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Study Number: CAPRISA 251

HIV Incidence Provincial Surveillance System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa

PROTOCOL

Version 1.0 5 May 2014

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LIST OF ACRONYMS AND ABBREVIATIONS

AE	Adverse Event
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
BREC	Biomedical Research Ethics Committee
CDC	Centers for Disease Control and Prevention
CD4 Cell count	Cluster of differentiation four cell count
CI	Confidence Interval
CAPRISA	Centre for the AIDS Programme of Research in South Africa
CRF	Case Report Form
EIA	Enzyme Immuno-Assay
EA	Enumeration Area
EDTA	Ethylenediaminetetraacetic acid
FBO	Faith Based Organisation
FRR	False Recent Rate
GCLP	Good Clinical Laboratory Practices
GIS	Geographic Information Systems
GPS	Global Positioning Systems
KZN	KwaZulu-Natal
HAART	Highly Active Antiretroviral Therapy
HCT	HIV Counselling and Testing
HIPSS	HIV Incidence Provincial Surveillance System
HIV	Human Immunodeficiency Virus
LAg	Limiting Antigen-Avidity
HSV-2	Herpes simplex virus type 2
IRB	Institutional Review Board
MDRI	Mean Duration of Recent Infection
MMC	Medical Male Circumcision
MOP	Manual of Procedures
NGO	Non-governmental organisation
NICD	National Institute for Communicable Diseases
NSP	National Strategic Plan for HIV and AIDS, STIs and TB
pNAAT	Pooled nucleic acid amplification tests
PB	Peripheral blood
PCR	Polymerase chain reaction
PDA	Personal data assistant
NIH	National Institutes of Health
PEP	Post-exposure prophylaxis

PrEP	Pre-exposure prophylaxis
PEPFAR	President's Emergency Plan for AIDS Relief
PMTCT	Prevention of Mother To Child Transmission
QA/QC	Quality Assurance/Quality Control
RCT	Randomized Clinical Trial
RITA	Recent infection testing algorithm (RITA) for HIV
RNA	Ribonucleic acid
SACEMA	The South African Centre for Epidemiological Modelling and Analysis
SAG	South African Government
SOP	Standard Operating Procedure
STI	Sexually transmitted Infection
TB	Tuberculosis
The Global Fund	The Global Fund to Fight AIDS, Tuberculosis and Malaria
USAID	United States Agency for International Development
USG	United States Government
UNAIDS	United Nations Joint Programme on HIV/AIDS
WB	Western Blot
WHO	World Health Organization

1) SCHEMA

Study Number: CAPRISA 251 **HIV Incidence Provincial Surveillance System (HIPSS)** **A longitudinal study to monitor HIV incidence trends in KwaZulu-Natal, South Africa**	
Background:	South Africa is at the epicentre of the HIV pandemic with an estimated 5.4 million people living with HIV/AIDS. With its many partners, South Africa has successfully rolled-out and scaled-up a broad range of HIV-related programmes. Despite improvements in HIV related morbidity and mortality, the rate of new HIV infections remain unacceptably high. In response to the provincial and national priorities to better monitor HIV incidence in high prevalence areas, the HIV Incidence Provincial Surveillance System (HIPSS) will be established in two sub-districts in the province of KwaZulu-Natal.
Purpose:	To establish population-level HIV incidence Provincial Surveillance System (HIPSS) platform in a household-based representative sample of men and women.
Study Site:	The sub-districts of Vulindlela and the Greater Edendale in the uMgungundlovu municipality of KwaZulu-Natal, South Africa.
Study population:	Household population.
Study size:	Two sequential cross sectional surveys with 10 000 individuals selected randomly in the age group 15-49 years will be conducted one year apart. From the cross sectional surveys two sequential observed cohorts of approximately 6400 HIV uninfected individuals in the age group 15-35 years will be selected to participate in the longitudinal follow-up.
Study Design:	HIPSS will establish population level HIV incidence cohorts in two districts in KwaZulu-Natal in order to monitor changes in HIV incidence in association with the scale-up of prevention efforts in a "real world", non-trial setting. HIPSS will rely on a combination of methodologies. This study is designed to be cross-sectional with two embedded cohorts. Baseline and follow-up measurements will be undertaken using a structured questionnaire and biological specimens. The sequential cohorts of HIV uninfected individuals (15-35 years of age) selected from a representative sample of households will be followed up at month 12 and assessed for HIV infection. Population level changes in HIV incidence will be measured. HIPSS will further provide an opportunity to evaluate laboratory tests for recent infections (TRIs) for estimating population level HIV incidence using the recent infection testing algorithm (RITA)
Study Duration:	Approximately 4 years in total

Study Hypothesis:	The intensified HIV prevention and treatment endeavours of the DOH and PEPFAR partners will have a substantial impact on the HIV incidence among men and women 15-35 years in the Vulindlela and Greater Edendale districts.
Primary Objective:	To measure HIV incidence at two time points in a household-based representative sample of men and women.
Secondary Objectives:	1. To determine the prevalence of HIV infected individuals, CD4 counts in these individuals and proportion on ART and ART naïve with detectable and undetectable viral load. 2. To determine changes in the rate of new HIV infections over time 3. To determine the association of behavioural and psychosocial factors and exposure to HIV prevention programmes with new HIV infections. 4. To determine the prevalence and incidence of pulmonary tuberculosis (TB), sexually transmitted infections (STIs) and hepatitis (Hep) B and C infection. 5. To compare cohort derived HIV seroconversion data with laboratory HIV incidence assay data. 6. To determine the community HIV viral load. 7. To inform the provincial and national departments of health on models of HIV incidence surveillance systems. 8. To determine the levels of transmitted HIV drug resistance
Statistical considerations:	The sample size of 10 000 per baseline survey with a longitudinal cohort of 6400 individuals will have 84% power to detect a reduction of 30% in the HIV incidence rate at a 5% significance level given HIV prevalence of 20%, loss-to-follow-up of 15% per annum and an initial HIV incidence rate of 3 per 100 person years. HIV incidence rate will be calculated for each cohort. The incidence rate ratio of the two cohorts will be calculated to quantify the change in HIV incidence between the two time periods. The association of new HIV infections and predictive variables measured at baseline and in the longitudinal cohort will be assessed. The prevalence and incidence of TB, STIs and Hep B and C will be measured at baseline and at follow-up.

2) INTRODUCTION

2.1 LITERATURE REVIEW AND BACKGROUND

2.1.1 The HIV Epidemic in South Africa and KwaZulu-Natal

South Africa has been ravaged by the effects of the Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS). With an estimated 5.4 million people living with HIV/AIDS [1] the country is at the epicentre of the HIV pandemic and accounts for nearly one sixth of the global disease burden. National, annual, anonymous seroprevalence surveys among pregnant women utilising public sector health care facilities demonstrate that HIV prevalence increased from 0.8% in 1990 to 30.2% in 2010 (figure 1) [2]. The HIV prevalence in the age group 30-34 years increased from 41.5% in 2009 to 42.6% in 2010 whilst the prevalence in the 15-24 year age remained as high as 21.8% in 2010. These national HIV prevalence data mask geographical variations and in 2010, HIV prevalence was reported to be 18.4% (95%CI 16.1-21.1) in the Northern Cape in contrast to the 39.5% (95% CI 38.0–41.0) in the province of KwaZulu-Natal (KZN). Similarly five districts within KZN have recorded HIV prevalence above 40%. These trends in HIV prevalence have continued both provincially and nationally [2].

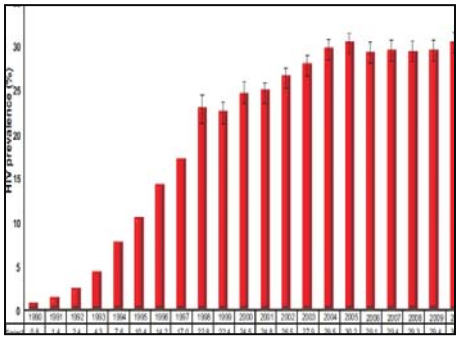


Figure 1: HIV prevalence trends among pregnant women in South Africa, 1990-2010

The South African National HIV Prevalence, Incidence, Behaviour and Communication Survey of 2008 has estimated an overall HIV prevalence of 10.9% (95% CI 10.0-11.0) with a prevalence of 16.9% (95% CI 15.5-18.4) in the 15-49 year age group [3]. More importantly the province of KZN remains the worst affected with a prevalence of 15.8% (95% CI 13.4-18.6). Amongst young people in KZN, the prevalence in the 15–24 year age group was 15.3% (95% CI 11.8-19.7) compared to the national estimate of 8.7% (95% CI 7.2−10.4). The prevalence in young women aged 15-19 years was 6.7% compared to 2.5% in young men of the same age group [3].

The majority of new infections in South Africa are heterosexually acquired with the highest incidence rates occurring in young women. This characteristic of the epidemic reflects the age-sex distribution of HIV with young women acquiring HIV infection about 5-7 years before men and are 1.3 to 12 times more likely to be infected than their male counterparts. Figure 2 illustrates the temporal trends in age-sex disparities in HIV prevalence from two population based surveys undertaken in 1992 and 2005 [4, 5]. The greater burden of HIV infection in women as well as the early rise in HIV infection in young women compared to men remains consistent [6, 7]. This age-sex difference in HIV prevalence highlights that age-disparate sexual coupling between young women and older men as an important contributor to the HIV epidemic in South Africa [8].

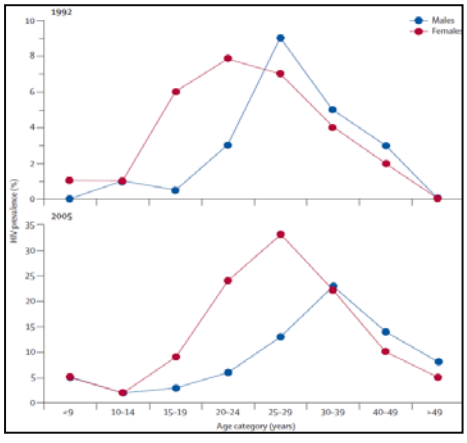


Figure 2: Age and sex disparities in HIV infection in South Africa, 1992 and 2005

In the generalised hyper-endemic epidemic setting of South Africa, efforts to alter HIV epidemic trajectories have to take this pattern of HIV acquisition in young women into account. Despite HIV

prevention efforts, young people continue to acquire new HIV infections sustaining an already unprecedented high prevalence of HIV infection. This study will be undertaken in KZN, the province with the highest national HIV prevalence.

2.1.2 HIV Incidence in KwaZulu-Natal

The spread and changes over time of HIV is tracked through measuring the rate and distribution of new HIV infections (incidence) in a population. Incidence measures the rate of HIV transmission and the change in incidence over time is a key measure of the impact of HIV prevention programmes. The gold standard method for estimating HIV incidence is through prospective cohort studies that measure the rate of new infections in a well-defined group of at risk individuals followed over time. However, prospective cohort studies that measure HIV incidence are logistically difficult to implement, prone to biases that can distort the resulting estimates of HIV infection observed and very expensive to undertake. More recent estimates of HIV incidence rely on mathematical modelling, indirect estimates derived from prevalence in young people (15–24 years) [9] assuming that the HIV prevalence difference in single year of age differs between the age strata and represents incident HIV infections, or using laboratory-based assays to distinguish recent from established long-term HIV infections, independent of the age of the source population.

In South Africa, several cohort studies have been conducted to measure HIV incidence. Between 2002 and 2005, results from preparatory studies for microbicide trials showed high HIV incidence rates among women recruited from several urban and rural sites [10-13]. Among the 5,753 women screened, the prevalence of HIV infection was 43%, whilst the HIV incidence rate was 6.6/100 women-years (wy). Multivariate analysis found that seroconversion rates were highest among women who were <24 years old, single and not cohabiting, and who had incident sexually transmitted infections (STI). Similar high HIV incidence rates have also been reported from other studies.in South Africa The overall HIV incidence was 5.5/100wy (95% CI 2.5 to 10.4) in Bloemfontein, 3.0/100wy (95% CI 0.4 to 10.8) in Rustenburg [14], 6.5/100wy (95%CI 4.4–9.2) in Vulindlela, 6.4/100wy (95%CI 2.6–13.2) in Durban 14.8/100wy (95% CI 9.7, 19.8) in Ladysmith, 6.3/100wy (95% CI 3.2, 9.4) in Edendale, and 7.2/100 wy (95% CI 3.7, 10.7) in Pinetown [13]. HIV incidence remains exceptionally high in certain districts compared to other HIV monitoring sites. Amongst sexually active women in the CAPRISA 004 tenofovir gel trial, the HIV incidence rates in 18-40 year old urban (Durban) and rural (Vulindlela) women was 9.0/100wy (95%CI 5.3-14.3) and 9.1/100wy (95%CI 6.6-12.3) respectively in the placebo gel arms [15].

In 2009, based on mathematical modelling the annual HIV incidence in adults aged 15-49 was highest in KwaZulu-Natal (2.3%) and lowest in Western Cape (0.5%) (EPP estimates, March 2010). Based on the three population based household surveys and the recent infection testing algorithm (RITA), the HIV incidence rate among men and women aged 15–49 years was estimated to be 2.0 per each year per 100 susceptible individuals (/100pyar) (uncertainty range: 1.2–3.0/100pyar). The highest incidence rate was among 15–24 year-old women, at 5.5/100pyar (uncertainty range: 4.5–6.5). In the period 2005–2008, incidence among men and women aged 15–49 was estimated to be 1.3/100 (uncertainty range: 0.6–2.5/100pyar), though this change from 2002–2005 was not statistically significant [16]. Thus it is clear from several data sources that HIV incidence rates remain high in KZN.

2.1.3 HIV Prevention programmes in KwaZulu-Natal

Over the past decade a considerable number of HIV prevention intervention programmes have been developed, implemented, and evaluated. Whilst KZN is known to be the epicentre of the HIV epidemic in South Africa there are reports that the battle is being won slowly [17]. In 2010 the South African government launched the massive HIV prevention and treatment campaign to alter the face of the AIDS epidemic locally [18]. The campaign aimed for a 6 fold increase in HIV testing, increase in HIV treatment provision, rigorous implementation of prevention of mother to child transmission

(PMTCT) of HIV, medical male circumcision (MMC) and sexual assault care through the provision of post exposure prophylaxis (PEP) have been the prominent programmes employed in the HIV prevention strategy resulting in

- HIV Antenatal prevalence has stabilised around 40%.
- PMTCT of HIV has reduced the HIV transmission rate from 22% in 2008 to 2.8% in 2010.
- Aggressive expansion of the anti-retroviral treatment programme is the largest in South Africa and by mid-2011 reached the target of universal access to treatment as the total number of people receiving treatment reached 1.79 million [19].
- More than 2 million people in KZN have had an HIV test and know their HIV status.
- MMC launched in 2010 has exceeded 105 000 young men.
- The cure rate for uncomplicated TB has risen to 57.6% and defaulters have reduced from 12.9% in 2007 to 6.6 in 2012.

2.1.4 HIV Prevention Intervention Research in the study area

Sexual transmission of HIV remains the primary route of infection accounting for approximately 90% of all cases. Despite the provision of HIV counselling and testing, peer education, treatment of STIs as well as condom promotion and provision delivered as integrated HIV prevention packages through health care settings; HIV incidence rates remain persistently high in young women. Several research studies undertaken in the study area have focussed on behavioural and biomedical interventions and are either completed or are on-going. These studies have been undertaken to enhance awareness, knowledge and provide evidence on HIV prevention strategies.

Key behavioural research recently completed in the district is the Phase III Randomized Controlled Trial of Community Mobilization, Mobile Testing, Same-Day Results, and Post-Test Support for HIV. The trial randomised communities to receive community-based HIV voluntary counseling and testing (CBVCT) intervention plus standard clinic-based VCT (SVCT), or SVCT alone . The CBVCT intervention has three major strategies: (1) to make VCT more available in community settings; (2) to engage the community through outreach; and (3) to provide post-test support. These strategies were designed to change community norms and reduce risk for HIV infection among all community members, irrespective of whether they participated directly in the intervention. A community-level intervention based on modifying community norms can change the environmental context in which people make decisions about HIV risk, and has the potential to alter the course of the HIV epidemic in developing countries [20-22].

Since the impact of the HIV epidemic is greatest among young people, the CAPRISA 007 RHIVA (Reducing HIV in Adolescents) trial, a cluster-randomised controlled trial assessed the impact of a school-based intervention of incentivised behaviour change on HIV incidence in grade 9 and 10 children in 14 Vulindlela schools. The trial has completed two years of follow-up and the results are expected to be available in mid-2013 [23, 24]

Research into the development of PrEP either as microbicides (gel or cream) for topical use or as a tablet for oral use has received unprecedented attention and support as a potential female controlled option. With over 60 candidate microbicides in development and 11 clinical trials testing six non-virus specific products the results have been disappointing with none demonstrating a protective effect for HIV. Several pre-clinical studies in different animal models proved tenofovir, an antiretroviral nucleotide reverse transcriptase inhibitor, as a promising antiretroviral agent whether administered as pre-exposure or post-exposure prophylaxis to prevent simian immunodeficiency virus (SIV). The results from the CAPRISA 004 trial of 1% tenofovir gel used intravaginally was the first major breakthrough to demonstrate the gels ability to reduce HIV acquisition by 39% and HSV-2 by 51% [15]. More than two thirds of the enrolled participants in the CAPRISA 004 trial were from the Vulindlela district and many of these women continue to participate in the CAPRISA 008 trial. CAPRISA 008 is an open-label randomized controlled trial to assess the implementation, effectiveness and safety of 1% tenofovir gel provision through family planning services in KwaZulu-

Natal, South Africa. This study is important as it will pave the way for women to readily access the gel following licensure.

Similarly tenofovir and truvada [containing two drugs: tenofovir disoproxil fumarate (TDF-300 mg) and emtricitabine (FTC-200 mg)] taken as daily single oral dose reduced the risk of HIV acquisition in MSM, IDU, heterosexual men and women and in heterosexual HIV-1 sero-discordant partnerships [25, 26]. Despite these positive results, the FEM PrEP trial testing a daily single oral dose of Truvada and the VOICE (Vaginal and Oral Interventions to Control the Epidemic) trial testing daily single oral dose of Truvada or tenofovir or daily single topical dose tenofovir gel were not able to demonstrate a protective effect in women against HIV acquisition and these results were attributed to lower levels of adherence to drug regimens [27]. These studies of ARVs as PrEP (oral and/or topical) therefore provide hope to millions of women as viable HIV prevention options to transform the global response to the HIV/AIDS epidemic. The key evidence will be come from the confirmatory trial currently being undertaken by the Follow-on African Consortium for Tenofovir Studies (FACTS) [28].
Against the sustained high HIV incidence rates research studies on behavioural and biomedical HIV prevention interventions are expected to continue and escalate in the district so that they provide the best level of evidence in terms of effectiveness or efficacy.

2.1.5 The Provincial government programmes

The government has initiated several structured social and biomedical programmes to serve the people at ward level, translating to all districts and all households in all municipalities. These programmes work collectively with the community in building the nation through better health care including HIV/AIDS. These programmes include but are not limited to.

Operation Sukuma Sakhe

Operation Sukuma Sakhe is a call by the provincial Premier for the people of KwaZulu-Natal to be resolute in overcoming the issues that have destroyed the communities such as poverty, unemployment, crime, substance abuse, HIV and AIDS and TB [29]. Operation Sukuma Sakhe spells out initiatives implemented by the different government sector departments. To rebuild the fabric of societies and the nation, the delivery of these initiatives are operationalized through a partnership with communities, stakeholders such business, civil society and government. Through social mobilization and the integrated role of the communities and delivery of government services, the target is to achieve the outcomes in more sustainable way by creating jobs through building access roads, community facilities and human settlements. In addition traditional communities as custodian land owners will be facilitate the granting of leases for the building of schools, crèches, health facilities, commercial and other developments. Thus the government structured programmes are meant to serve the people beginning at the household, at the ward level, translating to districts and to municipalities. Government collectively believes that the partnerships through Operation Sukuma Sakhe will key to building this nation together.

The implementation of Primary Health Care (PHC) re-engineering

As part of the health sector's contribution to the overall government strategy [30] of "A Long and Healthy Life for All South Africans" the Minister of Health has a signed performance agreement (the negotiated service delivery agreement – the NSDA) with the President where he has committed himself and the Members of the Executive Council (MECs) of the nine provinces to four main outputs:

- Increasing life expectancy
- Decreasing maternal and child mortality
- Combating HIV and AIDS and decreasing the burden of disease from tuberculosis
- Strengthening Health System Effectiveness

A three streams approach to PHC re-engineering has been adopted by the Department of Health (DoH). These three streams are:

i. A ward based PHC outreach team for each electoral ward;
ii. Strengthening school health services;
iii. District based clinical specialist teams with an initial focus on improving maternal and child health.

National Health Insurance (NHI)

The National Health Insurance (NHI) [31] is a financing system that will ensure that all South Africans are provided with essential healthcare, regardless of their employment status and ability to make a direct monetary contribution to the NHI Fund. The NHI will offer a defined service package of comprehensive health services from primary health care, to specialised secondary care, and highly specialised tertiary and quaternary levels of care. The benefits provided will cover preventive, promotive, curative and rehabilitative health services. Thus the emphasis will be placed on prevention of disease and promotion of health in contrast to the present healthcare system which focusses on managing disease and disease complications. The key components of the NHI are:-

- Comprehensive service Package within the Context of District Heath Services
- Service Delivery
- Health Systems Strengthening
- Health Financing

2.1.6 Development of partner programmes including PEPFAR

In the KZN province, PEPFAR is providing funding to 89 partners that implement activities in facilities and communities throughout the province. The partners who carry out these activities represent non-governmental organisations (NGOs), faith based organisations (FBOs), and South African government (SAG) agencies. The focus of many of these partners is national but support organizations provincially and locally [32].

Program Areas

The following table identifies the PEPFAR program areas in which partners work to provide services in South Africa. They are described in detail below.

Table 1: PEPFAR activities in KwaZulu-Natal province

Prevention	Care	Treatment	Other
• Counselling & Testing • Prevention of Mother to Child Transmission (PMTCT) • Prevention of Sexual Transmission • Blood Safety • Injection Safety • Male Circumcision • Comprehensive prevention services for Most at risk populations • Comprehensive prevention services for people living with HIV/AIDS	• Adult and paediatric Care and Support • TB/HIV • Orphans and Vulnerable Children	• ARV drug supply • Adult Treatment • Paediatric Treatment • Laboratory Infrastructure and services	• Strategic Information • Health Systems Strengthening • Human Capacity Development • Monitoring and Evaluation

2.1.7 Biomarkers for Measuring HIV Incidence

Trends in HIV incidence can be tracked by applying the incidence assay testing to samples from repeat cross-sectional surveys in the same population. Over the past several years the recent infection testing algorithm (RITA) for HIV, based on tests for recent infection (TRIs) has been developed. However, prior to implementation of a testing programme for recent infection in surveillance settings, test-specific prerequisites, such as calibration, validation, and quality assurance, and other test-specific performance characteristics that may influence interpretation, epidemiological considerations that may guide application, and practical operational considerations for implementation in surveillance settings are to be considered. When properly and judiciously applied, the capacity to estimate incidence from existing programmes that conduct surveillance for prevalent HIV-1 infection will enhance the capacity for more precise and timely analysis of the dynamics of the epidemic and the effectiveness of public health interventions.

Prior to the development of HIV antibodies, early markers of HIV infection include the presence of viral RNA and p24 antigen. The nucleic acid amplification test (NAAT) for detection of HIV-1 RNA and the p24 antigen assays are both highly sensitive and specific, with HIV-1 RNA having an added advantage of being detected much earlier than p24 antigen [33, 34]. HIV-1 RNA testing was developed for the purpose of patient monitoring and has more recently been adopted as a way to identify acutely infected individuals by pooling HIV seronegative samples. Surveillance programmes utilized NAAT testing of pooled HIV seronegative specimens to to estimate HIV incidence. A further advance in diagnosing acute HIV infection for estimating HIV incidence has been the development of fourth generation HIV-1 assays, detecting p24 antigen and HIV antibody simultaneously [35]. However, the detection levels of these assays differ as key viral and serological markers evolve in acute HIV infection.

Tests developed to estimate HIV incidence according to immunologic biomarkers of HIV disease progression in cross-sectional samples from HIV-infected persons have been developed [36]. These are being evaluated to establish a strategy for developing a standard, accurate, inexpensive, and commercially available kit to test for recent HIV infections. An HIV-positive specimen is classified as recent or non-recent by the TRI, based on whether it falls above or below a pre-defined threshold for the assay. In the case of the BED capture enzyme immunoassay (BED assay), one of the TRI [37], this cut-off is the normalized BED optical density threshold, below which a specimen tests as a recent infection. Annualized HIV incidence rates are estimated by applying the number testing as recent, the seroconversion interval established for the test and the number in the at-risk population.

The advantage of TRIs is that their use does not require following participants over time or assumptions about mortality, but on one HIV-positive sample collected at one point in time, resulting in an appealing and inexpensive alternative for estimating incidence in comparison to other methods. The accuracy of TRIs, however, is challenged by host and viral factors that may influence antibody production and normal progression through the assay-defined threshold for recent and non-recent test results. Namely, a non-constant proportion of true long-term infection in the sample has been shown to misclassify as recent on the assay, even after many years of infection, resulting in an overestimate of true population incidence (up to 2-4 times mathematically modelled or cohort estimates in the same population). Misclassification is can be particularly high among persons on ART and those with very low CD4 cell counts; therefore individual level data on ART and CD4 cell counts are collected to exclude such persons from the incidence analysis. These misclassifications had been observed more markedly with first generation assays like the BED, however, the new assays, like the Limiting antigen (LAg) Avidity EIA, have overcome many of these issues and are less likely to be affected by AIDS or low CD4 counts. Whilst assay misclassification rates have been shown to vary substantially across countries [38-41], using adjustment factors, assay-derived estimates could be calibrated to correct for misclassification, or incorporated into the mathematical formula to improve incidence estimates [42, 43].

A further approach to identifying recent HIV infection is to investigate antibody avidity that is the maturity of the HIV antibody response which increases over time following seroconversion. Antibody avidity is believed to be more robust than antibody titre because it is a functional property of maturing

antibodies. Antibodies of low avidity are usually indicative of recent infection and could be used for HIV-1 incidence determination. Several new assays are currently being evaluated to determine their accuracy in distinguishing recent from long term HIV infection and estimation of HIV incidence on a population level. These include the *rIDR-M-Avidity Index Assay (rIDR-M AI EIA)* developed by the CDC GAP Serology/Incidence laboratory. This test is an avidity index assay using a recombinant protein (*rIDR-M*) which incorporates 3 sequences derived from the immunodominant region (IDR) of gp41; representing divergent HIV-1 subtypes A through E (group M). This assay uses a pH3.0 buffer to dissociate low avidity antibodies characteristic of recent infection. The greater the proportion of high avidity antibodies remaining bound increases the avidity index, therefore indicating long-term infection [44]. The *Bio-Rad Avidity EIA* is a modification of the GS HIV-1/HIV-2 Plus O EIA (Redmond, MA). This assay uses 0.1M diethylamine (DEA) to dissociate low avidity antibodies characteristic of recent infection. The greater the proportion of high avidity antibodies remaining bound increases the avidity index, therefore indicating long-term infection. The *gp41 Less-Sensitive(LS) EIA* developed by the CDC GAP Serology/Incidence laboratory uses the same recombinant multi-subtype protein (rIDR-M). The principle is similar to the original LS assays in that the dilution of specimen is greatly increased to 1:10,000 (two-step dilution), which increases the separation between low antibody titre characteristic of recent infections and high antibody titre characteristic of long-term infections. The *Limiting antigen (LAg) Avidity EIA* developed by the CDC GAP Serology/Incidence laboratory is an avidity-based assay that uses the same recombinant multi-subtype protein (rIDR-M), but at a limited coating concentration, such that it is even easier to dissociate low avidity antibodies. In contrast to other avidity assays, the *LAg* requires only a single well as opposed to two wells; therefore, allowing for an increased number of specimens to be tested, is easier to perform and is able to dissociate low avidity antibodies more readily [37, 44, 45]. Furthermore, the LAg avidity EIA has been extensively evaluated and is the only commercially available avidity-based HIV-1 incidence assay.

HIPSS will use the LAG avidity EIA as the select TRI and test samples to estimate recent HIV infection from the cross sectional survey. The test has also been shown to be useful in different populations and subtypes to estimate HIV-1 incidence in cross-sectional specimens as part of HIV surveillance [46].

2.1.8 Surveillance of transmitted HIV drug resistance

Accurate surveillance of transmitted HIV drug resistance in areas with high HIV incidence and ART coverage is important to inform regimen choices and support programmatic efforts to prevent resistance. Studies using samples collected from ante-natal clinics in KwaZulu-Natal suggest that low to moderate levels of HIV-1 drug resistant variants have been circulating since 2008. These samples were collected from young women (less than 21 years of age) in their first pregnancy; criteria used as a sub-optimal surrogate of recent infection. In order to accurately assess the levels of transmitted resistance in KZN, we hope to access confirmed incident cases for HIV-1 drug resistance genotyping.

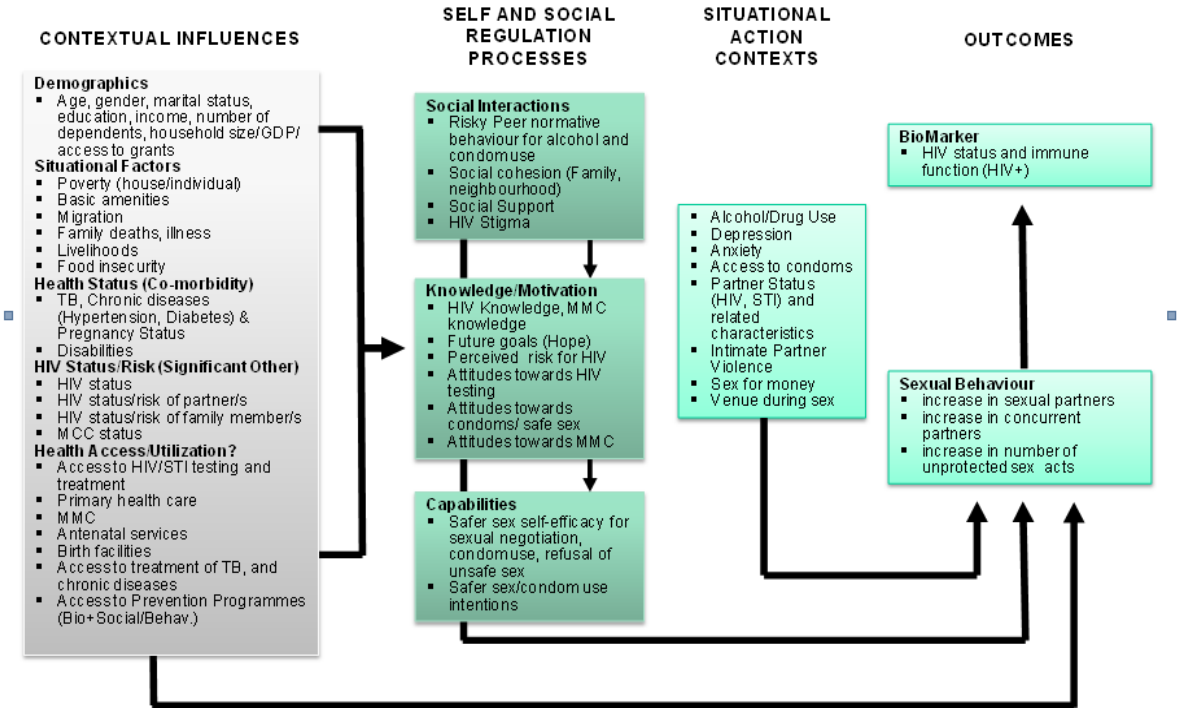
Sequencing of the pol gene will performed using an in-house assay certified by the Virology Quality Assessment Program (VQA). The procedure involves generation of a nested PCR amplicon spanning the entire protease and p66 and p51 regions of the reverse transcriptase genes. Genotypic resistance is defined as the presence of resistance mutations associated with impaired drug susceptibility, using the Stanford University HIV Drug Resistance Database Calibrated Population Resistance Tool (http://cpr.stanford.edu/cpr.cgi) and the 2009 transmitted drug resistance mutation list.

2.1.9 Psycho-social and Behavioural Measures

Theoretical Models of health, behavioural health and prevention have been useful in guiding determinant studies of HIV risk [47]. Historically, these models have often neglected the larger familial and social-cultural context, crucial determinants of HIV risk. In this regard, the National Institutes of Health [48] recently noted that effective behavioural research simultaneously targets multiple risk factors, integrates behavioural interventions into the environment, and intervenes at multiple levels [49, 50]. For the purpose of the present study we employed Social Action Theory

(SAT) [49-51] to guide the development of our socio-economic and behavioural measures and the analytical method. More specifically, SAT is a model of behaviour change that emphasizes the context in which behaviour occurs, and developmentally driven self-regulatory and social interaction processes that affect adaptive behaviour. SAT has been previously adapted in studies of high risk behaviour [49, 50]. For the purposes of the present study, it is speculated that high risk sexual behaviours and HIV outcomes are influenced by a) contextual influences (e.g., macro-stressors including socioeconomic issues, sociodemograhic profile including general health status, and access/use of resources); b) self-regulation (motivation and capabilities), c) social regulation (family resources, peer norms, social support and stigma) and d) affective/ situational action contexts in which sexual behaviours occur (depression, alcohol use, characteristics of sexual partner, presence of intimate partner violence, type of sexual encounter, venue during sex). In this regard, HIPSS will assess individual level data to understand socio-demographic and behavioural factors which enhance or modify risk for HIV infection.

Figure 4 : Modified Social Action Theory



2.1.10 HIV related co-morbidities

HIV infected individuals are at high risk for a wide range of illnesses. Among the most severe are the AIDS defining opportunistic infections and HIV/AIDS related co-morbidities. These infections have a significant impact on clinical presentation, disease progression, quality of life and in some individuals may enhance mortality. Some of the diseases and conditions also serve as important markers for on-going risks and impact on health services and HIV treatments. The co-morbidities include STIs which greatly increase the risk of HIV transmission. Tuberculosis (TB) including MDR and XDR TB is a greater threat to a person infected with HIV relative to an HIV uninfected person such that HIV increases the risk of disease acquisition and progression to active TB. Hepatitis B and C when chronic, increase the risk of severe liver disease, including cirrhosis and liver cancer. Both Hep B and C though unlikely to worsen the course of HIV infection, however, HIV infection is likely to accelerate the Hep B and C disease progression to cirrhosis and liver cancer which may further limit HIV treatment options. Thus, HIPSS will screen for these infections to understand the extent of co-morbidities which impact on health services.

2.2 STUDY JUSTIFICATION

South Africa has over 5.4 million people living with HIV, which means that one in six South African is HIV positive. The rates of new HIV infections are not declining significantly. There are thus major challenges that need to be addressed collectively by South Africans to improve prevention efforts to stem the tide of new infections, and to ensure appropriate care and treatment for those already infected.

The establishment of HIPSS over time will make the following important contributions to assess the impact of HIV prevention efforts and to ensure appropriate care and treatment for those already infected:

- Monitoring the impact of combination HIV prevention programming is an urgent global and local need. As opposed to ‘‘efficacy’’, which measures a program’s individual-level effect under highly controlled conditions, ‘‘impact’’ (or community-level effectiveness) is the effect of a program on a population level as measured by changes in incidence, prevalence, mortality, and/or other ultimate outcomes of interest.
- The KZN Provincial Government, PEPFAR partners and other local organisations are scaling-up intensive, multi-pronged prevention interventions including HCT, MMC, and early treatment for HIV and comprehensive prevention services. It is important to collect localized and detailed information about the HIV response in a geographic area that has the ability to look more closely at associations between the scale-up of prevention efforts and changes in HIV incidence in a “real world”, non-trial setting.
- HIPSS will establish population-level HIV prevalence at baseline and monitor the impact of the scale up of ART on prevalence.
- HIPSS will monitor HIV incidence over time as new bio-medical technologies become available including pre-exposure prophylaxis (PrEP) (oral and/or topical), post exposure prophylaxis (PEP), vaginal or anal microbicides whether through existing research settings or through post trial access and the impact of HIV treatment as prevention.
- South Africa has considerable experience in the use of a variety of methods to estimate HIV incidence. HIV incidence is a sensitive indicator of the impact prevention and treatment programmes. HIV incidence estimation however poses methodological challenges and on-going efforts are needed to strengthen our ability to accurately measure incidence. HIPSS will provide the ability to evaluate different laboratory assays and as well as potentially introducing additional laboratory components.
- As HIPSS will obtain information on HIV prevention and treatment programmes at the household level, it is expected that a significant number of people will seek HCT services.
- HIPSS activities and outputs are aligned with the new National and Provincial AIDS Strategic plan and will provide valuable information to the province to enable the implementation of the surveillance strategy across other districts. HIPSS will be implemented in close consultation with the District Health Management team and so approaches and results identified as a priority will be aligned to the needs of the District, Provincial and National health systems.
- . However, setting up district level surveillance systems will provide detailed information about the HIV response in the specific geographic areas and the ability to look more closely at associations in scale-up of prevention efforts on changes in HIV incidence. While the HSRC household survey is extremely valuable to monitor the HIV epidemic in South Africa its large geographic coverage and cross sectional methodology makes it difficult to assess more localized incidence dynamics with any statistical power.

