Mbongolwane & Eshowe

HIV Impact in Population Survey

Final report

Funded and Sponsored by:
Médecins Sans Frontières

Waverley Business Park, Building 20, Office 303 A&B

Mowbray, Cape Town 7925, South Africa

Conducted by:

Epicentre

8 rue Saint Sabin, 75010 Paris, France

& Médecins Sans Frontières

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List of abbreviations and acronyms

AE	Adverse event
AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal care
ARV	Antiretroviral drug
ART	Antiretroviral therapy
CAB	Community Advisory Board
CAPRISA	Centre for AIDS prevention and research in South Africa
DBS	Dry blood spots
DOH	Department of Health
EA	Enumeration Area
ELISA	Enzyme-linked immunoabsorbent assay
FRR	False Recent Rate
GPS	Global Positioning System (GPS)
HCT	HIV Counselling and Testing
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
HSA	Health Service Area
KZN	KwaZulu-Natal
LAG	Limiting antigen assay, a test for recent infection
MSF	Médecins Sans Frontières
NAAT	Nucleic acid amplification test
NHLS	National Health Laboratory Service
NICD	National Institute for Communicable Diseases
PCR	Polymerase Chain Reaction
PMTCT	Prevention Mother-to-Child Transmission

QC	Quality control
RITA	Recent Infection Testing Algorithm
RNA	Ribonucleic acid
SOP	Standard Operating Procedure
TB	Tuberculosis
UCT	University of Cape Town
UNAIDS	Joint United Nations Programme on HIV/AIDS
VL	Viral load
WHO	World Health Organization

Definitions

Acute HIV infection	Negative serology, positive NAAT
Avidity tests	Test for strength of antibody response to HIV antigens (weaker response is evidence of recent HIV infection)
HIV positive/negative	HIV status defined by serological rapid HIV test algorithm
HIV uninfected	HIV negative results of serology and NAAT
Household	Group of people who live together and provide themselves jointly with food and/or other essentials for living, or a single person who lives alone Member of the household resident: a person who belongs to the household and lives within it 4 or more nights a week (in the last month) Member of the household non-resident: a person who belongs to the household and does not live within it 4 or more nights a week (in the last month)
Incidence assays	Assays which determine whether HIV seropositive individuals likely acquired infection recently or have long term infection (includes BED, avidity and others)
Incident HIV cases	Acutely or recently infected
Long term HIV infection	Cases classified as non-recently infected through the Recent Infection Testing Algorithm.
Mean RITA duration	The average length of time that people with newly acquired infection in the population are to be classified by the RITA as having recently acquired infection
Migrant	A person who has moved place of residence within the last 10 years International migrant (immigrant or emigrant): a person who has crossed a national boundary

	Internal migrant (in-migrant or out-migrant): a person who has moved within their country
	Circular migrant: a person who is linked to their original household through communication, regular visits and cash remittance, from another place of work
Place of usual residence	The place where the person spends 4 nights a week on average
Recent HIV infection	Cases classified as recently infected through the RITA
Visitor	Person who slept in the house the night preceding the interview but does not belong to the household

Collaborative institutions, study investigators and roles

Epicentre Paris, France	**Dr. Helena Huerga** Principal Investigator	Study oversight Substantial input into study design, protocol development and implementation, data analysis, report writing and publications.
	Dr. David Maman **Dr. Jean-François Etard** Co-Investigators	Input into study design, protocol development, data analysis plan, report writing and publications.
	Ms. Jihane Ben Farhat Statistician	Statistical analyses
	Ms. Malika Bouhenia Field study coordinator	Coordination of the study in the field
Médecins Sans Frontières CIDER, University of Cape Town Cape Town, South Africa	**Dr. Gilles Van Cutsem** Co-Principal Investigator	Study oversight. Substantial input into study design, protocol development, data analysis plan, report writing and publications.
	Dr. Carol Metcalf **Dr. Indira Govender** **Dr. Ruggero Giuliani** **Dr. Matthew Reid** **Ms. Katherine Hilderbrand** **Mr. Emmanuel Fajardo** Co-Investigators	Input into study design, protocol development, data analysis plan, report writing and publications.
National Institute for Communicable Diseases (NICD) Johannesburg, South Africa	**Prof. Adrian Puren** Co-Investigator	Laboratory oversight. Input into study design, protocol development, report writing and publications.

Summary

Background: The prevalence of HIV in KwaZulu-Natal is one of the highest in the world. Accurate data on HIV prevalence, HIV incidence and antiretroviral therapy (ART) coverage are essential to define appropriate strategies of intervention. We assessed HIV prevalence, HIV incidence and ART coverage in Mbongolwane and Eshowe in KwaZulu-Natal, South Africa. Other HIV care services indicators were also evaluated.

Methodology: Cross-sectional population-based survey. A cluster sampling and geospatial random selection was used to identify the households visited. Persons aged 15-59 years living in the area were eligible. Face-to-face interviews were carried out followed by rapid HIV testing on site and blood collection for CD4 count, ART levels and viral load in HIV positive cases. ART coverage was defined as the proportion of HIV positive on ART (detectable blood levels) among those eligible according to current National Guidelines. Incidence was estimated using HIV LAg-Avidity assay corrected by viral load and ART status.

Results: In total 3566 households were visited, 6688 individuals were eligible and 5649 (84.5%) were included: 62.3% women and 37.7% men. Overall HIV incidence was 1.2 (95%CI: 0.2-2.1) per 100 person-year (PY) and 2.9 (95%CI: 1.2-4.7) per 100PY in women aged 15 to 29 years. Overall HIV prevalence was 25.2% (95%CI: 23.6-26.9). Prevalence in women was twice that of men: 30.9% (95%CI: 29.0-32.9) vs 15.9% (95%CI: 14.0-18.0). Prevalence reached 56.0% (95%CI: 51.7-60.3) in women aged 30-39 years. Participants older than 19 years, female, not married, with a lower education level than tertiary, having moved residency in the past 10 years (migrant) and having more than one sexual partner were more likely HIV infected. ART coverage was 75.0% (741 on ART/988 eligible) and was higher in women than in men: 78.5% vs 63.9% ($p<0.001$). Coverage increased with age: 60.5% in younger than 30 years vs 81.3% in older ($p<0.001$). Only 11% (1/9) of eligible men aged 20 to 24 were on ART. Among all individuals, 81.4% declared to have had an HIV test previously (88.4% of women vs 69.8% of men, $p<0.001$). Young people 15-34 years, men and those with more than one partner or no partner in the previous 12 months were more likely not tested for HIV. Among HIV positive participants, 75.8% were aware of their status prior to the survey. In the 20 to 24 year age group, 43.1% and 83.3% of women and men respectively were not aware of their status. In addition the factors associated to being untested for HIV, never having married was associated to being unaware of the HIV infection. Overall 27.5% of HIV positive participants had a CD4 count below 350 cells/µl and 25.9% between 350 and 499 cells/µl. Of individuals not on ART, 33.1% had a CD4 count below 350 cells/µl and 26.7% had a CD4 between 350 and 499. Viral suppression (<1000 copies/ml) was achieved in 90.3% of individuals who self-reported being on ART for more than 6 months. Among those not virologically suppressed, resistance to at least one ARV drug was found in 61.2% (30/49). Of the total population HIV infected, 57.1% (796/1423) had less than 1000 copies/ml. ART intake and being a women were independently associated to virological suppression

Conclusions: Overall HIV transmission is moderate in Mbongolwane and Eshowe areas. However a high number of new infections occur in young women. HIV remains an important health problem in the area with more than one

quarter of the population affected by the disease. Overall, access to HIV testing and ART is relatively high in the area, as well as ART coverage for those in need of treatment. However, young people seem to have more difficulties to access HIV testing and treatment. HIV programmes should maintain quality of care while developing strategies to test, link and treat young people aged 20 to 30 years. Novel interventions for HIV prevention in young women are urgent.

1. Introduction

1.1. Background

KwaZulu-Natal has an HIV prevalence among the highest in the world. In 2012, HIV adult prevalence in South Africa was estimated to be 18.8% in 15-49 years old (1). However, HIV prevalence in the country is heterogeneous and KwaZulu-Natal (KZN) has the highest HIV prevalence of the 9 provinces in South Africa: 27.9% (1). In 2011, the prevalence of HIV among pregnant women attending public sector antenatal clinics (ANC) in uThungulu District in KZN was 33.4% (2). Overall HIV incidence in the country has been estimated to be 1.7 per 100 persons-year (PY) and 2.3 per 100PY in women (1). Although the incidence of HIV in the district is unknown, in periurban areas of Kwazulu-Natal, HIV incidence rates of 6.3 to 14.8 per 100 PY have been found in women 18 to 35 years (1). In 2012, the proportion of HIV infected people on antiretroviral treatment (ART) was 28.3% in the country (1).

1.2. Médecins Sans Frontières (MSF) in South Africa

Médecins Sans Frontières (MSF) has been working with local health authorities in South Africa for more than 10 years to pilot, implement, and support scale-up of HIV and TB management and care. In 2001, MSF started the first public sector antiretroviral therapy (ART) programme in the country in Khayelitsha, a large township in the Cape Metropole of the Western Cape Province, working in partnership with the Provincial Government of the Western Cape and the City of Cape Town municipality.

In 2011, MSF in partnership with the KZN Department of Health (DOH) launched a community-based "Treatment as Prevention" pilot project in Mbongolwane and Eshowe HSAs. This project has been gradually implemented from 2011 to the end of 2013 and it was still in progress at the time of the survey. The goal of the project, named *Bending the Curves*, was to decrease the incidence of HIV infection and TB; and to reduce HIV- and TB-related morbidity and mortality by increasing access to, and coverage of, HIV- and TB-related services, by implementing a comprehensive package of interventions to promote prevention, early diagnosis, linkage to care, early treatment, and retention in care for HIV and TB, using novel community-based approaches. Two novel interventions were planned in the intervention package but were not implemented at the time of the survey: 1) Early initiation of ART in HIV-infected individuals satisfying one or more of the following criteria: CD4 count below 500 cells/µl; HIV-positive partner of an HIV-negative individual; TB patients and pregnant women regardless of CD4 cell count. 2) Prevention of Mother-to-Child Transmission (PMTCT) Option B+, i.e. initiation of life long ART in all HIV-positive pregnant women, regardless of their CD4 cell count (3).

From 2011 to the date of the survey, MSF has been supporting the DOH HIV program in the community and in several ART facilities. These facilities are: Mbongolwane Hospital and its 5 feeder clinics and 2 feeder clinics of Eshowe Hospital. Eshowe Hospital and Siphilile Clinic were not supported by MSF at the time of the survey. The support provided by MSF has included prevention activities such as condom distribution and support for medical male circumcision; various forms of large-scale community-based HIV counselling and testing (mobile units visiting community sites, schools and farms; community workers visiting households; and stand-alone testing sites in urban areas); implementation of point of care CD4 testing, support for linkage to care; training and mentoring of health staff in facilities to facilitate decentralization of ART initiation and management to peripheral clinics; and implementation of a community model of care for people living with HIV stable on treatment to more easily access medication (adherence clubs and community ART groups) to improve retention in care.

1.3. HIV care and ART in South Africa

The South African National Guidelines for HIV care and ART initiation have been reviewed in several occasions in the past years (4). Up to July 2011, ART initiation was recommended at a CD4 count threshold of 200 cell/µl. Guidelines were then reviewed and in line with international recommendations (5) the CD4 count threshold for ART initiation was raised to 350 cell/µl. In addition, ART initiation was recommended in case of TB diagnosis regardless of the CD4 count. Regarding PMTCT, option A was used up to March 2013 and option B since April 2013.

1.4. Evidence on prevention of HIV

HIV prevention and treatment go hand-in-hand and a combination of multiple, behavioural and biomedical, interventions are necessary for effective HIV prevention (6). Declines in HIV prevalence in Uganda, Kenya and Zimbabwe have been attributed to population-level reductions in risk behaviour (7–9). HIV incidence estimates derived from national household surveys suggest that HIV incidence in South Africa has begun to decline amongst youth 15 to 19 years of age (10). This may be attributable to substantial increases in HIV testing uptake and condom use, as other risk factors for HIV infection including age at sexual debut, age mixing, and multiple sexual partnerships, have not changed in recent years (11).

Over the past few years, there have been several advances in interventions for the prevention of HIV. Biomedical interventions that have been shown to be efficacious by means of randomised controlled trials include medical male circumcision (12–14); providing HIV-infected people with ART to prevent HIV transmission to their HIV-negative partners (15); and providing pre-exposure prophylaxis (PrEP) to people at risk of becoming infected, using antiretroviral drugs (ARVs) (16,17). Medical male circumcision has been endorsed by the king of the Zulu nation, King Goodwill Zwelithini, and is already promoted by the KZN DOH.

There is currently a great deal of interest and debate around the potential benefits of early ART initiation for improving HIV prevention (by reducing HIV transmission) and for minimising HIV-related morbidity and mortality among those already infected (18). This intervention is referred to as *Treatment as Prevention*. The clinical trial HPTN 052, which studied the impact of early ART treatment among HIV-positive individuals on HIV incidence in their serodiscordant partner, showed a 96% reduction in transmission of HIV in those who were on ART (15). This suggests that increasing ART coverage and thus the number of seropositive people with an undetectable viral load should lead to a reduction in HIV incidence. Mathematical models suggest that HIV incidence reduction is feasible if HIV infected individuals access diagnosis and treatment early in the course of infection (19,20).

An important risk of ART scale-up and long-term ART use is the potential for individuals to develop viral resistance, necessitating a switch to second-line drugs, and eventually third-line drugs and beyond. There is also a risk that individuals with resistant virus will transmit resistant virus to others (21). It is therefore important to monitor the frequency and types of antiretroviral resistance in the population.

1.5. Measuring ART coverage, HIV incidence and HIV prevalence

It is expected that the implementation of these new HIV prevention strategies will result in increased ART coverage and viral load (VL) suppression among those on ART leading to lowered infectivity and a reduction in HIV incidence. Measuring HIV incidence, HIV prevalence and ART coverage on a repeated or ongoing basis, is important in order to assess the impact of the interventions.

The most accurate way of measuring HIV incidence is by means of prospective cohort studies. The method is expensive, time consuming and complex, and is impractical in population-based interventions. In the last decade, several assays have been developed to differentiate recent from longstanding infections (22,23). The avidity assays (24,25), a new generation of tests, aim to differentiate the strength of the bond between the viral antigen and the specific antibody (26,27). These tests have showed promising results and are recommended by the World Health Organisation (WHO) for assessing HIV incidence in a population (28). The assay-based approach involves the use of one or more serological laboratory tests that are able to classify HIV infections in a population according to whether or not they were acquired in the recent past (generally within four to 12 months). Classification using one or more assays of this kind, or a combination of assays and other relevant information about the recency of HIV infection, such as HIV viral load and exposure to ART to account for the false recency rate (FRR) defines an HIV Recent Infection Testing Algorithm (RITA).

Population-based HIV prevalence surveys usually follow a cross-sectional design with the general population as the study subjects. A cross-sectional study is designed to estimate a key indicator such as HIV prevalence at one point in time to obtain a measure of the current level of the epidemic (29). ART coverage can be estimated using the same type of study.

1.6. Study justification

Assessing the baseline parameters of the HIV epidemic in an area is critical for the planning and implementing of multiple and complex interventions. The aim of the survey was to provide a baseline assessment of the HIV situation among the population of Mbongolwane and Eshowe where MSF was launching a new pilot HIV program.

The goal was to provide baseline information on ART coverage, HIV incidence and HIV prevalence in Mbongolwane and Eshowe areas. This study would help the DOH and MSF with planning and defining priority interventions concerning HIV diagnosis and care in the area. The results of the survey would also enable assessment of the impact of the pilot HIV program if it was repeated over time.

1. Study objectives

1.1. Primary objective

To assess ART coverage among HIV infected individuals in need of ART in Mbongolwane and Eshowe.

1.2. Secondary objectives

- To estimate HIV prevalence
- To estimate HIV incidence
- To assess viral load suppression among HIV infected on ART
- To measure the prevalence of antiretroviral drug (ARV) resistance among individuals on ART and among incident cases
- To assess HIV testing coverage and to describe use of HIV counselling and testing services
- To assess access to HIV care and ART
- To assess access to HIV prevention of mother-to-child transmission
- To describe migration dynamics and access to HIV care among migrants
- To estimate male circumcision coverage and to describe male circumcision practices

2. Methods

2.1. Study design and population

The study was a cross-sectional population survey. People aged 15-59 years old living in Mbongolwane and Eshowe HSA were eligible for enrolment in the study.

2.2. Source population and site

Mbongolwane, Eshowe and Catherine Booth constitute the three Health Service Areas (HSA) of uMlalazi Municipality, one of the six municipalities of uThungulu District, located in KZN province, South Africa. The main town in the municipality is Eshowe, located about 140km north of Durban. Administratively uMlalazi Municipality is divided in 26 Electoral Wards. The area where MSF operates in uMlalazi Municipality in the Eshowe and Mbongolwane HSAs corresponds to Wards 1-14, with a catchment population of approximately 120,000 (30). According to the 2011 Census, 61,179 people aged 15 to 59 were living in 25,106 households in the area covered by the survey.

