IN SEARCH OF REASON: PREVENTION OF MOTHER-TO-CHILD TRANSMISSION (PMTCT) FAILURES IN THE ERA OF PROGRAMMATIC SCALE-UP IN SOWETO, SOUTH AFRICA

by

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In the
Faculty of Health Sciences

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ABSTRACT

The 2008 scale-up of South African public sector prevention of mother-to-child transmission (PMTCT) to an AZT/sdNVP regimen led to significant reductions in vertical HIV transmission, yet incident paediatric infections continue. The objectives of this study were to 1) identify mothers of newly HIV-infected infants, and assess whether they received per-guideline PMTCT antiretroviral (ARV) regimens, and 2) qualitatively explore contextual factors contributing to these prescription failures and MTCT risk. Eligible women included birthmothers of HIV-infected infants in Soweto. Participants (n=45) first completed a questionnaire, and then a focus group or structured interview. Through triangulation of data, it was determined that 29 mother-infant pairs (64%) did not receive per-guideline PMTCT ARV regimens. Identified issues of importance include preterm birth, delayed antenatal care attendance, operational difficulties implementing PMTCT, and HIV-related stigma. While improved PMTCT regimens are available, social and structural factors must be addressed to ensure access to and uptake of prevention services.

Keywords: PMTCT; Vertical HIV transmission; Paediatric HIV; HIV health services; South Africa
DEDICATION

I dedicate this paper to the study participants.
ACKNOWLEDGEMENTS

This project involved a dedicated team and I thank everyone for their contributions. Most importantly, I would like to express gratitude to each of the participating mothers. Thank you for sharing your experiences with us.

Thank you to the staff of the PHRU in Soweto – especially, to Matamela Makongoza and Lindelwe Sikakane for your help facilitating focus groups and conducting interviews. It was a wonderful experience to work with you both. Also, a special thanks to Saucy Warnasuryia for the logistical study support as well as the gracious hospitality provided by you and your family in South Africa. Thank you for welcoming me to your country and into your home!

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# TABLE OF CONTENTS

Approval........................................................................................................................... ii
Abstract.............................................................................................................................. iii
Dedication........................................................................................................................... iv
Acknowledgements.......................................................................................................... v
Table of Contents........................................................................................................... vi
List of Figures ................................................................................................................ vii
List of Tables .................................................................................................................. viii
Glossary ........................................................................................................................... ix

**BACKGROUND** .............................................................................................................. 1
Vertical HIV Transmission: Scientific Discoveries and Missed Opportunities .............. 1
PMTCT in South Africa: Access and Scale-up ................................................................. 3

**INTRODUCTION** .......................................................................................................... 6

**METHODS** .................................................................................................................. 8
Setting ................................................................................................................................. 8
Eligibility and Recruitment ............................................................................................... 8
Data Collection ................................................................................................................ 9
  Question Content ........................................................................................................ 10
  Measures ....................................................................................................................... 10
Data Analysis .................................................................................................................. 11
Ethical Considerations .................................................................................................... 12

**RESULTS** .................................................................................................................... 14
Background Characteristics ............................................................................................. 14
Evaluation of PMTCT ARV Regimens .......................................................................... 17
Qualitative Findings ........................................................................................................ 19
  i) Delayed ANC Attendance ..................................................................................... 19
  ii) HIV-Associated Stigma ....................................................................................... 21
  iii) Lack of Knowledge and Mixed Messages ............................................................ 23

**DISCUSSION AND CONCLUSIONS** ........................................................................... 25

**FINAL REMARKS** ...................................................................................................... 30

**REFERENCE LIST** ..................................................................................................... 31
LIST OF FIGURES

Figure 1: Concurrent triangulation approach .................................................. 12
Figure 2: PMTCT ARV regimen evaluation......................................................... 18
LIST OF TABLES

