CAPRISA 055 PROTOCOL

Temporal trends in HIV infection in rural KwaZulu-Natal – implications for research and programmatic priority setting

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CAPRISA
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1. INTRODUCTION

HIV seroprevalence surveys amongst antenatal clinic attendees are important for monitoring trends of HIV infection in countries where heterosexual transmission is dominant. The annual, anonymous HIV seroprevalence surveys amongst antenatal clinic attendees in South Africa have to date provided a reliable picture of the evolving HIV epidemic in South Africa. Recent data from UNAIDS suggests that as the HIV epidemic matures at a country level within country differences in HIV infection become more pronounced and highlight the need for HIV seroprevalence surveys in rural communities to be strengthened for better informing and targeting HIV interventions. We propose to continue to monitor trends in HIV infection among antenatal clinic attendees to enable us to track changes in the evolving epidemic in this rural community, compare these trends to national and provincial data, monitor the impact of enhancing specific primary care services and the conduct of HIV and AIDS related research in this community, and utilise the data from these surveys to better inform service provision and research priorities in this setting.

Subsequent to the unlinked anonymous survey being initiated, the two dose nevirapine intervention for positive mothers was introduced as well as anti-retroviral treatment for persons with CD4 counts < 200 cells/ml or WHO clinical stage 3 / 4 disease. We propose an anonymous chart review to determine the uptake of voluntary counseling and testing (VCT) and acceptance of prevention of mother to child transmission (PMTCT) interventions among the survey population. By determining the VCT uptake and HIV prevalence among ANC clients in this context and comparing it to the HIV prevalence in the anonymous survey we will be able to determine the coverage of the PMTCT intervention and inform additional efforts and / or interventions required to enhance service provision to reduce mother to child transmission of HIV and enhance maternal health and outcomes.

The literature focuses on the relationship between viral load and mother to child transmission, and it is well established that a high viral load greatly increases the probability of mother to child transmission. However, little is known about the relationship between the mother’s CD4 count and WHO defined HIV clinical stage and mother to child transmission. We propose unlinked anonymous testing of infants at the 6 week post-partum visit to determine HIV prevalence among these infants and to help clarify the relationship between mother’s CD4 count and HIV clinical stage and mother to child transmission of HIV. This will help establish the efficacy of available PMTCT interventions as well as incident HIV infections during pregnancy and help inform policy regarding frequency and timing of intra-partum HIV testing.

South Africa is in the grips of a devastating epidemic with young women 15 to 24 years of age most affected. The 2008 National HIV and Syphilis Prevalence Survey (DoH, 2008) records an alarming 45.7% prevalence in uMgungundlovu District. This high prevalence is consistent with the increase from 40.1% in 2006 to 43.9% in 2008 in the seven primary health care clinics in Vulindlela. Of grave concern is the increase from 16.6% in 2006 to 20.8% in 2008 in women <20 years. As the majority of less than 18 year old boys and girls are in school this is an appropriate venue to validate this increasing high HIV prevalence in young women. To minimize introducing bias into this validation process we propose to conduct the linked anonymous survey amongst Grades 8 -12 learners regardless of age and sex; in six selected high schools in the Vulindlela district [CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS)]. Key demographic data on school, grade, age and sex will be recorded for the purposes of this study. In addition, data will be collected on presence of parent and/or guardian/caregiver, as well as availability of parent/guardian Identification Documents to inform the development of the informed consent/assent process for future adolescent studies in this community. HIV testing will be undertaken on dried blood spot specimens collected following study information and informed consent from learners. All learners will be encouraged to know their HIV status and provided with information on HIV counseling and testing services that they could access through the local public sector primary health care clinics and the CAPRISA Vulindlela Clinical Research Site at Mafakathini. With the recent introduction of HIV counseling and testing (HCT) in schools, all learners will be encouraged to receive their results at a scheduled follow-up visit through small group pre-test counseling followed by individual receipt of results and individual post-test counseling. CAPRISA has established the Youth Friendly Services operational at the CAPRISA Vulindlela clinical research site and all learners will be encouraged to access these services. The HIV prevalence in the general youth population will allow us to compare and validate the HIV prevalence in the pregnant <20 year age group from the antenatal survey population in Vulindlela.
2. SPECIFIC AIMS

i. Determine temporal trends in HIV infection amongst first time antenatal clinic attendees utilizing public sector facilities

ii. Indirectly estimate the HIV incidence in this population through modeling

iii. Directly estimate HIV incidence through new testing algorithms

iv. Establish the relationship between age of sexual partner and HIV infection in this population

v. Monitor trends in terms of age of participants and HIV prevalence infection

vi. Compare the HIV prevalence between the National and Provincial Department of Health estimates and that obtained from this rural community

vii. To guide the development of an HIV/AIDS surveillance programme and inform the HIV/AIDS response for the Umgungundlovu Health District Health (D22)

viii. Compare HIV prevalence between unlinked anonymous testing and that obtained via voluntary counseling and testing (VCT) in this rural community

ix. Understand the utilization of available prevention of mother to child transmission (PMTCT) services and the efficacy of those services

x. Determine the relationship between CD4 count, WHO defined HIV clinical stage of infected mothers and mother to child transmission

xi. Determine HIV prevalence amongst infants born approximately 18 – 22 weeks after the unlinked anonymous testing of first time antenatal clinic attendees utilizing public sector facilities

xii. Determine the HIV prevalence amongst a general youth population of grade 8 to 12 learners (males and females) ≥ 12 years of age in the six selected high schools in the Vulindlela district

xiii. Determine HIV transmission clusters indicative of sexual networks in schools through HIV phylogenetic analysis.

HYPOTHESES TO BE TESTED

In contrast to the national and provincial HIV seroprevalence estimates and the rising HIV related morbidity and mortality, the HIV prevalence in this rural community is continuing to rise.

Utilization of available VCT at antenatal clinics is low as is utilization of available PMTCT interventions.

HIV prevalence amongst youth aged ≥ 12 years of age in the general population is as high as the HIV prevalence amongst ≥ 12 years of age pregnant women attending primary health care clinic in Vulindlela.

3. BACKGROUND AND SIGNIFICANCE

The Joint United Nations Programme on HIV/AIDS (UNAIDS, 2004) estimates that almost 40 million adults and children were living with HIV/AIDS at the end of 2003. The burden of infection is most apparent in sub-Saharan Africa with almost 28 million infections, of which 3 million were newly acquired in 2003. Far from leveling off, rates of infection remain on the increase.

Although introduced late, heterosexual transmission of HIV has spread rapidly and by the end of 2002, it was estimated that 5.3 million South Africans are HIV infected (Dept of Health, 2002). To track the trends in HIV infection the Department of Health conducts anonymous annual sentinel surveillance amongst first time antenatal clinic attendees. Over the years these studies have demonstrated the national sero-prevalence to be 0.76% in 1990; 10.5% in 1995; and 26.5% by 2002. HIV infection is distributed unevenly across the nine provinces in South Africa, with KwaZulu-Natal consistently experiencing the highest prevalence. The HIV prevalence in this province has increased from 1.6% in 1990 to 18.2% in 1995 to 36.5% in 2002 (Dept. of Health, 2002). The epidemic occurs disproportionately amongst young, Black women, with more than 60% of infections occurring in the 20-30 year age group and is best described as “explosive” with no sign of saturation (Abdool Karim and Abdool Karim, 2002).

In the past two years whilst the national HIV surveys demonstrate a stabilisation in the HIV estimates we have observed a substantial increase in HIV estimates amongst antenatal clinic attendees utilising PHC clinics in Vulindlela. To date this data has been utilised to enhance the antenatal, voluntary
counselling and testing (VCT), and family planning services in the district in partnership with the KwaZulu-Natal Department of Health and to initiate a range of research projects to better understand factors driving the patterns of HIV infection and to test new HIV prevention technologies in this community, and provide Highly Active Anti-retroviral therapy to infected individuals through the CAPRISA Vulindlela Research Facility. We propose to continue to monitor trends in HIV infection among antenatal clinic attendees to enable us to track changes in the evolving epidemic in this rural community, compare these trends to national and provincial trends, monitor the impact of enhancing specific primary care services and the conduct of HIV and AIDS related research in this community, and utilise the data from these surveys to better inform service provision and research priorities in this setting.