In summary, South Africa has one of the highest rates of HIV in the world. The province of KZN with the highest infection rate in the country is taking a leading role in implementing a combination of programmes for HIV prevention and treatment at an unprecedented pace. It is vital to describe changes in the rate of new HIV infections resulting from implementation of these interventions. The study described in this protocol seeks to document changes in HIV incidence and examine factors that

may contribute to this change so that other districts, provinces, countries and programs can develop and implement HIV prevention strategies to rapidly monitor anticipated changes in HIV incidence.

2.3 AUDIENCE AND STAKEHOLDER PARTICIPATION

Stakeholders include the KZN HIV and AIDS Directorate from the Office of the Premier, the district offices of the KZN Departments of Health, Education and Social Services, PEPFAR and its implementation partners. Local non-governmental implementing partners in the district involved in the implementation of prevention programmes, other donors and the population of the district will also participate.

HIPSS is a joint endeavour of KZN Department of Health, PEPFAR partners in KZN, the Centers for Disease Control and Prevention (CDC), the National Institute for Communicable Diseases (NICD), Epicentre, Centre for the AIDS Programme in South Africa (CAPRISA), Stellenbosch University's South African National Research Foundation Centre of Excellence in Epidemiological Modelling and Analysis unit, SACEMA and HEARD.

2.4 GENERAL STUDY APPROACH

HIPSS will establish population level HIV incidence cohorts in two districts in KwaZulu-Natal in order to monitor changes in HIV incidence in association with the scale-up of prevention efforts in a "real world", non-trial setting. HIPSS will provide an opportunity to evaluate the Limiting antigen (LAg) Avidity EIA as a TRI for estimating population level HIV-1 incidence.

HIPSS will rely on a combination of methodologies. This study is designed to be cross-sectional with two embedded cohorts. The longitudinal follow up of the cohorts of HIV uninfected individuals (15-35 years of age) selected from a representative sample of households will measure population level changes in HIV incidence in the district.

2.5 HYPOTHESES

The intensified HIV prevention and treatment endeavours of the DOH and PEPFAR partners will have a substantial impact on the HIV incidence among men and women 15-35 years in the Vulindlela and Greater Edendale districts.

3) STUDY OBJECTIVES

3.1 PRIMARY OBJECTIVE

The primary objective of the study is to measure HIV-1 incidence at two time points in a household-based representative sample of men and women.

3.2 SECONDARY OBJECTIVES

To determine the prevalence of HIV infected individuals, CD4 counts in these individuals and proportion on ART and ART naïve with detectable and undetectable viral load. To determine changes in the rate of new HIV infections over time

To determine the association of behavioural and psychosocial factors and exposure to HIV prevention programmes with new HIV infections.
HIV Counselling and Testing (HCT)

- Medical Male Circumcision (MMC)

- Post Exposure Prophylaxis (PEP)
- Pre-Exposure Prophylaxis (PrEP) (oral and/or topical)
- Male and female condom use
- Sexual partner exposure to ARV treatment
- Behaviour change information, training and communication
- Contextual influences, knowledge, motivational factors, capabilities, social interactions, affective states, situational contexts in which sex occurs and sexual risk behaviours

To determine the prevalence and incidence of pulmonary tuberculosis (TB), sexually transmitted infections (STIs) and hepatitis (Hep) B and C infection.

To compare cohort derived HIV seroconversion data with laboratory HIV incidence assay data.

To determine the community HIV viral load.

To inform the provincial and national departments of health on models of HIV incidence surveillance systems.

To determine the levels of transmitted HIV drug resistance

To determine the levels of transmitted HIV drug resistance

4) STUDY DESIGN

HIPSS will establish two sequential household representative cross sectional surveys of 10 000 individuals in each survey. Consenting procedures, baseline assessments and cohort accrual and enrolment are scheduled to take 6 to 9 months. From these surveys HIV incidence will be measured with the laboratory TRIs and RITA algorithms. Each sequential cohort of approximately 6400 HIV uninfected individuals will be followed up at month 12 and assessed for HIV infection.

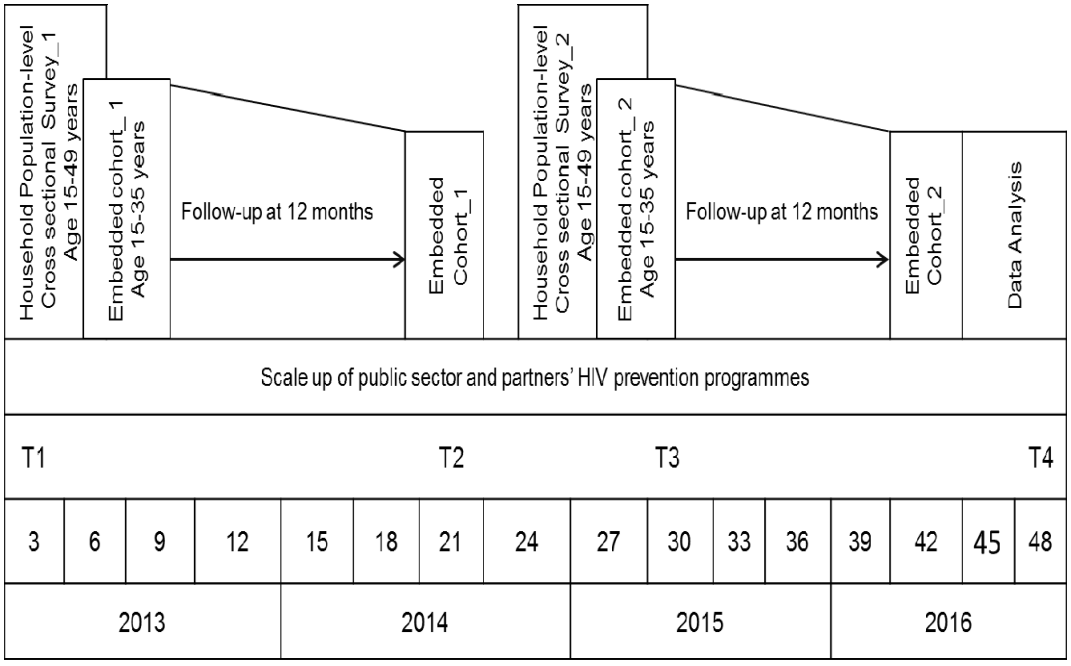


Figure 5: Study design and timelines

4.1 STUDY TIMELINES

The timeline for HIPSS are shown in Table 2.

Table 2: Schedule of timeline for HIPSS

YEAR	2013	2014	2015	2016
Protocol development	X			
Submit protocol for review to CDC and UKZN BREC for Ethics review	X			
Translate study instruments	X			
Recruitment and training of research staff	X			
Procurement of supplies and laboratory preparations	X			
Data collection for baseline for cohort 1	X			
Data collection at 12 months (follow-up cohort 1)		X		
Data collection for baseline for cohort 2		X		
Data collection at 12 months (follow-up cohort 2)			X	
Laboratory processing	X	X	X	
Interim analysis and report		X	X	
Data analysis			X	X
Writing of reports			X	X
Dissemination & discussion of results with stakeholders				X

4.2 HOW STUDY DESIGN MEETS OBJECTIVES AND ADDRESSES RESEARCH QUESTIONS

The study design incorporates laboratory and cohort derived methods to measure HIV incidence. Monitoring the change in the HIV incidence rate over time will offer insights into the role of public sector programmes in reducing the rate of new HIV infections in the cohort and in the general population, if a reduction is observed.

Blood samples from persons identified as HIV-infected during baseline surveys will be collected to measure HIV-1 RNA viral load. These data will be used to determine the proportion of HIV infected persons on ART and ART naïve with detectable and undetectable viral load in the community to impact HIV incidence in the general population.

Surveys of sexual risk behaviour and exposure to risk reduction programmes for men and women will be administered as part of the baseline and at follow-up. Repeat measures of sexual risk behaviours

and exposures to sexual risk reduction campaigns over time, allows for examination of whether risk behaviour changes may be coincident with reduced HIV incidence, if observed.

Using structured standardised questionnaires exposure information on services to HCT, time to accessing of services for HIV, TB, STIs, PEP, PrEP (oral and/or topical) and to district wide public sector health programmes will be obtained.

4.3 MONITORING AND EVALUATION OF DATA FROM PROGRAMMES

The ability to evaluate the stated hypotheses is centred, in part, on the district HIV prevention, care and treatment programmes. The geographical mapping of district HIV prevention, care and treatment programmes will be collected in real-time to critically evaluate the coverage in relation to the study sample. The key indicators for HCT, MMC, PEP, PMTCT, ART eligibility and initiation will be obtained from district health data and from information collected by PEPFAR and other partner organisations. The cumulative number of clients accessing these services will be further disaggregated by age and gender. Whilst the district health data may have limitations in completeness and accuracy, individual-level information on exposure to HIV prevention and treatment programmes will be collected from study participants through the questionnaire and correlated to determine the uniformity of services available and coverage of HIV programmes.

4.4 LIMITATIONS TO THE STUDY DESIGN

The HIPSS approach of a population-based, repeated longitudinal cohort study to evaluate changes in HIV incidence consequential to the district prevention and treatment initiatives; does not allow one to attribute changes in HIV incidence to any specific intervention or combination of interventions. At most this study will be able to give an accurate picture of HIV incidence over time in men and women. The effectiveness of individual district wide interventions needs to be evaluated with a different study design, including more districts.

The sampling strategy is expected to represent the attributes of the population and therefore the selection of a random sample. However, should survey staff encounter difficulties in the field and choose to select participants outside the sampling framework; we would expect to lose the representativeness of the population. Eligible participants who are not available or refuse will be replaced by an alternate individual predetermined in the sampling frame, however, only following authorisation of senior study staff member. The current sampling strategy has taken into account that the younger population are overrepresented as the highest HIV incidence rates are expected to occur in the younger age groups.

We anticipate a 15% annual lost-to-follow-up rate among cohort participants because of people moving away from the district. We have catered for the impact of this loss by increasing the sample size appropriately.

Data on sexual behaviours and other sensitive issues will be self-reported and are thus subject to potential under-reporting or social desirable bias. To limit the extent of the bias, field staff will be trained on how to put participants at ease, to manage sensitive situations and assured of

confidentiality. Staff will also not be sourced from the same community as that under study to minimise familiarity potentially leading to biased responses.

The comparison of HIV incidence rates will not allow causal interpretation of individual programmes as the sole mechanism influencing observed change in HIV incidence rates or in sexual risk behaviours and could be influenced by other modifying factors. The use of a district wide household representative sample in each HIV incidence cohort does allow a valid assessment of the population-based change in HIV incidence in men and women 15-35 over time.

4.5 PREVENTION EFFECTIVENESS

By combining: 1) the baseline HIV incidence rate among men and women; 2) the expected HIV acquisition risk reduction (if observed) and; 3) the expected number of infections averted based on the projected 30% reduction in HIV-1 incidence through the HIV prevention and treatment interventions, we will estimate the number of HIV infections averted due to these programmes among men and women in the population (as a proxy measure for population-level 'impact' of prevention programmes), however the study is not designed to do a detailed cost effective study of each of the interventions.

5) STUDY POPULATION

5.1 STUDY SETTING

The region, uMgungundlovu District Municipality, is located in central KwaZulu-Natal and is extremely diverse in terms of topography, climate and soils; the region presents a rich and complex natural environment with limited resources offering unique development opportunities. The region incorporates habitation in traditional settlements or farmlands through to informal, rural settlement and urban living. HIPSS will be established in Vulindlela and Greater Edendale, two sub-districts of uMgungundlovu.

Vulindlela is situated to the west of Pietermaritzburg and northwest of the Greater Edendale area within the boundaries of uMsunduzi and uMgeni municipalities. The sub district is approximately 28 000 hectares in extent. This rural community has a population of just over 150 000 and is predominantly Zulu speaking. The majority of the land belongs to the traditional authority through the iNgonyama Trust and is made up of 9 wards, of which 5 are under the traditional leadership of the Amakhosi and 4 are under the ward counsellors of the local government municipal system.

The Greater Edendale area is the second largest urban centre within the Kwa-Zulu Natal province and is the main economic hub within the uMgungundlovu District Municipality. Its location has a strong influence on the regional channels of investment, movement and structuring of the provincial spatial framework for growth and development. The Greater Edendale area is situated some 10km south-west of the uMsunduzi City Centre. The two areas are linked by a dual carriage way which is more popularly known as the Edendale Corridor. This route serves not only as a path for economic growth but also as connection between various outlying rural areas in the north, including Vulindlela, to the city. Edendale is divided into two areas, the first

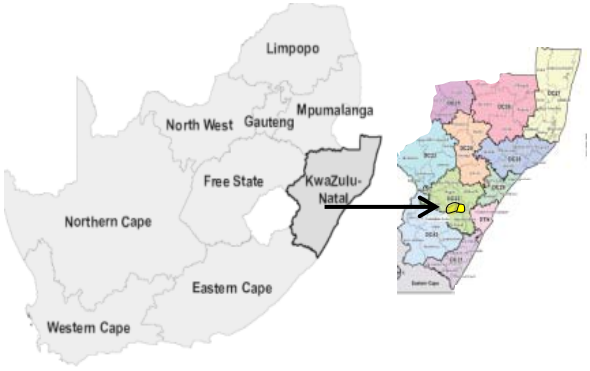


Figure 6: Schematic map showing the location of Vulindlela and The Greater Edendale sub-districts

of which is categorized as the traditional area of Edendale proper, where virtually all land is privately owned. The second area however, is regarded as the more contemporary area of Edendale and it is here that all land vests within the ownership of either the state or the provincial government. Much of the Greater Edendale Area is densely developed with both formal and informal housing, supported in some areas by ancillary land uses and facilities. The current population within the Edendale area is about 210 000 people which comprises approximately 36% of the city's population.

There are 7 and 9 PHC clinics in the Vulindlela and the greater Edendale sub-districts respectively. Trained nurses provide comprehensive primary health care, including family planning services, voluntary HIV counselling and testing, sexually transmitted infection (STI) treatment, antenatal care, treatment of opportunistic infections and minor ailments. They are linked by ambulance to the regional referral hospitals, Grey's Hospital (about 30 minutes away) providing optimal tertiary level of health care to people of the Western area of KwaZulu-Natal and Edendale Hospital (about 20 minutes away) a Regional and District level hospital providing comprehensive services. In addition, there are about 60 community based organizations in the district representing a variety of civic interests such as youth, women, religion, politics, and housing. Several of these organizations are currently providing HIV prevention and home-based care services to these communities and have links with the CAPRISA Vulindlela Clinical Research Site.

As part of the on-going epidemiological studies, CAPRISA has monitored the HIV prevalence in pregnant women in Vulindlela. The prevalence increased from 32.4% (95%CI 27.6-37.6) in 2001 to 40.0% (95% CI 35.2-44.8) in 2010. About a third of pregnant women surveyed were less than 20 years of age and about 20% were already HIV infected. The HIV epidemic in this district is being fuelled by high incidence rates, estimated at 11.2% per annum in young women under the age of 20 years. Between March 2004 and February 2005 we assessed the feasibility of establishing sexually experienced cohorts in Vulindlela. Results indicate that of the 981 volunteers,14-30 years of age, 35.7% (95% CI 32.7–38.8) were already HIV positive and the HIV incidence rates was 6.5 (95% CI 4.4–9.2) /100pyo. Similarly, in the greater Edendale area, of the 1084 volunteers 18-35 years of age, 46.1% (95% CI 43.1-49.1) were HIV positive and the HIV incidence rate was 6.3 (95% CI 3.2–9.4) /100pyo. These data underscore the persistently high HIV incidence rates in young women. The impact of HIV infection in this community was apparent by the disproportionately high AIDS related mortality rate of 5.2 (95%CI 2.9-7.5) /100pyo in young women 20-24 years of age [52].

5.2 SOURCES OF HOUSEHOLD-BASED STUDY POPULATION

We will use a two-stage cluster-based sampling of enumeration areas (EA) to randomly select households and recruit a household-representative sample of men and women. The two areas, the Vulindlela and the greater Edendale will be considered as the strata. The EA sampling frame has been triangulated from the Census 2011, the 2007 Community survey data (StatSA Community Survey) together with aerial imaging of dwellings supplied by Geo Terra Image (GTI) to obtain population number of household and persons on EA level. The sampling frame is further adjusted to the 2009-2010 GTI counts, other district council estimates, and StatsSA's released 2011 midyear estimates of population numbers per province, according to the 2009 province boundaries, race, five year age groups and gender. This EA data is used as the sampling frame and consists of demographic information, estimated population counts of number of households, number of people as well as numbers per population group, gender and per five-year age interval. The study area consists of an estimated 95641 households with a total of 367906 individuals. Of these, an estimated 176418 are males and 191515 are females. A total of 217278 are in the age range 15-49 years and 164302 are in age range 15-35 from whom we will recruit for the cross sectional and follow-up cohort respectively. From a total of 409 EAs, 164 EAs will be drawn randomly from the two districts. In the case that the EA data changes, we would use the most up to date EA data. This would not change the sampling process as the proportion of EAs selected to the total number of EA in the study sub-districts will remain the same. Within an enumeration area the households will be drawn systematically with a

random start in a serpentine pattern. Study staff will identify households and use the Global Positioning Systems (GPS) receiver to record the geographic coordinates of each randomly selected household. We will enrol 61 households from each enumeration area. Sampling will continue until 10 000 households have been enrolled. Should a selected household be abandoned, refuse to complete the composition form or the members away for an extended period of time the household on the right side of the selected house, when facing the entrance of the selected household, will be used as a replacement. All replacement household will be authorised by a supervisor.

Once a household is selected, a list will be made of all the individuals who reside in the household and meet the eligibility criteria for the study. These individuals will be numbered and the handheld device will select one of these individuals at random to be included in the study. Only one individual per household will be selected and enrolled in the study. Should the selected individual refuse to participate the next randomly selected individual may be selected. Should this second individual also refuse the household would be replaced. The above mentioned procedure for household replacement will be followed where the household on the right side of the selected, when facing the entrance, will be used as a replacement.

5.3 PARTICIPANT ELIGIBILITY

Residents of the identified study area will be eligible for inclusion in this study. Individuals must meet all of the following criteria at enrolment in order to be eligible for inclusion in the study.

5.3.1 Inclusion Criteria

Cross sectional Survey

- Household volunteers 15-49 years of age, inclusive of men and women
- Household residents <18 years of age to provide assent and parental, guardian, caregiver or household representative completing the household composition form to provide consent.
- Residing in the selected household
- Willing to provide written informed consent either in English or isiZulu
- Willing to participate in this study
- Willing to undergo study procedures
- Willing to provide clinical samples of peripheral blood, urine, sputum and self-collected vulvo-vaginal swab samples (females)

Cohort follow-up from the cross sectional

- Including all of the above except household volunteers 36-49 years of age, inclusive of men and women
- HIV Negative

5.3.2 Exclusion Criteria

Cross sectional Survey

- Non-residents from the study area.
- Refusal by participant to participate in the study
- Refusal by participant to provide clinical samples of peripheral blood, urine, sputum and self-collected vulvo-vaginal swab samples (females)
- Unable to provide necessary assent or consents
- Cognitive or mental challenges (based on the assessment of the participants ability to comprehend the study information provided)

- Stated intent to leave study indefinitely for work or any other reason in the next 12 months

Cohort follow-up from the cross sectional

- HIV Positive

5.4 JUSTIFICATION FOR INCLUDING MINORS 15-<18 YEARS OF AGE

Several large studies have consistently shown that HIV prevalence and incidence are dramatically high in young people 15 to 18 years of age. A unique feature of the HIV epidemic in this region is the age-sex differences in HIV acquisition and the vulnerability of young girls acquiring HIV infection about 5-7 years earlier than men; and having a 3-6 fold higher rate of HIV infection compared to young boys in the same age group [53, 54]. Although the national HIV prevalence estimates in prenatal women have stabilised, the continuing high prevalence in younger pregnant girls is of concern. In young pregnant 10 to 14 year old girls the HIV prevalence increased from 7.9% (95% CI 3.7-14.6) in 2009 to 9.1% (95% CI 5.1-15.8) in 2010, whilst the prevalence in the 15-19 year old girls increased from 13.7% (95% CI 12.9-14.7) in 2009 to 14.0% (95% CI 13.1-14.9) in 2010. Data from the national population-based survey conducted in 2008 estimated HIV prevalence in young people aged 15–24 years to be 15.3% (95% CI 11.8-19.7) in the province of KwaZulu-Natal compared to the national estimate of 8.7% (95% CI 7.2–10.4). The prevalence in young girls aged 15-19 years was 6.7% compared to 2.5% in boys of the same age group [6]. These data repeatedly underscore the importance of heterosexual transmission driving the epidemic in this region influenced by key epidemiological factors such as age and gender.

5.5 JUSTIFICATION FOR EXCLUSION OF SUB-SEGMENTS OF THE POPULATION

Except for the exclusion criteria described above, persons <15 years of age will be excluded from study participation. Whilst the age of consent in South Africa for having an HIV test is 12 years and to preferably include those <15 years in this study, the ethical considerations related to confidentiality, anonymity, protection of children, informed consent, in-country regulatory laws preclude their participation despite them being sexually active and at risk for HIV infection.

Based on current knowledge on HIV incidence, more than 80% of new HIV infections are acquired in young people less than 24 years of age [53, 54]. Thus the study sample to include younger population is intended to enhance the efficiency of the study, rather than the inclusion of an older population where fewer incident infections are expected to occur and therefore reducing the power of the study.

Persons with a stated intention to leave the study area indefinitely may be more easily lost-to-follow-up. Substantial attrition from these persons could reduce the power of the study, and ultimately jeopardize the ability of the study to detect differences in the key study outcomes.

5.6 CASE DEFINITIONS

The following case definitions will be used throughout the study to establish participant study eligibility and outcomes.

5.6.1 HIV status

HIV status will be determined following testing of PBS using the HIV testing algorithm **(Appendix A)** and reported as:

- **Confirmed HIV-negative**: HIV seronegative and NAAT negative as per the HIV testing algorithm.
- **Confirmed HIV-positive**: HIV seropositive as per the HIV testing algorithm
- **HIV indeterminate**: Indeterminate based upon the HIV testing algorithm and may require testing with additional laboratory tests.
- **HIV-positive Prevalent Infection**: HIV seropositive as per HIV testing algorithm.
- **HIV-positive Recent Infection (Cross sectional Survey)**: HIV positive and recent classification by LAg Avidity EIA and HIV-1 RNA viral load assay as per HIV testing algorithm in the cross sectional survey.
- **HIV-positive Acute Infection (Cross sectional Survey**): HIV seronegative and viral RNA positive as per HIV testing algorithm.
- **HIV-positive Incident Infection (Cohort follow-up)**: HIV seropositive as per HIV testing algorithm at the 12 month follow-up, confirmed with parallel testing of baseline (HIV antibody negative) and follow-up sample (HIV antibody positive)

5.6.2 Male circumcision status

Male circumcision status will be determined by using a validated question on whether they have had a traditional male circumcision or whether they have had medical male circumcision carried out by a qualified health care professional including the use of visual representation. This approach has been found to be more reliable in South Africa where traditional circumcision is widely practised by some cultural groups.

5.6.3 Household

A household will be defined as a group of people who share a physical structure such as a compound or homestead and who consume or make some contribution to food and other shared household resources. Households will be eligible for participation in this study if they are within the predefined study area.

5.6.4 Household resident

A household resident is defined as an individual who:

- has been sharing a physical structure such as a compound or homestead and who has been consuming or making some contribution to food and other shared household resources;
- is a person listed by the head of household as being a household resident (but not a guest who stayed in the house the prior night) on the Household Composition Form (Appendix B)
- any household resident who commutes for various time periods
- any person 15-49 years of age who is not related to the family but considered to be a guest/s who stayed at the household overnight ***will not be considered as a household resident and excluded from participating in HIPSS;***

5.6.5 Head of household

The head of household is defined as the person who is recognized within the household as being the head irrespective of gender.

6) STUDY PROCEDURES

The schedule of study assessments and procedures for HIPSS are shown in Table 3.

Table 3: Schedule of study assessments

Measurement	Cross Sectional survey / Baseline cohort	Cohort Follow-up survey visit at month 12

Informed consent/ Assent	X	Review of consent
Demographic data and locator information and fingerprinting	X	X (for confirmation)
Questionnaire administration	X	X
Sample collection • Peripheral blood sample (25ml) equivalent to about 5 teaspoons, first-pass urine (10-20 mls), sputum and self-collected vulvo-vaginal swab samples (females) and cough induced sputum samples.	X	X

6.1 CROSS SECTIONAL SURVEY

As described in section 5.2 a random sample of EAs will be selected for the study. Proportional to the relative size of the EA, for each selected EA, the households will be drawn systematically with a random start in a serpentine pattern. A single household member meeting the inclusion and exclusion criteria selected randomly will be invited to participate in the study.

A flow diagram of the recruitment, consent, fingerprinting and sample collection, questionnaire and cohort recruitment can be found in appendix C. All procedures completed in the cross sectional survey will serve as the baseline/enrolment for the selected cohort.

6.1.1 Recruitment

Study staff will approach households included in the sample and make appropriate introductions, provide information about the study and identify the head of household or designee. Once agreeable the household composition form will be completed to capture age and gender and basic socio-demographic profile of all usual household members excluding overnight visitors. From this information, household members who are 15-49 years of age will be identified as eligible to participate in the cross sectional survey.

One randomly selected individual who meets the eligibility criteria will be asked to participate in the study. Those who decline will be thanked for their time and asked to provide basic information about their reason for declining to assist in characterizing the impact of refusal on study outcomes. Those who agree to participate will be asked to designate a relatively private location either inside or outside their home where the remainder of activities may be conducted with as much privacy as possible and prepared for baseline assessments and enrolment.

6.1.2 Baseline Assessments and Enrolment

Once agreeable study staff will provide study information, procedures that will be undertaken, that they will be compensated minimally for their time and obtain written informed consent or assent (Appendix D) from the individual and/or parent or guardian consent if indicated. Only individuals meeting the study eligibility criteria will be asked to provide fingerprints and enrolled into the study. Participants will be asked to provide detailed locating information to assist with future contact. These will include telephone numbers, usual hangouts, names of family members/friends who can be contacted for tracking participants with information as to whether the participant agrees to such contact by study staff will be requested (Appendix F).

No personal identifiers will be documented on any study related data collection instruments. Each participant will be assigned a unique study number that will be linked to the structured questionnaire to be administered by study staff using a handheld PDA.

Trained staff will administer the questionnaire to obtain:-

- Demographic data
- HIV testing history
- Sexual behaviour history
- Exposure to information, education, prevention and treatment programmes for HIV
- MMC status (males)

Trained phlebotomist will collect the required peripheral blood sample (25ml) equivalent to about 5 teaspoons. Participants will be guided to collect 10-20 mls of first-pass urine sample, sputum and self-collected vulvo-vaginal swab samples (females).

If after consenting to participate in the survey a participant then refuses to continue with participation, then he or she will be reclassified as refusing to participate in the study, and no further study procedures will be conducted. These individuals will be asked to provide basic information about their reason for declining via the Refusal Pre-cohort Survey Forms (part of the baseline survey form Appendix G for Females and Appendix H for Males).

6.1.3 Linkage to care and Referrals

Prior to commencing the survey, parallel HCT services will be set up to make HIV testing available to participants and family members. As per South African Department of Health HCT policy guidelines [55] any person 12 years and older could access HCT services independently. Participants who would like to know their HIV status will be offered a choice of being tested by qualified staff using HIV rapid testing kits and algorithms approved by the SA DoH or being referred to a SA DoH accredited parallel HCT facility or being provided with information on where to access HCT for themselves, partners and family members through public sector facilities or other NGOs providing the service in the district (Appendix A). Referral systems will be set up to ensure that participants and family members who tests HIV positive can access treatment and care services through the local health care facilities. Participants who test HIV positive will be referred into treatment and care programmes. Records will be kept of individuals being referred.

As per Department of Health guidelines participants with signs and symptoms of STIs and / or TB will be referred to PHC services in the district to access care and services. All Participants laboratory results for HIV, STIs and / or TB will be sent to the nearest Department of Health clinic. Participants will be given a card with their barcode on and the name of the clinic where their results will be sent. Participants will be encouraged to visit the clinic to obtain their results and receive appropriate counselling and referrals to access care and treatment. Records will be kept of individuals being referred to determine the number of people returning for results and follow-up care.

Participants completing the baseline survey will be informed that they might be contacted for the follow-up survey approximately 12 months later.

6.1.4 Interim telephonic contact

Study staff will attempt to contact study participants at 3 month intervals by telephone after enrolment to update locator information and, if needed, approximately two weeks before their scheduled follow-up visit. Participants will be provided with a study helpdesk telephone number to call for updating their information or for seeking information regarding the study assessments and anticipated scheduled visits. For this contact participants will not be compensated. Participants determined to have moved within or outside the district will be visited at their current residence or at an alternative location of their choice at the time of follow-up assessment.

6.2 COHORT FOLLOW-UP

From the enrolment visit participants for the longitudinal cohort follow up will be contacted and informed via SMS that they are eligible for the study participation. Patients will not be informed of

their HIV status determined by this study. Selected participants will be visited again at their place of residence or at a location of their choosing for a follow-up visit at 12 months after enrolment. For the follow-up appointment, several attempts will be made by study staff to establish contact in person and complete the follow-up visit activities. The following procedures/assessments will be performed at the follow-up study visit:

- Verification of the participant's identity and participation in the study.
- Selection of a relatively private location either inside or outside the participant's home, so that the follow-up visit may take place with as much privacy as possible, as appropriate.
- Review of the study goals, informed consent and procedures.
- Study staff administered completion of follow-up questionnaire using a PDA. Participants will be asked questions about their MMC status, HIV testing history, sexual behaviour history and exposure to information, education, prevention and treatment programmes for HIV in the last 12 months.

All participants will have the required blood samples collected and guided to provide, first-pass urine sample, sputum and self-collected vulvo-vaginal swab samples (Females).

Participants who decline to participate in the scheduled follow-up visit will be thanked for their time and asked to provide basic information about their reason for refusal to assist in characterizing the impact of refusal on study outcomes. This information will be documented in the appropriate Follow-up cohort Survey refusal Form (Part of Appendix F)

6.3 PARTICIPANT RETENTION

Once a participant has enrolled in the study, the study staff will make every reasonable effort to retain them for the entire study period. Every effort will be made to maintain lost-to-follow-up rates at a minimum. A lost-to-follow-up rate of 15% of the enrolled cohort is anticipated. Study enrolment and retention will be monitored by the protocol team. Study staff will endeavour to achieve high levels of follow-up and implement the following procedures to achieve high retention rates:

- Thorough description of the study visit schedule and procedural requirements during the informed consent process
- Explanation of the importance of adhering to follow-up study visit to the overall success of the study.
- Accurate and complete completion of locator information form with multiple means to contact participants and to include place of residence and important landmarks for study contact.
- Flexibility in scheduling time and location of follow-up visit
- Use of appropriate telephonic contact and timely visit reminder
- Immediate tracking and follow-up of missed visit.
- Mobilization of trained field staff to track and make contact with participants, especially those who might have relocated.
- Community education to increase awareness about HIV/AIDS and importance of HIV prevention.
- Seeking support of community advisory boards, advocacy groups and others in support of the study.

6.4 STUDY ASSESSMENTS

6.4.1 Sample collection, processing and archiving

All procedures completed in the cross sectional survey will serve as the baseline for the selected cohorts.

During the cross sectional survey and at the cohort follow-up visit, trained phlebotomists will collect two tubes of peripheral blood samples in pre labelled ethylenediaminetetraacetic acid (EDTA) and plain tubes. Approximately 10mls blood will be collected in each tube. In addition, participants will be guided to collect first-pass urine sample (10-20ml), sputum and self-collected vulvo-vaginal swab samples (females). Sample transportation, processing and archiving procedures will be described in the Manual of Operations (MOP). These include handling, labelling, transport, chain of custody, assay procedures, proficiency testing and quality assurance procedures. Briefly all samples will transported under appropriate temeprature conditions to maintain sample integrity. All remaining samples will be catalogued for confirmation of laboratory tests if indicated and stored for future testing. All data linking participants' personal identifiers and participant identification (PID) number or study results will be maintained securely with access to a limited number of study staff.

6.4.2 Demographic and Behavioural Assessments

Demographic, psychosocial and behavioural data will be collected from all enrolled participants in the cross sectional survey and at the cohort follow-up study visit using structured questionnaires administered by trained study staff. Questions will cover issues related to knowledge/motivations, capabilities and social norms related to sexual patterns. Further, affective states (use of alcohol, indicators of depression), partner characteristics (including number, type (regular/casual) and concurrency of sexual partners; condom use, knowledge of own and sex partner/s HIV status), intimate partner violence and venues where sexual contact occurs will be collected. For those who report having known they were HIV infected prior to enrolment into the study, information on date of HIV diagnosis, linkages to HIV medical and psychosocial care, date of initiation of antiretroviral drug use will be collected.

6.4.3 Exposure to HIV prevention and treatment programmes

Participants will be asked about exposure to any informational, educational, behavioural and/or biomedical prevention, treatment and psychosocial support programmes for HIV through the DoH, NGOs, and/or PEPFAR partners in the district. These include but are not limited to exposure to HCT, MMC, PMTCT, ART provision, screening and treatment for TB, STI, family planning services and PEP. Information on access to PrEP (oral and/or topical) through research organisations will be obtained. Information on access to HIV care and self-reported ART use will be collected from all participants found to be HIV positive at the study enrolment visit.

6.5 STUDY FORMS

All information sheets, assent, informed consent forms and questionnaires will be translated into the local isiZulu language and pre-tested during the preparatory work. Consent forms and Information Sheets will be paper-based. Questionnaires will be administered by study staff using personal digital assistant (PDA) electronic handheld device in order to achieve data quality and to achieve efficiencies in data capture and data management.

The paper questionnaire will be integrated into the PDA with appropriate selection options (i.e. single response, multiple response, open ended questions, drop down lists, etc.). This ensures that the data are captured as accurately as possible. Questions that are compulsory will be such that the interviewer cannot proceed without filling in a response. Where appropriate, responses will be coded to improve the speed. Proper skip patterns will be incorporated to ensure that only required questions are completed.

The PDAs also have a global positioning system (GPS) built in so that the household coordinates are stored for proper household identification. Information on the name of the interviewer, date, time will be captured through an access code. Navigational GPS will be used to further assist the field teams to get to the households and the movement of the teams will be monitored using a tracking GPS. The

tracking will enable management to ensure that field teams are entering the EAs and households. The value of using this approach is that it ensures that the field teams are conducting the survey in the defined areas, which is critical in implementing an effective nationally representative sample.

The PDAs send the data to the server whenever there is an internet signal. This safeguards the data in the event that the PDS is lost or stolen.

The following forms will be used in the survey:

Household Composition Form (Appendix B): This form will direct questions and answers between the staff and the head of the household or designee to determine household compositions and to identify potential participants in the household.

Refusal Form (Appendix F): This form will contain a single question about the reason an individual declined participation to help characterize how those who refuse may differ from those who agree to participate. This form will be used at baseline and for those refusing to continue participation at the follow-up visit.

Refusal Form after Consent (Appendix G and H): Part of this form will be used when, if after consenting to participate in the survey a participant then refuses to continue with participation, then he or she will be reclassified as refusing to participate in the study, and no further study procedures will be conducted. These individuals will be asked to provide basic information about their reason for declining.

Locator, Enrolment and follow-up visit forms (Appendix F): These forms will be used to obtain and update detailed locator information including questions about contact telephone numbers, usual hangouts, and names of family members/friends who can be contacted for tracking participants and whether the participant agrees to such contact by study staff.

Cross sectional Survey [Baseline (Appendix G and H): and **Cohort Follow-up (Appendix I and J)** questionnaires: These questionnaires will be administered using the PDA and will consist of questions on the following:

- Demographic information to include age, gender, marital status, occupation, employment and educational status. Location of home urban or rural and proximity to national roads and socioeconomic status.
- Psycho-social information to include knowledge/motivational issues, capabilities, social norms and affective states/situational contexts related to sexual risk behaviours
- Behavioural information to include number, type (regular/casual), concurrency of sex partners, condom use, knowledge of own and sex partner(s) HIV status, engagement in transactional sex and exposure to intimate partner violence.
- HIV Status Information. Questions about HIV testing history date of last HIV test, HIV results and current HIV treatment, exposure to and treatment for TB and STIs. Contraceptive use.
- Male Circumcision Status (for males only). Circumcised yes/no; acceptability and access to MMC.

Termination Form (Appendix I and J Part of the follow up survey form). This form will be completed for individuals who have enrolled in the study but discontinue further participation. The reasons for discontinuation will be recorded.

