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CAN A ROUTINE PERI-PARTUM HIV COUNSELLING AND TESTING SERVICE FOR WOMEN IMPROVE ACCESS TO HIV PREVENTION, EARLY TESTING AND TREATMENT OF CHILDREN?

Karl-Gunter Technau

A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfillment of the requirements for the degree of Master of Science in Medicine

Johannesburg, 2009

DECLARATION

I, Karl-Gunter Technau, declare that this dissertation is my own work. It is being submitted for the degree of Master of Science in Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

……..

…2nd … ……..day of……November, 2009.

To Ntokozo and Your late Mother

May the improvement of PMTCT in South Africa

Always remember that mothers can never be replaced

Presentations Arising from this Study

1.) Technau K, Kotlolo H, Machepha J, Mofokeng Y, Khan S, Phakathi T, Jordan A, Sherman G. **The Accuracy of a Verbal versus a Documented HIV-NEGATIVE Status in the Postnatal Ward.** Oral. Annual South African Congress of Midwives, 2008, Light of the Nations Church, Polokwane, Limpopo province, South Africa, 2nd – 5th December 2008.

2.) Technau K, Khan S, Phakathi L, Phakathi T, Machepha J, Jordan A, Kotlolo H, Coovadia A, Sherman G. **Implementation and Impact of Dual PMTCT therapy in Johannesburg, South Africa.** Oral. South African AIDS Conference, 2009, Durban Convention Centre, Durban, Kwazulu Natal, South Africa, 31st March – 3rd April 2009.

3.) Technau K, Jordan A, Kotlolo H, Thomas L, Sherman G. **Peri-partum HIV Testing Protocol improves PMTCT in High Prevalence Setting.** Poster. 5th International Aids Society Conference on HIV Pathogenesis Treatment and Prevention, 2009, Cape Town, South Africa, 19th – 22nd July 2009 and published in Reviews in Antiviral Therapy, 2009; 6:59, Abstract P_52 for the 1st International Workshop on HIV Pediatrics. 17th – 18th July 2009, Cape Town, South Africa.

4.) Technau K, Sherman G. **Identification of HIV-positive women at the time of delivery improves PMTCT coverage.** (manuscript in preparation)

Abstract

Context

Prevention of mother to child transmission (PMTCT) of HIV relies on identification of HIV-positive pregnant women at the first antenatal visit and at time points thereafter. As not all women who attend antenatal care initially agree to test or maintain an HIV-negative status the lack of re-establishing HIV prevalence at delivery may result in missed prevention opportunities and a false impression of PMTCT coverage.

Objectives

To assess whether a routine peri-partum HIV counseling and testing service improves access to HIV prevention, testing and care of infants by identifying additional HIV-positive women at the time of delivery.

To assess the effect on the PMTCT coverage indicator when HIV prevalence is re-established in the delivery population.

Design and Patients

All women 18 years or older with live births in the labour and postnatal wards of the Rahima Moosa Mother and Child Hospital (RMMCH) were interviewed and invited to enrol irrespective of their need to retest/test for HIV or their potential refusal of an HIV test. Rapid HIV antibody tests were offered to women who had no HIV result, reported an HIV-negative result performed more than six weeks prior to delivery or reported an HIV result discrepant with her documented result.

Test acceptance and HIV prevalence were calculated for the enrolled population. The rate of return and results for early infant diagnosis in HIV-exposed infants and the follow-up of infected infants were documented. HIV polymerase chain reaction (PCR) results for infants not returning to the facility were retrieved from the National Health Laboratory Services database.

Results

Between 9th April 2008 and the 23rd of September 2008 there were 5169 women with live births. A total of 3684 (71.3%) of the 5169 women delivering were interviewed and 2419 (46.8%) were enrolled. Of the women enrolled, 2140 (88.5%) reported a known HIV status and 490 (22.9%) of these were HIV-positive. After counseling and testing, an additional 101 HIV-positive women were identified increasing the number of HIV-positive women by 20.6%. An additional 177 women were identified as being HIV-negative. The true infant PMTCT coverage increased by 17% as a result of newly identified HIV-positive women. Of 591 HIV-exposed infants identified, 284 (48.0%) underwent PCR testing at RMMCH or surrounding facilities and 16 (5.6%) tested PCR-positive. Of the infants expected to return to RMMCH for PCR testing 155/203 (76.4%) antenataly diagnosed versus 12/83 (14.5%) newly diagnosed women returned with their infants ($p<0.001$). Ten HIV-infected infants were diagnosed at RMMCH of which nine were in care with six initiated on antiretrovirals.

Conclusion

A large number of additional HIV-positive mothers were identified by the peri-partum HIV counseling and testing protocol allowing more infants to access prevention however infant follow-up rates were disappointing especially in the newly diagnosed group. This approach has the potential to improve delivery of PMTCT and knowledge of HIV status in similar clinical settings in South Africa. Good documentation of antenatal HIV results and better links between maternal and child health services as well as infant feeding counseling need attention. Additional support for newly diagnosed HIV-positive women may enhance their chances of returning for infant diagnosis and ongoing maternal care.

Acknowledgements

This study would not have been possible without its frontline workers. To the counsellors Joyce Machepha, Boitumelo Mofokeng assisted by Lebogang Phakathi, thank you for seeing, interviewing and counseling countless mothers and providing them with hope and support. To the meticulous and enthusiastic data managers, Themba Phakathi, Vincent Kgakgadi and Rivka Lilian, your effort and patience is appreciated. Sonjiha Khan, thank you for coordinating all the HIV tests and ensuring such high quality lab work. To those that assisted with phlebotomy, Sandra Knight and Kedisaletse Phiri, your service is not forgotten. The support and enthusiasm of the postnatal nursing staff is highly appreciated, especially that of Sr Hellen Kotlolo. The financial support provided by ECHO, CDC and PEPfAR for the employment of staff and other support is very gratefully acknowledged. I would like to thank my mentors, Professor Keith Bolton, Professor Ashraf Coovadia and Sister Annie Jordan for their guidance. Finally, to my supervisor, Professor Gayle Sherman, your insight, inspiration and support as well as patience and wisdom leave me very grateful for this opportunity.

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Nomenclature

AFASS	Referring to Infant Feeding Practice as: Acceptable, Feasible, Affordable, Sustainable and Safe
AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Clinic
ART	Antiretroviral Therapy
AZT	Zidovudine – Antiretroviral drug
CD4 Count	CD4 Cell Count (expressed as 10^6/litre)
CDC	Centers for Disease Control and Prevention, USA
DOH	Department of Health
HIV	Human Immunodeficiency Virus
HIV PCR	HIV DNA Polymerase Chain Reaction Test – Roche Amplicor Version 1.5
MDG	Millennium Development Goal
MTCT	Mother to Child Transmission
NSP	South African National Strategic Plan for HIV and Sexually Transmitted Infections 2007-2011
PMTCT	Prevention of Mother to Child Transmission
RMMCH	Rahima Moosa Mother and Child Hospital (previously Coronation Women and Child Hospital)
sdNVP	Single dose Nevirapine – Antiretroviral drug
VCT	Voluntary Counseling and Testing for HIV
WHO	World Health Organisation

Chapter 1 – Introduction

1.1 South Africa in the Context of the Global HIV Pandemic

The prevalence of HIV infection in South Africa is alarming, especially in the female population of child-bearing age as it fuels the epidemic in children. At least 90% of paediatric HIV infections are preventable and as a result of MTCT [1]. The annual antenatal maternal prevalence of HIV published by the national DOH is shown in Figure 1.1 [2].

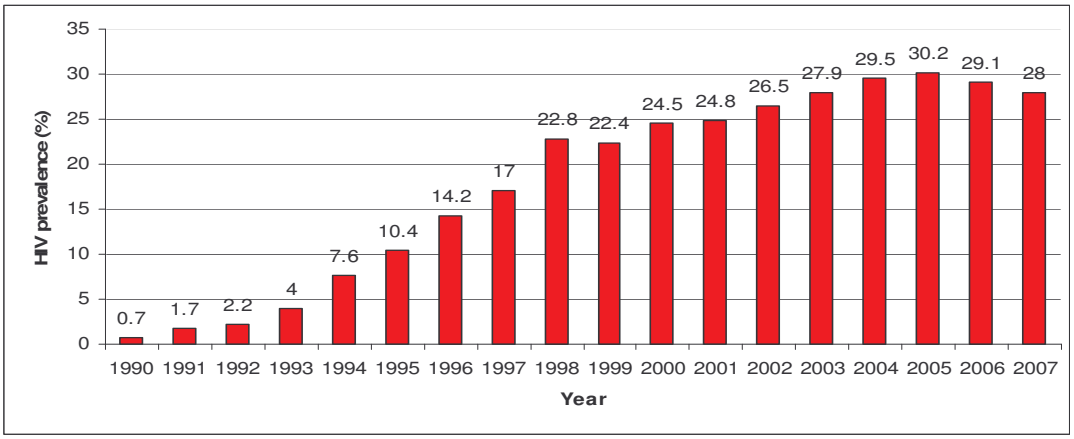


Figure 1.1: Annual Antenatal Prevalence – South Africa 1990-2007

Since the birth rate in South Africa is estimated at one million per annum, in 2007 an estimated 280 000 HIV-exposed infants were born. The exact incidence of paediatric HIV in South Africa is currently unknown because the vertical transmission rate of HIV is not readily available due to weak information systems. Estimates vary between models (Actuarial Society of South Africa and Stats SA)

and lie between 23.7% and 30% transmission from mother to child [3, 4]. Without the actual vertical transmission in 2007 being known, these models suggest that there would have been between 66 000 and 84 000 new infections in the year 2007. In 2006 it was estimated that about 200 000 to 300 000 children were living with HIV [5]. When the global estimates of children living with HIV are examined for 2007 (Figure 1.2) [1], the significance of the South African contribution to the global paediatric prevalence becomes evident comprising between 270 000 to 370 000, and making up 14% to 19% of the global two million.

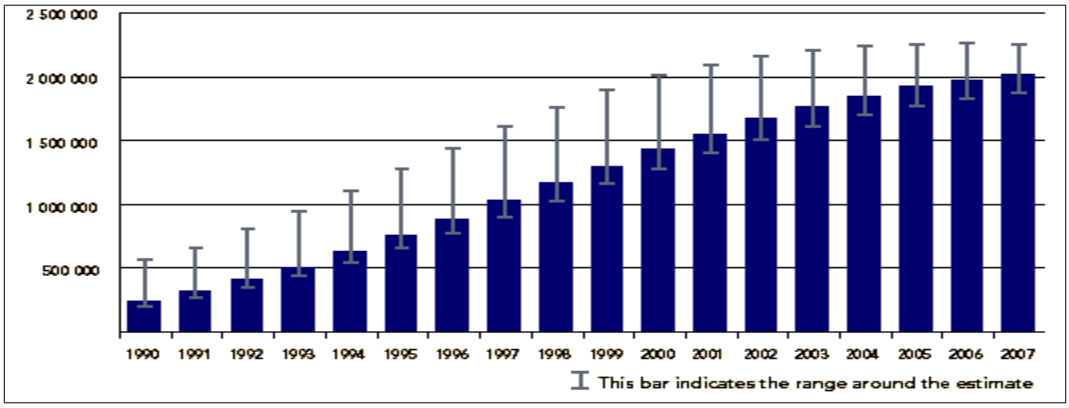


Figure 1.2: Number of Children under 15 years of age living with HIV globally 1990-2007

1.2 The Impact of HIV on Paediatric and Maternal Care in South Africa

HIV is still the major cause of paediatric and maternal mortality despite the availability of effective triple ART [6, 7] and has caused a reversal of the decrease in infant and under-5 mortality seen between 1975 and 1994. South Africa committed itself to achieving the MDG's for 2015 in 2000 and goals 4 and 5 aim to

achieve reduced maternal and child mortality by 2015, notably a two thirds reduction of under-five mortality [8]. Apart from the impact on mortality, the HIV epidemic has led to an overwhelming burden on the health care system as well as on the morale of health care workers. The management and prevention of paediatric and maternal HIV and related mortality is an important part of woman and child health in South Africa.

PMTCT should begin prior to pregnancy, as described by the four-pronged strategic approach of the World Health Organisation (WHO) [9]:

- Prevent HIV in potential parents (includes emphasis on VCT and messages of staying HIV-negative)
- Prevent unwanted pregnancy (includes family planning and contraception)
- Prevent HIV transmission to the child
- Care and support for HIV affected individuals

The South African DOH released the revised PMTCT guidelines on the 11th of February 2008 [10]. They incorporate the above points in theory but in practise, the South African PMTCT program starts antenataly, omitting the first two prongs of the WHO approach which are meant to be addressed through other programs (e.g. the VCT program). The South African PMTCT program includes VCT of the pregnant woman, counseling regarding feeding choices, prophylactic anti-retroviral drugs, free replacement formula feeds for six months if exclusive formula feeding is chosen by the mother and a virological HIV test (HIV DNA PCR) on the baby

done at six weeks of age. Additional HIV testing is to be performed where an infant is breastfed and for all HIV-exposed infants at 18 months of age.

The new protocol has been well received and implementation has begun in all nine provinces. The main addition to the sdNVP regimen is AZT given to the pregnant woman from 28 weeks of gestation until delivery and then to the baby for one to four weeks. However, successful and reproducible models for implementing this program to achieve the NSP target of reducing vertical transmission to <5% by 2011 are scarce [11]. The PMTCT program is a vital but underutilised tool for preventing morbidity and mortality in both women and children and urgently requires optimisation. The national uptake of the sdNVP PMTCT protocol before the introduction of AZT was thought to be 30% but estimates of uptake vary from 15% to 78% [5].

Providing pregnant women and infants with antiretroviral prophylaxis has been shown since 1993 as an effective intervention (ACT076 trial) [12]. Administering sdNVP can achieve almost a 50% reduction in HIV transmission rates [13]. Further, there is evidence of transmission under 2% if AZT together with sdNVP is used as adopted in the new South African guidelines [14]. Giving sdNVP and AZT to the newborn has been demonstrated to be effective, even when only the infant receives the dose [15, 16]. As these studies could not ethically have a control arm that did not offer any post-exposure prophylaxis, the risk of transmission had to be compared with historical reports. In both studies the transmission rate at six to eight weeks was around 15% whereas the transmission risk in infants with

absolutely no intervention had been reported as 25% at birth with an additional 16% occurring during breastfeeding [15, 17].

The feeding choices for HIV-infected mothers have been extensively investigated, showing that correct feeding techniques, either exclusive breast or formula feeding, have protective effects in terms of HIV transmission to infants. Pitfalls in poor feeding choices made without adequately considering the AFASS criteria put forward by the WHO, have highlighted the significant challenges that face both health care workers and mothers in this regard because of the high mortality that can be associated with poorly considered exclusive formula feeding [18]. More effort is now required to translate lessons learnt into large scale operational success.