Establishing surveillance amongst focused communities aim to concentrate resources and yield information that is most useful in reducing the spread of HIV and in providing care for those infected. Whilst systems have been established for the surveillance of HIV infection amongst ANC clinic attendees and high-risk groups, only selected public primary health care clinics throughout South Africa are used as sentinel sites for the primary surveillance of ANC attendees. The data provides useful information amongst the select group of women, with the most recent report suggesting “a stabilization of HIV prevalence rates”. However, data from these sentinel sites may be transferred reliably from one population to another and fail to capture the diversity or explain changes over time with advancing HIV epidemics in communities outside these sentinel sites. Thus ideally assessments should be based on well-designed studies conducted in populations where interventions programmes would be applied. As a consequence of changes in the local HIV epidemiology, intervention effectiveness against these changes over time need to be considered and evaluated, thus the motivation of annual surveillance of HIV prevalence within this community.

The prevalence of HIV infection will be anonymous, unlinked cross-sectional survey recommended by the US Centre for disease control and the World Health Organisation. The HIV tests results will not be linked to a specific person and will provide unbiased accurate data on the current status and direction of HIV epidemic in the study population. The surveillance of HIV prevalence within this community will enable us to prepare strategies to manage HIV/AIDS. A comprehensive HIV prevention programme together with AIDS care and management is currently integrated with the Mafakathini PHC services for family planning and antenatal clinic patients within CAPRISA research facility at Vulindlela. The comprehensive programme includes family planning and antenatal care, management of sexually transmitted infections, cervical cancer screening, pre and post HIV test counseling, referral to the department of health's prevention of mother to child transmission of HIV infection, referral to CAPRISA treatment project for accessing AIDS care and management, follow up of family planning cohorts for the incidence rates of HIV and STIs. By estimating the prevalence annually will allow us to establish the need for ongoing and future services for those infected and affected by HIV and allow us to strengthen our existing prevention programmes.

Utilization of VCT is an essential gateway for uptake of PMTCT interventions. In addition, if uptake of VCT is high among antenatal clients, it may be possible to utilize PMTCT VCT statistics for surveillance purposes and discontinue unlinked anonymous testing, reconciling the ethical dilemma of unlinked anonymous testing in a high HIV prevalence population where an effective prevention intervention exists. However, baseline comparisons of the HIV prevalence of these two populations and utilization of PMTCT services are needed to determine the feasibility of this transition. An anonymous chart review will determine the VCT prevalence rate in the anonymous unlinked survey population and the coverage of the PMTCT intervention. This will inform additional efforts and / or interventions required to enhance service provision to reduce mother to child transmission of HIV and enhance maternal health and outcomes.

Determining the HIV prevalence among 6 week post-partum infants will enable assessments of efficacy of the PMTCT intervention, incident HIV infection in the mother that could have occurred after her first ANC visit and determine the role of mother’s immune status on HIV transmission to the infant. This additional data will be invaluable for informing and enhancing service provision to reduce mother to child transmission and enhance maternal health and health outcomes.

The 2008 National HIV and Syphilis Prevalence Survey (DoH, 2008) records an HIV prevalence of 45.7% in uMgungundlovu District, which is consistent with a similar high prevalence of 43.9% found in the 2008 CAPRISA antenatal survey. In addition to overall high prevalence, the HIV prevalence has increased from 16.6% in 2006 to 20.8% in 2008 in young women <20 years of age. The increasing pregnancy rate and HIV prevalence in this age group is alarming, and amenable to focused interventions specifically tailored to young people.
The annual antenatal HIV seroprevalence surveys conducted amongst antenatal clinic attendees by CAPRISA in the Vulindlela District in uMngungundlovu has been an appropriate method to monitor the temporal trends in HIV infection and future HIV care needs in this rural community. However, antenatal surveys have been reported to bias and either over or underestimate true population HIV prevalence. We propose to validate the increasing HIV prevalence in young women by comparing the antenatal clinic HIV prevalence data with a general youth population of a school-based cohort of a similar age. This data will help to improve our estimates of population-level HIV rates in this area. For epidemiological surveillance, estimating HIV prevalence among learners will be central to HIV prevention and understanding of transmission dynamics in generalized, hyperendemic HIV prevalence settings.

4. PRELIMINARY STUDIES
CAPRISA Antenatal Clinic HIV-1 surveys: We have conducted seven anonymous HIV-1 sero-surveys among first visit antenatal clinic attendees utilizing the seven primary health care clinics in Vulindlela from 2001 – 2006. The prevalence of HIV-1 infection has increased from 32.4% in 2001 to 42.6% in 2004, decreasing to 37.9% in 2006, but again increased to 40.9% in 2008. The age specific prevalence for the 2004 to 2008 surveys is presented in Table 1. Of significance is that almost a third of pregnant women were teenagers, among whom 17.4% (10.7 – 26.6) were HIV infected.

Table 1: Temporal trends in overall and age specific HIV prevalence in pregnant women attending antenatal clinics in Vulindlela, 2004-2008

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2005</th>
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<tr>
<td></td>
<td>N=552</td>
<td>N=361</td>
<td>N=333</td>
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<tr>
<td></td>
<td>% (95%CI)</td>
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<td>% (95%CI)</td>
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<tr>
<td>&lt;20</td>
<td>26.8 (20.6-32.8)</td>
<td>22 (14.2-29.8)</td>
<td>16.6 (9.2-24.2)</td>
<td>13.0 (7.2-18.8)</td>
<td>20.8 (13.0-28.4)</td>
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<tr>
<td>20-24</td>
<td>54.8 (47-62.4)</td>
<td>37.8 (28.8-46.8)</td>
<td>48.4 (38.6-58.4)</td>
<td>36.4 (26.8-46)</td>
<td>39.2 (30.8-47.6)</td>
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<tr>
<td>25-29</td>
<td>66.2 (56-76.4)</td>
<td>50.8 (38.2-63.4)</td>
<td>51.0 (36.8-65.4)</td>
<td>60.4 (47.8-73)</td>
<td>60.8 (49.6-72.0)</td>
</tr>
<tr>
<td>30-34</td>
<td>53.8 (41.8-66.0)</td>
<td>56.8 (42.2-71.4)</td>
<td>51.4 (34.8-68)</td>
<td>55.6 (39.4-71.8)</td>
<td>59.6 (45.6-73.6)</td>
</tr>
<tr>
<td>&gt;35</td>
<td>9.8 (6.18.8)</td>
<td>34.2 (18.6-50)</td>
<td>33.4 (15.6-51.2)</td>
<td>42.2 (26.4-57.8)</td>
<td>39.3 (21.2-57.4)</td>
</tr>
</tbody>
</table>

Prevalence | 42.6 (38.4-46.6) | 37.4 (32.4-42.4) | 37.6 (32.4-42.8) | 34.4 (29.4-39.2) | 40.9 (36.0-45.8) |
5. RESEARCH DESIGN AND METHODS

a. Study site
As in previous years this study will be undertaken in the Umgungundlovu Health District Health (D22) – sub-district D225 (Vulindlela), a rural community in the KwaZulu-Natal Midlands about 150 kms from Durban which has a total population of approximately 400 000. Since 1990 there have been several initiatives to improve living conditions in the area through development of roads and access to water and electricity. Employment opportunities exist within Vulindlela through the forestry projects and in the neighboring towns of Howick and Pietermaritzburg. Participants for this proposed study will be recruited from the 14 primary health care clinics in the district (Elandskop, Mpumuzza, Mpophomeni, Mafakathini, Sondeloni, Songonzima and Taylors) and include one clinic in each of the municipalities of uMshwathi, uMgeni, Mpofana, Impendle, uMkhambathini and Richmond. On average, each clinic has first time prenatal attendees of 500 per annum. The validation phase will occur in a sample of learners ≥ 12 years of age attending two high schools in the district.

Study Design and Procedures

Purpose: Measure temporal trends in HIV infection in rural KwaZulu-Natal for research and programmatic priority setting

Study population:
CAPRISA Antenatal Survey: Pregnant women presenting for antenatal care and infants presenting for their 6 week post-natal / expanded programme for immunizations (EPI) visit.
CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS): Learners ≥ 12 years of age attending high schools in the district are considered to be a general youth population. Previous studies conducted in Vulindlela confirm that majority of youth in this age group (>80%) attend school. This survey will be undertaken in the schools among all registered learners to minimize selection and participation bias and compromise the validity of the surveillance data.

Design:
CAPRISA Antenatal Survey: Cross sectional study in two phases and a review of antenatal clinic (ANC) chart data

- **Phase I:** Peripheral blood specimens collected on all first visit antenatal clinic attendees during October and November will be tested anonymously for HIV. The specimens will be collected at the same time as the National Department of Health’s Annual HIV Seroprevalence Survey collection.
- **Phase 2:** Heel prick dried blood spot specimen collection from all infants presenting for their 6 week post-natal / EPI visit in March and April at the seven participating antenatal survey clinics for unlinked anonymous HIV antibody and PCR testing.