Missed visit Form (Appendix B part of the composition form). This form will be completed for individuals who after exhausting all attempts to contact have failed and have missed the visit.

6.6 RECRUITMENT AND TRAINING OF STUDY STAFF

The field staff will be recruited from the local and neighbouring areas. Based on the applications and the credentials submitted, they will be short-listed and the preferred individuals will be invited to the screening interviews. During the interviews, the prospective candidates will be assessed on their comprehension, interviewing skills, counselling and other skills relevant to the positions they applied for. The phlebotomist and/or nurses will be assessed on the phlebotomy specific practice and procedures. For the supervisors, they will also be assessed on the management skills with focus on their experience in the similar role.

Prior to initiation of the study, and again prior to the follow-up assessments, all study staff will participate in a multi-day study-specific training. The curriculum of the training will cover, but will not be limited to the following: rationale, purpose and scientific objectives of the study; study design and methodology; conduct of study assessments, tracking of participants, completion of study forms, and data collection; staff responsibilities; locating and recruiting participants; procedures for enrolling participants into the study; universal precautions, communication skills, safety in the field, ethical guidelines for research including participants' rights; procedures for obtaining informed consent and confidentiality requirements.

Study staff will receive a hands-on training on data collection and procedures. Role playing and mock interviews will be an essential component of the training and protocol team members will act as both the trainer and the mock respondent. The trainer will take the staff through each step of the interviewing process, from enrolling participants to ending the interview and completing any necessary forms. Within the interview itself, the trainer will demonstrate both the interviewing task being required of them as well as the response task being required of the participant. Question-by-question instructions and the use of any visual or recall aids will be reviewed. Study staff will also be paired together with each taking a turn at interviewing their partner. This method more closely resembles an actual interview and the performance of each staff member can be more carefully monitored as the trainers walk around to observe and provide individual instruction.

Study staff will be given a chance to practice both the English and isiZulu versions of all the assessments in order to discuss and resolve any issues. Study staff responsible for collection of blood samples and conduct laboratory analyses will receive training in universal precautions, sample collection and testing of study samples.

All staff will be trained in Good Clinical Practice (GCP), in Human Subjects Protection (HSP) quality control (QC) and quality assurance (QA), safety, post-exposure prophylaxes (PEP), methods of records keeping, and maintenance of laboratory related study files. There will be additional training days scheduled during the study for refresher training. During these refresher trainings, study staff will review study procedures and discuss any challenges encountered. In addition, all study staff will receive a Field Operations Procedures Manual which will serve as a procedural guide during actual data collection. Additionally, all staff will be required to sign a confidentiality agreement as part of the employee contract**.**

7) STATISTICAL CONSIDERATIONS

7.1 REVIEW OF STUDY DESIGN

HIPSS will establish two sequential cross sectional household representative surveys, 12 months apart. Each cross sectional survey will consist of 10000 individuals to measure established and recent HIV infections and complete baseline assessments. Two sequential cohorts of 6400 HIV negative individuals drawn from the cross sectional sample will be followed up at month 12 to measure HIV incidence. Consenting procedures, baseline assessments and cohort accrual for each survey is

scheduled to take at least 6 to 9 months with a follow-up visit 12 months later, thus the total study duration for the two surveys is expected take a total of 42 months. Whilst data cleaning will continue prospectively, data analysis and write-up will be done in the six month period after the follow-up visits of cohort 2 have been completed.

7.2 ENDPOINTS

7.2.1 Primary Endpoint

The primary endpoint will be HIV status at the 12 month follow-up visit and the date of HIV infection will be assumed to be the midpoint between the last negative HIV test result and the first positive HIV test result.

7.2.2 Secondary Endpoints

The secondary endpoints will be assessed in the cross sectional survey at baseline and in the cohort 12 months later using a combination of laboratory tests (CD4 cell counts, HIV-1 RNA viral load, ARV use, pulmonary tuberculosis, STIs, Hep B and C) and the responses from the interviewer administered structured questionnaires. The questionnaires will be used to assess the factors associated with new HIV infections. HIV incidence from the cohort will be compared to the laboratory HIV incidence estimation.

7.3 ACCRUAL, FOLLOW-UP, SAMPLE SIZE AND STATISTICAL POWER

The HIV incidence rate in the recently conducted longitudinal studies among women from the Vulindlela and the Greater Edendale area was 6.5 and 6.3 per 100 person years respectively. We have little or no data on HIV incidence on men from these districts. However, cross sectional surveys have shown that HIV prevalence is at least 5 times higher in young girls compared to young boys in the 15-24 year age groups and assume a slightly lower population based HIV incidence rate. Table 4 shows the sample sizes required to observe the percentage reduction in HIV incidence based on the assumptions of an HIV incidence rate of 3 per 100 person years; 80% power, 80% of cohort between 14 and 35, 20% HIV prevalence and 15% loss to follow-up

Table 4: Sample size calculations for the two sequential cross sectional surveys and the two embedded cohorts for detecting various levels of reduction in HIV incidence over time.

Reduction in HIV infections	0.4	**0.3**	0.25	0.2	0.15	0.1
Infections required for 80% power	120	**247**	379	631	1189	2828
Person years needed	5000	**9686**	14438	23370	42847	99228
Person years adjusted for loss to follow-up (HIV neg)	5883	**11396**	16987	27496	50411	116746
Number HIV negative in entire cohort	7353	**14245**	21234	34370	63014	145932
Size in entire cohort (i.e both first and second cohort combined)	9192	**17807**	26542	42963	78767	182415

The sample size of the cohort study will have 84% power to detect a 30% reduction in the incidence rate at a 5% significance level given HIV prevalence of 20%, loss-to-follow-up of 15% per annum and an initial HIV incidence rate of 3% p.a. If we enrol 10 000 households we would expect about 80% of the individuals who are included to fall within the age range 15-35. This means that 8000 individuals are eligible to be enrolled in the longitudinal cohort. Among these we expect an HIV prevalence of 20%, thus 6400 individuals will be eligible for the HIV negative cohort. If we assume a loss to follow-up of 15%, 5440 individuals will be expected to have follow-up data in the cohort. With an incidence rate of 3 per 100 person years in the first cohort and an incidence rate 30% lower in the second cohort, we will observe 277 HIV infections in the two cohorts combined. Table 5 shows the sample size calculation based on 10000 households. We assumed a low design effect, because we believe that the enumeration areas are not very heterogeneous, and we are including only one person from each household. In addition, we have a relatively small number of households in each of the enumeration areas. We set the design effect at 1.1. This means that we will have 84% power to detect a difference of 30% between the two cohorts.

Table 5: Number of enrolled participants, required to achieve the targeted effective number of person years.

	Time point	
	T1 and T2	**T3 and T4**
Cross sectional survey (Baseline) (age range 15-49 years)		
Number at baseline	10000	10000
HIV Prevalence	20%	20%
Number expected to be HIV negative	8000	8000
Longitudinal follow-up cohort (age range 15-35 years)		
Design effect	1.1	1.1
Number of individuals in the HIV negative cohort	6400	6400
Assumed HIV Incidence rate	3%	3% reduced by 30%
Loss to Follow-up adjustment	15%	15%
Number expected to be retained in cohort	5440	5440
Number of HIV endpoints assumed	163	114
Total number of endpoints assumed across both cohorts	277	
Probability of Correct Inference	84%	84%

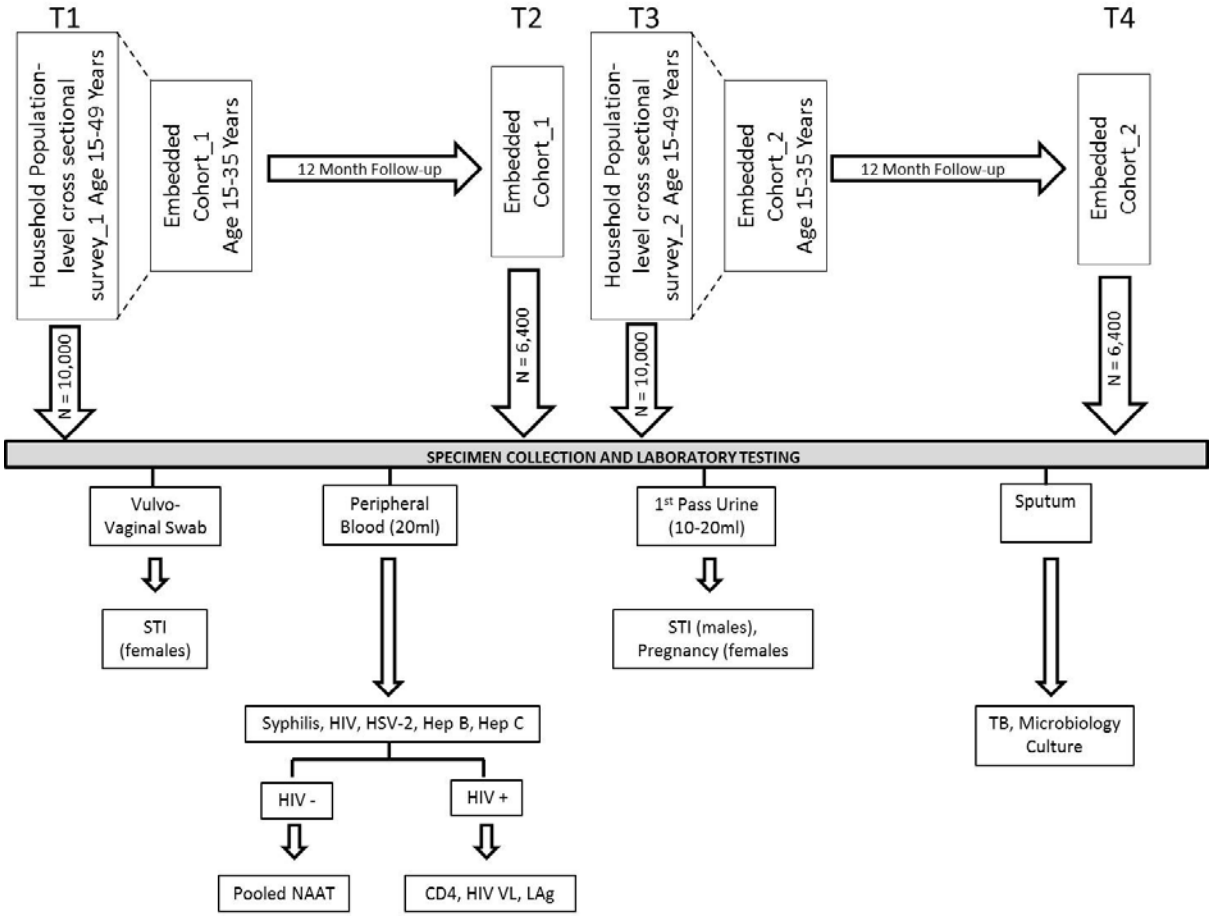
7.3.1 Cohort Accrual

The overall statistical approach follows from the goal of establishing an HIV surveillance platform. The cross sectional surveys will measure established and recent HIV infections. The longitudinal

cohort is a critical platform to estimate HIV incidence in a household-representative sample in two districts in the province of KZN following roll-out and scale-up of HIV prevention and treatment programmes. The random selection of EAs, households and individuals within the household is designed to achieve a district representative sample of individuals to minimise bias.

7.4 LABORATORY

7.4.1 Laboratory Specimens



The following biological specimens will be collected for laboratory testing in the cross sectional survey and at the month 12 cohort follow-up visit:
Peripheral Blood Sample (25mls) or (about 5 teaspoons)

- HIV antibody testing
- CD4 cell count
- Plasma for HIV-1 RNA Viral Load and resistance testing
- Pooled NAAT testing
- HIV recent infection testing using Limiting Antigen Avidity (LAg) assay
- Western Blot (if indicated)
- ARV measurement (if indicated)
- Syphilis serology
- HSV-2 serology
- Hep B and C serology

First-pass urine sample (10-20mls) (males)

- STI testing (*N. gonorrhoeae, C. trachomatis, T vaginalis*, HSV-2 and HPV)

First-pass urine sample (10-20mls) (females)

- Pregnancy testing

Self-collected vulvo-vaginal swab samples (females)

- STI testing (*N. gonorrhoeae, C. trachomatis, T vaginalis*, bacterial vaginosis, HPV and HSV-2)

Sputum sample

- Microbiological culture
- Tuberculosis (TB) Testing: GeneXpert MTB/RIF (Cepheid, Inc)

All remaining samples will be archived for confirmation of any discrepant or uncertain results and for future testing if indicated.

All samples will be transported to the laboratory on the day of collection. During transport, samples will stored in a cooler box. All processing and storage of samples will occur within 6 hours of sample collection. The HIV testing, viral load and CD4 cell count tests will be processed immediately. The remaining samples will be seperated, aliquoted and stored. The laboratory will adhere to standards of good laboratory practice; the study-specific procedures manual; standard operating procedures for proper collection, processing, labeling, transport, and storage of specimens. Specimen collection, testing, and storage will be documented using the laboratory information systems (LIMS), LabWare® as described in the study specific procedures manual. All laboratory testing and storage of samples will be conducted using the unique PID only with no other identifiers on the samples

7.4.2 Laboratory Testing

As described in section 6.1.2 trained phlebotomists will collect samples from participants in the household. The cross sectional and the follow-up month 12 study visits HIV testing procedures will be guided by the HIV testing and interpretation algorithm **(Appendix A)**.

HIV Testing: All samples will be tested with 4th generation HIV enzyme immunoassays (EIAs) to test for HIV antibodies and antigens.

CD4+ cell count measurement: Study participants who test HIV EIA positive will have CD4+ cell count testing.

HIV-1 RNA viral load measurement: Participants who test HIV seropositive will have individual HIV-1 RNA viral load measurements.

Test for Recent infection (TRI) for HIV: Participants who test HIV seropositive will be tested for recency by the LAg Avidity EIA and HIV-1 RNA viral load.

Pooled nucleic acid amplification tests (pNAAT) for HIV: Participants who test HIV EIA negative will have the pNAAT assay performed on plasma samples. Any sample pools testing positive will be disaggregated for individual quantitative testing of HIV-1 RNA. pNAAT will be used in this study to identify individuals with acute HIV-infection who have not seroconverted and therefore do not have detectable antibody. The use of pNAAT for HIV RNA detection is to account for acutely HIV-infected individuals in the absence of HIV antibodies.

Testing for sexually transmitted infections will be conducted on stored samples from the cross sectional survey (baseline) and at follow-up from a first-pass urine sample from males and on self-collected vulvo-vaginal swab samples from females. Serum samples will be screened for active syphilis using the qualitative Rapid Plasma Reagin (RPR) test. All reactive samples will undergo testing with the quantitative RPR and further testing with the *Treponema pallidum* haemagglutination test (TPHA). HSV-2 antibodies will be measured using the Kalon HSV-2 ELISA test.

Testing for Hepatitis B and C infection will be conducted on stored serum samples from the cross sectional survey (baseline) and at follow-up.

Testing for pulmonary tuberculosis will be conducted on sputum samples collected at the cross sectional survey (baseline) and at follow-up for the detection of *Mycobacterium tuberculosis* including rifampicin resistant strains. Pulmonary tuberculosis will be diagnosed by a combination of microbiological culture and the detection of specific *M. tuberculosis* and rifampicin resistance DNA sequences by polymerase chain reaction with the GeneXpert MTB/RIF (Cepheid, Inc).

Testing for HIV-1 genotype resistance test (GRT) will utilise the in-house human HIV-1 GRT which has been considered essential for HIV-1drug resistance monitoring. This assay could provide early diagnosis of drug resistance in patients adhered to antiretroviral therapy and prevent the cause of treatment failure. In addition, GRT results would be an important factor for Highly Active Antiretroviral Therapy (HAART) regimen selection. The in-house GRT includes the entire protease and partial reverse transcriptase region (up to codon 335) in the pol open reading frame. These regions are amplified where the well-defined protease inhibitor (PI) and reverse transcriptase inhibitor resistance-related mutations are positioned. The amplicon is subsequently used as a sequencing template to generate approximately 1.3kb of sequence data. HIV-1 RNA is reversed transcribed using the Superscript III RT enzyme (Invitrogen) and a 1.3kb fragment of the HIV-1 pol gene is amplified by nested PCR using AmpliTaq Gold (Applied Biosystems) and specific primers. Amplicons will be sequenced using the BigDye v3.1 cycle sequencing kit and run on an ABI 3130 automated sequencer. Sequences will then be submitted to the Stanford Drug Resistance Database (http://hivdb.stanford.edu) for the detection of resistance mutations

Testing for ARVs (where indicated) will utilise the High-performance liquid chromatography (HPLC) method for measurement of ARVS. Plasma samples for ARVS will be tested post study and where indicated.

Collection and shipping of specimens
All samples will be collected according to methods described in the manual of operations (MOP) and in the standard operating procedures (SOPs) for proper collection, processing, labelling, and transport of specimens to the laboratories.

7.4.3 Sample Storage and Possible Future Research Testing

All remaining plasma and serum samples from peripheral blood samples collected from each study participant at the time of study entry, seroconversion (if applicable), and study exit will be stored. In addition, study participants will be asked to provide written informed consent and assent for their samples to be stored beyond the end of the study for possible future research testing (Appendix E). Any residual samples of participants who do not consent to long-term storage and additional testing will be destroyed at the end of the study, after all protocol-required and quality assurance testing has been completed.

7.4.4 Quality Assurance of Laboratory testing

Randomly selected archived samples will be sent to the National Institutes of Communicable Diseases (NICD) for quality assurance of HIV testing. All testing will follow laboratory specified protocols which include quality checks and assurance programmes.

The study laboratory plan will include the procedures for sample management (e.g. chain of custody, handling, labelling and transport), assay procedures, proficiency testing and quality assurance procedures and sample storage procedures. Good laboratory practices (GLP) will be followed for all laboratory testing. The MOP will be used for all test and Quality Control procedures. Procedures will be in place for performing and documenting the quality of a sample, including storage under appropriate temperature conditions and transport conditions, monitoring of equipment and temperatures, and function indicators. An effective QA/QC system will be maintained to ensure integrity of the samples will be in place at the laboratory site. Each stored sample will have a unique identifier which is unlinked from the study participant's name. The samples will be stored for ten years.

7.4.5 Biohazard Containment

As the transmission of HIV and other blood-borne pathogens can occur through contact with contaminated needles, blood, and blood products, appropriate precautions will be employed by all personnel in the drawing of blood and shipping and handling of all specimens for this study, as currently recommended by South African guidelines on biohazard containment.

7.5 DATA MANAGEMENT

The use of PDA allows for data collection and real time data entry. Data from the PDAs will be uploaded to the Epicentre server daily. This server will be housed in a secure data centre.

Data quality on PDAs will be assured in the following ways:

- PDA-based questionnaires specifically ensure that study staff completes certain fields with legitimate range of values in each field. Skip patterns are enforced by the PDA. "Illegal" data entries (e.g. vaginal infections being documented for a man) are automatically rejected by the PDA and study staff is prompted about the problem. The PDA has Geographic Information System (GIS) capability which enables field managers to determine that field staff is in the correct EA. The GIS capability also ensures that the field worker is at the correctly sampled household.
- Quality improvement of home-based recruitment, enrolment, informed consent, interviews, data collection, data handling, forms processing, data management and other study operations will be on going. Study staff on a weekly basis will review the key indicators for each of the procedures. Following this any areas of concern will be defined, assessed and the areas of improvement will be verified. The possible solutions will be considered and action plans developed for improvement, including implementation, communication, and measuring/monitoring. The action plans implemented will be further measured and monitored to ensure success.

- The advantage of using PDA as opposed to manually paper based data capture are as follows:
  - Enable the survey team to get the field teams quickly and accurately into the sampled areas and track their progress
  - Field managers are able to track when field teams have entered or left a particular area and monitoring field team travelling habits to prevent abuse (e.g. speeding, travel after hours)
  - Tracking provides a historical record of the fieldwork, for quality control and field payment purposes.
  - Real time data monitoring and quality control. As the data comes from field it will be loaded on a central system and will be quality controlled for accuracy. Any missing data fields will be relayed to the field team concerned and supervisors will need to re-visit the respondent to capture the missing fields.

7.5.1 Data Storage and Disposition

Questionnaire data collected from the field will be stored on the server of the PDA service provider which is housed in the Amazon Data Centre. The server is secure and has state of the art security. The Data is backed up and has built in redundancy. Once a week the questionnaire data (excluding the identifying information such as name, GPS location or finger print) will uploaded onto the CAPRISA server. The only identifying information that will be received by CAPRISA will be the participant identifying number thereby protecting the participant's privacy.

All HIV-related laboratory data will be stored in a dedicated excel spreadsheet designed to reduce the manual entry of data (Appendix M and N). All laboratory results will be merged in the CAPRISA database using the participant identifying number.

The data downnloads will be stored on a secure server in a data management centre at CAPRISA to be jointly maintained by CAPRISA, Epicentre and CDC. The data centre will provide excellent

security and reliability including physical access control, online protection through a firewall to protect against hacking and viruses. The data will be backed up every four hours.

CAPRISA, Epicentre, and CDC will have equal access to the data and access will be a secure logon that is password protected with SMS verification. The user will only have access to the information that they have the rights to view. CDC staff is not engaged and will not have access to participants identifying information.

The name of the participants and the response to the questionnaire will be linked by a bar code and stored in databases to protect participant's privacy.

Once the study is complete a back up of the data excluding the identifying information will be archived and the identifying information deleted from server of the service provider.

7.6 DATA ANALYSIS

7.6.1 Descriptive analyses

Descriptive analyses will include: a description of all eligible individuals refusing participation, screened but refused to participate, individuals consenting and enrolling in the study, including those lost to follow-up.

7.6.2 Analysis of primary objective

To measure HIV incidence at two time points in a household-based representative sample of men and women.

Only participants who tested HIV negative at enrolment will be included in this analysis. The person-years in follow-up will be calculated as the difference between the date of the enrolment HIV test and the 12 month HIV test for participants who tested HIV negative. Where participants tested HIV positive at the 12 month visit the date of HIV infection will be assumed to be the midpoint between the last HIV negative test and the first HIV positive test. To achieve a population HIV incidence rate, the total number of seroconversions will be divided by the total number of person years. The incidence rate will be calculated with a 95% confidence interval. Incidence rates will also be given by age group and sex.

7.6.3 Analysis of secondary objectives

To determine the prevalence of HIV infected individuals, CD4 counts in these individuals and proportion on ART and ART naïve with detectable and undetectable viral load.

The proportion of HIV-infected men and women, in HIV care, ART use, detectable and undetectable viral loads in the cross sectional survey (baseline) will be measured. Logistic regression will be used to compare any engagement in care and any ART use in the HIV infected persons and to assess any differences in proportions in men and women.

To determine changes in the rate of new HIV infections over time

HIV incidence rate will be calculated as described under the primary objective for each of the cohorts. The incidence rate ratio of the two cohorts will be calculated to quantify the change in HIV incidence between the two time periods. A 95% CI will also be given. Poisson approximations will be used to calculate CIs for incidence rates. The CIs for the incidence rate ratios (IRRs) will be calculated using the F-distribution. Comparisons of HIV incidence from the two cohorts over two time points will assume a Poisson distribution of seroconversions in the follow-up time in each cohort.

To determine the association of behavioural and psychosocial factors and exposure to HIV prevention programmes with new HIV infections.

The association of new HIV infections and several predictive variables measured at the baseline cohort survey will be assessed. If the data allows for survival analysis appropriate survival analysis methods will be used to calculate the hazard ratio. However, since there is only one follow-up visit it might also be appropriate to do the analysis using multivariate logistic regression. If the duration of follow-up is similar for most participants the logistic regression will be favoured and of the duration of follow-up varies by many months between participants then survival analysis methods will be used.

Variables collected in the baseline survey could be included in the analysis, including the following: demographic information,(age, gender and area residing in), psycho-social variables, partner characteristics, situational factors associated with sexual practices, sexual behaviours, HCT, MMC, condom use, exposure to behaviour change information, training and communication.

To determine the prevalence and incidence of STIs, Hep B and C

The prevalence of STIs (panel to include gonorrhoea, chlamydia, trichomoniasis, HSV-2 and syphilis, HPV), Hep B and C in the cross sectional survey (baseline) will be calculated overall and individually with 95% CI. The overall prevalence and the prevalence of each STIs, Hep B and C by age and sex and the prevalence of HIV and STIs co-infection will also be calculated. Participants who test negative for STIs, Hep B and C at enrolment will be included for measuring STIs, Hep B and C incidence. The person years in follow-up will be calculated as the difference between the date of the enrolment and at the 12 month follow-up for participants who tested negative for STIs, Hep B and C. Where participants test positive for STIs Hep B and C at the 12 month visit the date of infection will be assumed to be the midpoint between the last negative test and the first positive test. To achieve a population incidence rate, the total number of laboratory confirmed STIs, Hep B and C infections will be divided by the total number of person years. The incidence rate will be calculated with a 95% CI. Incidence rates will also be given by age group and sex.

To determine the prevalence and incidence of pulmonary TB

The prevalence of pulmonary TB (as defined in section 7.4.2) in the cross sectional survey (baseline) will be calculated with 95% confidence intervals (CI). The prevalence of TB by age and sex and the prevalence of HIV and TB co-infection will also be calculated. Only participants who tested negative for TB at enrolment will be included for measuring TB incidence. The person years in follow-up will be calculated as the difference between the date of the enrolment and at the 12 month follow-up for participants who tested TB negative. Where participants test positive for TB at the 12 month visit the date of infection will be assumed to be the midpoint between the last TB negative test and the first TB positive test. To achieve a population TB incidence rate, the total number of laboratory confirmed TB infections will be divided by the total number of person years. The incidence rate will be calculated with a 95% CI. Incidence rates will also be given by age group and sex.

To compare cohort derived HIV seroconversion data with laboratory HIV incidence assay data

The LAg-Avidity EIA assay derived incidence will be compared to the incidence rate derived from the prospective cohort using parameters recommended for the assay. We will use the latest available-at-analysis-time data on false recent rates of the chosen algorithm (using data from CDC and the Consortium for the Evaluation and Performance of HIV Incidence assays, http://www.incidence-estimation.com/page/cephia-overview) to estimate the locally applicable FRR [56]

Assay-based HIV incidence is calculated as the number of recent infections divided by the population at risk (those testing HIV-negative plus those recently seroconverting), then annualized by multiplying by 365 divided by the estimated length of mean seroconversion duration for the assay (or 130 days for the LAg-Avidity EIA assay; 95% CI 118–142 days).

To calculate the incidence as an annual instantaneous rate (I_r) the following formula will be used:

$$I_r = \frac{R - \varepsilon P}{(1-\varepsilon)\omega N}$$

Where the survey counts (N, P, R) are as follows:

N = number of HIV negative individuals in the survey

P = number of HIV positive individuals in the survey

R = number of individuals classified incidence assay positive

The calibration parameters are as follows:

ω = mean incidence assay duration specified in units of years

ε = false recent rate (FRR) of the incidence assay

Confidence intervals are computed using a delta method approximation which may include the error, assumed to be normally distributed, associated with calibration parameters. The coefficient of variation (C_v) is computed as follows:

$$C_v = \sqrt{\frac{1}{P}\left(\frac{N+P}{N} + \frac{(P-R)R[1+\varepsilon/(1-\varepsilon)]^2}{[R-\varepsilon/(1-\varepsilon)(P-R)]^2}\right) + \frac{\sigma_\omega^2}{\omega^2} + \frac{\sigma_\varepsilon^2 (P-R)^2}{(1-\varepsilon)^4[R-\varepsilon/(1-\varepsilon)(P-R)]^2}},$$

where

σ_ω is the standard deviation of the mean RITA duration (assumed normally distributed)

σ_ε is the standard deviation of the FRR (assumed normally distributed).

The 95% confidence interval (CI) for I_r is then computed as:

$$I_r \pm 1.96 \times I_r C_v$$

To determine the community HIV viral load

Community HIV viral load is the mean viral load measurement of a community and can be used as an indicator of continued HIV transmission and ART uptake and coverage within a community. The community viral load in this study will be calculated as the arithmetic mean and will provide a baseline measurement for future HIV and ART surveillance.

To determine the levels of transmitted HIV drug resistance

Rates of transmission of resistance will be determined by calculating point prevalence with confidence intervals according to threshold levels of low (<5%), moderate (5-15%) and high (>15%). All 277 expected incident cases will be genotyped and sequences analyzed

7.6.4 Additional analyses

Sexual risk behaviour will be described for participants in the cross sectional survey (baseline) and at the follow-up visits. This analysis will be conducted in both HIV-infected and HIV-uninfected participants and results will be given by age and sex.

7.6.5 Controlling for potential confounding variables

For all analyses of the primary outcome, we will control for potential confounding variables by either stratification or including the variable(s) as covariates in the multivariate analyses.

8) STUDY MONITORING

8.1 MONITORING AND EVALUATION OF STUDY PERFORMANCE

HIPSS Steering Committee consisting of the PI and the protocol team members will ensure that the study's implementation and follow-up is scientifically sound, ethical, and of high quality. The members of the CAPRISA Research Support Group will contribute to the informed consent procedures, questionnaire design and administration, play a key role in monitoring a random number of informed consent procedures and will monitor the assent procedures for participants <18 years of age. The committee will meet quarterly or more or less frequently if needed either through face to face meeting or through teleconference to review the study and updated information. Any necessary adjustments to the study /cohort sample sizes, cohort follow-up durations, time period between surveys/cohorts, or other additions /modifications to the study will be at the discretion of the Principal Investigator and the protocol team. Study team meetings will be held weekly to monitor progress and to resolve any operational challenges.

The study will be monitored by the Study Quality Assurance Team. The monitoring will be undertaken according to the Study Quality Assurance Plan and will consist of on-going monitoring of study progress and safety of study participants by the Protocol Team in accordance with ICH, GCP guidelines. The Investigators will allow CDC study monitors to inspect study facilities and documentation (e.g., informed consent forms, clinic and laboratory records, other source documents and data collection instruments eg PDAs), as well as observe the performance of study procedures. The Investigators will also allow inspection of all study-related documentation by study sponsors. Study monitoring will be conducted by staff adequately trained on this study. Monitoring shall commence shortly after enrolment of the first participant and at regular intervals thereafter. Any issues or findings related to participants' safety or any compromise on scientific integrity will be reported immediately to the PI or designee.

8.2 INTERIM REVIEWS AND ANALYSIS

Study operations will be reviewed by a study monitoring committee to assess study conduct, timelines and study quality. Reviews are planned annually, with additional reviews as needed on an ad-hoc basis.

8.3 LIMITATIONS OF STUDY

We anticipate a 15% annual lost-to-follow-up rate among cohort participants at follow-up due largely to employment related movements or migration. There is a possibility that those who migrate and those who do not are different from each other in meaningful ways related to HIV infection risk. We have mitigated the effect of the migration on the evaluation by incorporating lost-to-follow-up into study calculations to ensure sufficient power is maintained.

Data on sexual behaviours (such as past/current number of partners, condom use, etc.) and history of STI symptoms will be self-reported and are thus subject to potential recall and social desirability bias. However, efforts will be made to ensure that the study staff recruiting, enrolling, interviewing and performing the blood sample collection will not be from within the community to minimise reporting

bias, concerns about stigma and disclosing personal information during data collection. There is also a possibility that self-reported exposure to prevention programmes may be incorrect.

Persons who are in institutions such as prisons are not included in the study; persons who are transient and thus not at home during enrolment are also not captured.

9) HUMAN SUBJECTS CONSIDERATIONS

9.1 ETHICAL CONSIDERATIONS

The study will be conducted under the oversight of the University of KwaZulu-Natal's Biomedical Research Ethics Committee (BREC) Internal Review Board (IRB). No study activities will begin until all approvals have been obtained. Subsequent to the initial review and approval, BREC will review the protocol at least annually. The study protocol, informed consent forms, participant recruitment materials, and other requested documents will be reviewed and approved by BREC. Any future amendments will be conducted in full compliance of BREC requirements prior to implementation. Study staff will make every effort to protect study participants privacy and confidentiality and provide support and referral to external agencies should this be required.

9.2 INFORMED CONSENT PROCESS

Verbal consent will be obtained from the head of the household for the household composition assessments. The head of the household will be informed that he/she will be compensated with an item to the approximate value of R10 for responding to the household composition form. Each potential study volunteer will be informed about the study and complete the English or isiZulu consent form prior to enrolment, in accordance with 21 CFR Part 50 and ICH GCP guidelines. The study volunteer will be informed that he/she will compensated with an item to the approximate value of R25 for their time should they wish to continue with study participation and for responding to the demographic, behavioural questionnaire and for the collection of biological samples. The consent / assent forms that will be used in this study are:

- Individual consent form for participants 18 years and older
- Parental/guardian consent for participants 15-<18 years of age
- Individual assent form for participants 15-<18 years of age
- Sample storage consent form

All consent forms and data collection forms will be translated from English into isiZulu. Back translations will also be completed and reviewed by a bilingual independent source in order to ensure accuracy of translated information. Before beginning the informed consent process, the potential volunteer will be asked to select a relatively private location either inside or outside their home, so that the study activities may be conducted in as much privacy as possible, as appropriate. The informed consent discussion will take place in either English or isiZulu. Participants will be given the opportunity to choose their preferred language. Prior to initiation of any study procedures, all potential volunteers will be given a printed copy of the consent form in either English or isiZulu depending upon their preference. A staff member will then read the consent form aloud to the participant. At this time, potential participants will be informed that their participation in the study is voluntary and that they may withdraw at any time. Withdrawal from the study will have no effect on the participant's access to health facilities or HIV related care in the district. Further, participants will be informed that they do not have to answer questions that make them uncomfortable and that any information that they disclose during the course of the study will be considered confidential (i.e., no personal identifiers will be used and only summary information across all participants will be

reported). Participants will have the potential risks and benefits of the study explained to them as well. After the consent form has been read aloud, potential volunteers will be invited to ask questions about any aspect of the study and their participation. If they agree to participate in the study, literate participants will document their provision of informed consent by signing their name on the consent document. Non-literate volunteers will be asked to identify a person that they would be comfortable to serve as an impartial witness to support them through the consent process after which the volunteer could provide a fingerprint to indicate consent and to be signed by the witness. Volunteers will be provided with a copy of their informed consent form, should they wish to receive it.

The study team will involve the community in establishing recruitment procedures through its community engagement strategies. The study team will draw on its prior experience with this community through its Community Research Support Group (CRSG) by disclosing information in culturally and linguistically appropriate formats. The study team will work with the community to obtain assents / consent in culturally and linguistically appropriate formats. As per South African Laws and Guidelines, the team will seek parental / guardian consent and individual assent from all individuals who are <18 years of age. We estimate that about 20% of the individuals will be <18 years of age, and will require parental /guardian consent. It is anticipated that some <18year olds will not have a parent, or legal guardian, available to provide consent, e.g. migrant, sick hospitalised or deceased parents and in such instances we will identify a care giver / "guardian" of the child, who will then provide consent for that child's participation in the research.

9.3 FINGERPRINT SCANNING

All eligible participants will be asked to provide a finger print. The finger print device will be attached to the mobile data collection device. The finger print will be scanned and stored on the data collection server with the identifying information. At the second visit during the participants identification will be verified using the stored finger print. We will be integrating biometric verification capabilities (via fingerprint scanning) into our Android mobile application. The figer print devices will be configured to support the a USB fingerprint scanner will be connected directly to the fieldworker's device. Software installed on the fieldworker's device to handle fingerprint extraction and matching. The participants will be informed on the purpose of the collection of the finger print and that these fingerprints will not be used for any other purposes.

9.4 POTENTIAL RISKS

The study protocol involves minimal risk to participants ie the collection of peripheral blood samples. As part of this study, participants will be asked questions on personal information and sensitive topics, including sexual behaviour, HIV status, access to care and treatment for HIV and male circumcision. It is possible that some individuals may experience discomfort from taking part in these study activities. Study staff will be trained to address any potential stress or discomfort that may result from study participation and to help make participants feel comfortable. As part of the informed consent procedure, all potential participants will be informed that they do not have to disclose personal information which they are uncomfortable sharing and that they can withdraw from the study at any time. There is a potential risk for participants to be "presumed" to be HIV positive by community members as study staff makes household visits for the survey. We plan on minimising these misconceptions through extensive and on-going community engagement process informing the community on the planned survey. Volunteers who may be HIV-infected may not have disclosed to family members and therefore feel distressed in responding to questions related to HIV. However, study staff will support study participants assuring them that all responses and information will remain confidential

There could also be a slight risk of discomfort to participants associated with blood collection. Feelings of discomfort could include feeling ill and/or having injection site complications such as slight bruising or tenderness. Study staff will be trained in how to deal with these complications and will refer participants to local health facilities for additional care, as needed. Although every effort will be made to keep volunteer information confidential, complete confidentiality cannot be guaranteed. Participants will be informed of this potential breach of confidentiality as part of the informed consent process. Study staff will be trained in maintaining confidentiality of study participants and of any information collected.