1.3 Access to PMTCT - Maternal Testing

If a pregnant woman is not identified as being HIV-infected, there is currently no avenue for her HIV-exposed infant to access the PMTCT program. Furthermore, the woman's chances of accessing HIV treatment are compromised putting her ability to function as a caregiver for her child at risk.

Low uptake of PMTCT in South Africa is worrying and increased HIV testing (NSP Goal 8) in women is seen as key to improving this situation [11]. Pregnant women access the PMTCT program via HIV rapid testing performed during pregnancy

usually at the first ANC visit. Retesting during pregnancy and around delivery is recommended by the CDC [19], the WHO [20] and is part of the NSP [11] but is difficult to implement [21]. Three publications highlight the potential dangers of not retesting: refusal of an antenatal HIV test was associated with a high (44%) maternal HIV prevalence in Johannesburg [22], seroconversion in late pregnancy was around 5% at Chris Hani Baragwanath Hospital [23] and global screening at an immunisation service in Kwazulu Natal showed significant discrepancies between verbally reported and actual maternal HIV status respectively where 6.7% women who reported a negative status were HIV-positive [24].

The issue of HIV testing during pregnancy has been widely studied since the time that HIV was discovered and paediatric AIDS occurred in clinical settings. Paediatric AIDS was linked with the virus now known as HIV in 1985 [25] and in December 1985 the Mortality and Morbidity Weekly Report (MMWR) of the CDC published guidelines for the approach to pregnant women and prevention of transmission [26]. In the years following this, these guidelines were expanded with the introduction and registration of the first HIV rapid tests to be used in pregnancy. Most countries now have extensive PMTCT and HIV testing guidelines tailored to suit the country's population, HIV prevalence and specific needs.

Currently, in South Africa, the HIV status established at the antenatal clinic is not written onto the woman's antenatal card in plain text. It is written as a code using a standardised coding mechanism that relies on the first letter of the mother's name and that of her own mother. This code has to be decoded by labour ward and

postnatal staff for the mother to be identified as either HIV-positive or negative. This system is a controversial issue offering confidentiality of the mother's HIV status but problems with correct decoding and identification of HIV-positive women at the various points of care.

The new South African PMTCT policy places an emphasis on routinely offered testing for pregnant women. The issue of HIV testing in labour for women who were not tested during antenatal care has also been studied extensively, both in terms of test-acceptance and impact on efficacy of PMTCT [27, 28]. Essentially the emphasis is always to be placed on antenatal testing and repeat testing but for those women not identified antenataly for whatever reason, one study concludes: "Rapid HIV testing and counseling in labour is a useful practice in high prevalence settings" [29]. Testing around the time of labour opens the door for mother-infant pairs to access some antiretroviral prophylaxis when there was not that opportunity during the pregnancy. If diagnosed pre-delivery there is a chance to administer the doses of sdNVP and AZT to the mother and if only diagnosed post-delivery the baby can be given post-exposure prophylaxis in the form of sdNVP and AZT. Evidence has also come to light that the vertical HIV transmission to infants from mothers who are unaware of their HIV status is higher than in those who know that they are HIV-positive [24]. Maternal HIV infection during late pregnancy or during breast feeding may account for up to 40% of infections in infants according to a study in Botswana [30]. These are very important findings that emphasize the need to prevent HIV in pregnant women and retest during later pregnancy and lactation.

Loss to follow-up from PMTCT both antenataly and postnataly is a serious problem. Manzi et al report a cumulative loss to follow-up of more than 75% between initial maternal test and six-month postpartum visit in a district hospital setting in Malawi [31].

Lessons learnt from these studies should be used to develop useful protocols for the South African setting. To institute programs it is advisable to establish the success of published best practice and experience in large local settings. Should such a protocol, tried out in a routine public service setting show similar successes one can motivate for its wider spread duplication and adoption in similar settings throughout the country. This study thus aims to investigate whether a peri-partum HIV testing protocol for women at delivery translates into improved access to PMTCT, early testing and treatment of children.

1.4 Infant PCR Testing – PMTCT Impact

Apart from addressing whether or not routine counseling and testing identifies significant numbers of new women for the PMTCT program, the question of whether a routine counseling and testing service identifies additional HIV-exposed infants around delivery and translates into a lower transmission rate arises.To document a reduced transmission rate following a “post-exposure only” intervention, treated infants have to be tested which has proven to be complicated by loss to follow-up [32].

1.5 Study Setting

1.5.1 History of RMMCH PMTCT Involvement

RMMCH has a history of proactive involvement in the PMTCT program that has operated since 1997 [32, 33, 34]. The program at RMMCH offers all the components recommended by the South African national PMTCT guidelines. The facility has been host to various research protocols and staff members have been and are currently active members of provincial and national PMTCT working groups. Widely published research includes:

- Early Infant testing research [32, 33] which validates infant PCR testing at six weeks of age and shows that it is feasible in low-resource settings to both diagnose infants as well as assess PMTCT efficacy
- Programmatic research on starting women on triple ART during pregnancy and other aspects of PMTCT patient flow [34] which highlights that a focussed and monitored system of referral from antenatal to ART clinics reduces the time pregnant women have to wait for ART initiation significantly as well as highlighting the effectiveness of triple ART for PMTCT

1.5.2 The Obstetric Services at RMMCH

The “catchment area” that the hospital serves is predefined but differs depending on the service provided.

1. The RMMCH antenatal clinic functions at two levels each having different catchment areas:
    a. It provides primary antenatal care to pregnant women from the geographical area surrounding the hospital.
    b. It acts as a secondary level referral centre for high risk women from designated surrounding clinics.

2. The RMMCH delivery service also functions at different levels:
    a. It is the delivery site for all women from the surrounding geographical area.
    b. It is the delivery site for designated clinics in the surrounding area that do not have a labour ward.
    c. It is the referral centre for obstetric emergencies and obstetric “high risk” women from the surrounding clinics and hospitals.

Therefore the population that delivers at the hospital is not the same as the population that booked for antenatal care at the hospital. Similarly, HIV testing rates and prevalence rates documented at the hospital’s antenatal clinic cannot be assumed to apply to the population that delivers at the hospital. The HIV testing

rate at the hospital's antenatal clinic has been more than 95% over the last three years (personal communication, Lebogang Phakathi, PMTCT data manager, RMMCH). The HIV prevalence in the labour ward is unknown as it has not formed part of routine PMTCT reporting requirements, but will depend on the quality of HIV testing and counseling provided at RMMCH ANC and other centres.

RMMCH has an annual number of deliveries of approximately 10 000 to 12 000 translating into roughly 850 to 1000 deliveries per month which are accommodated by the following obstetric ward services:

- Antenatal Ward (30 beds) with a high care unit (three beds)
- Labour Ward Admissions Ward (ten beds)
- Labour Ward (six stage rooms/beds)
- Postnatal Wards
    - Normal Deliveries (22 beds – between 700-800 admissions per month)
    - Post-Caesarean Section Ward (20 beds – approximately 200 admissions per month)
- Note on stillbirths: Due to the psychological trauma associated with stillbirths, women whose babies are not alive at birth are admitted to the gynaecological wards of the hospital for postnatal care.
- Note on women with infants born before arrival at hospital: Women who deliver before they reach the hospital are admitted in the same postnatal ward as women who deliver at the hospital.

The time from presenting in labour to discharge post-delivery is generally less than 24 hours. Despite this short time it presents a window of opportunity because it is the one time that the vast majority of pregnant women (including those that delivered their infants before reaching the hospital on time) are in the hospital and as such a “captive population” to maximise service delivery.

Pregnant women in labour are admitted to the labour ward admissions ward and it is at this point that their antenatal cards are checked by the attending staff. Decisions regarding provision of prophylactic ART for PMTCT are initiated here.

1.5.3 RMMCH Postnatal Ward Population

Given the diversity of the postnatal population at RMMCH, a pilot survey was done in the postnatal wards in 2007 to identify the major groups that make up this population. They were identified and are briefly described below:

Women who had attended antenatal services before, came from:

- RMMCH ANC: located on the same premises as the delivery ward. It serves the local area just west of the Johannesburg central business district. The communities are diverse in terms of socio-economic status, but consist predominantly of low to middle income women largely residing in houses.
- Witkoppen Health Centre ANC – a government/non-governmental partnership site located north of Johannesburg and serving largely low

income women from informal settlements. The site does not have facilities to deliver women and hence refers all women who booked there antenataly to RMMCH for delivery.

- Diepsloot ANC – a government clinic situated within the Diepsloot township north of Johannesburg. The township originated in the last twenty years and is largely an informal settlement. A high number of foreigners as well as refugees live in this area and it was affected by social unrest during the study period. There is no delivery facility and all deliveries are referred to RMMCH.
- Discoverers Community Health Centre ANC – a government clinic situated west of Johannesburg serving a large area which includes both informal and formal settlements, many of which have been in existence longer than the Diepsloot area. The facility has a delivery ward where low-risk women are delivered. Any concerns or signs of risk trigger a referral to RMMCH for delivery.
- Other clinics that women had booked at included various other smaller clinics like clinics in other provinces or even other countries as well as private facilities.

Unbooked Women:

- “Unbooked” women arrive for delivery without history or documentation of having booked for antenatal care.

1.5.4 PMTCT Interventions at RMMCH

At each point the intervention depends on the knowledge of the health care worker that the woman needs the intervention i.e. the woman tells the health care worker her status and/or it is clearly documented (by means of the coding system) in her antenatal card. RMMCH offers the following services to HIV-infected pregnant women and their infants as recommended by the national PMTCT policy.

Antenatal:

- After diagnosis as HIV-positive, women are offered CD4 count testing and a bedside Haemoglobin assay.
- CD4 Count greater than 200 x 10^6/litre:
  - If the Haemoglobin level is more than 8 g/dl women are given AZT 300mg twice daily to take home when they are at 28 weeks of gestation or more. If the Haemoglobin level is less than 8g/dl women are investigated for causes of anaemia before commencing AZT.
- CD4 Count less than 200 x 10^6/litre:
  - Women are fast tracked onto triple ART started at antenatal clinic once the woman has completed readiness counseling.
- General counseling is done on the topics of adherence to ART (AZT or triple treatment), infant feeding choices of either exclusive breast or exclusive formula feeding and women are issued with sdNVP to be taken as soon as labour commences. Women are also informed about the need

to have their babies tested when they reach six weeks of age and that the baby will need to be given AZT and NVP syrup after being born.

Labour and Delivery:

- sdNVP is taken by the mother and for those who had not received the tablet antenataly, it is dispensed in the ward.
- AZT 600mg is given on arrival and AZT 300mg is continued 12 hourly if labour is prolonged. AZT to the mother is then stopped once the infant has been delivered.

Postnatal:

- Infants are given sdNVP (0.6ml=6mg) syrup and commenced on AZT (1.2ml=12mg) syrup to be continued twice daily for either seven or 28 days (28 days if the mother received less than four weeks of antenatal ART prophylaxis).
- Infant feeding choice is rediscussed and mothers electing to exclusively formula feed are issued with their first tins of NAN Pelargon milk.
- All HIV-exposed infants are referred for HIV PCR testing at six weeks of age which is preceded by a registration and information visit when the baby is two weeks old. Women who had initially booked at clinics other than the RMMCH antenatal clinic are referred back to those clinics for HIV PCR testing.

Infant Visits:

- Two week registration, counseling and information session.
- Six week infant test, all infants started on cotrimoxazole prophylaxis.
- Ten week return for test results, cotrimoxazole stopped if infant is HIV-negative and not being breastfed.
- Breastfed infants are kept in follow-up and on cotrimoxazole and retested (if initially HIV-negative) six weeks after the cessation of breastfeeding.
- All HIV-infected infants are immediately referred into the HIV follow-up clinic at the same location where their care is continued.

Since the program's inception, there has been an emphasis on routine and early infant follow-up for HIV-exposed infants with provision of cotrimoxazole prophylaxis for all HIV-exposed infants until they could be proven to be uninfected. Routine infant HIV PCR testing was introduced in 2004 at the age of six weeks. The "source" of these routinely tested HIV-exposed infants has largely consisted of those infants born to women who were diagnosed as HIV-positive during their antenatal clinic attendance at RMMCH or other local clinics. It follows that infants born to mothers tested at antenatal clinics with high testing rates had the best chance to be identified at delivery, benefiting from both maternal and infant ARV prophylaxis and then being referred on for PCR testing. Babies born to women who did not know their HIV status at the time of delivery were unlikely to receive any ARV prophylaxis or be referred since there was no protocol in place for this.

Since 2005, all infant tests done routinely (i.e. at six weeks of age in babies known to be exposed) have been captured on an electronic database to facilitate statistics reporting. All HIV-infected infants are referred to the HIV treatment clinic for monitoring and initiation of antiretroviral therapy when indicated. This flow of patients has made it possible to present information on clinical progression and need for ART in HIV-infected infants [35, 36]. The rate of HIV transmission to infants born to HIV-infected women has been demonstrated to be under 10% in this largely formula fed population [32, 33, 34].

The program requires that infants born at RMMCH, but originating from antenatal clinics further afield be tested at those clinics rather than at RMMCH. Outreach and training provided the necessary skills and since 2006 a process of "down-referral" for infant testing ensued which has led to a reduction in the routine infant testing at RMMCH. Since then and with the advent of AZT provision in March 2008, there has been a growing emphasis on maternal testing rates at the antenatal and delivery services to ensure that there were no missed opportunities in terms of enrolling pregnant women into the PMTCT program.

1.5.5 Monitoring and Evaluation of PMTCT

The five main indicators used by the South African DOH to report on the quality of PMTCT before the introduction of AZT to the protocol are described below. The process of establishing new indicators and reporting tools to accommodate the addition of AZT is still in progress. The indicators are described to show the

reporting framework and to point out that the concept of “HIV testing uptake” and “HIV prevalence” in women is very much the focus of only the antenatal indicators (1-3). The labour ward and infant testing indicators (4 and 5) rely very heavily on HIV testing antenataly as well as on accurate communication of results (on the antenatal card) to the delivery and postnatal staff. The coding system of HIV results on the antenatal card is another systematic issue that has to work properly before the communication of the woman’s HIV status at the time of labour is possible, if the woman does not voice it herself. Only with this chain intact do the indicators show meaningful results.