2.3. Inclusion and exclusion criteria

Inclusion criteria

- Age 15 to 59 years
- Living in Mbongolwane and Eshowe area (Wards 1 to 14 of uMlalazi Municipality) at the time of the survey
- Member of the household visited by the survey team or visitor to this household
- Able and willing to provide informed consent

Exclusion criteria

- Any person present in the household visited by the survey team who neither is a member of the household nor is a visitor

2.4. Sampling

2.4.1. Sample size

To assess an ART coverage of 50% (95%CI: 45-55%), assuming that the prevalence in the age range 15-59 years old was 20%, the proportion of people in need of ART was 55% and a design effect of 1.3, under standard alpha=0.05 and power=80%, 4538 subjects were needed.

To assess an HIV incidence of 2.0% (95%CI: 1.3-2.7%) under the same hypothesis, assuming a mean duration of recent infection (MDRI), the average length of time that people with newly acquired infection in the population are to be classified by the recent infection test algorithm as having recently acquired infection, of 239 days with 95% confidence intervals of [214 days; 265 days] (31), and a False Recent Rate (FRR) of 1% with 95% confidence intervals of [0.4%; 1.6%] (32), 5626 subjects were needed. The sample size was calculated using the McWalter and Welte formula (33,34).

A sample size of **5600** subjects was used. Assuming an average of 2.4 people per household and a response rate of 75%, 3126 households were required to visit.

2.4.2. Sampling method

A multistage stratified cluster probability sampling was used for the selection of households. All the eligible members of a household were invited to the study. In total, 125 clusters of 25 households each were included. The number of clusters per Ward was selected with probability proportional to population by the 2011 Census. Google Earth maps from 2011 were used to sample the households to be visited. Field staff used Global Positioning System (GPS) receivers to find the geographic coordinates of each household.

2.5. Procedures

2.5.1. Community mobilization and participant recruitment

Mobilization was done through several channels before starting the survey: information on radio spots, meetings with community leaders and health facilities workers, information in schools. A leaflet and a poster were created to explain the purpose of the survey, how the participants were selected and the study procedures. They were distributed in the different areas were the survey was going to be conducted.

Meetings were organised with the community leaders to explain the study and have an opportunity to discuss potential issues and concerns. These stakeholders included local community leaders, district authorities and religious leaders. Continued dialogue with these stakeholders was ensured to maintain community engagement prior to and during the course of the study.

Targeted community mobilization was done in the areas where households were selected for inclusion the week before the arrival of the survey teams. Two mobilizers informed the neighborhood using a microphone installed on a car, and then they informed directly the community going door to door. They also met the community leaders of the area, asked about special events that could be happening in the neighborhood and collected information about the

best time for the survey teams to come in each house. Mobilization was particularly enhanced in urban areas, where the reluctance of participation to the survey was higher.

In order to reach a maximum of eligible individuals in their houses the survey teams visited the houses from Tuesday to Sunday. Time slots from early morning to late evening were covered in different days of the week in order to maximize the possibilities of finding the eligible participants in their houses. Since traditions, religious and social life were not the same in all the survey areas, the teams' working hours were also adapted according to the area they were going to visit. Each team visited 25 households per week.

Due to the importance that blood has in the Zulu culture, the survey teams made a particular effort in explaining the purpose of collecting and storing blood and the use of it.

2.5.2. Interviews

Face-to-face interviews were carried out with the help of a questionnaire. Interviewers first introduced the study to the head of household or if not present, to a household representative, and asked written informed consent to answer the household questionnaire. Following the consent process, the interviewer completed the household questionnaire, which listed household members and visitors, their month/year of birth, relation to the head of household, ages, number of nights sleeping in the house per week, in order to determine eligible participants. Information about household members who died recently or moved away from the household was also collected, including age and sex. Eligibility was verified with each individual prior to the consent process.

For any household member or visitor who was eligible and interested in participating, the interviewer obtained individual written informed consent to participate in the study. After consent was obtained, the interviewer conducted individual face-to-face interviews in a private area within the household or near to it. Items asked in the questionnaire instrument included:

- ***Background demographic characteristics:*** Gender, age, place of birth, education, marital status, occupation.
- ***Migration:*** Type of migration, duration of migration, destination/origin of migration.
- ***Antenatal and Delivery Care (for women):*** number of pregnancies and children, antenatal care visits, place of delivery, breastfeeding.
- ***Circumcision (for men):*** Circumcision, method for circumcision, place of circumcision.
- ***HIV Testing:*** HIV testing history, knowledge of HIV status, place of testing, date of testing, knowledge of HIV testing centres.

Following the interview, the interviewer proposed a rapid HIV test with pre- and post-counselling according to the National Guidelines for HIV Counselling and Testing (HCT) (35). Individuals who were not aware of their positive

status or who were not receiving care were counselled and informed about the closest centre where they could receive HIV care. They were also given a referral letter.

For individuals found to be HIV positive and for individuals not willing to perform an HIV test but willing to provide blood for anonymous testing in the laboratory, the interview continued including questions on ***HIV care and ART***: Date of first positive HIV test, place of follow-up, ART intake and date of start, PMTCT history, knowledge of HIV care and ART centres.

A qualified nurse collected venous blood from all participants. A total of 15 ml of venous blood was collected in three 5ml EDTA tubes from participants reported positive or indeterminate after HIV testing and from participants willing to participate in the study but not willing to know their HIV status. A total of 5ml of in one 5ml EDTA tube was collected from participants reported negative after HIV testing. Participants with a positive result on the rapid HIV test were tested for CD4 count, ARV drug levels, HIV recent infection test, HIV viral load (if on ART for more than 6 months), and drug resistance (if viral load was higher than 1,000 copies/ml). Participants with a negative result on the rapid HIV test were tested for acute HIV infection.

2.5.3. Laboratory procedures

HIV testing was done on the spot directly at participants' households. Other biological analyses were done in the UCT Department of Pharmacology laboratory at Groote Schuur Hospital in Cape Town, at Global Clinical and Viral Laboratory in Durban, and in collaboration with the National Institute for Communicable Diseases (NICD), a Division of the National Health Laboratory Service (NHLS) in Johannesburg.

2.5.4. HIV testing

All participants were offered confidential HCT carried out by trained counsellors. HCT was optional and was not a prerequisite to participation in the survey. Those who elected not to have HCT had blood drawn for anonymous tests done in the laboratory for study purposes.

Among participants who elected to have HCT in order to learn their HIV status, HIV testing was performed, after pre-counselling, using whole blood obtained by finger-prick at the participant's house. Rapid tests were done following a serial algorithm using Determine Rapid HIV-1/2 Antibody as screening test followed if positive by Unigold Rapid HIV test kit for confirmation. The tests were done by certified lay counsellors.

Those who tested positive with both tests were considered positive. Those with discordant results (Determine positive, Unigold negative) had a third "tiebreaker" test using ELISA done at Global Clinical and Viral Laboratory in Durban. Results were made available at the HIV care facility of their choice.

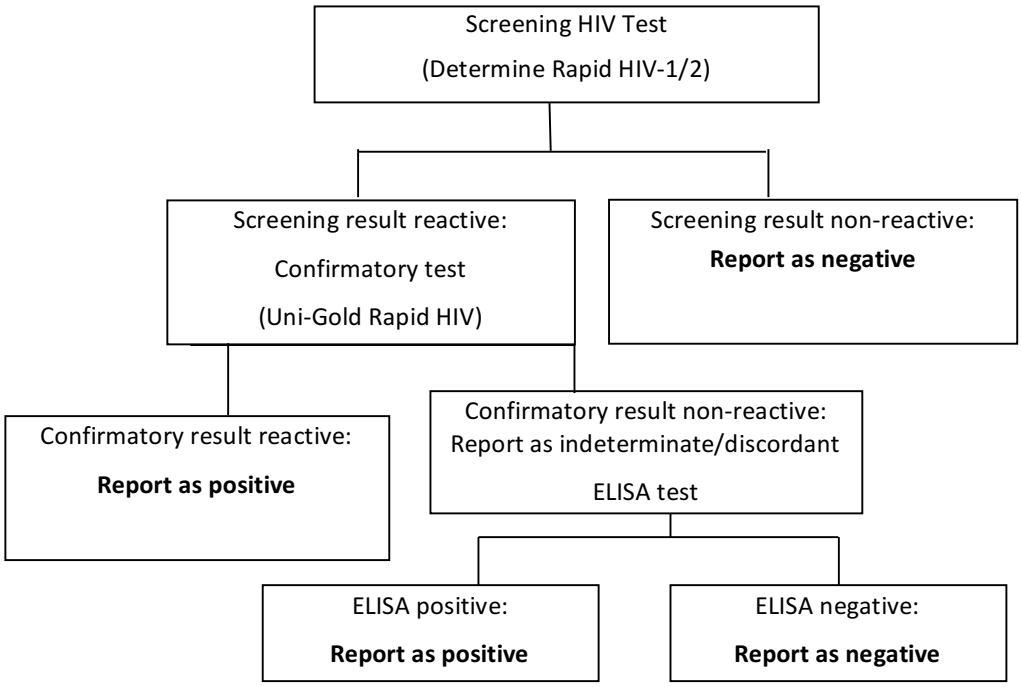

Figure 1: Serial HIV testing algorithm, HIV Counselling and Testing Policy guidelines, South Africa

2.5.4.1. CD4 count determination and plasma separation

Venous blood samples were transported in a cooler box to the MSF/Epicentre office in Eshowe and from there transported every evening to Global Clinical and Viral Laboratory in Durban. CD4 count was performed using a FACSCalibur™ device from Becton, Dickinson and Company (BD) according to standard manufacturer's instructions on samples reported as HIV positive.

Two dry blood spots (DBS) samples were prepared using the venous blood samples from each participant. The remaining 2 blood tubes from HIV positive participants and the tube from HIV negative participants were centrifuged for plasma extraction.

2.5.4.2. Viral Load and HIV-1 genotypic analysis

Viral load was performed for participants on ART for more than 6 months (determined by questionnaire) at Global Clinical and Viral Laboratory in Durban using a NucliSens EasyQ HIV-1 v2.0 assay from Biomerieux according to

manufacturer's instructions. The test could quantify HIV-1 RNA over the range of 20 copies to 20 million copies for 0.5ml sample.

HIV-1 genotyping was carried out at the Centre for AIDS Prevention and Research in South Africa (CAPRISA) on samples from participants on ART with VL higher than 1,000 copies/ml and on the first 100 specimens from participants classified as recently infected according to the RITA. TRUGENE HIV-1 Genotyping assay from Siemens Healthcare Diagnostics was used. Genotypic resistance was interpreted according to the Stanford University algorithm for HIV drug resistance.

2.5.4.3. ARV drug detection

Qualitative testing for ARV drug levels was performed for all HIV positive participants using DBS samples in the UCT Department of Pharmacology laboratory at Groote Schuur Hospital in Cape Town. Testing included the following drugs: nevirapine, efavirenz and lopinavir which covered all ARV regimens in use in the public sector in the area. A LC MS/MS qualitative assay was used for the drug presence determinations. Filter paper spots were punched out (3.2mm punches) and extracted. This technique detects presence or absence of the drugs down to 0.2 micrograms /ml. Considering that the therapeutic drug monitoring target for trough concentration is 1 microgram/mL at 24 hours for both lopinavir and efavirenz and is 3 micrograms/mL at 12 hours for nevirapine, a positive result was expected if the last dose was taken as prescribed. The assay should therefore be positive for all adherent patients and some partially adherent patients taking nevirapine or efavirenz, which have long half-lives. Quality controls (cut off limits) were analysed with each batch of samples as well as negative controls. Each batch was reviewed by the analyst in charge of the project and then quality controlled by another. Samples were analysed in batches.

2.5.4.4. Incidence Testing

Incidence testing was performed at NICD laboratory in Johannesburg. Specimens from participants confirmed to be HIV positive by ELISA were tested to determine recent versus long term HIV infection using incidence assays. These tests included the single-well limiting antigen avidity EIA (LAg-Avidity EIA) and modified BIORAD HIV 1/2+O Avidity incidence assays.

Limiting Antigen Avidity Enzyme Immunosorbent Assay (LAg-Avidity EIA)

LAg-Avidity EIA testing was conducted as described in detail by Duong *et al* (25) following the CDC protocol. In brief, the Limiting Antigen Assay is a simple serological assay that detects increasing avidity antibody maturation following

seroconversion and can be used for detecting recent HIV-1 infection. The assay has similar performance among individuals infected with different subtypes and across different populations (24,25).

Diethylamine based-avidity assay

The Genetic Systems™ HIV-1/HIV-2 PLUS O (BioRad, Redmond, WA) was conducted following the manufacturer's specifications. The high sensitivity and specificity of this assay conferred by the presence of highly conserved recombinant proteins and synthetic peptides is an advantage for detecting antibodies from any sample type (36,37).

Acute infection testing

Patients determined HIV negative by the rapid test algorithm outlined above were tested by Nucleic Acid Amplification Testing (NAAT) for detection of acute infection. A specimen pooling strategy followed by disaggregation to test for individual pool members was used. Initial pool sizes of 6-10 specimens were used. Any positive pools identified by a qualitative NAAT test were disaggregated to individual specimens and tested by means of a quantitative assay. The pooling testing was performed using Roche AMPLISCREEN method and the individual NAAT testing was performed using the Roche CAP/CTM method.

2.5.4.5. Plasma storage

Two plasma aliquots of 1 ml each were stored for up to 5 years at the Global Clinical and Viral Laboratory in Durban. These samples were kept in reserve for retesting using new assays of recent HIV infection.

2.5.4.6. Laboratory Quality Control

Global Clinical and Viral Laboratory is accredited by the South African National Accreditation System (SANAS) and participates in the United Kingdom National External Quality Assessment Service (NEQUAS). NICD participates in the Proficiency Testing quality assurance programme that includes quality control for molecular diagnostics and virology quality assurance.

2.6. Ethical considerations

2.6.1. Protocol Review

This protocol approved by the UCT Human Research Ethics Committee (HREC) and the Health Research Committee of the Health Research and Knowledge Management Unit of KZN DOH, in South Africa. In addition, it was approved by the Comité de Protection de Personnes de Paris in France.

2.6.2. Informed consent

Written informed consent was sought after complete explanation of study procedures and implications of study participation (risks/benefits). Informed consent documents (consent forms and information leaflets) were available in English and Zulu. The informed consent process was carried out in English or Zulu, depending on the preference of the participant, and in a private area chosen by the participant either inside or outside the house.

Informed consent was obtained in a three-part process.

1/Consent for the Household questionnaire was obtained prior to starting the questionnaire from the head of the household or the person willing to answer the household questionnaire.

2/Consent from each individual found eligible for the survey was then sought which included consent for the questionnaire, HIV testing and for drawing blood samples and performing the biological tests. HIV testing was proposed to be done on site (result given to the participant) or at the laboratory (anonymous testing). Eligible individuals who did not consent for HIV testing and other biological tests were not included in the study. A special consent procedure was used to obtain consent for participation of minors aged 15 to 17 years old (see below).

3/Consent from those found HIV positive was sought for storing blood samples up to 5 years.

Among potential participants aged 15 to 17 years old, permission was first obtained from the minor's parent, guardian or main caregiver (if the minor was not living with a parent) following the consent procedures described above. If the parent/guardian/caregiver granted permission, informed consent was then obtained from the minor using the same consent documents and procedures described above. Minors had the option of refusing to participate even if the parent/guardian/caregiver had given permission for the minor to participate.

2.6.3. Confidentiality

All study-related information was stored securely at Epicentre/MSF facilities. All participant information was stored in locked file cabinets in areas with access to study staff only. All laboratory specimens, reports, data collection instruments, process logs, and administrative forms were solely identified with the patients study ID number to maintain participant confidentiality.

All databases were password-protected for security of access. Forms, lists, logbooks and any other listings that link participant ID numbers to other identifying information were stored in separate locked filling cabinets accessible only to the data manager and principal investigator or appropriate designee.

During the household listing, field staff used GPS receivers to establish and record the geographic coordinates of each of the clusters. For confidentiality reasons, no data on individual household geographic coordinates was kept after the end of the survey.

2.7. Data management, storage and disposition

2.7.1. Data management

Paper based questionnaires and laboratory forms were used for collection of socio-demographic, HIV testing and HIV care information. Laboratory registers, laboratory information management systems (LIMS) or other electronic laboratory data were used to capture laboratory data, depending on the standard procedures of each laboratory.

2.7.2. Data analysis and definitions

The primary objective was to determine ART coverage in uMlalazi Municipality, KwaZulu-Natal. The secondary objectives aimed at assessing the impact of the HIV epidemic and the HIV programs in the area: HIV prevalence, HIV incidence, proportion of HIV-infected people on ART with viral failure and drug resistance, proportion of incident patients with transmitted drug resistance, HIV testing coverage, access to HIV care, prevention of mother-to-child transmission coverage, and circumcision coverage.

ART coverage: Proportion of HIV infected individuals on ART (ARV drugs detected in blood) among HIV infected individuals in need of ART.

Three estimations were done according to 3 scenarios of ART eligibility:

- Scenario 1: PMTCT Option A & ART initiation if CD4<350 cells/µl (South Africa national guidelines from August 2011 to March 2013)
- Scenario 2: PMTCT Option B & ART initiation if CD4<350 cells/µl (South Africa national guidelines at the time of the survey)
- Scenario 3: PMTCT Option B+ & ART initiation if CD4<500 cells/µl (MSF strategy for the area to be implemented from April 2014)

HIV incidence: Number of new HIV infections per 100 person-years.
HIV prevalence: Proportion of HIV positive individuals among those tested
Viral load suppression: Proportion of HIV infected with VL suppression (<1000 copies/ml) among HIV infected individuals on ART for more than 6 months
HIV testing coverage: Proportion of the individuals who had been tested prior to the survey.
HIV infection awareness: Proportion of HIV positive individuals who already knew their status.