Table 1: Characteristics of participating mothers ................................................................. 15
Table 2: Infant characteristics and delivery information ......................................................... 16
<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
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<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>ANC</td>
<td>Antenatal Care</td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral Therapy</td>
</tr>
<tr>
<td>ARV</td>
<td>Antiretroviral</td>
</tr>
<tr>
<td>AZT</td>
<td>Zidovudine [nucleoside reverse transcriptase inhibitor (NRTI)]</td>
</tr>
<tr>
<td>BBA</td>
<td>Born Before Arrival (on route to healthcare facility)</td>
</tr>
<tr>
<td>BI</td>
<td>Boehringer Ingelheim</td>
</tr>
<tr>
<td>CAD</td>
<td>Canadian Dollars</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>DNA-PCR</td>
<td>Deoxyribonucleic Acid – Polymerase Chain Reaction</td>
</tr>
<tr>
<td>FGD</td>
<td>Focus Group Discussion</td>
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<tr>
<td>HAART</td>
<td>Highly Active Antiretroviral Therapy</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HIVNET</td>
<td>HIV Network for Prevention Trials</td>
</tr>
<tr>
<td>MTCT*</td>
<td>Mother-to-Child Transmission of HIV</td>
</tr>
<tr>
<td>NVP</td>
<td>Nevirapine [non-nucleoside reverse transcriptase inhibitor (NNRTI)]</td>
</tr>
<tr>
<td>PACTG</td>
<td>Paediatric AIDS Clinical Trials Group</td>
</tr>
<tr>
<td>PHRU</td>
<td>Perinatal HIV Research Unit (Soweto, South Africa)</td>
</tr>
<tr>
<td>PMTCT</td>
<td>Prevention of Mother-to-Child Transmission of HIV</td>
</tr>
<tr>
<td>PWC</td>
<td>Paediatric Wellness Clinic (PHRU, Soweto, South Africa)</td>
</tr>
<tr>
<td>RNA</td>
<td>Ribonucleic Acid</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>sdNVP</td>
<td>Single-Dose Nevirapine</td>
</tr>
<tr>
<td>SI</td>
<td>Structured Interview</td>
</tr>
<tr>
<td>TAC</td>
<td>Treatment Action Campaign (South Africa)</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>ZAR</td>
<td>South African Rand</td>
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*Throughout this paper, the acronym “MTCT” is used, as it is most consistent with the current body of literature. However, the author acknowledges that “PTCT” (parent-to-child transmission) is a more appropriate term, emphasizing the role of both parents in vertical transmission.*
BACKGROUND

Vertical HIV Transmission: Scientific Discoveries and Missed Opportunities

Medical advances have nearly eliminated paediatric HIV in many settings worldwide, yet an estimated 430,000 children were newly infected in 2008 – the majority through mother-to-child transmission (MTCT) (1). This statistic speaks to a striking disconnect between research findings and their translation into successful public health practice. First theorized in 1982, the mechanism of MTCT is now well understood to occur during pregnancy, labour, or breastfeeding (2,3). Despite decades of research in this field, extreme inequities in treatment access and outcomes exist across the globe – with less than half of HIV-positive pregnant women in lower-resource countries receiving an antiretroviral (ARV) intervention to prevent transmission to their infants in 2008 (1). Without intervention, the risk of MTCT is estimated to be between 15-30%, and up to 45% with extended breastfeeding (4,5).

Researchers began investigating the possibility of MTCT risk reduction with the use of antiretroviral therapy (ART) in the late 1980s. A major breakthrough arrived in 1994, with the PACTG 076 trial documenting a reduction in risk of approximately two-thirds using a short-course zidovudine (AZT) regimen, compared to placebo (6). From there, additional studies confirmed these findings and new ARV agents were tested and approved for use in pregnancy (7). Importantly, it was established that the risk of transmission corresponded to maternal HIV RNA viral load (8). Accordingly, researchers acknowledged that ARV regimens that could
reduce such levels to ‘undetectable’ would be the most effective at minimizing MTCT risk.

These crucial findings were quickly translated into routine clinical practice in many high-resource settings around the world, and treatment recommendations were updated as newer, more efficacious regimens were developed (9). Ultimately, it was established that utilizing ARVs in combination (“highly active antiretroviral therapy”, or HAART) was the most effective way to reduce viral load and correspondingly, prevent vertical transmission. Today, many countries document MTCT rates of less than 2%, due to the use of HAART in pregnancy in conjunction with precautions taken during delivery and modifications in infant feeding (9,10).

In stark contrast, lower-resource, high HIV-prevalence settings faced a multitude of barriers to the timely implementation of PMTCT programming (9). Initially, the costs of antiretroviral therapy, alongside a high prevalence of co-morbidities and poorly functioning healthcare systems, made many assume that ART provision was near impossible in such settings (11). These factors necessitated the conduction of strategic research examining the prospect of using simpler, more affordable ARV regimens to reduce MTCT in resource-constrained areas.

In 1999, findings from the HIVNET 012 randomized trial demonstrated that providing a single dose of maternal nevirapine (sdNVP) at the onset of labour and to the infant within 72 hours post-delivery significantly decreased the risk of transmission compared to a short-course AZT regimen, from 25% to 13% (as of 14-16 weeks post-delivery) in a breastfeeding population (12). These findings were of vital importance as they documented the effectiveness of a simple, low-cost intervention for preventing MTCT – sparking the “first impetus” for the large-scale
advocation of treatment-based approaches to HIV/AIDS in resource-constrained settings (13).

In 2000, pharmaceutical company Boehringer Ingelheim (BI), the NVP patent holder, announced free provision of the drug to developing countries for a period of five years (14). A number of countries in sub-Saharan Africa participated in this provision program, and such sdNVP-based programs remain the mainstay of prevention of mother-to-child transmission (PMTCT) programs in many resource-limited settings.