1) **HIV testing rate in new antenatal women (new=first visit)**
    a) Numerator: New ANC attendees tested for HIV
    b) Denominator: All new ANC attendees
2) **HIV positivity rate amongst antenatal women**
    a) Numerator: New ANC attendees tested HIV-positive
    b) Denominator: New ANC attendees tested for HIV (1a)
3) **Nevirapine uptake rate in women (dispensing at ANC)**
    a) Numerator: number of ANC attendees given sdNVP to take home
    b) Denominator: New ANC attendees tested HIV-positive (2a)
4) **Nevirapine uptake rate in babies**
    a) Numerator: Nevirapine doses given to babies
    b) Denominator: Babies born to HIV-positive women
5) **HIV positivity rate in babies**
    a) Numerator: infants with positive PCR Results
    b) Denominator: Infants PCR tested

It is apparent that the first three indicators are more closely related to each other than the last two. Looking at the indicators listed above (specifically the denominator of the fourth indicator), one can see that this indicator only reflects reality if the number “infants born to HIV-positive mothers” is a true reflection of the number of HIV-positive women who delivered. With the introduction of AZT the indicators containing “Nevirapine” will be adjusted to include “dual-” or “multi-therapy” PMTCT. There is an inherent assumption that women know their status when they arrive for delivery or, that they will automatically be tested if they do not know their status. The following questions arise: How accurate is the reported number “Infants born to HIV-positive women” at RMMCH? How big is the gap between the total delivering population and the population of women who know their HIV status? Can routine testing around delivery improve this gap if it exists and improve access of infants to both prophylactic ART as well as infant testing? Monitoring and evaluation of the PMTCT program is crucial to improve service delivery and facilitate financial planning locally and at higher levels. The purpose of operational research around PMTCT at RMMCH is aimed at finding effective, affordable and reproducible interventions that prevent HIV infection and improve access to care in terms of the NSP 2007-2011.

Chapter 2 - Study Objectives and Hypothesis

2.1 Objectives

A. To assess the impact of a routine peri-partum maternal HIV testing service in the ante- and postnatal wards at RMMCH on the PMTCT program as measured by:
    1. An increase in number of women identified as being HIV-infected as a result of peri-partum HIV testing
        - Assess the ANC/pre-delivery HIV Testing dynamics for the whole and for each of the major groups that make up the RMMCH delivery population
            - Percentage of women knowing their HIV status on arrival for delivery
            - Percentage of women with improved knowledge of their HIV status (either changed status or found out their status for the first time) on leaving the facility post-delivery
        - Assess the reliability of verbal and documented HIV-negative status for women retested
    2. An increase in number of women and infants accessing prophylactic PMTCT medication around the time of delivery
    3. An increase in infants accessing early routine HIV testing
    4. The rate of transmission of HIV to the HIV-exposed infants identified

5. An increase in HIV-infected infants accessing HIV-related care
    - Access to prophylaxis against opportunistic infections
    - Access to the paediatric comprehensive HIV care, management and treatment (CCMT) service at RMMCH

B. To estimate the effect of a routine peri-partum testing service on the accuracy of the standard reported infant PMTCT uptake indicator.

2.2 Primary Null Hypothesis

Routine peri-partum HIV testing and counseling of women in the ante- and postnatal wards does not improve access to HIV prevention, testing and treatment for their infants.

Chapter 3 – Methods

3.1 Patient Selection and Sample Size

The study assessed an intervention at an operational level in the delivery and post-delivery service at RMMCH. A convenience sample of 2500 women, half of the population of women expected to deliver at RMMCH over the six-month study period, was chosen. Two full-time counsellors interviewed the women and obtained written informed consent for the study. Enrolment was conducted seven days a week between 07h00 and 16h00 on weekdays and 08h00 and 12h00 on weekends. Women discharged from the postnatal service on weekend afternoons or after 16h00 during week day afternoons were thus not enrolled in the study. On busy days an additional counsellor, usually stationed in the antenatal clinic, assisted the study counsellors to ensure that as many women delivering at the facility as possible were captured.

The counsellors did regular daily ward rounds in all obstetric wards, including the post-Caesarean section ward and the ward where mothers were admitted following normal vaginal deliveries. They interviewed all women with live births. The counsellors aimed to include all women on their register (Appendix A) which was an existing tool before the start of the study and part of the monitoring routine in the hospital aimed at assisting the nursing staff to capture accurate routine statistics and ensure identification of HIV-infected women. While entering the women on the register the counsellors had to ask questions regarding their HIV

status, booking site as well as postnatal plans. At this point women were invited to join the study and written informed consent (Appendix B) was obtained for those that agreed.

Eligibility Criteria:

1. Any woman arriving at the hospital in labour
2. Any mother in the postnatal ward having delivered a live baby.
3. Enrolment in the study occurred irrespective of the maternal HIV status (i.e. HIV-positive, HIV-negative or unknown) and the mother's willingness to undergo an HIV test.

Exclusion Criteria:

1. Women under the age of 18 years at the time of interview
2. Any women presenting without a live birth (e.g. miscarriage, stillbirth or voluntary termination of pregnancy).

Rapid HIV testing as per the national DOH protocol was considered necessary and offered if

- the woman's HIV status was unknown,
- there was a discrepancy between the HIV-status verbally reported by the woman and the status documented on the patient held antenatal card,
- the woman reported her status but no status was documented,
- the woman reported or had a documented HIV-negative status which was established more than six weeks ago.

If the offer of an HIV test was accepted, written informed consent for the test was obtained (Appendix B). Results were made available prior to discharge from the ward and generally within 45 minutes of venesection. Appropriate counseling and PMTCT related interventions were provided and efforts were made to ensure privacy and confidentiality by doing the counseling in a separate room. After the diagnosis was given, each newly diagnosed HIV-positive woman was counseled and given emotional support as well as an appointment for her next visit. Although rapid HIV tests were used, these were not performed at the bed side. There were usually five to fifteen samples to process daily and it was more practical to venesect all women and perform the rapid tests in a batch. These samples were processed by the trained laboratory technician or if not available (e.g. weekends or public holidays) by trained counselors supervised by nursing staff or the attending doctor in a dedicated side room located in the paediatric HIV clinic.

Women who were either known to be HIV-positive or who were newly diagnosed as positive following the above-mentioned testing protocol received the PMTCT interventions according to standard protocol at RMMCH.

A CD4 Count test was submitted for women newly diagnosed as HIV-positive with a return date for results two weeks later to coincide with the date of infant registration visit before testing. Since women who were diagnosed HIV-positive antenataly generally had CD4 count results and had their CD4 counts routinely repeated at the two week infant registration visit, their CD4 counts were not done at the time of delivery. The intended feeding choice as well as the intended infant

follow-up site was documented (Appendix A). HIV testing of partners and other children was offered to all HIV-positive women. If women brought their infants back to RMMCH for PCR testing, results were obtained directly from the laboratory as part of the clinic service. For all infants who did not return and may have been tested elsewhere, the National Health and Laboratory Service (NHLS) database was searched using infant surname and date of birth as identifiers to improve the quality of data and minimise the effect of loss to follow-up.

3.2 Explanation of Study Terms:

- Arrival status: This refers to the HIV status reported/stated by a woman when first interviewed in the delivery and/or post-delivery setting. This is also referred to as the “verbal status” in the results section. In terms of treating or preventing HIV the status reported verbally and therefore assumed to be “known” by individual women is conceptually important as it lays the foundation for women to acknowledge the need for and accept any treatment.

- Documented status: This is the HIV status that was found documented in the antenatal clinic card carried by the woman. The decision whether or not a woman was offered an HIV test or a retest depended on both verbal and documented status but in cases of uncertainty the documented status took precedence, i.e. if a woman said (verbal status) that she was tested HIV-

negative less than six weeks ago, but her antenatal card (documented status) showed that her HIV-negative result came from a test done more than six weeks ago, she would be offered a test. Similarly all women with discrepant verbal and documented status or with no documented status were offered a retest.

- Departure status: This refers to the HIV status newly established or already known to the woman by the time she was discharged post-delivery and had thus had the opportunity to go through the testing or retesting process that was offered.

An analysis was done for all women who reported an HIV-negative status and went on to have an HIV test to assess the negative predictive value (NPV) of a verbally reported HIV-negative status compared to a documented HIV-negative status.

3.3 Rapid HIV Tests

The standard HIV testing algorithm according to the DOH PMTCT policy [10] is represented below:

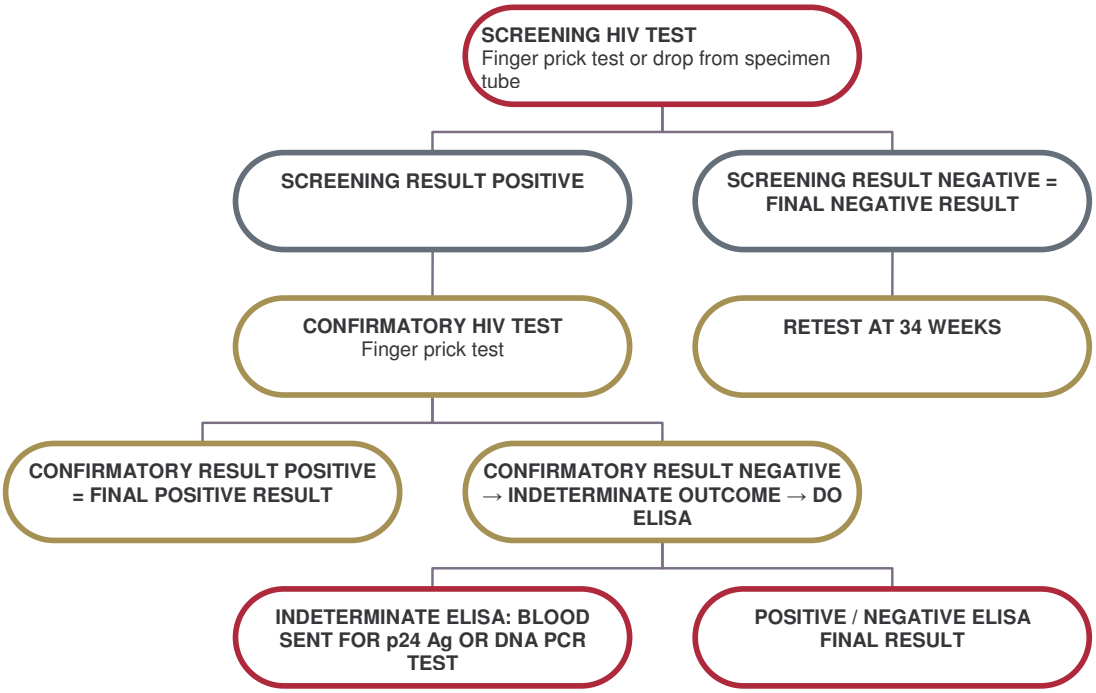


Figure 3.1: South African DOH Rapid HIV Testing Algorithm

The test kits on government tender during the study period were the SD Bio-line HIV-1/2 Version 3.0 (Standard Diagnostics Inc., Hagal-dong, Korea) as the screening test and the Acon HIV 1/2/0 Tri-line Rapid Test Device (Acon Laboratories, Inc., San Diego, USA) as the confirmatory test. During the study period counsellors and nurses involved with antenatal care raised concerns about these tests yielding false positive results and preferred using the 4th generation HIV Ag/Ab ELISA (Abbott Laboratories, Wiesbaden, Germany) tests done by the NHLS. To establish the validity of these concerns, 400 Determine^{TM} HIV-1/2 (Abbott Laboratories, Illinois, USA) were purchased and run concurrently with 400 antenatal standard protocol HIV tests. Accuracy of the individual kits and the DOH Rapid HIV test algorithm was determined by comparing the results with an HIV ELISA test for the first 200 tests run. Subsequently, 200 samples were run

checking all HIV-positive results with an HIV ELISA test. The DOH protocol includes an HIV ELISA test only if there is a discrepancy between the two rapid test results. The Determine kit has been available since 1989 and is considered a well validated, highly sensitive and specific rapid HIV test including in viral subtypes prevalent in Africa [37]. It is not routinely used in South Africa because it is not on state tender but it was used in this instance to provide an alternative if other tests performed poorly in the validation process.

3.4 Patient Consent and Ethical Considerations

Consent for HIV testing outside of the study was routinely sought in writing as per standard practise (Appendix C) and women had the choice to refuse an HIV test. Informed consent for involvement in this study was sought with consent for an HIV test where necessary at the same time (Appendix B). All patient information was kept confidential as per standard practise. A submission was made to the ethics committee of the University of the Witwatersrand to report on the study findings as well as to enrol patients in the study and this was unconditionally approved on the 4th of April 2008 (Protocol number M080203 – Appendix D).

3.5 Statistical Methods and Analysis

Results were captured on the register (Appendix A) and the information was entered into a Microsoft Access 2003 database. Data was checked prior to and following entry into the electronic database. For the purposes of confidentiality of the study group, a separate database was extracted from the main database which did not contain any patient identification other than a study number and this was only available to the principal investigator. All consent forms and paper registers (Appendix A) containing routinely collected data were locked away. Only the principal investigator knew which women were part of the study when women returned for infant testing. Data gathered from the Microsoft Access database were analysed using Microsoft Excel spreadsheets as well as SAS version 9.1 (2002-2003 by SAS Institute Inc., Cary, NC, USA). Basic descriptive statistical methods where used in the analysis of the data. Statistical comparisons were performed using the Chi-square test for categorical variables and for non-parametric data with small numbers the Fisher Exact test was used.

3.6 Measurable Outcomes

Pregnant Women and Mothers:

From the routinely completed ward register (Appendix A):

I. Total number of women interviewed
II. Total number of women enrolled in the study

Women from the latter group were then stratified into the following groups

1. Women with positive HIV status
2. Women with unknown HIV status who either
    a. Refused an HIV test or
    b. Tested HIV-positive or
    c. Tested HIV-negative
3. Women with negative HIV status (stratified further into reported versus documented and into those tested less than six weeks ago, six to twelve weeks ago or more than twelve weeks ago) who either
    a. Refused an HIV test or
    b. Tested HIV-positive or
    c. Tested HIV-negative

All women were stratified according to their original booking site, and per booking site women were stratified according to points 1) and 2) above

HIV-exposed Infants:

Outcomes were stratified according to: two groups of infants:

1. Infants born to women with a known HIV-positive status at the time of delivery because PMTCT services had been accessed antenataly.
2. Infants born to women whose HIV-positive status was first established in the peri-partum period as a result of this study and who then accessed

PMTCT services around the time of delivery. This group also included infants born to women who had initially tested HIV-negative during antenatal care.

These two groups were then compared with regard to their

1. Total numbers
2. Type of PMTCT drug intervention accessed
3. Rates of return for early infant testing at six weeks of age and concurrent initiation of cotrimoxazole prophylaxis
4. Vertical transmission rates at six weeks of age
5. Rates of access to the RMMCH CCMT service for antiretroviral therapy for infants diagnosed as HIV-infected.