In addition to the cross-sectional portions, an anonymous review of antenatal clinic (ANC) statistics at each clinic will be undertaken for the patients presenting during Phase I. The purpose of this review is to:

- Establish uptake of VCT and the results of the HIV tests.
- Establish whether CD4 testing was undertaken among clients who test HIV positive and the results of the test and what proportion were offered the PMTCT intervention and uptake of the intervention
- Determine what proportion of those with CD4 counts < 200 cells/ml were able to be initiated on anti-retroviral treatment

CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS): Cross sectional study among registered grade 8-12 learners ≥ 12 years of age in two selected high schools in the Vulindlela district review is to:

- Establish anonymous anonymous HIV antibody testing on dried blood spot specimens collected from grades 8 to 12 learners attending two six selected secondary schools within the Vulindlela District. All learners will be encouraged to know their HIV status and to receive their results at a scheduled follow-up visit through small group pre-test counseling followed by individual receipt of results and individual post-test counseling. CAPRISA has established the Youth Friendly services operational at the CAPRISA Vulindlela clinical research site and all learners will be encouraged to access these services including HIV counselling and testing within the context of pre and post test counseling for HIV and ongoing care (Appendix 2b) or be referred to the primary health clinics in the district.
Study duration:
Four Six months during two three separate two month intervals

CAPRISA Antenatal Survey
Phase 1: October – November of each survey year
Phase 2: March – April of the following year

CAPRISA Linked Anonymous youth Seroprevalence Survey (CLAySS
April – May of each year

Primary Endpoint
- Prevalent HIV amongst first time antenatal clinic attendees and high school learners ≥12 years of age in the district.

Secondary Endpoints:
- Indirectly estimate the HIV incidence in this population
- Establish the relationship between age of sexual partner and HIV infection in this population
- Monitor trends in terms of age of participants and HIV prevalence infection
- Compare the HIV prevalence between the National and Provincial Department of Health estimates and that obtained from this rural community
- To establish an annual surveillance programme for HIV prevalence
- Compare HIV prevalence between unlinked anonymous testing and that obtained via voluntary counseling and testing (VCT) in this rural community
- Understand the utilization of available prevention of mother to child transmission (PMTCT) services
- Determine the relationship between CD4 count and/or WHO defined clinical stage and mother to child transmission
- Determine HIV prevalence and incidence rates amongst 6 week old infants born approximately 18 – 22 weeks after the unlinked anonymous testing of first time antenatal clinic attendees utilizing public sector facilities
- Determine HIV prevalence amongst learners ≥ 12 years of age in the general population in grades 8 to 12 attending two selected high schools within the Vulindlela District.
- Validate and compare the antenatal clinic-based age specific HIV prevalence for the <20 year age group to the age specific HIV prevalence in learners ≥ 12 years of age
- Determine HIV transmission clusters indicative of sexual networks in schools.

b. Measurements

1. Measurement of Exposure variable
Patient's age, current partner's age, clinic, whether current pregnancy is the first pregnancy, if previous pregnancies had occurred, the year of the previous pregnancies, highest level of school attended, occupation, if mother's HIV status is known (yes or no), if known, mother's HIV status (positive or negative) and whether the pregnancy is intended (yes or no) will be the exposure variables collected at the phase I and phase II blood specimen collection visits. Phase II will also collect infant's age and use of nevirapine during pregnancy.

The anonymous chart review will record patient age, gestational age, offering of VCT, acceptance of VCT, HIV test result, CD4 count, WHO defined clinical stage of HIV, offering of nevirapine, and acceptance of nevirapine for all first antenatal visit clients presenting for care during phase I of the study.

Learner's age, current grade and gender will be the exposure variables collected with gender-neutral wording of the survey questions on sexual practices. Data collected on possession of South African Identification book, presence of parent and/or guardian/caregiver, as well as availability, accessibility, willingness or reluctance of parent/guardian to provide consent will inform the development of the informed consent/assent process for future adolescent studies in this community.

2. Measurement of outcome variables
CAPRISA Antenatal Survey: HIV testing will be performed on serum using the standard EIA Antibody assays by Enzygnost (Dade Behring) (CAPRISA Dade Behring HIV ELISA SOP number : LDBH013), using the BEP 2000 (CAPRISA BEP 2000 SOP number : QBEP004), a fully automated microtitre plate analyser using photometric measurement. HIV testing will be performed on plasma of ELISA negative
specimens using the COBAS AmpliPrep/COBAS TaqMan HIV-1 Test to detect RNA using the COBAS AmpliPrep Instrument for automated specimen processing and COBAS TaqMan Analyzer or COBAS TaqMan 48 Analyzer for automated amplification (Roche Diagnostics) (CAPRISA Roche Diagnostics HIV PCR SOP number : LP-CRL-017) HIV ELISA testing will be performed on dried blood spots for maternal antibodies to determine HIV exposure status and then ELISA positive specimens will undergo pooled PCR testing via NASBA Nuclisense VL at the Africa Centre Lab, DDMRI, Nelson R. Mandela School of Medicine, University of Kwa Zulu Natal. Results will be recorded as negative or positive.

**CAPRISA Linked Anonymous youth Seroprevalence Survey (CLaySS)**: HIV ELISA testing will be performed on dried blood spot samples for detecting antibodies to HIV using the the Vironostika Uniform 11 Assay, Biomerieux. ELISA antibody negative samples will undergo pooled PCR testing via NASBA Nuclisense VL for screening for acute HIV infection. Results will be recorded as negative or positive.

c. Study participant identification and recruitment

**CAPRISA Antenatal Survey**: All pregnant women and all 6 week post-natal / EPI infants attending the Umgungundlovu Health District Health (D22) – subdistrict D225 (7 clinics) (Vulindlela) PHC clinics for Phase I & II.

**CAPRISA linked anonymous Youth Seroprevalence Survey (CLaySS)**: learners from grades 8 to 12 attending six high schools located within the Vulindlela District will be informed of the survey and invited to participate. There are 7 primary health care clinics in the district and the CAPRISA Vulindlela clinical research site which offer HIV testing in the context of pre and post test counseling including the CAPRISA youth friendly services to which all learners will be encouraged and referred to for counseling and testing for HIV and ongoing support and care.

There have been several ongoing discussions and consultations with several stakeholders informing them and sharing of the ANC data and broader HIV prevention and treatment efforts in the district. The devastatingly high HIV prevalence among young women from these surveys provided impetus for proposed research in schools jointly with the DoE and DOH. The primary concern of community leadership has led to our invitation by the community to conduct research in this district to help them strengthen their prevention efforts in young people.

Community engagement processes were established through Community Research Support Groups (CRSG) consisting of stakeholders including health service providers and traditional leaders from community structures. The community liaison officer (CLO) works closely with all CRSG members on a regular basis to disseminate information on and highlight the need for HIV prevention and treatment, epidemiology of the HIV epidemic in South Africa, prevention strategies and the rationale for conducting HIV prevention research. The CLO with the CRSG through the local leadership have consulted the Schools Governing Bodies (SGB) who have expressed their concern on the status of the HIV epidemic in the community and consider the importance of validating the HIV prevalence in young women. Additionally, they have considered that the HIV information provided to learners during the surveillance will be educational, enhancing learner’s knowledge on HIV, HIV prevention and treatment and available resources within the community.

1. **Inclusion Criteria**: All pregnant women attending the clinics for their first antenatal visit will be included in phase I of the study. All infants attending the clinics for their 6 week post-natal / EPI visit will be included in phase II of the study. A sample of learners ≥12 years of age attending six high schools within the Vulindlela District.

2. **Exclusion criteria**: Women coming in for repeat visits and already tested during the study survey. Infants coming in for repeat visits and already tested during the study survey.

