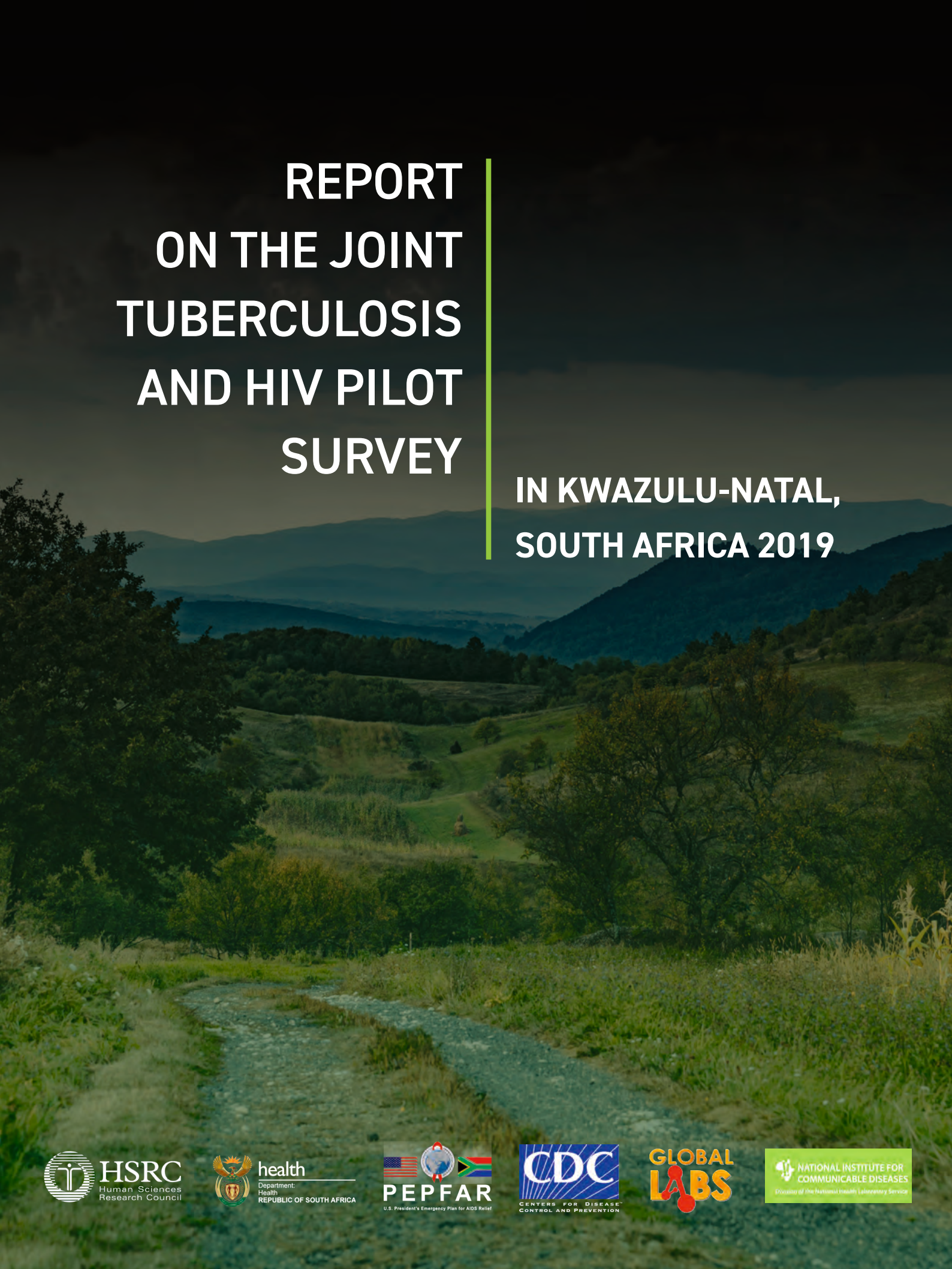
REPORT ON THE JOINT TUBERCULOSIS AND HIV PILOT SURVEY

IN KWAZULU-NATAL, SOUTH AFRICA 2019



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PEPFAR U.S. President's Emergency Plan for AIDS Relief

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NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES Division of the National Health Laboratory Service

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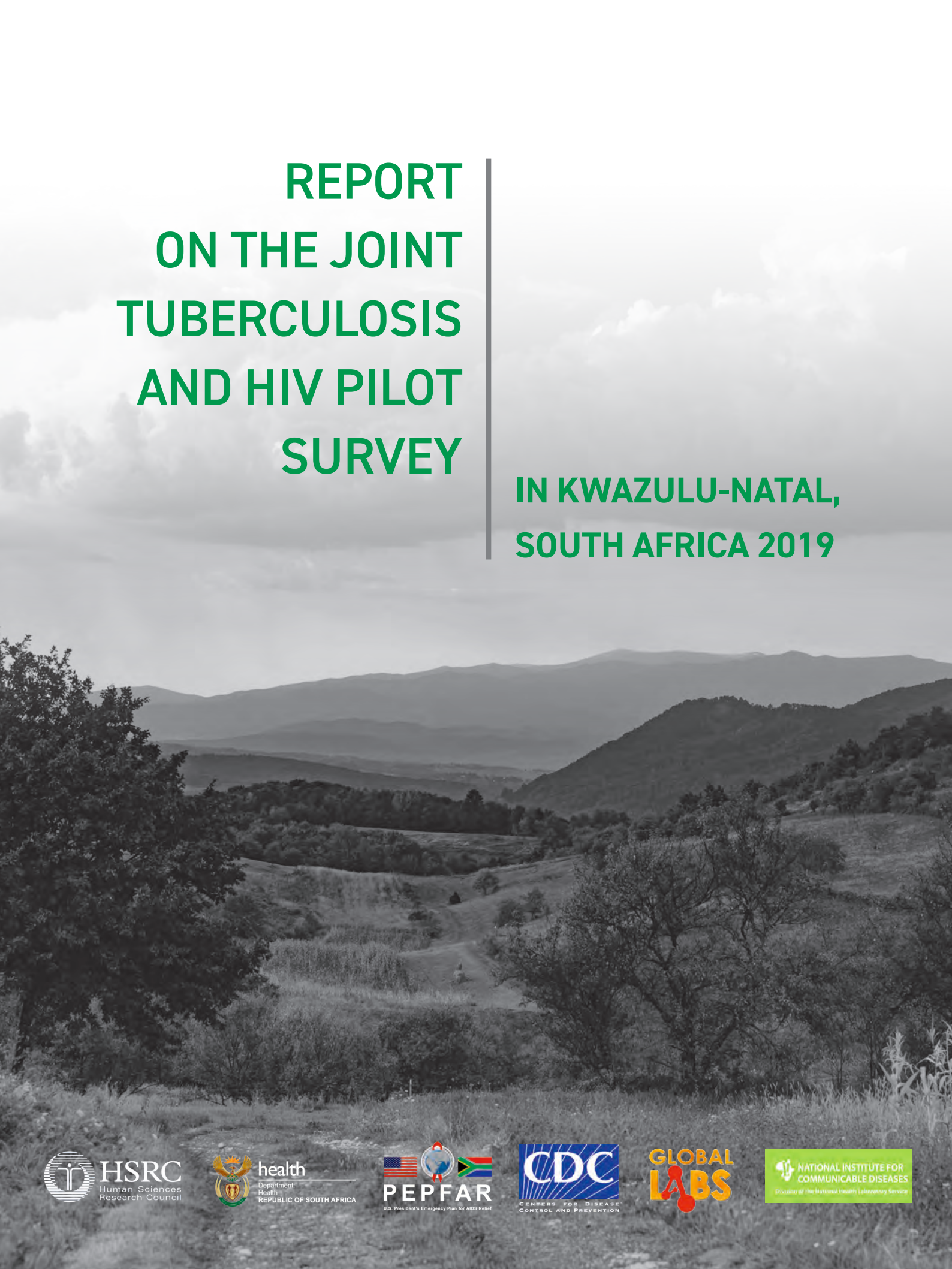

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ACRONYMS AND ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
CASI	Computer Assisted Self Interviewing
CDC	United States Centers for Disease Control and Prevention
CXR	Chest X-Ray
DBS	Dried blood spot
DNA	Deoxyribonucleic acid
DR	Drug resistance
EA	Enumeration area
EIA	Enzyme immunoassay
EID	Early infant diagnosis
FGD	Focus group discussion
GCVL	Global Clinical and Viral Laboratories
HH	Head of the household
HIV	Human immunodeficiency virus
HIVDR	HIV drug resistance
HSRC	Human Sciences Research Council
ID	Identification
IT	Information technology
KI	Key informants
KII	Key informant interviews
KZN	KwaZulu-Natal
LAg	Limiting antigen
MO	Medical officer
M.tb	*Mycobacterium tuberculosis*
NDoH	National Department of Health

NICD	National Institute for Communicable Diseases
OD	Optical density
OD*n*	Normalised optical density
PCR	Polymerase chain reaction
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PHIA	Population-based HIV impact assessment
PLHIV	People living with HIV
QA	Quality assurance
REDCap	Research Electronic Data Capture[new line]
RITA	Recent infection testing algorithm
RNA	Ribonucleic acid
RT	Rapid test
SABSSM	South African National HIV prevalence, Incidence, Behaviour and Communication Survey
SABSSMV	The fifth South African National HIV prevalence, Incidence, Behaviour and Communication Survey
SAL	Small area layer
SAMRC	South African Medical Research Council
SOP	Standard operating procedure
STI	Sexually transmitted infection
TB	Tuberculosis
TPS	National TB prevalence survey
UNAIDS	Joint United Nations Programme on HIV/AIDS
VL	Viral load
WHO	World Health Organisation

Survey-related definitions

Urban Areas: Geographic areas classified as urban by the 2011 South African National Census.

Rural Areas: Geographic areas classified as rural by the 2011 South African National Census.

Household: A group of persons who normally live and eat together. These people may or may not be related by blood but make common provisions for food or other essentials for living, and they have only one person whom they all regard as the head of the household (HH).

Head of household: The person who is recognised within the household as being its head and is 18 years or older. In the absence of an adult household head, younger members of the household who are accepted to be head by household members will be considered to be heads of the household.

Emancipated minors: Those aged 14-17 years who are married, or earn independent incomes, or have a living arrangement separate from their family.

Cluster Survey Site (Hub): This is a temporary central location within the cluster where all survey activities such as data collection and biomedical testing are conducted.

TB case definitions

Bacteriologically Tuberculosis positive (Bacteriologically TB positive): Identification of Mycobacterium tuberculosis, deoxyribonucleic acid by GeneXpert Ultra and/or isolation of Mycobacterium tuberculosis complex by culture from at least one of the sputum samples.

New TB patient: A patient who has never had TB treatment or has taken TB treatment for less than four weeks.

Previously treated TB patient: A patient with a prior history of TB treatment for at least four weeks and either relapsed, defaulted or failed treatment.

Currently on TB treatment: A patient who is currently registered for TB treatment.

HIV case definitions

HIV antibody positive: A respondent whose final test result is positive using the South African national HIV rapid testing algorithm or on laboratory HIV testing.

Incident/recent case of HIV: This refers to persons newly infected with HIV. In general, HIV incidence is expressed as the estimated number of persons newly infected with HIV during a specified time period (e.g., a year), or as a rate calculated by dividing the estimated number of persons newly infected with HIV during a specified time period by the number of persons at risk for HIV infection.

New diagnosis of HIV infection: This refers to individuals newly diagnosed with HIV, but who may have been infected years before being diagnosed.

Viral Load suppression: This is when antiretroviral therapy reduces a person's viral load (VL) to an undetectable level of <1000 copies/mL at the most recent viral load test. Viral suppression does not mean a person is cured – HIV still remains in the body. If antiretroviral therapy is discontinued, the person's viral load will likely return to a detectable level.

EXECUTIVE SUMMARY

Background

South Africa has a high infectious disease burden with overlapping Human Immunodeficiency Virus (HIV) and tuberculosis (TB) epidemics. People living with HIV (PLHIV) are vulnerable to drug-resistant TB, and HIV is associated with multi- and extremely-drug resistant TB epidemics and outbreaks.

South Africa has conducted population-based national HIV prevalence, behaviour and communication surveys since 2002. These studies, which include dry bloodspot samples, have more recently included analyses of HIV incidence, antiretroviral drug uptake, recency of HIV infection, and viral load suppression. The National Department of Health (NDoH) conducted its first TB prevalence survey in 2017 and that survey included symptom screening, sputum samples and mobile chest x-rays.

Although there are different criteria for HIV and TB surveillance studies – including variations in sample size, sampling methods and, on and off-site testing approaches, sample collection procedures, storage and transport logistics – there is potential to conduct joint surveys. Benefits include data collection within the same sampling framework and timeframe, obtaining insight into HIV-TB coinfection, and avoiding cost duplication.

To explore these possibilities, a pilot Joint HIV-TB survey was conducted by the Human Sciences Research Council (HSRC) in collaboration with the United States Centers for Disease Control (CDC) and Prevention in partnership with the NDoH, Global Clinical and Viral Laboratories, and the National Institute for Communicable Diseases (NICD).

Methods and preparatory steps

The pilot survey utilised the same sampling frame as the recent National Tuberculosis Prevalence Survey which is based on small areas layers as building blocks for clusters. Two clusters in KwaZulu-Natal were selected – Marburg (urban) and uMgayi/the Ridge (rural) and the survey was conducted between August and September 2019.

Sampling was conducted at the household level, with all eligible residents in the sampled households invited for attendance at the cluster survey hub for screening and testing. Common questionnaires were administered to all households, and there were separate questionnaires for children 11 years or younger, 12 – 14-year-olds stionnaires and computer-assisted self and people aged 15 years and older.

Screening, sample collection and testing at the survey hubs included 1) Rapid HIV tests; 2) blood sample collection for central laboratory testing for HIV, viral load, Limiting Antigen Avidity assay, HIV drug resistance; 3) chest X-ray images for respondents 15 years and older; 4) sputum sample collection for Xpert Ultra testing and culture for TB from respondents aged 15 years and older with presumptive TB; 5) random (point of care) blood glucose and blood cholesterol measurement from respondents aged 15 years and older; and 6) blood pressure, weight and height from respondents aged 15 years and older.

Ethical approval for the pilot study protocol was received from ethical committees of the HSRC and the Center for Global Health, of the CDC. Fieldworkers received training in ethics and survey procedures. Modest in-kind reimbursements were provided to survey

respondents. Survey instruments and procedures included English and isiZulu materials and interviewer-administered questionnaires and computer-assisted self-interviewing (CASI) options. Data were collated and managed using the Research Electronic Data Capture (REDCap) system.

Recruitment of fieldwork staff included drawing on personnel who had previously worked on either HIV or TB surveys or studies.

Pre-survey visits included engagement with community stakeholders and information sharing about the forthcoming survey. Community volunteers were recruited through leadership structures in each cluster. These volunteers were flexible members of the field survey team and they served a liaison function with local authorities and their community about the survey.

A situation assessment was conducted in each cluster after which there was a pre-listing, followed by the household census and interviews. Household members were assigned a study identity number and invitations were handed out to participants to visit the survey hub at a convenient time.

Implementation

Hub activities involved a multi-station arrangement whereby respondents were briefed on the procedures, consented and enrolled. Individual questionnaires (per age category) were completed, mostly by an interviewer and by using CASI with a proportion of respondents. The questionnaires included screening questions for TB, and questions about HIV and TB risk factors.

Chest X-rays (CXR) were administered, point of care tests conducted, and anthropomorphic measurements were taken, when applicable. Blood samples were drawn (including by venepuncture, finger prick, or heel prick), and HIV rapid testing was conducted. Respondents then proceeded to the Medical Officer (MO) station where their CXR was assessed. Two sputum specimens were obtained from participants identified as having presumptive TB (from TB screening questions and CXR) – one for Xpert Ultra testing and the other for TB culture. On completion of these procedures, the respondents could exit the hub.

Dried blood spot, plasma and sputum samples were appropriately labelled and packaged – including giving attention to cold chain conditions – and conveyed to respective laboratories via a courier. Biomarker tests included Xpert®MTB/RIF Ultra and MGIT 960 for sputum, HIV rapid testing for DBS (Dried blood spot) cards and HIV antibody testing, viral load testing using the Abbott platform, Limiting Antigen Avidity enzyme immunoassay for HIV recency, and genotyping for HIV drug resistance. Respondents could access the results of these laboratory tests at the clinic in the cluster at various time points including four days for sputum Xpert results, eight weeks for sputum culture, 12 weeks for HIV viral load, discrepant serology and infant diagnosis, and six months for HIV drug resistance.

To support understanding of the implementation process, a small-scale qualitative study comprising focus group discussions (FGDs) and key informant interviews was conducted with various staff and volunteers in the cluster. Field staff diaries and field observations provided additional data points.

Data for the cost estimates were gathered via a combination of top-down and bottom-up approaches including personnel, travel, training, equipment, supplies, building (hub and field lab), sample transportation, communication, central lab tests and other miscellaneous costs. The components that constituted the cost elements for the survey were identified and weights were assigned to the TB and HIV aspects respectively, based on actual invoice costs and on inputs from the project team. Cluster specific costs were also computed. For the hypothetical scaled up survey, it was assumed that the scope and cost components would be similar to those of this pilot survey. Total and per respondent cost in the pilot survey are presented in 2019 South African Rand (ZAR). Total and per respondent cost in the projected scaled up were presented in 2020 ZAR. Costs were also presented in USD of the same year, i.e., 2019 USD for the pilot and 2020 USD for the scaled-up.

Lessons learned

Joint survey: This joint TB-HIV pilot survey was successfully implemented in two geo-types (urban and rural) in KwaZulu-Natal, South Africa. The survey successfully combined TB and HIV components, including the collection of venous blood samples for HIV testing – an approach that has not yet been implemented in the series of national HIV surveys previously undertaken in South Africa. Overall, the biomarker data obtained was of good quality, with only a few missing variables. Qualitative and cost data were also formally collected for the first time since such information is typically not included in standard population-based TB and HIV surveillance surveys.

Response rate at households: Overall, 78.6% of the households were interviewed. However, within those households, the household-level response rate achieved – ~99% overall, and in each cluster was high. For this survey, the response rate was higher than in the most recent national HIV and TPS completed in South Africa.[3] The high response rate was potentially due to the inclusion of all households in the selected clusters, as well as the interest in the additional general health tests and measurements offered to respondents.

Response rate at the hubs: Although almost all eligible people accepted an invitation to the hub, in the end, less than half attended the services at the hub and were enrolled. Therefore, despite the high household-level response, the overall survey participation rate (enrolment at the hub) among all people who were eligible was low, with only 47.8% of all eligible individuals enrolled in the survey. This could be because invitations to the hub could be accepted without the guarantee that these individuals would attend the hub. Furthermore, some invitations were accepted by proxies. The participation rate could also have been influenced by the fact that some people may not have been keen to travel to and spend time at the hub despite transport being provided, and concerns regarding excessive time spent at the hub or distance and other factors such as community tension, which were reported from the qualitative interviews.

Uptake of HIV testing: Uptake of HIV rapid testing was relatively high, with nearly 68% of those who enrolled accepting testing. More than 60% of those enrolled also gave a venous blood sample suggesting moderate levels of acceptability of venous blood draws for population-based HIV surveillance in these two sites.

Uptake of TB screening and testing: Uptake of CXR was high as was sputum sample submission. None of those eligible for CXR declined it and almost all respondents submitted two sputum samples.

Uptake of additional tests and measurements: Uptake of additional health tests and measurements was high above 90% uptake for each test, and these were reported (in the qualitative interviews) to have been attractive to respondents and drove participation.

Organisation of activities: The organisation of activities at the hub was intended to ensure time efficiency. The survey was arranged in such a way that informed consent for all procedures was the first activity after the group information session. Overall, this process was efficiently carried out in general, although bottlenecks occurred in administering the informed consent and the CASI questionnaires. Problems with CASI were linked to preceding funding restrictions that had a knock-on effect on procuring, programming, and testing the devices, while problems with reading legibility and confidence with the electronic interface caused delays in data input by respondents.

Hub-based laboratory: The hub-based laboratory was labour intensive and prolonged hub operating hours.

Time in the field: The duration of the project and time required for household census and hub activities was not always adequate to reach the survey sample due to various dynamics in the field – for example, the terrain in the rural cluster was challenging to access, and in both clusters some people worked outside the cluster, leaving their homes early and returning late in the evening – which made it difficult for them to participate on the study. TB surveys, including the TPS, include a flexible schedule that can extend the time in each cluster which could increase participation. In this pilot, this option was not implemented given time and budget constraints.

Training: Although all members of the field team passed the competency testing conducted after training, it was evident that more intensive training would have been beneficial given that staff with more experience in HIV tended to gravitate towards HIV surveillance protocols and vice versa for those more experienced in TB. **Processing of blood and sputum samples was successful overall, as was transportation to various laboratories for testing.**

- **Costs:** The main cost element in the pilot survey was staff costs which accounted for close to 50% of the overall survey costs. This was followed by travel and laboratory test costs each accounting for about 15% of the overall cost. The unit cost of the HIV component was ZAR 6,916 (US$ 494) per participant in rural areas and ZAR 11,382 (US$ 813) per participant in urban areas. The unit cost for the TB component was lower than that of the HIV component, i.e., ZAR 6,300 (US$ 450) per participant in rural area, and ZAR 7,840 (US$ 560) per participant in urban areas. The lower response rate in urban areas may partially explain the higher per participant cost compared to that in rural areas. The projected costs of a hypothetically scaled TB-HIV survey is ZAR 236,667,676, US$ 16,904,834 for a sample of 35,479 respondents translating to a respondent cost of ZAR 12,147 (US$ 868). The respondent cost for the fifth South African National HIV prevalence, Incidence, Behaviour and Communication Survey (SABSSMV) (participants 0 years+) was estimated at ZAR 2,138 (US$ 152) while that for the National TB prevalence survey (TPS) was ZAR 2,479 (US$ 177). It should be noted that the designs of the projected hypothetical joint survey, SABSSMV and the TPS are

different thus limiting a direct comparison of costs. The hypothetical joint survey and the TPS collect data both at the household and at a hub. The hub creates additional costs for transportation of participants and from the hub and set up and running costs which include a mini field laboratory for the hypothetical survey. The hypothetical survey also includes venous blood draws in addition to DBS samples, and rapid HIV testing at the hub, whereas SABSSMV and the TPS used DBS samples only, with optional HIV rapid testing provided by service providers operating separately from the survey teams in SABBSMV.

Actions for consideration

Taking the various successes and challenges into account, we propose a survey design where the household and individual questionnaires, the spot sputum sample and the HIV RT were offered and completed in the household, with respondents only attending the hub for CXR, venous blood draws and for review by the medical officer. We also suggest making use of a satellite laboratory that could operate independently of the screening and testing.

A number of actions for consideration are made with respect to the pilot including refinements related to 1) extending time allocations for training; 2) sustaining community buy-in while in the field; 3) improving flexibility of day allocations in the field to address variations between clusters; 4) refining the survey design to incorporate administering questionnaires, HIV rapid testing, and collecting the spot sputum sample at the household interview stage; 5) addressing questionnaire length and challenges with CASI; 6) utilising a satellite network of laboratories rather than emphasising on-site laboratory processes; and; 7) potentially conducting a further pilot in other cluster settings.

Introduction

Globally, people living with the Human Immunodeficiency Virus (HIV) are 19 times more likely to fall ill with tuberculosis (TB) than those who are not living with HIV. TB is a leading cause of death among people living with HIV (PLHIV), accounting for around one-third of Acquired Immunodeficiency Syndrome (AIDS) deaths in 2018.

South Africa has a high infectious disease burden with overlapping HIV and TB epidemics. The country has the largest HIV epidemic in the world, with an estimated 7.9 million PLHIV in 2017 and an HIV prevalence of 20.6% among people aged 15-49 years. South Africa has the eighth highest TB incidence globally, with 615,000 cases in 2019, 58% of whom were PLHIV. People living with HIV are vulnerable to drug-resistant TB, and HIV is associated with multi- and extremely-drug resistant TB epidemics and outbreaks.

Many high HIV and TB burden countries, including South Africa, conduct national population-based surveys to help monitor the responses to the HIV and TB epidemics. Population-based HIV and TB surveys include people who are not necessarily in contact with the health system, and this allows for population-based rather than facility-based estimates.