3.7 Expected Beneficial Outcomes not Directly Measured

An increased number of women would be more knowledgeable about HIV and their own HIV status. If they tested negative they would potentially benefit by maintaining a negative HIV status. If they tested HIV-positive they would benefit by accessing care for themselves and their families. HIV-positive women would be able to prevent future pregnancies or plan them more carefully taking into consideration risks to themselves and a future child. These benefits would address both the first two prongs of the WHO PMTCT approach, albeit for future pregnancies in these individuals. There could also be a benefit in terms of general

increased knowledge and awareness about HIV infection and its consequences and available treatments which could lead to greater compliance later with HIV care.

3.8 Funding

Funding for the counsellors and data-capturers was secured through a PEPfAR (President's Emergency Plan for AIDS Relief, USA) grant through the US Centers for Disease Control and Prevention directed at work promoting identification of HIV-infected infants early in life. The HIV preventative and treatment related service delivery of the RMMCH Empilweni HIV Clinic was supported by the University of the Witwatersrand Paediatric HIV Clinics, also known as ECHO (Enhancing Children's HIV Outcomes). Computers and software at RMMCH were used to capture and analyse results.

Chapter 4 – Results

4.1 Source of Study Population – Women 18 Years or Older

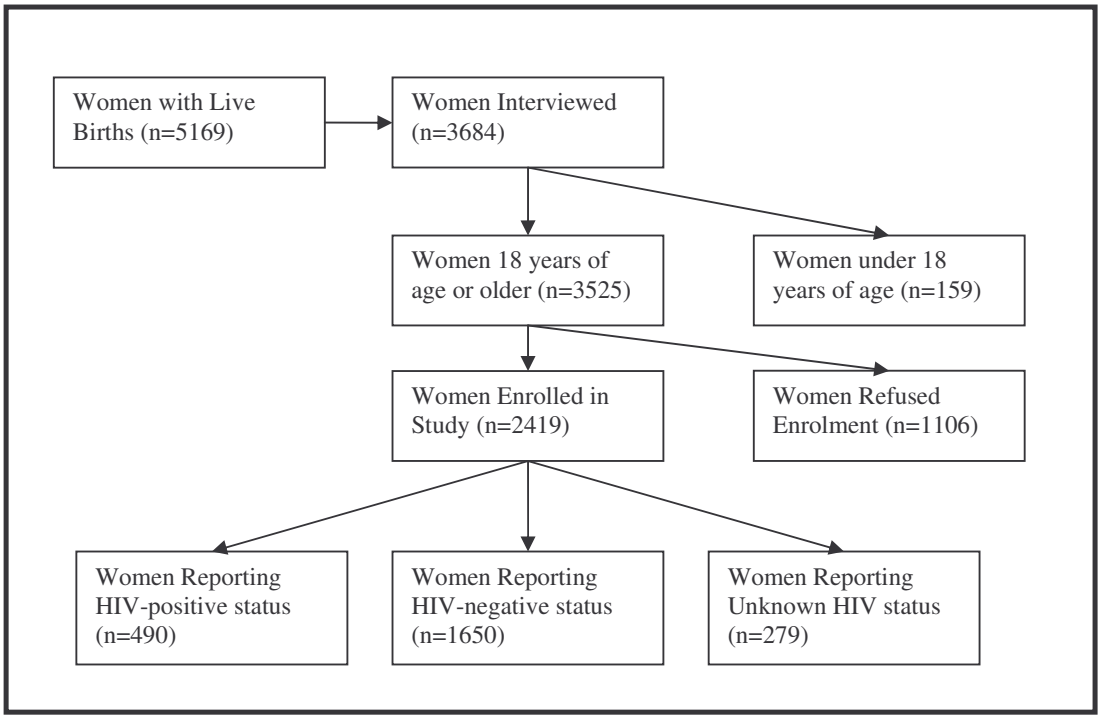


Figure 4.1: Overview of Study Population. The women interviewed were a subset of the women with live births during the study period and enrolled women formed a subset of the women interviewed with those under the age of 18 years being excluded.

During the study period of 167 days (five and a half months between the 9th of April and the 23rd September 2008), 3684 (71.3%) women out of 5169 women with live births were interviewed around the time of delivery in the RMMCH obstetric wards. Of the 3684 women interviewed, 2419 (65.7%) were enrolled in the study. This means that during the study period 46.8% of all women with live births were enrolled, slightly less than the 50% convenience sample aimed for in the study

design. The study aimed to enrol half the women presenting for delivery, but the counsellors' working hours, consent refusal and the fact that about 5% of women delivering were under 18 years old meant that only 46.8% of the total delivering population was enrolled.

Figures 4.2 and 4.3 highlight the diversity of the enrolled population in terms of antenatal booking history.

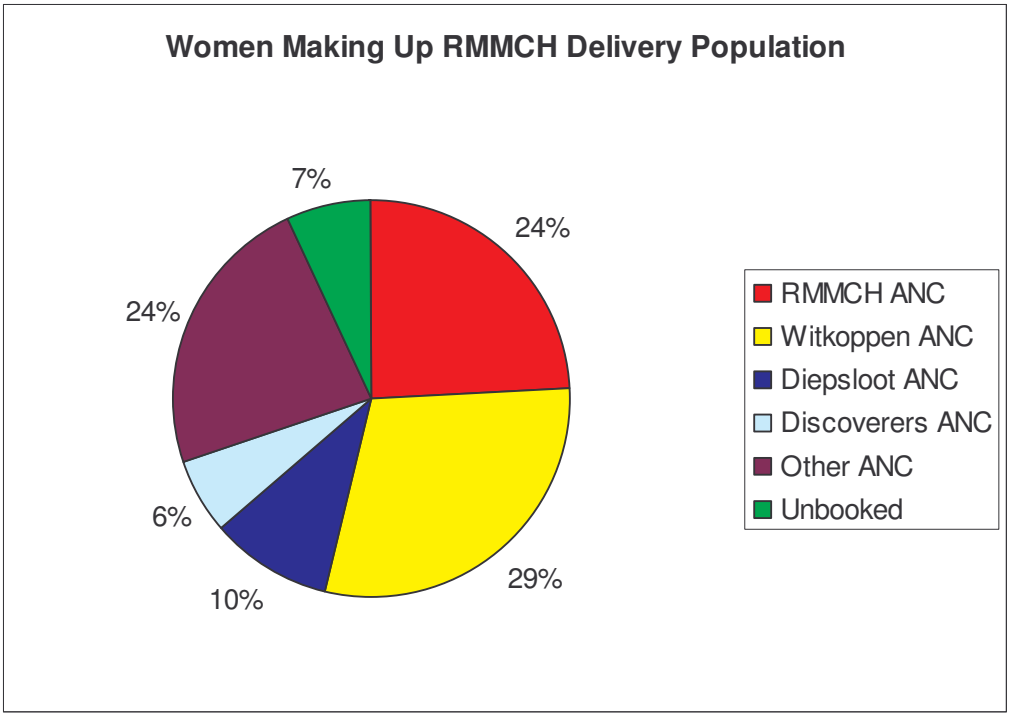


Figure 4.2: Booking History of Enrolled Women (n=2419)

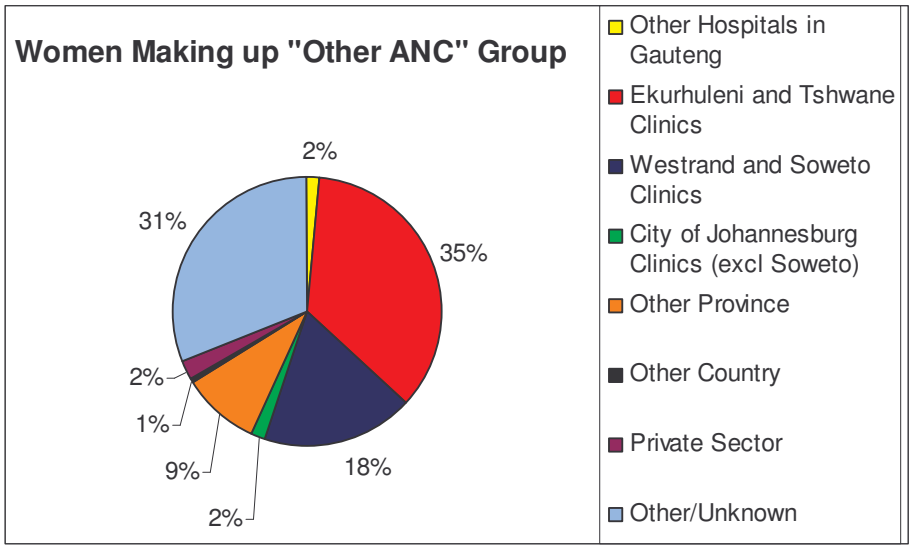


Figure 4.3: Geographical Distribution of Antenatal Bookings in the "Other ANC" Group (n=568). A large percentage (24% in Figure 4.2) of the enrolled population received antenatal care outside the RMMCH catchment area with more than 57% booking at antenatal clinics in Gauteng province. The "Other/Unknown" group in this figure were women who had evidence of having received antenatal care, albeit that the clinic name had not been captured by the counsellors.

4.2 Study Progress and Representativity of the Study Sample

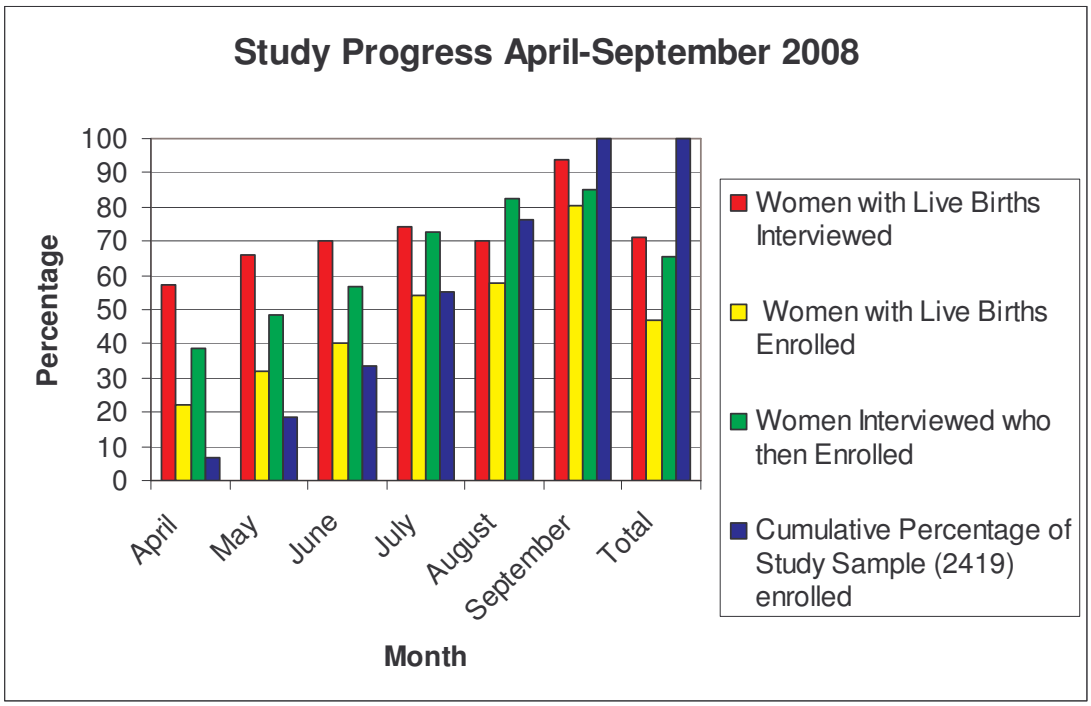


Figure 4.4: Progress of Study Recruitment Over Time. The study enrolment pattern changed over time as progressively higher percentages of interviewed women were enrolled [ ]. In the first three months 36% of the study sample was enrolled.

Although two thirds of the study sample was enrolled in the second three months of the study creating the potential for bias, the study results did not change over time.

Baseline variables routinely collected at RMMCH for the interviewed population were compared to the enrolled population to determine whether statistically significant differences were evident (Table 4.1). The median age of all women interviewed excluding those that were under 18 years of age (n=3525) was 25.94

years and the median age of the enrolled group was 25.85 years. Both groups had the same inter-quartile range of 22.5 to 30.6 years and no statistically significant difference was found (p=0.70) between the two groups. No other baseline variables (e.g. parity) were available for comparison.

Contribution by each subgroup	**Interviewed** (n=3684)	**Enrolled** (n=2419)	**p-value (Chi-square)**
RMMCH ANC	900 (24.4%)	577 (23.9%)	0.61
Witkoppen ANC	1060 (28.8%)	710 (29.4%)	0.63
Diepsloot ANC	373 (10.1%)	238 (9.8%)	0.72
Discoverers ANC	232 (6.3%)	150 (6.2%)	0.88
Other ANC	857 (23.3%)	568 (23.5%)	0.84
Unbooked	262 (7.1%)	176 (7.3%)	0.81
Women knowing their HIV status on arrival for delivery	3246 (88.1%)	2140 (88.5%)	0.67

Table 4.1: Comparison of Interviewed and Enrolled Women Delivering at RMMCH. No significant differences were noted in the distribution of antenatal booking history or knowledge of HIV-status on arrival between interviewed and enrolled population of women.

The convenience sample of 2419 enrolled women comprising 46.8% of all live births during the study period was representative of the 3684 interviewed women who comprised 71.3% of all women with live births during the study period. Bias in remaining 28.7% of women cannot be excluded however it was unlikely on grounds that the women that were not interviewed were different only in terms of being discharged during weekend afternoons or late weekday afternoons. The study outcomes therefore apply to at least 71% of all women delivering live births at RMMCH.

4.3 Accuracy of HIV Rapid Tests and Algorithm

HIV ELISA results on samples from 200 pregnant women were used as the standard against which the performance of individual rapid test kits and the DOH testing algorithm were measured (Table 4.2).

		HIV Status (HIV ELISA result)		Statistical Indicators			
		Positive	Negative	Sens	Spec	PPV	NPV
SD Bio-line HIV-1/2 Version 3.0	Positive	27	0	100%	100%	100%	100%
	Negative	0	173				
Acon HIV 1/2/0 Tri-line Rapid Test Device	Positive	27	2	100%	98.8%	93.1%	100%
	Negative	0	171				
Determine™ HIV-1/2	Positive	27	0	100%	100%	100%	100%
	Negative	0	173				
DOH Serial Rapid Algorithm	Positive	27	0	100%	100%	100%	100%
	Negative	0	173				

Table 4.2: Accuracy of Rapid Kits and Serial DOH Algorithm. No false positive or false negative results were noted when the routine rapid test algorithm was used despite the Acon HIV 1/2/0 Tri-line test yielding two false positive results. “Sens” = sensitivity, “spec” = specificity, “PPV” and “NPV” = positive and negative predictive value respectively.