3. Results

3.1. Household population

3.1.1. Demographic characteristics of the household population

In total, 3566 households were visited and 2377 (66.7%) were included. The outcomes of the households visited are presented in table 1. The inclusion rate among the households eligible was 77.8%. The refusal rate among contacted households was 10.3% (274/2651). The median number of people in the household was 6 (IQR: 3-8). The range varied from 1 to 30 people. The median age of the people living in the household was 22 years (IQR: 12-37).

Table 1: Outcomes of the households visited during the survey

	n	%
Included	2,377	66.7
Refused	274	7.7
No household member at home or no competent responder	344	9.6
Dwelling vacant or address not a dwelling	222	6.2
Dwelling destroyed	217	6.1
Household absent for extended period	41	1.1
Dwelling not found	9	0.3
Other	82	2.3
Total	3,566	100

In the households included in the survey, 14428 people were listed as family members or visitors by the head of the household. Among the 8637 (59.9%) aged 15-59 years, 8360 (96.8%) were family members of the household and 277 (3.2%) were visitors. Among the 8360 family members, 6522 (78.0%) were resident in the household and 1838 were non-residents (see figure 1). Of the residents, 3863 (60.2%) were women and 2556 (39.8) were men. The median age was 27 (IQR: 19-40). A majority had been living there for at least 3 years. Only 398 (6.2%) had arrived in the household less than 3 years prior to the survey. Of the 1838 family members non-residents in the household, 844 (45.9%) were women and 994 (54.1%) men. The median age was 29 (IQR: 23-37). Two thirds were living in another municipality of KZN.

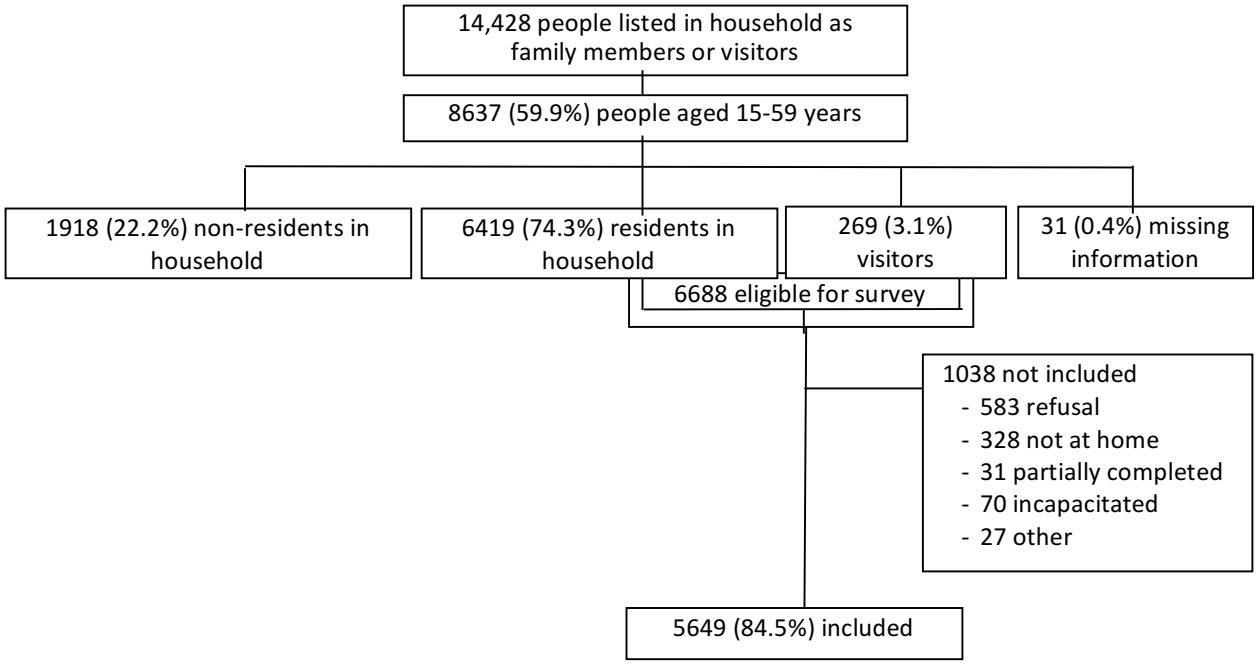

Figure 1: Flow chart of eligibility and inclusion

3.1.2. Mortality and migration of the household population

In total, 87 people had died in the 8.15 months prior to the survey. The mortality rate was 8.6/1000 persons-year (PY) overall, 7.2/1000 PY for women and 10.4/1000 PY for men. Among those aged 15-59 years, the mortality rate was 8.0 /1000 PY, 4.1/1000 PY for women and 13.1/1000 PY for men. The age distribution of the deceased people is shown in table 2.

Regarding out-migration, 308 people had left the household in the previous 8 months. The out-migration rate was 30.6/1000 PY overall, 24.1/1000 PY for women and 38.7/1000 PY for men. Among those aged 15-59 years, the out-migration rate was 46.5/1000 PY, 35.1/1000 PY for women and 61.0/1000 PY for men. The median age of those who had left the household was 28.0 years (IQR: 22.0-34.0), which was similar in women and men: 27.0 vs 28.0 years. The main reason for migration was work-related and the most frequent destination was another municipality within KZN. None declared a destination outside South Africa.

Table 2: age distribution of the deceased people during the 8 months prior to the survey

	Women		Men		Total	
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
0-14	4	10.8 (3.1-31.4)	5	10.6 (4.1-25.1)	9	10.7 (5.2-21.4)
15-29	5	13.5 (5.9-27.9)	4	8.5 (3.0-22.1)	9	10.7 (5.9-18.6)
30-44	7	18.9 (8.5-37.1)	15	31.9 (21.0-45.3)	22	26.2 (17.9-36.6)
45-59	2	5.4 (1.3-19.8)	16	34.0 (21.1-50.0)	18	21.4 (13.2-32.9)
>60	19	51.4 (34.7-67.7)	7	14.9 (6.8-29.5)	26	31.0 (21.8-41.9)
Total	**37**	**100**	**47**	**100**	**84**	**100**

3.2. Population of individuals

3.2.1. Individuals eligible & included

In total, 6688 individuals were eligible and 5649 (84.5%) were included. The gender distribution of the individuals eligible and included is presented in table 3. The inclusion rate was 87.8% among women and 79.5% among men. The median age of the individuals eligible and included was 27 years (IQR: 20-40) and 26 years (IQR: 19-40) respectively.

Table 3: Gender distribution of the individuals eligible and included

	Eligible		Included	
	n	%	n	%
Women	4008	59.9	3518	62.3
Men	2680	40.1	2131	37.7
Total	6688	100	5649	100

3.2.2. Sociodemographic characteristics of participants

The socio-demographic characteristics of the 5649 survey participants are presented in table 4. A majority of the participants had never been married, had completed primary or secondary school, were living in rural areas and were students or were not working. A higher proportion of women were married or living together, had never gone to school and were not working. Conversely, a higher proportion of men were living in farms and were students at the time of the survey. Majority of the students belonged to the age group 15-19 years: 77.9% aged 15-19 years, 18.1% aged 20-24 years, and 4.0% aged 25 or more years.

Concerning the participants' mobility, 761 (13.5%) had moved their residence in the 10 years prior to the survey (see table 5). A majority (53.4%) of those who had moved were living in another municipality within KZN before and an important proportion (39.0%) were living in the same municipality where the survey took place. The main reason for moving was family/friends related. The median delay from last move was 25.9 months (IQR: 7.9-54.7).

Of the total number of participants, 246 (4.4%) were visitors (see table 6). A majority were living in the surveyed municipality and an important proportion in another municipality within KZN. The frequency of visits was high for most of them: more than once a month for 97 (68.8%) of the 141 living in Umlalazi and 47 (51.1%) of the 92 living in another municipality of KZN.

Table 4: Participants socio-demographic characteristics

	Women	Men	Total	Women vs men
	n (%)	n (%)	n (%)	p
Marital Status (n)	3515	2129	5644	
Never Married	2448 (69.6)	178 (83.9)	4234 (75.0)	<0.001
Married/Living Together	905 (25.8)	294 (13.8)	1199 (21.2)	<0.001
Divorced/Separated	65 (1.9)	39 (1.8)	104 (1.8)	NS
Widowed	97 (2.8)	10 (0.5)	107 (1.9)	<0.001
Education (n)	3518	2130	5648	
No schooling	319 (9.1)	112 (5.3)	431 (7.6)	<0.001
Primary	1448 (41.2)	963 (45.2)	2411 (42.7)	0.003
Secondary	1625 (46.2)	988 (46.4)	2613 (46.3)	NS
Tertiary	126 (3.6)	67 (3.2)	193 (3.4)	NS
Place birth (n)	3518	2131	5649	
Umlalazi Municipality	2873 (81.7)	1780 (83.5)	4653 (82.4)	NS
Other municipality within KZN	574 (16.3)	308 (14.5)	882 (15.6)	NS
Province other than KZN	63 (1.8)	25 (1.2)	88 (1.6)	NS
Country other than South Africa	8 (0.2)	18 (0.8)	26 (0.5)	<0.001

Place residence (n)	3518	2131	5649	
Urban	246 (7.0)	143 (6.7)	389 (6.9)	NS
Semi urban	253 (7.2)	186 (8.7)	439 (7.8)	0.04
Rural	2969 (84.4)	1742 (81.8)	4711 (83.4)	0.01
Farm	50 (1.4)	60 (2.8)	110 (2.0)	<0.001
Occupation (n)	3518	2131	5649	
Farmer, Forestry	176 (5.0)	141 (6.6)	317 (5.6)	0.01
Soldier, Policeman	1 (0.0)	12 (0.6)	13 (0.2)	<0.001
Sales, Service worker	78 (2.2)	77 (3.6)	155 (2.7)	0.002
Factory worker	11 (0.3)	31 (1.5)	42 (0.7)	<0.001
Clerical	16 (0.5)	2 (0.1)	18 (0.3)	0.02
Professional/Manager	105 (3.0)	42 (2.0)	147 (2.6)	0.02
Student	876 (24.9)	756 (35.5)	1632 (28.9)	<0.001
Housewife/husband	439 (12.5)	26 (1.2)	465 (8.2)	<0.001
Construction	71 (2.0)	245 (11.5)	316 (5.6)	<0.001
Cleaning/Maid	213 (6.1)	17 (0.8)	230 (4.1)	<0.001
None	1418 (40.3)	631 (29.6)	2049 (36.3)	<0.001
Other	114 (3.2)	151 (7.1)	265 (4.7)	<0.001

NS: non-significant

Table 5: Participants' mobility characteristics

	Women	**Men**	**Total**	**Women vs men**
	n (%)	n (%)	n (%)	p
Moved residence in 10 year (n)	3518	2131	5649	
Yes	457 (13.0)	304 (14.3)	761 (13.5)	NS
No	3061 (87.0)	1827 (85.7)	4888 (86.5)	NS
Place of residence before (n)	456	303	759	
Umlalazi Municipality	193 (42.3)	103 (34.0)	296 (39.0)	0.02
Other municipality within KZN	234 (51.3)	171 (56.4)	405 (53.4)	NS
Province other than KZN	23 (5.0)	19 (6.3)	42 (5.5)	NS
Country other than South Africa	6 (1.3)	10 (3.3)	16 (2.1)	NS
Reasons for moving (n)	456	302	758	
Family/Friends	289 (63.4)	157 (52.0)	446 (58.8)	0.002
Work related	114 (25.0)	113 (37.4)	227 (30.0)	<0.001
Studies related	43 (9.4)	29 (9.6)	72 (9.5)	NS
Other	10 (2.2)	3 (1.0)	13 (1.7)	NS

NS: non-significant

Table 6: Residence and frequency of visits of the participants who were visitors

	Women	Men	Total	Women vs men
	n (%)	n (%)	n (%)	p
Place of residence (n)	137	109	246	
Umlalazi Municipality	79 (58.1)	63 (57.8)	142 (58.0)	NS
Other municipality within KZN	52 (38.2)	40 (36.7)	92 (37.6)	NS
Province other than KZN	4 (2.9)	3 (2.8)	7 (2.9)	NS
Country other than South Africa	1 (0.7)	3 (2.8)	4 (1.6)	NS
Frequency of visits (n)	136	106	245	
Once a month or more	87 (64.0)	65 (60.0)	152 (62.0)	NS
More than 2 times a year	24 (17.7)	23 (21.1)	47 (19.2)	NS
1-2 times a year	18 (13.2)	14 (12.8)	32 (13.1)	NS
Less than once a year	7 (5.2)	7 (6.4)	14 (5.7)	NS

NS: non-significant

3.2.3. Incidence

Incidence was calculated using LAg-Avidity Index (AI) EIA and Biorad HIV-1/HIV-2 PLUS O assays results corrected by viral load at a threshold of 100 copies/ml and antiretroviral treatment drug exposure tested in blood. The estimation was done using the McWalter and Welte formula(34) with an estimated Mean Duration of Recent Infection (MDRI) of 130 days for LAg assay and 220 days for Biorad assay.

Since the FRR of the assay varies for each particular population, sensitivity analyses were performed using a range of FRR values from 0.6% to 1.4%. The overall incidence based on the LAg AI assay ranged from 0.8 (95%CI: 0.0-1.8) to 1.5 (95%CI: 0.7-2.3) new cases per 100 persons-year (PY) depending on the FRR used. The figure 2 shows the variation of the incidence point estimates and the 95% confidence intervals according to the different FRR values. Considering an FRR of 1%, the overall incidence was 1.2 (95%CI: 0.2-2.1) cases/100 PY, higher in women and particularly in the group aged 15 to 29 years (table 7). Based on the 2011 census population for the surveyed area and according to this incidence rate, there would be 549 new HIV infections per year in the overall population and 401 new HIV infections per year in women 15-29 years. The figure 3 shows the variation of the incidence point estimate according to the different FRR values by gender and age group. Incidence varied from 2.5 to 3.1 cases/100 PY in women 15-29 years, from 0 to 0.3 cases/100 PY in women 30-59 years, from 0.8 to 0.9 cases/100 PY in men 15-29 years, and from 0 to 0.3 cases/100 PY in men 30-59 years.

Using Biorad assay and FRR values from 1.0% to 3.0%, the overall incidence based on the LAg AI assay ranged from 0.7 (95%CI: 0.0-1.8) to 1.7 (95%CI: 1.1-2.4) new cases/100 PY.

In addition, 2 (0.5%) acute infections were detected through NAAT out of the 4214 who tested negative on the rapid test. The incidence estimated using NAAT was 1.2 (0.0-2.9) new cases per 100 person-year.

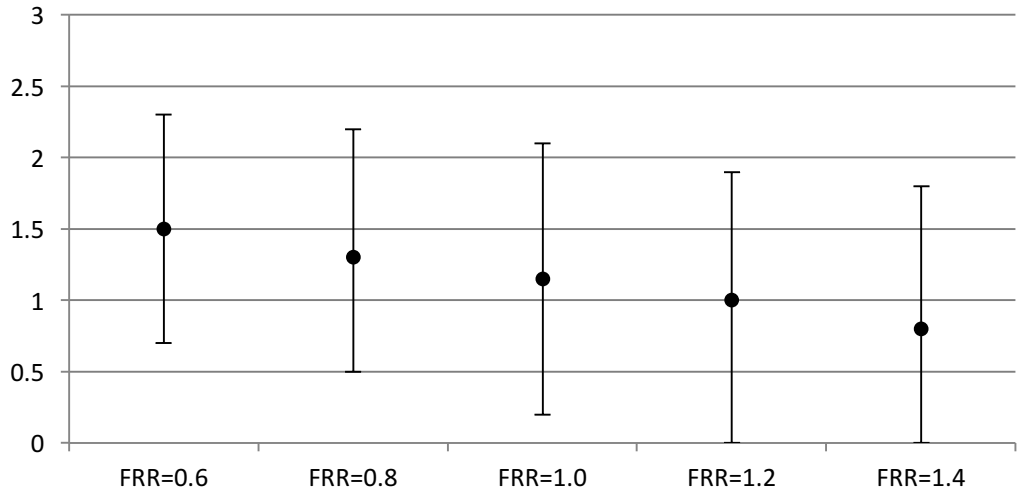

Figure 2: Incidence point estimates and 95%ci using Lag AI assay according to different test false recent rates

Table 7: Incidence estimation per gender and age group using Lag AI assay

	Women		Men		Total	
	/100 PY	(95%CI)	/100 PY	(95%CI)	/100 PY	(95%CI)
15-29 years	2.9	1.2-4.7	0.9	0.0-1.9	2.0	0.9-3.0
30-59 years	0.0	0.0-1.3	0.0	0.0-1.6	0.0	0.0-1.1
Overall	**1.6**	**0.2-3.0**	**0.6**	**0.0-1.5**	**1.2**	**0.2-2.1**

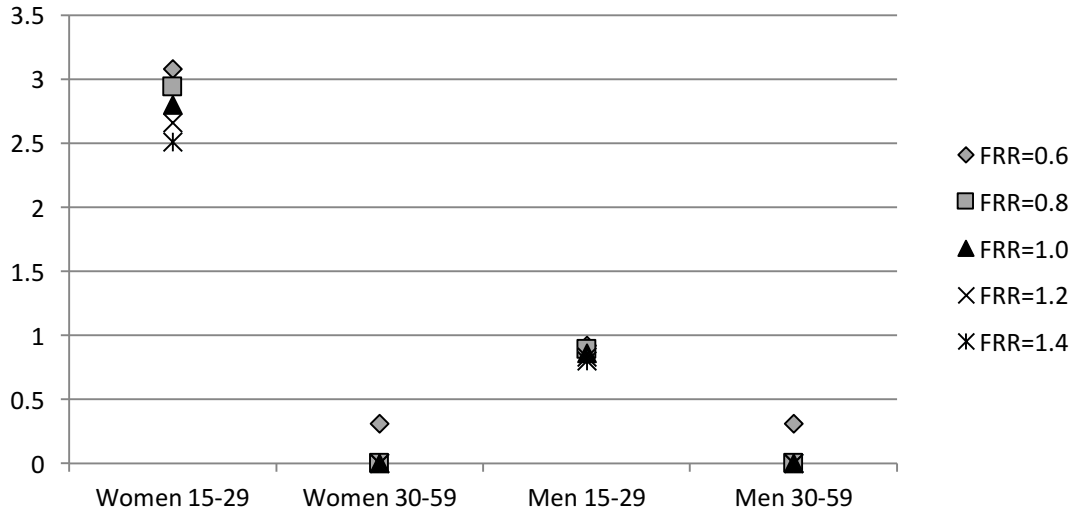

Figure 3: Incidence point estimates per gender and age group using LAg assay according to different test false recent rates

3.2.4. Prevalence

Ninety percent of the HIV tests were done on site. The others were done anonymously at the laboratory. In total, 1423 participants were HIV positive, 4223 HIV negative and 3 indeterminate. The overall prevalence was 25.2% (95%CI: 23.6-26.9). Prevalence in women was higher than in men: 30.9% (95%CI: 29.0-32.9) vs 15.9% (95%CI: 14.0-18.0). The highest prevalence was found in women aged 30-39 years: 56.0% (95%CI: 51.7-60.3). Figure 4 shows the HIV prevalence by gender and age group.