9.5 POTENTIAL BENEFITS

Participants would benefit from the study through receiving information on HIV and getting a broader understanding of HIV in the community, information on accessing general health care. Participants would benefit from this study as it would be possible for early referral to HIV counselling and testing services. In addition study staff would refer participants for management of HIV, TB, pregnancy or any other minor ailments, if necessary. Participants could also benefit from these referals as they would be able to access care and treatment much earlier.

Societal benefits of this study include gaining a better understanding of the methods to minimise HIV acquisition. The study will also contribute to the understanding of whether risk compensation is an unintended consequence of large-scale HIV prevention programs. In addition information from study participants will help refine projections of HIV infections that may be averted from prevention programs and the potential costs savings realized, compared to HIV care and treatment costs. The main member of the household completing the household composition form will receive a gift valued at R10 (+/-$1) Enrolled participants will receive an item to the approximate value of R25 (+/-$3) to compensatefor their time at each visit.

9.6 CONFIDENTIALITY

All study staff will receive training on procedures to protect participant confidentiality and Good Clinical Practices (GCP). In order to protect confidentiality, each participant will be assigned a unique study participant identification number (PID) so that their name is not linked to any of their personal data or laboratory results. The PID will be written on all data collection forms, HIV test results and will be matched only by this identification number, not by participants' names or other identifying information. A master list with each participant's name and their assigned identification number will be created and will be accessible to the Study Coordinator or designee

The master list will be securely maintained in password protected file at the local data management centre. All study data, including lab results, will be stored securely in the study offices. All databases will be encrypted and password protected. Study data will be accessible only to study staff directly involved in this study. Personal locating information, including participant's name, address and phone numbers, will be stored separately from study data in a filing cabinet in a secure room in the office.

All study consent forms will include the contact information of Principal Investigator and local IRB if participants have questions about the study; if they wish to withdraw themselves as a participant; if they have concerns about their rights as a study participant; or if they believe that have been harmed by the study. All staff that through the course of their work have knowledge of or access to personal information about participants will be required to sign a confidentiality agreement as part of their employee contract.

For this study extensive information will be collected from study participants, these include personally identifying or potentially identifying information such as GPS coordinates, address, first names, family or friends names, listing of family members sensitive sexual and behavioural information. Given the sensitive nature of all these data, study staff will be trained so as not to divulge

any study related information to any person/s outside of the study team. In addition study related information will be delinked and stored with staff having limited access to such information.

9.7 IDENTIFYING, MANAGING, AND REPORTING ADVERSE EVENTS

As HIPSS is an observational cohort study, standard adverse event (AE) reporting will not be undertaken; there are no anticipated adverse events. All unanticipated problems will be documented and immediately reported to the Principle Investigator. These unanticipated problems will be discussed and a verbal and/or written action plan will be devised and implemented within 48 hours of the initial report. The study team will maintain written documentation on all events, including details of the action plan and event resolution. If necessary, a formal report will be sent to BREC and to reported to CDC on the CDC's Incident Report Form 1254. Reporting of unanticipated problems will be the responsibility of the Principal Investigators of this study and all procedures will be included in staff training.

9.8 ACCESS TO CARE AND SERVICES

As this study is determining the DOH and PEPFAR partner programmes associated with changes in HIV infections over time, study staff will remind participants on where they could access health care and any other social support services. Details of linkage to care and referrals are in Section 6.1.3

9.9 COMMUNITY PARTNERSHIP

CAPRISA has established its presence in the area since 2001 and has created strong community programmes. Through the teams consultative and advocacy engagements, a strong Community Research Support Group (CRSG) has been established. The CRSG membership includes local community leaders, traditional leaders, leadership of local HIV/AIDS organisations, previous study participants, local health service provider representatives and HIV positive local community members. The CAPRISA community programme in partnership with the CRSG's are involved in creating and awareness on HIV, STIs, and HIV related research studies, HIV treatment and impact of HIV treatment at a community level. Similarly the CRSG members are actively involved in reviewing all study documentation; inform the community and other community organisation in the districts on CAPRISA related studies and will do the same for HIPSS. Thus the CRSG members play a key role in being the interface between the researchers and community members serving as advocates for the community's best interests and ensuring that the researchers are aware of any concerns within the community about the research being conducted. The CRSG also plays an important role in reviewing study educational materials, consent forms and Zulu translations of documents to be shared with study participants.

9.10 STUDY RECORDS

Complete, accurate, and current study records will be maintained and stored in a secure manner, throughout the study. All study records will be maintained for a period as required by the funders.

9.11 PROTOCOL DEVIATIONS/NEW & UNEXPECTED FINDINGS/CHANGES TO THE STUDY ENVIRONMENT

All protocol deviations, new/unexpected findings and changes to the study environment will be documented and immediately reported to PI and or designate. If necessary, a formal report will be sent to the appropriate IRBs. Reporting of such incidents will be the responsibility of the PI of this study. Any discussions, issues, and complaints related to the study will be reviewed promptly to ensure close monitoring of the impact of the study on participants. Appropriate action will be taken to resolve or deal with all issues accordingly.

10) DISSEMINATION, NOTIFICATION, AND REPORTING OF RESULTS

10.1 USE OF INFORMATION AND PUBLICATIONS

All abstracts and manuscripts developed in line with the study's' primary and secondary objectives for presentation at conferences and publication in peer-reviewed scientific journals will be in collaboration with investigators from the study. Analysis of data to answer novel research questions will be governed by CAPRISA, CDC and Epicentre policies.

Written material summarizing the findings from this study will be made available to participants and study staff upon completion of the study.

11) APPENDICES LIST

Appendix A:	HIV testing and interpretation algorithm.
Appendix B:	Household Composition Form (including household refusal, missed visit)
Appendix C:	Workflow diagram of the Study in the field
Appendix D:	Partcipant Information sheet and Informed Consent and Assent forms for enrolment
Appendix E:	Partciant Information sheet and Informed Consent and Assent forms for sample storage
Appendix F	Participant Identification Form
Appendix G	Female Cross Sectional Questionnire
Appendix H	Male Cross Sectional Questionnire
Appendix I	Female Cohort Questionnire
Appendix J	Male Cohort Questionnire
Appendix M	HIV Serology Testing Data Management Tool (Excel File)
Appendix N	HIV Limiting Antigen Avidity EIA Data Management Tool (Excel File)

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APPENDIX A - HIPSS HIV TESTING ALGORITHM

The purpose of the laboratory testing for HIV is to classify participants identified as HIV positive from the cross sectional surveys as either having recent or established infections. In the cohort HIV seroconversion will be confirmed in those having tested negative at baseline and testing positive at follow-up, 12 months later. Detailed methodology for the testing is described in the MOP.

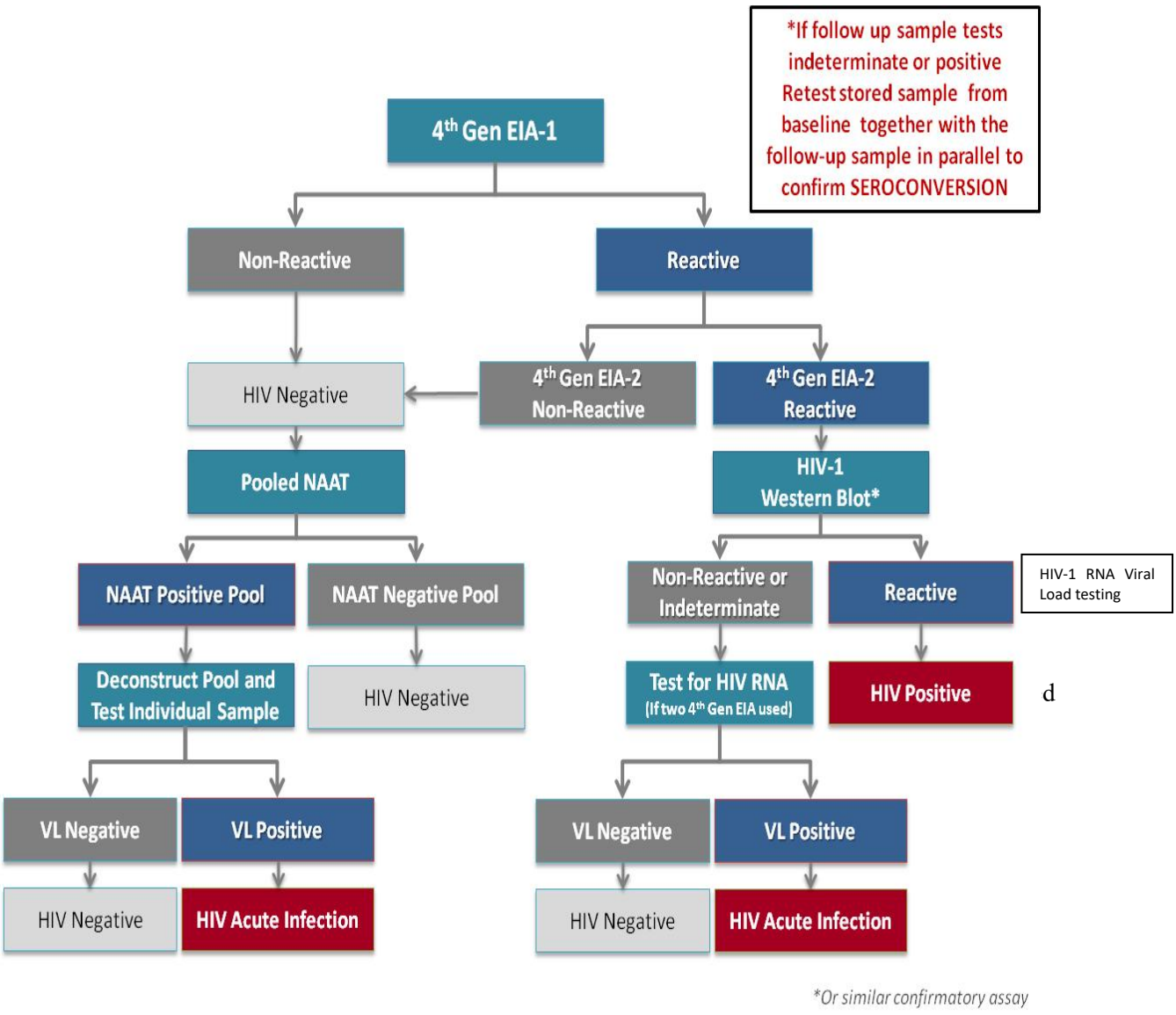
Figure 1 shows the testing and interpretation algorithm for HIV serology and NAAT testing

Figure 2 shows the collection of specimens and tests to be performed.

Figure 3 shows the limiting antigen aviditiy EIA testing algorithm

Figure 4 illustrates the South African Department of Health, HIV Counselling and Testing Algorithm

Figure 1- HIV Testing Algorithm



Viral Load testing

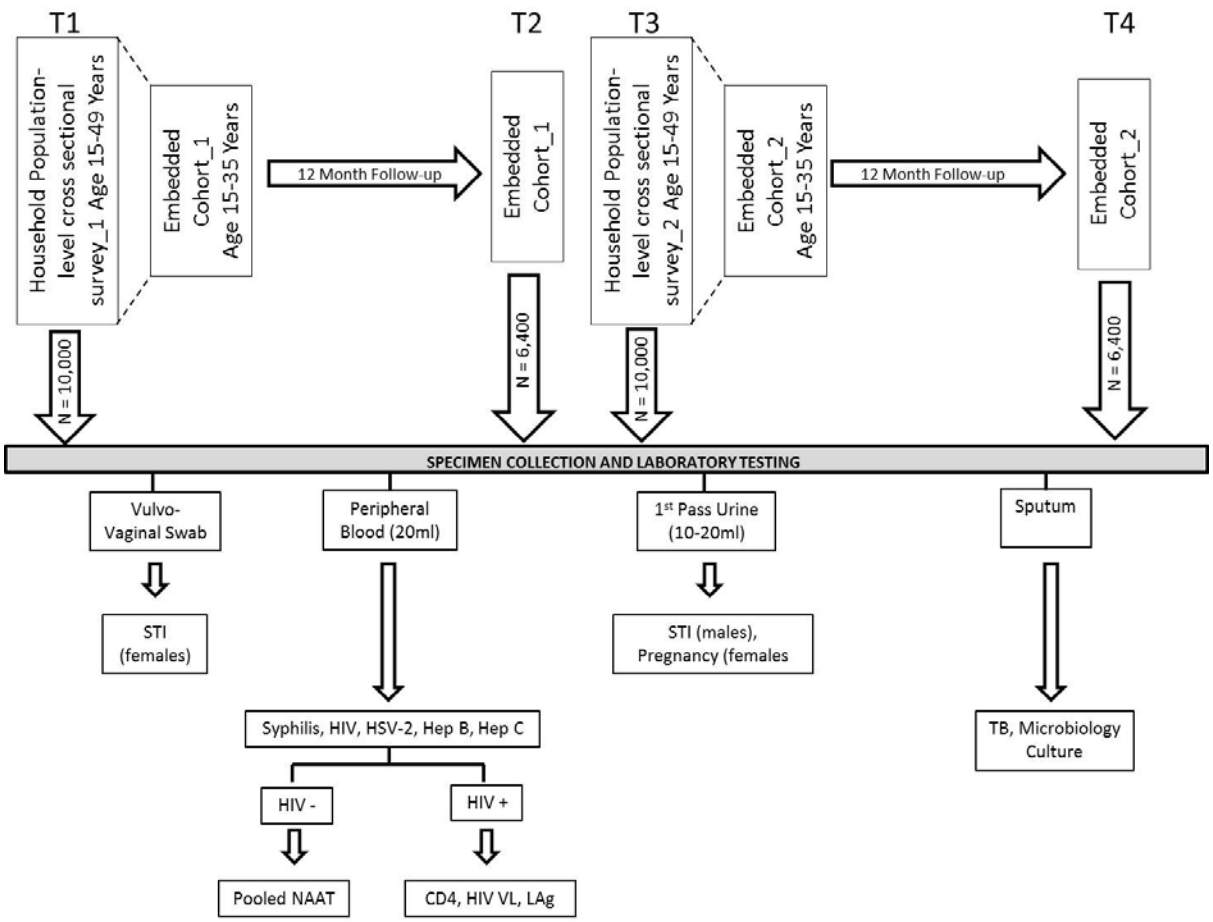


Figure 3: Limiting Antigen Avidity EIA Testing Algorithm

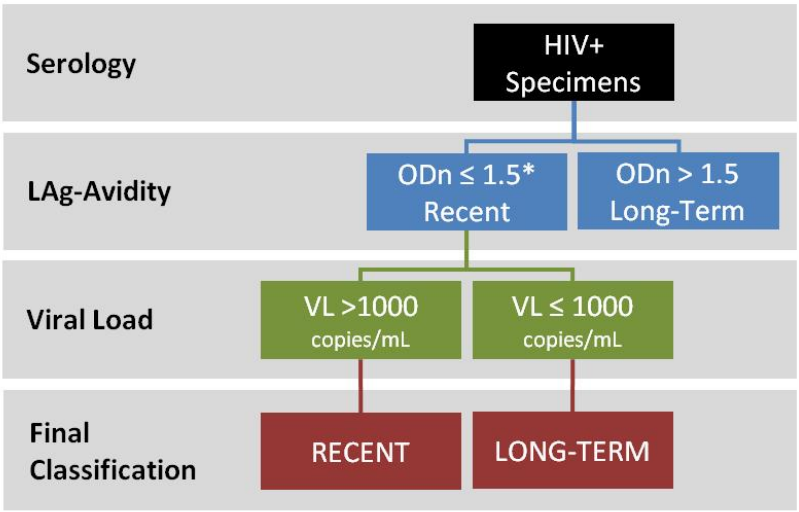


Figure 4: South African Department of Health, HIV Counselling and Testing Algorithm

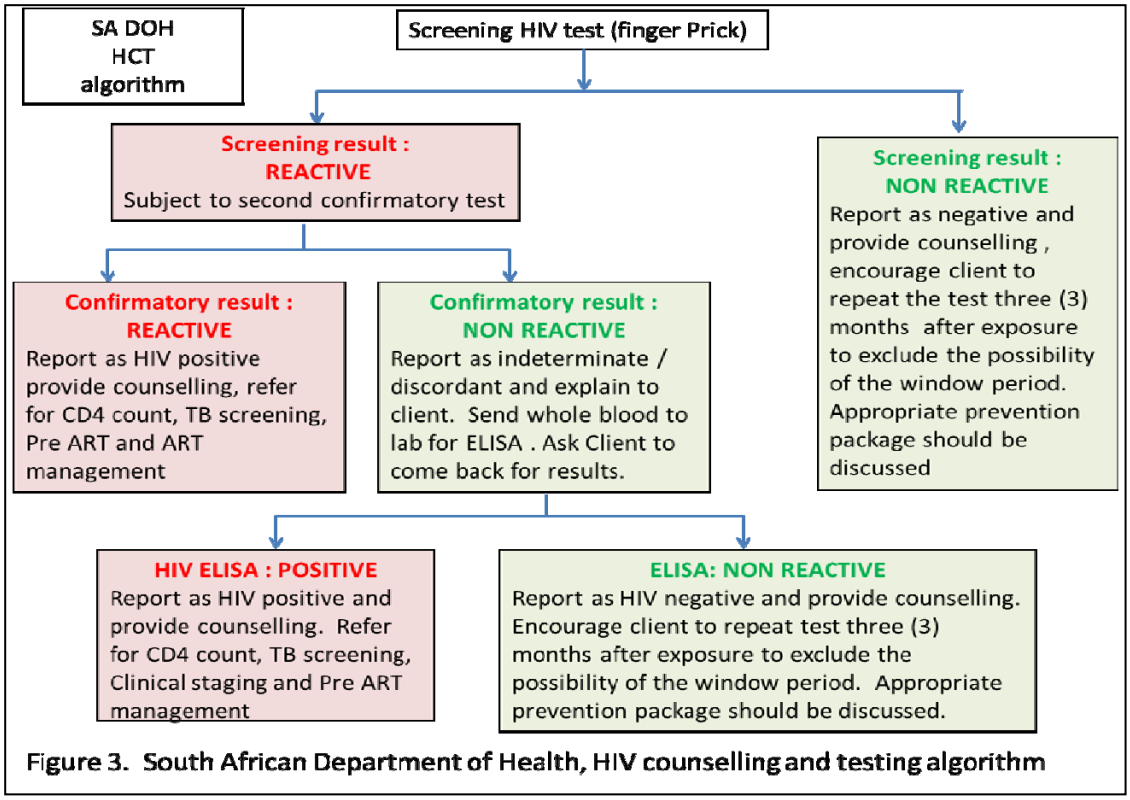


Figure 3. South African Department of Health, HIV counselling and testing algorithm

APPENDIX B - HOUSEHOLD COMPOSITION FORM

Title of Study: HIV Incidence Provincial Surveillance System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa

Section 1 – Household Identification

HH ID number		GPS coordinate	
Team ID		Supervisor	
Attempts to survey household			
1. Date	Time DD/MM/YYYY	Time DD/MM/YYYY	Time DD/MM/YYYY
2. Staff ID			
3. Result *			
4. Next visit Date and time			

	5.1 Member Selected (1):	5.2 Enrolment status (1)**
	5.3 Replacement Selected (2):	5.4 Enrolment status (2)**

***Result options:**
a) 1-members listed, 2-HH refused, 3-HH absent for extended time, 4-vacant or destroyed → replace HH (all replacement HHs must be signed off by supervisor).
b) 5-postponed, 6-no one at home → repeat visit and record preferred time of day for the repeat.

**** Enrolment Status**
(Rule: if 1st HH member refuses replace with 2nd selected member, if 2nd member refuses replace HH)
1-consented, 2-refused + replaced, 3-refused+HH replaced 4-not found + replaced 5-not found + HH replaced.

Section 2 – List Household members (ask for each member of the HH)

List the household members defined as an individual who:

- has been sharing a physical structure such as a compound or homestead and who has been consuming or making some contribution to food and other shared household resources;
- is a person listed by the head of household as being a household resident (but not a guest who stayed in the house the prior night) on the Household Composition Form (Appendix B)
- any household resident who commutes for various time periods
- any person who is not related to the family but considered to be a guest/s who stayed at the household overnight ***will not be considered as a household resident and excluded from participating in HIPSS;***

18 years and older starting with the oldest member

First name	Age	Gender (Male/Female)	Relationship to head of house?*	What is their education status?**	Have you been involved in any income generating activities in the last 7 days?[1]	What is their employment status?***	Do they receive any grants – which grant?****	Selected	Enrolment Status

[1] The definition of employment is such that if an individual has engaged in work related activities in the last 7 days, they are considered employed (Stats SA)

* **Relationship to head of HH** - 01 = Head, 02 = partner, 03 = child, 04 = Son-in-law or daughter-in-law 05 = grandchild.06 = parent 07 = Parent-in-law 08 = brother/sister, 09 = niece/nephew, 10 =other relative, 11 = adopted/foster/ step child 12 = not related, 98 = don't know

** **Education**: 1-No schooling/ crèche/ pre-primary, 2-Primary (grade 1 – 7), 3-Incomplete secondary (grade 8 – 11/NTC1/NTC2), 4-Completed secondary (grade 12/NTC3), 5-Tertiary (diploma or degree with completed grade 12)[2].

***Employment status:** 1-Student not working, 2- House wife, 3-Retired, 4-Illness, invalid, disabled or unable to work, 5-Part time worker, 6-Cannot find any work, 7 – Retrenched., 8- Contract worker e.g. Mine worker resting according to contract, 8- other specify _____.

****Grant type:** 1-Old-age grant, 2-Disability grant, 3-Child-support grant, 4-Care dependency grant, 5-Foster child grant, 6-War veterans' grant, 7-Grant-in-aid, 8-Social relief of distress grant.

[2] Source: Leibbrandt et al 2010

Less the 18 years of age

First name	Age	Relationship to head of house*	What is their education status?**	Have you been involved in any income generating activities in the last 7 days?[3]	What is their employment status? ***	Do they receive any grants – which grant?****	Do they live with their mother?	If no, is their mother alive?	Do they live with their father?	If no, is their father alive?	Selected	Enrolment Status

* **Relationship to head of HH:** - 01 = Head, 02 = partner, 03 = child, 04 = Son-in-law or daughter-in-law 05 = grandchild.

[3] The definition of employment is such that if an individual has engaged in work related activities in the last 7 days, they are considered employed (Stats SA)

06 = parent 07 = Parent-in-law 08 = brother/sister, 09 = niece/nephew, 10 =other relative, 11 = adopted/foster/ step child 12 = not related, 98 = don't know

** **Education:** 1-No schooling/ crèche/ pre-primary, 2-Primary (grade 1 – 7), 3-Incomplete secondary (grade 8 – 11/NTC1/NTC2), 4-Completed secondary (grade 12/NTC3), 5-Tertiary (diploma or degree with completed grade 12)[4]

***Employment status: 1-Student not working, 2-House wife, 3-Retired, 4-Illness, invalid, disabled or unable to work, 5-Part time worker, 6-Cannot find any work, 7 – Retrenched., 8- Contract worker e.g. Mine worker resting according to contract, 8- other specify _____.

**** **Grant type:** 1-Old-age grant, 2-Disability grant, 3-Child-support grant, 4-Care dependency grant, 5-Foster child grant, 6-War veterans' grant, 7-Grant-in-aid, 8-Social relief of distress grant.

[4] Source: Leibbrandt et al 2010

Section 3 – HH economic status

Definition of a household: Share the same resources (income contribution and cooking pot).

1. Indicate the main source of water for this household.[5]	
☐ Piped (tap) water in dwelling/house ☐ Piped (tap) water in yard ☐ Borehole in yard ☐ Rain-water tank in yard ☐ Neighbour's tap ☐ Public/communal tap ☐ Water-carrier/tanker	☐ Borehole outside yard ☐ Flowing water/stream/river ☐ Stagnant water/dam/pool ☐ Well ☐ Spring ☐ Other (specify)_____ ☐ No response
2. What type of toilet facility is used by this household?[6]	
☐ Flush toilet connected to a public sewerage system ☐ Flush toilet connected to a septic tank ☐ Chemical toilet ☐ None	☐ Pit latrine/toilet with ventilation pipe ☐ Pit latrine/toilet without ventilation pipe ☐ Bucket toilet ☐ Other (specify)_____ ☐ No response
3. What is the main source of energy/fuel for this household?[7]	
• Electricity from mains • Electricity from generator • Gas • Paraffin • Wood • Coal	☐ Candles ☐ Animal dung ☐ Solar energy ☐ Other, (specify) ☐ None ☐ No response

[5] Used in the General Household Survey, and NIDS and Africa Centre
[6] Used in the General Household Survey, NM HIV survey and Africa Centre
[7] Used in the General Household Survey, NM HIV survey and Africa Centre

4. What is the main source of income of this household[8]	
☐ Salary and/or wages ☐ Remittance (migrant worker sending money home) ☐ Pension or grants	• Sales of farming products • Other non-farming income • No income • Other (specify)_____ • No response
5. Does anyone in this household receive a social grant, pension or social relief assistance from the Government?[9]	
☐ No ☐ No response	• Yes (list grants received and number) ☐ Old-age grant _____number ☐ Disability grant_____number ☐ Child support grant_____number ☐ Care dependency grant_____number ☐ Foster child grant_____number ☐ War veterans grant_____number ☐ Grant-in-aid_____number ☐ Social relief of distress_____number ☐ Did not respond
6. What is the TOTAL MONTHLY INCOME in this household before tax? Please include all sources of income i.e. salaries, grants, pensions, income from investment, etc. [10]	
☐ No income ☐ R1 – R500 ☐ R501-2,500 ☐ R2,501-6,000	• R6,001-16,000 • R16,001-30000 • Greater than R30,000
7. Does your household owe money to the bank or micro lender?	
☐ No ☐ Owe less than R500	• Owe R1,001 – 1,500 • Owe R1,501- 2,000

8 Used in Labour Force Survey
9 Used in the General Household Survey
[10] Used in the Labour Force Survey, (HSRC HIV survey asks for open ended question total income HH____)

☐ Owe less between R501 to 1,000	• Owe more than R2,000 • Did not respond
8. Does your household have money saved in a bank or in a stokvel?	
☐ No ☐ less than 500 ☐ between 501 to 1,000	• Between R1,001 – 1,500 • Between 1,501- 2,000 • More than R2,000 • Did not respond
9. Do any of the household members own at least one of these items?[11] (select each item owned).	
☐ Radio ☐ Hi-Fi stereo , CD player, MP3 player ☐ Television ☐ Satellite dish ☐ Video cassette recorder, DVD player ☐ Computer ☐ Camera ☐ Cell phone ☐ Electric stove ☐ Gas stove ☐ Paraffin stove ☐ Microwave ☐ Kettle ☐ Fridge/freezer	☐ Washing machine ☐ Sewing/knitting machine ☐ Lounge suite ☐ Private motor vehicle in running condition ☐ Commercial motor vehicle in running condition ☐ Motorcycle/scooter ☐ Bicycle ☐ Donkey cart or ox cart ☐ Plough ☐ Tractor ☐ Wheelbarrow ☐ Livestock ☐ Hoe, spade or garden fork

[11] Assets (durable goods) serve as an indicator of socio-economic status. LSM standard question This question was asked in HSRC HIV survey, Africa Centre

Section 4 – Food security

10. Did your household run out of money to buy food during the past year?[12]	
☐ No ☐ Did not respond	• Yes → Has it happened 5 or more days in the past 30 days? ☐ No ☐ Yes ☐ Did not respond
11. Did your household cut the size of meals during the past year because there was not enough food in the house?	
☐ No ☐ Did not respond	• Yes → Has it happened 5 or more days in the past 30 days? ☐ No ☐ Yes ☐ Did not respond
12. Did your household skip any meals during the past year because there was not enough food in the house?	
☐ No ☐ Did not respond	• Yes → Has it happened 5 or more days in the past 30 days? ☐ No ☐ Yes ☐ Did not respond
13. Did your household eat a smaller variety of foods during the past year than you would have liked to, because there was not enough food in the house?	
☐ No ☐ Did not respond	• Yes → Has it happened 5 or more days in the past 30 days? ☐ No ☐ Yes

[12] Used in HH survey

	☐ Did not respond
14. Does your household have a vegetable food garden	
☐ No ☐ Currently planting a garden	• Yes
15. Is any member of your household attending a financial education support groups or programme?	
☐ No ☐ Currently planting a garden	• Yes

Section 5: Household access to health services and health status

16. Has any member of this household accessed general health care services in the last 12 months? [13]	
☐ No ☐ Did not respond	• Yes → Where do they normally go? ☐ Government Hospital - Edendale ☐ Government Hospital -Northdale ☐ Government Hospital -Greys ☐ Government Clinic (provide list) ☐ Caprisa - Vulindlela clinic ☐ Mobile unit ☐ Private hospital ☐ Private Doctor ☐ Workplace clinic ☐ School clinic ☐ Sangoma/inyanga ☐ Faith-based healer ☐ Other _____
17. Do any household members have a mental disability?	
☐ No ☐ No response	☐ Yes ☐ Mental illness____no. ☐ Intellectual disability____no.

[13] CAPRISA standard questions used in this geographical area

18. Do any household members have a physical disability?	
□ No □ No response	□ Yes → Which disabilities are they suffering from? □ □ Diabetes/blood sugar _____number □ A stroke_____number □ High blood pressure, _____number □ No sight, _____number □ No hearing, _____number □ No speech, _____number □ Asthma, wheeze, emphysema___number
19. Has any of the household members had TB in the last 12 months?	
□ No □ No response	• Yes → How many_____

Section 6- Household change in composition & deaths

20. Has the number of people living in this household changed in the last 12 months?	
□ No □ No response	• Yes → Increased by_____ → Decreased by _____
21. Has anyone died in this household in the last 12 months?	
□ No □ No response	• Yes → How many _____

22. Answer the following question for each person who died.					
What was the age at their last birthday of the person who died?	Relationship to head of the household? (see list)	What was their gender? (Male/Female)	What did they die of (Violent cause i.e. Road accident/assault or poor health)?	What symptoms did they have (see list, can pick more than one)? *	Did they contribute financially to this household? (yes/No) **

***What symptoms did they have :** Weight loss, Diarrhoea, Night sweats or Prolonged Fever, Oral Thrush , Vulvo vaginal thrush , Pulmonary TB, Pneumonia, Dementia, Painful or burning feet, Skin problems, Bedridden for more than 50% of the time in their last month, No response.

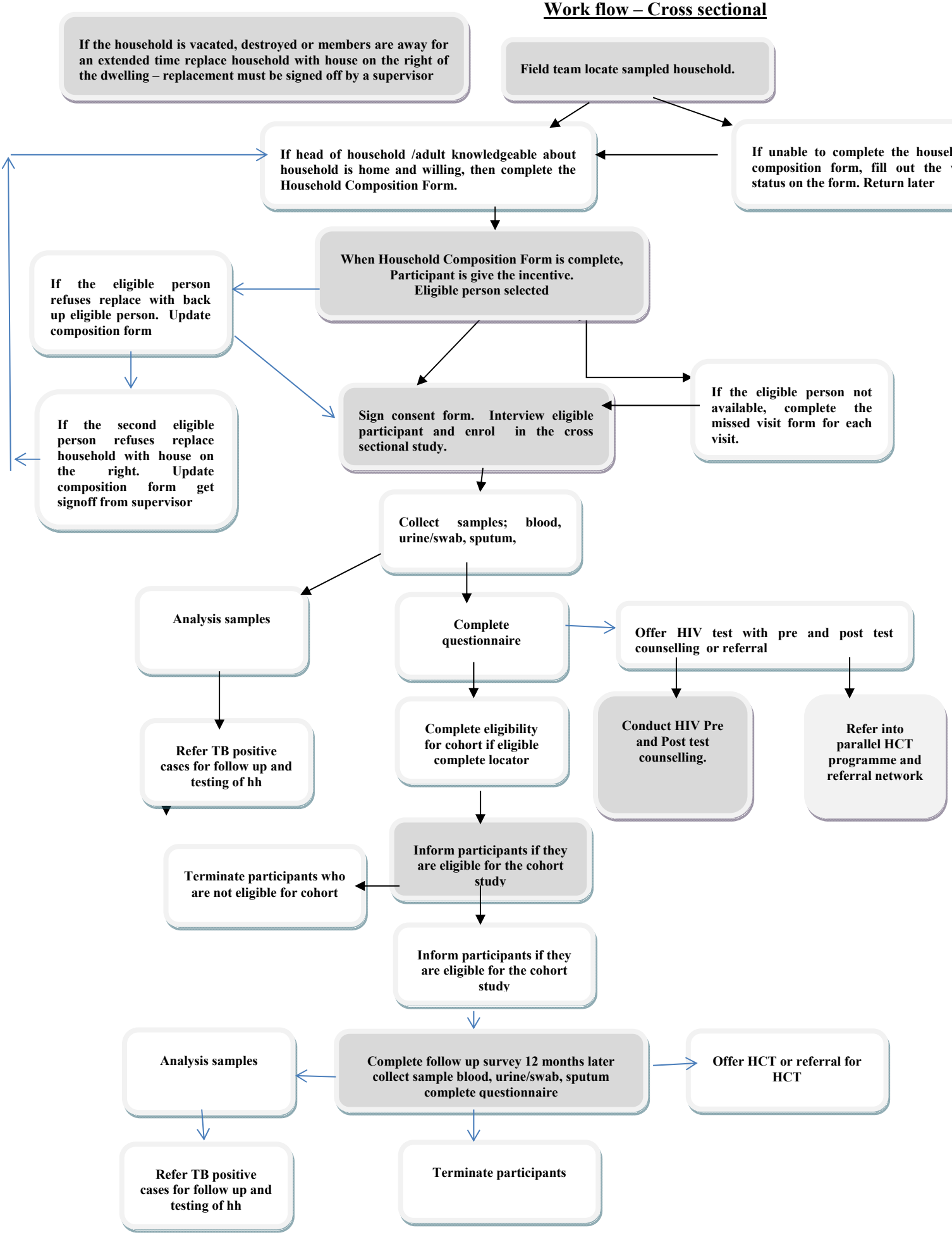
****Relationship to head of the household**: Is the head of the household, Wife/husband/ partner, Son/daughter/step child/ adopted child, Father/mother/step father/step mother, Brother/sister/step brother/step sister, Grandchild/great grandchild, Grandparent/great grandparent, Mother or father in law, Son or daughter in law, Other relation (e.g. aunt, uncle), No relation[14].

[14] SASA 2012 questionnaire

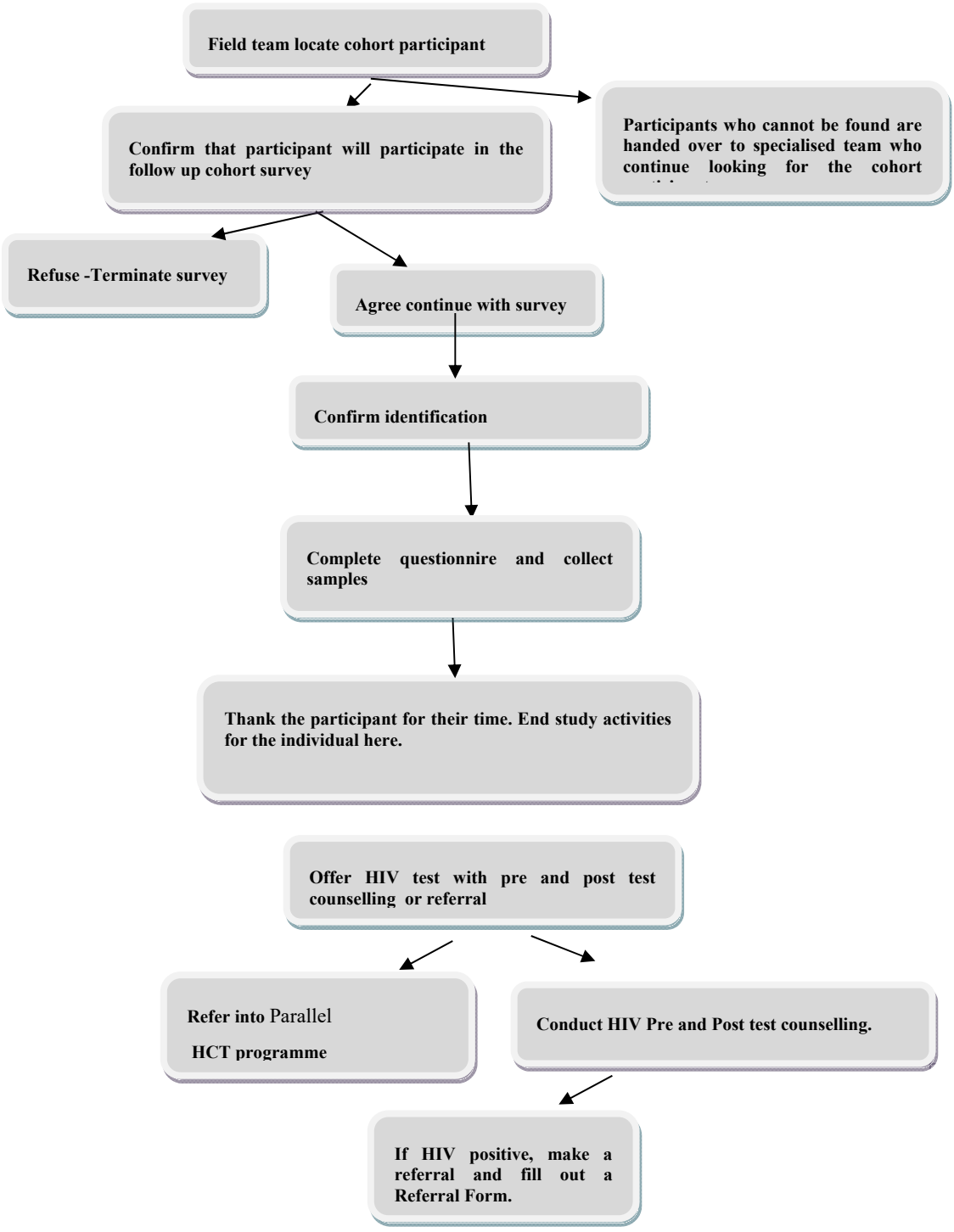
APPENDIX C – WORKFLOW DIAGRAM

The workflow diagram provides an overview of the field work for the cross sectional study on the page below and the cohort on the following page.