Population-based Impact Assessments (PHIA) for HIV have been conducted in 14 countries in West, East and Southern Africa as part of the support provided by the United States President's Emergency Plan for AIDS Relief (PEPFAR).[6,7] These surveys explore progress against the 90-90-90 targets and guide for HIV policy and funding priorities towards HIV epidemic control. The surveys inform relevant for national programmes, PEPFAR, the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), other donors and multilateral organisations such as the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organisation (WHO).

1.1 HIV surveillance in South Africa

South Africa has implemented antenatal HIV surveys since 1990, with the most recent survey having been conducted in 2017. As of 2017, knowledge of HIV status, antiretroviral treatment and viral suppression data have also been collected through the antenatal survey to inform the 90-90-90 fast-track commitments and the goal of ending AIDS by 2030. While antenatal surveys derive HIV data from pregnant women, population-based surveys link HIV status to demographic and other factors related to HIV as well as providing information on knowledge, behaviour and other aspects of HIV.

Population-based HIV prevalence, behaviour and communication surveys have been conducted in South Africa every three to four years through the Human Sciences Research Council (HSRC) since 2002. HIV incidence and other serological analyses were included as of 2005 and the most recent survey was completed in 2017.[3] As of 2012, the analysis was conducted on the use of antiretroviral drugs (ARVs), thus allowing for national estimates of antiretroviral therapy (ART) uptake. The 2012 and 2017 surveys also included testing of blood samples for recency of HIV infection, viral load (VL) testing (to determine viral load suppression (VLS) among PLHIV) and HIV drug resistance testing (2017 only for HIV drug resistance testing).[3]

1.2 TB surveillance in South Africa

In 2017, the NDOH embarked on its first-ever national survey to estimate the prevalence of bacteriologically confirmed pulmonary TB among young people and adults aged 15 years and older. This survey aimed to inform the South Africa National TB Control Programme about the epidemiology of TB disease and to inform ways in which TB control could be improved. Data on TB status were collected through TB symptom screening, sputum samples and mobile CXRs.

While the South African National HIV Survey includes information regarding knowledge of TB as well as TB diagnosis self-report, the South African National TB survey includes HIV testing of respondents who are presumed to have TB based on screening.

1.3 Potential for a Joint TB and HIV Survey

While the potential exists to integrate the HIV and TB surveys, there are several considerations that need to be addressed. For example:

- The prevalence of HIV and TB vary, with the lower prevalence of TB potentially requiring a much larger sample size (20,000 for HIV vs >30,000 for TB).
- HIV surveys of young people and adults gather blood spot samples by finger prick, or from infants by heel prick, using simple equipment. Transporting these blood samples to laboratories for later analysis is not complex. By contrast, TB prevalence surveys require additional equipment such as mobile CXR machines, radiographers or clinicians to read CXR data in real-time, and equipment and materials for transporting sputum samples under cold chain conditions. Field sites and laboratories are also necessary for conducting cluster activities and processing TB samples.
- Gathering blood spot samples for HIV testing and analysis is feasible for all ages. In contrast, TB surveys lend themselves to gathering data on young people and adults aged 15 years and older, as a definitive diagnosis of paediatric active TB in children and adolescents is more difficult. Specifically – it is difficult for children to produce sputum samples; TB in children is generally paucibacillary, and; CXRs are not suitable for use in healthy children with a low risk of TB disease.

Taking these considerations into account, it remains relevant to explore the potential for a joint TB and HIV population-based surveys in settings where there is a close relation in the incidence of both diseases. Benefits of doing so include:

- Collecting data for both diseases using the same sampling framework within the same timeframe.
- Obtaining insight into HIV-TB co-infection epidemiology.
- Leveraging resources and infrastructure to the benefit of data collection for HIV and TB and avoiding cost duplication of certain expenses.[1]
- Preventing survey fatigue if the same areas are sampled.

1 Anecdotally TB prevalence survey designs appear to have a substantially lower cost (ZAR 1,646.29) (≈ US$ 118) per TB survey respondent vs ZAR 3,573.14 (≈ US$ 297) per HIV survey respondent).

CHAPTER 2

Study aims and objectives

TB at the country level is monitored through national TB notification and registration systems as well as national TB prevalence surveys. TB prevalence surveys offer the best way for directly measuring the number of TB cases in relation to demographic characteristics including age, sex and locality. This data allows for TB incidence to be estimated, while also allowing for modelling of the impact of HIV co-infection and ART on the distribution of disease duration. Such surveys have been conducted in 29 countries.

Given that the feasibility of conducting a population-based TB-HIV survey is under-explored, the present study assesses the potential for a combined TB-HIV survey in South Africa. The Human Sciences Research Council (HSRC) in collaboration with the United States Centers for Disease Control and Prevention (CDC) conducted the pilot HIV-TB pilot study in 2019 in partnership with the NDoH, Global Clinical and Viral Laboratories (GCVL), and the National Institute for Communicable Diseases (NICD).

2.1 Aims

The pilot study applied the design and platform of the recently completed South Africa National Tuberculosis Prevalence Survey (TPS) – which includes a hub design – to pilot and determine the feasibility of a joint TB-HIV survey in South Africa, and to inform the potential for future full-scale TB-HIV surveys.

2.2 Objectives

The primary objectives of this pilot did not include conventional survey objectives such as HIV or TB prevalence. Instead, the pilot survey had the following objectives:

1. Determine the uptake of combined TB and HIV measures in the survey.
2. Assess the data quality of collected interviews and biomarker measures.
3. Estimate the costs of a hypothetically scaled-up joint TB-HIV survey and compare the cost per respondent of a joint TB-HIV survey to that of separate TB and HIV surveys.

Secondary objectives included: 1) Exploring the impact of additional non-HIV-related biomarkers on HIV survey participation; 2) Exploring the feasibility of using Computer Assisted Self Interviewing (CASI) to collect sensitive data in the quantitative aspect of the survey; 3) Documenting lessons learned to inform the scale-up of future joint TB- HIV surveys and assessments; Determining the time required to complete survey activities at the cluster hub per respondent and per cluster levels.

Methods

3.1 Design and Sampling

The same cluster-sampling frame as the TPS was employed. This sampling frame uses the 2011 census small area layers (SALs) as the building blocks for cluster selection. Convenience sampling was used, and the criteria for the selection of clusters was as follows:

- None of the clusters or areas included in the TPS or the 5th South African National HIV prevalence, Incidence, Behaviour and Communication Survey (SABSSMV)[3] were selected – in order to avoid 'survey fatigue' among residents in these areas.
- The selected clusters were those where the majority of the people spoke the same languages, i.e. one was English and the other isiZulu (which is the dominant language in the province).
- The selected clusters were adjacent to, or near, a prior TB prevalence survey cluster or a prior HIV survey cluster to allow for the comparison of survey uptake.
- The selected clusters included an urban and rural area.

The selected clusters – Marburg (urban) and uMgayi/the Ridge (rural) – were in KwaZulu-Natal (KZN) Province. This province was identified as best suited for the pilot study because it has a high HIV prevalence of 18.1% among people of all ages in 2017[3] and TB incidence of 511/100,000 in 2017. Additionally, the province has rural and urban areas within close proximity to each other, making it easier to select suitable clusters. The HSRC has an office in the province which allowed for on-hand support during survey implementation. Logistics for specimen handling transportation and maintenance of the cold chain could also be assessed under anticipated field conditions since the sites are nearly 700 kilometres distant from the TB testing laboratory, which is located in Gauteng Province.

Within a selected cluster, all conventional households (HHs) were eligible for inclusion into the survey (following TPS design). Non-conventional HHs (institutional or congregate settings, including prisons, hospitals, hotels, offices, diplomatic compounds, schools, universities, dormitories and student hostels) were excluded.

3.2 Sampling of respondents

All eligible persons in all HHs in selected clusters were offered survey enrolment. The inclusion and exclusion criteria in this survey were a hybrid of conventional HIV and TB survey inclusion criteria. The inclusion criteria were:

- Persons of all ages who were in HHs within the selected clusters (following HIV survey design).
- Persons who had slept in these HHs for at least five nights of the previous two weeks (a hybrid between TB and HIV survey designs).
- Persons who provided informed consent (assent and parental or guardian consent were required for those aged younger than 18 years).

The exclusion criteria were:

- Persons who were not willing to travel to the survey hub where screening activities were being conducted.
- Persons who are mentally incapacitated.
- Persons who did not speak English or isiZulu.
- Persons with a total hearing impairment, i.e. are deaf.
- Persons under the age of 15 years were not eligible for TB screening and testing.[2]

3.3 Measures

3.3.1 Questionnaires

The pilot survey administered four questionnaires, including HIV-TB questions, namely:

1. A household questionnaire that was administered to the head of the household (administered at the household).
2. A questionnaire for parents or guardians of children aged 11 years or younger (administered at the hub).
3. A questionnaire for children aged 12 to 14 years (administered at the hub).
4. A questionnaire for people aged 15 years or older (administered at the hub).

2 The exclusion of persons < 15 years for TB measures is based on the difficulty of sputum collection, the low yield for children compared to the adult population (Van Der Werf MJ, Borgdorff MW. How to measure the prevalence of tuberculosis in a population. Trop Med & Int Health. 2007 12(4):475-84). Further, TB in children is more often extra pulmonary which is not possible to diagnose in the context of this survey. In addition, the WHO TB prevalence survey guidance handbook exclude children in national TB prevalence surveys-World Health Organization; 2011:Tuberculosis prevalence surveys: a handbook

Table 1 shows the modules included in the household questionnaire.

Table 1: Household questionnaire modules, TB-HIV Pilot Survey, South Africa, 2019

Section / Module	Household information	Personal information
Geographic location of household	×	
Interview details	×	
Refusal particulars	×	
Source, availability, and safety of potable water	×	
Type of sanitation and sharing of facilities	×	
Energy sources	×	
Household amenities and assets	×	
Housing: Number of rooms in dwelling	×	
Type of dwelling	×	
Material of roof and walls of dwelling	×	
Vulnerability: Qualitative measure of income	×	
Vulnerability: Food insecurity	×	
Relationship of members		×
*Sex		×
*Age		×
*Race		×
Language		×
*Receipt of government social support grants		×
*Duration of stay in the household		×

** For all people in the household*

Table 2 shows the various modules included in the individual questionnaire.

Table 2: Individual questionnaire modules, TB-HIV pilot Survey, South Africa, 2019

Questionnaire module	Children aged 0–11 years (reported by parent/ guardian)	Children aged 12–14 years (self-reported)	Youth & Adults aged 15 years and older (self-reported)
Demographics	×	×	×
Orphan status	×	×	× (under age 20 years only)
Education	×	×	× (under age 19 years only)
Knowledge, attitudes, beliefs and values about HIV and AIDS and about HIV-related practices and behaviours (KABP)		×	×
Sexual history		×	×
Sexually Transmitted Infections (STI)			×
Delivery and care details	× (for respondents under age 2 years)		×
Contraception		×	×
Male circumcision	×	×	×
HIV testing and risk perception	× (for respondents under 2 years)	×	×
Drug and alcohol use	× (5–11 years, exposure to use within household)	× (including exposure to use within household)	×
Health status	×	×	×
Violence in relationships			×
Tuberculosis history			×
TB symptom screening			×

3.3.2 Screening and Biomarkers

The following tests were offered and conducted:

- Rapid HIV testing was offered to respondents of all ages at the survey hub.
- Central laboratory testing for HIV antibodies.
- Testing for VL, Limiting Antigen Avidity (LAg) assay, HIV drug resistance (HIVDR) in HIV positive samples. The LAg assay was done in HIV positive samples from respondents who were older than 2 years.
- Chest X-ray images for respondents 15 years and older.
- Xpert Ultra testing and culture for TB of sputum samples with presumptive TB.
- Random (point of care) blood glucose and blood cholesterol measurement in participants aged 18 years and older.
- Single Blood pressure reading in participants aged 18 years and older.
- Weight measurement in participants aged 18 years and older.
- Height measurement in participants aged 18 years and older.

3.4 Ethical considerations

The survey protocol was approved by the HSRC Research Ethics Committee (REC: 11/20/02/19) and by the Center for Global Health (CGH) of the Centers for Disease Control and Prevention (CDC), (CGH HSR Tracking # 2019-178). The CGH designated the research activity as involving human subjects but in which CDC involvement does not constitute engagement in human subject research. The survey adhered to international ethical standards as well as to the South African Children's Act of 2007. The ethical review took much longer than anticipated due to the complexity of this survey, and because the Research Ethics Committee (REC) did not have a clear understanding of the survey design. These issues were resolved after the Principal Investigator met with the chair of the committee and committee members.

Fieldwork staff were trained in research ethics and on the procedures for informed consent to ensure that voluntary consent and assent was obtained from respondents. The respondent's choices of not responding to a particular question were respected. All adults (18 years and older) who agreed to participate were required to provide written or verbal (where the respondent was illiterate) consent, in either English or isiZulu. Respondents under the age of 18 years signed an assent form, and their legal guardian signed the informed consent for their participation as prescribed by the South African Children's Act of 2007 (see Appendix 7).

Confidentiality during the individual interviews was maintained by placing the individual interview stations at a distance apart from each other and also apart from other survey activities (see Section 3.5.5). All other survey procedures were conducted away from other respondents. Data was collected using password-protected tablets.

Respondents were provided with reimbursement for their time spent on the survey. The reimbursement was valued at R50 (US$ 3.57 was ZAR1:US$14 at the time of the survey) and included items such as airtime vouchers, food vouchers, washing powder, soap bars for adults, and puzzles, toys, drawing books and crayons for children. These items were chosen based on the experience from the 2017-2019 TPS and advice from volunteers within the community.

3.5 Survey Preparatory work

Survey preparatory work included engaging with collaborating partners, preparing Standard Operating Procedures (SOPs) for survey processes – including the survey training and field manual, translation of survey materials into isiZulu (translation procedures included forward and back translation of survey communication materials, informed consent documents, and questionnaires), programming and testing the electronic tablets used for data collection, refining the HIV testing processes, procurement of survey materials, and completing administrative processes including recruiting field staff. Training materials were adapted from materials used in training for the TPS, and The fifth South African National HIV Prevalence, Incidence, Behaviour and Communication Survey (SABSSMV). Training was conducted from 12-20 August 2019.

Funding preparations were determined by the completion of the national TB prevalence survey and the funding model. Both these factors resulted in delayed initiation of preparatory activities.

3.5.1 Data collection and capture system

Data were collected and managed electronically using Research Electronic Data Capture (REDCap), and the data server was hosted at the HSRC. REDCap is a web-based secure application that is designed to support data capturing for research studies. REDCap was selected as the data collection system for the following reasons:

- It has an intuitive interface for validating data entry such as range checks, cross-validation procedures, and skip patterns.
- It provides an audit trail useful for data manipulation and exporting procedures.
- It provides easy procedures for exporting and downloading to most statistical packages.
- It provides procedures for importing data from external sources. This is relevant to this pilot survey because of the various data elements that were generated from different sources, such as the laboratory, the questionnaires, And the CXR readings

The questionnaires, screening and biomarker results forms were programmed on REDCap.

Computer-Assisted Self Interviewing (CASI)

As an alternative to interviewer-administered questionnaires (individual questionnaires at the hub), the survey also made use of the CASI system whereby survey respondents aged 15 years and above, could complete part of the questionnaire on their own. Several tablets were designated for this aspect. CASI was included to assess: 1) the feasibility of using this method with respondents who may not have used self-administered electronic data collection devices previously; 2) potential to reduce socially desirable answers to sensitive questions such as those about risk and sexual behaviour; and 3) whether it could shorten the duration of the interview. Respondents for CASI were systematically selected on arrival at the hub – every fifth participant enrolled was selected for CASI.

3.5.2 Survey staff and training

Staff composition

The survey staff comprised of a central team, a core field team (fieldworkers), and volunteers from the community. The central team comprised survey investigators, HSRC project management team members, the administrative teams, and staff from the collaborating institutions and laboratories. The core field team comprised a fixed member – namely one team leader, one Medical Officer (MO), one receptionist (the individual tasked with receiving respondents at the hub), five interviewers, three phlebotomists (for blood sample collection and HIV testing services), three nurses (one professional nurse and two assistant nurses), one radiographer, one field IT technician, one data checker, and one driver.

The majority of the core field staff team had been part of the national TB prevalence survey or/and the SABSSMV HIV prevalence survey. They were therefore trained and experienced in the administration of interviews, collecting blood (DBS) and sputum specimens, and in general survey procedures. The community volunteers were flexible members of the field team and were individuals who were from each survey area. These volunteers supported the survey team in liaising with local authorities and their community about the survey. They also conducted the pre-listing, supported community awareness about the survey, accompanied fieldworkers to conduct household interviews, supported hub activities (directing respondents between the different stations at the hub), as well as followed up with respondents where this was needed. The community volunteers were people who are well-known in their community. (See Appendices 1 and 2 for additional information.)

Training

Although most field staff had experience, all staff were trained to ensure they performed optimally for our study. Training of the field team was conducted by members of the central team in Durban over nine days during August 2019. The training covered the survey protocol, informed consent procedures, administration of the survey questionnaires, blood sample collection and handling of blood samples in the field, HIV rapid testing, and sputum specimen collection and handling in the field.

The training was based on the survey Field Operations Manual and SOPs (These documents can be made available upon request). It included combined sessions for all the field staff so that the entire team understood all the processes of the survey. Breakaway sessions were conducted that focused on roles assigned to particular team members. The combined sessions were intended to equip team members to undertake multiple roles and tasks in the survey – for example, the team members who were assigned to the 'receptionist' role were trained to obtain informed consent and to administer the survey interviews, and phlebotomists were trained to conduct some of the measurements such as weight and height and to administer survey interviews. This approach drew on lessons derived from the implementation of the TPS.

All team members were trained to understand the overall survey eligibility criteria and the criteria for each of the different survey screening and testing processes. Training included a dry practice run of survey field activities including setting up a mock hub at the training venue. This was a simulation without participants. The phlebotomists and nurses attended a further two-day training period for blood sample collection and HIV testing at GCVL, where laboratory HIV antibody testing was conducted. GCVL staff were also responsible for the sample processing that was conducted at the hub.

3.6 Fieldwork

Fieldwork was undertaken from the 26th August to 3rd September 2019 in the first cluster, and from 6th September to 15th September 2019 in the second cluster. This included: 1) pre-survey visits; 2) pre-listing activities; 3) the main data collection activities of household interviews and hub-based activities.

3.6.1 Pre-survey visits

Pre-survey visits were conducted in each cluster. The visits aimed to:

- Engage with government structures in the area about the survey.
- Engage with the local leaders ('gatekeepers') within communities including political, religious and traditional leaders and local associations regarding the survey.
- Sensitise the community about the survey.
- Sensitise and obtain support from local clinics and the local TB coordinator regarding the survey. This served to alert them to expect referrals from the survey for various issues and any linkage to care of survey respondents.
- Explain the purpose and procedures of the survey and obtain stakeholder and community consent.
- Complete a situation assessment to determine accessible and suitable areas to set up the survey hub. The survey hub was the area where survey screening and testing was conducted. The visit, therefore, identified the equipment and supplies that would be needed – e.g. tents, potable water, generators for electricity, mobile toilet facilities.
- Identify accommodation for the field team.
- Verify cluster boundaries.
- Obtain information about the terrain in the area to inform decisions about the types of vehicles that would be needed by the survey team.
- Recruit volunteers from the community to support the survey.
- Train the volunteers on their tasks and roles.
- Understand the safety challenges and measures to put in place for the safety of the survey team and equipment.

The pre-visits were conducted within two weeks of implementation of other field activities.

Community engagement and awareness

Community engagement and awareness activities were undertaken to inform all relevant community structures and local leaders in the selected clusters about the survey to facilitate community buy-in, awareness about the survey, and support for the smooth implementation of field activities. These engagement and awareness activities included meetings with various leaders, community meetings, and media engagements to disseminate information about the survey and encourage participation.

A variety of communication and mobilisation strategies were adopted in the two clusters. These were determined by the communication platforms that were available and accessible to the community in each cluster. Door-to-door visits and distribution of pamphlets about the survey were used in both clusters. Posters were also distributed in strategic places across the clusters (Appendix 3) and local radio stations and local newspapers carried information about the survey. In the rural cluster, information was broadcast in the community using a loudspeaker from a vehicle that travelled across the cluster and a community meeting (Imbizo) was also held. In the urban cluster, social media (WhatsApp and Facebook groups) were used.

3.6.2 Pre-survey listing

Pre-survey listing (enumerating the population in the cluster) was conducted before the main survey data collection activities began and were undertaken by volunteers from the community. The volunteers in each cluster were trained to conduct the pre-listing activity. Pre-listing generated updated information regarding the number of households and the population size in the cluster to ensure that the target sample would be reached. It also provided an opportunity for one-on-one awareness about the survey to members of households in the cluster. Pre-listing was conducted over 2-3 days and entailed enumerating all people in each household in the cluster by age and sex and recording this information on the survey pre-listing form.

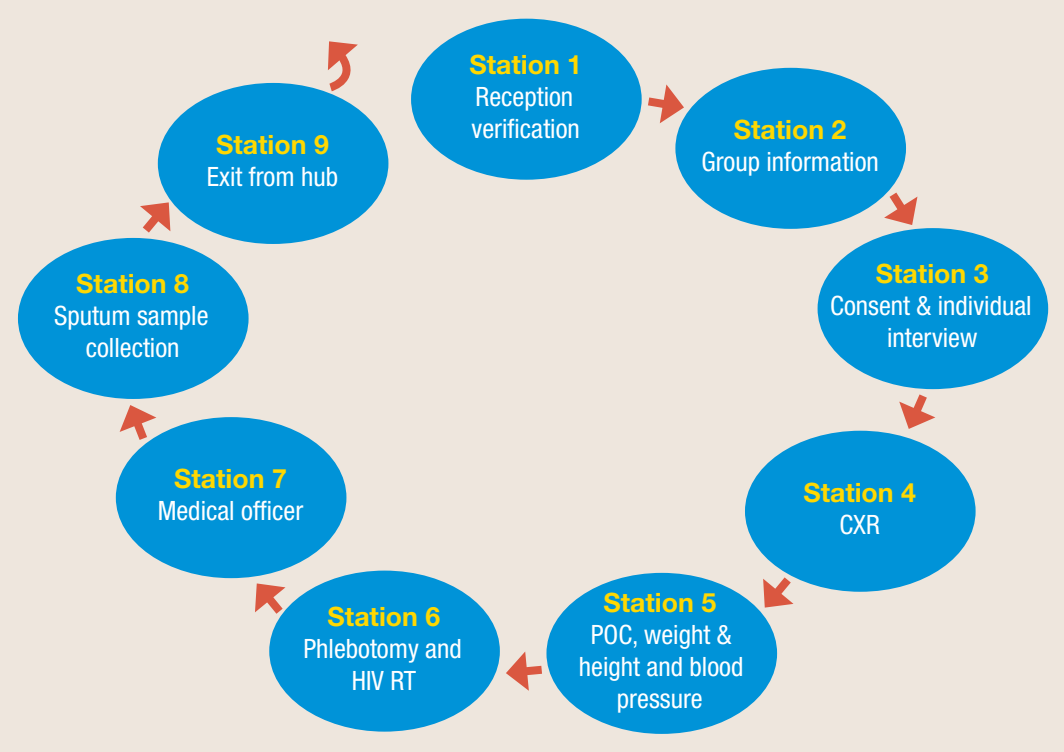
3.6.3 Household interviews, survey census and an invitation to the hub

Household interviews took place after completion of pre-listing and were largely conducted over 2-3 days. The survey field team members visited all households in the cluster, provided more information about the survey, and administered the household questionnaire to heads of households for consent to participate. Each household was assigned a household identity number (household ID). The household questionnaire included a census of all household members. Each member was assigned a census identity number. Members of the household who met the survey inclusion criteria were invited to attend the survey hub for screening and testing and were issued with barcoded invitation slips. These invitation slips contained information about the place where the hub was located, and the date when they should attend. The date was a flexible arrangement, and those who were invited were informed that they could also attend at a time that was convenient to them within hub operating hours during survey implementation in the cluster. In households where there was no one at the time of the visit or where the head of the household was not present were re-visited up to 3 times. Individuals who were eligible to participate in the survey but could not attend and/or be transported to the hub – for example, because they were bed-ridden or severely disabled – were offered the option to complete some of the hub activities at home (individual interview, sputum sample collection, blood sample collection). Arrangements were made for this to be done once hub activities were underway.

3.6.4 Hub activities

Figure 1 shows the organisation of the hub activities into stations. The activities completed at each station are further described in detail below. Participants could exit at any point if they wished to do so. They would specify if they were changing their mind about participation.