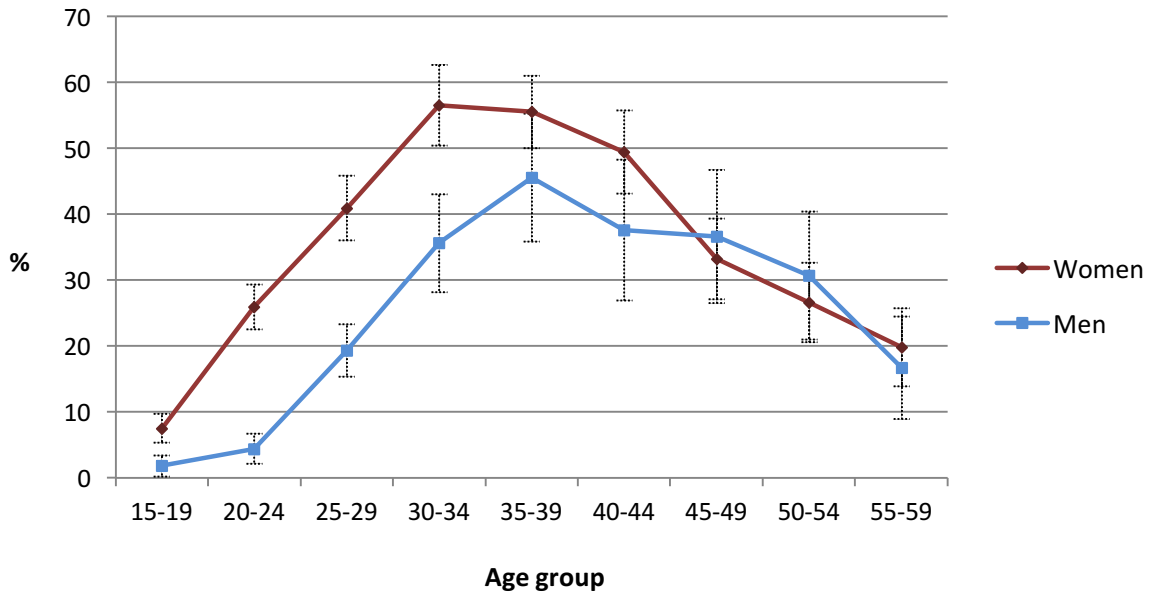

Figure 4: HIV prevalence by gender and age group

In a multivariate analysis, being older than 19 years, female, not being married, lower education level, being mobile and having more than one sexual partner were associated with an increased risk of being HIV infected. The area of residence (urban, rural, farm) was not associated with an increased risk of positivity. Not using a condom was associated with a lower likelihood of being HIV infected (table 8).

The factors associated with being HIV infected were similar in women and men (table 9). The main differences were the stronger association between HIV positive status and older ages in men due to the low prevalence in the group 15-19 years, the lack of association for men never married, and the stronger association between HIV positive status and having more than one sexual partner in women. Being circumcised was a protective factor in men. Among women with a sexual partner, the proportion of those with more than one sexual partner was small: 5.1% (103/2137). However, HIV prevalence was much higher in this group compared to women with only one partner: 61.5% (67/109) vs 34.0% (69/2028). The proportion of recent infections in this group was also higher than in women with only one partner: 6.0% (4/67) vs 2.5% (17/674). Median age was 26 years (IQR: 21-31) in women with more than one partner and 29 years (IQR: 23-40) in women with only one partner.

Table 8: Factors associated with HIV positive status

	Crude			Adjusted		
	OR	95%CI	p	OR	95%CI	p
Age group						
15-19	1			1		
20-24	4.3	3.2-5.9	0.001	3.6	2.6-5.0	<0.001
25-29	11.8	8.6-16.1		10.7	7.7-14.8	
30-34	25.0	17.8-35.1		26.0	18.1-37.4	
35-39	29.3	20.6-41.7		32.9	22.6-48.1	
40-44	21.6	15.1-30.9		25.1	17.1-36.9	
45-49	12.4	8.7-17.9		16.3	11.0-24.3	
50-54	8.7	6.1-12.5		12.1	8.1-18.0	
55-59	5.2	3.5-7.7		7.9	5.1-12.2	
Gender						
Male	1			1		
Female	2.7	2.3-3.1	<0.001	3.3	2.8-4.0	<0.001
Marital status						
Married/Living together	1			1		
Never married	0.7	0.6-0.9	<0.001	1.7	1.4-2.2	<0.001
Divorced/Separated/ Widowed	1.9	1.4-2.7		2.1	1.4-3.0	
Education						

Tertiary	1			1		
Primary/Secondary	1.5	1.0-2.2	0.01	2.7	1.7-4.2	<0.001
No schooling	2.0	1.2-3.1		2.5	1.5-4.2	
Area of residence						
Rural	1			1		
Urban/Farms	1.4	1.1-1.6	0.01	1.1	0.9-1.5	0.42
Mobility						
Not moved/Not visitor	1			1		
Moved/Visitor	1.3	1.1-1.6	0.003	1.3	1.1-1.6	0.01
Number of partners						
1	1			1		
>1	0.9	0.7-1.2	<0.001	1.7	1.3-2.3	<0.001
0	0.5	0.4-0.6		0.5	0.0-8.8	
Use of condom						
Yes	1			1		
No	0.4	0.3-0.4	<0.001	0.3	0.2-0.3	<0.001
Missing	0.3	0.3-0.4		0.9	0.0-15.3	

Table 9: Factors associated with HIV positive status by gender (adjusted)

	Women			Men		
	OR	95%CI	P	OR	95%CI	P
Age group						
15-19	1			1		
20-24	4.5	3.2-6.5	<0.001	1.7	0.8-3.6	<0.001
25-29	10.7	7.4-15.5		10.1	5.1-19.8	
30-34	23.6	15.4-36.2		28.2	14.2-55.8	
35-39	26.4	17.0-40.7		42.3	20.8-86.0	
40-44	19.9	12.8-30.9		33.5	16.0-70.0	
45-49	11.4	7.3-17.7		38.6	17.6-84.6	
50-54	8.3	5.3-12.9		28.8	13.1-63.4	
55-59	5.7	3.5-9.2		15.0	6.2-36.1	
Marital status						
Married/Living together	1			1		
Never married	1.8	1.4-2.2	<0.001	1.1	0.8-1.7	0.34
Divorced/Separated/ Widowed	1.9	1.3-2.9		1.7	0.8-3.5	
Education						
Tertiary	1			1		
Primary/Secondary	2.8	1.7-4.5	<0.001	2.2	0.9-5.2	0.14
No schooling	2.6	1.5-4.6		2.4	0.9-6.4	
Area of residence						

Rural	1			1		
Urban/Farms	1.1	0.8-1.4	0.60	1.1	0.7-1.7	0.59
Mobility						
Not moved/Not visitor	1			1		
Moved/Visitor	1.3	1.0-1.7	0.02	1.3	0.9-1.9	0.13
Circumcised						
No	-	-	-	1		<0.001
Yes	-	-		0.5	0.3-0.8	
Number of partners						
1	1			1		
>1	4.9	3.0-8.0	<0.001	1.4	1.0-2.0	0.03
0	0.6	0.0-9.3		0.4	0.2-0.5	
Use of condom						
Yes	1			1		
No	0.2	0.2-0.3	<0.001	0.3	0.2-0.4	<0.001

3.2.5. HIV testing coverage and HIV status awareness

3.2.5.1. HIV testing prior to survey

In total 4598 (81.4%, 95%CI: 79.8-82.9) participants declared to ever having had an HIV test prior to the survey. A higher proportion of women declared having had an HIV test compared to men: 88.4% (95%CI: 86.8-89.9) vs 69.8 (95%CI: 67.2-72.4). Participants were tested a median of 3 times (IQR: 2-4). Almost half of them had their last test done in the previous 6 months (table 10). A majority of them were tested in the public sector (figure 5). Considering only participants who had their last test in the previous 12 months, a quarter were tested by MSF. A majority of the participants that had been tested by MSF in the years 2012-2013 were HIV negative (91.7%). The proportion of men tested by MSF was higher than in the public sector: 37.3% (95%CI: 34.1-40.6) vs 30.8% (29.3-32.3), and the median age was lower: 23 (IQR: 18-36) vs 28 (IQR: 21-40). Among participants HIV negative, 3254 (77.1%) declared to ever having had an HIV test prior to the survey. Participants HIV negative had been tested a median of 3 [2-4] times.

Table 10: Delay since last HIV test for participants tested prior to the survey

	Women		Men		Total	
	n	%	n	%	n	%
≤6 months	1515	48.7	701	47.1	2216	48.2
>6 -12 months	444	14.3	233	15.7	677	14.7
>12 -24 months	453	14.6	293	19.7	746	16.2
>24 months	635	20.4	241	16.2	876	19.1
Don't know	471	2.0	20	1.3	83	1.8

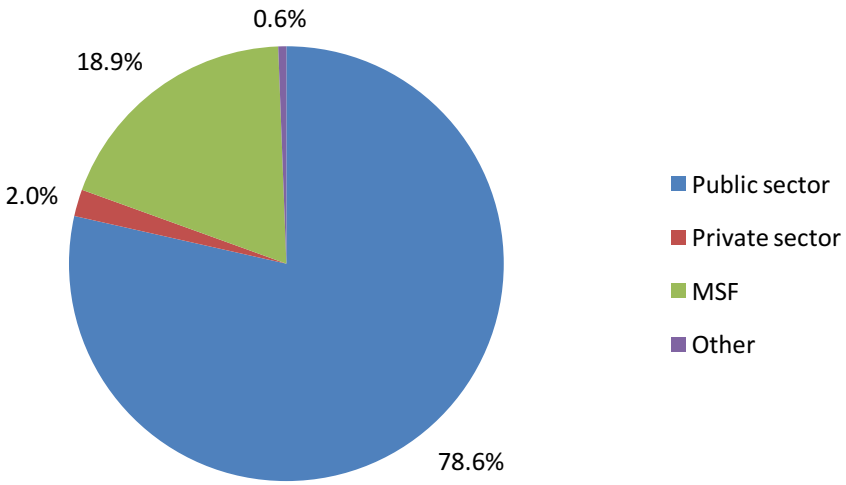

Figure 5: Place of HIV testing prior to the survey

Participants who declared not having done an HIV test prior to the survey were mainly men (63.6%), young (median age: 22 years, IQR: 17-34), never married (83.0%), and students (43.6%). They lived mainly in rural areas: rural (748, 85.3%), urban (63, 7.2%), semiurban (50, 5.7%), farm (16, 1.8%). Of the total 877 participants not tested, 334 (37.7%) were men less than 30 years all single and living in rural areas. The proportion of HIV infected among non-tested was 7.8% (69/877). The distribution of the households in the administrative ward subdivisions was relatively homogeneous. However, there were more participants who had not done an HIV test prior to the survey living in the wards 5, 7, 9, 10, 13, and 14, (which accounted for 8% to 13% in each), than in the wards 11 and 12 (which accounted only for 3-4% in each). In a multivariate analysis, factors associated to not being tested were young age, being a man, and having more than one partner or no partner in the previous 12 months (table 11,13).

Table 11: Factors associated to not being tested

	Crude			Adjusted		
	OR	95%CI	p	OR	95%CI	p
Age group						
15-19	1			1		
20-24	0.5	0.4-0.6	0.001	0.8	0.6-1.0	<0.001
25-29	0.4	0.3-0.5		0.7	0.5-1.0	
30-34	0.3	0.2-0.4		0.5	0.3-0.7	
35-39	0.2	0.2-0.3		0.4	0.3-0.6	
40-44	0.2	0.1-0.3		0.4	0.2-0.6	
45-49	0.4	0.3-0.5		0.7	0.4-1.1	
50-54	0.5	0.4-0.7		0.8	0.6-1.2	
55-59	0.6	0.4-0.8		0.9	0.6-1.4	
Gender						
Female	1			1		
Male	4.2	3.5-5.0	<0.001	4.4	3.6-5.3	<0.001
Marital status						
Married/Living together	1			1		
Never married	1.8	1.5-2.3	<0.001	1.0	0.7-1.3	0.22
Divorced/Separated/ Widowed	1.0	0.6-1.6		0.6	0.4-1.1	
Education						
Tertiary	1			1		
Primary/Secondary	1.6	1.0-2.6	0.16	1.1	0.7-1.9	0.37
No schooling	1.6	0.9-2.8		1.4	0.8-2.7	
Area of residence						
Rural	1			1		
Urban/Farms	0.8	0.6-1.1	0.13	0.9	0.7-1.2	0.47
Mobility						
Not moved/Not visitor	1			1		
Moved/Visitor	0.9	0.7-1.1	0.39	1.0	0.8-1.3	0.84
Number of partners						
1	1			1		
>1	2.4	1.9-3.1	<0.001	1.3	1.0-1.7	<0.001
0	3.0	2.5-3.5		2.5	2.1-3.1	

3.2.5.2. HIV positive status awareness

In total 1065 participants HIV positive were aware of their status before the survey, 351 were not aware and for 7 the information was not available. The overall HIV awareness ratio was 75.2% (95%CI: 72.9-77.4). Figure 6 shows HIV status awareness by gender and age group. The age groups less aware of their status were females 15-24 (40.4% not

aware) and males 15-34 (48.3% not aware) and 55-59 years (50.0% not aware). In a multivariate analysis, factors associated to not being aware of HIV infection were young age, being a man, being single, and having more than one partner in the previous 12 months (table 12, 13).