Despite the offering from BI, the South African government initially refused to introduce nationwide sdNVP programming (15). At the time, the government’s viewpoint was greatly influenced by the then president’s controversial views doubting an aetiological link connecting HIV infection to AIDS, alongside concern over the toxicity of ART (15-17). The decision of the South African government to delay the provision of freely donated NVP ultimately resulted in at least 35,000 paediatric HIV infections that could have been averted, and a loss of an estimated 1.6 million person-years of life from 2000-2005 (15).

PMTCT in South Africa: Access and Scale-up

Despite sustained government opposition, PMTCT services were finally made available in the South African public sector in 2002, under an order from the Constitutional Court (18). Advocates from the country’s Treatment Action Campaign (TAC) and other organizations employed a human rights approach to instigate provision, arguing that failure to provide sdNVP to pregnant HIV-positive women was against the country’s “right to health care services including the right to reproductive
health care" mandate (14). Further, in 2004 the South African government committed to providing HAART to all medically-eligible South Africans. Under these treatment guidelines, individuals (including pregnant women) with a World Health Organization (WHO) clinical stage IV (AIDS-defining) illness and/or a CD4 T-cell count of <200 cells/ml became eligible for lifelong HAART (19).

For pregnant women ineligible for HAART, sdNVP remained the available ARV strategy to prevent MTCT in the public sector until 2008. While perceivably one of the simplest PMTCT interventions, the implementation of the sdNVP strategy was challenging operationally – with a variety of contextual factors and health system constraints hindering access and uptake (20,21). Essentially, the regimen’s apparent simplicity was impeded by its small window of opportunity for intervention; with the potential prevention benefits being quickly negated if not administered and/or consumed within the indicated time frame (21). Of additional concern, the sdNVP regimen had no ability to prevent transmissions occurring in-utero prior to the onset of labour. This is an important limitation of the regimen, as an estimated 20% of MTCT instances occur prior to 36 weeks gestation in non-breastfeeding populations (3). Further criticism of the sdNVP strategy was due to its potential to create non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance (22,23). Essentially, mothers utilizing sdNVP for PMTCT may be at heightened risk of failing NNRTI-based HAART regimens taken in the future for their own health – with additional concern surrounding the creation of such resistance in exposed infants, as well (23). The unacceptability of sdNVP alone as a PMTCT regimen has been a theme echoed by experts in the field for years (“It’s time to move on from single-dose nevirapine”) (13,24,25).
For these reasons, in conjunction with further protest from the TAC, other advocates, and academics, and in accordance with evolving WHO PMTCT guidelines for resource-constrained settings, a dual therapy PMTCT ARV strategy was introduced for pregnant women ineligible for HAART in 2008 (26). The program included the provision of a short-course of maternal AZT initiated at 28 weeks gestation plus sdNVP at the onset of labour, with neonatal sdNVP administered within 72 hours of delivery and infant AZT prophylaxis for 7 or 28 days (depending on the duration of maternal therapy) (26). Encouragingly, alongside being a more efficacious ARV regimen (with transmission rates among those receiving AZT/sdNVP documented at 4.4% in one South African setting, compared to the sdNVP group at 7.2%), this new strategy allowed for intervention earlier on in pregnancy (21,27).
INTRODUCTION

When accessible and implemented appropriately, PMTCT programming represents one of the greatest achievements to date in HIV prevention efforts (9). While medical advances have led to the near elimination of vertical transmission and paediatric HIV in some settings, translating these scientific advances into practical successes in resource-constrained areas remains a challenge (5,9).

South Africa currently has the largest absolute number of HIV-positive persons worldwide (5). In 2008, the national antenatal care (ANC) HIV prevalence was 29%, an estimated 200,000 pregnancies occurred among HIV-positive women, and 73% were reported to have accessed PMTCT services (5,29-31). Despite free PMTCT access nationwide and the availability of the new AZT/sdNVP strategy since 2008, an estimated 59,000 infants were newly infected in 2009 (26,32).

While a more efficacious regimen, the country’s new PMTCT ARV strategy is also operationally more complex than sdNVP alone – involving a cascade of interventions that must be implemented in an appropriate and timely manner in order to maximize the prevention benefits (27,33). These interventions include antenatal HIV and CD4 testing, provision of maternal prophylactic ARV regimens (AZT or HAART, as indicated), administration of sdNVP to mother (if on AZT) and infant, and prescription of AZT for the appropriate length of time to the infant after birth (26).