Figure 1: Workflow and map of the stations at the hub, TB-HIV Pilot Survey, South Africa, 2019.



CXR – chest X-ray; POC – Point of care test point; HIV RT – HIV Rapid Test

Arrival at the survey hub-reception (Station 1)

Individuals who were invited for screening and testing presented at the hub starting from the third day of the main field activities. On arrival at the hub, they were directed to the reception station where they had to present the barcoded invitation slip for verification of their details using the data in the household interview database (See Appendix 4). Once successfully verified, each individual was issued a unique survey identity number (survey ID) and a site tracking sheet and was directed to the next station (the Group Information station- Station 2). Individuals who were randomly selected for self-administration of the individual questionnaire using CASI were selected after verification at the reception station.

To support recruitment where the number of people attending the hub was low (i.e. low recruitment pace, such as mornings and especially towards the completion of work in the cluster), people who presented at the hub without a hub invitation slip were assessed for eligibility for recruitment – the criterion being they lived within the boundary of the cluster and met the survey entry criteria (including people who lived in the selected cluster where there was no one at home at the time of the household visits). Their neighbours were informed about the study and told that researchers had visited their household. If these individuals presented to the hub without an invitation slip, their addresses were confirmed, and they were enrolled if they were within the selected. There were also a few households that were selected that could not be reached for the household interviews, and where occupants heard about the study and they presented at the hub. If they were confirmed as meeting the study entry criteria, they

were enrolled. Those who came from outside the cluster and those confirmed as visitors who had not slept in the household for at least five nights of the preceding two weeks were not enrolled. Where this was the case (i.e., where eligible individuals presented to the hub without an invitation slip), and where there had been no household interview and household census data collected, the household interview and household census information was completed, and those eligible were enrolled at the hub. Individuals who were not heads of households themselves were requested to return with the head of the household for the enrolment to be completed. Where those presenting were minors, it was required that they return with their legal guardian before they could be enrolled. For those reporting that they had lost or misplaced their invitation slips, identities were confirmed by asking about their identifier details – name, age, sex, address, area of the household, and date of the visit to their household. This information was cross-checked with the information in the household interview database. Where the details were verified, the individuals could proceed to be enrolled. Individuals whose details could not be verified with those in the household database, and those who were not eligible for participation, were not enrolled.

Group Information Session (Station 2)

At this station, detailed information about the survey was provided to a group of individuals. This included information about all procedures that were to be completed by each respondent who consented/assented to participate in the survey. There was also an opportunity for individuals to ask questions about the survey. Once all questions were answered, the individuals were directed to the consenting and individual interview station (station 3).

Consenting and individual interview (Station 3)

Consent/assent was obtained at this station, as described in Section 3.4 above. Individuals were considered enrolled in the survey after giving consent/assent. They were then referred to as respondents, and the individual interviews were then conducted as per the age of the respondent (Table 2). The respondents who were systematically selected for CASI were directed to complete the interviews on the tablets provided instead of the interviewer-administered interviews. As noted above, confidentiality during interviews was maintained by the physical distancing of individual interview stations. The interviews were linked to specific respondents by their survey ID.

Chest X-ray (Station 4)

After completion of the interview, respondents aged 15 years and older were asked to move to the CXR station where postero-lateral digital CXR images were taken. The images were labelled with the respondent's survey ID to link them to the interview data and data from other tests. The images were saved on two computers and were also transmitted to the central server located at the HSRC's main office in Pretoria. Safety measures were followed during chest radiography (respondents were provided with lead aprons for protection from radiation). For all females, the date of their last menstrual period was recorded and those who were potentially pregnant were not X-rayed.

Point of care tests and anthropometric measurements (Station 5)

Point of care random blood glucose and blood cholesterol measurements were offered to respondents 18 years and older. These respondents were also offered blood pressure tests (a single reading) as well as having their weight and height measurements taken.

Phlebotomy and HIV Rapid Testing (Station 6)

HIV rapid testing (RT) with pre- and post-test counselling was offered to all respondents. This was conducted in a private space away from other survey activities. Blood samples for RT and other HIV related tests were collected by venepuncture, finger prick, or by heel prick. Venepuncture was performed for respondents aged two years and older. When this was not successful, or if respondents declined venepuncture, a finger prick was done. A heel prick was used to obtain blood samples from children aged younger than two years.

HIV rapid testing

HIV RT was conducted according to the national guidelines for HIV RT (see Appendix 5). Test kits recommended by the NDOH and the KwaZulu-Natal province were used (ONE STEP Anti-HIV (1&2) Test, and BioTracer™ HIV 1/2 Rapid Card). Blood samples of respondents with indeterminate results as well as those of children aged younger than 18 months who tested HIV antibody positive on RT were sent for Deoxyribonucleic acid (DNA) Polymerase chain reaction (PCR) testing at a GCVL. These respondents and the parents/guardians of children aged younger than 18-months were informed that their results could be obtained from the clinic in the cluster after 12 weeks. The respondents and their parents/guardians of minors received a unique barcoded Laboratory Result Retrieval Form to use to obtain the test results from the clinic.

Medical officer (Station 7)

All respondents were seen at the MO station. At this station, the MO read and interpreted the CXR images of respondents who had undergone chest radiography. The CXR image reading and interpretation was conducted independently of the TB symptom screening findings – i.e. the MO was blinded to the symptom screening findings at the time of reading the CXR images. The MO classified the images as a) Normal with no abnormalities, b) Abnormal with abnormalities that are suggestive of TB and c) Abnormal with other abnormalities that are not suggestive of current TB. Respondents with CXR abnormalities that were suggestive of TB were deemed to have presumptive TB. After capturing the CXR findings, the MO then reviewed the symptom screening findings and used these together with the CXR findings to identify respondents who were eligible for sputum sample collection. The symptom screening included cough (persistent cough for ≥2 weeks or more or cough of any duration if HIV positive), unexplained fever for ≥2 weeks, drenching night sweats and unexplained weight loss (more than 1.5 kg in a month). Those who answered yes to any of these listed symptoms were eligible for sputum examination. As part of QA for CXR interpretation, all CXRs that were classified as 'Abnormal with changes suggestive of TB' and 20% of those classified as 'Normal' by the MO were sent to be re-read by a radiologist who was based offsite. The radiologist communicated any concerns about over or under reading with the MO.

Additionally, the MO discussed the results of all the other tests and measurements with the respondents and the parents/guardians of minors. HIV RT results were only discussed if the respondent wished to do so since they had received pre- and post-test counselling with the RT.

Sputum sample collection (Station 8)

Respondents who were eligible for sputum examination were requested to submit two sputum specimens, with the first specimen collected immediately (on the spot) and the second one collected an hour later. The first sample was earmarked for Xpert Ultra testing, while the second was for TB culture. To obtain good quality specimens of adequate volume, a survey nurse coached respondents on how to produce a sputum sample. Visual aids were used to facilitate coaching. The samples were collected in a sputum collection booth that was situated in a secluded place away from where the majority of the hub activities took place. The booth was situated to direct airflow away from the coaching nurse and other activities at the hub.

As part of the safety procedures, coaching nurses and all staff handling sputum samples on-site wore N95 Respirator masks. A few respondents, who were not able to give second sputum specimens after several attempts were asked to bring an early morning sputum specimen on the following day. The respondents were advised to collect it in a well-ventilated space at home, preferably outside of the house. Respondents who declined a CXR, or were unable to have it taken due to disability, or because of pregnancy were eligible for sputum examination regardless of the symptom screening findings. Respondents who were enrolled and interviewed at home were also eligible for sputum examination regardless of the symptom screening findings. The sputum samples from these respondents were collected at home, and no CXRs were taken.

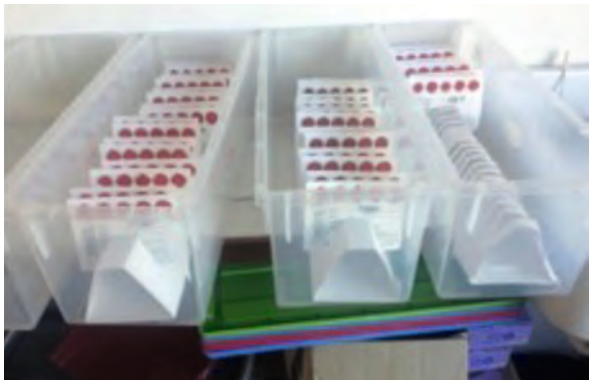
Sputum samples were collected into screw-top sputum jars and were stored in the refrigerator on site (for a maximum of 48 hours) before being sent by courier to the microbiology laboratory. The jars were labelled with barcodes that had the respondent's survey ID for linking to the questionnaire and other test data. Laboratory forms were completed for each sample to indicate if it was a first or second sample, the date of collection, and the date of dispatch to the laboratory. The form also included the names and surnames of the respondents to facilitate the tracing for treatment, and the reporting was that TB was found on testing the sputum samples.

Exit from the hub (Station 9)

On completion of all hub procedures, respondents were escorted to the exit station of the hub. At this station, the respondent site tracking card was reviewed to ensure that all relevant tests and procedures were completed. Respondents then received the reimbursement at this station. An exit register was maintained at this station.

3.7 Processing of blood samples at the hub

3.7.1 Dried Blood Spot samples



A portion of the blood sample collected from each respondent was spotted onto Whatman 97 Grade paper DBS cards to make DBS samples. Two DBS cards with 10 spots in total, (with approximately 75 µL of blood per spot) were prepared for respondents aged two years and older and one DBS card was prepared for children aged younger than two years. All DBS cards were labelled with the respondent's survey ID that was linked to the respondent questionnaire and other screening and testing data. DBS cards were allowed to dry for a minimum of 4 hours and were then individually packed into zip lock bags with desiccant to eliminate moisture. The DBS cards were maintained at room temperature on-site and during transportation to the laboratory.

3.7.2 Plasma samples

The blood samples collected by venepuncture were centrifuged on-site to separate the plasma and the blood cells. For each respondent, the plasma was aliquoted into three cryovials for central laboratory tests and storage. Samples were labelled with the respondent's survey ID that was linked to the respondent questionnaire and other test data. The plasma samples were stored between 2-8 °C in a fridge or in a cooler bag with gel ice packs on-site and during courier to the laboratory.

3.8 Specimen transportation

With the sputum and DBS and plasma samples going to different laboratories, two courier systems were in operation. The sputum samples were transported to the TB reference laboratory at the NICD in Johannesburg. The samples were triple packed (zip lock bag, canister, and sputum sample courier box) with absorbent material around each jar. Gel ice packs were placed in each box to maintain the cold chain and keep the samples viable. A log sheet with the respondents' survey IDs and a list of all the specimens being transported was completed for each batch of samples that were sent to the laboratory. The sputum samples were transported to the microbiology laboratory every second day.

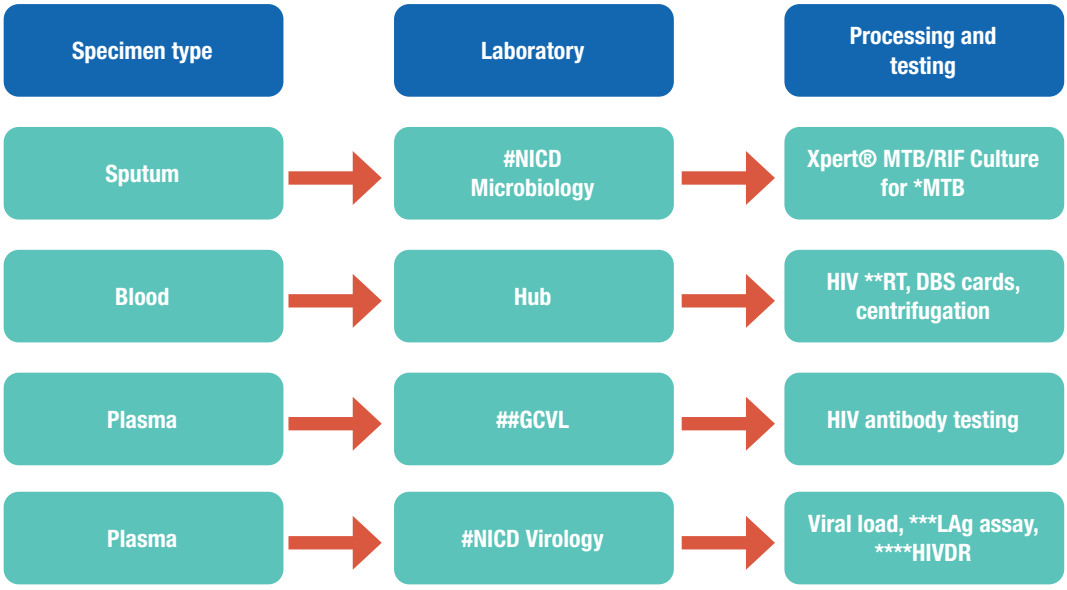
Plasma samples and DBS cards were transported to the GCVL in Durban daily. DBS samples were transported at ambient temperature, while the plasma samples were kept under cold chain conditions. All the daily sample dispatches were also accompanied by a log sheet of respondents' survey IDs and a list of all the specimens being transported.

3.9 Follow up of respondents

Follow up activities (phone calls, text messages, and door-to-door re-visits) were conducted to reach individuals who had not attended the hub 24 hours after the date and time of their invitation. These individuals were identified by comparing the hub and the survey census databases at the end of each day of hub activities.

3.10 Central laboratory testing

Figure 2: Summary of biomarker testing, TB-HIV Pilot Survey, South Africa, 2019



#NICD	National Institute for Communicable Diseases	**RT	Rapid Testing
##GCVL	Global Clinical and Viral laboratories	***LAg	Limiting Antigen
*MTB	Mycobacterium tuberculosis	****HIVDR	HIV drug resistance

Figure 2 summarises the biomarker testing in the survey and also indicates where testing was conducted. Testing and the other processes undertaken at the hub have been described above. The testing at the central laboratories is described below.

3.10.1 Microbiology: Sputum sample testing

Sputum samples were tested at the TB reference laboratory at NICD. The first sample was tested with Xpert® MTB/RIF Ultra (Xpert Ultra) while the second sample was for liquid culture on MGIT 960 (Becton Dickinson, USA) system. Xpert Ultra results were available within four days of sample receipt at the laboratory, and culture results were available after eight weeks.

3.10.2 HIV testing: HIV serology, incidence, viral load and HIV drug resistance testing

HIV Serology Confirmation

HIV serology testing of all samples was conducted at GCVL, an ISO 15189:2012 accredited laboratory. The Cobas HIV1/2 Combi Assay was used as a screen test with the Genscreen HIV1/2 Combi used as a confirmatory test and for QA of 10% of negative results on the screening test. The Bio-Rad Geenius™ HIV1/2 assay was used to confirm all positives, and the final HIV status was based on the Geenius™ Assay. For children under 18 months, the Roche Cobas Amplicor Taqman HIV1 DNA PCR was used to confirm HIV status.

HIV viral load (VL) testing

HIV VL testing was conducted at the virology laboratory at the NICD. Testing was conducted on HIV-positive samples using the Abbott platform (Abbott m2000 HIV Real-Time System, Abbott Molecular Inc., Des Plaines, Illinois, USA). This utilises a ribonucleic acid (RNA)-specific extraction procedure for DBS, thus minimising the problem of deoxyribonucleic acid contributing to the VL counts. The Abbott m2000sp and m2000rt open model protocol was used for automated extraction and sample preparation, and for real-time amplification and detection. The kit was supplied with three controls – negative, low positive, and high positive – and these were included in each run to determine the validity of the run and to calculate the VL concentrations of the samples. All analyses were conducted according to the manufacturer's instructions by certified laboratory staff.

HIV recency assay

HIV recency testing was conducted at the NICD virology laboratory. The recency algorithm utilised the Limiting Antigen Avidity enzyme immunoassay (LAg-Avidity EIA) which is based on the functional avidity of HIV-1 antibodies. The initial screening test was followed by a confirmatory test in triplicate for specimens with a normalised optical density (OD*n*) value of ≤2.0. Those with an OD*n* value of ≤1.5 were preliminarily classified as LAg recent infections. Specimens with a final OD*n* value of <0.4 were retested by the HIV diagnostic testing algorithm to confirm HIV-1 seropositivity.

Final determination of recency took into account the viral load, with all samples with an OD*n* value of ≤1.5 and with a viral load of ≥1000 copies/ml being classified as recently infected in the past year. Figure 3 shows the full Recent Infection Testing Algorithm (RITA). Specimens with OD*n* values ≤1.5 and suppressed VL, classified as <1000 copies/ml (due to elite controllers who naturally suppress their viremia or persons under suppressive ART),[3] were removed from the number of recent specimens and included in the number of long-term specimens. All remaining specimens with OD*n* values ≤1.5 and VL ≥1000 copies/ml have a final classification of recent infection.

Genotyping for HIV drug resistance

HIV positive specimens underwent HIV-1 pol and gp41 genotyping for the detection of HIV DR. This was conducted at the NICD virology laboratory. Drug mutations in the protease and reverse transcriptase and gp41 genes were interpreted according to the Stanford DR database. In-house specimens were used for quality control.

3 Figure 3: The Sedia HIV-1 LAg-Avidity EIA (for Serum or Plasma Specimens). Sedia Biosciences Corporation Portland, Oregon USA, 2016 (22)

3.11 Return of central laboratory results to respondents and linkage to care

Table 3 shows the laboratory test results that were returned to respondents. Results were returned to the clinic as soon as they were available, and this was dependent on the time required to conduct the testing. Positive Xpert Ultra results were sent to the survey project directors, who in turn sent the result to the clinic in the cluster and to the TB coordinator in the area for them to facilitate tracing of the respondent and initiation of TB treatment. The Xpert results were available within four days of sputum sample receipt at the laboratory. Sputum culture results were available eight weeks after sample collection and were also returned to the clinic manner.

The project directors actively engaged with the TB coordinators and the clinic manager to confirm receipt of the positive Xpert or culture results and tracing of respondents to initiate treatment. The community volunteers also supported the tracing of these respondents.

TB is a notifiable disease in South Africa and all diagnosed persons must be traced, notified, and placed on treatment. Respondent identifiers could therefore be used to trace all those with positive Xpert Ultra or culture results, and in addition, the TB programme has dedicated TB coordinators, who ensure that people who are diagnosed with TB are linked to care. HIV results for infants and those that were discrepant or indeterminant on RT, VL results and HIVDR results were returned to the clinic in each cluster.

Respondents could use the results retrieval voucher to access their results. The results were retained at the clinic for six months to allow respondents time to fetch them. The Community Health Workers (CHWs) and facility nurses assisted with the active linking of respondents to care when they requested this. HIV results were returned to the clinic with no direct tracing of respondents since HIV is not a notifiable disease in South Africa and the HIV programme relies on HIV positive people seeking care themselves or being linked to care by community-based organisations (CBOs) or non-governmental organisations (NGOs).

Table 3: Returning of central laboratory results to respondents, TB-HIV Pilot Survey, South Africa, 2019

Test Results	Returned to respondents and/ or health facility
Sputum Xpert results	Yes, through health facility and TB coordinator within 4 days
Sputum culture results	Yes, through health facility and TB coordinator after 8 weeks
HIV Viral load	Yes, through health facility, within 12 weeks
Discrepant HIV serology results	Yes, at household, within 12 weeks
HIV Infant diagnosis	Yes, within 12 weeks through health facility
HIV drug resistance	Yes, after 6 months, through a health facility

3.12 Quality assurance of interview, screening and testing data

QA of the data collected was guided by a data SOP. The on-site and off-site (office-based) data and information technology (IT) teams worked closely together to help resolve issues promptly. The office-based teams were available throughout field activities to support the field team. This was facilitated through an internal WhatsApp group whereby IT and data issues and updates could be communicated in real-time to troubleshoot and resolve timeously in addition to email and telephonic communication. Two office-based IT staff also visited the sites to provide on-site support to the field teams, including checking network connectivity and providing software and hardware support.

Real-time data checking and verification were conducted, and this included: 1) tracking entries into REDCap and addressing errors and discrepancies in real-time or as soon as was possible; 2) tracking the invitations to the hub; 3) verifying details of respondents at any station at the hub; 4) ensuring that respondent barcodes (the barcodes contained the survey IDs) were captured accurately; 5) ensuring that the questionnaire data was linked to the correct biomarker data for each respondent.

The QA process also included updating REDCap on the tablets and ensuring that all data were timeously uploaded to the HSRC server. The field IT staff also completed daily tracking sheets to report daily data summaries to the entire survey team via email. This also assisted in identifying missing data and other anomalies.

The laboratory staff verified each respondent's barcode ID with their tracking sheets at the laboratory to ensure the correct laboratory results were matched with the correct respondent.

Missing data

Pre-designed queries (reports) were set up in REDCap to identify missing data such as age, sex, race, and refusals at each station. These queries were run on-site every two hours on a daily basis by the data checker. Whenever missing data were identified, the data checker consulted the tracking sheets and the survey database to source these data. For missing information that could not be traced from the tracking sheets or the other sections of the database, the data checker and the team leader would attempt to contact the respondent directly to obtain the information.

Once data collection was completed, the data management and analysis team also checked all survey data reports. They also conducted further checks for missing data and sourced the data from hardcopy tracking sheets where this was possible.

3.13 Qualitative data collection

A qualitative research component was included in the survey to provide an opportunity to explore subjective views, understanding, perceptions, feelings and meanings (ideas conveyed or intended to be conveyed) that respondents constructed around their experiences of the implementation of the survey. The qualitative component of fieldwork included a range of qualitative data collection methods such as field staff diaries, notes from debriefing reports, key informant interviews (KIIs), focus group discussions (FGDs), and observations of fieldwork processes and procedures during survey implementation.

The KIIs were conducted with volunteers at the rural cluster. The first FGD was held with eight volunteers who supported the survey. The remaining two FGDs were held with survey field staff.

The first field staff FGD comprised 10 respondents including 4 field staff members who were interviewers, the MO, 3 field staff members who were responsible for IT aspects (including central HSRC IT staff members), the field staff members who had been assigned the role of receptionist, and the driver. The second field staff FGD had 7 respondents including the team leader, 2 phlebotomists, three nurses and 1 field staff member who was an interviewer. Field observations were conducted by the survey Principal Investigators, Project Directors, and individuals from collaborating laboratories.

The FGDs were conducted in English by experienced facilitators. These were audio-recorded and notes of the sessions were also taken by a member from the HSRC survey team experienced in qualitative data collection. An open-ended approach to interviews was adopted and guided by five identical questions for KIIs and focus group respondents (see Appendix 9). This approach allowed respondents a level of flexibility as to how they responded to the questions individually and as a group. It also allowed the facilitator and the note taker an opportunity to probe emerging issues to gain a deeper understanding of dynamics that were at play during the survey implementation process.

A final focus group exit interview was conducted with all staff. The interview also used the diaries to document staff experience, lessons learned and actions for consideration. The majority of staff used their field diaries to document personal experiences and frustrations during fieldwork. It was therefore allowed that these be retained by staff to protect their privacy.

The data provided an opportunity to capture views from members at all levels of the survey team (from the volunteers all the way to the MO).

3.14 Data collection for cost estimates

A combination of top-down and bottom-up approaches was used to collect cost data. The predominant source of data was administrative records detailing staff costs and invoices for procured items and services. These data were supplemented with information obtained from other relevant sources that included the actual time HSRC staff spent on the project (obtained from the relevant staff) as well as imputed prices of items used that were not purchased for the pilot. These supplementary data were obtained from the project management team and included prices of items from previous surveys, items that were being rented such as tablets used for data collection, and other donated items and services. These data were captured onto pre-designed excel sheets and used to compute the costs of the pilot survey.

To estimate the cost of a hypothetically scaled-up joint TB-HIV survey, a survey design plan was drawn up with the help of a survey statistician. As in the pilot, this design envisaged a hub-based survey and took into account key parameters such as expected sample sizes for both survey components (i.e. HIV and TB), disease prevalence rates, as well as the HIV incidence rate (as is the case for PHIAS) and viral load suppression. Thereafter, a survey implementation plan was developed and the hypothetical scaled-up survey was appropriately costed.

Data analysis and results

This section presents the results for 1) interview, screening and testing; 2) qualitative interviews and observations, 3) cost data, which are presented in succession.