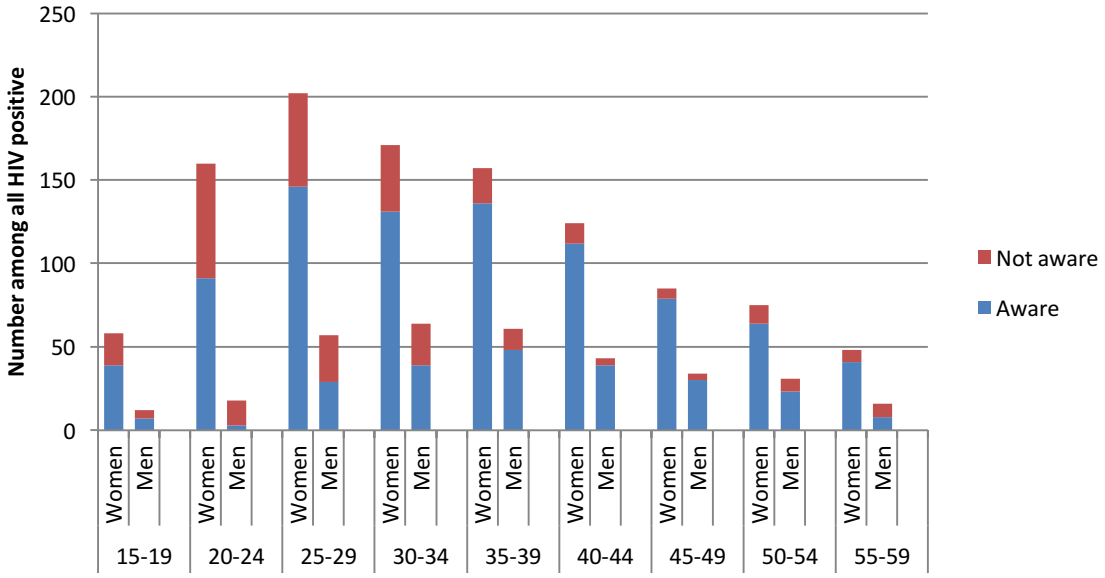

Figure 6: HIV status awareness by gender and age group

Table 12: Factors associated to not being aware of HIV infection

	Crude			Adjusted		
	OR	95%CI	p	OR	95%CI	p
Age group						
15-19	1			1		
20-24	1.7	1.0-3.0	<0.001	1.8	1.0-3.3	<0.001
25-29	0.9	0.5-1.6		0.9	0.5-1.6	
30-34	0.7	0.4-1.3		0.7	0.4-1.2	
35-39	0.4	0.2-0.7		0.3	0.2-0.7	
40-44	0.2	0.1-0.4		0.2	0.1-0.4	
45-49	0.2	0.1-0.4		0.2	0.1-0.4	
50-54	0.4	0.2-0.8		0.4	0.2-0.9	
55-59	0.6	0.3-1.3		0.7	0.3-1.7	
Gender						
Female	1			1		
Male	1.8	1.3-2.4	<0.001	1.8	1.3-2.6	<0.001
Marital status						
Married/Living together	1			1		
Never married	2.3	1.6-3.2	<0.001	1.6	1.1-2.4	0.05
Divorced/Separated/	1.3	0.7-2.4		1.3	0.7-2.6	

	Crude			Adjusted		
	OR	95%CI	p	OR	95%CI	p
Widowed						
Education						
Tertiary	1			1		
Primary/Secondary	0.7	0.3-1.4	0.20	0.5	0.2-1.2	0.20
No schooling	0.5	0.2-1.1		0.7	0.3-1.9	
Area of residence						
Rural	1			1		
Urban/Farms	1.1	0.8-1.5	0.56	1.0	0.7-1.4	0.92
Mobility						
Not moved/Not visitor	1			1		
Moved/Visitor	1.3	1.0-1.8	0.06	1.2	0.8-1.6	0.35
Number of partners						
1	1			1		
>1	2.8	1.9-4.1	<0.001	2.2	1.4-3.4	<0.001
0	0.8	0.6-1.0		1.0	0.7-1.4	

Table 13: Summary of factors associated with not being tested for HIV and not being aware of HIV positive

	Untested for HIV			Unaware of HIV positive status		
	Adjusted OR	95%CI	p	Adjusted OR	95%CI	p
Age group						
35-44	1			1		
15-24	2.3	1.7-3.2	<0.001	5.7	3.5-9.2	<0.001
25-34	1.7	1.2-2.4		2.8	1.9-4.2	
45-59	2.1	1.4-3.0		1.3	0.8-2.1	
Gender						
Female	1			1		
Male	4.4	3.7-5.3	<0.001	1.8	1.3-2.6	<0.001
Marital status						
Married/Living together	1			1		
Never married	1.0	0.7-1.3	0.19	1.6	1.1-2.3	0.07
Divorced/Separated/Widowed	0.6	0.4-1.1		1.3	0.6-2.5	
Number of sexual partners						
1	1			1		
>1	1.3	1.0-1.7	<0.001	2.2	1.4-3.3	<0.001
0	2.7	2.2-3.3		1.0	0.7-1.4	

Model includes: level of education (no schooling, primary/secondary, tertiary), area of residence (rural, urban/farms), and mobility (non-migrant, migrant/visitor)

3.2.5.3. Year and place of HIV testing for individuals aware of their positive status

Last HIV test in individuals aware of their positive status was done a median of 39.6 months (95%CI: 15.5-74.0) – 3.3 years prior to the survey. Participants declared having been tested from the year 1990 to the year of the survey (Figure 7). A majority had been tested in the public sector. A small proportion (3.3%) had been tested by MSF.

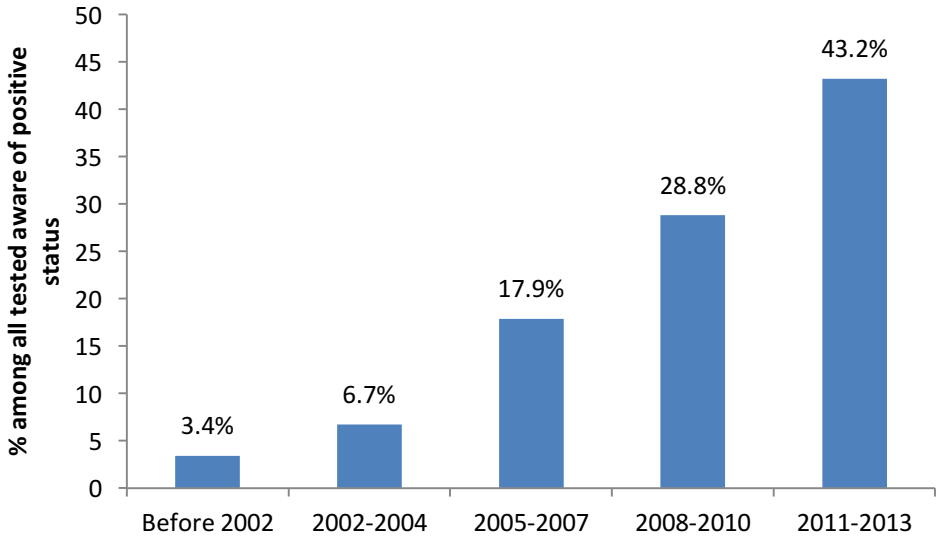

Figure 7: Year of HIV test for individuals aware of their positive status

3.2.6. ART initiation & ART coverage

3.2.6.1. ART initiation

In total 812 had ever initiated ART and 741 (91.3%) were still on ART at the time of the survey as determined by drug levels in blood. Among all HIV infected individuals, 52.1% were on ART. Among those aware of their status this proportion was 69.6%.

The median time since ART initiation for the participants on ART was 31.0 (IQR: 12.4-61.0) months. Participants had initiated ART from the year 1992 to the year of the survey. More than half of them had initiated ART from 2010 to 2013 (Figure 5). Almost sixty percent of the HIV patients in care were followed up in Eshowe Gateway Clinic, Mbongolwane Hospital and Eshowe Hospital (Table 14).

In a multivariate analysis ART initiation increased with age and women were more likely to be initiated on ART while those never married or with more than one sexual partner in the previous 12 months were less likely initiated on ART (table 15).

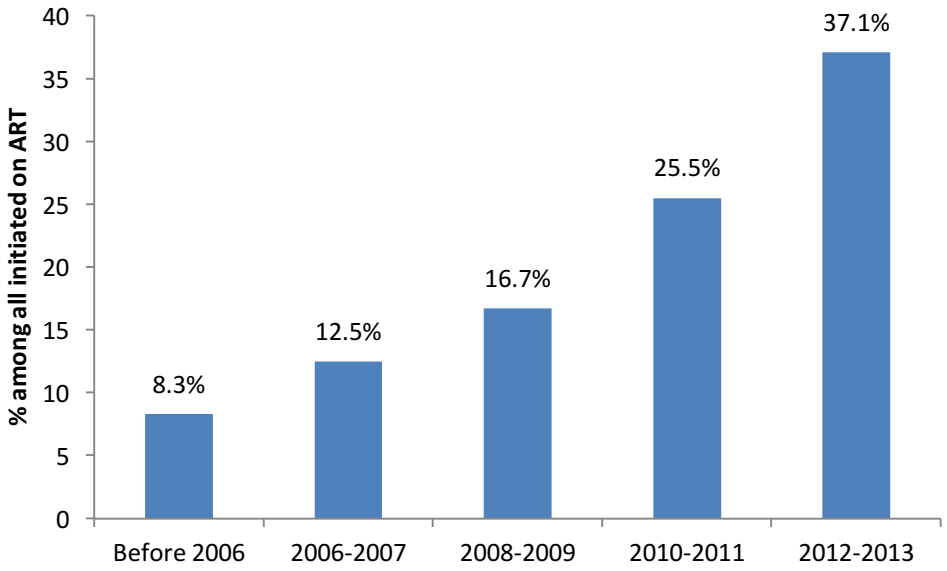

Figure 8: Year of ART initiation for the participants initiated on ART

Table 14: HIV facilities where individuals on care are followed up

	ART initiated		ART not initiated		Total	
	n	%	n	%	n	%
Eshowe Gateway Clinic	130	21.9	28	25.2	158	22.4
Eshowe Hospital	113	19.1	10	9.0	123	17.5
Mbongolwane Hospital	87	14.7	9	8.1	96	13.6
King Dinizulu Clinic	74	12.5	14	12.6	88	12.5
Ntumeni Clinic	52	8.8	12	10.8	64	9.1
Siphilile Clinic	39	6.6	17	15.3	56	8.0
Samungu Clinic	25	4.2	7	6.3	32	4.5
Osungulweni Clinic	18	3.0	4	3.6	22	3.1
Ngudwini Clinic	17	2.9	2	1.8	19	2.7
Mathungela Clinic	5	0.8	0	0	5	0.7
Other	32	5.4	8	7.2	40	5.7
Don't know	1	0.2	0	0	1	0.1
Total	**593**	**-**	**111**	**-**	**704**	**-**

Table 15: Factors associated to ART initiation

	Crude			Adjusted		
	OR	95%CI	p	OR	95%CI	p
Age group						
15-19	1			1		
20-24	0.5	0.2-0.9	<0.001	0.5	0.3-1.1	<0.001
25-29	1.0	0.5-1.9		1.2	0.6-2.3	
30-34	1.4	0.7-2.5		1.6	0.9-3.1	
35-39	3.6	1.9-7.1		3.9	1.9-7.8	
40-44	4.6	2.3-9.2		4.7	2.2-9.8	
45-49	4.8	2.2-10.1		4.5	2.0-10.1	
50-54	2.5	1.2-5.3		2.1	1.0-4.7	
55-59	2.4	1.1-5.3		1.7	0.7-4.1	
Gender						
Male	1			1		
Female	1.4	1.1-1.9	0.01	1.4	1.0-2.0	0.03
Marital status						
Married/Living together	1			1		
Never married	0.4	0.3-0.6	<0.001	0.6	0.4-0.8	0.003
Divorced/Separated/ Widowed	0.9	0.5-1.5		0.8	0.4-1.5	
Education						
Tertiary	1			1		
Primary/Secondary	1.7	0.8-3.6	0.22	2.3	1.0-5.2	0.02
No schooling	2.1	0.9-4.8		1.3	0.5-3.3	
Area of residence						
Rural	1			1		
Urban/Farms	0.8	0.6-1.1	0.17	0.9	0.6-1.3	0.56
Mobility						
Not moved/Not visitor	1			1		
Moved/Visitor	0.8	0.6-1.0	0.07	0.9	0.6-1.2	0.44
Number of partners						
1	1			1		
>1	0.4	0.3-0.6	<0.001	0.5	0.3-0.8	<0.001
0	2.1	1.6-2.9		1.9	1.3-2.7	

3.2.6.2. ART coverage

ART coverage according to the National Guidelines at the time of the survey was 75.0% (95%CI: 72.0-77.8). ART coverage was higher in women than in men: 78.5% (95%CI: 75.8-81.0) vs 63.9% (95%CI: 56.7-70.5), p<0.001. See table 16. Coverage increased with age: 60.5% in younger than 30 years vs 81.3% in older (p<0.001). See figure 9.

Of the 247 participants eligible according to the National Guidelines but not on ART, 161 (65.2%) were women and 189 (76.5%) had less than 40 years. The median age was 30 years (IQR: 24-38). If guidelines were changed to CD4<500 and PMTCT B+, there would be 164 additional participants eligible for ART not on treatment. Age and sex distributions were similar for them: 122 (74.4%) women and 130 (79.3%) less than 40 years. The median age was 30 years (IQR: 25-37). See figure 10.

Table 16: ART coverage according to the different ART initiation strategies by gender

		CD4<350 & PMTCT A	CD4<350 & PMTCT B	CD4<500 & PMTCT B+
Women	Eligible	735	750	872
	On ART	589	589	589
	ART coverage	**80.1**	**78.5**	**67.5**
Men	Eligible	238	238	280
	On ART	152	152	152
	ART coverage	**63.9**	**63.9**	**54.3**
Total	Eligible	973	988	1152
	On ART	741	741	741
	ART coverage	**76.2**	**75.0**	**64.3**

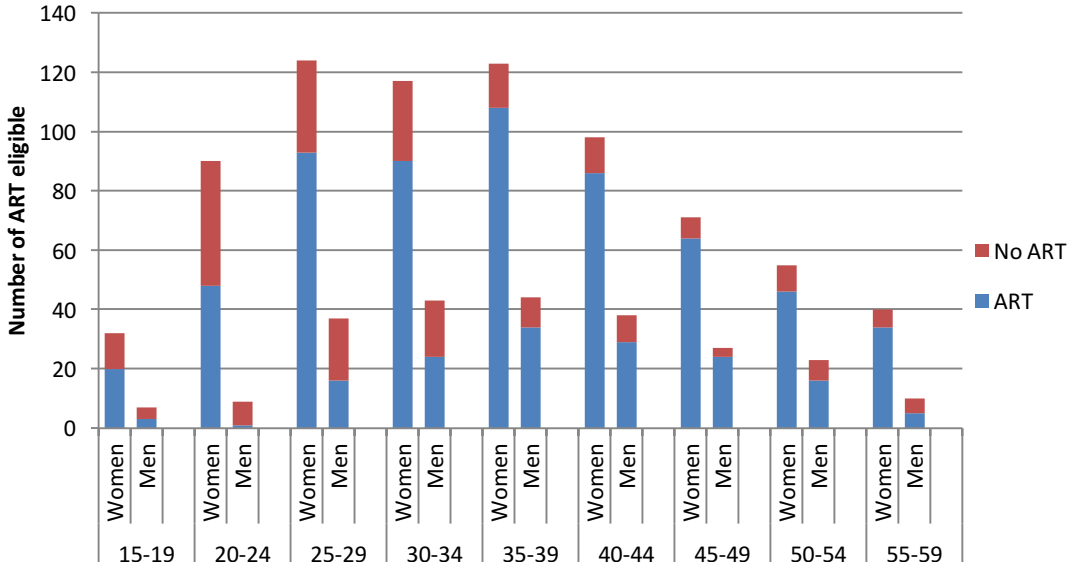

Figure 9: ART coverage according to national guidelines (CD4<350 & PMTCT B) at the time of the survey by gender and age group

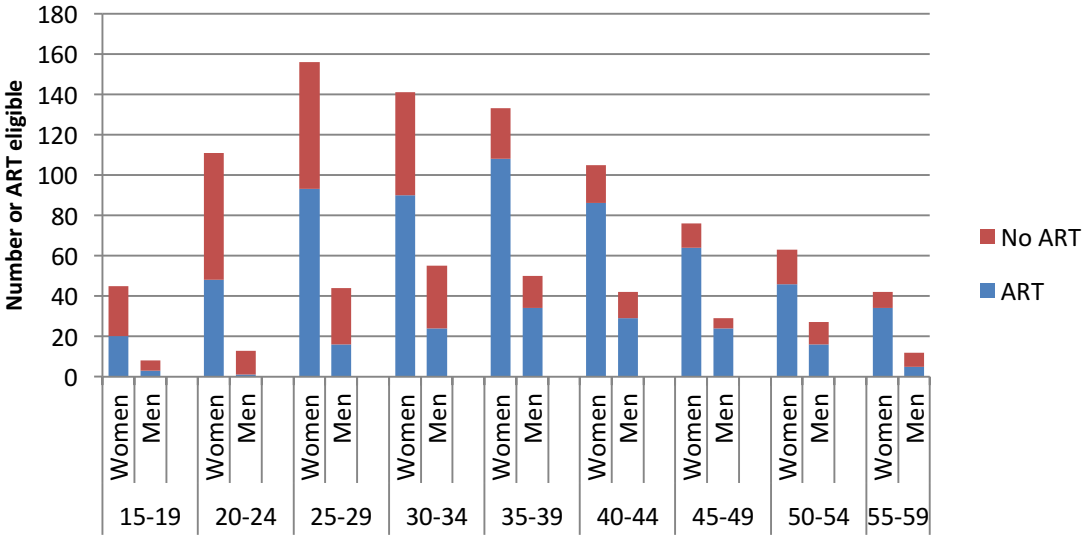

Figure 10: ART coverage according to 2013 WHO recommendations (CD4<500 & PMTCT B+) by gender and age group

3.2.6.3. Comparison of self-reported ART and tested ART

Self-reported vs blood-tested ART intake agreement was 91.9% (kappa=0.84). In total, 58/741 (7.8%) participants with a positive blood test declared not taking ART and 52/712 (7.3%) self-reporting ART intake had a negative blood test (table 17). ART intake agreement was similar in women and men: 91.9% (kappa=0.84) vs 92.0% (kappa=0.84) and lower in those aged <25 years compared to ≥25 years: 88.4% (kappa=0.70) vs 92.6% (kappa=0.85). Among individuals <25 years: 15/64 (23.4%) with positive blood test declared no ART and 12/61 (19.7%) with negative

blood test self-reported ART intake. ART coverage was 75.0% using blood-tested ART and 72.1% using self-reported ART.