Work flow – Cross sectional



Cohort survey workflow



APPENDIX D – PARTICIPANT INFORMATION SHEET, INFORMED CONSENT AND ASSENT FORMS FOR ENROLMENT

Title of Study

KZN HIV Incidence Measurement System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South AfricaVersion 1.0 5 May 2014

INFORMATION TO PARTICIPANTS

I am a member of a research team working with Epicentre and CAPRISA, University of KwaZulu-Natal. We are undertaking a study to find out whether services that are provided by government and other organizations on HIV information, education, prevention and treatment are having an effect by reducing the number of new HIV infections amongst the people in this community. To date we do not have any reliable information on who is becoming infected and why. Knowing more about HIV programmes and whether these have an effect on HIV infection rates will help us improve HIV prevention and treatment programs. In the case of the individules who are already infected with HIV, we wish to understand whether they are getting the necessary HIV care and treatment services that they require. For those individules who are not infected with HIV we will try and understand whether they have received information on HIV and how to protect themselves from becoming infected with HIV.

We will be asking about 10000 men and women between the ages of 15-49 year from the communities of Vulindlela and Greater Edendale to take part in the study. Some of these people will be contacted about a year later.

In order to know more about HIV and other infections and whether the programmes are working, we would like to ask a few questions about your health, your experiences and about yourself. This should take about 30 minutes of your time. If you agree to this, we will obtain this information from you and collect your finger prints but we will not write down your name together with the information that you give us, so no-one will know who the information comes from. In addition, to participate in the study we will request you to give us a small amount of blood, about 5 teaspoons (3 tubes), which the nurse will collect and ask you to give us some of your urine and for females we will ask you to give us a sample from your vagina. If you do not agree to your samples being collected then you will not be able to participate in the study. We will not write any names on the samples, we will only use numbers, so there will be no way of knowing who the sample came from. There is no limit on how long the blood, urine and vaginal samples will be stored and may be tested for other infections. If you do not want us to store the sample then we will destroy the sample as soon as the tests are completed for this study.

We will be happy if you take part in the study and you are free to take part, but if you do not wish to then please just say so and we will stop now. Also if you wish to stop at any time in the interview you will be free to do so.

If you agree to take part in the study, study staff will use a tracking device called Global Positioning System or GPS to determine the location of your house. This information will be transmitted to a central database and access to this information will be restricted to study data management staff. Should we need to contact you for a follow-up visit the data management staff will provide the field staff with the information needed to assist them in locating your house.

If you agree to take part in the study, study staff will also ask you to provide your finger prints which will be scanned and stored in a central database. This information will also be restricted to study data management staff. Should we need to contact you for a follow-up visit the data management staff will provide the field staff with the information needed to assist them in locating you.

On completion of the household composition assessments, the main member or head of the household will be compensated with an item to the approximate value of R10 and volunteers who enrol into the study will be compensated with an item to the approximate value of R25 for their time.

The results of the tests conducted on the sample provided by you will be available from your local Department of Health clinic linked to your barcode. We will provide you with a card with your bar code and the name of the clinic where your results will be sent to enable you to collect your results.

This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (Approval number BF269/13).

In the event of any problems or concerns/questions you may contact Dr Ayesha Kharsany on (031) 260 4555. CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or the study Field co-ordinator, Mr David Khanyile on 083 393 0603, EPICENTRE or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus, Govan Mbeki Building
Private Bag X 54001, Durban, 4000, KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Thank you for your time.

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1. 0 5 May 2014

INFORMED CONSENT FORM FOR ENROLMENT OF VOLUNTEERS 18 YEARS AND OLDER TO PARTICIPATE IN HIPSS

If the volunteer cannot read, this form must be read to the volunteer exactly as written, in the volunteer's language of choice, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study.

INTRODUCTION
Good Afternoon, my name is _____(Field Staff Name) from Epicentre and we are conducting a research study in collaboration with CAPRISA, Epicentre, the Provincial Department of Health, KwaZulu-Natal and the Centers for Disease Control and Prevention in South Africa (CDC).

The Principal Investigator of study is
Dr Ayesha BM Kharsany
2nd Floor Doris Duke Medical Research Institute
Nelson R Mandela School of Medicine
Private Bag 7, Congella 4013, Durban, South Africa
PHONE: 031-260 4555

BACKGROUND
You are being invited to participate in a research study that seeks to understand the HIV epidemic in this region. The study is being undertaken to find out whether services that are provided by government and other organizations on HIV information, education, prevention and treatment are having an effect by reducing the number of new HIV infections amongst the people in this community. To date we do not have any reliable information on who is becoming infected and why. Knowing more about HIV programmes and whether these have an effect on HIV infection rates will help us improve HIV prevention and treatment programs. In the case of the individules who are already infected with HIV, we wish to understand whether they are getting the necessary HIV care and treatment services that they require. For those individules who are not infected with HIV we will try and understand whether they have received information on HIV and how to protect themselves from becoming infected with HIV.

In this study we expect to include about 10,000 people, 15-49 years, from two sub-districts of the uMgungundlovu district municipality in KwaZulu-Natal (Vulindlela and Greater Edendale). This will be done at two different points in time. About half of the 10,000 people sampled in both time points will be followed up approximately 12 months later. The study will include both men and women.

PURPOSE OF THE STUDY
The purpose of this research is to understand and know

- The number of people who are HIV infected and whether they have proper and easy access to care and treatment programmes
- The number of people who are HIV uninfected and whether they have proper and easy access HIV prevention programmes
- The number of people who are becoming HIV infected and why

YOUR PARTICIPATION IS VOLUNTARY

Please read (or have someone to read to you) this Consent Form in the language of your choice in order to make sure that you are given enough information about taking part in this research study. If you agree and you qualify to take part in this study, you will be asked to sign this consent form (or make your mark on the form in the presence of a witness). The study staff will then enroll you in this research. They will also give you a copy of this consent form to keep. Participation in this study is voluntary and you should not hesitate to ask about anything you are not clear about during the study. You have been selected through a number provided by a computer programme. If you agree to join the study we hope that you answer the questions truthfully and to the best of your ability. We want to re assure you that none if the information you provide will be shared with anyone in the community or any person outside the study.

PROCEDURES

The study will involve the following procedures

The study staff would have used the tracking device called Global Positioning System or GPS to determine the location of your house. This information will be transmitted to a central database and access to this information will be restricted to study data management staff. Should we need to contact you for a follow-up visit the data management staff will provide the field staff with the information needed to assist them in locating your house.

After you have agreed (consented) to participate in this research, the study staff will take a copy of your fingerprints. This is done to ensure that all information we collect from you today, and in the future, is correctly assigned to one and the same person. This will also help us to keep all the information in such a way that no one can access it and link it to you. Every time we make contact with you we will confirm your identify through your fingerprint by compareing it with the fingerprint taken during your first visit.

Once you join this study, we will try to stay in contact with you for future visits. We will ask for your name, physical address, phone number, and other contact information. This will also help us to provide you with any updates on the study in the future.

Enrolment

At this visit

We will capture your fingerprints so what we can match this at your follow up visit.

We will ask you some questions about:

- Your age, who you live with, and what kind of work you do.
- Whether you have had an HIV test and know your HIV status.
- Your sexual behaviors and information on your sex partners. We will not ask the name(s) of your sex partners.
- Whether you know about the programmes on HIV information, education, prevention and treatment offered by the government and different research organizations. Whether you have used these services and how good you think they were.
- We will collect the following samples from you. If you do not agree to your samples being collected then you will not be able to participate in the study.

We will take about 5 teaspoons of blood from your arm to check for

- HIV and if needed we will measure your CD4 cell count and HIV viral load.
- HIV related testing in a laboratory.
- HSV-2, syphilis, hepatitis B and C infections

We will ask you to cough intensely to provide a little bit of your sputum

- to screen for tuberculosis (TB)

We will ask you to provide a small amount of urine

- to test for sexually transmitted infections (STIs) in males
- to test for pregnancy in females

We will ask the females to self collect a vaginal swab sample

- to test for sexually transmitted infections

At this visit you are free to ask study staff any questions you may wish to ask.
This visit will take about 30 minutes of your time.
The study staff will also inform you that some people in the study might be eligible for the follow-up study. Should you be eligible for the follow-up study, a staff member will contact you telephonically and arrange to complete a follow-up visit approximately 12 months (one year) later.

The results of the tests conducted on the sample provided by you will be available from your local Department of Health clinic linked to your barcode. We will provide you with a card with your bar code and the name of the clinic where your results will be sent to enable you to collect your results.

Please note that we will not share any of your information or any of the samples collected from you or the results of the tests with anyone not related to the study.
At the completion of this visit the study staff will compensate you with an item to the value of approximatly R25 and thank you for joining the study.

Follow-up visit
About half the number of people who entered the study will be asked to come back for the follow up survey about 12 months after their first visit. However, we will first check whether you qualify for the follow-up visit and if you do, then the study staff will contact you by telephone and arrange for this vist. If on your scheduled study visit day you are not available, the study staff will return several times to complete your study visit. We may also ask your family members to assist us in making contact with you if we are unable to contact you directly.

At this visit
We will compare your finger prints given at this visist with information given during the first visit to confirm your identification.
We will ask similar questions as we would have asked in the first visit.
We will take about 5 teaspoons of blood from your arm to check for

- HIV and if needed we will measure your CD4 cell count and HIV viral load.
- HIV related testing in a laboratory.
- HSV-2, syphilis, hepatitis B and C infections

We will ask you to cough intensely to provide a little bit of your sputum

- to screen for tuberculosis (TB)

We will ask you to provide a small amount of urine

- to test for sexually transmitted infections (STIs) in males
- to test for pregnancy in females

We will ask the females to self collect a vaginal swab sample

- to test for sexually transmitted infections

This visit will take about 30 minutes of your time and at the completion of this visit the study staff will compensate you with an item to the approximate value R25 and thank you for completing the follow-up visit.

RISKS AND/OR DISCOMFORTS
You may feel uncomfortable or anxious about some of the questions you are asked. You are allowed to refuse to answer any question that you do not want to answer. The risks of drawing blood are very rare. These include possibly a little pain from the needle stick, bruising, lightheadedness, and rarely infection where the needle entered the arm, however, the study staff will assist you in coping with these.

BENEFITS
Your participation in this research could help us learn more about HIV in the uMgungundlovu district, more importantly about how HIV information, education, prevention and treatment programs are

working. We hope that you benefit from this study as it would be possible for you to access early referral to HIV counselling and testing services. In addition study staff would refer you for the management of HIV, TB, pregnancy or any other minor ailments, if necessary. We hope you benefit from these referals as you would be able to access care and treatment much earlier.

CONFIDENTIALITY
The study staff will do everything they can to keep your participation in the study private. Access to the GPS location of your house, your finger prints and records will be restricted and limited to the study staff. You will be given a study number so that we do not use your name. This number and your name will only appear together on one form. The form will be kept in a locked file to which only certain study staff will have access to. All data collection instruments, blood samples, blood samples in storage, laboratory result sheets will not contain your name or personal information, will be maintatined and archived for study purposes only and will remain confidential. It will not be possible for people looking at any of these forms to know that they belong to you. Any reports or work that will be written and shared with the public will not make it possible for any individule to be identified in these reports. We will keep all information from your study records private to the extent allowed by law**.** Any samples collected will remain in storage without your name but with a number, they will not be discarded and the results of the testing will be used in the analysis.

COSTS FOR BEING IN THE STUDY
There is no cost to you for being in the study.

COMPENSATION
You will receive a item to the approximatly value of R25 for each visit day to thank you for your time and effort.

RIGHT TO REFUSE OR WITHDRAW
It is your choice to be in this study. If you decide not to take part, it will not affect your healthcare in any way. If you choose to take part in the study and change your mind at any time, then you can stop being in the study. Should you withdraw from the study the samples collected from your last visit will be included for all the testing for that visit. However, you will need to inform us if you do not wish for us to use any of the information collected from you and/or the results from the tested samples.Your participation is entirely voluntary.

REASONS WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT

You may be removed from the study without your consent for the following reasons:

- The investigator decides that continuing in the study would be harmful to you.
- The study is cancelled by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC).
- Other administrative reasons.

STUDY APPROVAL
This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number BF269/13).

PERSONS TO CONTACT
In the event of any problems or concerns/questions you may contact Dr Ayesha Kharsany on (031) 260 4555. CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or the study Field co-ordinator, Mr David Khanyile on 083 393 0603, EPICENTRE or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus, Govan Mbeki Building
Private Bag X 54001, Durban, 4000, KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

Thank you for your time.

CONSENT STATEMENT AND SIGNATURE PAGE FOR VOLUNTEERS 18 YEARS AND OLDER

I have read this form, or someone has read it to me. I was given time to ask questions. I agree to be in this study and also be part of the follow-up visit in approximately 12 months' time, if I qualify. I know that after choosing to be in this study, I may withdraw at any time. My participation is voluntary.

_____	_____	_____
Volunteer name (print)	Volunteer signature	Date
_____	_____	_____
Study staff member who administered consent (print)	Staff staff signature	Date
_____	_____	_____
Witness' name (print)	Witness' signature	Date

Was a copy of the signed copy given to the volunteer: ☐Yes ☐No

If no, why not:_____

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1. 0 4 5 May2014

PARENT / GUARDIAN/ CARE GIVER INFORMATION SHEET AND CONSENT FORM FOR VOLUNTEERS YOUNGER THAN 18 YEARS TO PARTICIPATE IN HIPSS

ADMINISTRATIVE PAGE

If the volunteer is younger than 18 years of age, this administrative section must be completed prior to completing the assent form for enrolment.

1. Has the volunteers age been verified?

   □Yes □No

2. If yes, indicate below how the participant's age has been verified:

   □ Birth Certificate

   □ Identification Document (ID)

   □ Other: Specify_____.

3. Who has provided consent for this volunteer to participate in this study?

   □ Parent

   □ Legal Guardian

   □ Care giver

   □ Other_____

_____	_____	_____
Study staff member (print)	Staff staff signature	Date

If you have indicated NO to Question 1 or in 3 above there is no adult consent, please do not proceed any further.

Staff Note: If the volunteer cannot read, the assent form must be read to the volunteer exactly as written, in the volunteer's language of choice, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study.

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1.0 5 May

INFORMED CONSENT FORM FOR PARENT / GUARDIAN / CARE GIVER TO CONSENT FOR ENROLMENT OF VOLUNTEERS YOUNGER THAN 18 YEARS TO PARTICIPATE IN HIPSS

If the child volunteers parent/guardian/care giver cannot read, this form must be read to the volunteers parent/guardian/care giver exactly as written, in their language of choice. A witness must sign this form to confirm that the correct information was given and has freely consented for the child/ward to be in this study.

INTRODUCTION

Good Afternoon, my name is _____(Field Staff Name) from Epicentre and we are conducting a research study in collaboration with CAPRISA, Epicentre, the Provincial Department of Health, KwaZulu-Natal and the Centers for Disease Control and Prevention in South Africa (CDC).

The Principal Investigator of study is
Dr Ayesha BM Kharsany
2nd Floor Doris Duke Medical Research Institute
Nelson R Mandela School of Medicine
Private Bag 7, Congella 4013, Durban, South Africa
PHONE: 031-260 4555

Since your child/ward is younger than 18 years of age, but older than 14 years of age, you as the parent / guardian / caregiver may provide consent for your child/ward to participate in this study. This does not mean that your child/ward has to agree to be in the study.

- If you as the parent / guardian /caregiver agrees to your child/wards participation in the study, we will still require your child/ward to agree to participate in this study.
- **Assent** is a term used to describe your child/wards agreement to participate in this study because your child/ward is under 18 years of age. The permission given by you as the parent / guardian / caregiver is called **consent**. We would like to receive both consent from you and assent from your child/ward to participate in this study since your child/ward is under 18 years of age.
- Your child/ward can agree to take part in this study at a later date, but prior to study completion.
- The consent form will describe to you the purpose of the study, study procedures, the type of inofrmation that we will be collecting, the risks and benefits of participating in this study, and your child/wards rights as a study participant.

I will give you and your child/ward information about this study and talk to you today about what your child/wards participation would involve. If you and your child/ward agrees to be part of this study and your child/ward qualifies to participate, I will further give you and your child/ward information about the procedures that you will undergo, what we will expect from you and your rights as a participant.

BACKGROUND
Through you, your child/ward is being invited to participate in a research study that seeks to understand the HIV epidemic in this region. The study is being undertaken to find out whether services that are provided by government and the many research organizations on HIV information, education, prevention and treatment are having an effect by reducing the number of new HIV infections amongst the people in this community. To date we do not have any reliable information on who is becoming infected and why. Knowing more about HIV programmes and whether these have an effect on HIV infection rates will help us improve HIV prevention and treatment programs. In the case of the individules who are already infected with HIV, we wish to understand whether they are getting the necessary HIV care and treatment services that they require. For those individules who are not infected with HIV we will try and understand whether they have received information on HIV and how to protect themselves from becoming infected with HIV.

In this study we expect to include about 10,000 people, 15-49 years, from two sub-districts of the uMgungundlovu district municipality in KwaZulu-Natal (Vulindlela and Greater Edendale). This will be done at two different points in time. About half of the 10,000 people sampled in both time points will be followed up approximately 12 months later. The study will include both men and women.

PURPOSE OF THE STUDY
The purpose of this research is to understand and know

- The number of people who are HIV infected and whether they have proper and easy access to care and treatment programmes
- The number of people who are HIV uninfected and whether they have proper and easy access HIV prevention programmes
- The number of people who are becoming HIV infected and why

YOUR CHILD/WARDS PARTICIPATION IS VOLUNTARY
Please read (or have someone to read to you) this Consent Form in the language of your choice in order to make sure that you are given enough information about your child/ward taking part in this research study. If you agree and your child/ward qualifies to take part in this study, you will be asked to sign this consent form (or make your mark on the form in the presence of a witness). Your child/ward will also have to give permission that is assent. The study staff will then enroll your child/ward in this research. They will also give you a copy of this consent form to keep. Your child/ward will also receive a copy of the form where he/she has given his/her permission. Participation in this study is voluntary and you should not hesitate to ask about anything you are not clear about. Your child/ward has been selected through a number provided by a computer programme. If you agree for your child/ward to take part in the study. we hope that he/she will answer the questions to the best of his/her ability. We want to re assure you that none if the information your child/ward provides will be shared with anyone in the community or any person outside the study.

PROCEDURES
The study will involve the following procedures

The study staff would have used the tracking device called Global Positioning System or GPS to determine the location of your childs/wards house. This information will be transmitted to a central database and access to this information will be restricted to study data management staff. Should we need to contact your child/ward for a follow-up visit the data management staff will provide the field staff with the information needed to assist them in locating your childs/wards house.

After you have agreed (consented) and your child/ward has agreed (assent) to take part in the study, the study staff will take a copy of your child/wards fingerprints. This is done to ensure that all information we collect from your child/ward today, and in the future, is correctly assigned to one and the same person. This will also help us to keep all the information in such a way that no one can access it and link it to your child/ward. Every time we make contact with your child/ward we will

confirm the indentity of your child/ward through their fingerprints and compare it with the fingerprints taken during your child/wards first visit.

The results of the tests conducted on the sample provided by your child will be available to them at their local Department of Health clinic linked to their barcode. We will provide your child with a card with their bar code and the name of the clinic where their results will be sent to enable them to collect their results.

Once your child/ward has joined this study, we will try to stay in contact with your child/ward for future visits. We will ask for your child/wards name, physical address, phone number, and other contact information. This will also help us to provide your child with any updates on the study in the future.

Enrolment

At this visit

We will capture your child/wards fingerprints so what we can compare this at the follow up visit.

We will ask your child/ward some questions about:

- His/her age, who he/she lives with, and whether they are in school or working.
- Whether he/she has had an HIV test and know their HIV status.
- Some sensitive questions on sexual behaviors and if they are having sex and with whom. We will not ask the name(s) of any of their sex partners.
- Whether your child/ward knows about the programmes on HIV information, education, prevention and treatment offered by the government and different research organizations. Whether your child/ward has used these services and how good they think they were.
- We will collect the following samples from your child . If you or your child does not agree to samples being collected then he/she will not be able to participate in the study.

We will take about 5 teaspoons of blood from your child/wards arm to check for

- HIV and if needed we will measure the CD4 cell count and HIV viral load.
- HIV related testing in a laboratory.
- HSV-2, syphilis, hepatitis B and C infections

We will ask your child/ward to cough intensely to provide a little bit of sputum

- to screen for tuberculosis (TB)

We will ask your child/ward to provide a small amount of urine

- to test for sexually transmitted infections (STIs) in males
- to test for pregnancy in females

We will ask the females to self collect a vaginal swab sample

- to test for sexually transmitted infections

At this visit your child/ward will be free to ask study staff any questions he/she may wish to ask.

This visit will take about 30 minutes of your child/wards time.

The study staff will also inform your child/ward that some people in the study might be eligible for the follow-up study. Should your child/ward be eligible for the follow-up study, a staff member will contact him / her telephonically and arrange to complete a follow-up visit approximately 12 months (one year) later.

Please note that we will not share any of your child/wards information or any of the samples collected from your child/ward or the results of the tests with anyone not related to the study.

At the completion of this visit the study staff will compensate your child/ward with an item to the approximate value of R25 and thank him/her for joining the study.

Follow-up visit

About half the number of people who entered the study will be asked to come back for the follow up survey about 12 months (one year) after their first visit. However, we will first check whether your child/ward qualifies for the follow-up visit and if your child/ward does, then the study staff will contact your child/ward by telephone and arrange for this vist. If on your child/wards scheduled study visit day, your child/ward is not available, the study staff will return several times to complete their study visit. We may also ask you and your family members to assist us in making contact with your child/ward if we are unable to contact your child/ward directly.

At this visit
We will capture your child/wards fingerprints and compare it to the prints taken during the first visit.
We will ask similar questions as we would have asked in the first visit.
We will take about 5 teaspoons of blood from your child/wards arm to check for

- HIV and if needed we will measure the CD4 cell count and HIV viral load.
- HIV related testing in a laboratory.
- HSV-2, syphilis, hepatitis B and C infections

We will ask your child/ward to to cough intensely to provide a little bit of sputum

- to screen for tuberculosis (TB)

We will ask your child/ward to provide a small amount of urine

- to test for sexually transmitted infections (STIs) in males
- to test for pregnancy in females

We will ask the females to self collect a vaginal swab sample

- to test for sexually transmitted infections

This visit will take about 30 minutes of your child/wards time and at the completion of this visit the study staff will compensate your child/ward with an item to the approximatly value of R25 and thank your child/ward for his/her time and completing the follow-up visit.

RISKS AND/OR DISCOMFORTS
Your child/ward may feel uncomfortable or anxious about some of the questions that the study staff may ask. Your child/ward will be allowed to refuse to answer any questions that he/she does not want to answer. The risks of drawing blood are very rare. These include possibly a little pain from the needle stick, bruising, lightheadedness, and rarely infection where the needle entered the arm, however, the study staff will assist your child/ward in coping with these.

BENEFITS
Your child/wards participation in this research could help us learn more about HIV in the uMgungundlovu district, more importantly about how HIV information, education, prevention and treatment programs are working. We hope that your child/ward benefits from this study as it would be possible for your child/ward and for family members to access early referral to HIV counselling and testing services. In addition study staff would refer your child/ward for further screening and management of HIV, TB, pregnancy or any other minor ailments, if necessary. We hope your child/ward benefits from these referals as your child/ward would be able to access care and treatment much earlier.

CONFIDENTIALITY
The study staff will do everything they can to keep your child/wards participation in the study private. Access to the GPS location of your childs/wards house, your child/wards finger print records will be restricted and limited to the study staff. Your child/ward will be given a study number so that we do not use his/her name. This number and your child/wards name will only appear together on one form. The form will be kept in a locked file to which only certain study staff will have access to. All data collection instruments, blood samples, blood samples in storage, laboratory result sheets will not contain your child/wards name or personal information. It will not be possible for people looking at any of these forms to know that they belong to your child/ward. Any reports or work that will be

written and shared with the public will not make it possible for any individual to be identified in these reports. We will keep all information from your child/wards study records private to the extent allowed by law**.** Any samples collected will remain in storage without your child/wards name but with a number, they will not be discarded and the results of the testing will be used in the analysis.

COSTS FOR BEING IN THE STUDY
There is no cost to your child/ward for being in the study.

COMPENSATION
Your child/ward will receive item to the aproximate value of R25 for each visit day to thank him/her for their time and effort.

RIGHT TO REFUSE OR WITHDRAW
It is yours and your child/wards choice to be in this study. If you or your child/ward decide not to take part, it will not affect your child/wards healthcare in any way. If you or your child/ward chooses to take part in the study and change your mind at any time, then you can stop being in the study. Should your child/ward withdraw from the study the samples collected from his/her last visit will be included for all the testing for that visit. However, your child/ward will need to inform us if he/she does not wish for us to use any of the information collected from him/her and/or the results from the tested samples.Your child/wards participation is entirely voluntary.

REASONS WHY YOUR CHILD/WARD MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT

You child/ward may be removed from the study without your consent or or his/her assent for the following reasons:

- The investigator decides that continuing in the study would be harmful to your child/ward.
- The study is cancelled by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC).
- Other administrative reasons.

STUDY APPROVAL
This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number BF 269/13_).

PERSONS TO CONTACT
In the event of any problems or concerns/questions you may contact Dr Ayesha Kharsany on (031) 260 4555. CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or the study Field co-ordinator, Mr David Khanyile on 083 393 0603, EPICENTRE or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus, Govan Mbeki Building
Private Bag X 54001, Durban, 4000, KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Thank you for your time.

CONSENT STATEMENT AND SIGNATURE PAGE FOR PARENT / GUARDIAN / CARE GIVER OF VOLUNTEERS YOUNGER THAN 18 YEARS

I have read this form, or someone has read it to me. I was given time to ask questions. I agree for my child/ward to be in this study and also be part of the follow-up visit in approximately 12 months' time, if my child/ward qualifies. I know that after choosing for my child/ward to be in this study, I may withdraw my consent at any time. I know and agree that my child/ward taking part in the study is voluntary.

_____	_____	_____
Parent / Guardian / Care giver Name (print)	Parent / Guardian / Care giver Signature	Date
_____	_____	_____
Study staff member who administered consent (print)	Staff staff Signature	Date
_____	_____	_____
Witness Name (print)	Witness Signature	Date

Was a copy of the signed copy given to the volunteer: □Yes □No

If no, why not:_____

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1.0 5 May 2014

ASSENT FORM FOR VOLUNTEERS YOUNGER THAN 18 YEARS TO PARTICIPATE IN HIPSS

ADMINISTRATIVE PAGE

If the volunteer is younger than 18 years of age, this administrative section must be completed prior to completing the assent form for enrolment.

1. Has the volunteers age been verified?

   □Yes □No

2. If yes, indicate below how the participant's age has been verified:

   □ Birth Certificate

   □ Identification Document (ID)

   □ Other: Specify_____.

3. Who has provided consent for this volunteer to participate in this study?

   □ Parent

   □ Legal Guardian

   □ Care giver

   □ Other_____

_____	_____	_____
Study staff member (print)	Staff staff signature	Date

If you have indicated NO to Question 1 or 3 above, please do not proceed any further.

Staff Note: If the volunteer cannot read, the assent form must be read to the volunteer exactly as written, in the volunteer's language of choice, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study.

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1.0 5 May 2014

ASSENT FORM FOR THE ENROLMENT OF VOLUNTEERS YOUNGER THAN 18 YEARS TO PARTICIPATE IN HIPSS

If the child/ward volunteers cannot read, this form must be read to the volunteer exactly as written, in their language of choice. A witness must sign this form to confirm that the correct information was given and the child/ward has freely assented to be in this study.

INTRODUCTION

Good Afternoon, my name is _____(Field Staff Name) from Epicentre and we are conducting a research study in collaboration with CAPRISA, Epicentre, the Provincial Department of Health, KwaZulu-Natal and the Centers for Disease Control and Prevention in South Africa (CDC).

The Principal Investigator of study is
Dr Ayesha BM Kharsany
2nd Floor Doris Duke Medical Research Institute
Nelson R Mandela School of Medicine
Private Bag 7, Congella 4013, Durban, South Africa
PHONE: 031-260 4555

Since you are younger than 18 years of age, but older than 14 years of age, your parent / guardian / caregiver may provide consent for you to participate in this study. This means that you as a child/ward also has to agree to be in the study.

- If your parent / guardian /caregiver agrees to your participation in the study, we will still require for you as a child/ward to agree to participate in this study.
- **Assent** is a term used to describe your agreement to participate in this study because you are under 18 years of age. The permission given by your parent / guardian / caregiver is called **consent**. We would like to receive both assent from you and consent from parent / guardian /caregiver for you as a child/ward to participate in this study since you are a child/ward under 18 years of age.
- You can can agree to take part in this study at a later date, but prior to study completion.
- The assent form will describe to you the purpose of the study, study procedures, the type of inofrmation that we will be collecting, the risks and benefits of participating in this study, and you as a child/ward, your rights as a study participant.

I will give you and your parent / guardian /caregiver information about this study and talk to you today about what your participation would involve. If you and your parent / guardian /caregiver agrees for you to be part of this study and if you qualify to participate, I will further give you and your parent / guardian /caregiver information about the procedures that you will undergo, what we will expect from you and your rights as a participant.

BACKGROUND

You are being invited to participate in a research study that seeks to understand the HIV epidemic in this region. The study is being undertaken to find out whether services that are provided by government and the many research organizations on HIV information, education, prevention and treatment are having an effect by reducing the number of new HIV infections amongst the people in this community. To date we do not have any reliable information on who is becoming infected and why. Knowing more about HIV programmes and whether these have an effect on HIV infection rates will help us improve HIV prevention and treatment programs. In the case of the individules who are

already infected with HIV, we wish to understand whether they are getting the necessary HIV care and treatment services that they require. For those individules who are not infected with HIV we will try and understand whether they have received information on HIV and how to protect themselves from becoming infected with HIV.
In this study we expect to include about 10,000 people, 15-49 years, from two sub-districts of the uMgungundlovu district municipality in KwaZulu-Natal (Vulindlela and Greater Edendale). This will be done at two different points in time. About half of the 10,000 people sampled in both time points will be followed up approximately 12 months later. The study will include both men and women.

PURPOSE OF THE STUDY
The purpose of this research is to understand and know

- The number of people who are HIV infected and whether they have proper and easy access to care and treatment programmes
- The number of people who are HIV uninfected and whether they have proper and easy access HIV prevention programmes
- The number of people who are becoming HIV infected and why

YOUR PARTICIPATION IS VOLUNTARY
Please read (or have someone to read to you) this Assent Form in the language of your choice in order to make sure that you are given enough information about taking part in this research study. If you agree and you qualify to take part in this study, you will be asked to sign this assent form (or make your mark on the form in the presence of a witness). Your parent / guardian /caregiver will also have to give permission that is consent. The study staff will then enroll you in this research. They will also give you a copy of this assent form for you to keep. Your parent / guardian /caregiver will also receive a copy of their form (consent) where he/she has given his/her permission. Participation in this study is voluntary and you should not hesitate to ask about anything you are not clear about. You have been selected through a number provided by a computer programme. If you agree to take part in the study we hope that you will answer the questions truthfully and to the best of your ability. We want to re assure you that none if the information you provide will be shared with anyone in the community or any person outside the study.

PROCEDURES
The study will involve the following procedures

The study staff would have used the tracking device called Global Positioning System or GPS to determine the location of your house. This information will be transmitted to a central database and access to this information will be restricted to study data management staff. Should we need to contact you for a follow-up visit the data management staff will provide the field staff with the information needed to assist them in locating your house.

After you have agreed (Assent) and your parent / guardian /caregiver has agreed (Consent) for you to take part in the study, the study staff will take a copy of your fingerprints. This is done to ensure that all information we collect from you today, and in the future, is correctly assigned to one and the same person. This will also help us to keep all the information in such a way that no one can access it and link it to you. Every time we make contact with you we will indentify you through your fingerprints and compare it with the fingerprints taken during your first visit.

The results of the tests conducted on the sample provided by you will be available from your local Department of Health clinic linked to your barcode. We will provide you with a card with your bar code and the name of the clinic where your results will be sent to enable you to collect your results.

Once you have joined this study, we will try to stay in contact with you for future visits. We will ask for your name, physical address, phone number, and other contact information. This will also help us to provide you with any updates on the study in the future.

Enrolment

At this visit

We will capture your fingerprints so what we can match this at your follow up visit.

We will ask you some questions about:

- Your age, who you live with, and whether you are in school or working.
- Whether you had an HIV test and know your HIV status.
- We will ask some sensitive questions on sexual behaviors and if you are having sex and with whom. We will not ask the name(s) of any of their sex partners.
- Whether you knows about the programmes on HIV information, education, prevention and treatment offered by the government and different research organizations. Whether you have used these services and how good you think they are.
- We will collect the following samples from you. If you do not agree to your samples being collected then you will not be able to participate in the study.

We will take about 5 teaspoons of blood from your arm to check for

- HIV and if needed we will measure the CD4 cell count and HIV viral load.
- HIV related testing in a laboratory.
- HSV-2, syphilis, hepatitis B and C infections

We will ask you to cough intensely to provide a little bit of your sputum

- to screen for tuberculosis (TB)

We will ask you to provide a small amount of urine

- to test for sexually transmitted infections (STIs) in males
- to test for pregnancy in females

We will ask the females to self collect a vaginal swab sample

- to test for sexually transmitted infections

At this visit you will be free to ask study staff any questions you may wish to ask.

This visit will take about 30 minutes of your time.

The study staff will also inform you that some people in the study might be eligible for the follow-up study. Should you be eligible for the follow-up study, a staff member will contact you telephonically and arrange to complete a follow-up visit approximately 12 months (one year) later.

Please note that we will not share any of your information or any of the samples collected from you or the results of the tests with anyone not related to the study.

At the completion of this visit the study staff will compensate you with an item to the approximate velue of R25 to thank you for joining the study.

Follow-up visit

About half the number of people who entered the study will be asked to come back for the follow up survey about 12 months (one year) after their first visit. However, we will first check whether you qualify for the follow-up visit and if you do, then the study staff will contact you by telephone and arrange for this vist. If on your scheduled study visit day, you are not available, the study staff will return several times to complete your study visit. We may also ask your family members to assist us in making contact with you if we are unable to contact you directly.

At this visit

We will capture your fingerprints and match it to the prints taken during the first visit.

We will ask similar questions as we would have asked in the first visit.

We will take about 5 teaspoons of blood from you child/wards arm to check for

- HIV and if needed we will measure the CD4 cell count and HIV viral load.

- HIV related testing in a laboratory.
- HSV-2, syphilis, hepatitis B and C infections

We will ask you to cough intensely to provide a little bit of sputum

- to screen for tuberculosis (TB)

We will ask you to provide a small amount of urine

- to test for sexually transmitted infections (STIs) in males
- to test for pregnancy in females

We will ask the females to self collect a vaginal swab sample

- to test for sexually transmitted infections

This visit will take about 30 minutes of your time and at the completion of this visit the study staff will compensate you with anitem to the approximate value of R25 and thank you for your time and for completing the follow-up visit.

RISKS AND/OR DISCOMFORTS

You may feel uncomfortable or anxious about some of the questions that the study staff may ask. You will be allowed to refuse to answer any questions that you do not want to answer. The risks of drawing blood are very rare. These include possibly a little pain from the needle stick, bruising, lightheadedness, and rarely infection where the needle entered the arm, however, the study staff will assist you in coping with these.

BENEFITS

Your participation in this research could help us learn more about HIV in the uMgungundlovu district, more importantly about how HIV information, education, prevention and treatment programs are working. We hope that you benefit from this study as it would be possible for you and your family members to access early referral to HIV counselling and testing services. In addition study staff would refer you for further screening and management of HIV, TB, pregnancy or any other minor ailments, if necessary. We hope you benefit from these referals as you would be able to access care and treatment much earlier.