4.1 Household and individual interview, screening and biomarker data

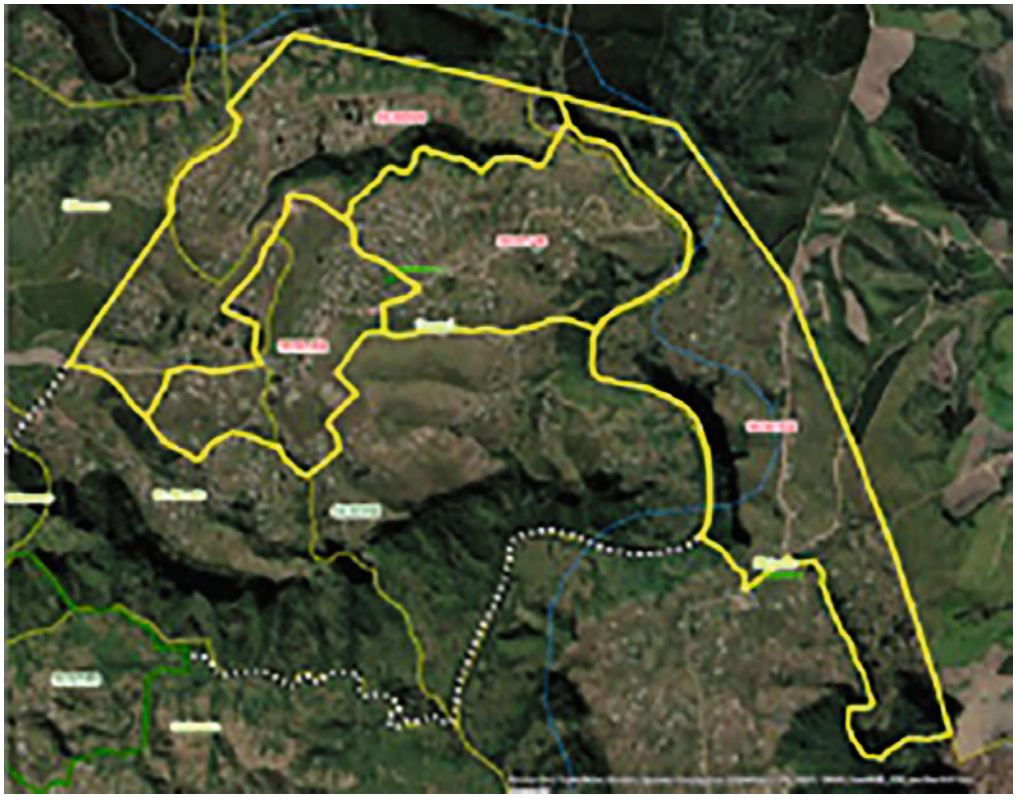
Data from the household interviews, the individual interviews, survey screening and testing were cleaned and then analysed using STATA statistical software version 12.0 (Stata Corporation, College Station, USA). Basic descriptive analyses were conducted with results present as counts and percentages. Graphical displays were performed for data at the cluster levels.

4.1.1 Community entry and pre-listing

The survey was generally well-received in both clusters. In each cluster, the stakeholders (government structures, local leaders) who were consulted during pre-visits facilitated community entry and community buy-in. They also supported activities to create awareness about the survey, such as the distribution of posters about the survey. The community leaders in each cluster provided or facilitated the allocation of space for the survey hub and the community leaders arranged for volunteers from the community as per the criteria requested for the survey – namely, that the volunteers had to be people who were well known and trusted in the community.

Figure 3a: Map of Marburg cluster (urban cluster), Joint TB/HIV Pilot Survey, South Africa, 2019; not to scale

Figure 3b: Map of uMgayi cluster (rural cluster), Joint TB/HIV Pilot Survey, South Africa, 2019; not to scale



Pre-listing identified 2,159 people in the two clusters, 62% of whom were 15 years and older (Table 4). The urban cluster had more people aged 15 years and older (80.9%), while the rural cluster had 47.3% aged 15 years and older.

Table 4: Population identified during pre-listing by cluster and age group, TB-HIV Pilot Survey, South Africa, 2019

Age group	Total	Urban cluster	Rural cluster
15 years and above	1,349 (62.4%)	790 (80.9%)	559 (47.3%)
< 15 years	810 (37.5%)	186 (19.1%)	624 (52.7%)
Total	**2,159**	**976**	**1,183**

4.1.2 Survey census and household interviews

Table 5 shows the response at the household level. Out of the 462 households approached, 363 heads of the households consented and completed the survey census –a household interview response of 78.6%. In the rural cluster, the household interview response was 99.5% and 62.2% in the urban cluster.

Table 5: Household level response, TB-HIV Pilot Survey, South Africa, 2019

	Total number of households visited	Number of households that participated *n*(%)	Number of household that did not participate *n*(%)	
			Households that refused the interview	Households where there was no response
Urban cluster	259	161 (62.2)	48 (18.5)	50 (19.3)
Rural cluster	203	202 (99.5)	1 (0.5)	0
Total	**462**	**363 (78.6%)**	**49 (10.6)**	**50 (10.8)**

The household census identified a total of 1,290 people who were eligible to participate in the survey, 543 (42.1%) of whom were in the urban cluster. Among these, 1,280 (99.2%) accepted invitations to attend the hub (Table 6).

Table 6: Individuals who accepted the invitation to the hub by cluster, TB-HIV Pilot Survey, South Africa, 2019

Cluster	Number of individuals eligible to participate	Individuals who accepted the invitation at the household level *n*(%)
Urban	543	542 (99.8)
Rural	747	738 (98.8)
Total	**1,290**	**1,280 (99.2)**

4.1.3 Participation at the hub

Overall, 616 (48.1%) of the 1,280 individuals who accepted the invitations to attend the hub ultimately attended and were enrolled in the survey (Table 7). Among these 616, participants the male and female enrolment rates at the hub were 39.5% and 55.1%, respectively. Of those who were 15 years and older, 913 accepted the invitation, and 438 (48%) attended and were ultimately enrolled. Of the 73 adolescents aged 12-14 years, 30 (41.1%) were ultimately enrolled, and among children aged 0-11 years, 148 (50.3%) were ultimately enrolled. In the rural cluster, 738 accepted the invitation and 409 (55.4%) were ultimately enrolled, whereas, in the urban cluster, 542 accepted the invitation and 207 (38.2%) were ultimately enrolled.

Table 7: Enrolment at the hub by sex, age and cluster, TB-HIV Pilot Survey, South Africa, 2019

	Individuals who accepted the invitation at HH (*n*)	Individuals who attended the hub and where enrolled *n*(%)
Total	**1,280**	**616 (48.1)**
Sex		
Male	576	228 (39.5)
Female	704	388 (55.1)
Age group (years)		
0-11	294	148 (50.3)
12-14	73	30 (41.1)
15+	913	438 (48.0)
Cluster		
Urban	542	207 (38.2)
Rural	738	409 (55.4)

Figures 4 and 5 show participation at the hub in each cluster by sex and by age group among those who accepted the invitation in each cluster. In the rural cluster, participation by women was 63.3% and by men was 59.0%. In the urban cluster participation was 43.7% for women, and 23.5% for men. In the rural cluster, participation was 55.5% among those aged 15 years and older, 47.8% among adolescents, and 57.0% among children. In the urban cluster, the proportions were 39.5% for those aged 15 years and older, 29.6% for those aged 12-14 years, and 34.5% for those aged 0-11 years. Respondents in the urban cluster were older – median age 49 years, interquartile range (*IQR*) 22-65, than those in the rural cluster – median age 30 years (*IQR* 11-66).

Figure 4: Participation at the hub in each cluster by sex, TB-HIV Pilot Survey, South Africa, 2019

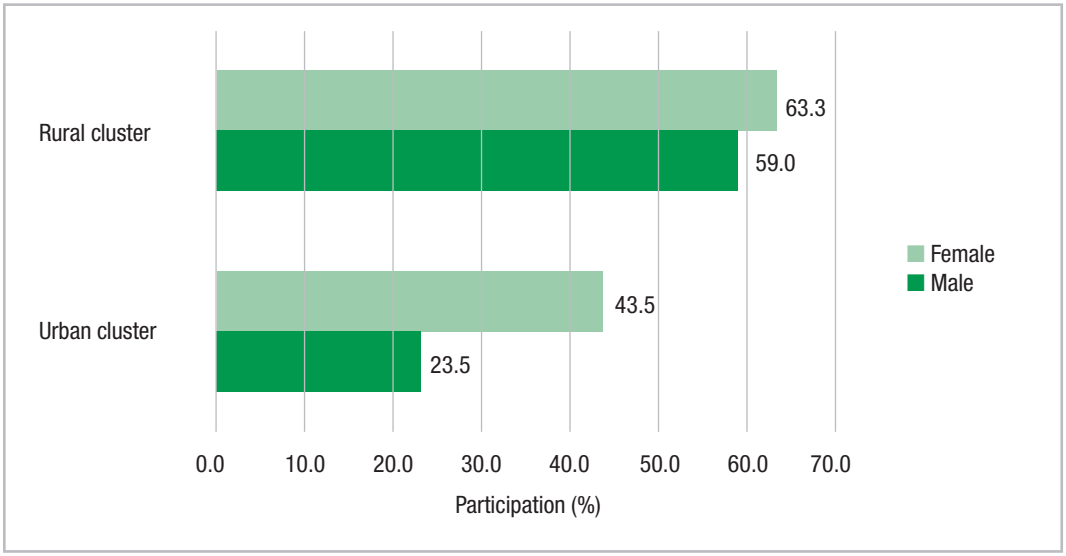
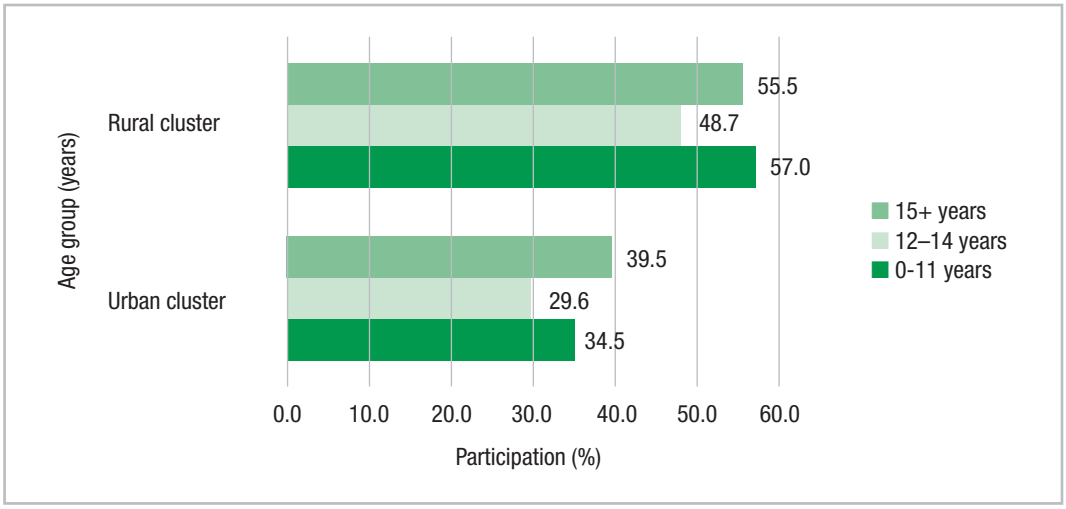


Figure 5: Participation at the hub in each cluster by age group, TB-HIV Pilot survey, South Africa, 2019



4.1.4 TB screening and testing

Among the 438 respondents who were aged 15 years and older, 120 (27.4%) had symptoms and/or CXR findings that were suggestive of TB and therefore met the eligibility criteria for sputum examination for *Mycobacterium tuberculosis* (*M.tb*). The majority of these respondents, 72.5% (87/120) were from the rural cluster. In this cluster, 32.3% (87/269) were eligible for sputum examination compared to 19.5% (33/169) in the urban cluster. The majority of those who were eligible for sputum examination in the urban cluster were older people – 60.6% (20/33) were 65 years and older – whereas in the rural cluster approximately half (50.6% (44/87)) were younger than 45 years old.

Table 8 shows the number and results of the sputum samples that were tested. A total of 120 samples were processed by Xpert Ultra and 3 tested Xpert Ultra positive – 2 samples were from respondents in the rural cluster and 1 from the urban cluster. One hundred and nineteen samples underwent culture and none were positive for *M. tb*, 5 (4.2%) were contaminated and 3 were positive for non-tuberculous mycobacteria.

Table 8: TB testing and results among respondents aged 15 years and older, TB/HIV Pilot Survey, South Africa, 2019

	Total n (%)	Urban cluster n (%)	Rural cluster n (%)
Respondents screened for TB	438	169	269
Samples received for Xpert Ultra[#]	120/ 438 (27.4)	33/169 (19.5.2)	87/269 (32.3)
Samples rejected	0	0	0
Positive Xpert Ultra	3/120 (2.5)	1/33 (3.0)	2/87 (2.3)
Trace Xpert Ultra	1 (0.8)	0 (0)	1 (1.1)
Negative Xpert Ultra	116 (96.7)	32 (97.0)	84 (96.6)
Samples received and processed for culture	119	32	87
Samples rejected	0	0	0
Culture positive for *Mycobacterium tuberculosis complex*	0 (0)	0 (0)	0 (0)
Culture negative *Mycobacterium tuberculosis complex*	111/119 (93.3)	28/32 (87.5)	83/87 (95.4)
Culture positive for *non-Tuberculous mycobacterium*	3 (2.5)	2 (6.3)	1 (1.1)
Contaminated	5 (4.2)	2 (6.3)	3 (3.4)

 # % of respondents screened for TB by symptoms and CXR

4.1.5 HIV Testing

A total of 423 respondents had HIV RT at the hubs in the two clusters. This translates to 32.8% (423/1,290) of all those who were eligible to participate in the survey, 33.0% (423/1,280) of those who accepted invitations to attend the hub and 68.7% (423/616) of those who attended and were enrolled in the survey. Among those with an RT, 7.8% (33/423) tested positive, the majority (32, 97.0%) were from the rural cluster. In the rural cluster, 10.8% of those who had an RT tested positive compared to 0.8% who tested positive in the urban cluster. (Table 9).

A total of 387 respondents gave a venous blood sample for plasma HIV testing in the laboratory. This translates to 30.0% (387/1,290) of those eligible to participate, 30.2% (387/1,280) of those who accepted the invitation to the hub, and 62.8% (387/616) of those who attended the hub and were enrolled on the survey. Of the 387 respondents, 59 (15.2%) tested positive. By cluster, 20.1% (57/284) in the rural cluster were positive compared to 1.9% (2/103) in the urban cluster. (Table 9)

Overall, more respondents tested for HIV in the rural cluster than in the urban cluster. In the rural cluster, 72.4% gave a blood sample for RT compared to 61.4% in the urban cluster. For venous blood samples, 69.4% in the rural cluster gave a sample compared to 49.8% in the urban cluster.

Viral Load suppression (VLS) was defined as a viral load that was less than 1,000cp/ml. Of the 59 HIV positive plasma samples, 49 (83.0%) had VLS.

Table 9: HIV testing, HIV results and viral load results, TB-HIV Pilot Survey, South Africa, 2019

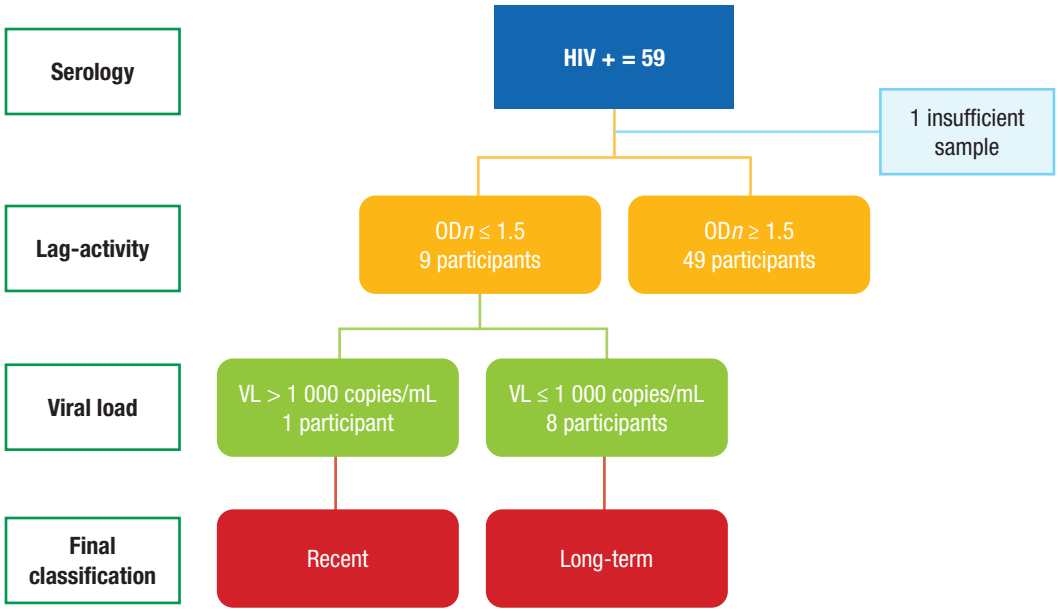
Number of respondents	Total *n* (%) *n* = 616	Urban cluster *n* (%) *n* = 207	Rural cluster *n* (%) *n* = 409
HIV RT sample#	423 (68.7)	127 (61.4)	296 (72.4)
Tested positive	33 (7.8)	1 (0.8)	32 (10.8)
Venous blood sample for plasma	387 (62.8)	103 (49.8)	284 (69.4)
Tested positive**	59 (15.2)	2 (1.9)	57 (20.1)
Viral load^	59	2 (100)	57 (20.1)
Samples ≥1,000 copies/ml^	10 (17.0^)	1 (0.5^)	9 (15.8^)
Samples <1,000 copies/ml	49 (83.0^)	1 (0.5^)	48 (84.2^)

*# % of those enrolled, ** % among those tested, ^%among those who tested HIV positive*

A total of 243 people disclosed their previous test results, among whom 57.2% took an RT and 62.5% gave a venous blood sample. Of those who tested positive on RT, three reported their last test as HIV negative. Of those who tested negative on RT, two reported their last test as positive, which could be attributed to reporting bias in people who may have engaged in risky behaviour. All the survey RT results were confirmed and were consistent with the results from laboratory testing on plasma samples.

Figure 6 presents the results of the RITA, among the 59 HIV positive respondents who gave a venous blood sample. One sample was insufficient for LAg testing. Of the remaining 58 samples that were tested, one was classified as a recent infection.

Figure 6: Flow of the final LAg classification, Joint TB-HIV Pilot Survey, South Africa, 2019



4.1.6 Point of care tests and anthropometric measurements

Among the 415 respondents who were 18 years and older and eligible for random and point of care glucose and cholesterol testing and blood pressure and anthropometric measurements, 365 (87.9%) had a random blood glucose test done, and 363 (87.5%) had a blood cholesterol test done. Blood pressure, weight, and height measurements and BMI calculations were conducted for 380 (91.6%) respondents. The blood pressure measurements are not shown.

Table 10: Glucose and cholesterol tests, and BMI measurements, TB-HIV Pilot Survey, South Africa, 2019*

	Total	Urban cluster	Rural cluster
Respondents with a random blood glucose reading mmol/L**	365	142	223
Median (*IQR****)	5.4 (4.7-6.5)	5.9 (4.7-8.1)	5.2 (4.6-5.9)
Respondents with a cholesterol reading mmol/L**	363	140	223
Median (*IQR****)	4.5 (3.7-5.3)	4.5(3.8-5.4)	4.4 (3.7-5.2)
Respondents with a Body Mass Index calculated	380	153	227
Underweight	13 (3.4%)	8 (5.2%)	5 (2.2)
Normal weight	106 (27.9%)	43 (28.1%)	63 (27.8)
Overweight & obese	261(68.7%)	102 (66.7%)	159 (70.0)

**These tests and measurements applied only to those 18 years and older*
***Mmol/L: millimoles/litre*
****IQR: interquartile range*

4.2 Analysis and results from the qualitative component of the survey

The findings presented below are extracted from data collected from the following sources: 1) field staff diaries; 2) notes from debriefing meetings (*n*=15); 3) observations of activities in both clusters by members of the HSRC survey team; 4) KIIs (*n*=5); 5) FGDs (*n*=3). To better account for how the survey was implemented the qualitative results are organised using the different stages followed during implementation – i.e. preparatory activities such as cluster entry and communication, recruitment of respondents, setting up of the hub process, and how the hub functioned. Emerging actions for consideration are also presented.

These qualitative data give voice to the experiences of the people interviewed in this case field staff, volunteers and selected survey partners and also reveal the complexities of survey implementation that are of value to future studies.

Due to budgetary and time constraints, the analysis and interpretation of the qualitative data collected did not follow the time-intensive iterative qualitative research process – for example, developing of themes, organising the analysis around the themes, and attempting to identify patterns from the data. Instead, a simpler content analysis approach was followed using the 5 questions developed for the interview guides as an organising method (Appendix 9).

Given that the sampling plan for collecting the data was purposive; all the people interviewed were selected to provide information about their experience of the survey. This is commonly referred to as a 'surface' approach to the analysis.

4.2.1 Communication community entry and social mobilisation

The comprehensive community engagement and social mobilisation component aimed to raise awareness about the survey in the two clusters. Volunteers from the community also assisted with mobilisation activities which included the distribution of survey flyers and facilitating entry into households. Social mobilisation included the following:

- 3 radio interviews and 2 newspapers interviews conducted in local languages.
- WhatsApp messages created and shared among local community groups.
- Facebook messages created and shared among local community groups.
- A community imbizo (community gathering or meeting) held to introduce the survey in the rural cluster.
- A community talk held to introduce the survey at a community clinic in the urban cluster.
- Pamphlets dropped off at households in the clusters.
- Posters about the survey distributed in the clusters (The posters included the dates and the venue of the hub in each cluster).
- Communicating with various stakeholders including different religious entities so that they shared this information with their congregations or religious group.

The communication aspect of this pilot survey relied on free publicity – i.e. free interviews on community radio stations and free media placements in community newspapers. Given the budgetary limitation as well as the scale of this pilot, the survey budget line for communication only catered for printing the posters and flyers.

Communication activities generated considerable interest in the survey in and outside the cluster. As a field team member observed: *The fact that volunteers had gone before us… It made it easy for them [respondents] to agree to participate.*

Nonetheless, FGD respondents reported that there were challenges concerning community members who were not part of the target population as they did not reside within the selected clusters, and yet presented at the hub wanting to participate in the survey. The experience showed that while the communication was targeted and successful, it also drew interest for people outside the boundaries of the targeted clusters which was problematic: As a volunteer noted: *That [social mobilisation] actually did help but it also caused a bit of confusion because the people out of the cluster also wanted to come. So you'll actually get people coming to the hub, but they are out of the boundary.*

It was also reported and observed that some members of the community in the rural cluster did not understand the selection procedures the survey used, namely why some households were part of the survey, and some were not. This occurred despite clarification being given during the community imbizo and also during census-taking and issuing of invitations to the hub.

Community members who presented themselves at the hub were shown a map and informed of the survey process. Even so, being turned away was not well accepted. The issue was compounded by the fact that there were people who presented at the hub without invitation cards and yet were eligible to participate and were thus enrolled. This latter category was referred to as 'walk-ins' – a term that was adapted from the TPS and included people whose households were selected for the survey. They had not received invitation slips because there had been no one at home during visits for the household interview and the census. The household interview and census data for these individuals were collected at the hub, and they were enrolled in the survey. Some had been missed by the household interview process but had heard from neighbours about the survey and therefore presented at the hub. Since they met the survey criteria and the survey sample had not been reached, they were enrolled.

In the rural cluster, some of those who presented at the hub reported that they had travelled long distances, despite transport being made available for those who needed it. Some were elderly and some pregnant women and mothers with babies or young children and had used limited resources for transport to the hub. In these instances, the procedures that had been scheduled for the household were then conducted at the hub, and the individuals could be enrolled. Lastly, some individuals who presented during periods where there were no or very few respondents in the hub – in a context where the survey had not reached the targeted enrolments – were enrolled into the survey if they were from within the cluster and met the survey inclusion criteria. Household interviews and census data were also collected at the hub, and the individuals were enrolled in the survey.

Accepting and enrolling individuals who presented at the site without the survey hub invitation cards but who met the survey criteria while turning others away – i.e. accepting those who met the survey inclusion criteria while turning away those who did not meet the inclusion criteria – led to tensions in the community in the rural cluster. These tensions related to some individuals sharing that they had been accepted without the survey invitation while others were not accepted because they did not meet the criteria. This practice as described above is widely accepted in TB prevalence surveys, especially where participation is low.