Table 17: Self-reported and blood-tested ART intake among HIV positive participants

	ART blood-tested			
ART self-reported	Positive	Negative	Missing	**Total**
Yes	655	52	5	**712**
No	58	593	22	**673**
Missing	28	10	0	**38**
Total	**741**	**655**	**27**	**1,423**

3.2.7. HIV seeking behaviour and people in care

Among 1065 HIV positive who knew their status, 930 (87.3%) sought care, 910 (85.4%) did a CD4, 880 (82.6%) received the CD4 result, 812 (76.2%) had initiated ART and 741 (69.6%) were still on ART at the moment of the interview. Of the 253 participants not initiated on ART, 128 were still in care at the time of the survey. Overall, 869 (81.6%) participants were followed for their HIV infection at the moment of the interview. A large majority of people were receiving care in the public sector (97.3%) and in uMlalazi municipality (90.4%). Another 9.6% were receiving care in other municipalities of KZN. The median delay since the last consultation was 1.1 month (IQR: 0.4-2.7) for participants not on ART and 0.6 months (IQR: 0.1-1.0) for participants on ART. The reasons for stopping HIV follow-up were different for participants initiated on ART and not initiated: the main reason for participants initiated on ART was that they had moved away, whereas those not initiated declared that they did not have a specific reason for stopping (Table 18).

Table 18: Reasons to stop HIV care according to ART initiation

	Not initiated on ART n (%)	**Initiated on ART n (%)**	**Total n (%)**
No specific reason	21 (42.9)	1 (7.1)	22 (34.9)
Moved away	6 (12.2)	3 (21.4)	9 (14.3)
Transport cost / Too far	3 (6.1)	2 (14.3)	5 (7.9)
Stop PMTCT	3 (6.1)	1 (7.1)	4 (6.3)
Thought cured	3 (6.1)	1 (7.1)	4 (6.3)
No one attending	2 (4.1)	0	2 (3.2)
Unfriendly staff	2 (4.1)	1 (7.1)	3 (4.8)
Scared/Denial	1 (2.0)	2 (14.3)	3 (4.8)
Side effects	0	2 (14.3)	2 (3.2)
Busy	2 (4.1)	0	2 (3.2)
Never started treatment	2 (4.1)	0	2 (3.2)
Other	4 (8.2)	1 (7.1)	5 (7.9)

3.2.8. CD4 count and viral suppression

3.2.8.1. CD4 count

Overall 385 (27.5%) of HIV positive participants had a CD4 count below 350 cells/µl and 363 (25.9%) between 350 and 499 cells/µl. The median CD4 count was 483 cells/µl (IQR: 332-665).

Considering the individuals not on ART, 218 (33.1%) had a CD4 count below 350 cells/µl (Table 19) and 176 (26.7%) had a CD4 between 350 and 499. The proportion of men with CD4 below 350 cells/µl was higher than women: 47.2% vs 27.8% ($p<0.001$). In terms of absolute numbers, those not on ART were women and participants aged 20 to 34 years (figures 11, 12) and majority were aged 20 to 34 years were . Changing the eligibility criteria from 350 to 500 would increase the number in need of ART 1.8 fold (from 218 to 394); a test and treat approach would increase this number 3 fold (from 218 to 659).

Table 19: CD4 count among participants HIV positive not on ART by gender

	Women		Men		Total	
	N	%	n	%	n	%
<350	133	27.8	85	47.2	218	33.1
350/499	133	27.8	43	23.9	176	26.7
>=500	213	44.5	52	28.9	265	40.2
Total	479	100	180	100	659	100

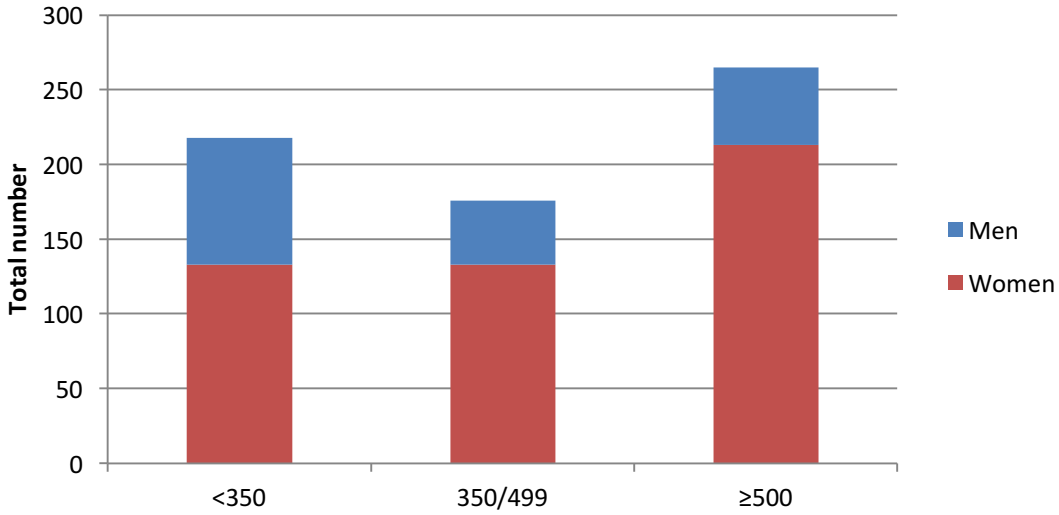

Figure 11: CD4 count distribution in men and women HIV positive not on ART

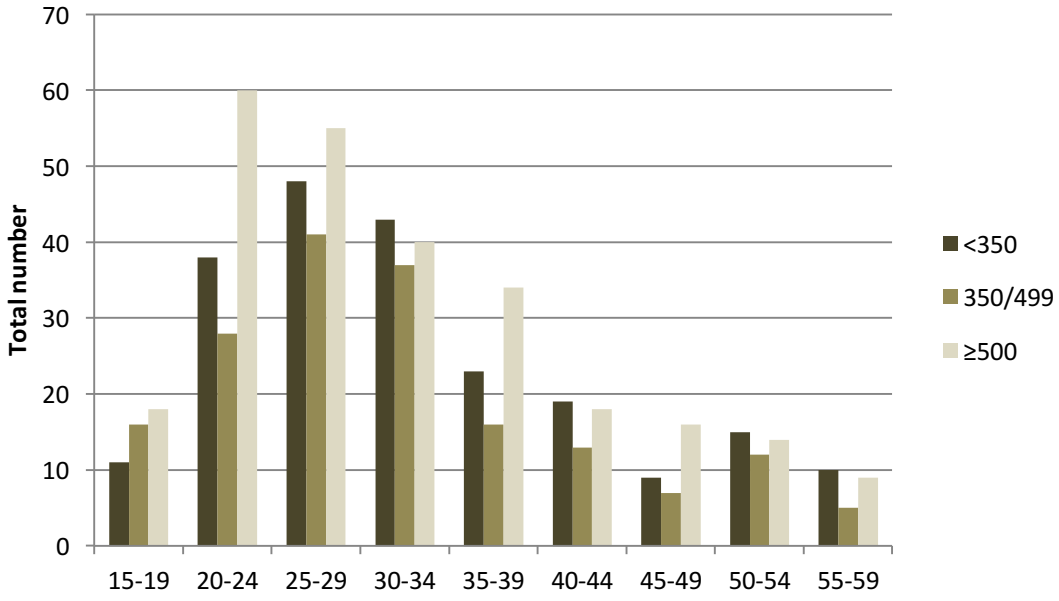

Figure 12: CD4 count distribution in HIV positive not on ART by age group

3.2.8.2. Viral suppression in participants on ART

Viral load suppression (<1000 copies/ml) was achieved in 90.3% of the participants who self-reported being on ART for more than 6 months. Viral load suppression at the threshold of 1000 copies/ml was not different according to gender or mobility (Table 20). The viral load distribution by gender is shown in Table 21.

Of the participants with ARV drugs detected in blood, 93.1% had less than 1000 copies/ml. Viral load distribution in this group was: 636 (86.0%) <100 copies, 53 (7.2%) 100-999 copies, 32 (4.3%) 1000-9999 copies, and 19 (2.6%) >=10000 copies.

Table 20: Virological suppression in participants HIV infected who self-reported being on ART for more than 6 months

	Virologically suppressed (<1000 copies/ml)		
	n/N	%	(95%CI)
Gender			
Women	431/473	91.1	88.3-93.3
Men	118/135	87.4	80.5-92.1
Visitor or moved residence in last 10 years			
Yes	102/110	92.7	86.6-96.2
No	447/498	89.8	86.6-92.3
Duration of ART			
More than 6m to 12 m	75/87	86.2	78.3-91.6
More than 12m to 24 m	99/107	92.5	85.9-96.2
More than 24 m	375/414	90.6	87.2-93.1
Total	549/608	90.3	87.6-92.5

Table 21: Viral load range in participants HIV infected who self-reported being on ART for more than 6 months

	Women		Men		Total	
	n	%	n	%	n	%
<100	408	86.3	107	79.3	515	84.7
100-999	23	4.9	11	8.2	34	5.6
1000-9999	22	4.7	5	3.7	27	4.4
≥10000	20	4.2	12	8.9	32	5.3
Total	473	100	135	100	608	100

3.2.9. Resistance in participants on ART

Resistance to at least one ARV drug was found in 61.2% (30/49) of the individuals who self-reported being on ART for more than 6 months and who were not virologically suppressed (≥1000 copies/ml). Considering only the individuals

not virologically supressed and with ARV drugs detected in blood, 21/29 (72.4%) were resistant. There was no difference in the proportion of resistance according to gender or mobility (Table 22).

The drugs to which resistance was found more often were efavirenz, nevirapine and lamivudine (Table 23). Of the 29 individuals on ART for more than 6 months and not virologically suppressed, 25 (86.2%) were on first line and 4 (13.8%) were on second line ART. Among those on first line, 18 (69.2%) had resistance to NRTI, 15 (57.7%) to RTI and 1 (3.9%) to PI. Among those on second line, 3 (75.0%) had resistance to NRTI, 3 (75.0%) to RTI and none to PI.

Table 22: Resistance to ART in individuals who self-reported being on ART for more than 6 months and who were not virologically supressed

	Any resistance		
	n/N	%	(95%CI)
Gender			
Women	22/36	61.1	43.9-75.9
Men	8/13	61.5	33.8-83.4
Visitor or moved residence in last 10 years			
Yes	4/8	50.0	18.8-81.2
No	26/41	63.4	45.3-78.4
Time of ART			
6-12 months	5/10	50.0	23.7-76.3
12-24 months	5/7	71.4	30.8-93.4
>24 months	20/32	62.5	43.3-78.4
ART line			
First line	18/25	72.0	49.6-87.1
Second line	3/4	75.0	20.4-97.2
Viral load			
<10,000 copies	12/22	54.6	33.1-74.4
≥10,000 copies	18/27	66.7	46.3-82.3
Total	30/49	61.2	46.7-74.0

Table 23: Resistance profile in HIV infected who self-reported being on art for more than 6 months and who were not virologically supressed

	Any resistance	
	n	%
Any resistance to PI	4	8.2
Any resistance to NRTI	24	49.0
AZT	2	4.1
D4T	7	14.3
TDF	6	12.2
3TC	23	46.9
ABC	22	44.9
DDI	10	20.4
FTC	23	46.9
Any resistance to NNRTI	29	59.2
EFV	29	59.2
NVP	29	59.2
ETR	10	20.4
RPV	10	20.8
Total	**30**	**61.2**

3.2.10. Viral suppression in HIV infected population

Of the total population HIV infected, 796/1423 (57.1%) were virally suppressed at a threshold of 1000 copies/ml. In 690/1423 (49.5%) participants, viral load was below 100 copies/ml. Viral load distribution in the population according to the diagnosis and ART status at the time of the survey is shown in figures 13 and 14. Average and median viral load according to the participants' characteristics is shown in table 24. In absolute number the participants with 1000 copies/ml or more were mainly people both undiagnosed or not on ART, particularly women aged less than 35 years and men less than 40 years (Figure 15). ART intake and being a women were independently associated to virological suppression (table 25).

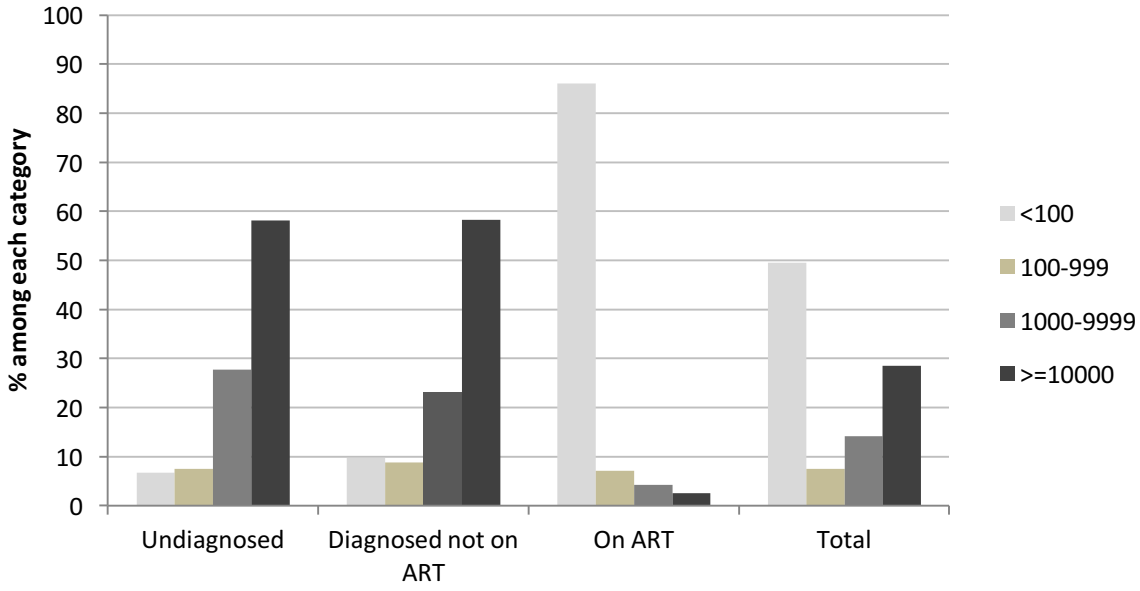

Figure 13: Distribution of viral load according the diagnosis and treatment status – proportions for each category

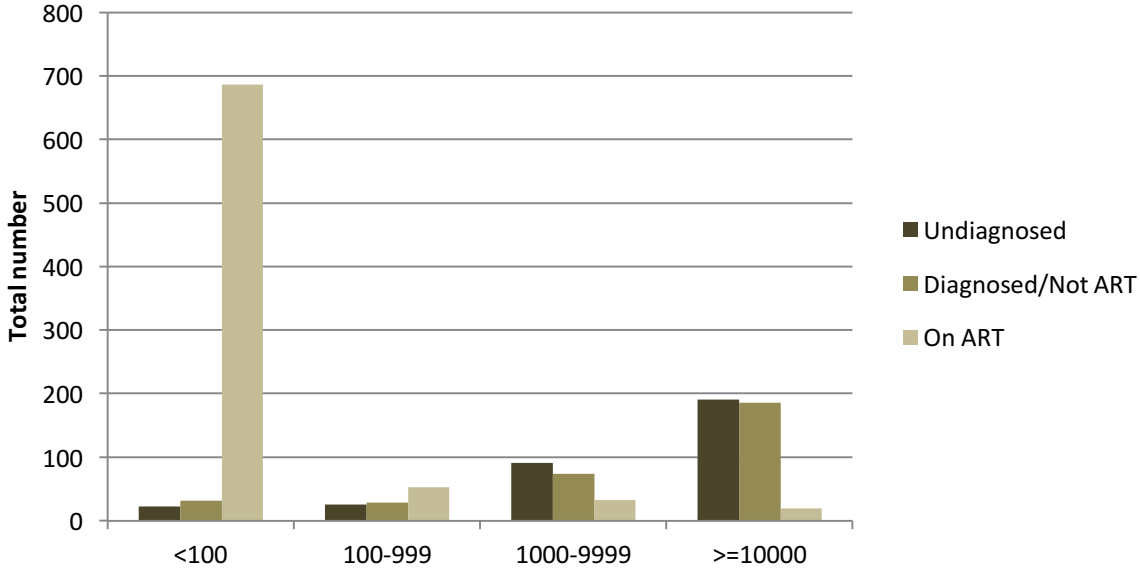

Figure 14: Distribution of viral load according to diagnosis and treatment status – absolute numbers for each category

Table 24: Mean and median viral load according to the participants characteristics

	N	Mean log 10 VL	Median log 10 VL (IQR)	% <1000 copies/ml	% <100 copies/ml
Diagnosis & treatment					
Undiagnosed	329	5.0	4.3 [3.5-4.9]	47 (14.3)	22 (6.7)
Diagnosed not on ART	319	5.3	4.3 [3.3-5.0]	59 (18.5)	31 (9.7)
On ART	740	3.5	0 [0-0]	689 (93.1)	636 (86.0)
Gender					
Women	1064	4.7	1.9 [0-4.0]	638 (60.0)	551 (51.8)
Men	331	5.1	3.2 [0-4.6]	158 (47.7)	139 (42.0)
Age group					
15-19	68	5.1	3.9 [1.7-4.7]	23 (33.8)	19 (27.9)
20-24	174	5.0	3.7 [1.4-4.6]	63 (36.2)	47 (27.0)
25-29	254	5.1	3.3 [0-4.5]	117 (46.1)	100 (39.4)
30-34	233	4.9	2.7 [0-4.3]	129 (55.4)	102 (43.8)
35-39	215	4.5	0 [0-3.5]	141 (65.6)	126 (58.6)
40-44	166	4.8	0 [0-3.5]	120 (72.3)	109 (65.7)
45-49	120	4.5	0 [0-2.7]	93 (77.5)	86 (71.7)
50-54	103	4.6	0 [0-4.4]	66 (64.1)	61 (59.2)
55-59	62	4.3	0 [0-3.7]	44 (71.0)	40 (64.5)
Overall	**1395**	4.9	**2.1 [0-4.2]**	**796 (57.1)**	**690 (49.5)**