   Men, women and children utilizing the Umgungundlovu Health District Health (D22) – PHC clinics for other health services will be excluded. Learners attending schools outside of the Vulindlela District will be excluded for the CAPRISA linked anonymous Youth Seroprevalence Survey (CLaySS). Learners <12 years of age will be excluded, but referred to clinics for counseling and testing for HIV.
**d. Time frame for proposed study**

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<td>Ethics amendment submission</td>
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<tr>
<td>Finalization of protocol</td>
<td>July of year of phase I survey</td>
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<tr>
<td>Meeting with DOH Primary Health Care Forum</td>
<td>June/July of year of phase I survey</td>
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<tr>
<td>Staff training</td>
<td>August/September of year of phase I survey</td>
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<tr>
<td>Specimen collection</td>
<td>October – November of year of phase I survey</td>
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<tr>
<td>Completion of specimen processing</td>
<td>December of year of phase I survey</td>
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<tr>
<td>Cleaning of phase I data and preliminary data analyses</td>
<td>January of year of phase II survey</td>
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<td>Dried Blood spot specimen collection</td>
<td>2 months of each year (preferably April and May)</td>
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<tr>
<td>Staff training</td>
<td>January / February of year of phase II survey</td>
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<td>Dried blood spot specimen collection</td>
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<td>Completion of specimen processing</td>
<td>May of year of phase II survey</td>
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<td>Cleaning of phase II data and final data analyses</td>
<td>June of year of phase II survey</td>
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<tr>
<td>Final report and feedback to services</td>
<td>July of year of phase II survey</td>
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<tr>
<td>Manuscript preparation</td>
<td>August of year of phase II survey</td>
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**e. Project Team**

<table>
<thead>
<tr>
<th>Name</th>
<th>Role</th>
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<tbody>
<tr>
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<td>Project Director</td>
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<td>Co-Investigator</td>
<td>Project Co-ordinator</td>
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<td>Mr Hilton Humphries</td>
<td>Co-Investigator</td>
<td>CAPRISA</td>
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<tr>
<td>Associate Prof Quarraisha Abdool Karim</td>
<td>Co-investigator</td>
<td>Associate Scientific Director, CAPRISA</td>
</tr>
<tr>
<td>Ms Nonhlanhla Yende</td>
<td>Co-investigator</td>
<td>Biostatistician</td>
</tr>
<tr>
<td>Ms Gethwana Mahlase</td>
<td>Co-investigator</td>
<td>Clinic liaison</td>
</tr>
<tr>
<td>Ms Nelisiwe Khuzwayo</td>
<td>Co-investigator</td>
<td>School liaison officer</td>
</tr>
<tr>
<td>Fanelesibonge Ntombela</td>
<td>Co-investigator</td>
<td>School and Community Liaison officer</td>
</tr>
<tr>
<td>Ms Natasha Samsunder</td>
<td>Co-investigator</td>
<td>Laboratory Manager</td>
</tr>
<tr>
<td>Prof T Ndungu</td>
<td>Co-Investigator</td>
<td>Laboratory Co-ordinator</td>
</tr>
<tr>
<td>Mr Jayraj Ramola</td>
<td>Data management support</td>
<td>CAPRISA Data Management</td>
</tr>
</tbody>
</table>

**f. Project management**

The project will be managed by the Principal Investigator, Dr Ayesha Kharsany, who will be responsible for overall quality of the study, adherence to the study protocol, analysis of study data, scientific integrity of the study results, interpretation of the study results and dissemination of the study findings. The Principal Investigator will also oversee the overall management of the project and will coordinate the transfer, cleaning and quality control of the study data. Dr Fröhlich will assist with the overall
management of the study at a site level. Ms Mlotshwa will be responsible for the coordination and implementation of the study. Nurses at all PHC clinics will be trained for each phase of the study on collection of peripheral blood specimens and select demographic variables for phase I and dried blood spots and select demographic variables for phase II. Telephonic contacts will be maintained with a designated staff member at the PHC clinics throughout both phase I and phase II to ensure quality of data collection. The Principal Investigator with Ms Mlotshwa, Maarschalk, Ms Ghetwana Mahlase and Ms Natasha Samsunder will train staff on providing information to learners on the objectives and procedures of the study, obtaining informed consent, dried blood spot specimen collection procedures and motivating referrals for counseling and testing for HIV. Mrs. Khuzwayo and Ms Ntombela will assist with oversight responsibilities for obtaining informed consent and Dried blood spot specimens from learners for the CAPRISA linked anonymous Youth Seroprevalence Survey (CLaySS). Additional CAPRISA nurses and counselors will be trained to support Ms Khuzwayo to obtain informed consent and sample collection. A driver will be appointed on a services rendered basis to collect all specimens on the days of specimen collection for all phases. These will be delivered to the CAPRISA RESEARCH Facility at Mafakathini clinic and shipped to CAPRISA RESEARCH laboratory in Durban. Ms N Samsunder and Prof T Ndungu will oversee the HIV laboratory testing of specimens. A CAPRISA research fellow will go to each of the seven clinics to conduct the retrospective chart review and assist with data analysis.

Dr Q Abdool Karim will advise on the overall epidemiological design and analysis of the study. Dr Kharsany will liaise with Mr. Ramota and the CAPRISA data management team to monitor the data capture and undertake quality assurance checks and provide statistical support. Drs Kharsany and Frohlich will be responsible for the data interpretation and manuscript preparation together with the study team. Dr Frohlich, Ms Mahlase, Mrs. Khuzwayo, Ms Ntombela and several CAPRISA staff members have already established links with the Department of Education, Department of Health, Schools governing bodies, Community Research Support groups, Traditional leadership and parents to provide information, rationale and purpose of the study. These information sessions are ongoing to facilitate the CAPRISA linked anonymous youth seroprevalence survey (CLaySS) for discussion of results prior to dissemination to the department of Health and for scientific publication.

g. Statistical considerations

1. Review of study design
This is a cross sectional study to be conducted in Vulindlela with approximately 350 participants in phase I and phase II. Since the anonymous chart review is in the phase I population, it is assumed the participant number will be the same or higher. During the CAPRISA linked anonymous Youth Seroprevalence Survey (CLaySS) all learners ≥ 12 years of age from the six selected schools will be eligible for participation.

2. Sample size/precision calculations
CAPRISA Antenatal Survey: We determined the precision of anticipated point prevalence estimates rather than a traditional sample size calculation, given that the size of the sample available for the study is limited by the number of women we know have attended the ANC clinics for a first visit. A retrospective analysis of antenatal clinic attendance patterns in the district for 2005 indicated an average of 1700 clinic attendees over 2 months at the clinics anticipated to be included in the survey. Participation rates among clinic attendees were usually high. If a 10% refusal rate is anticipated, we could expect 1530 participants to be enrolled in the study over 2 months in the Vulindlela district antenatal clinics. When the sample size is 1500, a two-sided 95% confidence interval for a single proportion using the large sample normal approximation will extend 2.25% from the observed proportion of 40% (NQuery Advisor 5.0) Subgroup analyses, according to women’s age and their partner’s age, and according to pregnancy history, will obviously have lower precision around point estimates.

CAPRISA Linked Anonymous youth Seroprevalence Survey (CLaySS): If the expected proportion is 20%, similar to the >20 prevalence rate in the 2008 antenatal survey, with a sample size of 246, a two-sided 95% confidence interval for a single proportion using the large sample normal approximation will extend 5%. If the expected proportion is one-third that rate, a sample size of 264 will be required to achieve a two-sided 95% confidence interval for a single proportion using the large sample normal approximation will extend 3% from the observed proportion for an expected proportion. (NQuery Advisor
5.0) Given that these confidence intervals are narrower than those in the antenatal survey, we believe that achieving at least this sample size in the Validation Phase will allow for antenatal survey estimates to be improved.

3. Study Endpoints
Prevalent HIV infection

4. Statistical analysis
All data will be analysed using SAS Software (SAS Institute, Inc. Carey NC)

Measurement of exposure variable
Select demographic characteristics
CAPRISA Antenatal Survey: For phase I and II analyses, mother’s age, father’s age, clinic, whether current pregnancy is the first pregnancy, if previous pregnancies had occurred, the year of the previous pregnancies, highest level of school attended by mother, mother’s occupation, if mother’s HIV status is known (yes or no), if known, mother’s HIV status (positive or negative) and whether the pregnancy is intended (yes or no) will be categorized and prevalence of HIV adjusted for these variables. Phase II analyses will include infant’s age and use of nevirapine during pregnancy.

CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS): Analyses will include gender, current grade and age for descriptive statistics and odds ratios will be calculated comparing these variables for HIV negative and HIV positive learners. Data collected on sexual practices, possession of South African Identification book, presence of parent and/or guardian/caregiver, as well as availability, accessibility, willingness or reluctance of parent/guardian to provide consent will inform the development of the informed consent/assent process for future adolescent studies in this community.

Measurement of outcome variable
Prevalent and Incident HIV: HIV prevalence and select demographic risk factors associated with HIV status will be measured using chi-squared tests for categorical data (participants age categories and partners age categories) and analysis of variance techniques for continuous variables (age, partners age). HIV prevalence (ELISA) and incidence (PCR) by age will be measured and reported using the two-tailed p-values and 95% confidence intervals. Year to year variations in HIV prevalence will be assessed using chi-square for trend. Chi-Square tests and logistic regression will be performed to obtain crude and adjusted relative risks.

h. Data collection and management

1. Study specific forms

CAPRISA Antenatal Survey: All data collection forms for phase I and phase II will record patient’s age, current partner’s age, clinic, whether current pregnancy is the first pregnancy, if previous pregnancies had occurred, the year of the previous pregnancies, highest level of school attended, occupation, if mother’s HIV status is known (yes or no), if known, mother’s HIV status (positive or negative) and whether the pregnancy is intended (yes or no). Phase II will also collect infant’s age and use of nevirapine during pregnancy.