CONFIDENTIALITY

The study staff will do everything they can to keep you participation in the study private. Access to the GPS location of your house your finger print and records will be restricted and limited to the study staff. You will be given a study number so that we do not use your name. This number and your name will only appear together on one form. The form will be kept in a locked file to which only certain study staff will have access to. All data collection instruments, blood samples, blood samples in storage, laboratory result sheets will not contain your name or personal information. It will not be possible for people looking at any of these forms to know that they belong to you. Any reports or work that will be written and shared with the public will not make it possible for any individual to be identified in these reports. We will keep all information from your study records private to the extent allowed by law**.** Any samples collected will remain in storage without your name but with a number, they will not be discarded and the results of the testing will be used in the analysis.

COSTS FOR BEING IN THE STUDY

There is no cost to you for being in the study.

COMPENSATION

You will receive an items to the approximate value of R25 for each visit day to thank you for your time and effort.

RIGHT TO REFUSE OR WITHDRAW

It is yours and your parent / guardian /caregiver choice for you to be in this study. If you or your parent / guardian /caregiver decide for you not to take part, it will not affect you healthcare in any way. If you or your parent / guardian /caregiver chooses for you to take part in the study and change your mind at any time, then you can stop being in the study. Should you withdraw from the study the

samples collected from your last visit will be included for all the testing for that visit. However, you will need to inform us if you do not wish for us to use any of the information collected from you and/or the results from the tested samples. Your participation is entirely voluntary.

REASONS WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR PERMISSION

You may be removed from the study without your permission for the following reasons:

- The investigator decides that continuing in the study would be harmful to you.
- The study is cancelled by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC).
- Other administrative reasons.

STUDY APPROVAL

This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number BF269/13).

PERSONS TO CONTACT

In the event of any problems or concerns/questions you may contact Dr Ayesha Kharsany on (031) 260 4555. CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or the study Field co-ordinator, Mr David Khanyile on 083 393 0603, EPICENTRE or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus, Govan Mbeki Building
Private Bag X 54001, Durban, 4000, KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za
Thank you for your time.

ASSENT STATEMENT AND SIGNATURE PAGE FOR VOLUNTEERS YOUNGER THAN 18 YEARS

I have read this form, or someone has read it to me. I was given time to ask questions. I agree to be in this study and also be part of the follow-up visit in approximately 12 months' time, if I qualify. I know that after choosing to be in this study, I may withdraw my assent at any time. I know and agree that my taking part in the study is voluntary.

_____	_____	_____
Volunteer Name (print)	Volunteer Signature	Date
_____	_____	_____
Study staff member who administered assent (print)	Staff staff Signature	Date
_____	_____	_____
Witness Name (print)	Witness Signature	Date

Was a copy of the signed copy given to the volunteer: □Yes □No

If no, why not:_____

APPENDIX E – INFORMED CONSENT AND ASSENT FORMS FOR SAMPLE STORAGE

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1.0 5 May 2014

INFORMED CONSENT FORM
FOR SAMPLE STORAGE FOR POSSIBLE FUTURE RESEARCH
FOR VOLUNTEERS 18 YEARS AND OLDER

The Principal Investigator of study is
Dr Ayesha BM Kharsany
2nd Floor Doris Duke Medical Research Institute
Nelson R Mandela School of Medicine
Private Bag 7, Congella 4013, Durban, South Africa
PHONE: 031-260 4555

INTRODUCTION
If you agree to take part in the HIPSS study, there may be some remaining blood, urine and vaginal swab samples (females) known as samples, taken from you during the study that might be useful for future research. You are being asked to agree to the storage of the left over samples for possible future research that will include additional testing. This is research that will be conducted in the future that may or may not be related to the HIPSS study.

This consent form gives you information about the collection, storage, and use of your samples for possible future research. The study staff will talk to you about this information. Please ask if you have any questions. If you agree to the storage of your samples for possible future research, you will be asked to note this on this consent form. You will get a copy of this form to keep.

HOW WILL YOU GET THE SAMPLES FROM ME?
The HIPSS study staff will collect your blood, sputum ask you to collect the urine sample and they will ask females to collect a vaginal swab as part of the HIPSS study that you have consented to. These samples are needed to carry out the regular tests for the research study. If you agree to have your specimens stored for possible future research, we will store the remainder of the samples after the tests for the HIPSS study have been completed.

HOW WILL YOU USE MY STORED SAMPLES?
Researchers at CAPRISA and elsewhere will use your samples to look for HIV and other infections, or for damage caused by such infections, or the body's response to infection. Researchers may also look at your genes (DNA), since genes can affect the way the body responds to infections in important ways. Your genes might make you more or less likely to get infected, or make the responses to infection or to treatment stronger or weaker. If you become infected with HIV your genes might also affect how fast or slowly you develop AIDS.

Your samples may be shared with colleagues both in South Africa and outside of South Africa however, your stored samples will be sent with only your confidential PID number and will not be

linked to any personal identifiers such as your name. All future research studies using your samples will be reviewed first by the CAPRISA Scientific Review Committee and a special committee at the Nelson R Mandela School of Medicine Biomedical Research Ethics Committee**. It is important for you to know that your samples will not be sold or used in products that make money for the researchers.**

WHERE WILL MY SAMPLES BE STORED?
If you agree to have your specimens stored they will be stored with your confidential PID number at special facilities that are designed to store blood samples safely and securely. The storage facilities are based at the CAPRISA research Laboratory, Doris Duke Medical Research Institute, Nelson R Mandela School of Medicine. The storage facilities are designed so that only approved researchers can have access to the samples.

HOW LONG WILL YOU KEEP MY SAMPLES?
There is no time limit on how long your samples will be stored for.

DOES STORAGE OF MY SAMPLES BENEFIT ME?
It is unlikely that you will have any direct benefit from the tests done on your stored specimens but there may be benefits to society of doing research on your stored specimens. These benefits may include learning more about HIV infection.

WHAT ARE THE RISKS?
There are few risks related to storing your samples. When future tests are done on the stored samples, there is a very small but possible risk to your privacy. Some genetic testing may be done on your stored samples. Researchers will not have access to your personal information and it will not be possible for investigators to contact you or your family about the results.

WHAT ABOUT CONFIDENTIALITY?
In order to keep your information private, your samples will be labelled with a code. Your personal information (name, address, phone number) will not be placed on the samples. Only the research staff will be able to link the code with your personal information. The results of tests done on your stored samples will not be included in your health records. Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

WHAT ARE MY RIGHTS?
If you decide not to sign this form, the samples described below will be collected from you and after all the HIPSS study related testing has been completed all remaining samples will be destroyed for any future testing.

STUDY APPROVAL
This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number BF269/13).

PERSONS TO CONTACT
In the event of any problems or concerns/questions you may contact Dr Ayesha Kharsany on (031) 260 4555. CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or the study Field co-ordinator, Mr David Khanyile on 083 393 0603, EPICENTRE or the UKZN Biomedical Research Ethics Committee, contact details as follows:

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Research Office, Westville Campus, Govan Mbeki Building
Private Bag X 54001, Durban, 4000, KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Thank you for your time.

CONSENT STATEMENT AND SIGNATURE PAGE FOR SAMPLE STORAGE VOLUNTEERS 18 YEARS AND OLDER

Please carefully read the statements below and think about your choice. No matter what you decide it will not affect your participation in the HIPSS study.

I agree to have my samples stored for future research and possible testing related to HIV and other infections.

☐Yes ☐No

_____	_____	_____
Volunteer Name (print)	Volunteer Signature	Date
_____	_____	_____
Study staff member who administered consent (print)	Staff staff Signature	Date
_____	_____	_____
Witness Name (print)	Witness Signature	Date

Was a copy of the signed copy given to the volunteer: ☐Yes ☐No

If no, why not:_____

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1.0 5 May 2014

INFORMED CONSENT FORM FOR PARENT / GUARDIAN / CARE GIVER TO CONSENT FOR SAMPLE STORAGE FOR VOLUNTEERS YOUNGER THAN 18 YEARS

The Principal Investigator of study is
Dr Ayesha BM Kharsany
2nd Floor Doris Duke Medical Research Institute
Nelson R Mandela School of Medicine
Private Bag 7, Congella 4013, Durban, South Africa
PHONE: 031-260 4555

INTRODUCTION
If your child/ward agrees to take part in the HIPSS study, there may be some remaining blood, urine and vaginal swab samples (females) known as samples, taken from your child/ward during the study that might be useful for future research. You are being asked to agree for the storage of the left over samples collected from your child/ward for possible future research that will include additional testing. This is research that will be conducted in the future that may or may not be related to the HIPSS study.

This consent form gives you information about the collection, storage, and use of your child/wards samples for possible future research. The study staff will talk to you about this information. Please ask if you have any questions. If you agree to the storage of your child/wards samples for possible future research, you will be asked to note this on this consent form. You will get a copy of this form to keep.

HOW WILL YOU GET THE SAMPLES FROM MY CHILD/WARD?
The HIPSS study staff will collect your child/wards blood, ask your child/ward to collect the urine sample and they will ask females to collect a vaginal swab as part of the HIPSS study that you have consented for your child/ward and your child/ward has assented to. These samples are needed to carry out the regular tests for the research study. If you agree to have your child/wards specimens stored for possible future research, we will store the remainder of the samples after the tests for the HIPSS study have been completed.

HOW WILL YOU USE MY CHILD/WARDS STORED SAMPLES ?
Researchers at CAPRISA and elsewhere will use your samples to look for HIV and other infections, or for damage caused by such infections, or the body's response to infection. Researchers may also look at your child/wards genes (DNA), since genes can affect the way the body responds to infections in important ways. Your child/wards genes might make your child/ward more or less likely to get infected, or make the responses to infection or to treatment stronger or weaker. If your child/ward becomes infected with HIV their genes might also affect how fast or slowly they develop AIDS.
Your child/wards samples may be shared with colleagues both in South Africa and outside of South Africa however, your child/wards stored samples will be sent with only their confidential PID number and will not be linked to any personal identifiers such as your child/wards name. All future research studies using your child/wards samples will be reviewed first by the CAPRISA Scientific Review Committee and a special committee at the Nelson R Mandela School of Medicine, Biomedical Research Ethics Committee**. It is important for you to know that your child/wards samples will not be sold or used in products that make money for the researchers.**

WHERE WILL MY CHILD/WARDS SAMPLES BE STORED?

If you agree to have your child/wards specimens stored they will be stored with your child/wards confidential PID number at special facilities that are designed to store blood samples safely and securely. The storage facilities are based at the CAPRISA research Laboratory, Doris Duke Medical Research Institute, Nelson R Mandela School of Medicine. The storage facilities are designed so that only approved researchers can have access to the samples.

HOW LONG WILL YOU KEEP MY CHILD/WARDS SAMPLES?
There is no time limit on how long your child/wards samples will be stored for.

DOES STORAGE OF MY SAMPLES BENEFIT ME?
It is unlikely that your child/ward will have any direct benefit from the tests done on the stored specimens but there may be benefits to society of doing research on your child/wards stored specimens. These benefits may include learning more about HIV infection.

WHAT ARE THE RISKS?
There are few risks related to storing your child/wards samples. When future tests are done on the stored samples, there is a very small but possible risk to your child/wards privacy. Some genetic testing may be done on your child/wards stored samples. Researchers will not have access to your child/wards personal information and it will not be possible for investigators to contact your child/ward or your child/wards family about the results.

WHAT ABOUT CONFIDENTIALITY?
In order to keep your child/wards information private, your child/wards samples will be labelled with a code. Your child/wards personal information (name, address, phone number) will not be placed on the samples. Only the research staff will be able to link the code with your child/wards personal information. The results of tests done on your child/wards stored samples will not be included in your child/wards health records. Every effort will be made to keep your child/wards personal information confidential, but we cannot guarantee absolute confidentiality. Your child/wards personal information may be disclosed if required by law.

WHAT ARE MY RIGHTS?
If your child/ward decides not to sign this form, the samples described below will be collected from your child/ward and after all the HIPSS study related testing has been completed all remaining samples will be destroyed for any future testing.

STUDY APPROVAL
This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval numberBF269/13).

PERSONS TO CONTACT
In the event of any problems or concerns/questions you may contact Dr Ayesha Kharsany on (031) 260 4555. CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or the study Field co-ordinator, Mr David Khanyile on 083 393 0603, EPICENTRE or the UKZN Biomedical Research Ethics Committee, contact details as follows:

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Research Office, Westville Campus, Govan Mbeki Building
Private Bag X 54001, Durban, 4000, KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Thank you for your time.

CONSENT STATEMENT AND SIGNATURE PAGE FOR PARENT / GUARDIAN / CARE GIVER FOR SAMPLE STORAGE FOR VOLUNTEERS YOUNGER THAN 18 YEARS

Please carefully read the statements below and think about your choice. No matter what you decide it will not affect your participation in the HIPSS study.

I agree to have my samples stored for future research and possible testing related to HIV and other infections.

☐Yes ☐No

_____	_____	_____
Parent / Guardian / Care giver Name (print)	Parent / Guardian / Care giver Signature	Date
_____	_____	_____
Study staff member who administered consent (print)	Staff staff Signature	Date
_____	_____	_____
Witness Name (print)	Witness Signature	Date

Was a copy of the signed copy given to the volunteer: ☐Yes ☐No

If no, why not:_____

Title of Study
KZN HIV Incidence Measurement System (HIPSS)
A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa
Version 1.0 5 May 2014

ASSENT FORM FOR SAMPLE STORAGE FOR POSSIBLE FUTURE RESEARCH FOR VOLUNTEERS YOUNGER THAN 18 YEARS

The Principal Investigator of study is
Dr Ayesha BM Kharsany
2nd Floor Doris Duke Medical Research Institute
Nelson R Mandela School of Medicine
Private Bag 7, Congella 4013, Durban, South Africa
PHONE: 031-260 4555

INTRODUCTION
If you agree to take part in the HIPSS study, there may be some remaining blood, urine and vaginal swab samples (females) known as samples, taken from you during the study that might be useful for future research. You are being asked to agree to the storage of the left over samples for possible future research that will include additional testing. Your parent / guardian / care giver will also need to asked and will need to consent to the storage of your sample for possible future research. This is research that will be conducted in the future that may or may not be related to the HIPSS study.
This consent form gives you information about the collection, storage, and use of your samples for possible future research. The study staff will talk to you about this information. Please ask if you have any questions. If you agree to the storage of your samples for possible future research, you will be asked to note this on this assent form. You will get a copy of this form to keep.

HOW WILL YOU GET THE SAMPLES FROM ME?
The HIPSS study staff will collect your blood, sputum, ask you to collect the urine sample and they will ask females to collect a vaginal swab as part of the HIPSS study that you have consented to. These samples are needed to carry out the regular tests for the research study. If you agree to have your specimens stored for possible future research, we will store the remainder of the samples after the tests for the HIPSS study have been completed.

HOW WILL YOU USE MY STORED SAMPLES?
Researchers at CAPRISA and elsewhere will use your samples to look for HIV and other infections, or for damage caused by such infections, or the body's response to infection. Researchers may also look at your genes (DNA), since genes can affect the way the body responds to infections in important ways. Your genes might make you more or less likely to get infected, or make the responses to infection or to treatment stronger or weaker. If you become infected with HIV your genes might also affect how fast or slowly you develop AIDS.
Your samples may be shared with colleagues both in South Africa and outside of South Africa however, your stored samples will be sent with only your confidential PID number and will not be linked to any personal identifiers such as your name. All future research studies using your samples will be reviewed first by the CAPRISA Scientific Review Committee and a special committee at the Nelson R Mandela School of Medicine Biomedical Research Ethics Committee**. It is important for you to know that your samples will not be sold or used in products that make money for the researchers.**

WHERE WILL MY SAMPLES BE STORED?
If you agree to have your specimens stored they will be stored with your confidential Participant Identification (PID) number at special facilities that are designed to store blood samples safely and

securely. The storage facilities are based at the CAPRISA research Laboratory, Doris Duke Medical Research Institute, Nelson R Mandela School of Medicine. The storage facilities are designed so that only approved researchers can have access to the samples.

HOW LONG WILL YOU KEEP MY SAMPLES?
There is no time limit on how long your samples will be stored for.

DOES STORAGE OF MY SAMPLES BENEFIT ME?
It is unlikely that you will have any direct benefit from the tests done on your stored specimens but there may be benefits to society of doing research on your stored specimens. These benefits may include learning more about HIV infection.

WHAT ARE THE RISKS?
There are few risks related to storing your samples. When future tests are done on the stored samples, there is a very small but possible risk to your privacy. Some genetic testing may be done on your stored samples. Researchers will not have access to your personal information and it will not be possible for investigators to contact you or your family about the results.

WHAT ABOUT CONFIDENTIALITY?
In order to keep your information private, your samples will be labelled with a code. Your personal information (name, address, phone number) will not be placed on the samples. Only the research staff will be able to link the code with your personal information. The results of tests done on your stored samples will not be included in your health records. Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

WHAT ARE MY RIGHTS?
If you decide not to sign this form, the samples described below will be collected from you and after all the HIPSS study related testing has been completed all remaining samples will be destroyed for any future testing.

STUDY APPROVAL
This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval numberBF269/13).

PERSONS TO CONTACT
In the event of any problems or concerns/questions you may contact Dr Ayesha Kharsany on (031) 260 4555. CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or the study Field co-ordinator, Mr David Khanyile on 083 393 0603, EPICENTRE or the UKZN Biomedical Research Ethics Committee, contact details as follows:

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Private Bag X 54001, Durban, 4000, KwaZulu-Natal, SOUTH AFRICA
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Email: BREC@ukzn.ac.za

Thank you for your time.

ASSENT STATEMENT AND SIGNATURE PAGE FOR SAMPLE STORAGE FOR VOLUNTEERS YOUNGER THAN 18 YEARS

Please carefully read the statements below and think about your choice. No matter what you decide it will not affect your participation in the HIPSS study.

I agree to have my samples stored for future research and possible testing related to HIV and other infections.

□Yes □No

_____	_____	_____
Volunteer Name (print)	Volunteer Signature	Date
_____	_____	_____
Study staff member who administered assent (print)	Staff staff Signature	Date
_____	_____	_____
Witness Name (print)	Witness Signature	Date

Was a copy of the signed copy given to the volunteer: □Yes □No

If no, why not:_____

APPENDIX F – PARTCIPANT IDENTIFICATION

Team ID

Participant Id number		**GPS coordinate**	
Team ID		**Supervisor**	

Section 1 : Eligibility for enrolment into the cohort

1. What is your age at your last birthday?	
☐ Older than 35 • **Not eligible for the cohort study. Thank participant and terminate interview**	☐ Between 15-35 • **Eligible for possible selection for enrolment in the cohort**
2. Are you planning to stay in this area for the next 12 months	
☐ No • **Not eligible for the cohort study Thank participant and terminate interview**	☐ Yes • **Eligible for possible selection for enrolment in the cohort**
3. Are you willing to be involved in a follow up survey should you be selected (cohort)	
☐ No • **Not eligible for the cohort study interview and complete the refusal section 3**	☐ Yes • **Enrol for possible selection for enrolment in the cohort. Complete section 2**

Section 2: Participant Identification

Note: Only collect information if participant is between 15 – 35 years

Explain to the participant that people who are of the eligible (between 15 to 35) will be randomly selected to be followed up. Not all people will be contacted. Those that are selected will be notified and re-interviewed in 12 months' time.

4. Participant first name	
5. Participant nick name	
6. Participants surname	
7. South African Identification number	
8. Home address + GPS coordinates	
9. Home telephone number (land line)	
10. Work telephone number (land line)	
11. Cell phone number	
Can you provide the name of a relative or friend that can assist us to contact you should the above numbers change? Please note that this person will not be told that the participant has been enrolled in the study rather they will be told it is a routine call to confirm their contact details for a date based that they have given permission to be enrolled in	
12. Friend / relatives first name	
13. Friend / relatives surname	
14. Friend / relatives Home telephone number	
15. Friend / relatives cell phone number	
16. Please indicate your prefered method of cummunication **(Please note that if we can not reach you by your prefered method we will try alternative methods and fianly a home visit)**	□ SMSCell phone callTelephone call on home phoneTelephone call at work phoneTelephone call to friend / relative land lineTelephone call to friend / relative cell phone □ Home visit

Section 3: Refusal to participate in the cohort

17. What are the reasons that you did not want to participate?[1]	
□ Participant declined to give a reasons for refusal	□ Need partner / parental consent and they will not allow it

□ I don't have time to participant in the survey □ I am ready know I am HIV positive □ I don't wish to be retested for HIV □ I don't want blood drawn again	□ Prefer to be tested away from home □ Prefer to test without a partner □ Fear breach of confidentiality □ I find the topics uncomfortable or embarrassing Other _____

Section 4

Finger Print scanning

4.1 Finger Print

Prompt: please place your finger print onto the scanning divice .

Scan the finger print

Section 5

Lab Samples

5.1 Prompt: Thank you for agreeing to participate. We will start with the lab test specimens.

Please note that your results will be available from your local Department of Health Clinic.

Give the participant a card with the linked barcode and write the name of the clinic were the results will be send on the car.

5.2Barcode

Scan the bar code in order to scan the barcode assigned to this participant's specimines

APPENDIX G – FEMALE CROSS SECTIONAL QUESTIONNAIRE

Female

Title of Study: HIV Incidence Provincial Surveillance System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the

uMgungundlovu District, KwaZulu-Natal, South Africa

Participant Identification

Participant Id number		GPS coordinate	
Team id		Supervisor	
Attempts to survey participant			
1. Date	Time DD/MM/YYYY	Time DD/MM/YYYY T	Time DD/MM/YYYY
2. Staff id			
3. Next visit Date and time			
4. Result*			

***Result options:**

a) 1-consented + figure scanned, 2-refused + replaced, 3-refused+HH replaced 4 not found + replaced 5 not found + hh replaced 1-Member consented

(Rule: if 1st HH to refuses replace with 2nd selected member, if 2nd member refused replace HH)

5. Confirm eligibility for the cross-sectional
Not eligible if yes to any of the following questions : □ Younger than 15 years of age □ Older than 49 years of age □ Non-residents from the study area. □ Refusal by participant to participate in the study □ Refusal by participant to provide clinical samples of peripheral blood, urine, sputum and self-collected vulvo-vaginal swab samples (females)

- Unable to provide necessary assent or consents
- Cognitive or mental challenges (based on the assessment of the participants ability to comprehend the study information provided)
- Stated intent to leave study indefinitely for work or any other reason in the next 12 months

If not eligible end the survey and thank participant and replace. Must obtain supervisor sign off

Section 1: Demographics

(age, gender, marital status, education, number of dependents)

6. Are you	☐ Male ☐ Female
7. How old were you at your last birthday?	Years _____.
8. What is your highest education qualification[15]	
☐ No schooling/ crèche/ pre-primary ☐ Primary (grade 1 – 7),- ☐ Incomplete secondary (grade 8 – 11/NTC1/NTC2)	☐ Completed secondary (grade 12/NTC3), ☐ Tertiary (diploma/ degree) ☐ No response
9. What is your home language? [16]	
☐ Zulu ☐ Xhosa ☐ Sotho	☐ English ☐ Afrikaans ☐ Other _____.
10. What is your race?[17]	
☐ African ☐ Coloured	☐ White ☐ Asian/Indian ☐ Other _____.
11. What is your nationality [18]	
☐ South African citizen → Do you have a SA identity document ☐ No ☐ Yes ☐ Refugee	☐ Non-citizen (Legal resident) → How many years have you lived in South Africa _____. ☐ Other_____
12. How long have you lived in this community?	

[15] Source: *Leibbrandt*, M. *et al*. (*2010*), "Trends in South African. Income Distribution and Poverty since the Fall of. Apartheid

[16] Source: SA National Health, Demographic and Behaviour Survey 2011

[17] Source: SA National Health, Demographic and Behaviour Survey 2011

[18] Source: SA National Health, Demographic and Behaviour Survey 2011

□ Always □ No response	□ YY____MM_____. → Where did you move from □ Within in this district □ Outside this district but within Kwazulu Natal □ Another province in South Africa □ Outside South Africa

13. In the last 12 months, have you been away from your home for more than one consecutive month?[19]	
□ No	□ Yes □ No response
14. What is your marital status?[20]	
□ Legally married □ Living together like husband and wife □ Divorced □ Separated, but still legally married	□ Widowed □ Single, but have been living together with someone as husband/wife before □ Single and have never been married/never lived together as husband/wife before

Section 2: Knowledge and motivation

15. Can you tell me all the ways that you know that HIV can be prevented?[21] (Do not read out options. Multiple responses are possible)	
□ Using a condom. □ Abstaining from sex. □ Sticking to one sexual partner. □ Having fewer sexual partners. □ Not having sex before marriage. □ Avoid contact with blood/using gloves.	□ Using drugs to prevent transmission of mother to child. □ Male circumcision. □ Taking ARV's within 72hours of being exposed to the HIV virus. □ Don't know.

[19] Source: SA National Health, Demographic and Behaviour Survey 2011
[20] Source : General Household Survey 2011, Statistics SA
[21] Source: SA National Health, Demographic and Behaviour Survey 2008

Perceived risk for HIV

16. How likely do you think you are you to contract HIV in the future?	
□ I am definitely going to be infected. □ I am probably going to get infected. → What are your reasons for believing so? (Multiple answers possible.) □ I am sexually active. □ I have many sexual partners. □ I don't use condoms. □ I don't always use condoms. □ I don't trust my partner. □ I am sick. □ My partner is sick. □ My partner died of AIDs. □ I had an accident/cuts. □ Other_____.	□ I probably won't get infected. □ I will definitely not get infected. → What are your reasons for believing so? (Multiple reasons possible). □ I have never had sex. □ I have abstained from sex. □ I am faithful to my partner. □ I trust my partner. □ I use condoms. □ I know my HIV status. □ My partner is circumcised. □ I do not have sex with sex workers. □ My ancestors protect me. □ God protects me. □ I am not at risk for HIV. □ Other_____

Perceived power to prevent HIV transmission

17. Please select the most appropriate option:[22]	Agree	Partially agree	Don't agree
□ It is the man who decides when to have sex. □ Men need sex more than women do. □ Men don't like using condoms. □ It is ok for a man to have more than one sexual partner.			

18. Select the most appropriate option:[23]	Agree	Uncertain	Disagree
□ Using a condom seems like an insult to my partner.			

[22] Source: Adapted from Pulerwtiz & Barker, (2008) and self-developed

[23] Source: Adapted from Pulerwtiz & Barker, (2008) and self-developed

☐ I don't enjoy sex with a condom.			

Perceived consequence of contracting HIV[24]

19. Select the most appropriate option:	Agree	Uncertain	Disagree
☐ AIDS is probably the worst disease I could get. ☐ My friends/family would disown me if I was to contract HIV. ☐ I am not afraid of contracting HIV as there are effective drugs to treat it.			

Attitudes to MMC

20. **Would you prefer your sexual partner to be circumcised?** [25]	
☐ No ☐ Doesn't matter	☐ Yes
21. Have you heard that circumcision has been shown to partly reduce the chance of HIV infection amongst men?	
☐ No ☐ Don't know	☐ Yes

Section 3 - Situational action context

Alcohol and drug use

22. Did you drink alcohol in the last year?[26]	
☐ No [If never skip the next section]	☐ Yes → How often do you have 5 or more drinks on one occasion? ☐ Never ☐ Less the monthly ☐ Monthly

[24] Source: Adapted from Pulerwtiz & Barker, (2008) and self-developed

[25] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

[26] Source : Heard Tavern intervention survey

	☐ Weekly ☐ Daily (or almost daily)
23. How often do you have sex after drinking?[27]	
☐ Never	☐ Always. ☐ Sometimes. → How often do you use a condom in these instances? ☐ Always ☐ Sometimes ☐ Never → Who do you have sex with in these instances? ☐ Stable partner. ☐ Casual partner. → Stranger.

Drug use

		Never	Monthly or less	2-4 times per month	2-3 times per week	4 or more times per week
	Dagga					
	Heroin					
	Cocaine					
	Glue					
	Tik					
	Wunga					
	Quh					
	Other addictive substances					

[27] Source: SA National Health, Demographic and Behaviour Survey 2008

[28] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

25. How often do you have sex after taking drugs (in last 6 months)?[29]		
☐ Always.	☐ Sometimes	☐ Never

Depression

We would like you to describe ways that you may have felt or behaved during the last week.

	Rarely (Less than 1 day)	Some of the time (1-2 days)	Occasionally (3-4 days)	All of the time (5-7 days)
26. I was bothered by things that don't usually bother me.[30]				
27. I had trouble keeping my mind on what I was doing.				
28. I felt depressed.				
29. I felt everything I did was an effort.				
30. I felt hopeful about the future.				
31. I felt fearful.				
32. My sleep was restless.				
33. I was happy.				
34. I felt lonely.				
35. I could not get going.				

36. Have you ever accessed treatment to assist you with depression?	
☐ No	☐ Yes → If yes, what services did you access? ☐ Doctor /nurse in a public facility. ☐ Private Doctor or

[29] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

[30] Source: CES-D10 Short form depression questionnaire

	nurse. □ Private Counsellor. □ Support group. □ EAP in the workplace. □ Medication. □ Other_____.

Section 4 - Social interactions

Access to social, financial and emotional support

37. What forms of support, in the last month, have you received from important people/organisations in your life?	**Tangible (money, food, care)**	**Educational/ Informational**	**Emotional/ Relational (support/ bonding)**
Biological Father			
Biological Mother			
Sibling			
Grandparent			
Other Family member			
Other community member			
Teacher			
Nurse/Doctor			
Internet/sites cafes/Social media			
Stokvels			
Church groups			
Taverns			
Sport/ youth clubs			
Traditional leadership structures			
Work friends or employer			
Other			

HIV stigma

38. Choose the best answer [31]	No	Yes	Unsure
□ People with HIV/AIDS should be ashamed.			
□ People with HIV/ AIDS must have done something wrong.			
□ I do not want to be friends with someone with HIV / AIDS.			

Section 5- HIV Status and risk

HIV status information

39. Have you been tested to see if you are HIV positive? [32]	
□ No → What are the reasons you did not have an HIV test? □ Do not need to test □ Do not want to know/am afraid. □ It's better not to know. □ Have to get my partners permission. □ Want to test with my partner. □ Don't know where to test/don't have access to testing. □ Other_____ [If no skip next section]	□ Yes → How many times have you had a test in your life time?____. → When was the last time that you had an HIV test?(give best approximate date)_____. → Did you get the result of this test? □ No □ Yes [If no skip to the next section]
40. Would you like me to refer you to our parallel HIV testing service?	
□ No	□ Yes

[31] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

[32] Source: Swaziland HIV Incident Measurement Survey, 2011

	If yes, refer the participant using the referral process
41. What was the result of your latest HIV test?[33]	
☐ Negative. ☐ Indeterminate. ☐ Did not respond.	☐ Positive. → Are you currently being provided with any of the following support or treatment? ☐ Nutritional support. ☐ Emotional support (support groups). ☐ Treatment buddy. ☐ Home based care. ☐ CD4 test. ☐ Viral load test. ☐ Financial support. ☐ Treatment of opportunistic infections. → Has a Doctor or Nurse told you that you need to take ARV's? ☐ No ☐ Yes → If yes, which dose pill did you take? ☐Have not started ARVs ☐Multiple dose ☐Fixed/single dose → Are you still taking ARV's? ☐No ☐Yes → Have you ever been pregnant while you were HIV positive? ☐No ☐Yes → Which of the following clinical services did you access while HIV positive and pregnant? ☐An HIV test at an antenatal visit.

[33] Source: Swaziland HIV Incident measurement Survey, 2011

	□Medication to prevent mother to child transmission. □Follow up care for HIV+ Women and their infants. □Counselling/support for breastfeeding. □Testing of your baby. □Infant milk formula. → Did your baby become infected with HIV? □No □Yes
42. Could you have been exposed to TB in the last 12 month? ("Please note all of the following that are true"?)	
□ I was in prison in the last 12 months □ I was in hospital in the 12 months	□ I was in contact with someone who has TB in the last 12 months □ I had contact with someone who has resistant TB (MDR or XDR) in the last 12 months □ I lived in a hostel or informal settlement in the 12 months
43. In the past 2 weeks have you had any of the following symptoms? <u>Select one or more the following</u>	
□ Unexplained persistent cough for more than 2 weeks □ Coughed up blood □ Loss of appetite □ Unexplained weight loss	□ Drenching night sweats □ Fevers □ None of the above □ Don't know □ Do not want to disclose **<u>If the participant answer yes to any of these questions flag for referral to TB screening and take a sputum sample</u>**
44. Have you ever been tested for TB?[34]	
□ No	□ Yes → Are you on TB treatment?

[34] Source: SA National Health, Demographic and Behaviour Survey 2011

	☐ No ☐ Yes
45. Has a doctor or nurse ever told you that you have TB?	
☐ No → If no, are you currently taking medication to prevent TB (IPT)? ☐ No ☐ Yes ☐ If yes when did you start taking this medication? MM__YY____ ☐ If no have you taken any IPT medication in last 12 months? ☐ No ☐ Yes	☐ Yes → What was the date when you were first diagnosed with TB? MM____YY_____ → When did you start your TB medication?MM____YY____. → Have you completed your treatment? ☐ No ☐ No did not take medication ☐ Yes
46. Has a doctor or nurse ever told you that you have an STI?	
☐ No → Do you currently have any possible symptoms of an STI such as ulcers and discharge area? ☐ No ☐ Yes → If yes may I refer your for STI screening to our parallel service? **<u>If the participant answer yes to any of these questions flag for referral to STI screening</u>**	☐ Yes → What was the date when you were diagnosed with a STI? MM____YY_____. → Have you completed your treatment? ☐ No ☐ Yes

47. Has a doctor or nurse ever given you medication to prevent you contracting HIV because you were exposed (Raped, touched blood etc.) to the HIV virus?	
□ No	□ Yes

Section 6 - Sexual history

I now have to ask you very sensitive questions on sex and other sex-related matters. Please remember that your name will not be recorded anywhere in this questionnaire and the information you give will be kept confidential.

Different people have different definitions of 'sex' or 'sexual intercourse.' For this study, sex can include several things, such as:

- Vaginal sex, which is when a man puts his penis in a woman's vagina.
- Anal sex, which is when a man puts his penis in another person's rectum or butt.

First Sex

48. Have you ever had sex?[35]	
□ No → What was the main reason for not having sex? □ No partner available. □ Do not want to have sex. □ Waiting for marriage. □ Religious reasons. □ Avoiding HIV or STI's. □ Avoiding pregnancy. □ Fear of authority. □ Other:_____ [Skip section on sexual history]	□ Yes → How old were you when you first had sex? □ ____years. □ Don't remember. □ Did not respond. → How old was your partner? □ ____years. □ Don't know. □ Did not respond. → Did you use a condom?[36] □ No □ Yes □ Don't remember → Were you forced to have sex? □ No

[35] Source: SA National Health, Demographic and Behaviour Survey 2011

[36] Source: SA National Health, Demographic and Behaviour Survey 2011

	☐ Yes ☐ Don't remember

Life time Sex

49. How many people have you had sex with in your life time? (It is ok to estimate the number if you don't remember exactly).[37]	_____ number.
50. How many people have you had sex with in the last 12 months?	
☐ Have not had sex in the last 12 months.	_____number. → How often did you use a condom when you had sex? ☐ Sometime ☐ Always ☐ Never → Have you ever taken ARV medication (PREP) to prevent getting HIV before you had sex? ☐ No ☐ Yes → What type of PREP did you take? ☐ Oral medication ☐ Gel → Did you know the HIV status of these partners? ☐ Yes, all of them. ☐ Yes, some of them. ☐ No, none of them.[38] → How many of these partners did you know were HIV positive? ☐ All of them. ☐ Some of them

[37] SOURCE: Swaziland HIV Incident measurement Survey, 2011

[38] SOURCE: Swaziland HIV Incident measurement Survey, 2011

	☐ None of them.

Last 3 sexual partners

Now I am going to ask you more details about the 3 most recent partners that you have had sex with. Please tell me about them starting with the most recent (newest) partner.

