterol AND attended referral: (if client was not referred, skip to next section)		
12.	If client was referred for high/low BP: were you initiated on treatment?	☐ Yes, date of initiation: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Not referred for high BP ☐ Don't know ☐ Refuse to answer
13.	If client was referred for high blood sugar: were you initiated on treatment?	☐ Yes, date of initiation: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Not referred for high blood sugar ☐ Don't know ☐ Refuse to answer

14.	If client was referred for high cholesterol: were you initiated on treatment?	☐ Yes, date of initiation: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Not referred for high cholesterol ☐ Don't know ☐ Refuse to answer
If client was referred to Gynecology AND attended referral: (if client was not referred, skip to next section)		
15.	If client was referred to Gynecology: Did you undergo further testing and/or treatment procedures?	☐ Yes, date of procedure: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Not referred to Gynecology ☐ Don't know ☐ Refuse to answer
15a.	If yes, what was the diagnosis?	☐ Pre-cancerous cells ☐ Cervical cancer ☐ Nothing ☐ Don't know ☐ Refuse to answer

15b.	If yes, date of diagnosis	[___][___] / [___][___][___] / 20[___][___]
15c.	If yes, have you been treated?	☐ Yes, date of treatment: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to treatment appointment yet ☐ Not referred to Gynecology ☐ Don't know ☐ Refuse to answer
15d.	If you need treatment, and you have not yet been treated, why not?	
If client was referred for FP and/or VMMC AND attended referral: (if client was not referred, skip to next section)		
16.	If client was referred for FP: were you put on any FP methods?	☐ Yes, date of initiation: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Don't know ☐ Refuse to answer
17.	If client was referred for VMMC: Did you get the procedure done?	☐ Yes, date of procedure: [___][___] / [___][___][___] / 20[___][___] ☐ No, why not: _____ ☐ Did not go to referral appointment yet ☐ Was not referred

		☐ Don't know ☐ Refuse to answer
"Thank you. This concludes our telephone survey."		
Questions 18 & 19 to be conducted by telephonic follow-up call by counsellors IF client used Linkage Navigators for any referral appointments reported in this survey		
18.	Was using the service of a Linkage Navigator helpful?	☐Yes, why: _____ ☐ No, why not: _____ ☐ Don't know ☐ Decline to answer
19.	Would you have preferred to have gone to your referral appointments alone?	☐Yes, why: _____ ☐ No, why not: _____ ☐ Don't know ☐ Decline to answer
Question 5 to be answered by counsellors or nurse after checking TIER.NET, if client was referred to ART		
20.	Was client linkage to ART confirmed by TIER.NET?	☐Yes, date: [___][___] / [___][___][___] / 20[___][___] ☐ No

APPENDIX K. PHD STUDY VARIABLES BY DATA SOURCE AND SOURCE DOCUMENT

Variable and Category Values	Variable Type and Category Definition	Data Source and Source Document
Demographics	**Independent Variables**	**Zazi HTS Health Screening Programme,** **HTS Client Demographics Form**
date	text (date_dmy)	
date_of_birth	text (date_dmy, Max: 1999-12-31)	
sex 1 2	Categorical Female Male	
race 1 2 3 4 5 6	Categorical Black White Coloured/mixed race Indian Asian Other	
nationality 1 2	Categorical South African Other	
ethnic_group 1 2 3 4 5 6 7 8 9 10	Categorical Zulu Sotho Tsonga Tswana Venda Xhosa North Sotho Ndebele Swazi Other	
marital_status 1 2 3 4 5 6	Categorical Single Married, including traditional or marriage Divorced Widowed Living together Other	
highest_education 1 2 3 4 5 6	Categorical No formal education Primary school High school Matriculated Tertiary education Other	
source_of_money 1 2 3 4 5 6	Categorical Employed Self-employed Social/Disability grant Parents Pension Other	
Demographics	**Dependent Variables**	**Zazi HTS Health Screening Programme,** **HTS Client Demographics Form**
age	Continuous [diff (date, date_of_birth)]	
age_cat 1 2	Categorical 18-24 (IF[diff (date, date_of_birth)≥18 & ≤24] 25-34 (IF[diff (date, date_of_birth)≥25 & ≤34]	