All data collection forms for the anonymous chart review will record patient age, gestational age, offering of VCT, acceptance of VCT, HIV test result, CD4 count, WHO defined clinical stage of HIV, offering of nevirapine, and acceptance of nevirapine.

CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS): Data collection forms will include age, current grade and gender. Data will be collected (Appendix 2a) on key sexual behavior practice, possession of South African Identification book, presence of parent and/or guardian/caregiver, as well as availability, accessibility, willingness or reluctance of parent/guardian to provide consent will inform the development of the informed consent/assent process for future adolescent studies in this community.

2. Data entry

The DataFax system has been setup for this study including the design of the case report forms (CRF) and will be employed for all future surveys. Any corrections or alterations to the dataset will be verified and authorized by the principal investigator after checking with the original source documents.
6. ETHICAL CONSIDERATIONS
   a. Ethical approval
   This protocol was approved was on 5 October 2004; amendment to include HIV-1 RNA PCR approved
   on 5 April 2005, amendment to include chart review approved on 20 August 2008, amendment to
   include learners – approved on 23 July 2010 by the Faculty of Health Sciences Biomedical Research
   Ethics Committee of the Nelson R Mandela School of Medicine, University of Natal (FWA #: 00000678).
   The protocol recertification for the year 2010 was received on 5 October, 2010
   b. Informed consent
   CAPRISA Antenatal Survey: For phase I, based on the Department of Health’s ethical considerations
   for HIV/AIDS Clinical and Epidemiological Research guidelines (Dept of health 2000), unlinked
   anonymous HIV testing is done for surveillance purposes. During the first antenatal visit peripheral blood
   specimen is routinely collected for purposes of syphilis testing. All specimens will be tested for HIV as
   “Unlinked and anonymous” without any personal identifiers; thus, informed consent will not be obtained.
   Because the chart review is of minimal risk, the data collection will not adversely affect the rights or
   welfare of the subjects, and it anonymous and without any personal identifiers, informed consent is not
   necessary per the Food and Drug Administration Good Clinical Practice 2007 Reference Guide (FDA
   2007).
   For phase II, informed consent for unlinked anonymous testing will be obtained from the parent or lawful
   guardian prior to drawing the dried blood spot specimen. See attached informed consent form (Appendix
   1). The person providing informed consent will be referred to voluntary counseling and testing centres for
   confidential HIV testing per the Department of Health’s ethical considerations for HIV/AIDS Clinical and
   Epidemiological Research guidelines (Dept of health 2000).
   CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS): If the learner is ≥ 12 years of
   age, HIV Testing information sheet will be provided to each learner (Appendix 2b) and all parents will be
   informed of the survey prior to implementation (Appendix 2c). Informed consent for linked anonymous
   testing will be obtained from each learner (Appendix 2d) and for long term storage of blood samples
   (Appendix 2e).

In 2007, South Africa’s amendment to the Children’s Act No 38 of 2005 came into effect, expanding the
scope of several existing children’s rights and granting new ones. The Act gives to children 12 years and
older rights relating to reproductive health, including access to contraceptives and to information on
sexuality and reproduction, and the right of consent to HIV/AIDS testing and treatment. These rights
reflect growing concern over the need to prevent HIV in the country’s youth. For instance, every child,
regardless of age, has the right to “have access to information on the prevention and treatment of ill-
health and disease, sexuality and reproduction. S130 of the act further propose that all children of 12
years of age should have the right to independently consent to HIV testing and children under 12 years
can also consent if they are of sufficient maturity and has the mental capacity to understand the benefits,
risks, social or other implications of the treatment or operation.

All learners 12 years and older will be provided with information to make an informed decision whether to
participate or not. Information on HIV, HIV testing, importance of the survey, encourage and motivate
learners to know their HIV status, the benefits of knowing ones status, referral to CAPRISA clinical
research site and to CAPRISA Youth Friendly Services or primary health care clinics in the district to
access HIV counseling and testing services.

Informed consent procedures
Several information sessions will be held with learner prior to the implementation of the survey to ensure
that learners have sufficient time in deciding whether they wish to participate or not. Members of the
School Governing body (SGB) will oversee the informed consent process to ensure voluntariness. If a
participant is unable to provide written consent, but consents verbally, a witness comprising either an
An educator or a member of the SGB will witness the informed consent process and sign on behalf of the participant certifying that informed consent had been given verbally by the participant. Furthermore, this person will also sign as witness to certify that informed consent had been given verbally by participant. All staff will be trained in informed consent procedures to ensure that voluntary informed consent is obtained for all learners. This research to be undertaken on learners will explicitly adhere to the new South African Children’s Act (No. 38 of 2005) which came into effect in 2007 [Bamjee et al. 2007; South Africa Department of Social Development (2007 June 29)].

The learner will be provided with an informational leaflet (appendix 2b) describing the benefits of knowing ones HIV status and referred to voluntary counseling and testing centres for confidential HIV testing per Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa (Department of Health, 2006).

c. Participant confidentiality

All peripheral blood specimen tubes and select demographic information forms will be identified only by a unique participant coded number to maintain participant’s confidentiality. Any information pertaining to the participant will not be released without the written permission of the participant.

**CAPRISA Linked Anonymous youth Seroprevalence Survey (CLAySS):** Several procedures will be implemented to ensure confidentiality. Interviews will be held with each individual learner in an area separated from the rest of the learners. No names of individual learners will be recorded either on the questionnaires or on the dried blood spot specimen collection filter paper. Each learner will be allocated a 9 digit unique identifier. HIV test results, age, current grade and gender of each learner will be linked using this number for analysis and therefore maintaining complete confidentiality as no names will be used. This 9 digit number will be prelabelled to prevent transcription and possible duplicate numbers allocation errors.

All data from questionnaires will transmitted electronically using Datafax and the HIV test results will be linked electronically to ensure and maintain confidentiality. All analysis will focus on overall and age specific HIV prevalence and not by school to ensure further confidentiality.

d. Risks

Study participants may experience some discomfort, feel faint or dizzy when having blood drawn. Some bruising or swelling may occur at the site where blood is drawn.

e. Potential Benefits

Participants may receive no direct benefit. Eligible positive pregnant mothers and infants will have access to ARV treatment through the CAPRISA AIDS Treatment Programme. Recommendations based on findings from this study will be provided to the Dept of Health and are intended to enhance maternal and infant services especially in relation to reducing HIV infection and treating AIDS.

**CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS):** All learners are likely to benefit from receiving information and education on HIV, HIV testing and encouraged to know their HIV status with referral to the primary health clinics in the district and CAPRISA Vulindlela Research facilities for HIV counselling and testing within the context of pre and post test counseling for HIV and ongoing care and to the CAPRISA Youth Friendly Services (Appendix 3) operational at the research site.

7. BIOHAZARD CONTAINMENT

As the transmission of HIV can occur through contact with contaminated needles, blood, and blood products, universal blood and secretion precautions will be observed by all nurses when drawing blood. Staff collecting dried blood spot specimens will receive training on collection and transportation of these. The blood specimen collected on the filter paper will be allowed to dry, kept away from direct sunlight, dust and not allowed to come into contact with any surface or each other. The dried filter paper will be placed into a Ziploc bag with desiccant package, air removed, plastic bag sealed and refrigerated until transported to CAPRISA research laboratory. All standard universal precautions for blood sample collection, transportation and processing will be adhered to.

8. USE OF INFORMATION AND PUBLICATION
Presentation and publication of the results of this study will be governed by CAPRISA policies. Any presentation, abstract or manuscript will be made available to CAPRISA Scientific Committee for review prior to submission.