In the situation of free, available, and more efficacious PMTCT strategies, there is an urgent need to investigate failures in PMTCT and to contextualize the current situations of mothers accessing care. While traditionally reported “progress indicators” of PMTCT are important in identifying absolute numbers of pregnant
women being tested for HIV and prescribed ARV regimens, these data are precluded by the fact that they do not evaluate whether or not mothers and infants received all components of the prescribed intervention (34). Importantly, the efficacy of PMTCT ARV regimens significantly diminishes in the absence of all indicated components – heightening the risk of MTCT (33).

This study seeks to gather information beyond progress indicators, taking a unique approach to data collection and analysis in order to more fully explore PMTCT in an urban South African setting in the era of PMTCT strategy transition from sdNVP to AZT/sdNVP and HAART. Through the use of a mixed qualitative-quantitative approach, the objectives of this study are to: 1) identify mothers of newly HIV-infected infants, assess whether or not they received per-guideline PMTCT ARV regimens, and ascertain where in the administration cascade instances of non per-guideline receipt occurred, and 2) qualitatively explore contextual factors and challenges contributing to these prescription failures and MTCT risk.
METHODS

Setting

This study was conducted at the Perinatal HIV Research Unit (PHRU) in 2009, more than one year after the change in national PMTCT guidelines to the dual AZT/sdNVP strategy. The PHRU is one of Africa’s largest HIV research and clinical care centres. A research division of the University of the Witwatersrand, the PHRU is housed at the Chris Hani Baragwanath Hospital in Soweto, South Africa. Soweto is an urban residential area located to the southwest of Johannesburg, with a population of approximately one million (35). In the greater Johannesburg area (including Soweto), the antenatal HIV prevalence is similar to the national average, at 30% (95% CI 27.9, 31.5) (31).

The PHRU provides HIV testing, treatment, and prevention services for adults and children, free of charge. HIV-positive infants and children are treated at the PHRU’s Paediatric Wellness Clinic (PWC). This clinic serves as Soweto’s primary site for infant DNA-PCR HIV testing, and is one of two major sites in the area providing specialized infant HIV care. Services provided by the PWC include HAART prescription, clinical monitoring, treatment of opportunistic infections, management of acute illnesses, counselling, and referrals as appropriate. As of August 2010, approximately 1,100 infants and children were being treated at the PWC (36).

Eligibility and Recruitment

Women were eligible to participate in this study if they were at least 18 years old, willing to provide voluntary informed consent, and had recently given birth to an HIV-infected infant receiving care at the PWC. To limit inclusion to mothers who
would have been eligible for dual AZT/sdNVP therapy throughout pregnancy, women
must have given birth between December 2008 and June 2009.

Participant recruitment occurred at the PWC, with clinic staff identifying
eligible women prior to their infant’s clinical appointment. A clinic nurse briefly
described the study and invited women to receive additional information from a study
representative in a private clinic room, if interested. Overall, 45 of 46 approached
women (98%) enrolled in the study.

Data Collection

Data were collected with the assistance of two local study
representatives/interviewers. These multilingual women had prior training and
experience in both qualitative and quantitative research methods, and also had
experience specifically with HIV-related research. Further training was provided
regarding PMTCT in the South African context.

After providing informed consent, each participant first completed an
interviewer-administered questionnaire. Then, the first 10 women were assigned to
participate in one of two focus group discussions (FGD), and the next 35 to
individual structured interviews (SI). The FGDs and SIs were conducted in the
preferred languages of the participants, and included English, Zulu, Sotho, and
Xhosa. FGDs were audio-recorded, translated into English, and transcribed verbatim
by the facilitator. SI responses were manually recorded in English.

FGDs lasted approximately one hour each, and SIs approximately 45 minutes
each. For their time and reimbursement of transport costs, participants were given
an honorarium of 50 ZAR, equivalent to approximately 7 CAD.
**Question Content**

Questionnaires elicited information on demographics, obstetric and PMTCT history, antenatal care, HIV testing, CD4 results (in pregnancy and at time of interview), type and duration of PMTCT regimens for mother and infant, delivery, infant feeding practices, and maternal postnatal HAART use.

Both FGD and SI questions were organized around three general topic areas: antenatal care, delivery and postnatal experiences, and infant feeding. Four main FGD questions were included, which were broad and open-ended: “Tell us about women’s experiences at the antenatal clinic”, “Tell us about women’s experiences delivering their babies”, “Tell us what you think about infant feeding options for HIV-positive mothers”, and “What do you think should be done in order to help prevent babies from becoming HIV-positive in Soweto?”. Built into this FGD guide were prompt questions to assist the group facilitator with directing the discussion towards identifying contextual barriers and challenges in PMTCT.

FGD data were used to guide the question structure of the SIs. SIs included both closed and open-ended questions in which participants were invited to list and share difficulties that HIV-positive women, both personally and in general, experience at antenatal clinics, delivery sites, and with infant feeding.