3 4	35-44 (IF[diff (date, date_of_birth)≥35 & ≤44] ≥45 (IF[diff (date, date_of_birth)≥45]	
marital_status_cat 1 2 3	Categorical Divorced/Widowed (IF marital_status = 3 or 4) Living together/Married (IF marital_status = 2 or 5) Single (IF marital_status = 1)	
highest_education_cat 1 2 3	Categorical Up to high school (IF highest_education = 1 or 2 or 3) Matriculated (IF highest_education = 4) Tertiary (IF highest_education = 5)	
Wealth Quintile Characteristics	**Independent Variables**	**Zazi HTS Health Screening Programme,** **HTS Client Demographics Form**
housing_living_on 1 2 3 4 5 6 7	Categorical Shack/ Zozo Flat/ cottage Room/ garage Hostel Shared house Stand alone brick house Other	
type_house 1 2 3 4	Categorical Permanent Rental Informal Other	
home_water_source 1 2 3 4 5	Categorical Tap water indoors Only outside tap water Well/ borehole Stream/ river/ pond Other water source	
type_of_toilet_facility 1 2 3 4 5	Categorical Flush toilet inside (connected to sewage) Outside pit latrine/ toilet Flush toilet inside (septic tank) No toilet facility Other toilet facility	
fuel_for_cooking 1 2 3 4 5 6 7	Categorical Electricity Gas Paraffin Coal Candles Firewood/ straw Other	
fuel_for_lighting 1 2 3 4 5 6 7	Categorical Electricity Gas Paraffin Coal Candles Firewood/ Straw Other	
household_have 1 2 3	Categorical Radio Computer Landline telephone	

4 5 6 7	TV Refrigerator Mobile phone/ cell phone None listed	
anyone_house_own 1 2 3 4 5 6	Categorical Bicycle Car/ truck Sheep/ goat/ cattle Motorcycle/ scooter Donkey/ horse None listed	
Wealth Quintile Characteristics	**Dependent Variables**	**Zazi HTS Health Screening Programme,** **HTS Client Demographics Form**
wealth_quintile 1 2 3 4 5	Categorical *See methods in text ≤20th percentile >20th percentile & ≤40th percentile >40th percentile & ≤60th percentile >60th percentile & ≤80th percentile >80th percentile & ≤100th percentile	
Risk Behaviour Characteristics	**Independent Variables**	**Zazi HTS Health Screening Programme,** **Data Collection Form**
drink_alcohol_last_year 1 2 3 4	Categorical Weekly Monthly Sometimes Never drank alcohol in the last year	
ever_smoked_cigarettes 0 1	Categorical No Yes	
Risk Behaviour Characteristics	**Dependent Variables**	**Zazi HTS Health Screening Programme,** **HTS Data Collection Form**
how_many_drinks_day 1 2 3 *ONLY IF [drink_alcohol_last_year] = 1 or 2 or 3*	Categorical 1-2 3-4 >4	
still_smoke_cig_now 0 1 *ONLY IF [ever_smoked_cigarettes] = 1*	Categorical No Yes	
how_many_cig_day 1 2 3 4 5 6 *ONLY IF [ever_smoked_cigarettes] = 1*	Categorical 1-2 Less than 5 10 20 30 More than 30	
HTS Health Screening Results	**Independent Variables**	**Zazi HTS Health Screening Programme**
height	Continuous text (number_1dp)	HTS Client Health Screening Results
weight	Continuous text (number)	HTS Client Health Screening Results
systolic1_BP	Continuous text (number)	HTS Client Health Screening Results

diastolic1_BP	Continuous Text (number)	HTS Client Health Screening Results
was_BP_redone 0 1	Categorical No Yes	HTS Client Health Screening Results
systolic2_BP	Continuous Text (number)	HTS Client Health Screening Results
diastolic2_BP	Continuous Text (number)	HTS Client Health Screening Results
HbA1c_results*	Continuous Text (number_1dp)	HTS Client Health Screening Results
HbA1c_low* 0 1 *(If RDT machine read 'low')*	Categorical No Yes	HTS Client Health Screening Results
random_glucose_results*	Continuous Text (number_1dp)	HTS Client Health Screening Results
random_glucose_low* 0 1 *(If RDT machine read 'low')*	Categorical No Yes	HTS Client Health Screening Results
total_cholesterol_results*	Continuous Text (number_1dp)	HTS Client Health Screening Results
total_cholesterol_low* 0 1 *(If RDT machine read 'low')*	Categorical No Yes	HTS Client Health Screening Results
syndromic_sti 1 2 3 4 5 6	Categorical Discharge Blood Sores Lower abdominal pain Burning when urinating No symptoms	HTS Client Health Screening Results
chlamydia_results* 1 2 3	Categorical Positive Negative Indeterminate	HTS Client Health Screening Results
syndromic_tb 1 2 3 4 5 6	Categorical Coughing Blood in sputum Weight loss Sweats TB contact No symptoms	HTS Client Health Screening Results
final_HIV_result 1 2 3	Categorical Reactive Non-reactive Indeterminate	HTS Client Health Screening Results
CD4_results	Continuous Text (number)	HTS Client Health Screening Results
HTS Health Screening Results	**Dependent Variables**	**Zazi HTS Health Screening Programme**
BMI	Continuous [weight]/([height]*[height)	HTS Client Health Screening Results
systolic2_BP *ONLY IF* *[was_BP_redone] = 1*	Continuous Text (number)	HTS Client Health Screening Results