Although the demarcation of the survey cluster areas and the enrolment criteria were explained, it seemed that these were not well understood by communities. A further complicating factor was that health care and many other services were very limited in these communities, and the survey was seen as coming to resolve health-related problems – especially due to the presence of a doctor.

Based on reported sentiment communicated by some of the people who were turned away, and by some community leaders in the rural cluster, this aspect has to be carefully managed as there is potential to create negative perceptions about research studies and possible disinterest in participation.

4.2.2 Pre-visit, pre-listing and household census

FGDs with volunteers and members of the field team identified the pre-visits and pre-listing activities as critical for community entry. These activities assisted in securing buy-in from the community and facilitated the recruitment of respondents. In addition, it was noted that the pre-visits achieved their objectives including 1) allowing the survey team to conduct detailed boundary mapping and to undertake introduction visits in the area thereby increasing the probability of reaching the targeted sample; 2) facilitating communication and engagement with the local clinics, police stations, religious entities, traditional leaders, and political leaders including ward committee members and councillors about the survey.

Communicating with and engaging with the local clinics facilitated referral of patients to the clinics for follow-up required to address health and other concerns detected by the survey. Engaging traditional structures (in the rural cluster) and political structures ensured that the team could implement the survey without any hindrances and interruptions.

Challenges that were reported in the process of implementing these activities included:

- The research team had to manage tensions related to the impression that the survey 'was brought' to the community by those community leaders who were the first to be approached, although meetings with the local traditional and political leadership were scheduled according to their availability. Several visits and constant communication during the pre-visit phase helped to reduce the tensions.
- Multiple visits (more than had been envisaged) were needed to strengthen community networks and identify possible sites for the hub.
- It was not easy to access and reach all the houses and residents in the clusters for the pre-listing activities and the household interviews. In the urban areas, many households were not occupied during the day because many of the household members were at work. Attempts to change the time for this activity to the evening were not successful in all areas as residents had concerns about their security and therefore declined to speak to the survey field teams in the evenings. In the rural cluster, the biggest challenge was reaching all the households in the cluster due to the geographic spread across the area and the difficult terrain which made some areas inaccessible – even by motor vehicle. As in the urban cluster, some households were also unoccupied during the day because occupants were working on farms or in the nearby towns and some only returned during the weekend or at the month-end.
- Some respondents mixed up the details of adult and child invitations to the hub. This had to be corrected when the respondents presented at the hub and was a time-consuming activity for staff. In addition, some staff members mixed the child and adult invitation slips and this also created delays at the hub reception station.

As a team member explained:

> *In order for us to check the data on the day of the screening, we used the barcodes, so you find that there was an issue, especially in Marburg. It became a challenge, but in the uMgayi/the Ridge (rural cluster), that was solved. Another problem that also came in the uMgayi/the Ridge area was the mixture [mix up] of invitations that were for kids that were given to adults, and then the one that was for adults, was given to kids. When people came for the screening you had to change that first before they could do anything, so that takes a lot of time (delay) and people are waiting already outside you know, for me that was the challenge you know.*

4.2.3 Volunteers supporting the survey

It was noted that volunteers from the survey communities were key to the successful implementation of the survey. The volunteers were trained for their tasks and roles by members of the core survey team. Volunteers reported that they felt equipped for the tasks they had to undertake.

Experiences from the TPS survey had shown that the most widely accepted approach for selecting community volunteers was for the community to select them independent of the survey team. Therefore, in both clusters, the survey team provided a list of skills that the volunteers needed to have, the tasks they were to perform and the duration over which they were required to support the survey. Leadership structures within the community were then left to recruit the volunteers.

FGD participants indicated that this approach possibly contributed to individuals related to or close to the community leaders being recruited for the volunteering opportunity. The field staff reported being made aware of complaints and accusations from some respondents who felt that the volunteering opportunity was exclusively for those who are politically aligned with certain leaders. The complaints and accusations were more common in the rural cluster which is a more closed community in comparison to the urban cluster. It was noted that these complaints were possibly due to tensions that already existed amongst various leaders in the cluster.

Based on the TPS and other community surveys, it is most difficult to choose volunteers without the involvement of community leaders and it is also not possible to please all members of the community. Once these complaints had come to the attention of the team leader, the field team managed these perceptions by preventing volunteers with ties to both political and traditional leaders from conducting activities in the community and rather allocated them tasks in the hub. In addition, members of the core survey team also took over tasks such as the initial interaction with people who attended the hub (engaging the people who presented at the entry point of the hub to identify individuals who were eligible and ineligible to participate by determining whether or not they resided within the cluster boundaries).

4.2.4 Location of the hub

In both clusters, the hub was located in a formal structure. In *Marburg* (urban cluster), the hub was located at a church, while in *uMgayi/the Ridge* (rural cluster) an unused building that had been a public health clinic was used. The unused building in the rural cluster was noted as the only possible venue which could be used as a hub within that community. It was on the main road used by public transport and opposite a shop. The project team had to organise cleaning of the site and to make provisions for water and ablution facilities, and arrangements for electricity before it could be used as the hub – a process that built on previous TPS experience among the survey team members who previously had to set up hubs using tents. In both clusters, the hub location was determined by community leaders and was set up a day before the hub activities.

It was reported that some people who lived on the outskirts of the clusters felt that the location of the hubs was not ideal due to the distance that they needed to travel to get there. However, based on the experience of implementing the TPS, arrangements had been made to transport individuals to and from the hubs so as to eliminate the inconvenience or barrier to recruitment of travelling or walking long distances to the hub. The longest distance that most people would have travelled to get to the hub, was 1.5 kilometres. While there were roads in the urban cluster, in the rural cluster the terrain of the areas was difficult and people travelled on footpaths or gravel roads.

In the urban cluster a few individuals who were not from a Christian based faith were uncomfortable attending hub activities in a church – this despite assurances by the local leaders and stakeholders that using the church building as the hub would be acceptable to people of all religions in the cluster. This site was also central and easily accessible, and the research team had been informed that the venue had previously been used to host events that were previously well attended irrespective of such concerns.

4.2.5 Consenting and individual interviews at the hub

It was reported that the consent form used was too long, and therefore, it took a long time to complete the informed consent process for individuals at the hub. As described in the methodology section, the respondents would have attended the information group session where a nurse took them through the information sheet. They then moved to the next station where they had to give informed consent after making up their minds about participation. Also as described in the methodology section, the consenting process was closely linked to the individual interview station: consenting and the individual interview were conducted by the same person at the same station. This meant that the time spent on consenting and on the questionnaire was long. This created a bottleneck since respondents could not attend other stations before consenting and completing the individual questionnaire.

Long waiting periods was the outcome – especially in the mornings since most of the respondents presented to the hub early in the morning with numbers tapering off toward the afternoon (this was more common in the rural cluster). It was reported and also observed that some people spent a long time at the hub – 2-3 hours for some – which was cumbersome for those who also brought and agreed for their children to participate. Waiting times discouraged some people who had been invited from presenting to the hub.

To address the long wait times at the consenting and individual interview stations, members of the field team who were at stations that were not busy were assigned to assist with consenting and the administration of individual interviews. It was possible to assign members of the field team to different tasks and roles because all field staff members (except the driver) were trained in consenting and administering the questionnaire.

> *In the team, we had few interviewers and we had a lot of respondents sitting waiting for hours to be interviewed. Once interviewed, they are also caught in a bottleneck in the blood section where they had another wait which had an impact on the time the hub closed. The lab staff were busier toward the end of the day and had to complete processing the samples and allow enough time for the DBS to dry. Based on this, the staff suggested that future studies should increase the number of interviewers and increase the number of people that are taking blood. Maybe that will shorten the process.* (Team member 9)

Since there were several tests offered in the survey, there was concern that some respondents were likely to forget what they had consented to at the consent stage as they moved across the hub – hence there was a need to remind them about this at each station. It was suggested that respondents should be reminded and referred to the consent forms at each station rather than only once at the consent and interview station.

4.2.6 CASI and questionnaire administration

It was reported and observed that self-administration of the questionnaire was not popular because the majority of respondents were intimidated or had difficulties reading the questions and operating the tablet. This was more pronounced among older respondents and also in the rural cluster where many people were not familiar with touch screen tablets. The length of the interview and the size of the tablet were also cited as challenges by the survey respondents who had been selected for CASI.

> *The self-administered questions… I think they need to be simplified so that any person can be able to go through and navigate all those questions. Some respondents had challenges. Some will take very long to complete each answer. It needs to be simple easy to move from one section to another, like if a person were to save and wait for the tablet some people they can't do that.* (Team member)

> *People will complain about the questionnaire being too long because they didn't know they were going to take so much time with the questionnaire. I would say the senior citizens is where we got the most complaints.* (Team member)

Emotional response to intimate partner violence (IPV) questions in the questionnaire

Respondents did not specifically raise any concerns with the contents of the questionnaire. The majority of respondents were said to have been comfortable answering questions and being interviewed by the interviewers (both males and females). However, the intimate partner violence (IPV) questions did elicit discomfort among two respondents who had been survivors of domestic violence and sexual assault. In these instances, nurses in the team together with the interviewer counselled the respondents. None of the respondents wanted to be referred for further assistance, and told the interviewers that they did not want to revisit the matter in another setting.

4.2.7 Chest X-rays

The provision of CXRs was appreciated by survey respondents, who indicated to the survey staff that it was not easy to access CXR services at the local clinics, that CXRs were not available from the mobile clinic services provided in the rural cluster, and that CXRs were expensive in the private healthcare sector. No challenges were noted with regard to this aspect of the survey. Respondents were processed efficiently, with minimum waiting times for CXR.

4.2.8 Point of care tests, blood pressure and weight and height measurements

The additional tests (random blood glucose, blood cholesterol) and health-related measurements (weight and blood pressure,) were reported to have been very popular and attracted many of the respondents to the survey. It was reported that respondents appreciated that they could receive their results recorded on a wellness card that they could take home.

The MO reviewed all the screening and test results (HIV RT only if respondents requested) and used her clinical discretion to determine referral to the local clinic for further assessment and/or management. It was also reported that the presence of an MO at the hub was one of the aspects of the survey that had also encouraged participation. However, it was observed that respondents then came with expectations for medical assessments and access to medication which was not the case in this survey. These expectations were managed well by the MO who had also experienced the same when working on the TPS.

4.2.9 Blood sample collection and processing on-site

Blood samples for central laboratory testing were collected by trained phlebotomists. Dried blood spotting, centrifuging, plasma separation, and aliquoting was done on-site. When bottlenecks occurred at the phlebotomy station, respondents were directed to other stations that were less busy. The challenges reported at the blood collection and processing station included respondents requesting additional tests from the blood draw. For example, one respondent requested blood group testing, and another requested screening for cancer. Apart from the bottlenecks during the phlebotomy process, the time needed to process the blood specimens (centrifuging and aliquoting of plasma) added extra time in the hub after all other survey processes were completed. This resulted in the hub shutting down late in the evening. To account for the additional time required to process the blood samples in the rural cluster, the survey team decided to limit the number of enrolments to around 50 per day and to set a cut off time to allow respondents into the hub. Individuals who arrived at the hub after the cut off time were not enrolled. As a team member observed: *At the hub, if we tried to see how many people we will do like 100. It means we will finish at 10-12 p.m. Especially the blood stations. It takes a lot of time.*

4.2.10 HIV rapid testing

Overall, there was high uptake of the rapid HIV test. It was reported that respondents indicated that they appreciated being tested by someone who did not live in their community because it meant that their results would not be communicated to others within the community. The survey respondents reported that the MO and nurses were caring and warm and also indicated that they have been treated very well by the survey staff at the hub.

Most of those who tested positive already knew their HIV status with only a few (*n*=3), who found out for the first time that they were HIV positive. The testing team managed this circumstance appropriately, and there was no instance of an emotional breakdown or other concerning reaction to the HIV RT result.

4.2.11 Patient referrals

Interviews with the staff working at the local clinics revealed that they appreciated the screening role that the survey had provided. In one clinic, the nursing sister highlighted how the survey had assisted in finding a TB patient who had been lost from care and had been untraceable.

4.2.12 Laboratory related considerations

In the interviews with the staff members from the NICD virology laboratory, it was noted that there was a preference for plasma samples (i.e. for viral load, LAg assay and HIV DR testing). Laboratory staff were satisfied with the sample quality, packaging, and courier.

The laboratory staff at GCVL expressed concerns regarding the costs and the logistics of using plasma samples for a scaled-up national survey. Their view was that viral load, LAg assay and HIVDR testing is achievable on DBS samples. They indicated that they felt that venous blood draws could reduce survey participation rates because people who know about and have participated in previous HIV surveys may not understand the reasons for changing the survey sampling from a finger prick to a venous blood draw.

The advantages and disadvantages of having laboratory-related processing at the hub were discussed. Completion of some of the sample procedures such as centrifuging, plasma aliquoting at the hub meant that the procedures at the central laboratory conducting HIV antibody testing could be completed much faster and more efficiently. However, completing these procedures at the hub took much longer than was anticipated. This meant that the blood sample processing station regularly closed late (between 20h00 and 21h00 at times). It was noted that closing the hub late raised concerns about the safety of the survey staff. A mixed approach, where all interviews could be conducted in the household with the hub reserved and screening tests only, was suggested as one way to address this issue.

It was reported that laboratory readiness to test the specimens had been impacted by delays in initiating and concluding the contracting process. This had affected the ability of the laboratory to firmly and timeously plan and hire staff for the survey.
A further challenge was the limited budget that was allocated for laboratory testing. This affected the number of field-based laboratory staff that could be engaged. During the implementation of the survey, it has become clear that more capacity was needed, and to facilitate completion of the survey this was provided at no additional cost to the survey.

4.2.13 IT-related processes

Several IT-related challenges were reported and observed. These included the delayed programming of the survey questionnaires on the survey tablets and the set-up for the CASI aspect of the survey. This meant that testing of the IT and data system before fieldwork was limited and this had an impact on the functionality of the IT system and tablets in the field. The problems encountered included inaccurate skip patterns in the questionnaire, errors in the screening algorithm for TB, and errors in the numbering of some questions. For example:

> *And the questionnaires for 12-14 years – alcohol questions – if a person says no, it will still ask more questions about [this]. I think there was a problem with the skipping* (Team member 12), and:

> *The symptoms questions were a problem because I think initially there was some issue with the coding 'yes', versus 'no'. So when the interviewer enters 'no' on any of the symptoms it was coming out as 'yes' or it then looked like there were more people who were eligible for sputum. The MO needed to decide whether this person needed to go for sputum or not it was a bit of a challenge there.* (Team member 11)

The team also reported that there were problems when moving between different sections of the questionnaire and when uploading data to the server. Internet connectivity was not stable – especially in the rural cluster – and this affected the speed at which data could be captured and uploaded to the server. However, the majority of these challenges were resolved by IT teams in field teams and those who were at the HSRC office. The lessons learned from addressing challenges in the first cluster (urban) were beneficially implemented to improve the IT functionality in the second cluster.

Interviews with the laboratory staff indicated that there were problems with the interface between the central laboratory data, the questionnaire and other screening and testing data. Some of the central laboratory data could not be captured directly onto Redcap.

4.3 Analysis and results of the survey costs

Cost data were collected for the following elements:

1. staff;
2. utilities;
3. supplies;
4. screening procedures;
5. laboratory procedures and tests;
6. courier of specimens;
7. courier of other survey materials;
8. travel;
9. trainings;
10. building, equipment, communication, and other miscellaneous items.

Given that a key objective of this survey was to ascertain the cost of conducting a joint TB-HIV survey, it was important to allocate costs to the TB or HIV component or jointly to both components depending on the delineation of items and/or services. While such cost assignment is straightforward for some cost elements (e.g. laboratory tests for HIV or TB), some costs elements are not readily classified (e.g. the buildings at the hubs, travel expenditure). In such cases, the costing and operational teams jointly assigned weights to both components based on the available information, knowledge of the project from its inception and experiences of implementing prior HIV and surveys and the TPS. Both financial and economic costs were calculated. Financial costs captured the actual costs incurred in implementing the survey. In addition to these financial costs, economic costs included imputed values for cost items not incurred but used in the pilot (e.g. tablets that had been used in previous surveys and buildings gifted for use as a hub at no rental cost), items/services not used (and therefore incurred no costs) in the pilot but anticipated for use in a national survey (e.g. communication/sensitisation services) and actual time (not billed time) spent on the project as indicated by some categories of personnel. Please refer to Appendix 13 for the economic cost figures.

4.3.1 Key assumptions: Total costs (aggregate and cluster-specific)

Most of the cost data came from personnel and other project-related records maintained by the finance and project management team. A key feature of the project information system was that most items were jointly invoiced. This reality conflicted with an ideal scenario for given the overlap of many costs and activities hence the costing exercise could not be based on separate costing for the components with joint costing only for joint activities. Consequently, where separate costs for the HIV and TB components were not available, the costing exercise relied heavily on weights informed by the expert opinion of the project management team.

Regarding assigning weights to both the HIV and TB components – while samples for TB testing is different the aggregate total cost is a straightforward accounting exercise not requiring these weights, the total costs for each component depend on the weights. Based on expert opinion from the program staff, it was determined that a weight distribution of 50:50 was appropriate for most of the cost elements (utilities, supplies, travel, non-specimen courier, training and reimbursement, building, equipment, communication, and other miscellaneous expenditures.

The specimen courier cost element was heavily concentrated on the TB component. Most of the specimen courier costs were incurred in transporting sputum samples to NICD in Johannesburg, hence a weight assignment of 95% in favour of the TB component and 5% to HIV (HIV samples were transported to GCVL in Durban, and aliquoted plasma samples were then sent in batches to the NICD laboratory in Johannesburg). In addition, the packaging requirements for the sputum samples for TB testing is different from those for HIV samples. Sputum samples required triple packaging and monitoring of the temperature en-route to the laboratory. The sputum samples were couriered every second day regardless of the number submitted. In contrast, HIV samples were partially processed at the hub and thereafter aliquoted plasma vials had a shorter transit to GCVL for the laboratory antibody testing, and thereafter plasma vials for additional testing (only the HIV positives) were shipped in larger batches to the virology laboratory at the NICD. These differences accounted for the heavier weighting in favour of the TB component for courier costs.

The laboratory cost element, which was slightly more weighted in favour of HIV, was informed by activities related to pre-test counselling, sample collection, post-test counselling, sample processing at the hub and testing in the laboratories (GCVL and NICD). The slightly higher weight assigned to HIV for laboratory testing was informed by laboratory-related costs. For the laboratory tests, we took into account the cascade of tests done based on the HIV antibody results.

The weight for the CXR procedure was 100% in favour of the TB component as this only applied to screening for TB.

The staff cost element was slightly weighted more in favour of the HIV component based on expert advice from the project management team. These weights are presented in Appendix 11 for both financial and economic costs. These weights were applied to the cost of each cost element to yield the associated costs for each component (HIV and TB), with their aggregation yielding the aggregate total costs for each survey component (i.e. TB and HIV).

For the cluster-specific costs, each cluster was allocated an equal weight (split 50:50) for a number of the cost elements (staff, supplies, non-specimen related courier, operational team's travel, equipment, communication, and other miscellaneous expenditure). Some cost elements such as cluster-specific buildings, utilities, and travel were exclusively allocated to only one cluster determined by the actual implementation of activities in each cluster. Other cluster-specific weights were allocated based on the cluster-specific number of respondents (e.g. reimbursements) or the relative number of tests conducted in each cluster (e.g. laboratory tests, and CXRs). Applying these weights yielded the cluster-specific cost for that cost element. These were aggregated to yield the total cost for each cluster.

To obtain cluster-specific costs for each survey component (i.e. HIV and TB) we assumed the same weights as obtainable in the aggregate case. For instance, it was assumed that the weight distribution for HIV-TB for the staff element in the aggregate sample (52:48) was the same in each cluster. The only difference was for cluster-specific cost elements where a zero weight was assigned where necessary (e.g. for 'utilities' a weight of zero was assigned to both HIV and TB in the rural cluster even though the weight distribution was 50:50 in the aggregate case). These cluster-component weights were applied to the above cluster-specific cost elements to yield the costs of each component per cluster.

4.3.2 Key assumptions and average costs (aggregate and cluster-specific)

The average cost (financial and economic) represents the cost per respondent as follows:

- Cost per respondent for the aggregate case (i.e. the entire survey).
- Cost per respondent for HIV and TB components respectively.
- Cost per respondent for each survey component.

In obtaining the aggregate cost per respondent, each cost element was divided by the number of respondents who were interviewed (*n*=616). The only exception was the laboratory test and the CXR components. For the laboratory tests, given the cascading nature of testing for individuals – often declining for subsequent HIV related tests – the test-related cost per respondent was computed as a summation of the per respondent cost of each testing procedure., To obtain the cost per respondent for the other tests, the relevant total cost was divided by the number of respondents who gave a venous blood sample for HIV and the number who did a CXR and those who gave a sputum sample for TB testing. Finally, the aggregate cost per respondent was estimated by summing up the cost per respondent for all the cost elements.

The weights used in the computations (aggregate and cluster-specific) across the cost elements are shown in Appendix 11. The TB component constituted 52% of the total financial costs, while the HIV component made up 48% of the total cost. The rural cluster accounted for 54% of the total cost, while urban represented 46% of the total survey cost. These weights were applied to the relevant costs to obtain the disaggregated costs (by survey component and by cluster). Table 11 shows the total financial costs of the pilot survey. The total financial cost for the pilot was approximately ZAR 4 million (approximately US$ 287,000). The TB component was approximately ZAR 2.1 million (approximately US$ 152,000), Table 11. The total cost in the rural cluster was approximately ZAR 2.2 million (approximately US$ 160,000) (Table 11). In Table 12 below, the per respondent costs are presented – i.e. financial costs per respondent taking into account the relevant tests per age group. The average cost per participant was ZAR 12,147 (US$ 868). Although the TB component accounted for the larger share of the total costs, the unit cost of the HIV component was higher than that of the TB component by 20.9%. Also, the unit cost in the urban cluster (ZAR 14,435/ US$ 1,031) exceeded that of the rural cluster (ZAR 11,246/ US$ 803) by 28%.

Table 11: Total financial costs, TB-HIV Pilot Survey, South Africa, 2019

S/No	Category	TC	HIV TC	TB TC	TC- M	TC-U	TC HIV(M)	TC HIV(U)	TC-TB(M)	TC-TB(U)
1	Staff	1,943,167	1,018,978	924,189	971,583	971,583	509,489	509,489	462,094	462,094
2	Utility-Marburg	4,298	2,149	2,149	4,298	0	2,149	0	2,149	0
3	Utility-UMgayi	35,553	17,776	17,776	0	35,553	0	17,776	0	17,776
4	Supplies	11,538	5,769	5,769	5,769	5,769	2,885	2,885	2,885	2,885
5	Total testing cost-no CXR	592,525	312,519	280,005	172,709	419,816	92,339	220,154	80,370	199,661
6	TB test – CXR	287,500	0	287,500	107,134	180,366	0	0	107,134	180,366
7	Specimen courier cost (by HSRC)	90,008	4,600	85,408	28,748	61,260	1,469	3,131	27,279	58,129
8	Non-specimen courier cost	12,968	6,484	6,484	6,484	6,484	3,242	3,242	3,242	3,242
9	Travel (Operational team)	602,527	301,263	301,263	301,263	301,263	150,632	150,632	150,632	150,632
10	Travel Marburg	140,558	70,279	70,279	140,558	0	70,279	0	70,279	0
11	Travel UMgayi	215,874	107,937	107,937	0	215,874	0	107,937	0	107,937
12	Training & Reimbursements	78,770	39,385	39,385	32,897	45,873	16,449	22,936	16,449	22,936
13	Other miscellaneous*	1,512	756	756	756	756	378	378	378	378
	Grand Total (ZAR)	**4,016,797**	**1,887,896**	**2,128,902**	**1,772,201**	**2,244,596**	**849,310**	**1,038,560**	**922,891**	**1,206,037**
	Grand Total (US$)	**286,914**	**134,850**	**152,064**	**126,586**	**160,328**	**60,665**	**74,183**	**65,921**	**86,146**

Note: TC = Total cost; M = Marburg; U = UMgayi; Amounts rounded to the nearest integer; *Miscellaneous items include printing of survey documents including manuals, flyers and information sheets, consent forms, and flyers, waste disposal, renting of mobile vans, etc.