		☐ No second partner, skip to next section.	☐ No third partner, skip to next section.
	Partner 1	Partner 2	Partner 3
51. Their first name/nick name.			
52. What is the nature of your relationship?[39]	☐ Husband. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.	☐ Husband. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.	☐ Husband. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.
53. What is the current age of your partner?[40]	_____ years.	_____years.	_____years.
54. Is this partner a member of your household?[41]	☐ No ☐ Yes	☐ No ☐ Yes	☐ No ☐ Yes
55. Month and year sexual relationship began.[42]	MM___ YY___	MM___ YY___	MM___ YY___
56. When did this sexual relationship end?	MM___ YY___ ☐ Not ended	MM___ YY___ ☐ Not ended	MM___ YY___ ☐ Not ended
57. Partner's sex?[43]	☐ Male	☐ Male	☐ Male

[39] SOURCE: Swaziland HIV Incident measurement Survey, 2011

[40] SOURCE: Swaziland HIV Incident measurement Survey, 2011

[41] Source: Africa Centre Demographic information 2010

[42] SOURCE: Swaziland HIV Incident measurement Survey, 2011

[43] SOURCE: Swaziland HIV Incident measurement Survey, 2011

	☐ Female	☐ Female	☐ Female
58. If male, is he circumcised? **(skip if patner female)**	☐ Circumcised at start of relationship. ☐ Not circumcised. ☐ Became circumcised during relationship. ☐ Don't know.	☐ Circumcised at start of relationship. ☐ Not circumcised. ☐ Became circumcised during relationship. ☐ Don't know.	☐ Circumcised at start of relationship. ☐ Not circumcised. ☐ Became circumcised during relationship. ☐ Don't know.
59. How many times did you have sex with this partner in the last 12 months?[44]	☐ Never in the last 12 months. ☐ Once. ☐ 2 – 5 times. ☐ 6 – 10 times. ☐ 10 – 20 times. ☐ More than 20 times.	☐ Never in the last 12 months. ☐ Once. ☐ 2 – 5 times. ☐ 6 – 10 times. ☐ 10 – 20 times. ☐ More than 20 times.	☐ Never in the last 12 months. ☐ Once. ☐ 2 – 5 times. ☐ 6 – 10 times. ☐ 10 – 20 times. ☐ More than 20 times.
60. How often did you use a condom when you had sex?[45]	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never
61. If you never used a condom with this partner, was it because you battled to access condoms when having sex with this partner?	☐ No ☐ Yes ☐ Sometimes	☐ No ☐ Yes ☐ Sometimes	☐ No ☐ Yes ☐ Sometimes
62. How often did you give or receive money/gifts so that you could have sex with this person?[46]	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never

[44] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[45] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[46] SOURCE: Swaziland HIV Incident measurement Survey, 2011

63. Did you and your partner have anal sex in the last 12 months?	□ No □ Yes If no, skip the next question.	□ No □ Yes If no, skip the next question	□ No □ Yes If no skip the next question.
64. How often did you and your partner use a condom when you had anal sex in the last 12 months?[47]	□ Never had anal sex. □ Always. □ Sometimes. □ Never.	□ Never had anal sex. □ Always. □ Sometimes. □ Never.	□ Never had anal sex. □ Always. □ Sometimes. □ Never.
65. When you were having a sexual relationship with this partner, do you think that he/she was HIV positive?[48]	□ No. □ Don't know. □ Yes. → Do you think that this partner was taking ARV's for HIV?[49] □ No. □ Yes. □ Don't know.	□ No. □ Don't know. □ Yes. → Do you think that this partner was taking ARV's for HIV?[50] □ No. □ Yes. Don't know.	□ No. □ Don't know. □ Yes. → Do you think that this partner was taking ARV's for HIV?[51] □ No. □ Yes. Don't know.
66. Have you told your partner your HIV status?	□ No. □ Yes.	□ No. □ Yes.	□ No. □ Yes.
67. Has this partner had any STI's in the last 12 months?	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.
68. Can you talk about safe sex with this	□ No. □ Yes.	□ No. □ Yes.	□ No. □ Yes.

[47] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[48] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[49] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[50] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[51] SOURCE: Swaziland HIV Incident measurement Survey, 2011

partner?	☐ Don't know.	☐ Don't know.	☐ Don't know.
69. Has this partner ever forced you to have sex when you did not want to?	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.

Section 7- Health access

Health status HIV, TB, chronic conditions, Pregnancy, disabilities

70. Have you suffered any of the following illnesses in the past 12 months?[52]	
☐ Heart disease. ☐ Stroke. ☐ Arthritis. ☐ Obesity (very over weight). ☐ High blood pressure. ☐ Diabetes. ☐ TB. ☐ Pneumonia. ☐ Cancer. ☐ Malaria.	☐ Depression/anxiety. ☐ Asthma. ☐ Hepatitis. ☐ STI's. ☐ Peptic Ulcers. ☐ Kidney disease. ☐ HIV. ☐ Other_____. → Are you accessing medical assistance for your illness ☐ No ☐ Yes

Access to contraception

71. Are you currently using a contraceptive method?	
☐ No → Why not ☐ Trying to fall pregnant. ☐ Cannot access	☐ Yes → Which kind ☐ Condoms. ☐ Injection 2 months (*Nur-Isterate*).

[52] Source: SA National Health, Demographic and Behaviour Survey 2011

contraceptive methods. ☐ No reason. ☐ My partner can not make me pregnant	☐ Injection 3 months (Depo Provera). ☐ Daily pill. ☐ IUCD. ☐ Spermicides. ☐ Rhythm/calendar/safe period/Withdraw/Thigh sex /Masturbation. ☐ Emergency contraception. ☐ Anal sex. ☐ Female sterilisation. ☐ Oral sex. ☐ Other _____. ☐ No response. → Are you able to access your contraceptive method whenever you need it? ☐ No ☐ Yes
72. Have you ever been pregnant?	
☐ No	☐ Yes → Were you still at school during your first pregnancy? ☐ No ☐ Yes → Did you return to school afterwards? ☐ No ☐ Yes → During your last pregnancy did you still have sex while pregnant? ☐ No ☐ Yes → Did you (still) use condoms? ☐ No ☐ Yes → How many children have you had in total ____.

	→ How many are still alive _____.

Exposure to prevention programmes.

73. In the past 12 months, from where/or whom have you received HIV information that has been useful to you?[53]	
☐ No one. ☐ Billboard. ☐ A child or learner of school going age. ☐ A religion/faith based organisation. ☐ The workplace. ☐ Community meeting. ☐ Traditional healer. ☐ AIDS or welfare organisation.	☐ Newspaper. ☐ Television. ☐ Clinic, hospital or doctor. ☐ Telephone help line. ☐ Pharmacy or chemist. ☐ Parent, family or care giver. ☐ Partner. ☐ Friend. ☐ Other.
74. Which of the following activities have you participated in, in the past 12 months?	
☐ Community meeting on HIV & AIDS. ☐ Membership of an HIV organisation e.g. TAC ☐ Volunteer for HIV activities e.g. fund raising. ☐ Attended a local HIV rally or march. ☐ Attended an HIV educational event in the workplace. ☐ Attended an HIV play or event. ☐ Attended a support group for HIV/AIDS.	☐ Cared for a person who is sick with AIDS. ☐ Helped a family who has someone sick with AIDS. ☐ Helped a family who lost a member as a result of AIDS. ☐ Other: _____. ☐ No response.
75. In the last 12 months, have you seen or heard any messages about the following topics related to HIV?[1]	
☐ Get an HIV test to know your status. ☐ Reduce your number of sex partners. ☐ Use condoms every time you have sex. ☐ Male circumcision for HIV prevention.	☐ ARV's are available at clinics to treat HIV. ☐ All pregnant women should get an HIV test. ☐ ARV's are available to women to prevent mother to child transmission. ☐ Other:_____.

[53] Source: SA National Health, Demographic and Behaviour Survey 2011

Complete the Eligibility Questionnaire for cohort

APPENDIX H – MALE CROSS SECTIONAL QUESTIONNAIRE

Title of Study: HIV Incidence Provincial Surveillance System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the

uMgungundlovu District, KwaZulu-Natal, South Africa

Participant Identification

Participant Id number		GPS coordinate	
Team id		Supervisor	
Attempts to survey participant			
1. Date	Time DD/MM/YYYY	Time DD/MM/YYYY T	Time DD/MM/YYYY
2. Staff id			
3. Next visit Date and time			
4. Result*			

***Result options:**

a) 1-consented + figure scanned, 2-refused + replaced, 3-refused+HH replaced 4 not found + replaced 5 not found + hh replaced 1-Member consented

(Rule: if 1st HH to refuses replace with 2nd selected member, if 2nd member refused replace HH)

5. Confirm eligibility for the cross-sectional
Not eligible if yes to any of the following questions : □ Younger than 15 years of age □ Older than 49 years of age □ Non-residents from the study area. □ Refusal by participant to participate in the study □ Refusal by participant to provide clinical samples of peripheral blood, urine, sputum and self-collected vulvo-vaginal swab samples (females) □ Unable to provide necessary assent or consents □ Cognitive or mental challenges (based on the assessment of the participants ability to comprehend the study information provided) □ Stated intent to leave study indefinitely for work or any other reason in the next 12 months If not eligible end the survey and thank participant and replace. Must obtain supervisor sign off

Section

Finger Print scanning

4.1 Finger Print

Prompt: please place your finger print onto the scanning divice .

Scan the finger print

Section

Lab Samples

5.1 Prompt: Thank you for agreeing to participate. We will start with the lab test specimines

5.2Barcode

Scan the bar code in order to scan the barcode assigned to this participant's specimines

Section 1: Demographics

(age, gender, marital status, education, number of dependents)

6. Are you	□ Male □ Female
7. How old were you at your last birthday?	Years _____.
8. What is your highest education qualification[1]	
□ No schooling/ crèche/ pre-primary □ Primary (grade 1 – 7) □ Incomplete secondary (grade 8 – 11/NTC1/NTC2)	□ Completed secondary (grade 12/NTC3), □ Tertiary (diploma/ degree) □ No response
9. What is your home language?[1]	
□ Zulu □ Xhosa □ Sotho	□ English □ Afrikaans □ Other _____.
10. What is your race?[1]	
□ African □ Coloured	□ White □ Asian/Indian □ Other _____.
11. What is your nationality[1]	
□ South African citizen	□ Non South African resident (non-citizen)

→ Do you have a SA identity document □ No □ Yes □ Other _____.	□ How many years have you lived in South Africa _____.
12. How long have you lived in this community?	
□ Always □ No response	□ YY____MM_____. → Where did you move from □ Within in this district □ Outside this district but within Kwazulu Natal □ Another province in South Africa □ Outside South Africa
13. In the last 12 months have you been away from your home for more than one consecutive month[1]	
□ No	□ Yes □ No response
What is your marital status?[54]	
□ Legally married □ Living together like husband and wife □ Divorced □ Separated, but still legally married	□ Widowed □ Single, but have been living together with someone as husband/wife before □ Single and have never been married/never lived together as husband/wife before

Section 2: Knowledge and motivation

HIV knowledge of prevention

14. Can you tell me all the ways that you know that HIV can be prevented?[1] (Do not read out options. Multiple responses are possible)	
□ Using a condom. □ Abstaining from sex.	□ Using drugs to prevent transmission of mother to child.

[54] Source : General Household Survey 2011, Statistics SA

□ Sticking to one sexual partner. □ Having fewer sexual partners. □ Not having sex before marriage. □ Avoid contact with blood/using gloves.	□ Male circumcision. □ Taking ARV's within 72hours of being exposed to the HIV virus. □ Don't know.

Perceived risk for HIV

15. How likely do you think you are you to contract HIV in the future?	
□ I am definitely going to be infected. □ I am probably going to get infected. → What are your reasons for believing so? (Multiple answers possible.) □ I am sexually active. □ I have many sexual partners. □ I don't use condoms. □ I don't always use condoms. □ I don't trust my partner. □ I am sick. □ My partner is sick. □ My partner died of AIDs. □ I had an accident/cuts. □ Other_____.	□ I probably won't get infected. □ I will definitely not get infected. → What are your reasons for believing so? (Multiple reasons possible). □ I have never had sex. □ I have abstained from sex. □ I am faithful to my partner. □ I trust my partner. □ I use condoms. □ I know my HIV status. □ My partner is circumcised. □ I do not have sex with sex workers. □ My ancestors protect me. □ God protects me. □ I am not at risk for HIV. □ Other_____

Perceived power to prevent HIV transmission

16. Please select the most appropriate option[1]:	Agree	Partially agree	Don't agree
→ It is the man who decides when to have sex. → Men need sex more than women do. → Men don't like using condoms. → It is ok for a man to have more than one sexual partner.			
17. Select the most appropriate option[1]:	Agree	Partially agree	Don't agree

□ Using a condom seems like an insult to my partner. □ I don't enjoy sex with a condom.			

Perceived consequence of contracting HIV

18. Select the most appropriate option:	Agree	Partially agree	Don't agree
□ AIDS is probably the worst disease I could get. □ My friends/family would disown me if I was to contract HIV. □ I am not afraid of contracting HIV as there are effective drugs to treat it.			

Attitudes to MMC

19. Have you heard that circumcision has been shown to partly reduce the chance of HIV infection amongst men?	
□ No □ Don't know	□ Yes

Section 3 - Situational action context

Alcohol and drug use

20. Did you drink alcohol in the last year?[1]	
□ No [If never skip the next section]	□ Yes → How often do you have 5 or more drinks on one occasion? □ Never □ Less the monthly □ Monthly □ Weekly □ Daily (or almost daily)

21. How often do you have sex after drinking?[1]	
☐ Never	☐ Always. ☐ Sometimes. → How often do you use a condom in these instances? ☐ Always ☐ Sometimes ☐ Never → Who do you have sex with in these instances? ☐ Stable partner. ☐ Casual partner. ☐ Stranger.

Drug use

		Never	**Monthly or less**	**2-4 times per month**	**2-3 times per week**	**4 or more times per week**
	22. Dagga					
	23. Heroin					
	24. Cocaine					
	25. Glue					
	26. Tik					
	27. Wunga					
	28. Quh					
	29. Other					

30. How often do you have sex after taking drugs?[1]		
☐ Always.	☐ Sometimes	☐ Never

Depression.

We would like you to describe ways that you may have felt or behaved during the last week.

	Rarely (Less than 1 day)	**Some of the time (1-2 days)**	**Occasionally (3-4 days)**	**All of the time (5-7 days)**
31. I was bothered by things that don't usually bother me.[1]				
32. I had trouble keeping my mind on what I was doing.				
33. I felt depressed.				
34. I felt everything I did was an effort.				
35. I felt hopeful about the future.				
36. I felt fearful.				
37. My sleep was restless.				
38. I was happy.				
39. I felt lonely.				
40. I could not get going.				

41. Have you ever accessed treatment to assist you with depression?

☐ No	☐ Yes → If yes, what services did you access? ☐ Doctor /nurse in a public facility. ☐ Private Doctor or nurse. ☐ Private Counsellor. ☐ Support group. ☐ EAP in the workplace. ☐ Medication. ☐ Other_____.

Section 4 - Social interactions

Access to social, financial and emotional support

42. What forms of support, in the last month, have you received from important people/organisations in your life?	**Tangible (money, food, care)**	**Educational/ Informational**	**Emotional/ Relational (support/ bonding)**
Biological Father			
Biological Mother			
Sibling			
Grandparent			
Other Family member			
Other community member			
Teacher			
Nurse/Doctor			
Internet/sites cafes/Social media			
Stokvels			
Church groups			
Taverns			
Sport/ youth clubs			
Traditional leadership structures			
Work friends or employer			
Other			

HIV stigma

43. Choose the best answer[1]	No	Yes	Unsure
□ People with HIV/AIDS should be ashamed.			
□ People with HIV/ AIDS must have done something wrong.			
□ I do not want to be friends with someone with HIV / AIDS.			

Section 5- HIV Status and risk

HIV status, HIV status of partner, HIV status of family members

HIV status information

44. Have you been tested to see if you are HIV positive?[1]	
☐ No → What are the reasons you did not have an HIV test? ☐ Don't need to test ☐ Do not want to know/am afraid. ☐ It's better not to know. ☐ Have to get my partners permission. ☐ Want to test with my partner. ☐ Don't know where to test/don't have access to testing. ☐ Other_____ [If no skip next section]	☐ Yes → How many times have you had a test in your life time?____. → When was the last time that you had an HIV test?(give best approximate date)_____. → Did you get the result of this test? ☐ No ☐ Yes [If no skip to the next section]
41 Would you like me to refer you to our parallel HIV testing service?	
☐ No	☐ Yes If yes refer the participant using the referral process
42 What was the result of your latest HIV test?[1]	
☐ Negative. ☐ Indeterminate. ☐ Did not respond.	☐ Positive. → Are you currently being provided with any of the following support or treatment? ☐ Nutritional support. ☐ Emotional support (support groups). ☐ Treatment buddy. ☐ Home based care. ☐ CD4 test. ☐ Viral load test. ☐ Financial support. ☐ Treatment of opportunistic infections.

	→ Has a Doctor or Nurse told you that you need to take ARV's? □ No □ Yes → If yes, which dose pill are you on? □Have not started ARV □Multiple dose □Fixed/single dose → Are you still on ARV's? □No □Yes
45. Could you have been exposed to TB in the last 12 month? **(**"Please note all of the following that are true"?)	
□ I was in prison in the last 12 months □ I was in hospital in the 12 months	□ I lived in a hostel or informal settlement in the 12 months □ I was in contact with someone who has TB in the last 12 months □ I had contact with someone who has resistant TB (MDR or XDR) in the last 12 months
46. In the past 2 weeks have you had any of the following symptoms? <u>Select one or more the following</u>	
□ Unexplained persistent cough for more than 2 weeks □ Coughed up blood □ Loss of appetite **<u>If the participant answer yes to any of these questions flag for referral to TB screening and take sputum sample</u>**	□ Unexplained weight loss □ Drenching night sweats □ Fevers □ None of the above
43 Have you ever been tested for TB1?	
□ No	□ Yes → Are you on TB treatment □ No

	☐ Yes
44 Has a doctor or nurse ever told you that you have TB?	
☐ No → If no, are you currently taking medication to prevent TB (IPT)? ☐ No ☐ Yes ☐ If yes when did you start IPT medication? MM__YY___ ☐ If no have you taken IPT medication in the last 12 months? ☐ No ☐ Yes	☐ Yes → What was the date when you were first diagnosed with TB? MM____YY_____. → When did you first start your TB medication? MM____YY____ → Have you completed your treatment? ☐ No ☐ Yes
45 Has a doctor or nurse ever told you that you have an STI?	
☐ No → Do you currently have any possible symptoms of an STI such as ulcers and discharge area? ☐ No ☐ Yes → If yes may I refer your for STI screening to our parallel service? **<u>If the participant answer yes to any of these questions flag for referral to STI screening</u>**	☐ Yes → What was the date when you were diagnosed with a STI? MM____YY_____. → Have you completed your treatment? ☐ No ☐ Yes
46 Has a doctor or nurse ever given you medication to prevent you contracting HIV because you were exposed (Raped, touched blood etc.) to the HIV virus?	
☐ No	☐ Yes

Section 6 - Sexual history

I now have to ask you very sensitive questions on sex and other sex-related matters. Please remember that your name will not be recorded anywhere in this questionnaire and the information you give will be kept confidential.

First

47 Have you ever had sex?[1]	
☐ No → What was the main reason for not having sex? ☐ No partner available. ☐ Do not want to have sex. ☐ Waiting for marriage. ☐ Religious reasons. ☐ Avoiding HIV or STI's. ☐ Avoiding pregnancy. ☐ Fear of authority. ☐ Other:_____ [Skip section on sexual history]	☐ Yes → How old were you when you first had sex? ☐ ____years. ☐ Don't remember. ☐ Did not respond. → How old was your partner? ☐ ____years. ☐ Don't know. ☐ Did not respond. → Did you use a condom?[1] ☐ No ☐ Yes ☐ Don't remember → Were you forced to have sex? ☐ No ☐ Yes ☐ Don't remember

Life time

48 How many people have you had sex with in your life time? (It is ok to estimate the number if you don't remember exactly).[1]	_____ number.
49 How many people have you had sex with in the last 12 months?	
☐ Have not had sex in the last 12 months.	_____number. → How often did you use a condom when you had sex? ☐ Sometime ☐ Always

	☐ Never → Have you ever taken ARV medication (PREP) to prevent getting HIV before you had sex? ☐ No ☐ Yes → What type of PREP did you take? ☐ Oral medication ☐ Gel → Did you know the HIV status of these partners? ☐ Yes, all of them. ☐ Yes, some of them. ☐ No, none of them.[1] → How many of these partners did you know were HIV positive? ☐ All of them. ☐ Some of them ☐ None of them.

Last 3 sexual partners

Now I am going to ask you more details about the 3 most recent partners that you have had sex with. Please tell me about them starting with the most recent (newest) partner.

		☐ No second partner, skip to next section.	☐ No third partner, skip to next section.
	Partner 1	Partner 2	Partner 3
50 Their first name/nick name.			
51 What is the nature of your relationship?[1]	☐ Wife. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.	☐ Wife. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.	☐ Wife. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.

52 What is the current age of your partner?[1]	_____ years.	_____years.	_____years.
53 Is this partner a member of your household?[1]	□ No □ Yes	□ No □ Yes	□ No □ Yes
54 Month and year sexual relationship began.[1]	MM___ YY___	MM___ YY___	MM___ YY___
55 When did this sexual relationship end?	MM___ YY___ □ Not ended	MM___ YY___ □ Not ended	MM___ YY___ □ Not ended
56 Partner's sex?[1]	□ Male □ Female	□ Male □ Female	□ Male □ Female
57 If male, is he circumcised? **(skip if partner female)**	□ Circumcised at start of relationship. □ Not circumcised. □ Became circumcised during relationship. □ Don't know.	□ Circumcised at start of relationship. □ Not circumcised. □ Became circumcised during relationship. □ Don't know.	□ Circumcised at start of relationship. □ Not circumcised. □ Became circumcised during relationship. □ Don't know.
58 How many times did you have sex with this partner in the last 12 months?[1]	□ Never in the last 12 months. □ Once. □ 2 – 5 times. □ 6 – 10 times. □ 10 – 20 times. □ More than 20 times.	□ Never in the last 12 months. □ Once. □ 2 – 5 times. □ 6 – 10 times. □ 10 – 20 times. □ More than 20 times.	□ Never in the last 12 months. □ Once. □ 2 – 5 times. □ 6 – 10 times. □ 10 – 20 times. □ More than 20 times.
59 How often did you use a condom when you had sex?[1]	□ Always □ Sometimes □ Never	□ Always □ Sometimes □ Never	□ Always □ Sometimes □ Never
60 If you never used a condom with this	□ No	□ No	□ No

partner, was it because you battled to access condoms when having sex with this partner?	☐ Yes ☐ Sometimes	☐ Yes ☐ Sometimes	☐ Yes ☐ Sometimes
61 How often did you give or receive money/gifts so that you could have sex with this person?[1]	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never
62 Did you and your partner have anal sex in the last 12 months?	☐ No ☐ Yes If no, skip the next question.	☐ No ☐ Yes If no, skip the next question	☐ No ☐ Yes If no skip the next question.
63 How often did you and your partner use a condom when you had anal sex in the last 12 months?[1]	☐ Never had anal sex. ☐ Always. ☐ Sometimes. ☐ Never.	☐ Never had anal sex. ☐ Always. ☐ Sometimes. ☐ Never.	☐ Never had anal sex. ☐ Always. ☐ Sometimes. ☐ Never.
64 When you were having a sexual relationship with this partner, do you think that he/she was HIV positive?[1]	☐ No. ☐ Don't know. ☐ Yes. → Do you think that this partner was taking ARV's for HIV?[1] ☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Don't know. ☐ Yes. → Do you think that this partner was taking ARV's for HIV?[1] ☐ No. ☐ Yes. Don't know.	☐ No. ☐ Don't know. ☐ Yes. → Do you think that this partner was taking ARV's for HIV?[1] ☐ No. ☐ Yes. Don't know.
65 Have you told your partner your HIV status?	☐ No. ☐ Yes.	☐ No. ☐ Yes.	☐ No. ☐ Yes.

66 Has this partner had any STI's in the last 12 months?	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.
67 Can you talk about safe sex with this partner?	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.
68 Has this partner ever forced you to have sex when you did not want to?	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.

Section 7- Health access

Health status HIV, TB, chronic conditions, Pregnancy, disabilities

69 Have you suffered any of the following illnesses in the past 12 months?[1]	
□ Heart disease. □ Stroke. □ Arthritis. □ Obesity (very over weight). □ High blood pressure. □ Diabetes. □ TB. □ Pneumonia. □ Cancer. □ Malaria.	□ Depression/anxiety. □ Asthma. □ Hepatitis. □ STI's. □ Peptic Ulcers. □ Kidney disease. □ HIV. □ Other_____. → Are you accessing medical assistance for your illness □ No □ Yes

Access to contraception

70 Are you currently using a contraceptive method?	
□ No → Why not □ My partner is trying to fall pregnant. □ Cannot access	□ Yes → Which kind □ Condoms. □ Spermicides.

contraceptive methods. □ My partner is using contraceptives □ My partner cannot fall pregnant □ No reason.	□ Rhythm/calendar/safe period/Withdraw/Thigh sex /Masturbation. □ Emergency contraception. □ Anal sex. □ Female sterilisation. □ Male sterilisation. □ Oral sex. □ Other _____. □ No response. → Are you able to access your contraceptive method whenever you need it? □ No □ Yes

Exposure to prevention programmes.

71 In the past 12 months, from where/or whom have you received HIV information that has been useful to you?[1]	
□ No one.	□ Newspaper.
□ Billboard.	□ Television.
□ A child or learner of school going age.	□ Clinic, hospital or doctor.
□ A religion/faith based organisation.	□ Telephone help line.
□ The workplace.	□ Pharmacy or chemist.
□ Community meeting.	□ Parent, family or care giver.
□ Traditional healer.	□ Partner.
□ AIDS or welfare organisation.	□ Friend.
	□ Other.

72 Which of the following activities have you participated in, in the past 12 months?	
□ Community meeting on HIV & AIDS.	□ Cared for a person who is sick with AIDS.
□ Membership of an HIV organisation e.g. TAC	□ Helped a family who has someone sick with AIDS.
□ Volunteer for HIV activities e.g. fund raising.	□ Helped a family who lost a member as a result of AIDS.
□ Attended a local HIV rally or march.	□ Other: _____.
□ Attended an HIV educational event in the	

workplace. ☐ Attended an HIV play or event. ☐ Attended a support group for HIV/AIDS.	☐ No response.

73 In the last 12 months, have you seen or heard any messages about the following topics related to HIV?[1]	
☐ Get an HIV test to know your status. ☐ Reduce your number of sex partners. ☐ Use condoms every time you have sex. ☐ Male circumcision for HIV prevention.	☐ ARV's are available at clinics to treat HIV. ☐ All pregnant women should get an HIV test. ☐ ARV's are available to women to prevent mother to child transmission. ☐ Other:_____.

Section 8

Male Circumcision

Now I would like to ask you about male circumcision. As a reminder, by male circumcision, I mean removal of the foreskin of the penis.

Before we begin, do you have any questions?

74 When you do NOT have an erection, would you say your penis is uncircumcised or circumcised?[1]	
☐ Uncircumcised → If uncircumcised, what are the reasons? ☐ I am scared of pain. ☐ I don't want an HIV test. ☐ I think it will change the way I enjoy sex. ☐ I think it's unnecessary. ☐ I think it looks strange. ☐ I do not need to be circumcised as I am not having sex. ☐ It is against my religion. ☐ My friends are not getting circumcised.	☐ Circumcised → If circumcised, what are the reasons? ☐ For hygienic reasons. ☐ To prevent diseases (HIV and STI's). ☐ For cultural reasons. ☐ To enhance my sexual performance. ☐ My friends are getting circumcised. ☐ My partner wants me to. ☐ Other_____.

☐ My partner doesn't want me to get circumcised. ☐ Other_____.	
75 When were you circumcised?	
YYYY_____ MM_____DD_____	
76 Who circumcised you?	
☐ Medical Circumcision ☐ Don't know	☐ Traditional Circumcision
77 On the day you got circumcised, did you have an HIV test?	
☐ No ☐ Don't know	☐ Yes
78 Did anyone influence your decision to get circumcised?[1]	
☐ No	☐ Yes → If yes, who was it? ☐ Friend/colleague ☐ Traditional leader or healer ☐ Parents ☐ Partner ☐ Other_____.

Complete the Eligibility Questionnaire for cohort

APPENDIX I – FEMALE COHORT QUESTIONNAIRE

Title of Study: HIV Incidence Provincial Surveillance System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the

uMgungundlovu District, KwaZulu-Natal, South Africa

Participant Identification

Participant Id number		GPS coordinate	
Team id		Supervisor	
Attempts to survey participant			
1. Date	Time DD/MM/YYYY	Time DD/MM/YYYY T	Time DD/MM/YYYY
2. Staff id			
3. Next visit Date and time			
4. Result*			

***Result options:**

a) 1-consented + figure scanned, 2-refused + replaced, 3-refused+HH replaced 4 not found + replaced 5 not found + hh replaced 1-Member consented

(Rule: if 1st HH to refuses replace with 2nd selected member, if 2nd member refused replace HH)

Note: This information will be kept in a separate database from the participant questionnaire. It will be linked by a barcode to the participant's questionnaire. The identification process and the questionnaire will be repopulated from the baseline responses.

5. Please can you confirm your name and surname	Are you “First name and surname”? (prepopulated by the database) ☐ No, I am not that person ☐ Yes, I am that person ☐ No, I don’t not wish to identify myself
6. Confirm ID.	☐ Failed - this is not the right person <u>Instruction: Discontinue survey</u> ☐ Failed, BUT this seems to be the right person Instruction: Call the supervisor who can make a decision to override the system based on agreed rules ☐ Confirmed Instruction: ID confirmed, continue with the consent and the cohort questionnaire

This form is held in a spate database to the questionnaire information

Female Cohort Questionnaire

Title of Study: HIV Incidence Provincial Surveillance System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa

Participant Id number		GPS coordinate	
Team id		Supervisor	

Section

Finger Print scanning

4.1 Finger Print

Prompt: please place your finger print onto the scanning divice .

Scan the finger print continue if verified

Section5

Lab Samples

5.1 Prompt: Thank you for agreeing to participate. We will start with the lab test specimines

Please note that your results will be available from your local Department of Health Clinic.

Give the participant a card with the linked barcode and write the name of the clinic were the results will be send on the card.

5.2Barcode

Scan the bar code in order to scan the barcode assigned to this participant's specimines

Section 1: Demographics

(age, gender, marital status, education, number of dependents)

1. In the last 12 months have you been away from your home for more than one month at all together?[55]	
☐ No	☐ Yes

[55] Source: SA National Health, Demographic and Behaviour Survey 2011

	☐ No response
2. What is your marital status?[56]	
☐ Legally married ☐ Living together like husband and wife ☐ Divorced ☐ Separated, but still legally married	☐ Widowed ☐ Single, but have been living together with someone as husband/wife before ☐ Single and have never been married/never lived together as husband/wife before

Section 2: Knowledge and motivation

HIV knowledge of prevention

3. Can you tell me all the ways that you know that HIV can be prevented?[57] (Do not read out options. Multiple responses are possible)	
☐ Using a condom. ☐ Abstaining from sex. ☐ Sticking to one sexual partner. ☐ Having fewer sexual partners. ☐ Not having sex before marriage. ☐ Avoid contact with blood/using gloves.	☐ Using drugs to prevent transmission of mother to child. ☐ Male circumcision. ☐ Taking ARV's within 72hours of being exposed to the HIV virus. ☐ Don't know.

Perceived risk for HIV

4. How likely do you think you are you to contract HIV in the future?	
☐ I am definitely going to be infected. ☐ I am probably going to get infected. → What are your reasons for believing so? (Multiple answers possible.) ☐ I am sexually active. ☐ I have many sexual partners. ☐ I don't use condoms.	☐ I probably won't get infected. ☐ I will definitely not get infected. → What are your reasons for believing so? (Multiple reasons possible). ☐ I have never had sex. ☐ I have abstained from sex. ☐ I am faithful to my partner. ☐ I trust my partner.

[56] Source : General Household Survey 2011, Statistics SA

[57] Source: SA National Health, Demographic and Behaviour Survey 2008

□ I don't always use condoms. □ I don't trust my partner. □ I am sick. □ My partner is sick. □ My partner died of AIDs. □ I had an accident/cuts. □ Other_____.	□ I use condoms. □ I know my HIV status. □ My partner is circumcised. □ I do not have sex with sex workers. □ My ancestors protect me. □ God protects me. □ I am not at risk for HIV. □ Other_____

Perceived power to prevent HIV transmission

5. Please select the most appropriate option:[58]	**Agree**	**Partially agree**	**Don't agree**
□ It is the man who decides when to have sex. □ Men need sex more than women do. □ Men don't like using condoms. □ It is ok for a man to have more than one sexual partner.			

6. Select the most appropriate option:[59]	**Agree**	**Uncertain**	**Disagree**
□ Using a condom seems like an insult to my partner. □ I don't enjoy sex with a condom.			

Perceived consequence of contracting HIV[60]

7. Select the most appropriate option:	**Agree**	**Uncertain**	**Disagree**
□ AIDS is probably the worst disease I could get. □ My friends/family would disown me if I was to contract HIV. □ I am not afraid of contracting HIV as there are			

[58] Source: Adapted from Pulerwtiz & Barker, (2008) and self-developed
[59] Source: Adapted from Pulerwtiz & Barker, (2008) and self-developed
[60] Source: Adapted from Pulerwtiz & Barker, (2008) and self-developed

effective drugs to treat it.			

Attitudes to MMC

8. Would you prefer your sexual partner to be circumcised? [61]	
☐ No ☐ Doesn't matter	☐ Yes

9. Have you heard that circumcision has been shown to partly reduce the chance of HIV infection amongst men?	
☐ No ☐ Don't know	☐ Yes

Section 3 - Situational action context

Alcohol and drug use

10. Did you drink alcohol in the last 12 months?[62]	
☐ No [If never skip the next section]	☐ Yes → How often do you have 5 or more drinks on one occasion? ☐ Never ☐ Less the monthly ☐ Monthly ☐ Weekly ☐ Daily (or almost daily)
11. How often do you have sex after drinking in the last 12 months?[63]	
☐ Never	☐ Always. ☐ Sometimes. → How often do you use a condom in these instances?

[61] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

[62] Source : Heard Tavern intervention survey

[63] Source: SA National Health, Demographic and Behaviour Survey 2008

	☐ Always ☐ Sometimes ☐ Never → Who do you have sex with in these instances? ☐ Stable partner. ☐ Casual partner. ☐ Stranger.

Drug use

		Never	Monthly or less	2-4 times per month	2-3 times per week	4 or more times per week
	12. Dagga					
	13. Heroin					
	14. Cocaine					
	15. Glue					
	16. Tik					
	17. Wunga					
	18. Quh					
	19. Other addictive substance					

20. How often do you have sex after taking drugs in the last 6 months?[65]

☐ Always.	☐ Sometimes	☐ Never

[64] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

[65] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

Depression

We would like you to describe ways that you may have felt or behaved during the last week.

	Rarely (Less than 1 day)	Some of the time (1-2 days)	Occasionally (3-4 days)	All of the time (5-7 days)
21. I was bothered by things that don't usually bother me.[66]				
22. I had trouble keeping my mind on what I was doing.				
23. I felt depressed.				
24. I felt everything I did was an effort.				
25. I felt hopeful about the future.				
26. I felt fearful.				
27. My sleep was restless.				
28. I was happy.				
29. I felt lonely.				
30. I could not get going.				

31. Have you ever accessed treatment to assist you with depression in the last 12 months?

☐ No	☐ Yes → If yes, what services did you access? ☐ Doctor /nurse in a public facility. ☐ Private Doctor or nurse. ☐ Private Counsellor. ☐ Support group. ☐ EAP in the workplace. ☐ Medication. ☐ Other_____

[66] Source: CES-D10 Short form depression questionnaire

	Rarely (Less than 1 day)	Some of the time (1-2 days)	Occasionally (3-4 days)	All of the time (5-7 days)
	.			

Section 4 - Social interactions

Access to social, financial and emotional support

32. What forms of support, in the last month, have you received from important people/organisations in last 12 months?	Tangible (money, food, care)	Educational/ Informational	Emotional/ Relational (support/ bonding)
Biological Father			
Biological Mother			
Sibling			
Grandparent			
Other Family member			
Other community member			
Teacher			
Nurse/Doctor			
Internet/sites cafes/Social media			
Stokvels			
Church groups			
Taverns			
Sport/ youth clubs			
Traditional leadership structures			
Work friends or employer			
Other			

HIV stigma

33. Choose the best answer [67]	No	Yes	Unsure
☐ People with HIV/AIDS should be ashamed.			
☐ People with HIV/ AIDS must have done something wrong.			
☐ I do not want to be friends with someone with HIV / AIDS.			

Section 5- HIV Status and risk

HIV status information

34. Have you been tested to see if you are HIV positive in the last 12 months? [68]

☐ No

→ What are the reasons you did not have an HIV test?

- ☐ Do not want to know/am afraid.
- ☐ It's better not to know.
- ☐ Have to get my partners permission.
- ☐ Want to test with my partner.
- ☐ Don't know where to test/don't have access to testing.
- ☐ Other_____

☐ Yes

→ How many times have you had a test in the last 12 months?_____times .

→ When was the last time that you had an HIV test?(give best approximate date)_____.

→ Did you get the result of this test?