**Measures**

To perform the assessment of PMTCT ARV regimens utilized, a definition of per-guideline care was developed based on the 2008 South African PMTCT strategy (26). Mother-infant pairs experiencing at least one of the following were classified as having a per-guideline PMTCT ARV “failure”: mother received no ARV intervention;
mother received sdNVP only; mother received AZT only; mother received prenatal AZT or HAART for less than two months; lack of HAART provision for qualifying (CD4 count <200 cells/ml) mothers; infant received no ARV intervention; infant received sdNVP only; infant received AZT only; and/or, provision of improper length of infant AZT prophylaxis based on length of maternal therapy (i.e., prescribed for 7 instead of 28 days). All classifications were based on maternal self-reports.

Data Analysis

Quantitative data obtained from the questionnaires were double-entered into Microsoft Office Excel to ensure accuracy. Descriptive statistics including frequencies, proportions, means, and standard deviations were then calculated using SPSS Statistics 17.0 (37).

Transcripts from both the FGDs and the SIs were hand-coded by two independent reviewers, and compared for consistency and agreement on emergent themes. Coders utilized a grounded theoretical methodology (38). Thematic and content analysis were conducted and recurrent themes were identified. Relevant quotes were selected from the FGD transcripts to exemplify and illustrate the themes.

Quantitative and qualitative data were then corroborated using a concurrent triangulation approach (Figure 1) (39). Triangulated data were used to conduct the assessment of per-guideline PMTCT ARV receipt. After determining the number of mother-infant pairs who did not receive or take per-guideline PMTCT ARV regimens, qualitative findings were used to explore possible contributory factors.
Ethical Considerations

Prior to participating, women were provided with an information booklet and consent form, and a study representative explained the objectives and procedures orally in the preferred language of the participant. Women were informed that participation was completely voluntary, that they were free to withdraw at any time, and that their refusal would in no way affect the care that they, or their infants, received from the PHRU. FGD participants were informed that with their acknowledgement and written consent, the sessions would be audio-taped and transcribed verbatim.

Participant confidentiality was strictly enforced during study conduction. All documentation of interview proceedings was collected using a study number. No identifying particulars of participants apart from demographic information including infant sex and date of birth were documented on any interview forms.
This study was granted ethical approval from the University of the Witwatersrand Human Research Ethics Committee (South Africa), and the Research Ethics Board of Simon Fraser University (Canada).
RESULTS

Background Characteristics

Table 1 lists demographic characteristics of the participating mothers. In total, 45 women participated in this study, of average age 28.7 years (SD=5.4, range 19-38). Mean gravidity (defined as the number of times ever pregnant) of mothers at time of study was 2.6 (SD=1.2, range 1-6), and mean parity (defined as the number of live births) was 2.4 (SD=1.1, range 1-5). Eleven percent of mothers reporting a prior delivery (4 of 37) had past experience with ARVs for PMTCT, with one mother reporting exposure to sdNVP in two prior pregnancies.

The majority of participants (n=42, 93%) attended ANC at some point in their pregnancy, with 86% of attendees (36 of 42) reporting their first ANC visit before seven months gestation.

Table 2 shows infant characteristics and delivery information. Of 45 infants, 29 (64%) were female. The mean gestational age of infants at birth was 8.5 months (SD=0.7) and mean birth weight 2.7 kg (SD=0.7, range 1.0-3.9). Fourteen infants (31%) were delivered preterm, defined as prior to 8.5 months gestation. More than half of the deliveries (n=26, 58%) occurred in a public hospital setting. Eight infants (18%) were delivered by caesarean section; six due to reported emergency complications. In terms of infant feeding, 38 mothers (84%) reported exclusive formula feeding, 1 (2%) exclusive breastfeeding, and 6 (13%) mixed-feeding (defined as a combination of breast milk and other liquids/foods).
Table 1: Characteristics of participating mothers

<table>
<thead>
<tr>
<th>Variable</th>
<th>n=45</th>
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<tbody>
<tr>
<td>Mean age (years), (SD)</td>
<td>28.7 (5.4)</td>
</tr>
<tr>
<td>Mean gravidity (SD)</td>
<td>2.6 (1.2)</td>
</tr>
<tr>
<td>Mean parity (SD)</td>
<td>2.4 (1.1)</td>
</tr>
<tr>
<td>Completed high school education, n (%)</td>
<td>22 (49)</td>
</tr>
<tr>
<td>ANC attendance in pregnancy, n (%)</td>
<td></td>
</tr>
<tr>
<td>Before 7 months gestation</td>
<td>36 (80)</td>
</tr>
<tr>
<td>After 7 months gestation</td>
<td>6 (13)</td>
</tr>
<tr>
<td>Did not attend</td>
<td>3 (7)</td>
</tr>
<tr>
<td>PMTCT in prior pregnancy*, n (%)</td>
<td>4 (11)†</td>
</tr>
<tr>
<td>Most recent** CD4 count (cells/ml), n (%)</td>
<td></td>
</tr>
<tr>
<td>&gt;350</td>
<td>19 (42)</td>
</tr>
<tr>
<td>201 – 350</td>
<td>11 (24)</td>
</tr>
<tr>
<td>≤200</td>
<td>12 (27)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (7)</td>
</tr>
<tr>
<td>HAART user**</td>
<td>8 (18)</td>
</tr>
</tbody>
</table>