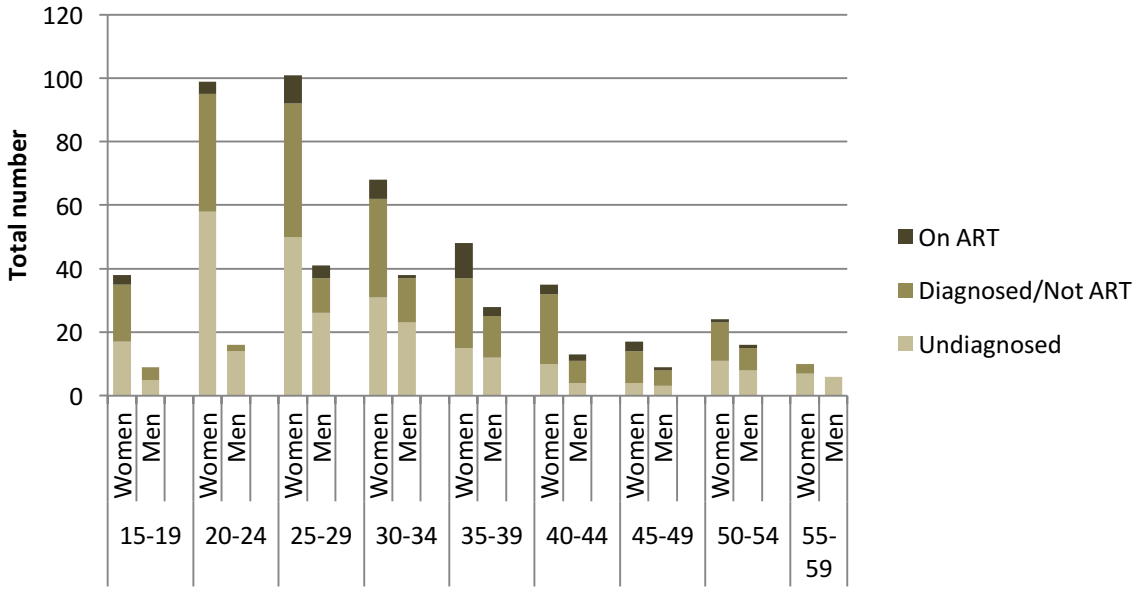

Figure 15: Participants with viral load ≥1000 copies/ml by gender and age group according to their diagnosis and treatment status

Table 25: Factors associated to viral load <1000 copies/ml in HIV infected participants

	Crude			Adjusted		
	OR	95%CI	p	OR	95%CI	p
Age group						
15-19	1			1		
20-24	1.2	0.6-2.2	<0.001	2.0	0.7-5.6	0.1
25-29	1.8	1.0-3.3		1.8	0.7-5.0	
30-34	2.8	1.5-5.3		3.4	1.2-9.5	
35-39	4.3	2.2-8.3		2.0	0.7-5.7	
40-44	6.0	3.0-12.1		3.4	1.1-10.4	
45-49	8.3	3.9-17.7		4.5	1.4-14.9	
50-54	4.2	2.0-8.7		2.9	0.9-9.7	
55-59	5.7	2.4-13.1		4.5	1.1-19.0	
Gender						
Male	1			1		
Female	1.7	1.3-2.3	<0.001	1.7	1.1-2.8	0.03
Marital status						
Married/Living together	1			1		
Never married	0.5	0.4-0.6	<0.001	1.1	0.6-1.8	0.30
Divorced/Separated/ Widowed	1.3	0.7-2.3		2.1	0.8-5.3	
Education						
Tertiary	1			1		
Primary/Secondary	1.7	0.8-3.5	0.03	1.5	0.4-5.0	0.13
No schooling	2.8	1.2-6.4		3.0	0.7-12.5	
Area of residence						
Rural	1			1		
Urban/Farms	0.7	0.5-1.0	0.04	0.8	0.5-1.4	0.47
Mobility						
Not moved/Not visitor	1			1		
Moved/Visitor	0.8	0.6-1.1	0.23	1.0	0.6-1.6	0.88
Number of partners						
1	1			1		
>1	0.4	0.3-0.6	<0.001	0.6	0.3-1.1	0.17
0	1.7	1.3-2.2		0.7	0.4-1.2	
ART intake*						
Yes	1			1		
No	0.01	0.0-0.02	<0.001	0.01	0.0-0.2	<0.001

* Blood-tested ART intake

3.2.11. Cascade of care

Figure 16 shows the different steps of the cascade of care in the HIV infected population. At the time of the survey, of all HIV infected participants, 74.8% were already diagnosed, 61.1% were in care, 52.1% were on ART, and 55.9% were virologically suppressed at a threshold of 1000 copies/ml. In addition, 48.5% had less than 100 viral copies/ml.

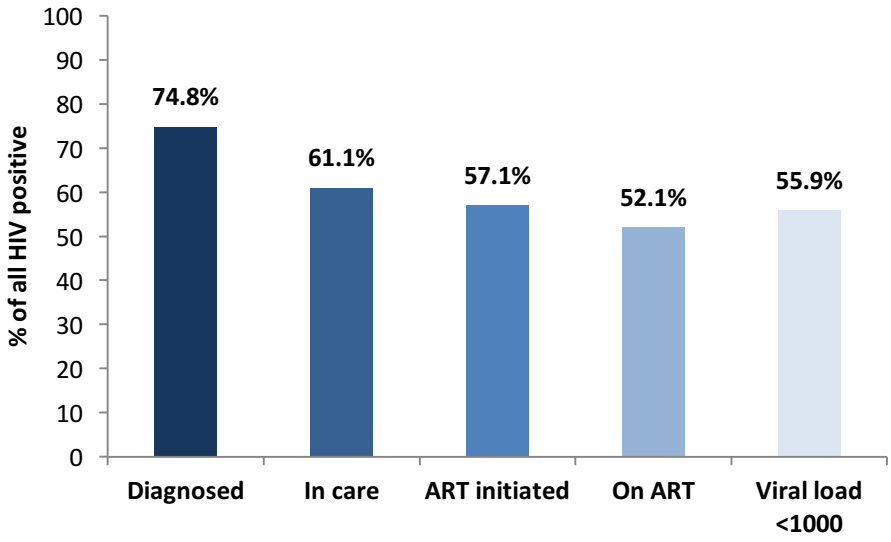

Figure 16: Steps of the cascade of care

3.2.12. Tipping point

The tipping point is the time when the number of ART initiations goes over the number of new infections in an area. We calculated the tipping point ratio in the 6 months previous to the survey in Mbongolwane and Eshowe areas. Considering a population of 61,179 people aged 15-59 living in the area, there would have been 274 new HIV infections in the 6 months previous to the survey; there were 894 new ART initiations. Therefore, the tipping point ratio at the time of the survey would be 3.3. This means that the tipping point was reached in the area. There were 3 persons starting ART per person newly infected.

3.2.13. Reproduction and PMTCT

3.2.13.1. Reproduction

In total, 2548 (72.4%) women had ever given birth. The median number of children per women was 2 (IQR: 1-4). At the time of the survey, 134 (3.8%) of the women were pregnant and 308 (8.8%) were breastfeeding. The proportion of women who had never given birth was higher among those with education compared with those with no education: 29.8% vs 5.0% ($p<0.001$).

HIV positive mothers had a higher proportion of children who had died than HIV negative ones: 11.0% vs 8.6% (p=0.004). This difference persisted when only mothers who had delivered in the 5 years prior to the study were considered: 5.3% vs 2.5% (p=0.01).

3.2.13.2. Antenatal care and PMTCT

In total, of the 1259 women who had delivered in the 5 years prior to the survey (2008-2013), 1214 (96.4%) had had at least one medical antenatal care (ANC) consultation, and 920 (73.1%) had had 3 or more ANC consultations (Table 26). The median number of ANC consultations was 6 (IQR: 5-7). The median month of pregnancy at the first ANC consultation was 4 months (IQR: 3-5).

A large majority of the women (97.8%) had been attended by health personnel at a health facility during their pregnancy and delivery (Figures 17 and 18). A total of 1003 (79.7%) women breastfed their children for a median duration of 9 months (IQR: 5-14).

Out of the 799 women who had delivered in the last 2 years (2011-2013), 745 (93.2%) had had an HIV test as part of their ANC, and 738 (99.1%) had gotten the results of the test.

The proportion of women with at least one ANC or at least 3 ANC consultations was not different among HIV positive and HIV negative: 97.3% vs 97.5% (p=0.90) and 72.9% vs 73.1% (p=0.90). However, the mean number of ANC consultations was higher among HIV positive women compared to negative: 6.4 vs 5.9 (p=0.01) and the mean month of pregnancy at first ANC was lower 3.9 vs 4.1 (p=0.01).

Overall, 3.9% (134/3463) women were pregnant at the time of the survey. The proportion of pregnant women was 3.3% (25/763) among those aged less than 20 years, and 2.2% (10/447) among those aged less than 18 years old.

Table 26: Antenatal care consultations for women who had delivered between 2008 and 2013

	Women who delivered N	At least 1 medical ANC n (%)	3 ANC or more n(%)	Mean number of ANC	Mean month of pregnancy at first ANC
Age					
15-19	136	131 (96.3)	106 (77.9)	5.8	4.3
20-24	408	396 (97.1)	306 (75.0)	5.9	4.2
25-29	341	333 (97.7)	256 (75.1)	6.3	3.9
30-34	172	164 (95.3))	121 (70.3)	6.1	3.9

35-39	122	118 (96.7)	80 (65.6)	5.9	4.0
40-44	56	48 (85.7)	34 (60.7)	6.8	3.8
45-49	20	20 (100)	14 (70.0)	6.2	3.9
50-54	4	4 (100)	3 (75.0)	5	4
55-59	0	0	0	0	0
Education					
No education	28	25 (89.3)	19 (76.0)	5.5	4.1
Primary	398	388 (97.5)	296 (76.3)	6.0	4.2
Secondary	782	753 (96.3)	569 (75.6)	6.1	4.0
Tertiary	51	48 (94.0)	36 (75.0)	6.5	3.5
Total	1259	1214 (96.4)	920 (73.1)	6.1	4.0

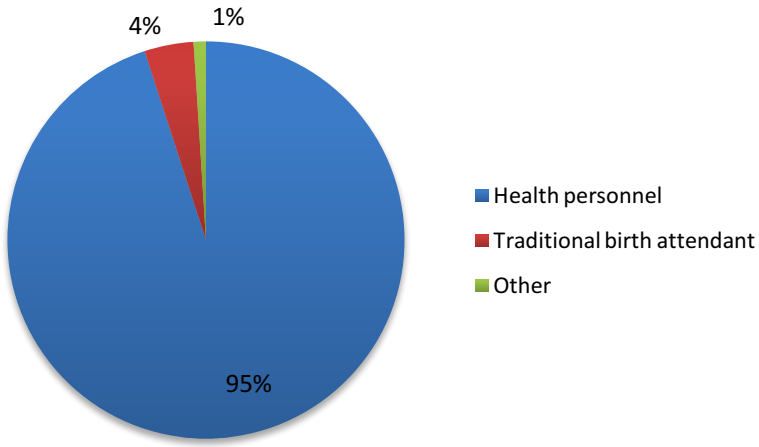

Figure 17: Type of attendant at delivery for women who had delivered between 2008 and 2013

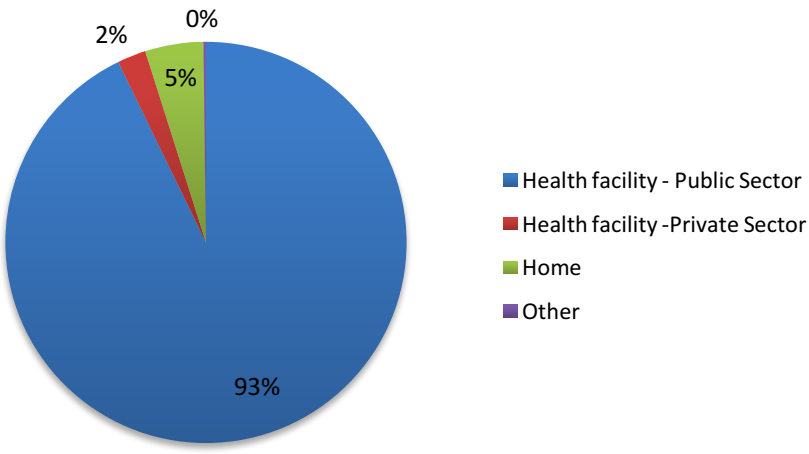

Figure 18: Place of delivery for women who had delivered between 2008 and 2013

3.2.14. Circumcision

Of the 2131 men included in the survey, 461 (21.7%) declared to have been circumcised. The median age of circumcision was 18 years (IQR: 16-22). The proportion of men circumcised by age group is shown in figure 19. A majority of the men had been circumcised in a health facility or in a circumcision camp (Figure 20).

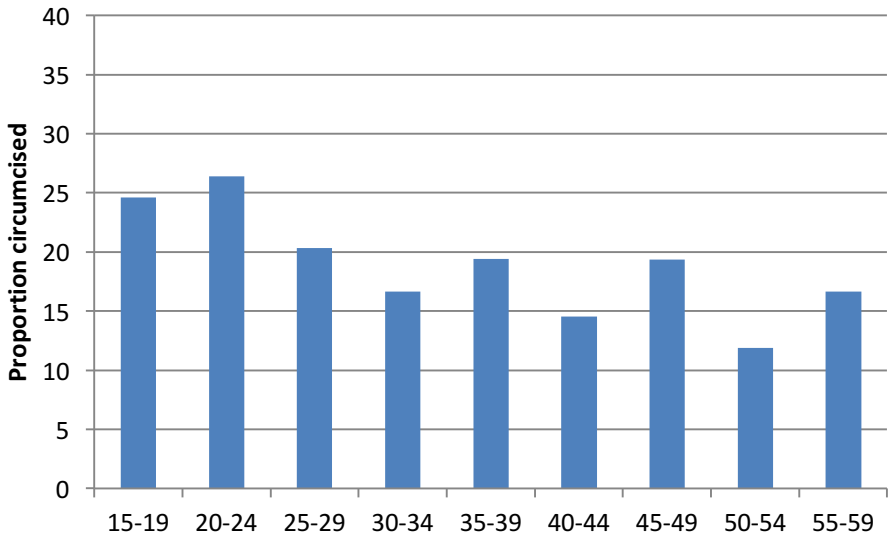

Figure 19: Proportion of men circumcised by age group

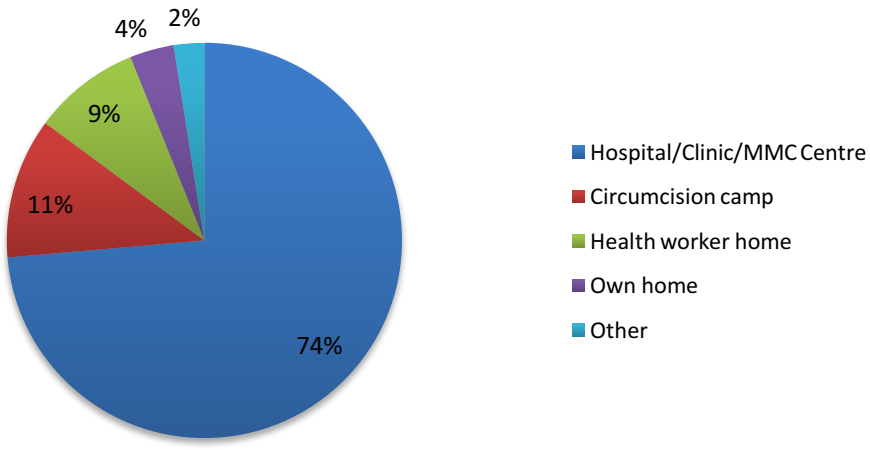

Figure 20: Place of circumcision for the men who declared to have been circumcised

3.2.15. Knowledge about HIV prevention and care

Table 27 shows the knowledge about HIV prevention and care by gender. A majority of the participants had heard about HIV and knew a place to get an HIV test. Overall, three quarters knew that HIV can be transmitted from mother to baby and that there are drugs to reduce transmission. Knowledge on HIV transmission from mother to baby was better among women compared to men: 79.8% vs 67.6% (p<0.001).