diastolic2_BP *ONLY IF [was_BP_redone] = 1*	Continuous Text (number)	HTS Client Health Screening Results
systolic_avg	Continuous =sum(systolic1_BP,systolic2_BP)/2	HTS Client Health Screening Results
diastolic_avg	Continuois =sum(diastolic1_BP,diastolic2_BP)/2	HTS Client Health Screening Results
BP_avg 1 2 3	Categorical High BP (IF systolic_avg>140 or diastolic_avg>90) Low BP [ELSE IF (systolic_avg>0 and systolic_avg<90) or (diastolic_avg>0 and diastolic_avg<60)] Normal BP [ELSE IF (systolic_avg>90 or diastolic_avg>60) and (systolic_avg<140 or diastolic_avg<90)	HTS Client Health Screening Results
HbA1c_cat* 1 2 3	Categorical High HbA1c (IF HbA1c_results ≥ 6.5) Low HbA1c (IF HbA1c_low = 1) Normal HbA1c (IF HbA1c_results < 6.5 and HbA1c_low = 0)	HTS Client Health Screening Results
random_glucose_cat* 1 2 3	Categorical High (IF random_glucose_results ≥ 11) Low (IF random_glucose_low = 1) Normal (IF random_glucose_results < 11 and random_glucose_low = 0)	HTS Client Health Screening Results
total_cholesterol_cat* 1 2 3	Categorical High (IF total_cholesterol_results ≥ 5) Low (IF total_cholesterol_low = 1) Normal (IF total_cholesterol_results < 5 and total_cholesterol_low = 0)	HTS Client Health Screening Results
Quality of Task-shifting	**Independent Variables**	**Zazi HTS Health Screening Programme,** **HTS Counsellor Recommended Referral Sheet**
BP_results_correct 0 1	Categorical No Yes	
glucose_results_correct* 0 1	Categorical No Yes	
chol_results_correct* 0 1	Categorical No Yes	
STI_results_correct 0 1	Categorical No Yes	
TB_results_correct 0 1	Categorical No Yes	
HIV_results_correct 0 1	Categorical No Yes	
Feasibility of Task-shifting/Clinic Flow Time Points	**Independent Variables**	**Zazi HTS Health Screening Programme**
time	text (time)	HTS Client Demographics Form
end_time	text (time)	HTS Client Demographics Form
pre_test_start_time	text (time)	HTS Client Counselling Form

pre_test_end_time	text (time)	HTS Client Counselling Form
screenings_start_time	text (time)	HTS Client Counselling Form
screenings_end_time	text (time)	HTS Client Counselling Form
post_start_time	text (time)	HTS Client Counselling Form
post_end_time	text (time)	HTS Client Counselling Form
start_time_data	text (time)	HTS Data Collection Form
form_end_time	rext (time)	HTS Data Collection Form
Feasibility of Task-shifting/Clinic Flow Time Points	**Dependent Variables**	**Zazi HTS Health Screening Programme**
reception_time	Continuous [diff (end_time, time)]	HTS Client Demographics Form
pretest_time	Continuous [diff (pre_test_end_time, pre_test_start_time)]	HTS Client Counselling Form
screenings_time	Continuous [diff (screenings_end_time, screenings_start_time)]	HTS Client Counselling Form
posttest_time	Continuous [diff (post_end_time, post_start_time)]	HTS Client Counselling Form
data_form_time	Continuous [diff (form_end_time, start_time_data)]	HTS Data Collection Form
total_HTS_time	Continuous [diff (post_end_time, pre_test_start_time)]	HTS Client Counselling Form
total_clinic_time	Continuous [diff (post_end_time, time)]	HTS Client Demographics Form & HTS Client Counselling Form
HTS Client Satisfaction with Clinic Flow Time	**Independent Variables**	**Evaluation of Zazi Study, HTS Client Clinic Exit Survey**
client_reception_time 1 2 3 4 5 97 98	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied Don't know Refuse to answer	
client_pretest_time 1 2 3 4 5 97 98	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied Don't know Refuse to answer	
client_screening_time 1 2 3 4 5	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied	