All variables are self-reported. Percentages may not equal 100% due to rounding.
Note: SD, standard deviation; ANC, antenatal care
* Defined as past exposure to sdNVP during labour for purposes of PMTCT
† Percentage of n=37 women of parity >1
** As of date of study participation
Table 2: Infant characteristics and delivery information

<table>
<thead>
<tr>
<th>Variable</th>
<th>n=45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex = female, n (%)</td>
<td>29   (64)</td>
</tr>
<tr>
<td>Mean gestational age at birth (months), (SD)</td>
<td>8.5  (0.7)</td>
</tr>
<tr>
<td>Preterm delivery (&lt;8.5 months), n (%)</td>
<td>14   (31)</td>
</tr>
<tr>
<td>Mean birth weight (kg), (SD)</td>
<td>2.7  (0.7)</td>
</tr>
<tr>
<td>Delivery location, n (%)</td>
<td></td>
</tr>
<tr>
<td>Public hospital</td>
<td>26   (58)</td>
</tr>
<tr>
<td>Local clinic</td>
<td>13   (29)</td>
</tr>
<tr>
<td>Home</td>
<td>3    (7)</td>
</tr>
<tr>
<td>Other/BBA</td>
<td>3    (7)</td>
</tr>
<tr>
<td>Delivery method, n (%)</td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>37   (82)</td>
</tr>
<tr>
<td>Caesarean – emergency</td>
<td>6    (13)</td>
</tr>
<tr>
<td>Caesarean – elective</td>
<td>2    (4)</td>
</tr>
<tr>
<td>Infant feeding method, n (%)</td>
<td></td>
</tr>
<tr>
<td>Exclusive formula</td>
<td>38   (84)</td>
</tr>
<tr>
<td>Exclusive breastfeeding</td>
<td>1    (2)</td>
</tr>
<tr>
<td>Mixed-feeding</td>
<td>6    (13)</td>
</tr>
</tbody>
</table>

All variables are self-reported. Percentages may not equal 100% due to rounding.
Note: SD, standard deviation; BBA, born before arrival on route to healthcare facility
Evaluation of PMTCT ARV Regimens

Through triangulation of quantitative and qualitative data, it was determined that 29 mother-infant pairs (64%) did not receive or take a PMTCT ARV regimen in accordance with the then current national guidelines. Of the 29 mother-infant pairs, inadequacies were noted in the regimens taken by 27 mothers and 13 infants. **Figure 2** displays the evaluation of regimens taken by these 29 mother-infant pairs.
**Figure 2: PMTCT ARV regimen evaluation**

Non-receipt of per-guideline PMTCT ARV regimen

\[ n=29^* \]

**Mothers**  
\[ n=27 \]
- No ARV intervention  
  \[ n=7 \]
- sdNVP only  
  \[ n=5 \]
- AZT or HAART <2 months  
  \[ n=11^{**} \]
- AZT 2+ months for HAART-qualifying mothers  
  \[ n=1 \]
- HAART  
  \[ n=1 \]

**Infants**  
\[ n=13 \]
- No ARV intervention  
  \[ n=2 \]
- AZT only  
  \[ n=1 \]
  + sdNVP  
  \[ n=10 \]
- No sdNVP  
  \[ n=0 \]

\*Number of mother-infant pairs  
**Of these 11, 1 mother was also HAART-qualifying (CD4 of <200 cells/ml)
Qualitative Findings: Exploring Contextual Factors Contributing to PMTCT Failures and MTCT Risk

Three main themes emerged from the qualitative component of this study, including 1) delayed ANC attendance due to fear of HIV testing, affecting initiation of care and appropriate timing of uptake, 2) HIV-associated stigma affects women’s decisions surrounding PMTCT, and 3) lack of knowledge and mixed messages surrounding ARV use and feeding options may heighten infant risk. Summarized findings of these themes are presented here.

i) Delayed ANC attendance due to fear of HIV testing, affecting initiation of care and appropriate timing of uptake

In this study, nine mothers (20%) either did not attend ANC or attended late in pregnancy (after seven months gestation), hindering the optimal timing of ARV initiation for purposes of PMTCT. Mothers discussed that it was well understood that ANC involved HIV testing, and that fear of testing, particularly for the first time, was a barrier to seeking out care. One young woman expressed fears surrounding testing positive, as follows:

“Some [women] are scared as they think that if they book [at ANC] they will be found to be HIV positive, and are not sure how they would deal with that.” (FGD participant, 22 years)

Another older woman expressed similar fears regarding testing at ANC, particularly as she suspected her status, as illustrated below:

“I didn’t book at an antenatal clinic because I was afraid that they would test me for HIV, so I avoided it as I told myself that I might be found to have this disease. This fear was due to a lack of knowledge. My husband died but I did not know what killed
him, you understand. So this is what I was running away from. I didn’t want to test.”