- ☐ No
- ☐ Yes

35. Would you like me to refer you to our parallel HIV testing service?

☐ No

☐ Yes

If yes refer the participant using the referral process

36. What was the result of your latest HIV test?[69]

[67] Source: Adapted from HEARD - SAB Tavern Intervention questionnaire and self-developed

[68] Source: Swaziland HIV Incident Measurement Survey, 2011

[69] Source: Swaziland HIV Incident measurement Survey, 2011

□ I have never tested □ Negative. □ Indeterminate. □ Did not respond.	□ Positive. → Are you currently being provided with any of the following support or treatment? □ Nutritional support. □ Emotional support (support groups). □ Treatment buddy. □ Home based care. □ CD4 test. □ Viral load test. □ Financial support. □ Treatment of opportunistic infections. → Has a Doctor or Nurse told you that you need to take ARV's? □ No □ Yes → If yes, which dose pill are you on? □No on ARVs □Multiple dose □Fixed/single dose → Are you still on ARV's? □No □Yes → Have you ever been pregnant while you were HIV positive? □No □Yes → If yes are you still pregnant □No □Yes → If no, which of the following clinical services did you access while HIV positive and pregnant? □An HIV test at an antenatal visit. □Medication to prevent mother to child transmission. □Follow up care for HIV+ Women and their infants.

	□Counselling/support for breastfeeding. □Testing of your baby. □Infant milk formula. → Did your baby become infected with HIV? □No □Yes
47. **Could you have been exposed to TB in the last 12 months? (**"Please note all of the following that are true"?)	
□ I was in contact with someone who has TB in the last 12 months □ I had contact with someone who has resistant TB (MDR or XDR) in the last 12 months	□ I lived in a hostel or informal settlement in the 12 months □ I was in prison in the last 12 months □ I was in hospital in the 12 months □
48. In the past 2 weeks have you had any of the following symptoms? Select one or more the following	
□ Unexplained persistent cough for more than 2 weeks □ Coughed up blood □ Loss of appetite □ Unexplained weight loss □ **If the participant answer yes to any of these questions flag for referral to TB screening and take sputum sample**	□ Drenching night sweats □ Fevers □ None of the above
49. Have you been tested for TB in last 12 months?70	
□ No	□ Yes → Are you on TB treatment □ No □ Yes
50. Has a doctor or nurse told you that you have TB in last 12 months?	

[70] Source: SA National Health, Demographic and Behaviour Survey 2011

□ No → If no, are you currently taking medication to prevent TB (IPT)? □ No □ Yes → If yes when did you start the IPT medication? MM___YY___ → If no have you taken IPT in the last 12 months? MM___YY____	□ Yes → What was the date when you were first diagnosed with TB? MM____YY_____. → When did you start your TB medication? MM____YY____ → Have you completed your treatment? □ No □ Yes
51. Has a doctor or nurse told you that you have an STI in the last 12 months?	
□ No → Do you currently have any possible symptoms of an STI such as ulcers and discharge area? □ No □ Yes → If yes may I refer your for STI screening to our parallel service? □ No **<u>If the participant answer yes to any of these questions flag for referral to STI screening</u>**	□ Yes → What was the date when you were diagnosed with a STI? MM____YY_____. → Have you completed your treatment? □ No □ Yes
52. Has a doctor or nurse ever given you medication to prevent you contracting HIV because you were exposed (Raped, touched blood etc.) to the HIV virus in the last 12 months?	
□ No	□ Yes

Section 6 - Sexual history

I now have to ask you very sensitive questions on sex and other sex-related matters. Please remember that your name will not be recorded anywhere in this questionnaire and the information you give will be kept confidential.

Different people have different definitions of 'sex' or 'sexual intercourse.' For this study, sex can include several things, such as:

- <u>Vaginal sex</u>, which is when a man puts his penis in a woman's vagina.
- <u>Anal sex</u>, which is when a man puts his penis in another person's rectum or butt.

Sex in last 12 months

53. How many people have you had sex with in the last 12 months?	
☐ Have not had sex in the last 12 months. Skip the rest of this section	_____number in last 12 months. → How often did you use a condom when you had sex? ☐ Sometime ☐ Always ☐ Never → Have you ever taken ARV medication (PREP) to prevent getting HIV before you had sex? ☐ No ☐ Yes → What type of PREP did you take? ☐ Oral medication ☐ Gel → Did you know the HIV status of these partners? ☐ Yes, all of them. ☐ Yes some of them. ☐ No, none of them.[71] → How many of these partners did you know were HIV positive? ☐ All of them. ☐ Some of them ☐ None of them.

Sexual partner in last 12 months

Now I am going to ask you more details about the 3 most recent partners that you have had sex in the last 12 months. Please tell me about them starting with the most recent (newest) partner.

		☐ No other partners in last 12 months skip to next	☐ No other partners in last 12 months skip to next section..

[71] SOURCE: Swaziland HIV Incident measurement Survey, 2011

		section.	
	Partner 1	Partner 2	Partner 3
54. Their first name/nick name.			
55. What is the nature of your relationship?[72]	☐ Husband. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.	☐ Husband. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.	☐ Husband. ☐ Regular partner. ☐ Casual partner. ☐ Commercial partner.
56. What is the current age of your partner?[73]	_____ years.	_____years.	_____years.
57. Is this partner a member of your household?[74]	☐ No ☐ Yes	☐ No ☐ Yes	☐ No ☐ Yes
58. Month and year sexual relationship began.[75]	MM___ YY___	MM___ YY___	MM___ YY___
59. When did this sexual relationship end?	MM___ YY___ ☐ Not ended	MM___ YY___ ☐ Not ended	MM___ YY___ ☐ Not ended
60. Partner's sex?[76]	☐ Male ☐ Female	☐ Male ☐ Female	☐ Male ☐ Female
61. If male, is he circumcised? **(Skip if female)**	☐ Circumcised at start of relationship. ☐ Not circumcised. ☐ Became circumcised during relationship.	☐ Circumcised at start of relationship. ☐ Not circumcised. ☐ Became circumcised during relationship.	☐ Circumcised at start of relationship. ☐ Not circumcised. ☐ Became circumcised during relationship. ☐ Don't know.

[72] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[73] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[74] Source: Africa Centre Demographic information 2010
[75] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[76] SOURCE: Swaziland HIV Incident measurement Survey, 2011

	☐ Don't know.	☐ Don't know.	
62. How many times did you have sex with this partner in the last 12 months?[77]	☐ Never in the last 12 months. ☐ Once. ☐ 2 – 5 times. ☐ 6 – 10 times. ☐ 10 – 20 times. ☐ More than 20 times.	☐ Never in the last 12 months. ☐ Once. ☐ 2 – 5 times. ☐ 6 – 10 times. ☐ 10 – 20 times. ☐ More than 20 times.	☐ Never in the last 12 months. ☐ Once. ☐ 2 – 5 times. ☐ 6 – 10 times. ☐ 10 – 20 times. ☐ More than 20 times.
63. How often did you use a condom when you had sex?[78]	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never
64. If you never used a condom with this partner, was it because you battled to access condoms when having sex with this partner in the last 12 months?	☐ No ☐ Yes ☐ Sometimes	☐ No ☐ Yes ☐ Sometimes	☐ No ☐ Yes ☐ Sometimes
65. How often did you give or receive money/gifts so that you could have sex with this person?[79]	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never	☐ Always ☐ Sometimes ☐ Never
66. Did you and your partner have anal sex in the last 12 months?	☐ No ☐ Yes If no, skip the next question.	☐ No ☐ Yes If no, skip the next question	☐ No ☐ Yes If no skip the next question.
67. How often did you and your partner use a condom when you had anal sex in the last 12 months?[80]	☐ Never had anal sex. ☐ Always. ☐ Sometimes.	☐ Never had anal sex. ☐ Always. ☐ Sometimes.	☐ Never had anal sex. ☐ Always. ☐ Sometimes. ☐ Never.

[77] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[78] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[79] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[80] SOURCE: Swaziland HIV Incident measurement Survey, 2011

	☐ Never.	☐ Never.	
68. When you were having a sexual relationship with this partner, do you think that he/she was HIV positive?[81]	☐ No. ☐ Don't know. ☐ Yes. → Do you think that this partner was taking ARV's for HIV?[82] ☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Don't know. ☐ Yes. → Do you think that this partner was taking ARV's for HIV?[83] ☐ No. ☐ Yes. Don't know.	☐ No. ☐ Don't know. ☐ Yes. → Do you think that this partner was taking ARV's for HIV?[84] ☐ No. ☐ Yes. Don't know.
69. Have you told your partner your HIV status in the last 12 months?	☐ No. ☐ Yes.	☐ No. ☐ Yes.	☐ No. ☐ Yes.
70. Has this partner had any STI's in the last 12 months?	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.
71. Can you talk about safe sex with this partner?	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.
72. Has this partner forced you to have sex when you did not want to in the last 12 months?	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.	☐ No. ☐ Yes. ☐ Don't know.

Section 7- Health access

Health status HIV, TB, chronic conditions, Pregnancy, disabilities

[81] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[82] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[83] SOURCE: Swaziland HIV Incident measurement Survey, 2011
[84] SOURCE: Swaziland HIV Incident measurement Survey, 2011

73. Have you suffered any of the following illnesses in the past 12 months?[85]	
□ Heart disease. □ Stroke. □ Arthritis. □ Obesity (very over weight). □ High blood pressure. □ Diabetes. □ TB. □ Pneumonia. □ Cancer. □ Malaria.	□ Depression/anxiety. □ Asthma. □ Hepatitis. □ STI's. □ Peptic Ulcers. □ Kidney disease. □ HIV. □ Other_____. → Are you accessing medical assistance for your illness □ No □ Yes

Access to contraception

74. Are you currently using a contraceptive method?	
□ No → Why not □ Trying to fall pregnant. □ Pregnant □ Cannot access contraceptive methods. □ My partner can't make me pregant □ No reason.	□ Yes → Which kind □ Condoms. □ Injection 2 months (*Nur-Isterate*). □ Injection 3 months (Depo Provera). □ Daily pill. □ IUCD. □ Spermicides. □ Rhythm/calendar/safe period/Withdraw/Thigh sex /Masturbation. □ Emergency contraception. □ Anal sex. □ Female sterilisation.

[85] Source: SA National Health, Demographic and Behaviour Survey 2011

	☐ Male sterilisation. ☐ Oral sex. ☐ Other _____. ☐ No response. → Are you able to access your contraceptive method whenever you need it? ☐ No ☐ Yes

Exposure to prevention programmes.

75. In the past 12 months, from where/or whom have you received HIV information that has been useful to you?[86]	
☐ No one. ☐ Billboard. ☐ A child or learner of school going age. ☐ A religion/faith based organisation. ☐ The workplace. ☐ Community meeting. ☐ Traditional healer. ☐ AIDS or welfare organisation.	☐ Newspaper. ☐ Television. ☐ Clinic, hospital or doctor. ☐ Telephone help line. ☐ Pharmacy or chemist. ☐ Parent, family or care giver. ☐ Partner. ☐ Friend. ☐ Other.
76. Which of the following activities have you participated in, in the past 12 months?	
☐ Community meeting on HIV & AIDS. ☐ Membership of an HIV organisation e.g. TAC ☐ Volunteer for HIV activities e.g. fund raising. ☐ Attended a local HIV rally or march. ☐ Attended an HIV educational event in the workplace. ☐ Attended an HIV play or event. ☐ Attended a support group for HIV/AIDS.	☐ Cared for a person who is sick with AIDS. ☐ Helped a family who has someone sick with AIDS. ☐ Helped a family who lost a member as a result of AIDS. ☐ Other: _____. ☐ No response.

[86] Source: SA National Health, Demographic and Behaviour Survey 2011

77. In the last 12 months, have you seen or heard any messages about the following topics related to HIV?[1]	
☐ Get an HIV test to know your status. ☐ Reduce your number of sex partners. ☐ Use condoms every time you have sex. ☐ Male circumcision for HIV prevention.	☐ ARV's are available at clinics to treat HIV. ☐ All pregnant women should get an HIV test. ☐ ARV's are available to women to prevent mother to child transmission. ☐ Other:_____.

APPENDIX J – MALE COHORT QUESTIONNAIRE

Male Cohort Identification

Title of Study: HIV Incidence Provincial Surveillance System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa

Participant Identification

Participant ID number		**GPS coordinate**	
Team ID		**Supervisor**	
Attempts to survey participant			
1. Date	Time DD/MM/YYYY	Time DD/MM/YYYY T	Time DD/MM/YYYY
2. Staff id			
3. Next visit Date and time			
4. Result*			

***Result options:**

a) 1-consented + figure scanned, 2-refused + replaced, 3-refused+HH replaced 4 not found + replaced 5 not found + hh replaced 1-Member consented

(Rule: if 1st HH to refuses replace with 2nd selected member, if 2nd member refused replace HH)

Note: This information will be kept in a separate database from the participant questionnaire. It will be linked by a barcode to the participant's questionnaire. The identification process and the questionnaire will be repopulated from the baseline responses.

7. Please can you confirm your name and surname	Are you “First name and surname”? (prepopulated by the database) ☐ No, I am not that person ☐ Yes, I am that person ☐ No, I don’t not wish to identify myself
8. Confirm ID.	☐ Failed - this is not the right person <u>Instruction: Discontinue survey</u> ☐ Failed, BUT this seems to be the right person Instruction: Call the supervisor who can make a decision to override the system based on agreed rules ☐ Confirmed Instruction: ID confirmed, continue with the consent and the cohort questionnaire

This form is held in a spate database to the questionnaire information

Male Cohort Questionnaire

Title of Study: HIV Incidence Provincial Surveillance System (HIPSS)

A longitudinal study to monitor HIV incidence trends in the uMgungundlovu District, KwaZulu-Natal, South Africa

Section

Finger Print scanning

4.1 Finger Print

Prompt: please place your finger print onto the scanning divice .

Scan the finger print continue if verified

Section

Lab Samples

5.1 Prompt: Thank you for agreeing to participate. We will start with the lab test specimens

Please note that your results will be available from your local Department of Health Clinic.

Give the participant a card with the linked barcode and write the name of the clinic were the results will be send on the card.

5.2Barcode

Scan the bar code in order to scan the barcode assigned to this participant's specimines

Section 1: Demographics

(age, gender, marital status, education, number of dependents)

1. In the last 12 months have you been away from your home for more than one consecutive month?[1]	
□ No	□ Yes □ No response
2. What is your marital status?[1]	
□ Legally married □ Living together like husband and wife	□ Widowed □ Single, but have been living together with

☐ Divorced ☐ Separated, but still legally married	someone as husband/wife before ☐ Single and have never been married/never lived together as husband/wife before

Section 2: Knowledge and motivation

HIV knowledge of prevention

3. Can you tell me all the ways that you know that HIV can be prevented?[1] (Do not read out options. Multiple responses are possible)	
☐ Using a condom. ☐ Abstaining from sex. ☐ Sticking to one sexual partner. ☐ Having fewer sexual partners. ☐ Not having sex before marriage. ☐ Avoid contact with blood/using gloves.	☐ Using drugs to prevent transmission of mother to child. ☐ Male circumcision. ☐ Taking ARV's within 72hours of being exposed to the HIV virus. ☐ Don't know.

Perceived risk for HIV

4. How likely do you think you are you to contract HIV in the future?	
☐ I am definitely going to be infected. ☐ I am probably going to get infected. → What are your reasons for believing so? (Multiple answers possible.) ☐ I am sexually active. ☐ I have many sexual partners. ☐ I don't use condoms. ☐ I don't always use condoms. ☐ I don't trust my partner. ☐ I am sick. ☐ My partner is sick. ☐ My partner died of	☐ I probably won't get infected. ☐ I will definitely not get infected. → What are your reasons for believing so? (Multiple reasons possible). ☐ I have never had sex. ☐ I have abstained from sex. ☐ I am faithful to my partner. ☐ I trust my partner. ☐ I use condoms. ☐ I know my HIV status. ☐ My partner is circumcised. ☐ I do not have sex with sex workers. ☐ My ancestors protect me. ☐ God protects me.

AIDs. □ I had an accident/cuts. □ Other_____.	□ I am not at risk for HIV. □ Other_____

Perceived power to prevent HIV transmission

5. Please select the most appropriate option[1]:	Agree	Partially agree	Don't agree
□ It is the man who decides when to have sex. □ Men need sex more than women do. □ Men don't like using condoms. □ It is ok for a man to have more than one sexual partner.			
6. Select the most appropriate option[1]:	Agree	Partially agree	Don't agree
□ Using a condom seems like an insult to my partner. □ I don't enjoy sex with a condom.			

Perceived consequence of contracting HIV

Select the most appropriate option:	**Agree**	**Partially agree**	**Don't agree**
□ AIDS is probably the worst disease I could get. □ My friends/family would disown me if I was to contract HIV. □ I am not afraid of contracting HIV as there are effective drugs to treat it.			

Attitudes to MMC

7. Have you heard that circumcision has been shown to partly reduce the chance of HIV infection amongst men?	
□ No □ Don't know	□ Yes

Section 3 - Situational action context

Alcohol and drug use

8. Did you drink alcohol in the last 12 months?[1]	
☐ No [If never skip the next section]	☐ Yes → How often do you have 5 or more drinks on one occasion? ☐ Never ☐ Less the monthly ☐ Monthly ☐ Weekly ☐ Daily (or almost daily)

9. How often do you have sex after drinking in last 12 months?[1]	
☐ Never	☐ Always. ☐ Sometimes. → How often do you use a condom in these instances? ☐ Always ☐ Sometimes ☐ Never → Who do you have sex with in these instances? ☐ Stable partner. ☐ Casual partner. ☐ Stranger.

Drug use

		Never	**Monthly or less**	**2-4 times per month**	**2-3 times per week**	**4 or more times per week**
	10. Dagga					

how often have you used:[1]	11. Heroin					
	12. Cocaine					
	13. Glue					
	14. Tik					
	15. Wunga					
	16. Quh					
	17. Other					

18. How often do you have sex after taking drugs?[1]		
□ Always.	□ Sometimes	□ Never

Depression.

We would like you to describe ways that you may have felt or behaved during the last week.

	Rarely (Less than 1 day)	**Some of the time (1-2 days)**	**Occasionally (3-4 days)**	**All of the time (5-7 days)**
19. I was bothered by things that don't usually bother me.[1]				
20. I had trouble keeping my mind on what I was doing.				
21. I felt depressed.				
22. I felt everything I did was an effort.				
23. I felt hopeful about the future.				
24. I felt fearful.				
25. My sleep was restless.				
26. I was happy.				

27. I felt lonely.				
28. I could not get going.				

29. Have you ever accessed treatment to assist you with depression in the last 12 months?	
□ No	□ Yes → If yes, what services did you access? □ Doctor /nurse in a public facility. □ Private Doctor or nurse. □ Private Counsellor. □ Support group. □ EAP in the workplace. □ Medication. □ Other_____.

Section 4 - Social interactions

Access to social, financial and emotional support

30. What forms of support, in the last month, have you received from important people/organisations in last 12 months?	**Tangible (money, food, care)**	**Educational/ Informational**	**Emotional/ Relational (support/ bonding)**
Biological Father			
Biological Mother			
Sibling			
Grandparent			
Other Family member			
Other community member			
Teacher			

Nurse/Doctor			
Internet/sites cafes/Social media			
Stokvels			
Church groups			
Taverns			
Sport/ youth clubs			
Traditional leadership structures			
Work friends or employer			
Other			

HIV stigma

31. Choose the best answer[1]	**No**	**Yes**	**Unsure**
□ People with HIV/AIDS should be ashamed.			
□ People with HIV/ AIDS must have done something wrong.			
□ I do not want to be friends with someone with HIV / AIDS.			

Section 5- HIV Status and risk

HIV status, HIV status of partner, HIV status of family members

HIV status information

32. Have you been tested to see if you are HIV positive in the last 12 months? [1]	
□ No → What are the reasons you did not have an HIV test? □ Don't need to test □ Do not want to know/am afraid.	□ Yes → How many times have you had a test in your life time?____. → When was the last time that you had an HIV test?(give best approximate date)_____.

□ It's better not to know. □ Have to get my partners permission. □ Want to test with my partner. □ Don't know where to test/don't have access to testing. □ Other_____	→ Did you get the result of this test? □ No □ Yes [If no skip to the next section]
33. Would you like me to refer you to our parallel HIV testing service?	
□ No	□ Yes If yes refer the participant using the referral process
34. What was the result of your latest HIV test?[1]	
□ I have never tested □ Negative. □ Indeterminate. □ Did not respond.	□ Positive. → Are you <u>currently</u> being provided with any of the following support or treatment? □ Nutritional support. □ Emotional support (support groups). □ Treatment buddy. □ Home based care. □ CD4 test. □ Viral load test. □ Financial support. □ Treatment of opportunistic infections. → Has a Doctor or Nurse told you that you need to take ARV's? □ No □ Yes → If yes, which dose pill are you on? □No on ARVs

	□Multiple dose □Fixed/single dose → Are you still on ARV's? □No □Yes

35. **Could you have been exposed to TB in the last 12 months?** (“Please note all of the following that are true”?)	
□ I was in prison in the last 12 months □ I was in hospital in the last 12 months	□ I lived in a hostel or informal settlement in the 12 months □ I was in contact with someone who has TB in the last 12 months □ I had contact with someone who has resistant TB (MDR or XDR) in the last 12 months
36. In the past 2 weeks have you had any of the following symptoms? Select one or more the following	
□ Unexplained persistent cough for more than 2 weeks □ Coughed up blood □ Loss of appetite □ Unexplained weight loss □ **If the participant answer yes to any of these questions flag for referral to TB screening and take sputum sample**	□ Drenching night sweats □ Fevers □ None of the above

37. Have you been tested for TB in last 12 months 1?	
□ No	□ Yes → Are you on treatment □ No □ Yes
38. Has a doctor or nurse ever told you that you have TB in last 12 months?	
□ No → If no, are you currently taking medication to prevent TB (INH)? □ No □ Yes → If yes when did you start INH medication? MM___YY__ → If no have you taken INH medication in the last year ? □ No □ Yes	□ Yes → What was the date when you were first diagnosed with TB? MM____YY_____. → When did you start your TB medication? MM____YY____ → Have you completed your treatment? □ No □ Yes
39. Has a doctor or nurse ever told you that you have an STI in last 12 months?	
□ No → Do you currently have any possible symptoms of an STI such as ulcers and discharge area? □ No □ Yes → If yes may I refer your for STI screening to our parallel service?	□ Yes → What was the date when you were diagnosed with a STI? MM____YY_____. → Have you completed your treatment? □ No □ Yes

If the participant answer yes to any of these questions flag for referral to STI screening	
40. Has a doctor or nurse ever given you medication to prevent you contracting HIV because you were exposed (Raped, touched blood etc.) to the HIV virus in last 12 months?	
□ No	□ Yes

Section 6 - Sexual history

I now have to ask you very sensitive questions on sex and other sex-related matters. Please remember that your name will not be recorded anywhere in this questionnaire and the information you give will be kept confidential.

Last 12 months

41. How many people have you had sex with in the last 12 months?	
□ Have not had sex in the last 12 months.	_____number. → How often did you use a condom when you had sex? □ Sometime □ Always □ Never → Have you ever taken ARV medication (PREP) to prevent getting HIV before you had sex? □ No □ Yes → What type of PREP did you take? □ Oral medication □ Gel → Did you know the HIV status of these partners? □ Yes, all of them. □ Yes some of them.

	□ No, none of them.[1] → How many of these partners did you know were HIV positive? □ All of them. □ Some of them □ None of them.

Sexual partners in last 12 months

Now I am going to ask you more details about the 3 most recent partners that you have had sex with in the last 12 months. Please tell me about them starting with the most recent (newest) partner.

		□ No second partner, skip to next section.	□ No third partner, skip to next section.
	Partner 1	Partner 2	Partner 3
42. Their first name/nick name.			
43. What is the nature of your relationship?[1]	□ Wife. □ Regular partner. □ Casual partner. □ Commercial partner.	□ Wife. □ Regular partner. □ Casual partner. □ Commercial partner.	□ Wife. □ Regular partner. □ Casual partner. □ Commercial partner.
44. What is the current age of your partner?[1]	_____ years.	_____years.	_____years.
45. Is this partner a member of your household?[1]	□ No □ Yes	□ No □ Yes	□ No □ Yes
46. Month and year sexual relationship began.[1]	MM___ YY___	MM___ YY___	MM___ YY___
47. When did this sexual relationship end?	MM___ YY___ □ Not ended	MM___ YY___ □ Not ended	MM___ YY___ □ Not ended

48. Partner's sex?[1]	□ Male □ Female	□ Male □ Female	□ Male □ Female
49. If male, is he circumcised? **(Skip if female)**	□ Circumcised at start of relationship. □ Not circumcised. □ Became circumcised during relationship. □ Don't know.	□ Circumcised at start of relationship. □ Not circumcised. □ Became circumcised during relationship. □ Don't know.	□ Circumcised at start of relationship. □ Not circumcised. □ Became circumcised during relationship. □ Don't know.
50. How many times did you have sex with this partner in the last 12 months?[1]	□ Never in the last 12 months. □ Once. □ 2 – 5 times. □ 6 – 10 times. □ 10 – 20 times. □ More than 20 times.	□ Never in the last 12 months. □ Once. □ 2 – 5 times. □ 6 – 10 times. □ 10 – 20 times. □ More than 20 times.	□ Never in the last 12 months. □ Once. □ 2 – 5 times. □ 6 – 10 times. □ 10 – 20 times. □ More than 20 times.
51. How often did you use a condom when you had sex?[1]	□ Always □ Sometimes □ Never	□ Always □ Sometimes □ Never	□ Always □ Sometimes □ Never
52. If you never used a condom with this partner, was it because you battled to access condoms when having sex with this partner?	□ No □ Yes □ Sometimes	□ No □ Yes □ Sometimes	□ No □ Yes □ Sometimes
53. How often did you give or receive money/gifts so that you could have sex with this person in last 12 months?[1]	□ Always □ Sometimes □ Never	□ Always □ Sometimes □ Never	□ Always □ Sometimes □ Never
54. Did you and your	□ No	□ No	□ No

partner have anal sex in the last 12 months?	□ Yes If no, skip the next question.	□ Yes If no, skip the next question	□ Yes If no skip the next question.
55. How often did you and your partner use a condom when you had anal sex in the last 12 months?[1]	□ Never had anal sex. □ Always. □ Sometimes. □ Never.	□ Never had anal sex. □ Always. □ Sometimes. □ Never.	□ Never had anal sex. □ Always. □ Sometimes. □ Never.
56. When you were having a sexual relationship with this partner, do you think that he/she was HIV positive?[1]	□ No. □ Don't know. □ Yes. → Do you think that this partner was taking ARV's for HIV?[1] □ No. □ Yes. □ Don't know.	□ No. □ Don't know. □ Yes. → Do you think that this partner was taking ARV's for HIV?[1] □ No. □ Yes. □ Don't know.	□ No. □ Don't know. □ Yes. → Do you think that this partner was taking ARV's for HIV?[1] □ No. □ Yes. □ Don't know.
57. Have you told your partner your HIV status?	□ No. □ Yes.	□ No. □ Yes.	□ No. □ Yes.
58. Has this partner had any STI's in the last 12 months?	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.
59. Can you talk about safe sex with this partner?	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.	□ No. □ Yes. □ Don't know.
60. Has this partner ever forced you to have sex when you	□ No. □ Yes.	□ No. □ Yes.	□ No. □ Yes.

did not want to in last 12 months?	☐ Don't know.	☐ Don't know.	☐ Don't know.

Section 7- Health access

Health status HIV, TB, chronic conditions, disabilities

61. Have you suffered any of the following illnesses in the past 12 months?[1]	
☐ Heart disease. ☐ Stroke. ☐ Arthritis. ☐ Obesity (very over weight). ☐ High blood pressure. ☐ Diabetes. ☐ TB. ☐ Pneumonia. ☐ Cancer. ☐ Malaria.	☐ Depression/anxiety. ☐ Asthma. ☐ Hepatitis. ☐ STI's. ☐ Peptic Ulcers. ☐ Kidney disease. ☐ HIV. ☐ Other_____. → Are you accessing medical assistance for your illness ☐ No ☐ Yes

Access to contraception

62. Are you currently using a contraceptive method?	
☐ No → Why not ☐ My partner is trying to fall pregnant. ☐ Cannot access contraceptive methods. ☐ My partner is on contraceptives	☐ Yes → Which kind ☐ Condoms. ☐ Spermicides. ☐ Rhythm/calendar/safe period/Withdraw/Thigh sex /Masturbation.

□ My partner cannot fall pregnant □ No reason.	□ Emergency contraception. □ Anal sex. □ Male sterilisation. □ Oral sex. □ Other _____. □ No response. → Are you able to access your contraceptive method whenever you need it? □ No □ Yes

Exposure to prevention programmes.

63. In the past 12 months, from where/or whom have you received HIV information that has been useful to you?[1]	
□ No one. □ Billboard. □ A child or learner of school going age. □ A religion/faith based organisation. □ The workplace. □ Community meeting. □ Traditional healer. □ AIDS or welfare organisation.	□ Newspaper. □ Television. □ Clinic, hospital or doctor. □ Telephone help line. □ Pharmacy or chemist. □ Parent, family or care giver. □ Partner. □ Friend. □ Other.

64. Which of the following activities have you participated in, in the past 12 months?	
□ Community meeting on HIV & AIDS. □ Membership of an HIV organisation e.g. TAC □ Volunteer for HIV activities e.g. fund raising. □ Attended a local HIV rally or march. □ Attended an HIV educational event in the	□ Cared for a person who is sick with AIDS. □ Helped a family who has someone sick with AIDS. □ Helped a family who lost a member as a result of AIDS. □ Other: _____. □ No response.

workplace. □ Attended an HIV play or event. □ Attended a support group for HIV/AIDS.	

65. In the last 12 months, have you seen or heard any messages about the following topics related to HIV?[1]	
□ Get an HIV test to know your status. □ Reduce your number of sex partners. □ Use condoms every time you have sex. □ Male circumcision for HIV prevention.	□ ARV's are available at clinics to treat HIV. □ All pregnant women should get an HIV test. □ ARV's are available to women to prevent mother to child transmission. □ Other:_____.

Section 8

Male Circumcision

Now I would like to ask you about male circumcision. As a reminder, by male circumcision, I mean removal of the foreskin of the penis.

Before we begin, do you have any questions?

66. Were you circumcised in the last 12 months?	
□ No (skip this section) □ Yes YYYY_____ MM_____DD_____	
67. Were you circumcised by a medical Doctor /Nurse or a Traditional Healer?	
□ Medical Circumcision □ Don't know	□ Traditional Circumcision
68. On the day you got circumcised, did you have an HIV test?	
□ No	□ Yes
69. Did anyone influence your decision to get circumcised?[1]	
□ No	□ Yes → If yes, who was it?

	☐ Friend/colleague ☐ Traditional leader or healer ☐ Parents ☐ Partner ☐ Other_____.

APPENDIX K – CONFIDENTIALITY AGREEMENT FOR RESEARCH STAFF

Confidentiality Agreement for Research Staff

Project title: HIV incidence Provincial Surveillance System (HIPSS)

Principal Investigator: Ayesha Kharsany

☐ I understand that all the information /that I will hear, record and/or transcribe is confidential

☐ I understand that the contents of the consent forms, questionnaires or interview can only be discussed with the researchers.

☐ I will not keep any copies of the information nor allow third parties to access them.

Research Staff members' signature:

_____

Research Staff's name:

_____

Date:

_____

Signature of PI:

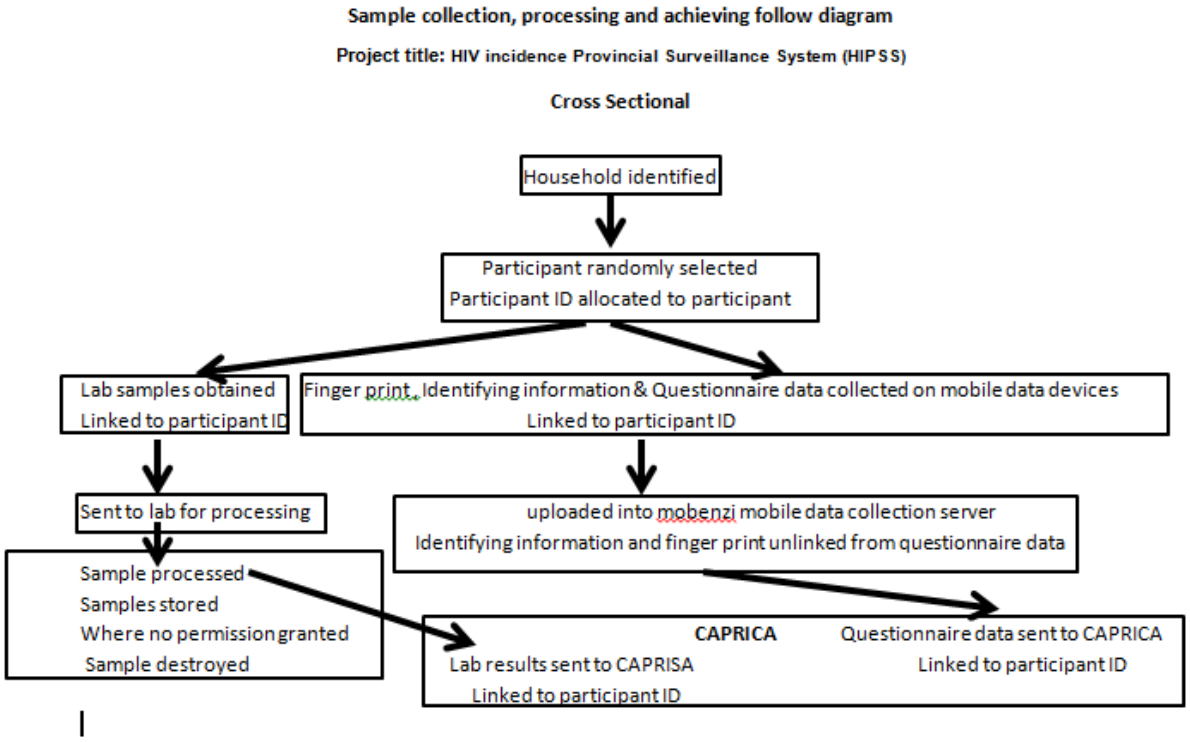
_____

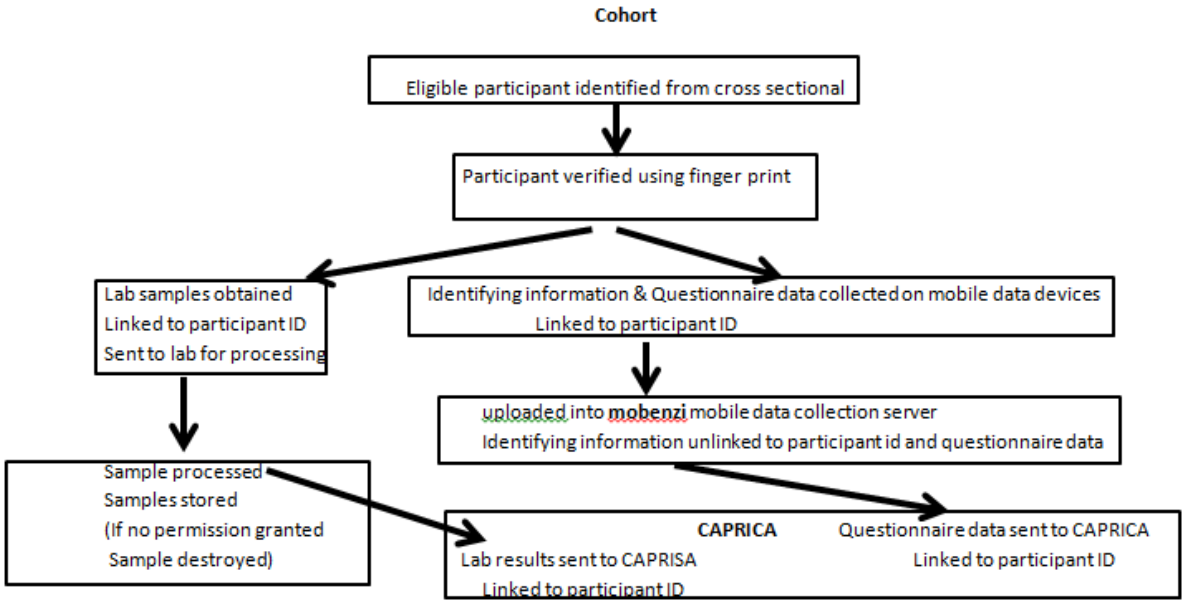
Name of PI: Ayesha Kharsany

_____

Note: The Research Staff member will be given a copy of this form to retain for her/his records

APPENDIX L – DATA MANAGEMENT




Cohort
Eligible participant identified from cross sectional
Participant verified using finger print
Lab samples obtained
Linked to participant ID
Sent to lab for processing
Identifying information & Questionnaire data collected on mobile data devices
Linked to participant ID
uploaded into mobenzi mobile data collection server
Identifying information unlinked to participant id and questionnaire data
Sample processed
Samples stored
(If no permission granted
Sample destroyed)
CAPRICA
Lab results sent to CAPRISA
Linked to participant ID
Questionnaire data sent to CAPRICA
Linked to participant ID