9. REFERENCES


10. BUDGET JUSTIFICATION

All peripheral blood and Dried blood spot specimens will be processed in the CAPRISA RESEARCH Laboratory, Durban.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>COST</th>
<th>QUANTITY</th>
<th>TOTAL COST</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV serum ELISA test</td>
<td>R67.00 per specimen</td>
<td>Approx. 350</td>
<td>R23,450.00</td>
</tr>
<tr>
<td>HIV plasma PCR test</td>
<td>R270.00 per positive specimen</td>
<td>Approx. 5</td>
<td>R1,350.00</td>
</tr>
<tr>
<td></td>
<td>R20 per negative specimen</td>
<td>Approx. 210</td>
<td>R4,200.00</td>
</tr>
<tr>
<td>HIV PCR repeat testing (+/- 10% of specimens)</td>
<td>R20.00 per specimen</td>
<td>Approx. 23</td>
<td>R460.00</td>
</tr>
<tr>
<td>HIV DBS ELISA test (phase 11)</td>
<td>R80.00 per specimen</td>
<td>Approx. 350</td>
<td>R35,000.00</td>
</tr>
<tr>
<td>HIV DBS PCR test</td>
<td>R350 per specimen</td>
<td>Approx. 140</td>
<td>R49,000.00</td>
</tr>
<tr>
<td>CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS) DBS</td>
<td>R80.00 per sample</td>
<td>Approx 350</td>
<td>R35,000.00</td>
</tr>
</tbody>
</table>
11. DISCLOSURES

Conflict of Interest: **None for PI and co-investigators**
INFORMATION TO PARTICIPANTS

CAPRISA anonymous postnatal survey to enhance PMTCT programmes

I am a member of a team working at CAPRISA, University of KwaZulu-Natal, who have been undertaking anonymous antenatal surveys in the 7 primary health care clinics in the Vulindlela area with the KwaZulu-Natal Department of Health (KZN DOH) to understand how HIV is spreading in Vulindlela.

As part of the antenatal care provided to pregnant women utilising public sector health facilities, the South African Department of Health provides services to reduce mother to child transmission of HIV (PMTCT intervention). HIV testing for pregnant women remains voluntary as is uptake of the PMTCT intervention for those mothers who are HIV infected. More recently, the National DOH introduced anti-retroviral (ARV) treatment for all HIV infected persons utilising public care facilities in South Africa who are eligible for treatment initiation according to their guidelines.

We are undertaking this study because we want to learn how many infected mothers or mothers at risk of getting infected with HIV are actually using the free HIV testing service provided at these PHC clinics. In addition, we want to establish whether infants born to infected mothers are benefiting from mothers being on treatment and/or how effective the PMTCT intervention is on the infant. In order to do this we would like to ask you a few questions about your experiences during your last pregnancy and a few questions about yourself – this will take 10-15 minutes. If you agree to this, we will write down this information but we will not ask or write down your name or any other information such as where you live. So no-one will know who the information comes from.

In addition, we would also like to take a small sample of blood from your child. In order to do this we would do a small finger or heel prick and place a few drops of blood on special paper. We use a lancet, not a needle or syringe. This sample will be tested for HIV infection. We do not write any names on the paper and so there will be no way of knowing who the sample came from. Because of this, we cannot give you back any results. If you agree to this, we will write down this information but we will not ask or write down your name or any other information such as where you live. So no-one will know who the information comes from.

There is no limit on how long the blood will be stored and may be tested for other infections. If you do not want us to store the sample then we will destroy the sample as soon as it is tested for HIV.

If you do not want to be interviewed (or the baby to have the blood sample) then please just say so and we will stop now. Also if you wish to stop at any time in the interview you are free to do so. If you do not wish to participate you are still free to attend the clinic in the normal way and to receive all treatment there as before.

Thank you for your time.

If you want more information or have any complaints then please contact either:

Janet Frohlich (Dr) Gethwana Mahlase
CAPRISA Vulindlela Site Manager CAPRISA Vulindlela Outreach
Telephone: 033 260 6852 Mobile: 082 894 6571
or
The Biomedical Research Ethics Committee, University of KwaZulu-Natal Ph. 031 260 2486
or The KZN Department of Health – Ph 033 897 1068
APPENDIX 1b: Informed consent for CAPRISA anonymous post-natal survey to enhance PMTCT programmes

I have read the explanation above and have had the opportunity to speak to a member of the project team. I understand the procedures explained above.

Tick box

<table>
<thead>
<tr>
<th>I agree to participate in this CAPRISA study of PMTCT services. I understand the purpose of the evaluation and know that I can stop the interview at any time.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I also agree to a blood spot being collected from my child</td>
</tr>
<tr>
<td>I also agree for the filter paper sample of blood being stored for up to 2 years</td>
</tr>
</tbody>
</table>

Name __________________________________ Signature ________________

I confirm that I have explained the purpose and nature of the Impact survey and that the above participant has understood the procedures including that the sample from her child will be tested for HIV. I also confirm that the participant freely agrees to participate in the survey

Witness _________________________________ Signature ________________

Date _________________________________
APPENDIX 2a: Data collection and Sample Tracking form for CAPRISA linked anonymous Youth Seroprevalence Survey (CLAYSS)

Study ID _ _ _ - _ _ - _ _ _ _
Date of collection dd _ _ m m m _ _ _ y y _ _

1. Learner gender : M / F
2. Learner grade :  8 / 9 / 10 / 11 / 12
3. Learner age _ _ OR Date of birth dd _ _ m m m _ _ _ y y _ _
4. Do you have a birth certificate? Yes/No
5. Do you have the South African identification book? Yes/No
6. Is your biological mother still alive? Yes/no (If no, skip to Question 8)
7. Does your biological mother live in your house? Always/Sometimes/Never
8. Is your biological father still alive? Yes/No (If no, skip to question 10)
10. Do you know if your parent/s have the South African identification book? Yes/No/Don't Know
11. Who is your guardian/caregiver in the absence of your mother/father?
12. Do you know if your guardian/caregiver has an ID book? Yes/No/Don’t Know
13. Have you ever engaged in sexual intercourse. Refused / No / yes
14. If yes :
   a. vaginal / anal / oral / other type to be specified
   b. How many sex partners have you had in total?
   c. What is the age of your oldest sex partner
15. Have you been informed about HIV testing services at CAPRISA and primary health care clinic in Vulindlela Yes/No
16. Specimen
   a. Dried blood spot specimen collection Yes / no  Sent: Yes /no
   b. Specimen collected by (Date, time, print name, signature)
   c. Specimen received by in lab (Date, time, print name, signature)

Return sheet to CAPRISA Laboratory (DDMRI)
APPENDIX 2b: Information sheet for learners

HIV Testing Information Sheet for Learners

South Africa is the worst affected country in the world for HIV infection. In 2008 an estimated 5.7 million South Africans were living with HIV and AIDS.

To understand how HIV is spreading in Vulindlela, for the last several years CAPRISA researchers together with the KwaZulu-Natal Department of Health have been testing pregnant women anonymously for HIV in the seven clinics in the Vulindlela area. However, the information from these surveys is limited to pregnant women only and does not tell us how much of HIV we have amongst young people who are not pregnant. We know from HIV testing surveys carried out in the rest of the country and world that most HIV infections occur in young people below 25 years of age. It is for this reason that it is important that you know your HIV status.

We are undertaking this study because we want to learn how many young people have HIV infection (Prevalence) so that this information will help in assisting young people in the community to avoid HIV, to design appropriate research to prevent new infections and on how to care for those who have HIV infection. After the study is done, we will hold meetings in the community to provide the results of the study.

The researchers will ask you a few questions and take a few drops of blood from your finger to check how big a problem of HIV is among young people in the community. The questionnaire contains detailed questions on sexual behaviour and you may refuse to answer any questions that you do not wish to answer. No names will be collected for this purpose and therefore your HIV result will not be linked to your name. We call this type of testing anonymous HIV testing. However, we still encourage you to get an HIV test done separately from this study and to know your HIV status.

To get an HIV test, you can go to one of the clinics in the district or you are welcome to attend the CAPRISA Vulindlela Research site in Mafakathini. All staff at these clinics are well trained to counsel you, test your blood for HIV infection and if needed will refer you for additional care.

At the clinics a trained counselor in a private room will counsel you, ask questions and explain to you in detail on the procedure for testing. This involves a prick of your finger tip to collect a few drops of blood. The test is done while you are waiting and usually takes between 20 to 30 minutes. Once your results are ready the counselor will give you your results in private, will explain the meaning of your results and what actions you should be taking in the future. If you are HIV negative you will receive risk reduction counseling to support you to remain negative. If you are HIV positive you will receive counseling to support you to understand your status and you will receive appropriate referral for further care.

If you feel that you would like to talk to someone about having an HIV test please feel free to talk trained staff at CAPRISA Vulindlela Clinical Research Site between 8h00 and 16h00 hours.

Primary Health Care Clinics in Vulindlela

- Mphophomeni Clinic
- Sondelani Clinic
- Taylors Halt Clinic
- Songonzima Clinic
- Elandskop Clinic
- Mafakathini Clinic
- Mpumuza Clinic
14 August 2011
Dear Parent,

Thank you for taking the time to read this letter. In order to understand how HIV is spreading in Vulindlela, for the last several years CAPRISA has been testing pregnant women for HIV in the seven clinics in the Vulindlela area in collaboration with the KwaZulu-Natal Department of Health. This information has been very useful; however, the information from these surveys is limited to pregnant women only and does not reflect the amount of HIV amongst young people who are not pregnant.