The subsequent 200 women tested demonstrated 100% specificity with the DOH algorithm using the HIV ELISA result as the standard and 100% sensitivity and specificity in comparison to the Determine™ test. Although the serial DoH

algorithm was 100% sensitive and specific, the false positive results for the confirmatory test (Acon) are worrying in that these highlight a potential for falsely diagnosing women as HIV-infected if the protocol is not correctly adhered to.

4.4 Enrolled Population and Study Objectives

4.4.1 Identification of Additional HIV-positive Women

HIV Status Reported by Women on Arrival for Delivery

The HIV status reported in the initial interview was a positive status in 490 (20.3%), a negative status in 1650 (68.2%) and an unknown status in 279 (11.5%) women (Figures 4.1 and 4.5).

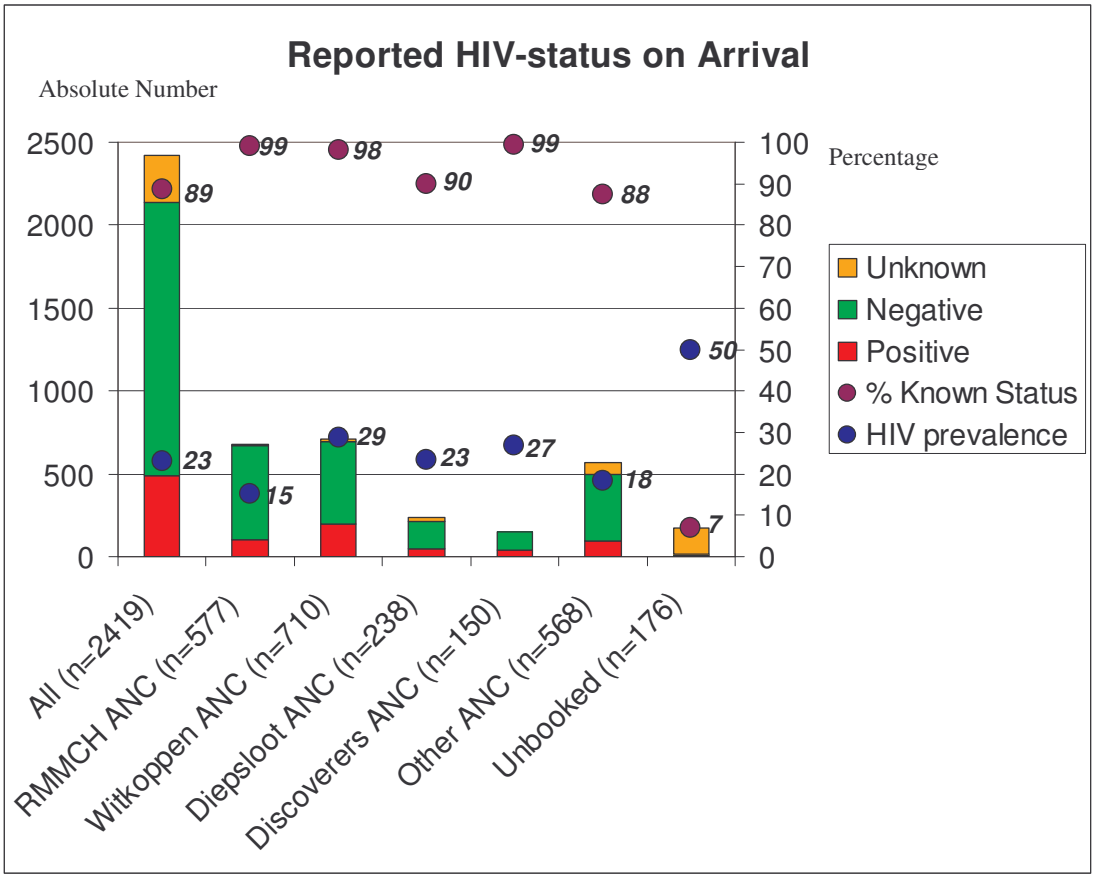


Figure 4.5: Reported HIV Status on Arrival. Knowledge of HIV status and HIV prevalence differs between groups of women from different antenatal sites.

A high percentage of women who booked at RMMCH, Witkoppen and Discoverers ANC reported knowing their HIV status in comparison to women booking at Diepsloot and other ANC's. Where women had not received antenatal care, there was both a strikingly low knowledge of their HIV status and high HIV prevalence. The heterogeneity with respect to knowledge of HIV status and HIV prevalence of the delivering population at the regional delivery site (RMMCH) in comparison to the antenatal clinic at RMMCH is highlighted.

Women Reporting an HIV-negative Status

Women reporting an HIV-negative status were offered a retest if they reported an HIV-negative status established more than six weeks prior to enrolment (Table 4.3).

	Total reported HIV-negative	Total offered retest	Retest Refused	Retest positive
All Women in group	1650	815 (49.4%)	47 (5.8%)	32 (4.2%)
Negative 6-12 weeks ago	815	402 (49.3%)	22 (5.5%)	17 (4.5%)
Negative >12 weeks ago		413 (50.7%)	25 (6.1%)	15 (3.9%)
RMMCH ANC	469	130 (27.7%)	8 (6.2%)	1 (0.8%)
Witkoppen ANC	496	281 (56.7%)	13 (4.6%)	2 (0.7%)
Diepsloot ANC	164	76 (46.3%)	7 (9.2%)	10 (14.5%)
Discoverers ANC	109	63 (57.8%)	5 (7.9%)	1 (1.7%)
Other ANC	406	260 (64.0%)	14 (5.4%)	18 (7.3%)
Unbooked	6	5 (83.3%)	0 (0%)	0 (0%)

Table 4.3: Test Acceptance and HIV Prevalence in Women Reporting an HIV-negative Status. The difference between refusal and positive testing rate in women reporting a negative result six to twelve weeks ago versus women reporting a negative result more than 12 weeks ago was not statistically significantly different on a chi-square test (p=0.72 and 0.67 respectively).

In total, 835 (50.6%) of 1650 women who reported an HIV-negative status had been tested within the preceding six weeks. Using the cut-off of having had an HIV test more than six weeks ago as a criterion for offering a retest revealed that 32

(4.2%) of this group had either seroconverted in late pregnancy or had reported their HIV status incorrectly. The highest rates of “seroconversion” were seen in the Diepsloot and “Other ANC” groups, the same two groups that had slightly lower knowledge of HIV status amongst ANC attendees (Figure 4.5).

These mother-infant pairs would have been missed had they not been offered a retest.

Women Reporting an Unknown HIV Status

All 279 women in this group were offered a test but 33 (11.8%) refused. Of the 246 (88.2%) who consented, 69 (28.0%) tested positive (Table 4.4).

	Total (n=279)	**Refused Test** (n=33)	**Test positive** (n=69)
RMMCH ANC	6	0 (0%)	2 (33.3%)
Witkoppen ANC	13	2 (15.4%)	5 (45.5%)
Diepsloot ANC	24	2 (8.3%)	7 (31.8%)
Discoverers ANC	1	0 (0%)	1 (100%)
Other ANC	71	12 (16.9%)	10 (16.9%)
Unbooked	164	17 (10.4%)	44 (29.9%)

Table 4.4: Test Acceptance and Prevalence in Women Reporting an Unknown HIV Status.

The percentage of women who refused a test has the total number as a denominator while the percentage of women who had a positive result has the number of women agreeing to a test as its denominator.

Although the numbers were small in women with unknown HIV status on arrival the HIV prevalence amongst those tested in this group approximated the prevalence figure for Gauteng (30.3%) from the 2007 anonymous survey [2].

Women reporting an HIV-positive status

Only seven (1.4%) of 490 women reporting an HIV-positive status were offered a retest because no supporting documentation of their status was evident on their antenatal records. All seven women were confirmed to be HIV-positive.

Reliability of a Reported HIV-negative Status

To establish the reliability of a verbally reported HIV-negative status on arrival, the retesting results were stratified according to whether the women had documentation of their status or not (Table 4.5).

Documented HIV Status	Total (n=1650 reported HIV-negative)	Refused Test	Retest Positive	NPV of reported Status
HIV-Positive	7 (0.4%)	0 (0%)	6 (85.7%)	14.3%
No Documentation	64 (3.9%)	4 (6.3%)	9 (15.0%)	85.0%
HIV-negative	1579 (95.7%)	43/744 (5.8%)	17 (2.4%)	97.6%

Table 4.5: Reliability of Reported HIV-negative Status. The 835 women not retested had documentation of a recent HIV-negative result (less than six weeks before).

Of all women who enrolled in the study there was one who was falsely diagnosed as HIV-positive according to her documented antenatal result. Women who reported a negative result when their antenatal card showed a positive result were more likely to be HIV-positive than women with no documentation or with a documented HIV-negative status as demonstrated by the increasing NPV. With a verbally reported HIV-negative status, women without documentation had a higher chance of being infected ($p<0.001$).

Change in Knowledge of HIV Status between Arrival to and Departure from RMMCH

The reported HIV status was compared to the departure status for all women after counseling and testing had been completed for those that qualified (Figure 4.6).

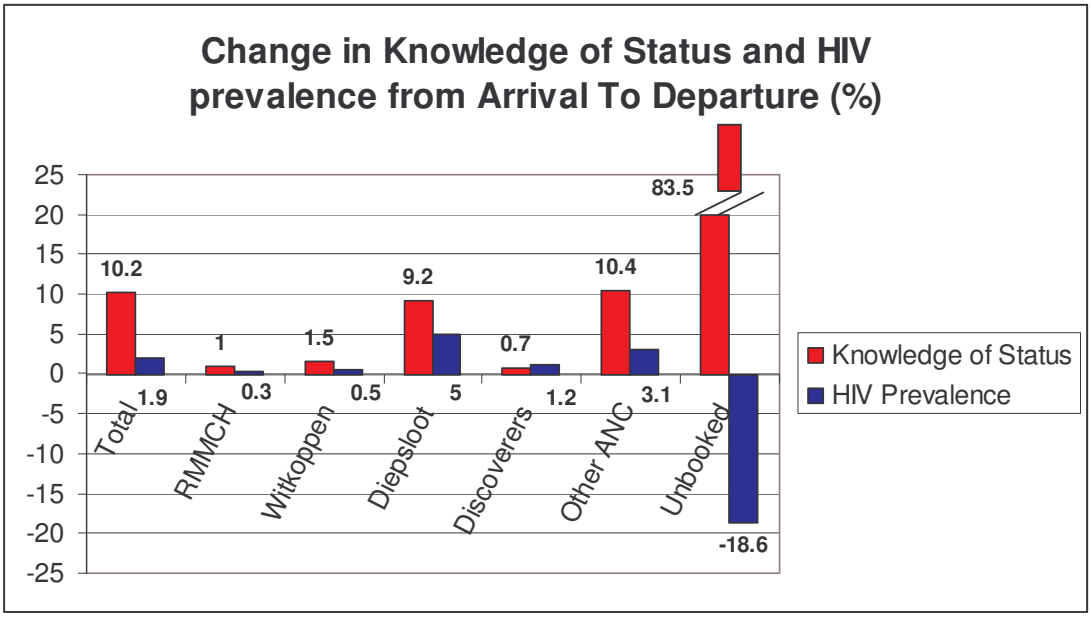


Figure 4.6: Change in HIV Prevalence and % Knowledge of HIV status. An increase in the level of knowledge of HIV status was seen in all groups but was highest in the unbooked group due to the high number of women of unknown status. The HIV prevalence increased in all groups except for the "Unbooked" group where it decreased from 50% to 31.4% as the number of tested women in this group increased from 12 to 159 women.

The difference in the number of women reporting a known HIV status on arrival versus those with a known HIV status on departure was 246 (10.2%) out of the total group of 2419 (Figure 4.6) with 33 (1.4%) of 2419 women leaving the postnatal service without a known HIV status. In addition 32 women who reported an HIV-negative status were shown to be HIV-positive after being retested. Therefore the number of women with improved knowledge of their status was actually 278 (11.5%) of 2419. They comprised 177 women with previously unknown HIV status that were newly identified as HIV-negative and 101 women newly diagnosed as HIV-positive comprising 7.3% and 4.2% of the enrolled

population respectively. The number of HIV-positive women identified increased by one fifth (20.6%) for the whole group (Table 4.6).

	Whole Group	RMMCH	Witkoppen	Diepsloot	Discoverers	Other ANC	Unbooked
A: Total Women	2419	577	710	238	150	568	176
B: Known HIV-positive on arrival	490	102	201	50	40	91	6
C: Newly diagnosed HIV-positive women	101	3	7	17	2	28	44
C as % of **A**	4.2	0.5	1.0	7.1	1.3	4.9	23.5
C as % of **B**	20.6	2.9	3.5	34.0	5.0	30.8	733

Table 4.6: Additional HIV-positive Women Identified. More than 4% of the total population were newly identified as HIV-positive originating predominantly from "Diepsloot", "Other ANC" and "Unbooked" subgroups.

Although only 872 (36%) of the total 2419 women (Figure 4.4) were enrolled in the first three months of the study, 39 (4.5%) were newly diagnosed as HIV-positive which is comparable to 101 (4.2%) of all 2419 women (Chi-square p-value=0.72). Identifying 101 additional HIV-positive women from the time of arrival for delivery to the time of departure represented a statistically significant increase in the number of infected women and therefore HIV-exposed infants identified (Chi-square $p<0.001$). Extrapolated over a one year period at RMMCH where there are 10 000 to 12 000 deliveries per annum there would be about 420 to 504 newly

diagnosed HIV-positive women amounting to 35 to 42 per month. Even if the study population was representative of only 71% of the women delivering live births, i.e. those interviewed during the study period, at least 25 to 30 additional HIV-positive women would be identified per month.

4.4.2 Increased Access to PMTCT Interventions

The process of interviewing and testing occurred largely in the postnatal as opposed to the labour ward since this was more practical and acceptable to the women. Counseling women for an HIV test at the time of the first stage of labour was not impossible but far less practical than after the delivery. Most women presented in the active rather than latent phase of the first stage and only eight of the 101 newly diagnosed women were tested pre-delivery. Those women who knew their HIV-positive status at arrival for delivery had usually (94.9% of cases) received PMTCT-related interventions like ART prophylaxis (Table 4.7) and counseling during their antenatal care. The 101 newly identified HIV-positive women were offered sdNVP and AZT syrup for their infants as well as infant feeding counseling. Of the eight women newly identified in the labour ward as being HIV-positive, six received sdNVP only and two received sdNVP and AZT (single) doses prior to the birth of their infants. The reason for the six women not receiving AZT was as a result of national guidelines recommending that women presenting in labour without having received AZT should receive only sdNVP. The two women who received single dose AZT should theoretically not have received

this. No multiple births were recorded in the enrolled women who were known or newly diagnosed HIV-positive.