97 98	Don’t know Refuse to answer	
client_posttest_time 1 2 3 4 5 97 98	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied Don’t know Refuse to answer	
client_nurse_time 1 2 3 4 5 97 98	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied Don’t know Refuse to answer	
HTS Client Satisfaction with HTS Services	**Independent Variables**	**Evaluation of Zazi Study,** **HTS Client Clinic Exit Survey**
satisfied_pretest 1 2 3 4 5 97 98	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied Don’t know Refuse to answer	
prepared_screenings 1 2 3 4 5 97 98	Categorical I feel very prepared I feel somewhat prepared I feel neutral I feel somewhat prepared I feel very prepared Don’t know Refuse to answer	
comfort_screenings 1 2 3 4 5 97 98	Categorical I feel very comfortable I feel somewhat comfortable I feel neutral I feel somewhat uncomfortable I feel very uncomfortable Don’t know Refuse to answer	
satisfied_posttest 1 2 3 4 5 97 98	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied Don’t know Refuse to answer	
helpful_nurse 1 2 3 4 5 97 98	I feel it was very helpful I feel it was somewhat helpful Neutral I feel it was somewhat unhelpful / waste of time I feel it was very unhelpful / waste of time I didn't see the nurse Don't know Refuse to answer	

client_experience 1 2 3 4 5 97 98	Categorical I feel very satisfied I feel somewhat satisfied I feel neutral I feel somewhat unsatisfied I feel very unsatisfied Don't know Refuse to answer	
client_like	Open-ended Response Notes	
client_dislike	Open-ended Response Notes	
Linkage to Care and Treatment Initiation	**Independent Variables**	**Evaluation of Zazi Study,** **HTS Client Linkage to Care Follow-Up Survey**
ART_LTC 1 2 3	Categorical No Yes Not applicable / Not referred	
ART_clinic_date	Continuous Text (date_dmy)	
explain_missed_ART_referral	Open-ended Response Notes	
ART_TI 0 1 98	Categorical No Yes Not applicable / Not referred	
ART_initiation_date	Continuous Text (date_dmy)	
explain_no_ART	Open-ended Response Notes	
STI_LTC 1 2 3	Categorical No Yes Not applicable / Not referred	
STI_clinic_date	Continuous Text (date_dmy)	
explain_missed_STI_referral	Open-ended Response Notes	
STI_TI 0 1 98	Categorical No Yes Not applicable / Not referred	
STI_treatment_date	Continuous Text (date_dmy)	
explain_no_STI_treatment	Open-ended Response Notes	
TB_LTC 1 2 3	Categorical No Yes Not applicable / Not referred	
TB_clinic_date	Continuous Text (date_dmy)	
explain_missed_TB_referral	Open-ended Response Notes	
TB_TI 0 1 98	Categorical No Yes Not applicable / Not referred	
TB_treatment_date	Continuous	

	Text (date_dmy)	
explain_no_TB_treatment	Open-ended Response Notes	
BP_LTC 1 2 3	Categorical No Yes Not applicable / Not referred	
BP_clinic_date	Continuous Text (date_dmy)	
explain_missed_BP_referral	Open-ended Response Notes	
BP_TI 0 1 98	Categorical No Yes Not applicable / Not referred	
BP_treatment_date	Continuous Text (date_dmy)	
explain_no_BP_treatment	Open-ended Response Notes	
glucoe_LTC* 1 2 3	Categorical No Yes Not applicable / Not referred	
glucose_clinic_date*	Continuous Text (date_dmy)	
explain_missed_glucose_referral*	Open-ended Response Notes	
glucose_TI* 0 1 98	Categorical No Yes Not applicable / Not referred	
glucose_treatment_date*	Continuous Text (date_dmy)	
explain_no_glucose_treatment*	Open-ended Response Notes	
TC_LTC* 1 2 3	Categorical No Yes Not applicable / Not referred	
TC_clinic_date*	Continuous Text (date_dmy)	
explain_missed_TC_referral*	Open-ended Response Notes	
TC_TI* 0 1 98	Categorical No Yes Not applicable / Not referred	
TC_treatment_date*	Continuous Text (date_dmy)	
explain_no_TC_treatment*	Open-ended Response Notes	
choose_active_linkage* 1 2 3 97 98	Categorical No Yes Not applicable / No referral Don’t know Refuse to answer	**Zazi Evaluation Study,** **HTS Client Clinic Exit Survey**
why_no_active*	Open-ended Response Notes	