We know from HIV testing surveys carried out in the rest of the country and world that most HIV infections occur in young people below 25 years. We would like to undertake a similar study with young people because we want to learn how many young people have HIV infection.

We are asking learners from schools in the Vulindlela district to participate in this study. We will ask each learner a few questions. The questionnaire contains detailed questions on sexual behavior and your child may refuse to answer any questions that they not wish to answer. We will also take a small spot of their blood. From this we will be able to learn how much HIV there is in young people.

The learners who would like to be a part of this study will be asked to give their consent to participate. Learners will be given a unique identification number that will not be linked to their names. This means that the blood spot and the questions asked will also not be linked to the learner’s name and that there is no way in which the HIV test result will be linked to the learner. We call this type of HIV testing Linked Anonymous Testing.

As per Government guidelines, anyone older than 12 years of age is allowed to access HIV testing without parent or guardian permission. However, we are writing to you to inform you of what we will be doing. If you would like more information, please contact Dr. Janet Frohlich, at the CAPRISA Vulindlela Research Site or call her on 27 (0) 33 260 6851 or Ms Gethwana Mahlase, CAPRISA Vulindlela Outreach, Mobile: 082 894 6571. Uyacelwa ukuba ukhumbule, noma ngubani ukuze azi ngesimo sakhe segciwane lengculazi.

Many Thanks - The CAPRISA Vulindlela Research Team
APPENDIX 2d: Informed consent form for learners: English Version
CAPRISA 055
Temporal trends in HIV infection in rural KwaZulu-Natal – implications for research and programmatic priority setting
CAPRISA linked anonymous Youth Seroprevalence Survey (CLAySS)

INFORMED CONSENT FORM FOR LEARNERS - 12 years and older - Version 3.0 – 14 August 2011

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

Background: I am a member of a team working at CAPRISA, University of KwaZulu-Natal. To understand how HIV is spreading in Vulindlela, for the last several years we have been anonymously testing pregnant women for HIV in the seven clinics in the Vulindlela area with the KwaZulu-Natal Department of Health. However, the information from these surveys is limited to pregnant women only and does not reflect the prevalence of HIV amongst young people who are not pregnant. We know from HIV testing surveys carried out in the rest of the country and world that most HIV infections occur in young people below 25 years. We are undertaking this study because we want to learn how many young people have HIV infection (Prevalence).

Procedures: In order to do this we would like to ask you a few questions about your health and experiences. We will also take a small sample of blood from you. To do this we will use a lancet to do a small finger prick. You may feel a small sting on your finger from the lancet. We will then place a few drops of your blood on a special paper. This is called dried blood spot (DBS) collection method. We will take this special paper to the CAPRISA Laboratory where we will test one spot of your sample for HIV infection. The remaining spots will be stored indefinitely and may be tested for other infections. If you do not want us to store the sample then we will destroy the sample as soon as it is tested for HIV. This process should take approximately 30 minutes.

Benefits: The benefits of your participation will help to inform research to help young people in the community to avoid HIV, to design appropriate research to prevent new infections and on how to care for those who have HIV infection. After the study is done, we will hold a meeting in the community to give the results of the study.

Confidentiality: When we collect your information and your blood on the special paper we will not use your name. We will only use a number and therefore no one will know the results would have come from you. Your name will not be revealed to anyone outside of the study team. Because your information and your HIV test result will not be linked to your name, we will not be able to give you back any results. We strongly encourage you to know your HIV status and attend the CAPRISA Vulindlela Clinic in Mafakathini or any of the clinics in the districts for HIV counseling and testing. However, it is important for you to know that the study records may be reviewed by the BREC to ensure that the research study is conducted safely and ethically.

Problems or Questions:
You will not be paid for taking part in this study. You can ask any questions you wish to the research staff. Participation in this study is voluntary, and it is okay if you don’t want to participate. Also, if you agree to participate and then change your mind, it is not a problem for you to stop.

If you want more information or have any complaints then please contact:
Dr. Ayesh Kharsany at 031-260 4558, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban
Dr. Janet Frohlich, at the CAPRISA Vulindlela Research Site or call her on 27 (0) 33 260 6851
Ms Gethwana Mahlase, CAPRISA Vulindlela Outreach, Mobile: 082 894 6571
The Biomedical Research Ethics Committee, University of KwaZulu-Natal Ph. 031 260 2486

Statement of Consent: CAPRISA Linked Anonymous Youth Seroprevalence Survey (CLAySS)
I have read the explanation above and have had the opportunity to speak to a member of the study team. I understand the procedures explained above.

Tick I agree to participate in this CAPRISA Linked Anonymous Youth Seroprevalence Survey (CLAySS)
I also agree to the Dried blood spot specimen collection method

I DO NOT agree to participate in this CAPRISA Linked Anonymous Youth Seroprevalence Survey (CLAySS)
Reason:

Participants Name __________________________ Signature _________________________ Date __________

I confirm that I have explained the purpose CAPRISA Linked Anonymous Youth Seroprevalence Survey (CLAySS) and that the above participant has understood the procedures including that the sample will be tested for HIV. I also confirm that the participant freely agrees to participate in the survey.

Study Staff Member __________________________ Signature _________________________ Date __________
Witness Full Name __________________________ Witness Signature _________________________ Date __________

To be completed staff member administering the Informed consent

Tick

Yes
Refused
No

Copy of signed copy of Informed consent given to participant

If not given, explain Why

Copy retained
APPENDIX 2d: Informed consent form for learners: isiZulu Version
CAPRISA 055
Temporal trends in HIV infection in rural KwaZulu-Natal – implications for research and programmatic priority setting
CAPRISA linked anonymous Youth Seroprevalence Survey (CLAYSS)
INFORMED CONSENT FORM FOR LEARNERS - 12 years and older - Version 3.0 – 14 August 2011

Uma ivolontiya lingakwazi ukufunda, lefomu kumlele ifundelwe ivolontiya njengoba ibhaliwe, nangolimi lwivolonti, kanti futhi ufakazi kumele asayinle leforn ukumqiniseka ukuthi ionke ulwazi olunikwe ivolontiya luyiqiso kanti futhi ivolontiya lingayencia ucwaningo ngokuzikhethela okukhuleleleke.

Isendelalelo: Ngiyungula lwewengu labasebenzi bakwa CAPRISA (isikhungo socwaningo ngqiciwane lesendelulela ngculaza uqobo) kwinywuesi yakwa Zulu Natal.

Ukuze sazi ngokubhebethethwa kwengciwane lendelwe endaweni yakwa Vulindlela, eminyakeni eyeledile besihloleliengciwane lwendelwe kwasbesifazane abakhulelele, ethemtholamelpilo eyisikhombisa ngokudonsa igazi elingahlanganiswe nagama lamuntu, sihlangene nomyango wezempiyo kwazu Zulu Natal.


Inzuzo: Ukungenela kwakho ucwaningo kuyoba nenjalo ocwanelengwe uolozioza intsha yomphakathi ekuvikilekeni kwisendulela nempilo, nokuhlela ucwaningo mayelana nokuvikilela ukuthetheleleka, nomu unkumakeleka labo asebethelelelekele ngqiciwane. Uma ucwaningo seluphelile siyoba nomhlanganiso womphakathi ukunikeza impumelula yocwaningo.


Ukukhelo eyoyithola ngikhathana kwakho ukuthetha ukuphi yomphakathi elapho kubasebenzi bocwaningo.

Ukuphawu

<table>
<thead>
<tr>
<th>Upuhawu</th>
<th>Ngiyavuma ukungenela ucwaningo lakwaCAPRISA Linked Anonymous Youth Seroprevalence Survey (CLAYSS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isizathu</td>
<td>Ngiyavuma futhi ukuthethwa kwagazi losimwe</td>
</tr>
<tr>
<td>Angivumi ukuzimbandakanya nalolucwaningo lwakaCAPRISA Linked Anonymous Youth Seroprevalence Survey (CLAYSS)</td>
<td></td>
</tr>
</tbody>
</table>

Ngiyavuma ukungenela uqobo ewenzise ukungeneni oluzosiza intsha yomphakathi ekuvikilekeni kwisendulela nempilo, nokuhlela ucwaningo mayelana nokuvikilela ukuthetheleleka, nomu unkumakeleka labo asebethelelelekele ngqiciwane. Uma ucwaningo seluphelile siyoba nomhlanganiso womphakathi ukunikeza impumelula yocwaningo.