The benefit of the study in providing additional PMTCT medications was inherently linked to the first objective of identifying more HIV-exposed women. This benefit could only be guaranteed for the doses administered by or under observation of the nursing staff. Once discharged from the hospital, the onus was on the mother to continue administering the AZT syrup. It was assumed that the support and counseling provided around the time of testing would have helped to encourage mothers to comply with treatment. This was not the case for at least two women where the reaction to the diagnosis resulted in refusal to comply with further PMTCT follow-up.

	HIV-positive Mothers and Exposed Infants	
	Known before delivery	**Newly diagnosed perinataly**
Total mother child pairs	490	101
PMTCT Drug interventions		
sdNVP and AZT to both a) mom > 4wks, baby 1 wk	120 (24.5%)	0 (0%)
b) mom < 4wks, baby 4 wks	189 (38.6%)	2 (2.0%)
HAART to mother and NVP, AZT to baby	83 (16.9%)	0 (0%)
NVP to both and 4-weeks AZT to baby	73 (14.9%)	6 (5.9%)
NVP and 4-weeks AZT to baby only	25 (5.1%)	91 (90.1%)
No prophylaxis	0 (0%)	2 (2.0%)
Infant Feeding Intention		
Exclusive breast-feeding	17 (3.5%)	6 (6.1%) of 98
Infant Follow-up Intention		
Infant follow-up at RMMCH	203 (41.4%)	83 (83.8%) of 99

Table 4.7: PMTCT Interventions in Known versus Newly Diagnosed HIV-positive Women. All the infants born to newly diagnosed HIV-positive women would not have received PMTCT-related interventions if the woman had not tested at the time of delivery. There were two mothers who refused to continue administering the prophylactic medications at home or to bring their infants for testing and these two and an additional mother refused to agree to exclusive feeding (breast or formula).

Of the women already known to be HIV-positive at the time of arrival for delivery, more than 60% had had some AZT and a quarter had received AZT for longer than four weeks by the time of delivery. Together with the 16.9% of women who were on triple therapy a total of 80% of women hailing from all antenatal clinics

had received PMTCT interventions according to the current PMTCT protocol. On the other hand 20% of all women previously diagnosed as HIV-positive had received no antenatal ART except sdNVP in 14.9%.

Exclusive formula feeding was the most commonly chosen infant feeding option by HIV-positive mothers. Women who were newly diagnosed as HIV-positive were requested to return to RMMCH for infant PCR testing and to receive their own CD4 count results from the sample submitted at diagnosis. More than 80% of these women reported an intention to return to RMMCH (Table 4.7).

4.4.3 Infant Follow-Up Dynamics

The cascade of events in following up HIV-exposed infants from the time of delivery is depicted in Figure 4.7.

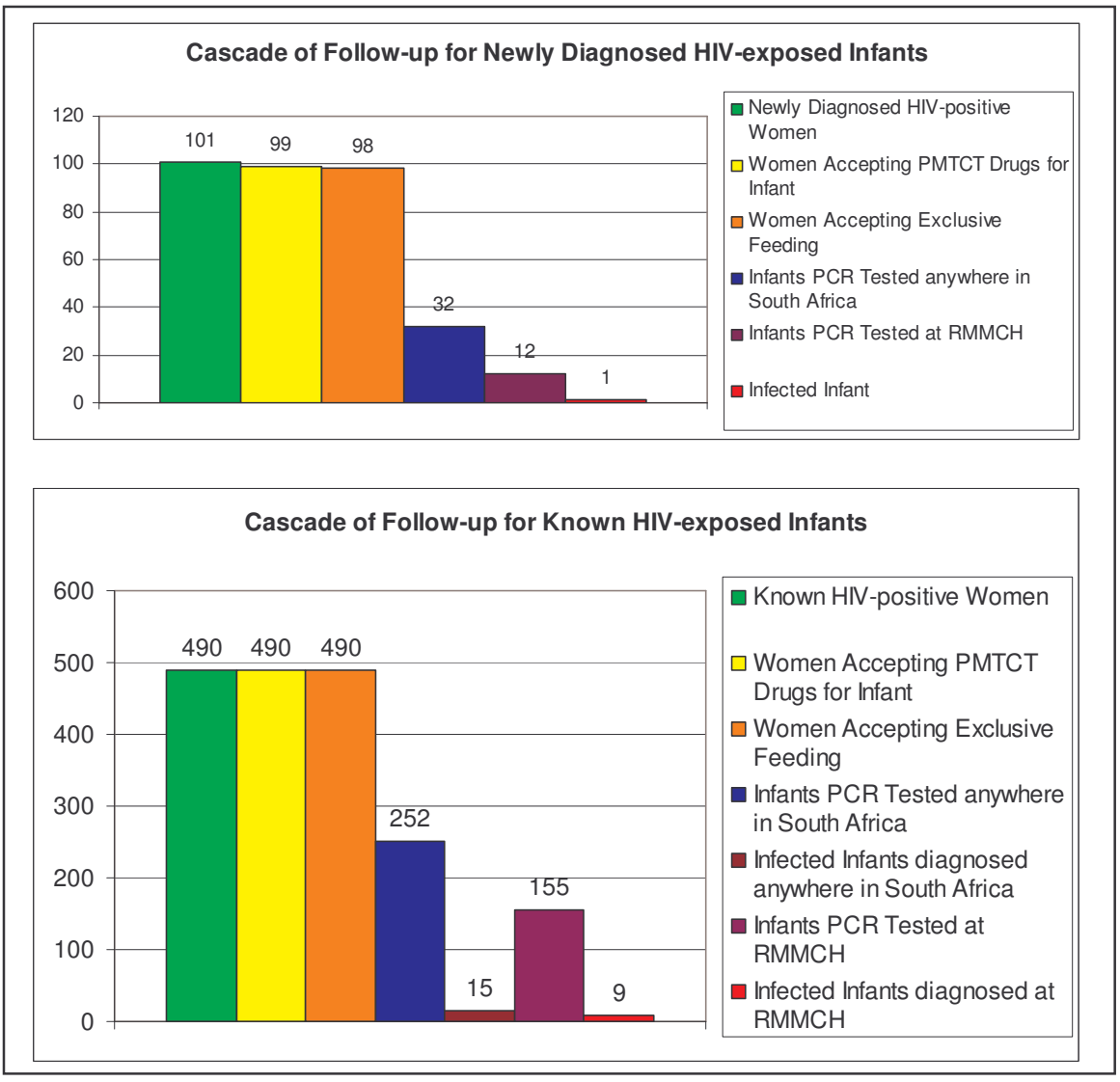


Figure 4.7: Cascade of Follow-up for Known and Newly Diagnosed HIV-exposed Infants.

After two mothers in the newly diagnosed group did not agree to continue follow-up the largest subsequent drop-off occurred with infant testing. As far as could be ascertained 49% and 67% of infants born to known compared to newly diagnosed HIV positive women respectively, did not receive a PCR test. The number of infants that received their PCR test result is unknown except for the infected infants diagnosed at RMMCH.

In total, 286 of the 591 (48.4%) HIV-exposed study infants were expected to attend the infant testing service at RMMCH (Table 4.7). Table 4.8 shows the follow-up and testing rates of these infants.

	All HIV-exposed Infants	**Infants expected for follow-up at RMMCH**		**p-value only for RMMCH tested infants**
		Infants known to be exposed before arrival for delivery	Infants newly diagnosed as exposed perinataly	
Total number expected	591	203	83	
Infants PCR tested and received cotrimoxazole	284 (48.0%)	155 (76.4%)	12 (14.5%)	<0.001 (Chi-square test)
PCR positive infants	16 (5.6%)	9 (5.8%)	1 (8.3%)	0.54 (Fisher exact test)

Table 4.8: Infant Follow-Up Dynamics. Cotrimoxazole prophylaxis was given to infants presenting at six weeks for an HIV test at RMMCH and it was assumed that other clinics followed the same protocol although this was not checked.

There were 97 PCR results (91 negative, six positive) traced from the NHLS database for infants born to women known to be HIV positive before arriving for delivery. Twenty results (all negative) were traced for infants born to women newly diagnosed by the study protocol. Combining traced results with the PCR results done at RMMCH, 32% (32/101) of infants to newly diagnosed mothers had a PCR done, although only 14.5% (12/83) of those expected to return to RMMCH arrived for PCR testing.

Loss to follow-up was a significant problem as 48 (23.6%) of 203 HIV-exposed infants identified antenataly and 71 (85.0%) of 83 newly diagnosed HIV-exposed infants due for testing at RMMCH did not return there. The rate of return in the newly diagnosed group was significantly lower (Table 4.8) showing that follow-up after a new maternal HIV diagnosis was poor. As the numbers were small the study objective of determining whether transmission rates differed between the known and newly diagnosed HIV-positive groups could not be answered. Of the ten infants diagnosed at RMMCH as HIV-infected nine were in care and one was lost to follow-up. Six infants had been initiated on ART (including the infant from a mother newly diagnosed at the time of delivery), two were awaiting ART initiation and one was being monitored for need of initiation.

4.4.4 Impact on Monitoring and Evaluation:

The **RMMCH antenatal attendees** formed less than a quarter of the **RMMCH delivering group** (Figure 4.2). This difference between the antenatal population and the delivering population at a facility is important because most national PMTCT indicators related to the identification of HIV-positive women focus on the monitoring of **antenatal** service delivery, for example antenatal testing rate and antenatal prevalence.

The HIV prevalence rate amongst women from different ANC services varied. The women attending RMMCH antenatal clinic had an HIV prevalence that was 10%

less than those attending the Witkoppen ANC. This demonstrates that the population of women attending the RMMCH delivery facility was heterogeneous with respect to their HIV risk. The HIV prevalence for the whole group (24.8%) was slightly lower than the national and Gauteng figures of 28.0% and 30.3% respectively for 2007 [2].

HIV prevalence at delivery is not a routine indicator of the PMTCT dataset. The “live births to HIV-positive women” form a subset of the “total live births” but there is no provision for distinguishing “live births to HIV-negative women” from “live births to women of unknown status” which are the other two subsets of “total live births”. A falsely low prevalence results if the number of “live births to HIV-positive women” is divided by “total live births” when not all women know their HIV status, yet the HIV prevalence at delivery is an important indication of how many infants should be receiving treatment and then proceed to infant testing following delivery. The HIV prevalence at delivery should not be much lower than the HIV prevalence found at antenatal services for the same population. The standard indicator of antenatal HIV prevalence versus the delivery HIV prevalence were compared to the study group HIV prevalence where 98.6% of women had a known HIV status (Figure 4.8).

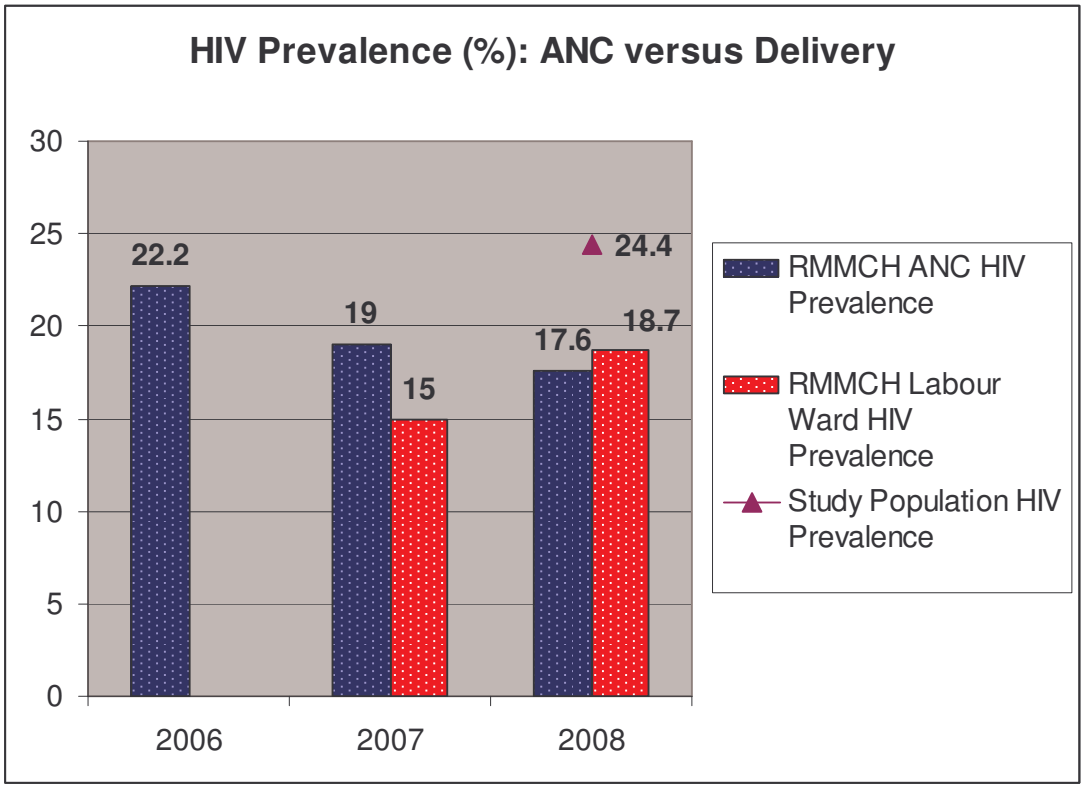


Figure 4.8: HIV Prevalence at RMMCH ANC versus RMMCH Delivery. The ANC HIV prevalence in 2008 (blue bars only) was statistically significantly lower than in 2006 ($p<0.001$). The downward trend of RMMCH ANC HIV prevalence is contrasted here with the upward trend of labour ward HIV prevalence from 15% to 18.7% ($p<0.001$). The HIV prevalence in both the labour ward and study group were calculated by dividing the number of "live births to HIV-positive women" by "total live births" without factoring in the number of women with unknown HIV status.

The downward trend in ANC HIV prevalence could be due to a decreasing prevalence in the local antenatal population. The increasing labour ward prevalence may reflect improved reporting as a consequence of this study and / or the higher HIV prevalence in women from ANC's other than RMMCH that fed into the delivery population. In enrolled women, a quarter of the total 2008 delivering population, the proportion of women with known HIV status increased by 10.2% to

98.6% between the time of arrival and departure from the delivery service (Figure 4.6). In 2008 the study HIV prevalence was significantly higher than the labour ward prevalence ($p<0.001$).

Figure 4.9 shows the number of known and additional theoretical number of HIV-exposed infants. There are potentially three groups of HIV-exposed infants: 1) those known to be HIV-exposed before the time of delivery, 2) those newly diagnosed as HIV-exposed due to the peripartum testing protocol, 3) those expected to be HIV-exposed where the mother refused a test. It was assumed that women who refused an HIV test had a high prevalence of 44% [22].