Table 12: Financial costs per respondent, TB-HIV Pilot Survey, South Africa, 2019

		I	II	III	IV	V	VI	VII	VIII	IX
S/No	**Category**	**AC**	**AC-HIV**	**AC-TB**	**AC-M**	**AC-U**	**AC-M-HIV**	**AC-U-HIV**	**AC-M-TB**	**AC-U-TB**
1	Staff	3,154	2,633	2,180	4,694	2,376	4,946	1,794	2,925	1,737
2	Utility-Marburg	7	6	5	21	0	21	0	14	0
3	Utility-UMgayi	58	46	42	0	87	0	63	0	67
4	Supplies	19	15	14	28	14	28	10	18	11
5	Total testing cost-no CXR	6,377	4,033	2,344	6,548	6,548	4,036	4,036	2,512	2,512
6	TB test – CXR	678	0	678	678	678	0	0	678	678
7	Specimen courier cost (by HSRC)	146	12	201	139	150	14	11	173	219
8	Non-specimen courier cost	21	17	15	31	16	31	11	21	12
9	Travel (Operational team)	978	778	711	1,455	737	1,462	530	953	566
10	Travel Marburg	228	182	166	679	0	682	0	445	0
11	Travel UMgayi	350	279	255	0	528	0	380	0	406
12	Training & Reimbursements	128	102	93	159	112	160	81	104	86
13	Other miscellaneous**;	2	2	2	4	2	4	1	2	1
	Grand Total (ZAR)	**12,147**	**8,103**	**6,704**	**14,435**	**11,246**	**11,385**	**6,917**	**7,844**	**6,295**
	Grand Total (US$)	**868**	**579**	**479**	**1,031**	**803**	**813**	**494**	**560**	**450**

*Note: I (n=616); II (n=387); III (n=424); IV (n=207); V (n=409); VI (n=103); VII (n=284); VIII (n=158); IX (n=266); AC for lab tests were determined by the cascade of the number of samples for each particular test; Amounts rounded to the nearest integer; AC= Average (i.e. unit) Cost; M=Marburg; U=uMgayi; * Miscellaneous items include printing of survey documents including manuals, flyers and information sheets, consent forms, and flyers, waste disposal, renting of mobile vans, etc.;*

To examine the relative influence of the various cost elements, we present the relative contribution of each item to the total cost in the aggregate case (Table 13). Staff constituted the largest cost element, accounting for 48% of the pilot survey cost. This was followed by the operational team's travel expenses, which constituted 15% of the total cost, and was in turn followed by testing costs at nearly the same percentage. Miscellaneous expenses contributed the least to survey costs.

The SABSSMV survey conducted in 2017 is estimated to have cost approximately ZAR 127 million (US$ 9,1 million) which translates to a respondent cost of ZAR 2,000 (US$ 138), lower than that in this survey (personal communication, HSRC). This difference could be attributed to the addition of the TB aspect (the hub and related TB screening and testing, as well the additional health-related measurements), and the inclusion of venous blood samples (together with the setting up the mini field laboratory) whereas the SABSSMV survey used DBS samples that were collected at the household. The costing approach may also result in different cost estimates, especially the economic vs. financial costs.

Table 13: Relative contribution of cost elements to total financial costs, TB-HIV Pilot Survey, South Africa, 2019

S/No	Category	Total cost (ZAR)	Total cost (US$)	Percentage
1	Staff	1,943,167.00	138,797.64	48.38
2	Travel (Operational Team)	602,527.00	43,037.64	15.00
3	Total testing cost-no CXR	592,525.00	42,323.21	14.75
4	TB test – CXR	287,500.00	20,535.71	7.16
5	Travel UMgayi	215,874.00	15,419.57	5.37
6	Travel Marburg	140,558.00	10,039.86	3.50
7	Specimen courier cost (by HSRC)	90,008.00	6,429.14	2.24
8	Training & Reimbursements	78,770.00	5,626.43	1.96
9	Utility-UMgayi	35,553.00	2,539.50	0.89
10	Non-specimen courier cost	12,968.00	926.29	0.32
11	Supplies	11,538.00	824.14	0.29
12	Utility-Marburg	4,298.00	307.00	0.11
13	Other miscellaneous*	1,512.00	824.14	0.04

** **Miscellaneous items include printing of survey documents including manuals, flyers and information sheets, consent forms, and flyers, waste disposal, renting of mobile vans, etc.*

4.3.3 Hypothetically scaled-up joint survey

To compute the cost of a hypothetical scaled up survey, a survey statistician drew up a survey design similar to this pilot based on key parameters, including the HIV and TB prevalence rates, the HIV incidence rate, VLS and the expected sample sizes for the HIV and TB components. We used this survey design to draw up a survey implementation plan that in combination with costs estimated from the present pilot survey informed the calculation of the relevant costs of a hypothetical scaled-up TB-HIV survey.

The costs of the scaled-up survey are based on the assumptions of a TB prevalence of 0.33%, an HIV prevalence of 20.5%, an HIV incidence of 0.79%, and VLS among HIV-infected respondents of 50%. For full details regarding the design considerations for the scaled-up survey and the inputs for the parameters in this section, see Appendix 12 The scaled-up survey follows a hub design, is estimated to be implemented in 122 clusters in twelve months. We envisaged that each urban cluster would include a hub while each rural cluster would contain between 1 and 1.5 hubs based on experiences in the rural cluster in the due present pilot. This would result in a total of 150 hubs. Seven fieldwork teams, each comprising 15 fieldworkers (105 fieldworkers in total) will take part in the survey. Fieldworker training (including refresher training) will take place over 18 days and will involve seven instructors.

The cost estimates, as well as the key assumptions for the scaled-up survey, are outlined in Table 14. The results indicate that without considering the potential economies of scale, the total cost of a national joint TB-HIV survey (using venous blood draws), in South Africa was estimated at ZAR 236 million (US$ 16.9 million). In the sensitivity analysis, we adjusted the estimates based on assumptions for each cost component in consultation with the administrative and project team. This resulted in a total cost of about ZAR 231.3 million (US$ 16.5 million).

The project costs of a scaled-up survey based on the design parameters described above are shown in Table 14.

Table 14: Cost projection of a hypothetical joint TB/HIV national survey

Activity	Assumptions due to changes in scope and/or efficiency	Data source	Unit cost	Quantity	Total cost
Training	The training cost (components and unit price) is comparable to that in the national TB survey.	The national TB survey (2017R), pilot survey. Airfare was estimated by financial experts using October 2020 market rates for each province.	Venue cost*: R108,040 per day Breakaway room: R4,615.38 per room day Accommodation: R1,310/person day Per diem: R150/person day Training allowance: R100/person day.	18 days, 112 respondents, 2 breakaway rooms.	ZAR5,838,191 US$ 417,014
Field monitoring trips	Two field supervision trips per province, implying 18 trips total	Field supervision cost per day from the national TB survey	R13,500 per trip in the national TB survey	18 trips.	ZAR 261,440 US$ 18,746
Equipment	Average equipment cost per hub is the same as that in the pilot. High-speed laptops for data analysis are fixed equipment costs.	Equipment cost per team from the pilot survey. Cost of a mobile van for X-ray machines from the pilot or TB survey from Faith.	R125,000 for high-speed laptops. R201,375 per team on other equipment costs. R12,500 per day for TB mobile van renting**.	7 teams, 150*14 van rental days.	ZAR 34,255,210 US$ 2,446,801
Human resource	No significant change in the staff structure and salary level compared to the pilot.	% LOE and salary and benefit of staff from the pilot survey.	Same as the pilot for each position.	Core project staff and 7 teams of field workers.	ZAR 62,922,379 4,494,456
Supplies	Average total supply cost per hub in a national scaled-up survey is the same as that in a pilot.	Hub-specific total cost of supplies for HIV & TB from the pilot is the same as as the unit cost.	R20,884.6 per hub.	150 hubs.	ZAR 3,383,305 US$ 241,665
Transportation	Travel costs for fieldworkers across clusters and courier cost for lab specimen and non-specimen shipping per cluster stays the same as the pilot.	The pilot survey.	R6,484 per cluster for non-specimen shipping; R45,004 per cluster for specimen shipping. For fieldworker travel, R138,429 per cluster in urban areas. R206,258 per cluster in rural areas.	55 clusters in rural area and 67 clusters in urban area.	ZAR 20,052,507 US$ 2,075,179

Activity	Assumptions due to changes in scope and/or efficiency	Data source	Unit cost	Quantity	Total cost
Buildings	Rental costs per hub in the pilot by rural/urban is representative of that in a national survey.	Building cost from the pilot by rural and urban.	R12,600 per hub in urban area; R27,400 per hub in rural area.	83 hubs in rural areas, 67 hubs in urban areas.	ZAR 3,112,128 US$ 222,295
Communication	Cost of sensitisation, public relations, etc. and airtime were captured under communication, mainly for hub-specific activities.	Communication cost per cluster from the pilot.	R45,500 per cluster.	122 clusters.	ZAR 995,080 US$ 428,220-
Utilities	No significant change in the utility cost per hub between the pilot and national survey.	Utility cost per hub from the pilot.	R44,298 per hub in rural areas, R68,552.9 per hub in urban areas.	83 hubs in rural areas, 67 hubs in urban areas.	ZAR 8,938,361 US$ 637,954
Central laboratory tests	No significant change in the central lab cost per hub between the pilot and national survey	Central laboratory costs by HIV and TB components from the pilot	Unit cost for HIV tests in the pilot (except the antiretroviral (ARV) availability) is: R4,032.7 Unit cost for TB culture and Gene Xpert combined is: R2,343.9	11451 of HIV tests for HV 6000 Gene Xpert tests and TB culture and based on ¼ of CXR and symptom screening	ZAR 65,061,196 US$ 4,647,228
Other	No significant change in the other cost per cluster (including prints, waste removal, mobile van rental for respondents and staff transportation, and diesel for generators) between the pilot and national survey. The rural hub would consume 70% of the cost for waste removal and mobile van rental.	'Other miscellaneous' cost per month from the pilot.	R31,066 per cluster in rural area, R17,466 per cluster in urban area.	55 clusters in rural area and 67 clusters in urban area.	ZAR 3,109,160 US$ 222083
Total					**ZAR 236,667,680 US$ 16,904,834**

**Venue cost included rental space, equipment, supplies, and conference meals.*
***The 12,500 per day for the x-ray mobile van renting was from the TB/HIV pilot. It's a loaded rate, including both equipment and staff costs for x-ray reading and results reporting.*
Central laboratory costs are not included in the HR cost projection.

CHAPTER 5

Lessons learned

5.1 Feasibility and uptake of survey

This joint TB-HIV pilot survey was successfully implemented in two geo-types (urban and rural) in KwaZulu-Natal, South Africa. The survey successfully combined TB and HIV components, including the collection of venous blood samples for HIV testing – an approach that has not yet been implemented in the series of national HIV surveys previously undertaken in South Africa. Qualitative and cost data were also formally collected for the first time since such information is typically not included in standard population-based TB and HIV surveillance surveys.

Funding

The funding model for this study included a restriction until a protocol was finalised and approved which had an impact on contracting and acquisition of particular services for third party providers and partners. Specifically, the laboratory partners could not be formally engaged before the lifting of restrictions, and the tablets that were to be used for data collection could not be acquired. This situation impacted survey readiness by limiting the timeframe that was available for Supply Chain Management processes and the time to conduct some of the preparatory work, such as programming and testing of data collection instruments. Thereafter, some of the funding for the fieldwork had to be utilised within a relatively short timeframe.

Response rate

Engaging with a range of local stakeholders in the cluster, including managers of the primary healthcare clinics in the area was beneficial to the survey. It created access for buy-in by the majority of the community members, helped manage any community-level concerns, and facilitated tracing of respondents who were diagnosed with TB and needed to be linked to treatment.

The household-level response rate achieved – ~99% overall, and in each cluster – was high and is higher than in the most recent national HIV and TPS completed in South Africa.[4] This could be because all households in the selected clusters were included as well as the interest in the additional general health tests and measurements were offered to respondents (not related to TB and HIV).

While the compensation for time taken was not intended to be an incentive, participation was supported by offering various items in kind. Puzzles and games for children were appreciated in the urban setting, whereas items more relevant to the household were preferred in the rural setting – for example, washing powder.

Although almost all eligible people accepted an invitation to the hub, in the end, less than half attended the hub and were enrolled. This could be because some invitations were accepted by proxy but could also be because people may not have been keen to travel to and spend time at the hub despite transport being provided. It was also noted that some of those who presented at the hub reported that they had travelled long distances and distance may have affected turnout. In addition, the fact that for some respondents, it took

4 Personal communication, HSRC

a considerably long time for some respondents to complete all hub activities could have discouraged others from attending. The average overall participation in the TPS was 66.1%[20].

HIV surveys select a sample of households in a SAL, and in both standard TB and HIV surveys, tests and investigations that are not directly related to TB or HIV are not included.[2,8,9,14] Uptake of HIV RT was relatively high, with nearly 68% of those who enrolled accepting HIV RT. This is higher than the uptake of RT in KwaZulu Natal province in SABSSMV, which was 36.6%.[3] More than 60% of those enrolled also gave a venous blood sample suggesting moderate levels of acceptability of venous blood draws for population-based HIV surveillance in the South African context.

Activities at the hub

The organisation of activities at the hub were intended to ensure time efficiency. The survey was arranged in such a way that informed consent for all procedures was the first activity after the group information session. This was immediately followed by the administration of the individual questionnaire – a key activity for TB screening as the part determining eligibility for sputum examination. This approach, unfortunately, contributed to bottlenecks as the questionnaire was overly long and time-consuming to implement. The delays at this station cascaded and created further bottlenecks at the field laboratory station. This, in turn, contributed to the delayed completion of the field laboratory processes and the late closure of the hub.

Although staff had been trained on gathering HIV-TB data simultaneously, previous experience in one or the other sometimes impeded following the procedures as required. They were also not aware of the pre-survey work (pre-visits, and communication) that had been done by the central team, as reflected in some of the inputs from the qualitative interviews. This impacted their understanding of and approach to some of the survey processes and challenges they faced. This was partly attributable to the truncated training process. However, experience built up and workflow improved as the fieldwork continued.

The pilot successfully collected and conducted the initial processing of venous blood at the mini-laboratory at the hub. This required several adequately qualified and trained staff and some specialised equipment (centrifuge, pipettes in the field). In this survey, one centrifuge of 36 tube capacity was available as well as two technical staff. However, to successfully complete all processes there was a need to avail more laboratory trained people to the hub.

There was a high uptake of TB screening. All those who were eligible for CXR consented to chest radiography and all those eligible for sputum sample examination gave a sputum sample. There also was high uptake of point of care tests and of the weight, height and blood pressure measurements – higher than uptake for all other screening and testing procedures. The high uptake of screening and testing can be partially attributed to community buy-in to the survey, as well as to how the survey was implemented. The survey with nurses and an MO, and availability of health screening tests and measurements could have given the impression of a clinical service being provided rather than a surveillance research project underway (as was also suggested in the qualitative data) and could partly explain the high uptake of screening and testing at the hub. Limited access to healthcare services in the rural clusters also likely contributed to the high uptake of testing where participation and testing were higher.

Processing of blood samples in the field laboratory at the hub was undertaken and completed successfully. The samples were then successfully couriered to the central laboratories, and all were received in viable format and were then successfully tested. The sputum samples were also handled appropriately, and none were rejected for testing. Only one respondent was unable to provide a second sputum sample suggesting that there was good coaching and follow up of patients for sputum samples. Given that such community-based surveys detect presumptive TB in people in the community (some of whom are asymptomatic but screen CXR positive in high HIV prevalence settings such as in KwaZulu Natal), it is not uncommon for such individuals to be unable to produce a sputum sample. For example, in the TPS 17.1% and 14.6% of sputum eligible respondents did not have a valid Xpert Ultra and culture result respectively.

5.2 Data collection system and quality of the data

One of the objectives of this pilot survey was to determine the quality of the data collected. Excluding the CASI aspect (see below), the quality of the data was generally comparable to that from SABSSMV and the TPS, with respect to missing and inaccurate data. The biomarker data were also largely complete, with only a small proportion of missing elements, and it was possible to link almost all the biomarker and questionnaire data.

However, several challenges were noted. Firstly, the CASI aspect was largely unsuccessful. This was due to the type of tablets used for data collection, which were small, the font size could not be adjusted, and there was no audio option. In addition, many of the mainly older respondents who were selected for CASI were not keen to use it because of limited experience with technology and difficulty reading the small text. Consequently, this data was of poor quality with many missing variables, and it could, therefore, not be used to assess the impact of CASI on collecting sensitive information. There was also limited time to test this aspect as was the case for all other data related components, including the programming and testing of all the other questionnaires and data entry forms.

Qualitative component

The qualitative component of the study, in particular, the insights from the collaborating laboratory partners highlighted several important issues that are relevant to this present pilot but also to other HIV and TB surveys in general.

It was evident that preparatory activities at the community level were critical for the implementation of the survey. While the communication was targeted and successful, it also drew interest for people outside the boundaries of the targeted clusters, which was problematic. Due to the nature of the survey and the services it provides, it is anticipated that this challenge is unavoidable. However, collaborations with local NGOs providing health-related services such as HIV testing could assist community members who do not meet the inclusion criteria but need health services.

Preparatory activities should be allocated adequate time to allow for sufficient consultation with all stakeholders to address any misunderstandings. This was well implemented by the survey team. Regarding misunderstandings of inclusion criteria – this was not a new experience as there have been similar experiences in prior HIV surveys as well as the TPS, and other surveys. These qualitative observations are generally addressed and not formally reported.

A suggestion to address the long waiting times at the hub from FGDs and KIIs was to increase the number of interviewers, depending on cluster geo-type and demographics – i.e. urban/rural or wealthy/poor – as this had some association with potential levels of enrolment.

The qualitative data showed where the hub operations could be adjusted to maximise enrolment and staff activity. This is included suggestions for a revised design of the survey to move some of the activities from the hub – specifically moving the individual interviews to the household and reserving the hub for screening and testing. This would reduce the time that respondents spend at the hub – especially during peak times.

Blood samples

The blood sample processing on-site was noted as a major activity that contributed to the hub operations stretching late into the night – in particular, when respondents were enrolled later in the day. This raised concerns about the safety of staff who were required to be at the hub beyond daylight hours.

Interviews with some of the laboratory staff highlighted possible obstacles of scaling up a survey of this design nationally. These included considerations regarding the acceptability of venous blood sample collection (although in this survey uptake among those who attended the hub was high), availability of staff for venous blood draws, availability of technicians for hub-based blood sample processing and feasibility of courier requirements. These were highlighted in the backdrop of the design of previous HIV surveys conducted in South Africa which have used DBS samples obtained by finger prick. Notably, many other countries have conducted PHIAs where venous blood is collection is accepted.

Addressing data collection challenges

In considering these challenges, a survey design where the household and individual questionnaires, the spot sputum sample and the HIV RT were offered and completed in the household, with respondents only attending the hub for CXR, venous blood draws and for review by the MO would represent a refinement. This could potentially increase participation, given that although almost all eligible people accepted an invitation to the hub, less than half attended the hub and were enrolled.

There are advantages to obtaining plasma samples for LAg assay, VL and HIVDR testing in comparison to DBS samples. Collaboration with existing laboratories such as those under the National Health Laboratory Service – which has 260 laboratories across South Africa – would enable quite an efficient collection and handling of venous blood samples. This would overcome the need for technical expertise and resources at the hub. Alternatively, temporary satellite laboratories that function independently from the hub (and can operate late with staff working in shifts if needed) to process samples from more than one hub could also be explored. Experiences from PHIAs that have used satellite laboratories can be drawn upon to inform the final decisions about handling blood specimens in the field.

Despite the high household-level response, the overall survey participation rate (enrolment at the hub) among all eligible people was low. Only 47.8% of all eligible individuals enrolled in the survey. In SABSSMV, the testing response rate was 61.1%. Preliminary data from adjacent clusters that were part of the national TB prevalence survey indicate enrolment at 71.0% (77.3% in the rural area and 64.6% in the urban area compared to 54.8% and 38.1% respectively in this pilot survey). This can be attributed to the design of the survey, where people had to leave their homes and attend the hub for enrolment. Furthermore, in keeping with TB survey design, invitations to the hub could be accepted by proxy whereby the head of the household could accept invitations to the hub for eligible members of their household in their absence, without the guarantee that these individuals would attend the hub. This is evident from the number of invitations (1,280) and the number of people who attended the hub and were enrolled (616). The low participation rate could also have been influenced by the time that some respondents spent at the hub, and the distance travelled by those who did not make use of the survey transport system. Some respondents spent up to three hours at the hub (especially during peak times) and could have discouraged others from attending. This issue was also highlighted in the qualitative data with certain bottle-neck areas in the hub being identified, and suggestions to consider a design where individual-level activities are split between the household and the hub to reduce the time spent in the hub.

The duration of the project and time required for household census and hub activities was not always adequate to reach the survey sample due to owing to various dynamics in the field – for example, the terrain of the area in the rural cluster was challenging to negotiate. In both clusters, some people worked outside the cluster, and therefore left their homes early and returned late in the evening, which made it difficult for them to participate in the study. TB surveys, including the TPS, include a flexible schedule that can extend the time in each cluster where this can increase participation. In this pilot, this option was not implemented given time and budget constraints.

Although findings from this pilot survey have limited generalisability, it is notable that there were more HIV positive respondents in the rural cluster than in the urban cluster. This is consistent with higher HIV prevalence in rural and poorer areas in South Africa. Furthermore, more respondents were eligible for sputum examination in the rural cluster, and these were mostly middle-aged – a finding that is consistent with the epidemiology of HIV-related TB in South Africa.

5.3 Cost data discussion

Cost data were retrospectively collected and most costs were jointly invoiced and were not disaggregated by cluster or survey component. However, we worked closely with the administrative and project team to make sure that the weights assigned were reflective of the resources devoted to each component. The nature of the survey also made it difficult to obtain data directly from the field staff to complement administrative records. Ideally, data should have been collected from fieldworkers ensure a more precise calculation of the economic cost. However, it was not feasible to administer the fieldworker cost data instrument during survey activities as it disrupted the multiple activities going on at the hubs. A few of the responses that were obtained were of poor quality and were not included in the analysis. For the economic cost calculation, we also collected these costs were supplemented by personnel responses indicating the actual time HSRC staff spent on the project.

The main cost element in the survey was the staff costs which accounted for close to 50% of the overall survey costs. This was followed by travel and testing costs each accounting for about 15% of the overall cost. The total cost for this pilot survey was ZAR 2.1 million (US$ 287,00), translating to a respondent cost of ZAR 3,409 (US$ 466). The SABSSMV survey conducted in 2017 is estimated to have cost approximately ZAR 127 million (US$ 960,000) which translates to a respondent cost of ZAR 2,000 (US$ 138), lower than that in this survey (personal communication, HSRC). This difference could be attributed to the addition of the TB aspect (the hub), and the inclusion of venous blood samples (together with the setting up of the mini field laboratory) whereas the SABSSMV survey only used DBS samples that were collected at the household.

Projected costs and potential efficiency gains

The TPS is estimated to have cost ZAR 87,231,760 (US$ 6,230,840), translating to a respondent cost of ZAR 2,479 (US$ 177) for the 35,191 respondents enrolled. The projected costs of a hypothetical TB/HIV national survey is ZAR 236.7 million or US$ 16.9 million for a sample of 35,479 respondents, translating to a respondent cost of ZAR 6,671 (US$ 476) which is higher than the respondent cost for the TPS (ZAR 2,479; US$ 177) and SABSSMV (ZAR 2,138; US$ 152). It should be noted that a direct comparison of the respondent costs of SABSSMV, the TPS and the hypothetical TB/HIV national survey is limited by differences in design and testing methodology of the surveys as summarised in Table 15. Firstly, differences in where data collection occurs may drive some of the cost differences. In the TPS and the hypothetical survey data collection occurs in the household (prelisting and then the household questionnaire with the census), and at the hub. In SABSSMV data collection only took place in the household. Another major difference is that where the hub is included there are additional costs for transporting people to and from the hub and for setting up and running the hub including requirements for the provision of water, electricity, tables, chairs, ablution facilities and tents or hire of a building). The TB survey design recommends that participants make the hub, but in both the TPS and the pilot survey it was necessary to provide transport for some of the participants especially in rural areas even though some could easily walk to the hub particularly in the urban cluster. A further additional cost difference and driver for the TPS and the hypothetical survey are reimbursements for participants an element not included in SABSSMV. The hypothetical survey also requires a higher cadre of field staff, including phlebotomists to draw venous blood and staff trained in pre- and post-HIV test counselling, professional nurses for safe sputum sample collection and handling, and a radiographer. These cadres of staff require higher salaries than the staff required in SABSSMV, where formal professional qualifications were not a requirement. The hypothetical survey further includes DBS samples as a backup in addition to venous blood draws and also requires laboratory equipment and materials (pipettes, centrifuge, cryovials etc), for initial processing of blood samples that are required in the field.