Linkage to Care and Treatment Initiation	**Dependent Variables**	**Zazi Evalution Study, HTS Client Linkage to Care Follow-up Survey**
LTC_time_ART	Continuous [diff (ART_clinic_date, date)]	
TI_time_ART	Continuous [diff (ART_initiation, date)]	
LTC_time_STI	Continuous [diff (STI_clinic_date, date)]	
TI_time_STI	Continuous [diff (STI_treatment, date)]	
LTC_time_TB	Continuous [diff (TB_clinic_date, date)]	
TI_time_TB	Continuous [diff (TB_treatment, date)]	
LTC_time_BP	Continuous [diff (BP_clinic_date, date)]	
TI_time_BP	Continuous [diff (BP_treatment, date)]	
LTC_time_glucose*	Continuous [diff (glucose_clinic_date, date)]	
TI_time_glucose*	Continuous [diff (glucose_treatment, date)]	
LTC_time_TC*	Continuous [diff (TC_clinic_date, date)]	
TI_time_TC*	Continuous [diff (TC_treatment, date)]	
LTC_cat_ART 1 2 3	Categorical Delayed (IF LTC_time_ART > 30 and ≤ 90) Successful (IF LTC_time_ART ≤ 30) Lost to follow-up (IF LTC_time_ART > 90 OR ART_LTC = 1)	
TI_cat_ART 1 2 3	Categorical Delayed (IF TI_time_ART > 30 and ≤ 90) Successful (IF TI_time_ART ≤ 30) Lost to follow-up (IF TI_time_ART > 90 OR ART_TI = 1)	
LTC_cat_STI 1 2 3	Categorical Delayed (IF LTC_time_STI > 30 and ≤ 90) Successful (IF LTC_time_STI ≤ 30) Lost to follow-up (IF LTC_time_STI > 90 OR STI_LTC = 1)	
TI_cat_STI 1 2 3	Categorical Delayed (IF TI_time_STI > 30 and ≤ 90) Successful (IF TI_time_STI ≤ 30) Lost to follow-up (IF TI_time_STI > 90 OR STI_TI = 1)	
LTC_cat_TB 1 2 3	Categorical Delayed (IF LTC_time_TB > 30 and ≤ 90) Successful (IF LTC_time_TB ≤ 30) Lost to follow-up (IF LTC_time_TB > 90 OR TB_LTC = 1)	
TI_cat_TB 1 2 3	Categorical Delayed (IF TI_time_TB > 30 and ≤ 90) Successful (IF TI_time_TB ≤ 30) Lost to follow-up (IF TI_time_TB > 90 OR TB_TI = 1)	
LTC_cat_BP 1 2	Categorical Delayed (IF LTC_time_BP > 30 and ≤ 90) Successful (IF LTC_time_BP ≤ 30)	

3	Lost to follow-up (IF LTC_time_BP > 90 OR BP_LTC = 1)	
TI_cat_BP 1 2 3	Categorical Delayed (IF TI_time_BP > 30 and ≤ 90) Successful (IF TI_time_BP ≤ 30) Lost to follow-up (IF TI_time_BP > 90 OR BP_TI = 1)	
LTC_cat_glucose* 1 2 3	Categorical Delayed (IF LTC_time_glucose > 30 and ≤ 90) Successful (IF LTC_time_glucose ≤ 30) Lost to follow-up (IF LTC_time_glucose > 90 OR glucose_LTC = 1)	
TI_cat_glucose* 1 2 3	Categorical Delayed (IF TI_time_glucose > 30 and ≤ 90) Successful (IF TI_time_glucose ≤ 30) Lost to follow-up (IF TI_time_glucose > 90 OR glucose_TI = 1)	
LTC_cat_TC* 1 2 3	Categorical Delayed (IF LTC_time_TC > 30 and ≤ 90) Successful (IF LTC_time_TC ≤ 30) Lost to follow-up (IF LTC_time_TC > 90 OR TC_LTC = 1)	
TI_cat_TC* 1 2 3	Categorical Delayed (IF TI_time_TC > 30 and ≤ 90) Successful (IF TI_time_TC ≤ 30) Lost to follow-up (IF TI_time_TC > 90 OR TC_TI = 1)	

***Variables only collected within integrated non-communicable disease – HIV testing services**