In PMTCT, “coverage” is defined as the proportion of HIV-exposed infants identified who receive appropriate ART. In the RMMCH postnatal ward every infant identified as HIV-exposed receives treatment unless the mother refuses. Therefore the only HIV-exposed infants who lost their opportunity for PMTCT prophylaxis completely are those whose mothers refused an HIV test. Irrespective of how many HIV-exposed infants remain unidentified, the reported “coverage” will remain 100%. The true “coverage” is that proportion of infants treated when the maternal HIV prevalence is extrapolated to include the group of women who refuse testing.

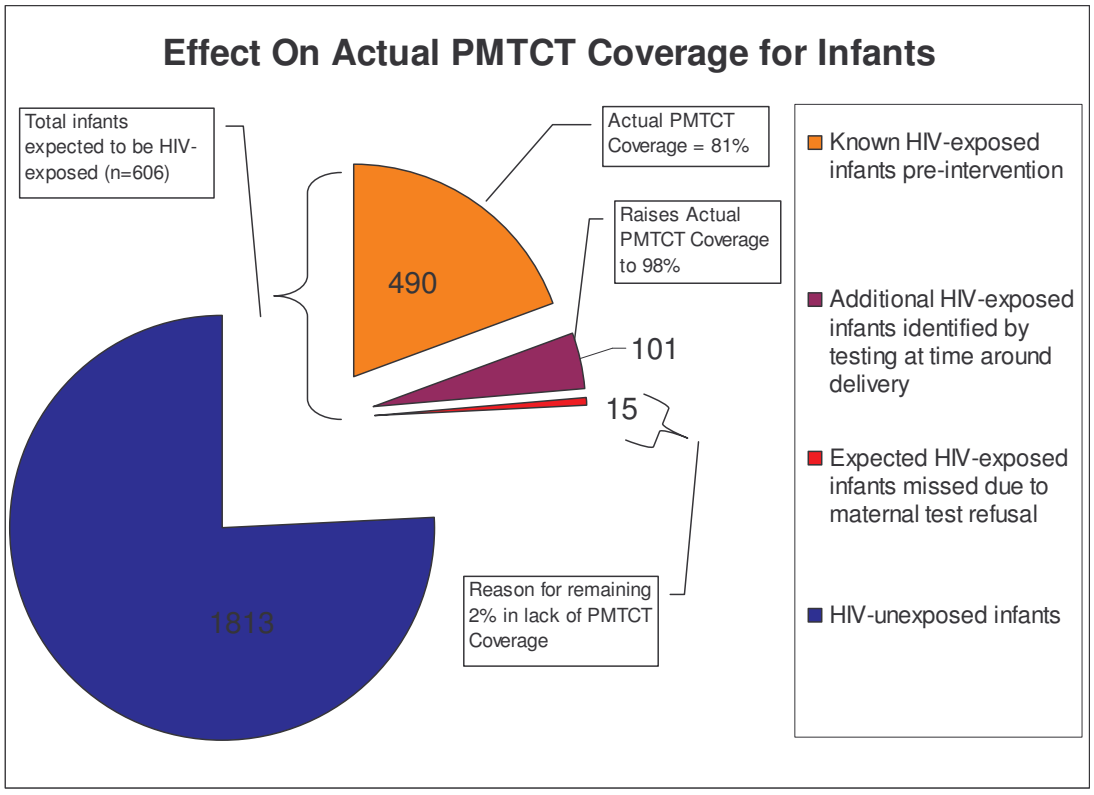


Figure 4.9: Prevalence and Numbers of HIV-exposed Infants – Coverage Discrepancies. The denominator of 'total number of HIV-exposed infants' was calculated as follows: Total number of HIV-exposed infants found by the time of departure from postnatal service (n=591) plus 44% of the women who refused an HIV test (n=33) resulting in a total of 606 expected HIV-exposed infants. There was a 17% increase in the true coverage of all HIV-exposed infants following the identification of additional HIV-positive mothers.

This provides evidence that a falsely reassuring picture is created if the ANC HIV-prevalence is assumed to be the prevalence at delivery and if no further HIV testing or recalculation of prevalence at the time of delivery is undertaken.

Chapter 5: Discussion

5.1 Increased Identification of HIV-positive Women

The study sample, although not random, was likely to be representative of women with live births at RMMCH during the study period. A large number (71%) of the total delivering population was interviewed and there were no significant differences between those enrolled and those interviewed. Results from the first half of the study sample were equivalent to those of the second half.

The proportion of women knowing their HIV status on arrival for delivery, antenatal booking distribution and median age were similar in the enrolled versus the interviewed population. Consent refusal was the main reason for not enrolling and age under 18 years excluded about 5% of women from enrolling. Entry into the study was allowed even if an HIV test was refused, therefore there was no reason to suspect that the effect of the intervention would be different if applied to all interviewed women but HIV-test refusal may have been higher in the women who declined to enrol.

Women not interviewed by the counsellors were those discharged on weekend afternoons or after the counsellors working hours during the week. High daily admission and discharge rates in the postnatal wards suggested that women not interviewed due to counsellor working hours were unlikely to differ significantly

from those interviewed. There was no reason to believe that those women discharged and not interviewed on a weekend or late weekday afternoon would have less chance of being HIV-infected. The counsellors interviewed women post-Caesarean section and after normal delivery irrespective of whether their infants were with them in the ward or required admission immediately post-delivery. Women that were enrolled in the study were in the same wards as those that refused to participate in the study. Although the recruiting process became more efficient over time, the actual results remained constant.

To ensure reliable HIV test results, the perception of poorly performing rapid tests on the DOH tender was investigated. Used according to the serial testing algorithm recommended by the DOH to screen for and then confirm a diagnosis of HIV, the rapid tests were 100% sensitive and specific. This information allayed fears expressed by nursing and counseling staff regarding reliability of the kits and the process of testing according to the DOH algorithm resumed. Validation of the algorithm also allowed for confidence in the results of determining HIV status in this study.

The study identified significant additional numbers of HIV-positive women ($p<0.001$). For every 25 women who participated in the study one additional HIV positive woman and her exposed infant were identified and provided with PMTCT-related interventions. The 4.2% of the study population newly diagnosed as HIV-positive is in itself important considering that it is higher than the national antenatal prevalence of some African countries (Ghana, Burkina Faso and Senegal) [1].

5.2 Change from HIV-negative to HIV-positive Status

The finding that just under 5% of women reporting an HIV-negative status and agreeing to a retest were found to be HIV-positive is alarming, although it is in line with previous experience in South Africa [23, 24]. For the 32 HIV-exposed infants in this group the transmission rate would have been reduced from 25-40% to 15% [15, 16, 17] therefore preventing HIV in three to eight infants. This assumes mothers continued administering the PMTCT prophylaxis and practiced their intended feeding method.

The significant conversion rate in women reporting an HIV-negative status shows that the six week period was a useful cut-off. Since women who tested HIV-negative more than twelve weeks ago had had more time to become HIV-infected than those testing HIV-negative six to twelve weeks ago, it was unexpected that the latter group did not have a higher rate of “seroconversion” than the group that had an HIV-negative result from six to twelve weeks ago, and this was unlikely to be influenced by those that refused a test since the two groups were similar in terms of test refusal.

Seroconversion between antenatal care and delivery does not necessarily reflect a recent HIV infection but may be accounted for by reporting and documenting errors by women or the healthcare service. This could be seen by the fact that the negative predictive value of the verbal HIV-negative status with documentation was higher than that without documentation. Documentation of the status was

more reliable than the woman's verbal report and could be as a result of denial of a positive HIV status. The highest rates of "seroconversion" were seen in the Diepsloot and "Other ANC" groups, the same two groups that had slightly lower knowledge of HIV status amongst ANC attendees possibly indicating room for improvement in HIV-testing services. It can be concluded though, that HIV retesting during later pregnancy and in the peri-partum period is a crucial part of PMTCT. Recent literature confirms that HIV incidence during pregnancy is higher than outside of pregnancy [38]. Furthermore experience in Botswana has demonstrated that when a PMTCT program improves, transmission of HIV from infection late in pregnancy and during breastfeeding accounts for almost half of vertical transmission [30].

For the 47 women reporting an HIV-negative status but refusing a retest it was not possible to determine their status but the group should not be overlooked as refusal of an HIV-test has previously been associated with a higher HIV-prevalence (Smith et al) although this was in women who had never tested before [22]. Of the total study group, 33 (1.4%) women were discharged from the postnatal ward with an unknown HIV status. Although a small number of women, they were at higher risk of being HIV-infected and therefore of having proportionately more HIV-exposed infants. Further work is required to devise ways of assisting women to test, dealing with specific reasons for refusal and possibly offering the infants of these women prophylaxis despite refusal of maternal testing. These issues were not investigated in this study and the ethical and public health arguments around them are beyond the scope of this discussion.

5.3 Newly Diagnosed HIV-negative Women

Although the emphasis is often placed on the identification of HIV-positive women during PMTCT-related activities, the most effective way of preventing HIV in children is preventing HIV in parents. As health care workers in a postnatal setting are primarily focussed on ensuring the protection of the HIV-exposed infant, the potential benefit of reinforcing health education and preventative efforts for HIV-negative women may be overlooked.

During the study, 7.3% of the total study population were newly identified as HIV-negative. Measuring the potential benefit of this improved “knowledge of HIV status” was not within the scope of this study, but the additional focussed counseling session that these women received may influence some of their future choices. Efforts such as these, that target the first two prongs of the WHO strategic approach to PMTCT should not be neglected, and should be incorporated into current programs.

5.4 Infant PMTCT Access

The issue of infants receiving interventions was inherently linked to the identification of new HIV-positive women. All newly identified HIV-exposed infants received sdNVP and the first dose of AZT from the nursing staff in the postnatal wards. The mothers were counseled on how to administer AZT to their infants and

on the importance of correct infant feeding practices. At the time of discharge from the postnatal ward it could not be guaranteed that the mother would comply fully with AZT administration or exclusive feeding and bring the infant back for a PCR test at RMMCH or any health care facility.

Considering that the dual therapy program was launched in April 2008, the distribution of PMTCT interventions which women diagnosed antenataly had accessed by the time they presented in labour reflected how quickly the AZT program had been implemented. Although the majority of women had received AZT for less than four weeks, almost a quarter of the mothers had received more than four weeks of AZT during their pregnancy. Just over 15% of mothers had started triple ART during their pregnancy. One would expect about 15-20% of antenatal HIV-positive women to require ART due to low CD4 counts in this setting as noted by Coovadia in 2004 [39]. Women attending the antenatal services described in this study seemed to be accessing appropriate care if identified as being HIV-positive antenataly although there is room for improvement as 5.1% of antenataly diagnosed women had not received or taken any prophylaxis by the time of delivery.

Infant follow-up of HIV-exposed infants remains a major challenge both nationally and at RMMCH with a marked loss to follow-up ranging from 24% of infants known to be HIV-exposed by delivery to 70% of HIV-exposed infants born to newly diagnosed HIV-positive mothers. One of the most important needs identified in this study was that all HIV-positive mothers, particularly those newly diagnosed around

delivery, need support in terms of taking the important step towards early infant testing. Improved counseling on infant testing and working towards acceptance of HIV diagnosis and disclosure may also be needed for both groups. This was highlighted by the fact that two mothers in the newly diagnosed group refused upfront to administer AZT to their infants and three mothers refused to exclusively formula or breastfeed. This showed that although there was benefit to many infants, there were a few individual mothers who struggled to accept the HIV-positive result given to them around the time of delivery. Therefore PMTCT programs should allow for additional counseling and support required by newly diagnosed HIV-positive women at the time of delivery.

Follow-up of infants was complicated by the fact that the study population seemed mobile as evidenced by the number of women delivering at RMMCH having booked at ANC services elsewhere in the province. The lack of continuity between antenatal, maternal and child health services, due to the vertical nature of the PMTCT program, may prevent good communication of HIV results between antenatal care and the point of delivery as well as poor infant follow-up.

The majority (93.9%) of HIV-positive mothers stated that they intended to formula feed rather than breast feed. A similar trend towards formula feeding had been noted in 2002 and 2006 at the same institution [32, 33, 34]. The WHO recommends that mothers should be assisted in choosing their preferred feeding method while taking into account the AFASS criteria. The overwhelming choice of formula feeding raises concerns because many women originated from very poor

areas like the squatter camps around Diepsloot. The skewed choice of infant feeding practices requires further assessment to establish whether the choices women made were well informed and whether quality of infant feeding counseling was adequate.

5.5 Infant Testing Outcomes

No meaningful comparison of transmission rates in infants of mothers with known and newly diagnosed HIV-positive status at delivery was possible because of the small number of PCR results available in the latter group. It is highly likely that the vertical transmission rate in the HIV-exposed infants identified at birth was reduced by the study interventions and that the HIV-exposed but uninfected infants benefited e.g. by feeding counseling to minimize postnatal transmission. Of the 32 infants born to newly diagnosed HIV-positive women at delivery that were tested, one infant was identified as HIV-positive and is currently receiving HAART. Identification of HIV positive women at delivery improved access to PMTCT prophylaxis for infants but did not translate into identification of these infants for early diagnosis in the majority of cases.

For the infants of women known to be HIV-positive by the time of delivery, the follow-up for testing was better and the 5.8% transmission rate was in line with what has previously been observed at RMMCH. All infected infants except one

were in care suggesting that the major challenge lies in getting infants back to facilities for testing rather than in the follow-up of confirmed infected infants.

The importance of knowing a negative HIV status, in this case for an infant, should not be overlooked because establishing a negative HIV status in an exposed infant provides the opportunity to reassure the mother. Further, each contact with the health care system is an opportunity to reinforce health education and counseling messages for the mother and to provide services such as CD4 counts and referrals to adult treatment centres.

5.6 Monitoring and Evaluation of the PMTCT Program

Identification of HIV-positive women antenataly allows the indicator of “Antenatal HIV prevalence” to be calculated but the study demonstrates that the HIV prevalence in the women delivering at RMMCH differed from the antenatal HIV prevalence because women from RMMCH ANC only comprise 24% of women delivering at RMMCH. Knowledge of HIV status in women from the RMMCH ANC compared to the whole delivering population was 99% and 89% respectively on arrival for delivery. The study intervention increased knowledge of HIV status by 10.2% leaving 2% of women without knowledge of their HIV status. The resultant HIV-prevalence, which increased by 1.9%, approximates the true prevalence at delivery, improves the infant PMTCT coverage significantly and provided a more honest measure of PMTCT program efficacy.

The variation in knowledge of HIV status between women from different antenatal clinics could be a reflection of the quality of testing coverage or counseling at these clinics. The wide variation of HIV prevalence between groups of women, notably a more than 10% difference between the women who booked at RMMCH versus those that booked in clinics that served predominately women from informal and poorer settlements (Witkoppen, Diepsloot and Discoverers) reflects that HIV-prevalence in communities may be related to socio-economic status.