Table 15: Comparison of the surveys: Comparison of surveys: TPS, SABSSMV, pilot TB/HIV survey and hypothetical joint TB/HIV national survey

Component	#TPS	##SABSSMV	Pilot TB/HIV survey	Hypothetical joint TB/HIV national survey
Population	**15 years+**	**All ages**	**All ages**	**15 years+**
Data collection site	Household and hub	Household	Household and hub	Household and hub
Transport for participants	Transport for participants to and from the hub	none	Transport for participants to and from the hub	Transport for participants to and from the hub
Participant reimbursement	reimbursement	none	reimbursement	reimbursement
Field staff	Professional nurses Radiographer	Experienced data collectors no professional qualification necessary	Professional nurses Radiographer Radiologist *Phlebotomists Laboratory technicians	Professional nurses Radiographer Radiologist *Phlebotomists Laboratory technicians
Field equipment and material	Mobile digital CXR equipment Sputum sample cups Refrigerator DBS collection materials	DBS collection materials	Mobile digital CXR equipment DBS collection materials Blood sample processing material (pipettes, centrifuge, cryovials) Sputum sample cups Refrigerator Weight scale Height measurement Glucometers and strips	Mobile digital CXR equipment DBS collection materials Blood sample processing material (pipettes, centrifuge, cryovials) Sputum sample cups Refrigerator
Sample processing	Central laboratory	Central laboratory	mini laboratory at the hub and central laboratory	mini laboratory at the hub and central laboratory

Component	#TPS	##SABSSMV	Pilot TB/HIV survey	Hypothetical joint TB/HIV national survey
Population	**15 years+**	**All ages**	**All ages**	**15 years+**
Sample transport	Cold chain requirement and 48-hour delivery for sputum samples Regular transport for DBS samples	Regular transport for DBS samples	Cold chain requirement and 48-hour delivery for sputum samples Cold chain and 8-hour delivery time for plasma samples Regular transport for DBS samples	Cold chain requirement and 48-hour delivery for sputum samples Cold chain and 8-hour delivery time for plasma samples Regular transport for DBS samples
Tests	CXR Optional DBS for HIV serology if screen positive for presumptive TB	Optional HIV rapid test DBS for HIV antibody test If positive viral load test HIV incidence related tests Antiretroviral exposure test HIV drug-resistant tests if viral load ≥1,000	CXR 15years+ HIV rapid test Venous blood draws for HIV serology. If HIV positive additional test; • viral load test • HIV incidence related tests • Antiretroviral exposure test • HIV drug-resistant tests if viral load ≥1,000 18years+; • Random blood sugar and cholesterol • Weight measurement • Weight measurement	

*#TPS-National TB prevalence survey, ## SABSSMV-Fifth South African National HIV prevalence, Incidence, Behaviour and Communication Survey; *Qualified and certified for pre and post HIV test counselling.*

The higher unit cost in the urban cluster can be partially explained by higher participation in the rural cluster. However, it is also likely that costs were higher in the urban cluster because it was the first cluster in which the survey was conducted. In this circumstance, the team were less experienced, less confident, and less efficient at time management. By way of example, most of the IT-related challenges were experienced and addressed in the urban cluster. Anecdotal evidence suggests that survey staff become more experienced and more efficient over time.

The amount of time spent at the hub varied between the respondents and was longest in those who consented to RT and were also eligible for sputum sample examination. Other bottlenecks in the completion of some of the procedures (individual interview and phlebotomy on some occasions) meant that respondents spent an average of 2 hours in the hub, with some spending up to 3 hours.

It is possible that with a refinement of the survey methodology, the per respondent cost could be reduced. Possible areas of cost reduction could include staff costs – the main cost element in this survey – and more widespread use of rapid testing including on-site GeneXpert testing, and on-site HIV RT with only a proportion of HIV positive samples tested at a laboratory for QA purposes since RT is used in clinical settings.

5.4 Strengths and limitations

This is the first study to formally conduct and report on this combination of TB and HIV surveillance measures using a WHO-recommended TPS design, including a qualitative and cost component that incorporates a hypothetical scale up in the South Africa context. We successfully completed all the key TB and HIV surveillance measures adhering to recommended WHO designs[22, 23]. There are, however, some limitations.

Several delays impacted preparation. Firstly, the ethics approval was delayed by the complex nature of the project resulting in numerous questions for the ethics committee members. An in-person meeting with the ethics committee finally resolved these questions. Delays in finalising of funding aspect also impacted some of the preparatory and instrument testing work.

The participation rate at the hub was very low due to the reasons outlined above. However, it is also possible that the period that was allocated for work in each cluster was inadequate. The time that was allocated was based on the experiences from the TPS, and this time was probably inadequate to accomplish both TB and HIV related activities, in particular in the rural cluster where the interest in participation was high. Furthermore, TB surveys, including the TPS, allow for a flexible schedule that can extend the time in each cluster where this can increase participation. In this pilot, this option was not implemented because of time and budget constraints.

The processes at the mini-field laboratory at the hub took a long time to complete. Therefore, when respondents were enrolled late in the day (such as those who have come after work or after other chores, or when there were many respondents at any given time in the hub a bottleneck was created that resulted in the field lab procedures running late into the evening (up until 20h00).

To address this challenge, the staff resorted to enrolling a prescribed number of respondents per day in the rural cluster. This was number was, however, lower than the numbers required to reach the target sample in the period allocated for work in the cluster. While this could have been addressed by working for an extended period in the cluster, budget constraints and staff fatigue were limiting factors. There is a strong possibility that participation, especially in the rural cluster is an underestimate of what could be realised.

Regarding staffing, while the intention had been to employ survey field staff who had implemented the national TB prevalence survey previously (since it had included HIV testing), this was not possible. The final field team comprised of a mix of staff who had worked in national HIV surveys, the national TB prevalence survey and other TB and HIV research studies. Overall, most staff had difficulties integrating requirements for both TB and HIV surveillance. Those most familiar with HIV tended to focus on the HIV aspects, and vice versa for those more familiar with the TB survey followed a similar path with TB components. This caused challenges and misinterpretation of some of the survey requirements and procedures and is also evident in some of the feedback from the qualitative interviews. Future surveys will require more in-depth training of field workers about integrating TB and HIV surveillance measures and requirements.

CHAPTER 6

Conclusions and considerations

This pilot survey was successfully conducted in two clusters in KwaZulu-Natal, with the survey team enrolling respondents of all ages, and completing all the surveillance measures. The uptake of TB and HIV measures by respondents was high, although overall participation was well below desired levels, and this requires further reflection and proactive planning in future surveys.

The quality of the data collected compared favourably to that from the recent HIV survey and the TPS. The cost per respondent was higher for HIV than for TB. The cost per respondent was higher than that in SABSSMV and in the TPS (as expected) given the differences in design and blood samples used for HIV related testing, as well as the combination of surveillance measures.

The results indicate the overall costs are high due to the need to accommodate more complex activities for both HIV and TB during fieldwork, a joint HIV-TB survey offers the benefit of delivering findings simultaneously within a common timeframe.

The following actions are offered for consideration:

6.1 Preparatory processes

Given that the ethical approval process was slowed due to the complexity of the survey and the need to provide more explanatory detail to the REC during the review process**,** in-person presentation by the principal investigators in the review process could facilitate early communication with RECs to pre-emptively respond to any questions and clarifications that are required.

Given that the funding model restricted the use of project funds to prescribed timeframes, thereby impeding engagement of laboratory and third-party partners and services and impacting survey readiness regarding Supply Chain Management processes, including timeous procurement and testing of the CASI devices, open channels of communication during the early phases of the project rollout could proactively address such constraints.

Given that field staff were recruited based on their previous experience in either HIV or TB surveys, and that it became apparent that staff experience did not readily flow towards integrated survey methods and protocols, and that the approach to training was constrained, emphasising training that is conducted over a longer period (more days, more time per day) could adequately focus on the integration of data collection process as well as the overall project including information on the pre-survey work (pre-visits, communication) regarding the context of the fieldwork. More detailed competency tests covering survey specific information and activities including assessments during a mock field exercise session could also be useful in informing the final selection of the field team members.

Given that engaging with a range of local stakeholders in the cluster including managers of the primary healthcare clinics in the area was beneficial to the survey (ensuring buy-in, helping manage tensions, facilitating tracing of TB patients lost to follow-up), community engagement could not only be retained as part of the pre-survey activities but also sustained throughout the fieldwork process.

Given that communication about a survey of this nature is critical for communities, and that in this pilot the communication aspect relied on free publicity (i.e. free interviews on community radio stations and free media placements in community newspapers due to budgetary limitation), a more complete and dedicated communication strategy could better support a scaled-up survey.

6.2 Activities at the hub

Given that the number of days allocated to various activities during fieldwork (household census and hub activities) was not always adequate to reach the survey sample due to owing to various dynamics in the field, more time could be allocated for these activities, including accommodating a flexible depending on the nature of the cluster. For example, in rural areas, the wider geographic spread of households requires more time for access, whereas, in urban areas, hub activities may need to accommodate people who are employed and cannot attend on weekdays. Additional considerations include staff fatigue and providing breaks between cluster activities.

Given that there was a considerable fall-off between acceptance of invitations to the hub and actual attendance and enrolment at the hub (due to acceptance of invitations by proxy, distance to the hub, and concerns with the appropriateness of the venue), hybrid approaches could be evaluated whereby the individual questionnaire, the spot sputum sample and the HIV RT are offered and completed in the household, with respondents only attending the hub for CXR, venous blood draws and MO review, or where all samples (sputum and blood) are completed in the household and the respondents attend the hub for CXR and MO review only.

Given that bottlenecks emerged due to the lengthy questionnaire (which followed the group consent procedure) and was vital for TB screening and determining eligibility for sputum testing, but which also had a knock-on effect on field laboratory processes and late closure of the hub, consent for each procedure could be undertaken at the station where it is done, and that respondents could access the different station in a flexible manner directed by which station are available to attend to respondents. In this way, some respondents could start the hub process at the screening or testing stations, while others start by completing the questionnaire. This could minimise bottlenecks at any point. There is also potential to increase the number of staff at each station beyond what was used in the TPS where only a short TB questionnaire was administered, and no formal HIV questionnaire was administered.

Given that the field mini-laboratory allowed for the successful processing of venous blood but was human and material-resource intensive in that several adequately qualified and trained staff and some specialised equipment (centrifuge, pipettes in the field) were required, existing laboratories such as those under the National Health Laboratory Service could be considered to provide support. Alternatively, the use of temporary satellite laboratories that function independently from the hub (and can operate late with staff working in shifts if needed) could also be explored. Experiences from PHIAs surveys could also be reviewed to inform the final decisions about handling blood specimens in the field.

Given that reimbursement of respondents included a range of options (interest in which varied by cluster) the range of choices could be retained but nuanced to the likely needs of the cluster. Given that the financial records and invoicing conventions used for the costing analysis were not suited to costing objective that sort to cost the TB and HIV elements separately (due to joint invoicing, lack of cluster disaggregation, data not directly available from field staff) it was necessary to use weights determined by administrative staff and the project team, attention could be given to disaggregation up-front and tracking costs during data collection.

6.3 Additional piloting

Given that fieldwork was conducted in two clusters, and that lessons learned have provided insights into refinements, there is potential to conduct further pilot testing in up to six additional clusters. For example, three rural clusters (e.g. two traditional areas and one farm), and four urban clusters (e.g. two informal settlements, a formal township, and residential flats). This could provide additional insights for a scaled-up survey including potential efficiency gains on human resources and other resources.

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Survey field staff and community volunteers

A1a: Survey field staff

No	Name	Main Role
1	Ms Tsatsawani Mkhombo	Team Leader
2	Dr Mmatsie Manentsa	Medical Officer
3	Ms Patience Gugulethu Sithole	Professional Nurse
4	Ms Nondumiso Perseverance Hlongwa	Assistant Nurse
5	Ms Thokozile Xulu	Assistant Nurse
6	Mr Musawenkosi Mkhize	Interviewer
7	Ms Delisha Naidoo	Interviewer
8	Ms Nisha Delall	Interviewer
9	Ms Ester Nkosi	Interviewer
10	Ms Nomcebo Meyiwa	Interviewer
11	Mr Simphiwe Phetha	Interviewer at reception station (Receptionist)
12	Ms Omaar Moshia	IT Technician
13	Mr Mnqobi Ndlela	Data Checker
14	Mr Derrick Biyela	Driver
15	Ms Sihle Gama	Phlebotomist
16	Ms Thobile Mthethwa	Phlebotomist

A1b: Community volunteers

No	Urban cluster	Rural cluster
1	Shara Govender	Nokulunga Chiliza
2	Charmane Govender	Thabisile Khwela
3	Tessa Pillay	Nongcebo Hlongwane
4	Aakira Maharaj	Nokukhanya Ngcobo
5	Damain Govender	Jackson Ngcobo
6	Melisha Pillay	Philani Bhengu
7	Flori Joseph	Phililе Mbelu
8	Arnold Perumal	Lucky Ngcobo

Training sessions

Session	Field team member
Use of tablet computers and entry of data into REDCap	All
Interview skills	All
Survey introduction and overview	All
Household interview and census	All
Reception at the hub	Receptionist/ Field data checker and IT technician
Group information session	Nurses and interviewers
Administering the individual screening questionnaire	Interviewers
Field CXR reading	MO
Glucose, cholesterol testing and BP, Height and weight measurements.	Nurses and phlebotomists
Blood collection, processing and storage and rapid HIV testing	Phlebotomists and nurses
Sputum collection, handling and storage on-site, preparation for the courier, completion of sample log sheets	Nurses
Data flow in the cluster and at the hub	Field IT technician
QA, field management and leadership	Team leader and MO

Survey communication pamphlet and Poster

The South Africa TB /HIV Prevalence Pilot Survey 2019
Needs Your Participation

Greetings resident of Marburg

Next week the Human Sciences Research Council will conduct a joint TB and HIV pilot survey in this area.

This survey is not only for this area; two areas selected within this province has been selected to participate in the survey. The survey aims to reach a total of 1,600 people in Kwazulu-Natal.

Field workers will visit specific homes to invite members of households within the selected areas, to participate in the survey. They will also provide more information about the exact venue, date and times that the survey will be in your area.

This pilot survey is very important to South Africa, as it will give an indication if HSRC and its partners can implement a larger survey in order to support efforts to find the best methods to fight TB and HIV. You are requested to welcome field workers, identified by their branded bibs and name tags, into your homes, and to support them in this process.

Join the TB prevalence survey in your area and take part in interviews. Only when we know, will we be able to end TB in South Africa.

South Africa **MUST** end **TB** and **HIV**
#itsinourhands **#**endTB **#**endHIV **#** ourSouthAfrica

Knowledge through research = Action

For further information call:

Team Leader:	Ms Tsatsi Mkhombo:	081 848 9985
Project Directors:	Mr Shandir Ramlagan:	082 355 2379
	Mr Sean Jooste:	079 624 1064
	Dr Olanrewaju Oladimeji:	062 258 3986
Project PI:	Dr Sizulu Moyo:	smoyo@hsrc.ac.za

HSRC Human Sciences Research Council

50/90 Years of humanities and social sciences

The South Africa TB /HIV Prevalence Pilot Survey 2019
Needs Your Participation

Greetings resident of The Ridge

Next week the Human Sciences Research Council will conduct a joint TB and HIV pilot survey in this area.

This survey is not only for this area; two areas selected within this province has been selected to participate in the survey. The survey aims to reach a total of 1,600 people in Kwazulu-Natal.

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HSRC Human Sciences Research Council

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Sequence at the hub

Day	Activity
Day 1	Household Census Listing, interviews and invitations- started
Day 2	Household Census Listing, interviews and invitations continues - completed
Day 3	Set up of survey hub and screening commences: Interviews, CXR, whole blood and sputum collection, point of care for Blood Pressure, Cholesterol and Glucose testing and data downloading
Day 4	Screening continued: Interviews, CXR, whole blood and sputum collection, point of care for Blood Pressure, Cholesterol and Glucose testing and data downloading. Mop up begins
Day 5-8	Screening continued: Interviews, CXR, whole blood and sputum collection, point of care for Blood Pressure, Cholesterol and Glucose testing and data downloading. Mop up continued
Day 9	Screening wrapped up: Census, Interview, CXR, DBS & sputum and closure of cluster operations. FGDs conducted by HSRC staff with the field staff

Survey invitation slip

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

HSRC
Human Sciences
Research Council

CENSUS ID

Principal Investigator: Dr Sizulu Moyo (Human Sciences Research Council)
Funding source: The US President's Emergency Plan for AIDS Relief (PEPFAR)
through the US Centers for Disease Control and Prevention (CDC)
(Cooperative Agreement #GH001629),

Joint Tuberculosis and HIV Pilot Survey

Good Day! The Human Sciences Research Council (HSRC) in collaboration with other research organisations is conducting a Joint Tuberculosis (TB) and HIV Pilot Survey, also called the combined TB/HIV pilot survey. The main purpose of this study is to find out if it is possible to do a joint (combined) TB and HIV survey in South Africa. You are being invited to take part in the survey activities that will be conducted at the survey hub that is located at ……(place) from ……(day)/……(month)/2019.You are invited because you agreed that you slept in this home for 5 nights of the last two weeks. At the hub you will be asked questions about your health including questions about HIV and TB. We will measure your weight how heavy you are), your height (how tall you are), your blood pressure (BP) blood glucose (amount of sugar in the blood), and cholesterol (amount of fat in the blood) if you are 18 years and older. This will provide opportunity for you to know about some aspects of your health. You will also be asked to give a blood sample for an HIV test, and other HIV related tests that are viral load (the amount of the HIV in the blood), recency of HIV infection (to see if infection with HIV happened recently), and resistance to antiretroviral drugs (ARVs) (whether the HIV drugs work well against the HIV). You will also be asked to take a chest X-ray, and if necessary, to give a sputum sample (phlegm) to be tested for TB. A chest X-ray and sputum sample will be taken from those who are 15 years and older. If your children are taking part, we will ask you questions about their health, if they are younger than 12 years. Those who are 12 years and older will be asked to answer questions on their own. We will also collect blood from the children for HIV testing if they agree. This will provide the opportunity to know one's HIV status, including that of children. Children will also be given opportunity to indicate whether they agree to give a blood sample. All the work will be done by specially trained people. Taking part in the study is strictly voluntary. We invite you to visit the hub, where you will be provided with more details about the study. You will receive a small packet of household items or airtime as reimbursement for your time. Children will also a small packet of household items or child friendly items, or airtime as reimbursement for their time spent on the study.

The meeting has been scheduled as follows:

Date: **Venue:** **Time:**

Please keep this slip safely, and bring it when you come to our site. We thank you for your time.

Participant name: | **Age** | **Sex**

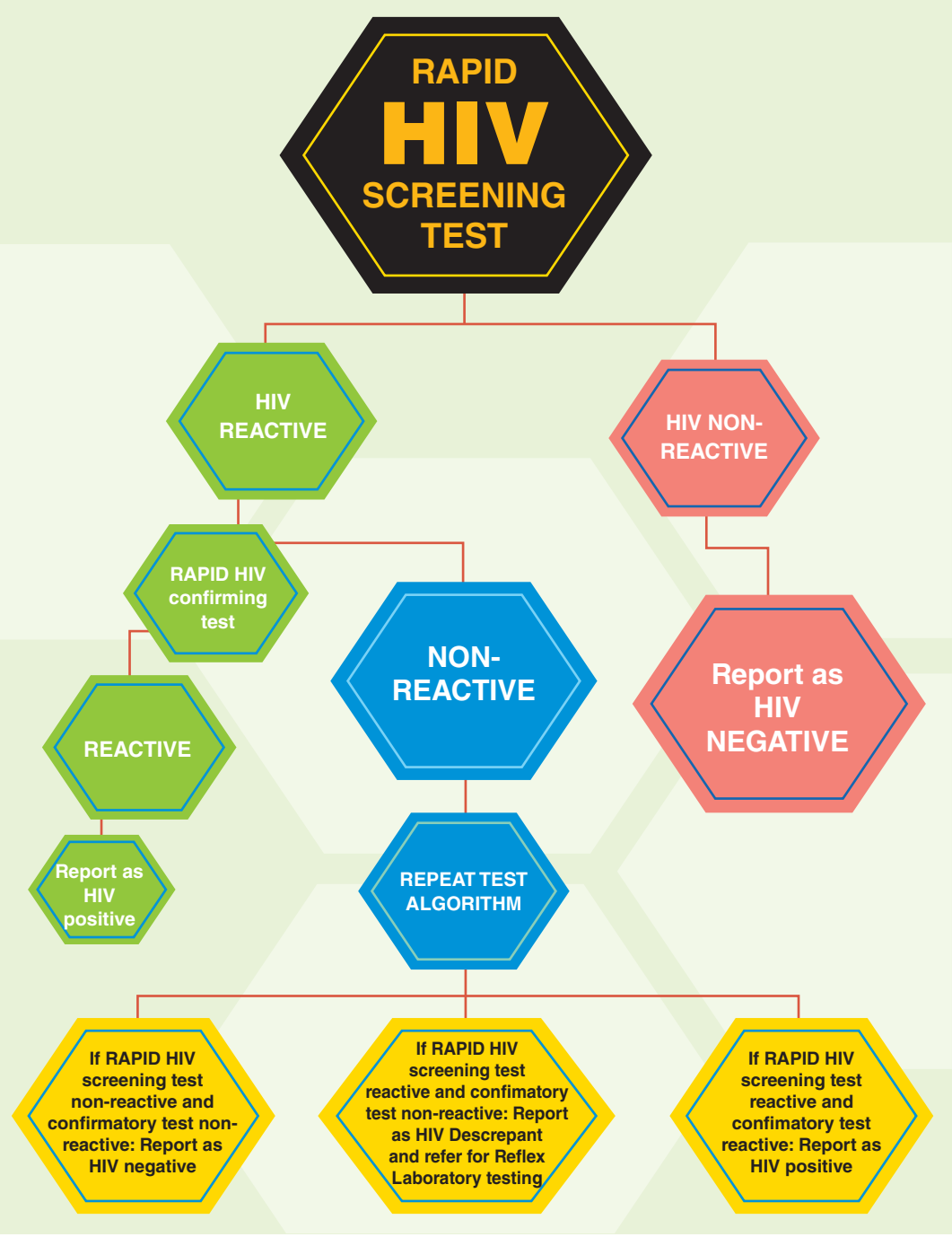
Race | **Child** | **Adult** | **Date** D D M M Y Y Y Y

Participant's address

Date the invitation is given D D M M Y Y Y Y

Field staff member»s name:

South Africa National Department of Health. National HIV testing services policy 2016



Field Measurement and Biomarker Form

Venue: _____

Dates: _____

Time: _____

Participate in the TB and HIV pilot survey

For further information call:

Team Leader:	Ms Tsatsi Mkhombo:	081 848 9985
Project Directors:	Mr Shandir Ramlagan:	082 355 2379
	Mr Sean Jooste:	079 624 1064
	Dr Olanrewaju Oladimeji:	062 258 3986
Project PI:	Dr Sizulu Moyo:	smoyo@hsrc.ac.za

If you are asked to participate, please give your time

Knowledge through research = Action

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Researching minors: Provisions of the Children's Act

The researcher has to comply with the mandatory reporting of child abuse as regulated in the Child Care Act (No. 74 of 1983 and the new Children's Act (No. 38 of 2005) as amended. Therefore, no direct questions were asked about child abuse in the survey. Secondly, information about a child's experience of sexual abuse that was given voluntarily by the respondents was to be handled on an individual (case-by-case) basis. The cases were to be dealt with by survey staff in consultation with the supervisors, principal investigators or project directors of the survey.

Field workers who encountered situations of child abuse were to inform the Project Directors who were to contact the appropriate service providers, such as social work offices and Child Protection Units in the respective areas. A copy of the referral form which included the following details the date of referral, age of the child, type of referral, and the referral agency was to be completed and submitted to the agency, and a copy was to be retained by the survey.

Minors aged 12-18 years

A minor decided whether to participate and assented (expressed their will) after parental or legal-guardian consent had been given. The parent or legal guardian assisted the minor to make an informed choice and either give their permission or not. Parental permission and minor's decision had to be consistent. Thus, if the minor decided not to participate, the parent could not override this decision.