(FGD participant, 38 years)

An additional participant articulated the fear of receiving the test, as it signified a conclusion regarding one’s HIV status:

“It is difficult [booking at ANC] because you know that since you are pregnant, this is the time when you will know whether you are positive or negative.” (FGD participant, 33 years)

However, participating mothers discussed the importance of ANC attendance and HIV testing to maximize the prevention benefits for their infants. Associated with this idea, they acknowledged the value of earlier and more frequent HIV testing in pregnancy, and initiation of ARVs sooner in pregnancy:

“Booking early, i.e., at 3 months is helpful so that if there is disease you can be treated in time, which may also protect the baby from being HIV positive.” (FGD participant, 33 years)

Another older woman echoed similar feelings surrounding the importance of early testing, even outside of pregnancy:

“First and foremost I would say that once you discover you are pregnant, you must get an HIV test as early as possible. If I had tested early enough perhaps there would have been a difference. It’s important to know your status even if you are not pregnant…” (FGD participant, 38 years)

Additionally, another mother emphasized the need for earlier initiation of treatment:
“I think this medication should be started sooner. As you can see they [other FGD participants] all took them but their babies are positive.” (FGD participant, 33 years)

While women had varied experiences with the ANC booking process and initiated care at different points in their pregnancies, in general they felt that booking was a straightforward process if you followed the guidelines of the local clinics, such as arriving very early in the morning and attending the clinic in closest geographic proximity to your home. Many women reported that disregarding clinic rules could potentiate a delay in obtaining care, as illustrated by one mother:

“At my local clinic we book as from Thursday. They take 10. If ever you are number 13 or whatever, you are told to come back next Thursday. Still if you don’t wake up early, you will go back the following Thursday. You will find the clinic full because you did not wake up; come next Thursday.” (FGD participant, 28 years)

Another woman attending a different ANC site reported a similar situation at her clinic:

“At the time I went to the clinic, they turned 3 people away because they wanted 6 people.” (FGD participant, 22 years)

ii) HIV-associated stigma affects women’s decisions surrounding PMTCT

Stigma surrounding HIV infection was discussed by the participants, particularly relating to receiving support from family and friends, and infant feeding. Firstly, women acknowledged that HIV-positive pregnant women without proper support may face additional challenges in adhering to PMTCT regimens. One women described the hopelessness that an HIV-positive test signified for her:
“When you get home [from the clinic] you are confronted straight away, ‘what did you get today?’ . This is not right and you get more stressed, contemplate suicide and stop thinking for your children. You even forget that if you get treatment you will live. When you are leaving a testing site, just after you have been tested, there is this feeling that when people look at you they already know this thing that’s in you. When they laugh, it’s as if they are laughing at you. You even wish to stay indoors.” (FGD participant, 31 years)

However, other women felt that HIV-associated stigma did not play a very important role in their daily lives, as illustrated by one mother:

“But nowadays issues surrounding HIV infection are different. Before people were like, so and so is positive, don’t get close to her she will infect you. But for now, I tell everyone, I don’t hide my status.” (FGD participant, 33 years)

HIV-associated stigma was also identified as an issue of importance in regards to infant feeding, specifically relating to the government-funded formula tins. These differ noticeably from store-purchased products due to a special government stamp indicative of the formula provision program for HIV-positive mothers. Women reported varying views:

“With me I peel off the paper, because they talk a lot. I used to hide the tin under my bed. I even put bricks to raise the bed. I peeled off the wrapper. It has an orange stamp, about 4 or 3 written lines, unlike the one from the shop.” (FGD participant, 31 years)

Another participant, however, explained that she was not as personally affected by the use of the government formula:
“I personally do not have a problem, but if someone finds you using Pelargon they suspect you are positive. I used to be shy. I used to pour it into a Lactogen tin. But now… if you come to my house you will find it on the table. One of my cousins was looking for a stamp on my Pelargon tin… Maybe her friends told her to check for a stamp. She found it, but I wasn’t bothered.” (FGD participant, 28 years)

iii) Lack of knowledge and mixed messages surrounding ARV use and feeding options may heighten infant risk