These findings emphasise the importance of analysing the delivering population separately to the antenatal populations in large centres to understand the dynamics as well as quality of testing at feeder clinics. It also provides an opportunity to strengthen referral systems and communication between facilities when this information is fed back to the feeder clinics. This process is ongoing between RMMCH and its referral sites.

The setting of RMMCH is that of a well established and well running PMTCT site. The improvement noted following this intervention may be greater in sites with a lower baseline of PMTCT service quality as measured by the percentage of women arriving for delivery with a known HIV status. To improve the accuracy of reporting of the PMTCT program the prevalence for the delivering group should be calculated and reported to enable more accurate calculation of the PMTCT coverage. Sites where the delivering group is made up largely of the local

antenataly booked women and where the antenatal clinic has excellent testing rates may not need this intervention.

The cost of this intervention was not measured but involved employment of counsellors and performing an increased number of HIV tests. Two full-time counsellors managed to cover almost three quarters of the delivering population. Employing one counsellor per 3500 deliveries to achieve a 17% or higher improvement in PMTCT coverage may prove a cost-effective intervention in a country like South Africa with high paediatric and maternal HIV burden. Training nursing staff in labour and postnatal wards to counsel and test women after hours could increase the benefits of this intervention.

5.7 Conclusion

The study intervention revealed beneficial outcomes as well as challenges that need to be considered in order to improve the South African PMTCT program. The significant number of newly identified HIV-positive mothers should be a prompt for similar facilities to engage in testing and retesting around delivery and in this way promote active HIV case finding and “re-recruitment” into the PMTCT program at the time of birth until such time as either the HIV prevalence drops or antenatal care escalates and improves to a level that obviates this need. Both HIV-positive and negative women, especially those newly diagnosed at the time of delivery, were a captive audience at the time of delivery and could benefit from proactive

health care interventions. This intervention improved infant PMTCT coverage by identifying a significant number of at-risk infants and providing them with access to HIV prophylaxis as well as a link to HIV testing and care. The intervention in itself was not ideal as HIV-positive women should be diagnosed in time to receive at least four weeks of antenatal AZT and to adjust to their diagnosis. The intervention is worthwhile currently though, because with relatively little effort significant numbers of HIV-positive and negative women are identified with benefit to themselves and their infants.

Routine peri-partum HIV testing and counseling of women in the ante- and postnatal wards does improve **access to** HIV prevention, testing and treatment for their infants but does not, in itself, translate into improved **outcomes of** care for HIV-exposed infants because more work is urgently required to find practical ways of improving rates of infant follow-up of HIV-exposed infants. Better integration of maternal and child health services, for example a Road to Health Card documenting HIV-exposure status more clearly or routine screening of infants for HIV-exposure at well baby clinics may improve infant care. Other areas that require further research into operational interventions include support and counseling for HIV-positive women, particularly those newly diagnosed as HIV-positive during late pregnancy or the peri-partum period. Feeding counseling and practices also need further attention. The peripartum counselling and testing protocol ensures that PMTCT coverage is reported more accurately which is a necessary step in improving PMTCT efficacy and working towards eradication of paediatric HIV.

Appendix A – Ward Register

Name Surname	Mother DoB* dd/mm/yyyy	Booking		Status reported by mother		Status on ANC card or in file (pls double check)		Testing now?		Lab no	Rslt†	PMTCT med To MOTHER	PMTCT med To BABY	If positive - Transfer out?‡	If positive - Feeding Choice
		Bookd	where	**Positive**	**Negative**, tested less than 6 wks ago	**Positive**	**Negative**, tested less than 6 wks ago	Not needed			P / N / Err	sdNVP / sdNVP+AZT for __ wks / ART for ____wks / None	sdNVP + AZT for 1 week / 4 weeks	Y…… / N	Breast / Formula
		Unbooked		**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	Yes	Refusd		P / N / Err				
		Bookd	where	**Positive**	**Negative**, tested less than 6 wks ago	**Positive**	**Negative**, tested less than 6 wks ago	Not needed			P / N / Err	sdNVP / sdNVP+AZT for __ wks / ART for ____wks / None	sdNVP + AZT for 1 week / 4 weeks	Y…… / N	Breast / Formula
		Unbooked		**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	Yes	Refusd		P / N / Err				
		Bookd	where	**Positive**	**Negative**, tested less than 6 wks ago	**Positive**	**Negative**, tested less than 6 wks ago	Not needed			P / N / Err	sdNVP / sdNVP+AZT for __ wks / ART for ____wks / None	sdNVP + AZT for 1 week / 4 weeks	Y…… / N	Breast / Formula
		Unbooked		**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	Yes	Refusd		P / N / Err				
		Bookd	where	**Positive**	**Negative**, tested less than 6 wks ago	**Positive**	**Negative**, tested less than 6 wks ago	Not needed			P / N / Err	sdNVP / sdNVP+AZT for __ wks / ART for ____wks / None	sdNVP + AZT for 1 week / 4 weeks	Y…… / N	Breast / Formula
		Unbooked		**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	**Unknown**	**Negative** 6-12 weeks ago / >12 wks ago	Yes	Refusd		P / N / Err				

* DoB = Date of Birth
† Result: P = Positive; N = Negative; Err = Error
‡ Relates to where the mother intends to have her HIV-exposed infant tested, either at RMMCH (N) or at another clinic (Y and name of clinic)

Appendix B – Study and HIV testing Consent form

1. INFORMATION SHEET CONCERNING THE PERIPARTUM HIV TESTING STUDY

The Human Immunodeficiency Virus which we call "HIV" is a very important health problem in South Africa. About one quarter of all pregnant women in South Africa are infected with the virus, and this means that they are "HIV-positive". When a person is HIV-positive it does not mean that they have "AIDS" which is the condition people get when HIV has already caused a lot of damage to the body. People who are HIV-positive can be treated with medicines called antiretroviral medicine (ARV's) to make sure that they do not get sick and get "AIDS" and to make sure that they can live a normal life.

For a mother there is a risk that her newborn baby may become infected with HIV if the mother is HIV-positive. **Not all babies** born to HIV-positive women become HIV-positive, only about one quarter of babies that are born to HIV-positive mothers do become HIV-positive if no preventative medicines (ARV's called Nevirapine and AZT or Zidovudine) are given. If we do give an HIV-positive mother or her baby these preventative medicines around the time of birth the risk becomes lower for her baby to become HIV-positive although there always remains some risk. It is important that an HIV-positive mother either only bottle feeds or only breastfeeds her baby without mixing the two or mixing breast milk with other food. We want to make sure that every baby born to an HIV-positive mother has a lower risk of getting HIV. An HIV-positive baby has a high risk of getting "AIDS" early in life and this is something we want to try avoid as well in those babies that still become infected despite the preventative medicines.

Many pregnant women in South Africa have an HIV test when they book at the clinic for their pregnancy **but not all women do**. Because HIV is transmitted through sex, it is very possible that a woman who was HIV-negative a few months ago, is now HIV-positive. That is why we, at Coronation Hospital, find it important to ask every woman who is about to deliver a baby or who has just delivered: Do you know your HIV result? And if not: Can we offer you an HIV test now to find out your result? Or did you have an HIV test a few months ago that said "HIV-negative" – so can we repeat the test now to make sure you did not become HIV-positive recently.

If the result of the test we do is "HIV-negative" it means that the woman can protect herself in the future in order to stay "HIV-negative" and most importantly, **she knows her result now**.
If the result is "HIV-positive" it means that the woman can take the necessary steps to remain healthy by living a healthy life style and finding out early whether or not she qualifies for ARV's yet. The other benefit is that preventative medicines can be given to her and/or her baby to prevent the baby from becoming HIV-positive as well, and even if the baby does become HIV infected, she can make sure that the baby is treated early and does not have to become very sick. Women who know they are HIV-positive can also make informed feeding choices to make sure they choose the feeding option best for them and their baby. Coronation hospital offers a routine service were all babies of HIV-positive mothers are tested for HIV when the baby is six weeks old, so that the mothers can find out early whether or not their baby became HIV infected.

Not every hospital asks all the women that deliver at that hospital whether they know their HIV result and not all women have the chance to get a test at the time of delivery. We believe that it may help many women if we do the testing at delivery but before we can recommend to other hospitals and clinics to do this we have to prove to them that it does help. To do this we have to do a "research study" on a large group of women at Coronation and report to the hospital management and the Department of Health whether or not it was helpful. For this reason we would like to invite you to let us use your test results without your name attached to write this report. It is important that all "research studies" that are done are approved first by the university involved and a special committee that decides if the study can proceed. Only if this is the case and only if all the participants' names are kept strictly secret can we do this. We have undertaken to comply with these conditions and for this reason we invite you to join this study as a participant. If you decide not to join or you decide to withdraw from the study after you have joined it this is absolutely fine and it will not affect your or your child's treatment at all, nor will it be held against you in any way.

2. SUBJECT CONSENT FORM FOR PERIPARTUM HIV TESTING STUDY

I understand what this study is about and have had all my questions about this study answered.
I understand that taking part in this study is my choice and that if I decide not to; it will not cause any problems with the treatment that my baby or I will receive at this hospital.
I may decide to stop taking part in the study at any time and my withdrawal from the study will in no way compromise the care my child or I receive.

All information from this study is strictly confidential and only the people involved in the study will have access to it.

If you would like to know more about this activity, please ask Dr Karl Technau who will be happy to answer your questions (011 470 9421 office hours or 082 687 3633 in case of emergency).

This process was approved by the Ethics Committee of the University of the Witwatersrand on 19th March 2008 [Protocol number M080203]. If you would like to have more information regarding the ethical considerations of the study, you are welcome to call the Chairperson of this committee at the following number

Professor P. Cleaton Jones
Committee for Research on Human Subjects, University of the Witwatersrand. Tel: 011 717 2229

I have been given a copy of the Information sheet and the consent form, which I have read, or its contents explained to me through an interpreter. I have had all my questions and concerns answered to my satisfaction by the clinic staff.

I understand that I may refuse to participate in this process or withdraw at any stage without giving a reason for doing so and this will in no way influence the way me or my child will be treated.

The health care worker(s) wish to test me for HIV infection. This is a test on my blood which will establish whether or not I have been infected with the virus, called HIV, which may cause AIDS. The reason for wanting to do the test are: 1. To diagnose my illness, 2. To give me the proper treatment, 3. To offer me access to further health care if I am found to be HIV-positive as well as help to keep my status HIV-negative if I am found to be HIV-negative, 4. If I have just had a baby and I am HIV-positive, medicine to help prevent the baby becoming HIV infected can be given although some babies may still become infected.

If the test shows me to be HIV-positive the result will be treated with confidentiality. A negative test is not an absolute guarantee that I am not infected because the test may show an "HIV-negative" result in people who have just become infected in the last few weeks

I, _____, agree to have an HIV test and would like to know my result, and I wish to participate in the peripartum HIV testing study.

Woman's signature: .....
Woman's name: .....
Date: .....
Witness signature: .....
Witness name: .....

Name and signature of person who obtained informed consent: .....

Appendix C – HIV consent for women not participating in study (in routine use at RMMCH)

Informed Consent for HIV Testing of Adults
Coronation Woman and Children Hospital

MINIMUM PROCEDURE FOR OBTANING INFORMED CONSENT FOR HIV TESTING

Date: _____ Name: _____

EXPLANATORY NOTES FOR CARE WORKERS

1. **WHAT IS INFORMED CONSENT?**
   - Informed consent is the legal requirement that is necessary before a doctor or other health care worker examines, investigates or manages a patient.
2. **INFORMED CONSENT FOR HIV TESTING MUST BE SPECIFIC AND EXPLICIT**
   - Consent to HIV testing is not covered by the usual contractual agreement which is implied when a patient consult a doctor. The reason is that the implications of a positive test in the present social climate may be extreme, (This may change as attitude to and Knowledge and understanding of HIV infection changes).
3. **WHAT DOES INFORMED CONSENT IMPLY IN THE CONTEXT OF HIV TESTING**

Informed consent implies that the patient has received minimum of the pre-test information and counseling and understanding the following

The reason or purpose for which the test is being performed.
The potential advantages of having his/her status determined, especially access of treatment
The influence the results of the HIV test may have on treatment.
The possible psycho-social impact of a positive test.

POST TEST COUNSELING

The principle of informed consent implies tat once the patient's test is known (positive or negative) appropriate counselling will follow. The health care worker should therefore ensure that the positive patients are directed to appropriate facilities where they will receive ongoing care and management.

DOCUMENTATION

It is recommended that a note be made in the patient's file/record that informed consent for HIV has been obtained and from whom.

EXPLANATORY NOTES FOR PERSONS OFFERED AN HIV TEST

TESTING

1. I / We / the health care worker(s) wishes to test you for HIV infection- Your consent (permission) is requested to do so.
2. This is a test on your blood which will establish whether or not you have been infected with the virus, called HIV, which may cause AIDS.
3. The reason(s) I want this test performed is/are
   - 3.1. To help me diagnose your illness
   - 3.2. To help me give the proper treatment
   - 3.3. In the context of pregnancy, we would like to offer you access to further health care if you are found to be HIV-positive as well as help to keep your status HIV-negative if you are found to be HIV-negative.
   - 3.4. If you have just had a baby and you are HIV-positive we would like to offer you and/or your baby preventative medicine to prevent the baby becoming HIV infected.

Because you asked to be tested for HIV infection

4. If the test is positive, treatment may have to be modified in your own interest. (Treatment should not be sub-optimal because of any perceived potential risk to the health care worker)
5. You should realize now that if the test shows you to be HIV-positive this means that:-

Your results will be treated with confidentiality
You may be able to make changes to your lifestyle, which will improve your quality of life
You are at risk of developing AIDS which at present can be treated but cannot yet be cured.
You may suffer discrimination in obtaining work, insurance and medical aid

Knowledge of your positive status will allow the heath care worker to proceed to screen you for treatment with effective Anti retroviral therapy.

Knowledge of your status as a new mother may help us to protect your baby from becoming HIV-positive.

6. A negative test is not an absolute guarantee that you are not infected.

SIGNATURE (PATIENT) _____ **pre-test**
SIGNATURE (HEALTH WORKER) _____ ☐

SIGNATURE (PATIENT) _____ **post-test**
SIGNATURE (HEALTH WORKER) _____ ☐

Appendix D – Ethics Approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Technau

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M080203**
PROJECT	Can a routine peripartum HIV counselling and testing service for women improve access to HIV prevention, Early testing..
INVESTIGATORS	Dr C G Technau
DEPARTMENT	Paediatrics
DATE CONSIDERED	08.02.29
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 08.03.19 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr G Sherman

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

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