If no parent was present, a legal guardian was substituted, either court-appointed or as indicated by the parent in a will (in accordance with Section 27 of the Children's Act). If there was no guardian, a foster parent by order of the Children's Court could be a substitute. If there was no foster parent, a caregiver could act in the capacity. In line with the Children's Act, a caregiver was defined as follows:

Any person other than a parent or guardian, who factually cares for a child and includes – a) a foster parent; b) a person who cares for the child with the implied or express consent of a parent or guardian of the child; c) a person who cares for the child whilst the child is in temporary safe care; d) the person at the head of a child and youth care centre where a child has been placed; e) the person at the head of a shelter; f) a child and youth care worker who cares for a child who is without appropriate family care in the community, and; g) the child at the head of a child-headed household.

If a minor (a child of 16 years and younger in a recognised 'child-headed household') was the caregiver, then a 'responsible person' – in line with Section 137 of the Children's Act – assisted them. The responsible person could have been appointed by the Children's Court, a government body or an NGO. If a minor was the caregiver and there was no supervisory adult, a trusted adult could be nominated by the minor, including but not limited to a social worker, community worker or teacher. Where it was found that a minor caregiver was so isolated that no responsible adult was available, the minor was not recruited into the survey and was regarded as a vulnerable child. Appropriate interventions were then to be initiated, outside of the research context, to support that child. However, no such cases were identified in the current survey.

Minors younger than 12 years

For minors younger than 12 years, permission was sought from the parent or substitute, as outlined above, as independent consent by such young minors is not generally permissible. The minor was asked to decide whether to participate, and permission from the parent could not override the child's decision.

To ensure the research was conducted according to the highest ethical standards, the following additional measures were implemented. Each section of the questionnaire included a short introduction, indicating what was covered in the section, explaining why the questions were asked, and assuring respondents about the confidentiality of their responses. The fieldworkers were trained in research ethics and in applying the ethical guidelines during their activities. Specific training was also given on how to manage children and any crises that could occur in the field. The team leader and the central survey team monitored the work to ensure compliance with all ethical provisions.

Modules by age group included in the individual questionnaire for joint TB-HIV pilot, 2019

Questionnaire module	Children aged 0 to 11 years (reported by parent/ guardian)	Children aged 12 to 14 years (self-reported)	Youth & Adults aged 15 years and older (self-reported)
Demographics: Age, sex, race, nationality, employment, marital status, the importance of religion.) Income, education, number of children, disability, migration	×	×	×
Orphan status: Parental survivorship (under 20 years) Age of child at death of a parent	×	×	× (under 20 years only)
Education: School attendance Reasons for missing school Educational attainment Safety at school	×	×	× × × × × (under 19 years only)
Knowledge, attitudes, beliefs and values about HIV and AIDS and about HIV-related practices and behaviours (KABP) & Tuberculosis (TB)		×	×
Sexual history: Sexual debut Partner history Sexual orientation and identity Transactional sex Concurrency Age mixing Condom use Use of other contraceptives		×	×
Sexually Transmitted Infections: Current and previous symptoms			×
Delivery and care details: Current pregnancy ANC services Breastfeeding, formula feeding, pre-mastication	× (for respondents under 2 years)		×

Questionnaire module	Children aged 0 – 11 years (reported by parent/ guardian)	Children aged 12 – 14 years (self-reported)	Youth & Adults aged 15 years and older (self-reported)
Contraception: Knowledge Ever and current use	(Only condom use)	×	×
Male circumcision: Circumcision status Age and place of circumcision Reasons Complications Knowledge	×	×	×
HIV testing and risk perception: Testing history Source & testing reason Antiretroviral treatment Risk perception	× (for respondents under two years)	×	×
Drug and alcohol use: Use & impact	× (five to 11years; exposure to use within the household)	× (including exposure to use within the household)	×
Health status: Perception of general health Hospitalisation	×	×	×
Violence in relationships: Occurrence of intimate partner violence (IPV)			×
Tuberculosis history: Current treatment Previous treatment			×
TB symptom screening: Cough (persistent cough for ≥2 weeks or more or cough of any duration if HIV positive). Unexplained fever for ≥2 weeks Drenching night sweats Unexplained weight loss (more than 1.5 kg in a month)			×

Key informant interviews and focus group discussion guide

1. **Tell me about the nature of your involvement in the study?**
   Probes: What was your role? Did the roles fit with your skills?

2. **Please share with me some of the highlights from the project?**
   Probes: What did the study do well?
   (Explore this question for the different aspects of the study training, entry, recruitment of respondents, processes at the hub, implementation and data collection, testing HIV and TB, transportation of samples, communication and study mobilisation, lab aspects).

3. **Please share with us some of the challenges you experienced during the implementation of the project, low points or areas that the project could improve?**
   Probe: What did not work well? Which aspects of the study were the most challenging?
   (Explore this question for the different aspects of the study training, entry, recruitment of respondents, processes at the hub, implementation and data collection, testing HIV and TB; transportation of samples, communication and study mobilisation, lab aspects)

4. **Looking back at the project, tell me what were the gaps that you identified?**
   Probes: What gaps did you come across?
   (Explore this question for the different aspects of the study training, entry, recruitment of respondents, processes at the hub, implementation and data collection, testing HIV and TB; transportation of samples, communication and study mobilization, lab aspects)

5. **Looking at the challenges and gaps you have mentioned to me, can you now tell me what needs to be improved or done better if we were to implement this project again?**
   Probes: What lessons did you learn? – focus more on the solutions and future surveys for this question - if already covered under question 3, this question can be left out)
   (Explore this question for the different aspects of the study training, entry, recruitment of respondents, processes at the hub, implementation and data collection, testing HIV and TB; transportation of samples, communication and study mobilization, lab aspects)

Weights used in financial cost analysis, Joint TB/HIV Pilot Survey, South Africa, 2019

	Cost elements	Component				Cluster weights (aggregate and component)			
S/No	Category	HIV (%)	TB (%)	M (%)	U (%)	HIV (%) – M	HIV (%) – U	TB (%) – M	TB (%) – U
1	Staff	52	48	50	50	52	52	48	48
2	Utility-Marburg	50	50	100	0	50	0	50	0
3	Utility-uMgayi	50	50	0	100	0	50	0	50
4	Supplies	50	50	50	50	50	50	50	50
5	Total testing cost-no CXR	53	47	29	71	53	52	47	48
6	TB test – CXR	0	100	37	63	0	0	100	100
7	Specimen courier cost (by HSRC)	5	95	32	68	5	5	95	95
8	Non-specimen courier cost	50	50	50	50	50	50	50	50
9	Travel (Operational Team)	50	50	50	50	50	50	50	50
10	Travel Marburg	50	50	100	0	50	0	50	0
11	Travel uMgayi	50	50	0	100	0	50	0	50
12	Training & Reimbursements	50	50	42	58	50	50	50	50
13	Other miscellaneous	50	50	50	50	50	50	50	50
	Grand Total	**47**	**53**	**44**	**56**				

Note: M = Marburg; U = uMgayi

Weights used in economic analysis, Joint TB/HIV Pilot Survey, South Africa, 2019

	Cost elements	Component				Cluster weights (aggregate and component)			
S/No	Category	HIV (%)	TB (%)	M (%)	U (%)	HIV (%) – M	HIV (%) – U	TB (%) – M	TB (%) – U
1	Staff	52	48	50	50	52	52	48	48
2	Utility-Marburg	50	50	100	0	50	0	50	0
3	Utility-uMgayi	50	50	0	100	0	50	0	50
4	Supplies	50	50	50	50	50	50	50	50
5	Total testing cost-no CXR	53	47	29	71	53	52	47	48
6	TB test – CXR	0	100	37	63	0	0	100	100
7	Specimen courier cost (by HSRC)	5	95	32	68	5	5	95	95
8	Non-specimen courier cost	50	50	50	50	50	50	50	50
9	Travel (Operational Team)	50	50	50	50	50	50	50	50
10	Travel Marburg	50	50	100	0	50	0	50	0
11	Travel uMgayi	50	50	0	100	0	50	0	50
12	Training & Reimbursements	50	50	42	58	50	50	50	50
13	Other miscellaneous	50	50	50	50	50	50	50	50
14	Building-Marburg	50	50	100	0	50	0	50	0
15	Building-uMgayi	50	50	0	100	0	50	0	50
16	Equipment	50	50	50	50	50	50	50	50
17	Communication	50	50	50	50	50	50	50	50
	Grand Total	**48**	**52**	**45**	**55**				

Note: M = Marburg; U = uMgayi

Design considerations for a hypothetically scaled-up, national joint HIV-TB survey

Rationale and opportunities

The main rationale for a joint HIV-TB survey is to generate superior information and to obtain improved cost and other efficiencies. A successful joint survey will inform both disease domains and ideally allow for the examination of TB as HIV's most important co-morbidity and vice versa. Furthermore, TB prevalence surveys often have per respondent cost of $100 or less, whereas PHIA – the current standard for national HIV household surveys – have cost several times higher. A joint survey ideally would lead to cost savings compared to PHIA alone and certainly have lower costs than separate TB and HIV surveys.

Challenges and possible solutions

There are, however, formidable challenges to a joint survey design:

Number of survey clusters: The primary objective of a TB survey is the estimation of national TB prevalence, whereas a PHIA's primary objective is to estimate subnational VL suppression. For this reason, TB surveys require far fewer survey clusters (often close to 50) than PHIA (often close to 500). For a truly joint survey design and to satisfy both survey domains primary objectives, the number of clusters would need to be closer to that required for subnational HIV VLS, while still collecting data via a central cluster location. That implies more effort than for a typical TB prevalence design, though perhaps less effort than for a typical HIV household survey design. Alternatively, a hybrid approach to sampling design may aim to satisfy both disease domains with large but incomplete overlaps in clusters and/or households.

Examination of TB/HIV co-infection: Assumptions around HIV and TB prevalence suggest that a joint survey with a sample size resembling that of a typical TB prevalence survey would likely yield well below 100 respondents with HIV/TB co-infection. One such hypothetical sample design, involving 6,000 respondents who are both tested for TB and HIV, yielded only 20 respondents with TB/HIV co-infection. Such small numbers, reminiscent of the observed numbers of PHIA respondents with recent HIV infection, are likely to impede in-depth analysis of TB/HIV co-infection and making analysis of co-morbidities less possible. However, the larger total sample sizes would still facilitate separate in-depth analyses of HIV and TB.

Age bands: The 1st generation PHIA also sampled children under 15 years of age, whereas the TB prevalence survey focuses on 15+ year-olds only. Meanwhile, 2nd generation PHIA generally dropped paediatric sampling as well, so that this may no longer be a constraint in a joint survey design.

Survey uptake: TB prevalence surveys generally have lower participation rates compared to PHIA or other surveys where data collection occurs within the household – possibly

due to the active effort that is required to reach the survey hub. Efforts would need to be made to attract enough candidate respondents to the cluster's survey hub. In this survey pilot, respondents were compensated for participation. Additional benefits attracting participation did or could include measurements of random glucose, HbA1C, total cholesterol, blood pressure, weight, or blood group determination. Such benefits would need to be identified in particular with younger and male potential respondents in mind, both of which traditionally are more reluctant to participate in surveys compared to older or female populations.

Interview duration and question understanding: The TB survey questionnaire is generally shorter than that used in HIV surveys such as PHIA and the interview duration in this joint pilot was cited by some as too long. A hypothetical joint survey would need to control total interview length carefully, and the PHIA questionnaire, in particular, would need to be trimmed to metrics essential for weighted data analysis and satisfying programming and monitoring requirements. Similarly, the piloted self-administered data collection mode (CASI) was a challenge to complete for some respondents, particular the older ones. The investigators note that unfortunately, the questionnaire structure was not sufficiently prepared for a CASI environment (No. reply options, open text fields, phrasing that was not always clear in self-administered mode), but could easily be done so in a joint survey.

Combining investigations of TB and HIV into a single cross-sectional population-based household survey provides possibilities for better understanding these interrelated epidemics but with several methodological challenges. The following text and accompanying spreadsheet are an attempt at drafting a sample design to meet objectives of both TB and HIV survey, while also obtaining an overlapping sample of individuals for the analysis of co-morbidities. The design is developed for South Africa given the availability of existing relatively recent inputs on both HIV and TB.

Geographies and Sample Design Objectives

Given the difference in prevalence, 0.33% for TB and 20.6% for HIV (and, possibly, more importantly, clustering effects) different geographies are needed. The typical geography used in most health surveys is the enumeration area or EA. At the time of definition, most statistical offices define EAs by an area covering 80-120 households, with a target of 100 households (typically redefined at the time of the census). EAs are too small for TB surveys where a minimum of 400 adults are needed, per site. An appropriate geographic unit for TB prevalence surveys for South Africa is the 'small area layer' or SAL, which combines EAs with a population of less than 500 with adjacent EAs within the same sub-place. In the case of a TB survey, a minimum of 184 households (2.72 adults 15 years and older), would be needed for a cluster 'take' of 500 adults. A two-stage approach would be appropriate, beginning with the selection of SALs followed by a selection of households and taking all eligible individuals. For a PHIA, a three-stage approach might be taken, starting with SALs, followed by EAs, and then households, and taking all eligible individuals in the household. Alternatively, the 2nd stage sample for a PHIA component could select from all the households selected for a TB survey as the 'take' per cluster for a PHIA are much smaller (related to design effects). Currently, an average of 35 households is selected from each EA for PHIA surveys. Taking a larger number of households per cluster increases the design effects, significantly depending on the phenomenon of interest. A sample for a PHIA component would require a subset of households (70 proposed here) per cluster, and a larger number of clusters.

Design Objectives (Sample Allocation and Design Effects)

1. PHIA: VLS at Provincial level with 95%CI of +/- 10%
2. PHIA: National Incidence RSE (relative standard error) of 30% or less
3. TB: National Prevalence with RSE of 12.5% or less (a 'relative precision' 'd' of 0.25)

The PHIA surveys have both national (HIV incidence) and sub-national (VLS) objectives. During the 1st round of PHIAs national incidence estimates requirements, given our understanding of the importance of proportion false-recency in lab analysis, played a greater role in sample design decisions. In the second round of the PHIAs, with inputs derived from PHIAv1 survey analysis and new assumptions, the role of VLS at the subnational level gained overall importance in sampling design and allocation. When national-level indicators are of central interest (as with TB), proportional (to population) designs are typically best, in that they keep design effects (DEFFs) lower; where subnational estimates are of interest, an equal-size (equal allocation between SNUs) are typically best but result in, at times, much larger design effects for national-level indicators. The impact on design effects for national-level indicators is dependent on the heterogeneity of the HIV epidemic that informs sample allocation by provinces. The allocation of the sample in PHIA surveys tend toward a non-proportional, more equal-size design, reflecting the heterogeneity of the epidemic (e.g., Mozambique versus eSwatini).

Given the competing demands associated with TB and PHIA surveys a combined sample strategy, with different geographies and 'takes', would need to be employed where only a portion of overlap would be possible (likely between 25%-40%, and dependent on the average size of SALs and number of TB Labs available and TB-PHIA clusters that could be visited).

In the proposed design a total of 122 SAL would be needed, 64 SALs for a TB-PHIA component and an additional 58 SAL-EAs (using a 3 stage sampling strategy: SAL-> EA -> HHs) exclusively for the PHIA component. In the 64 SALs selected for TB-PHIA components, 280 DUs/HHs would be selected with approximately 760 eligible adults. Following a complete household listing (needed for evaluation of changes in the probability of selections and calculation of weights), DUs/HHs for TB-component would be selected followed by a selection of 70 DUs/HHs for the PHIA component (from among the 280). All eligible adults from the 280 DUs/HHs would be eligible for the TB component, but only eligible adults from the 70 DUs/HHs would be eligible for both TB and PHIA components. As noted above, 58 SAL-EAs of the 122 SAL would be drawn (disproportionally by strata to meet sampling objectives) for only the PHIA component of the survey.

Inputs

Inputs for the sample design are primarily from the The South African National HIV prevalence, Incidence, Behaviour and Communication Survey (SABSSM) 2017 (response rates, adults per household, provincial HIV prevalence, national HIV incidence) and, for TB design inputs, from the National TB Prevalence Survey draft report sampling design discussion and appendix) and TB prevalence estimates based on 2013 case notification surveillance (in same draft report). The sample size calculations utilise the following assumptions:

Prevalence

- TB prevalence: 333/100,000 or 0.333%
- HIV prevalence: 20.5% (ranging from 12.6% in Western Cape to 27.0% in KwaZulu-Natal)
- HIV incidence: 0.79%

VLS among HIV-infected: 0.5 or 50% (a 'conservative' estimate approach for targets)

Clustering Effects

- Intraclass correlation coefficient (ICC) of 0.05 for VLS
- Intraclass correlation coefficient (ICC) of 0.000835 for TB prevalence
- Intraclass correlation coefficient (ICC) of 0.0 for HIV incidence

Specific to HIV recency testing

- Proportion false recent (PFR) = 0.000001%
- An adjustment factor 1.016 to account for MDRI and PFR is included for national HIV incidence estimation and associated variance calculations.

Households per cluster and response rates

- The average number of selected dwelling units per cluster= 280 for TB PSUs and 70 for PHIA only PSUs, which should yield an average of approximately 217 and 54 responding households per cluster, respectively (based on 77.7% overall household response [94.8% occupancy rate X 82.2% household response]).
- The actual number of selected dwelling units per cluster will reflect changes in the measure of size between the sampling frame and HH listing.
- The average number of de facto household members of 3.88 and adults 15 years and older of 2.72, which is based on the SABSSM 2012 (similar values found in SABSSM 2017).
- A testing rate of 63.6% among adult respondents (based on interview response of 92.2% and agreeing to a blood draw of 69.0% among those interviewed), based on SABSSM 2017.

Calculations

In the attached Excel spreadsheet 'Sampling_TB_PHIA_ZAF', response rates based on SABSSM 2017 are presented together with calculations of the number of expected cases from the sample design calculations for the TB, PHIA and overlapping samples (see first tab 'ResponseRates'). In the 2nd tab are the number of 'de facto' household members based on weighted output from SABSSM 2012, used as inputs for the number of adults 15+ expected in responding households. The main sampling design calculations are presenting in the 3rd tab 'TB_PHIA_Design' with all inputs presented in the 1st panel, rows 1 thru 30. In column C, basic inputs from the first two tabs are brought in: response rates in rows 9 thru 13, and household age composition in rows 14-20.

ICCs are a basic input for the PHIA sample calculations, and second round country designs are based on calculations of the 1st round dataset. The ICCs from earlier PHIA surveys for VLS range from 0.015 in Lesotho (LePHIA 2016) to 0.061 in Zambia (ZamPHIA 2015/16). A reasonable conservative 'guesstimate' of 0.05 is used in this design. An ICC for TB prevalence in South Africa was derived from sample design inputs for RSA from the most recent National TB Prevalence Survey (draft report) and use of the 'Lime Book.' Assuming a k value of 0.5, the cluster size of 500 and a prevalence of 333/100,000 indicates a design effect of 1.41. These parameters imply an ICC of around 0.000835. Calculations of the ICC are presented in the 4th tab 'ICC_Calculations' and based on the discussion in Appendix 2 of the report and triangulation of information from the sampling chapter of the Lime Book. ICCs for indicators of interest are presented in columns 21 thru 24.

Information on population distribution are presented in column F (rows 5-27) and for provincial HIV and TB prevalence in columns Q and T. Targets and steps for adjusting calculations are presented in rows 31-38 along with a summary of results for PHIA and TB components (from calculations below in the spreadsheet). Because in PHIA the provincial and national objectives are 'at odds', pulling the allocation of the sample in different directions, PHIA designs have made use of Excel's 'Solver' add-in, to allocate sample to achieve the smallest sample needed, given objectives. The initial calculation for the sample needed in each stratum are approximated in Panel 2 (Rows 60-73), based on sample inputs and a 'take' of 70 DUs/HHs per cluster. The initial calculations indicate the need for 120 PSUs (EAs) for the PHIA component of the survey.

A subset of PSUs is needed for the TB component (but with a larger number of households, involving SALs) and preferably with a proportional-to-population allocation to keep design effects down.

These calculations are covered in the second set of calculations. The results are presented in rows 40-57 for the sample needed for the TB component. (Sub-sampling is based on a fraction of the total number of PSUs for the PHIA component [Col I, Row 36) and redistributed by population by province in Col H, Rows 5-13). The 'fraction' used is changed until TB targets are met ('d', a relative precision of 0.25 or an RSE of 12.8%).

Results

A sample of 122 PSUs will be sufficient to meet TB-PHIA survey objectives of a) provincial VLS estimates with a 95%CI of +/-10%, b) national HIV incidence estimate with an RSE of 30% or less and c) a national TB prevalence with a 0.25 relative precision. Sixty-four (64) PSUs (SALs) with 280 DUs (to be sampled following a household listing), is expected to yield near 14,000 households responding, with around 24,000 adults (15+) agreeing to TB/HIV testing. Based on an initial estimate of TB prevalence of 0.00333 we can anticipate a 95%CI of +/-0.00085 (0.25% to 0.42%), or a relative precision of 0.25, or an RSE of 12.8%.

A subsample of 70 (of 280 DUs) would be selected from these households in these 64 SALs and combined with 70 DUs from each of 58 SAL-EAs sampled for the PHIA-component of the survey. The HIV component of the survey would be carried out in a total of 122 PSUs, with an expected 6,631 responding households and 11,451 persons (15+) agreeing to a blood draw and testing. This sample is expected to capture 1,735 HIV infected individuals 15-49, with at least 150 or more in each province, and should provide an estimate of viral load suppression (VLS) with a 95%CI of +/-10% or less. At a national level, the estimated 95%CI for VLS would be around 0.036 (or 3.6%). Based on these sample calculations, we would expect a national HIV incidence estimate with an RSE of 27% (95% CI of 0.38% to 1.2%).

Approximately 6,000 respondents are expected to be involved in both TB and PHIA components of the survey (¼ of TB-component respondents and ½ of PHIA-component respondents).

For analyses, three sets of weights will need to be developed: TB only, another for PHIA component (only), and a third for analysis of both TB-PHIA.

Conclusions

The different primary objectives for TB and HIV surveys as well as the vastly different prevalence of disease (TB) and outcomes of interest (VLS) demand different sample sizes and suggest widely diverging sample designs. This inherently impedes an efficient joint TB/HIV survey. Nevertheless, the substantial investments necessary to survey each disease domain, the relatedness of these two diseases and the anecdotally much lower TB survey costs continue to call for a common survey design.

Economic costs of the pilot survey

S/No	Category	Total cost	HIV (%)	TB (%)	HIV Total cost	TB Total cost	AC (N=616)	AC-HIV (N=387)	AC-TB (N=424)
1	Personnel	1,943,166.57	52%	48%	1,018,977.59	924,188.98	3,154.49	2,633.02	2,179,69
2	Utility-Marburg	4,298.03	50%	50%	2,149.02	2,149.02	6.98	5.55	5.07
3	Utility-Umgayi	35,552.87	50%	50%	17,776.44	17,776.44	57.72	45.93	41.93
4	Supplies	11,538.47	50%	50%	5,769.24	5,769.24	18.73	14.91	13.61
5	Total testing cost-no CXR	592,524.54	53%	47%	312,519.07	280,005.47	6,376.51	4,032.66	2,343.85
6	TB test_CXR	287,500.00	0%	100%	0.00	287,500.00	678.07	0.00	678.07
7	Specimen courier cost (by HSRC)	90,008.20	5%	95%	4,600	85,408.20	146.12	11.89	201.43
8	Non-specimen courier cost	12,968.41	50%	50%	6484,205	6,484.21	21.05	16.76	15.29
9	Travel PM	602,526.91	50%	50%	301,263.455	30,1263.46	978.13	778.46	710.53
10	Travel Marburg	140,558.05	50%	50%	70,279.025	7,0279.03	228.18	181.60	165.75
11	Travel Umgayi	215,873.59	50%	50%	107,936.795	10,7936.80	350.44	278.91	254.57
12	Training & Reimbursements	78,770.00	50%	50%	393.85	3,9385.00	127.87	101.77	92.89
13	Other miscellaneous	1,511.70	50%	50%	755.85	755.85	2.45	1.95	1.78
	Grand Total	**40,167.97**	**47%**	**53%**	**1,887,896**	**2,1289,013**	**12,147**	**8,103**	**6,704**
	Grand Total (US$)	**286,914**			**134,850**	**152,064**	**868**	**579**	**479**

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