Table 27: Knowledge about HIV prevention and care by gender

	Women	Men	Total
	n (%)	n (%)	n (%)
General knowledge			
Have heard about HIV	3429 (97.5)	2046 (96.0)	5475 (96.9)
Think circumcision can prevent HIV transmission	1947 (56.8)	1233 (60.3)	3180 (58.1)
Think HIV can be transmitted from mother to baby	2734 (79.8)	1384 (67.6)	4118 (75.2)
During pregnancy	2473 (72.1)	1251 (61.1)	3724 (68.0)
During delivery	2427 (70.8)	1166 (57.0)	3593 (65.5)
By breastfeeding	2390 (69.7)	1150 (56.2)	3540 (64.7)
Think there are drugs that can reduce mother to child transmission	2530 (92.6)	1156 (83.6)	3686 (89.6)
Know a place to get an HIV test	3360 (98.0)	1967 (96.1)	5327 (97.3)
Places named for HIV testing			
Public sector	3356 (95.4)	1955 (91.7)	5311 (94.0)
Private sector	923 (26.2)	595 (27.9)	1518 (26.9)
MSF	1692 (48.1)	1024 (48.1)	2716 (48.1)

Regarding the risk of contracting HIV, 20% of the participants declared that their risk of contracting HIV was high (Table 28). The proportion of women declaring a high risk of contracting HIV was higher that of men: 22.4% vs 16.4% (p<0.001).

Table 28: Reported risk of contracting HIV for participants who declared not being HIV infected

	Women		Men		Total	
	n	%	n	%	n	%
No risk	349	17.8	203	17.5	552	17.7
Low	836	42.7	595	51.2	1431	45.9
Moderate	332	17.0	173	14.9	505	16.2
High	439	22.4	190	16.4	629	20.2
Total	1956	100	1161	100	3117	100

3.2.16. Sexual behaviour

In total 1048 (18.6%) individuals declared that they had never had sexual intercourse and 1075 (19.1%) declared to have had the last sexual intercourse more than one year before the interview (Table 29). Sexual activity increased in the age group 20-24 years and decreased progressively from the age of 40 years both for women and men (Table 30). However, from 50 years old, women were less sexually active than men: 35.8% of women had had sexual intercourse in the year before the interview compared to 74.1% of men.

Regarding the youth, 60.1% (1509/2510) of the individuals 15-24 years declared a sexual intercourse in the past. This proportion was higher in urban areas compared to rural areas: 71.1% (95%CI: 66.3-75.5%) vs 58.2% (95%CI: 56.1-60.3%). Figure 21 shows the women and men aged 15-24 years who reported having had a sexual intercourse in the past. Eighty percent of the participants aged less than 18 years declared never having had sexual intercourse.

Table 29: Delay since last sexual intercourse by gender

	Women		Men		Total	
	n	%	N	%	n	%
Less than 1 year ago	2140	60.9	1380	64.8	3520	62.4
More than 1 year ago	783	22.3	292	13.7	1075	19.1
Never	591	16.8	457	21.5	1048	18.6
Total	**3514**	**100**	**2129**	**100**	**5643**	**100**

Table 30: Individuals who had sexual intercourse less than one year prior to survey by age and gender

	Women		Men		Total	
	n	%	n	%	n	%
15-19	217	28.1	210	30.9	427	29.4
20-24	501	80.4	348	80.0	849	80.2
25-29	418	84.3	257	87.1	675	85.3
30-34	261	85.3	149	82.8	410	84.4
35-39	216	76.9	114	85.1	330	79.5
40-44	169	67.3	89	76.1	258	70.1
45-49	170	65.6	67	72.8	237	67.5
50-54	116	41.1	78	77.2	194	50.7
55-59	72	29.6	68	70.8	68	41.3
Total	2140	60.9	1380	64.8	3520	62.4

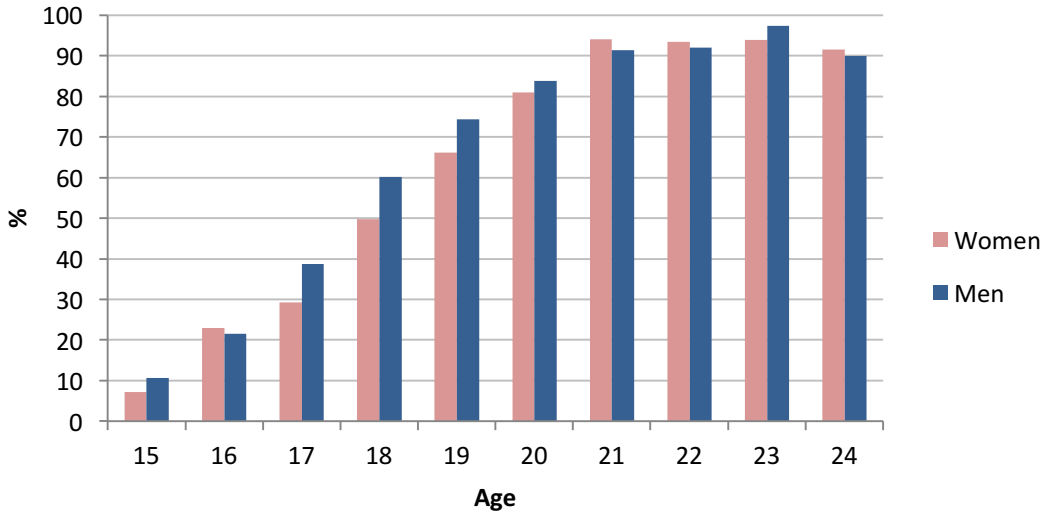

Figure 21: Participants 15-24 years who reported having had a sexual intercourse in the past

Concerning the use of condoms, in total 1691 (48.1%) participants declared to have used a condom during their last sexual intercourse and 2315 (65.9%) declared to always or sometimes use a condom during sexual intercourse (Tables 31, 32). The proportion of women who had used a condom during their last sexual intercourse was lower than that of men: 44.3% vs 54.0% (p=<0.001). The proportion of HIV positive participants who had used a condom during their last sexual intercourse was higher than that of HIV negative: 64.6% vs 41.2% (p=<0.001). There was no difference in the use of condoms among HIV positive participants by gender: 64.4% of women vs 65.3% of men (p=0.8). Participants HIV positive aware of their status used a condom in their last sexual intercourse more often than those not aware: 73.6 vs 34.8, p<0.001.

Table 31: Proportion of individuals declaring to have used a condom during the last sexual intercourse

	Women		Men		Total	
	n	%	n	%	n	%
15-19	111	51.6	145	69.0	256	60.2
20-24	231	46,1	224	64.4	455	53.6
25-29	204	49.0	142	55.3	34	51.4
30-34	133	51.0	64	43.0	197	48.0
35-39	99	45.8	64	56.1	163	49.4
40-44	86	50.9	44	49.4	130	50.4
45-49	52	30.8	26	38.8	78	33.1
50-54	23	19.8	23	29.5	46	23.7
55-59	7	9.7	13	19.1	20	14.3
Total	**946**	**44.3**	**745**	**54.0**	**1691**	**48.1**

Table 32: Frequency of condom use with the last sexual partner (participants declaring a sexual intercourse within 12 months)

	Women		Men		Total	
	n	%	n	%	n	%
Always	545	25.5	466	33.8	1011	28.8
Sometimes	776	36.3	528	38.3	1304	37.1
Never	814	38.1	385	27.9	1199	34.1
Total	**2134**	**100.0**	**1379**	**100.0**	**3514**	**100.0**

Of the participants who declared having had sexual intercourse in the 12 months previous to the survey, 2946 (83.9%) declared having had one partner, 512 (14.6%) two or three partners and 53 (1.5%) more than three partners. The median number of partners was 1 (IQR: 1-1). The range for the number of partners declared was 1-25. Men declared having two or three partners more often than women: 29.8% vs 4.8%, p<0.001 (see figure 22).

In total, 220 (3.9%) of participants declared at least one of the previous three people with whom they had sexual intercourse in the previous 12 months was a casual acquaintance, and 6 (0.1%) declared at least one transactional partner.

In total, 480 (8.5%) of participants reported concurrent partnerships (sexual partnerships that overlap) in the previous 12 months. This proportion was higher in men than in women: 19.0% vs 2.2%, p<0.001.

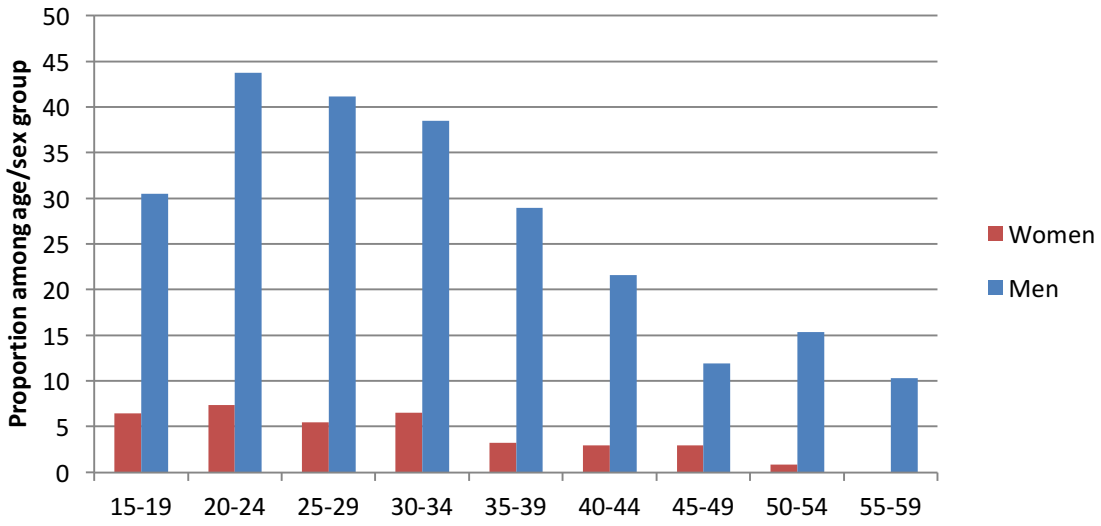

Figure 22: Proportion of women and men declaring more than one sexual partner per age group among participants with at least one partner in the 12 months prior to the survey

4. Discussion

We found in this survey an overall moderate HIV incidence in a range between 0.8 to 1.5 new cases per 100 persons-year and a high HIV incidence of 2.9 per 100 person-year in young women. HIV prevalence was high in the Mbongolwane and Eshowe areas, at 25.2%. Prevalence in women was double that of men and reached the highest rate, 56.0%, in women aged 30-39 years. Overall ART coverage was relatively high at 75.0%, and higher in women compared to men. In total 75.2% of the HIV positive individuals were aware of their HIV status. Virological suppression at a level of less than 1000 copies/ml was achieved in 90.3% of the individuals who self-reported being on ART for more than 6 months. Resistance to at least one ARV drug was found in 61.2% of the individuals on ART for more than 6 months who were not virologically supressed. Of the total population HIV infected, 52.1% were on ART, 57.1% had less than 1000 viral copies/ml.

The socio-demographic characteristics of the household and individual population in the study were similar to those found in the South African Census of 2011. There were more women than men living in the area, probably linked to the fact that men migrated out of the area more and had a higher mortality. A significant proportion of members of the family lived in another municipality but visited the household often. This group may play a role in the transmission of the HIV both in the area of the study and in the area where they live.

HIV incidence was estimated using 2 different assays with similar results. Incidence was extremely different according to the gender and the age groups. HIV incidence in young women 15-29 was very high while the estimates were moderate in men and older women. The trends by gender and age group were maintained when different values of FRR were used.

HIV prevalence increased quite rapidly in women from the age of 20 years with the peak in their 30s. In young and middle age men the trend was similar. However rates in men were much lower than in women and the increase in incidence started later and peaked later in life. From 45 years there were no differences in the prevalence by gender. High incidence in the past years, with recent decline associated with increased access to ART (and possible condom use) may explain current picture of very high prevalence with moderate incidence.

Visitors and individuals who had moved in the past 10 years were more likely to be HIV infected. Mobility and migration have been associated to HIV infection in other contexts. However, living in an urban versus a rural area was not associated with HIV status as might have been expected. Participants with more than one sexual partner in the previous 12 months were more likely to be HIV infected and this association was particularly strong in women.

The fact that people using a condom were more likely to be HIV positive may be a consequence of a more frequent use of condoms by individuals who are HIV infected and who know their positive status.

A large proportion of people declared that they had done an HIV test prior to the survey. Almost 90% of women had had a test compared to 70% of men. This difference may be at least partially explained by the testing during the ANC visits. HIV testing seems to be accessible in the area and awareness about the importance is high. On average, participants had already been tested 3 times prior to the survey. Youth, men and people with more than one sexual partner are more likely to be untested for HIV. In order to increase HIV testing coverage, strategies should be defined to make HIV testing accessible to these groups.

Overall HIV positive status awareness was also relatively high: three quarters of HIV infected people knew their status. Nevertheless, awareness was lower in specific age-gender groups, such as women aged 15-24 and particularly men aged 15-34 and 55-59 where almost half of them were not aware of their status. MSF out-of-facility, mobile, and community-based HIV testing seems to have had an impact on testing overall but the impact on diagnosing HIV infected is smaller. Almost 20% of the people tested had been tested by MSF but only 3% of the positive ones had had their test done by the organization.

Half of the HIV infected individuals were on ART. The median delay since ART initiation was relatively long: more than 2.5 years, and a quarter had initiated ART at least 5 years prior to the study. The ART program in the area seems to have begun a considerable number of years ago with a progressive increase in the number of ART initiations particularly since 2010. ART coverage was relatively good at 75%. Coverage was higher in women and increased with age. As for HIV testing, strategies of intervention should target specific groups with lower coverage such as men and young people 15-29 and those with more than one sexual partner.

Self-reported and blood-tested ART agreement was high in the overall population but lower among young people. The discrepancies may be explained by individuals denying their lack of adherence to treatment and individuals who preferred not to reveal their treatment probably due to stigma related reasons. Overall ART coverage estimations were not very different when using blood-tested or self-reported ART intake. Therefore, ART self-reporting can be a good tool for overall ART coverage estimations. However, blood testing for ART is preferable when assessing ART intake in young people.

Virological suppression (<1000 copies/ml) was high for participants on ART for more than 6 months, revealing a functional ART program in the area. Resistance to at least one ARV drug was detected in two thirds of those not

virologically supressed. Resistance to tenofovir (RTI used in first line treatment) was relatively low. However, a high proportion of the participants in this group had resistance to efavirenz (NNRTI used in first line treatment).

Overall viral suppression in the HIV infected population was relatively high, 57.1%. More than half of the HIV infected individuals were virologically supressed. However viral suppression was lower in young people particularly those aged 15 to 24 years: one third had <1000 copies/ml. These findings are in accordance with those on HIV awareness and ART coverage.

The knowledge about HIV prevention was relatively weak in this context where HIV testing and ART coverage were high. Only three quarters of the population knew that HIV can be transmitted from mother to baby. However, a large majority knew a place for HIV testing. HIV seems to be a concern in this area and a high proportion of participants considered that they were at moderate or high risk of infection.

The steps of the cascade of care showed a relatively low attrition over the cascade. The main drop occurred on HIV diagnosis, with an additional drop on people in care. In general, it seems that once people get diagnosed, treatment and viral suppression are achieved in a relatively high proportion. However, we need to take in consideration that each step of the cascade is a one-shot picture of the situation at the time of the survey. There is no link between one step and the previous one in the cascade and the results are not directly comparable with a prospective cohort cascade. In terms of the HIV dynamic in this population, the tipping point was achieved at the time of the survey with more than 3 ART initiations per new infection.

At the time of the survey, only 60% of the population declared that they were sexually active (sexual intercourse less than 1 year before the interview). A majority of the participants aged less than 18 years declared never having had a sexual intercourse. Concurrent partnerships were relatively high in men and low in women. The use of condoms was only moderate. There were no major differences in the use of condoms by age or gender except a decrease from the age of 45 years. However participants HIV positive used condoms more often than those HIV negative and this difference was larger between those HIV positive and aware of their status compared to those unaware. This reflects good health education on HIV transmission among diagnosed HIV positive people.

A limitation of this study was the cross sectional design, which means statements about causality cannot be made. This design is probably not the most adapted to describe the HIV epidemic in mobile populations. People not resident in the survey area but visiting family or friends may have an impact on HIV transmission in both locations. Self-reporting bias may also have occurred, although, the main results of the study were based on biological tests

including ARV testing in blood samples. Strengths of the study were the population-based design, the high inclusion rates and results based on biological tests.

This survey was conducted 2 years after MSF had started an intensive intervention to support the MoH TB & HIV services in the area, with the aim of increasing HIV testing, ART initiations, virological suppression among patients on ART, community TB/HIV literacy, condom distribution and medical male circumcision, as well improving the quality of TB/HIV services together with decentralization to primary care, nurse initiated management of ART.

In conclusion, overall HIV transmission is moderate in Mbongolwane and Eshowe areas. However a high number of new infections occur in young women. HIV remains an important health problem in the area with more than one quarter of the population affected by the disease. Overall, access to HIV testing and ART is relatively high in the area, as well as ART coverage for those in need of treatment. However, young people seem to have more difficulties to access HIV testing and treatment. HIV programmes should maintain quality of care while developing strategies to test, link and treat young people aged 20 to 30 years. Novel interventions for HIV prevention in young women are urgent. Surveys such as this are critical to evaluate ART programs and define strategies for intervention.

5. Acknowledgments

We would like to thank the study participants and their communities for their participation. Thanks to the survey team in the field for their tremendous work and motivation, and to MSF team in Eshowe, Cape Town and Brussels for their continuous support. We acknowledge ours partners from Global Laboratory in Durban, Groote Schuur Hospital in Cape Town, and SACEMA in Stellenbosch for their very valuable contribution to this survey.

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