Zimpilo:

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Isizathu</td>
<td>Ukungathanda ukuphi yobona eyozama ukuthetha kwagazi losimwe</td>
</tr>
</tbody>
</table>

Ukophawu

<table>
<thead>
<tr>
<th>Ngiyavuma ukungenela uqobo</th>
<th>Ngiyavuma ukungenela ucwaningo lakwaCAPRISA Linked Anonymous Youth Seroprevalence Survey (CLAYSS)</th>
</tr>
</thead>
</table>

APPENDIX 2d: Informed consent form for learners: isiZulu Version
CAPRISA 055 Protocol Version-5.2
14 August 2011
INTRODUCTION
You have decided to take part in a CAPRISA research study. The blood that is collected from you might be useful for future research. You are being asked to agree to the storage of this blood. This consent form gives you information about the collection, storage, and use of your blood. The study staff will talk with you about this information. Please ask if you have any questions. If you agree to the storage of your blood, you will be asked to sign this consent form. You will get a copy to keep.

HOW WILL YOU GET THE BLOOD FROM ME?
The researchers will collect blood through a finger-prick and place it onto blotting paper [Dried blot specimen (DBS)]. This paper with your blood will be kept and used for future research.

HOW WILL YOU USE MY BLOOD?
Your blood will only be used to confirm results with new tests when these are available or to confirm the type of HIV infection if it is present or to test for your body’s response to infection. No other kinds of testing will be done by anyone on your stored blood. The researchers do not plan to contact you with any results from tests done on your stored blood. This is because research tests are often done with experimental procedures, so the results from one research study are generally not useful for making decisions on managing your health. Your blood will not be sold or used directly to produce commercial products. Research studies using your samples will be reviewed by the CAPRISA Scientific Review Committee and a special committee at the Nelson R Mandela School of Medicine Ethics and Professional Standards Committee.

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

HOW WILL MY BLOOD BE STORED?
Your blood will be stored in special facilities that are safe and secure and only approved researchers will have access to these samples.

DOES STORAGE OF MY BLOOD BENEFIT ME?
There are no direct benefits to you. The benefit of doing research on stored blood samples includes learning more about HIV infection.

WHAT ARE THE RISKS?
We do not anticipate any risk as the stored blood samples are not linked to your name.

WHAT ABOUT CONFIDENTIALITY?
All blood samples will be labelled with a code that can only be traced back to the study and your personal information (name, address, phone number) will be protected. When researchers are given your stored blood to study, they will not be given your personal information. We will make every effort to keep your personal information confidential.

WHAT ARE MY RIGHTS?
Allowing your blood samples to be stored is completely voluntary. You may decide not to have any blood stored other than what is needed to complete this study and still be in this research study or any future study. If you decide now that your blood can be stored for future research, you may change your mind at any time. You must contact your study staff and let them know that you do not want your samples used for future research. Your blood will then not be used.

WHAT DO I DO IF I HAVE QUESTIONS?
For questions about the storage of your blood, contact
Dr Ayesha Kharsany at 031-260 4558, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban
Dr. Janet Frohlich, at the CAPRISA Vulindlela Research Site or call her on 27 (0) 33 260 6851
Ms Gethwana Mahlase, CAPRISA Vulindlela Outreach, Mobile: 082 894 6571
The Biomedical Research Ethics Committee, University of KwaZulu-Natal Ph. 031 260 2486

SIGNATURES
Please carefully read the statements below and think about your choice. No matter what you decide it will not affect your care. I agree to have blood spots collected for the purpose of storage and testing for future research related to HIV infection.

_____ Yes  _____ No
__________________________________________________________
Participant Name          Participant Signature            Date
(print)

__________________________________________________________
Study Staff Conducting   Staff Signature    Date
Consent Discussion (print)
INFORMED CONSENT FORM FOR Specimen Storage FOR LEARNERS - 12 years and older - Version 1.0 – 14 August 2011

ISINGENISO

Nizolithola kanjani igazi kimina?
Abacwaningi bazokuqhumboza umunwe bese bewucindezela ephepheni eliyisipesheli [Dried blot specimen (DBS)]. Leliphepha elinegazi lakho liyogcinwa ukuze lisetshenziswe ocwangweni oluzayo.

Niylisebenzisa kanjani igazi lami?

Nizoligcina isikhathi esisingakanani igazi lami?
Asikho isikhathi esinqunziwe sokuthi linyiogcinwa isikhathi esisingakanani igazi lakho.

Lizobekwa kanjani igazi lami?
Igazi lakho liyowulekhelelela endaweni eyisipesheli futhi evikelele, abacwaningi abavumelelelelele kuphela abhayokwazi ukufinyelelela kulamashampila.

Kuyangisiza yini mina ukuciniswa kwedwazi lami?
Akukho kusizakala okuthololayo wena ngokubeka kwegazi lakho. Usizo oluthololakala ngokuhlola igazi eligciniwe kuba ukufundza babanzeni ngokuthethuleka kwe-HIV.

Yini ubungozi?
Akukho ubungozi esibulindele ngoba amasamaphala egazi awanalo igama lakho.

Kuhamba kanjani mayelana nokuciniswa kwezimfihlo?
Wonke amasamaphala egazi ayoayelawuthuka ngehodha ekuyiyo eyowaxhumanisa nokuqawo kconti iminingwwelelela yakho (igama, idllesi nocingo) iyowoidwelela. Uma abacwaningi benikezwa igazi lakho ukuthi balihlole, ngeke banekezwe iminingwelelela yakho. Siyoqiniseka ngakho konke okusemdeleni umthi iminingwelelela yakho ivikelele, amasamaphala akho iminingwwelelela yakho.

Yini amalungelo ami?
Ukuqalamiselelela ukuthi ayovelilelela akho kungakudlondlela kwegazi lakho. Ukuqala umquma ukuthi lingabi khona igazi lakho eligciniwe ngaphandlesa kwakhelelelela ukuthi ukuthi ukuthi ukuthi umlubhlulela ngakho kale iminingwwelelela yakho. Siyoqiniseka ngakho konke okusemdeleni umthi iminingwelelela yakho ivikelele, amasamaphala akho iminingwwelelela yakho.

Kumele ngenzenjani uma ngenibezu?
Uma unemibuzo ngokuciniswa kwedwazi lakho, thintanano no Dr. Ayesha Kharsany at 031-260 4558, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban
Dr. Janet Frohlich, at the CAPRISA Vulindlela Research Site or call her on 27 (0) 33 260 6851
Ms Getwana Mahlase, CAPRISA Vulindlela Outreach, Mobile: 082 894 6571
The Biomedical Research Ethics Committee, University of KwaZulu-Natal Ph. 031 260 2486

AMASIGNESHA
Sicela ufundisise izitimatendle ezisingezansi bese ucbanga ngesinxumo sakho. Noma ikuphi okunqumayo angxe kwashintsha ukunakekelwa kwakho. Ngiyawuma ukuba igazi lami lithathwe ukuze linyiogcinwa laKwaCAPRISA kwegazi oluzayo lokuthethulela ngengculazi. _____ Yebo     _____ Cha

Igama lombambiqhaza                           Isignesha yombambiqhaza                           Usuku
(print)

Umsebenzi wocwanko(no print)                           Isignesha yomsebenzi                           Usuku

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CAPRISA 055 Protocol Version-5.2
14 August 2011
APPENDIX 3: CAPRISA YOUTH FRIENDLY SERVICES

Ekhayalethu CAPRISA Vulindlela Centre has a team of researchers, doctors, nurses, social workers, other health care workers and fieldworkers whose goal is to:

- Find ways of preventing HIV infection
- Treat those clients living with AIDS
- Provide a Youth Friendly Health Service

Ekhayalethu Centre Youth Health Services

Clinic days are normally on a Wednesday between 12:30—15:30 or you can call the clinic at (033) 260 6851 to find out when the next clinic day will be.

All information shared by study volunteers and clients attending the Ekhayalethu Centre is always private and confidential.

We are available to assist adolescents with services, information and support on a wide range of healthcare matters.

HIV Prevention & AIDS Treatment
- HIV risk reduction and testing
- Support services for HIV-infected and their families
- Peer education
- Treatment of opportunistic infections
- Nutrition
- Wellness Program and TB screening

Medical Services
- Complete physical examinations
- Medical Male Circumcision

Counselling
- Adherence counseling
- Sexual abuse support services referral
- Alcohol and substance abuse support services and referral
- Mom and Baby Program
- Violence prevention and treatment programs referral

Reproductive Health
- Birth Control advice and information
- Pregnancy testing
- Sexually transmitted diseases screening and treatment
- Condom distribution