Women expressed the need for provision of more information at the ANC clinics surrounding the use of ARVs in pregnancy. Many suggested that prior to and during their pregnancy, they wished they were given more information. Women voiced recognition that the local clinics were often overburdened and short-staffed, possibly limiting the resources available for PMTCT counselling. One woman articulated the questionable information she received at ANC regarding the use of PMTCT ARV regimens and their effectiveness:

“When I discovered I was HIV positive, my first option was to have an abortion because I had no intention of having a baby in being HIV positive. But the sister said the baby could be OK if given treatment. I asked her if she was 100% sure and she said with current research, it is possible for the baby to be alright. So I left it like that.” (FGD participant, 31 years)

In terms of infant feeding, women were provided with a variety of messages at both the ANC clinics and delivery sites. While some women reported that they were instructed and encouraged to formula feed, others were provided with all of the available options and information on the associated risks. Some mothers felt they
were not provided with enough counselling on any of the methods. Others reported confusion surrounding the information they were given:

“Regarding this bottle or cup feeding [formula feeding] there is confusion. In the same clinic, a sister tells you that breastfeeding is best for the baby and it will protect against illnesses, as the baby no longer gets infected that way if you don’t mix. Another tells you that you must not give breast milk, as it will make the baby positive. It’s the same clinic but different sisters have different stories about breastfeeding and cup feeding.” (FGD participant, 31 years)

Further confusion existed at the delivery sites in terms of instruction and messages provided by staff. Indeed, one young mother suggested that her infant did not receive any source of nourishment until a day after birth, due to disagreement and confusion at the delivery site:

“...He [newborn infant] didn’t eat till the following day because they insisted that I should breastfeed. I refused because I knew my status. They said I should till six months as there was no problem. I waited for my mother to bring the milk.” (FGD participant, 22 years)
DISCUSSION AND CONCLUSIONS

To the author’s knowledge, this study constitutes the first mixed-methods assessment of maternal and infant PMTCT ARV regimens utilized in Soweto using data obtained directly from the perspective of mothers. Using such an approach, it was possible to identify failures in the PMTCT ARV cascade that may have otherwise remained unreported. The qualitative findings further inform and enhance this PMTCT ARV evaluation, to include documentation of mothers’ lived experiences in this setting and provide insight into possible reasons for the inadequacies in PMTCT ARV administration and associated vertical transmissions.

The major finding of this study is that while ANC and PMTCT uptake was high among participants, a great number of per-guideline PMTCT ARV failures occurred. Importantly, of the 29 mother-infant pairs identified as not receiving adequate regimens, 25 of the mothers took either no, or a truncated length, of prenatal AZT or HAART. This finding may be explained in part due to the high proportion of infants delivered preterm (prior to 8.5 months gestation). It has been documented previously that pregnant women living with HIV are more likely to deliver early, especially in resource-constrained settings (40,41). At the time of study conduction, the national PMTCT guidelines allotted AZT prescription for women ineligible for HAART only beginning at 28 weeks gestation (26). Consequently, infants born early were relegated to sub-optimal regimens due to this systematic constraint – regardless of the timing and uptake of maternal care.

There is evidence demonstrating that when mothers receive an inadequate duration of ARVs in pregnancy, postnatal infant AZT prophylaxis provides a PMTCT
benefit (7). However, as reported here, a number of infants did not receive AZT prophylaxis for the optimal length, based on the duration of maternal therapy. This finding may be indicative of the need for improvement in PMTCT implementation and operational strategies at some sites. More specifically, this finding may speak to miscommunications between mothers and healthcare staff surrounding the length of maternal AZT or HAART prophylaxis taken in pregnancy.

Furthering this idea, three participating mothers were identified to have received prenatal AZT, even though their self-reported CD4 counts in pregnancy suggest they were eligible for HAART. This is a finding of significant concern, as the rapid initiation of full HAART regimens in pregnant women with advanced HIV infection is of critical importance (42). The aetiology of this failure is hypothesized to be delayed CD4 results from laboratories or healthcare worker confusion over increasingly complex PMTCT algorithms. While identified throughout this study, operational problems in PMTCT implementation are not a novel finding of this project (9,20,21,28).

Operational and systematic constraints were also evident through the provision of contradictory information surrounding PMTCT and infant feeding. Low-quality PMTCT counselling has been identified previously as a concern in South Africa (43). It is worth noting, however, that one contextually appropriate optimum method of infant feeding has not yet been consistently defined for all HIV-positive mothers (44). This may result in counsellors not feeling equipped to provide clear messages. Prioritizing the further training of healthcare staff and personnel may assist in alleviating this concern.
Although the complete avoidance of ANC among study participants was low, maternal refusal of care and non-adherence to prescribed regimens cannot be overlooked as factors contributing to MTCT in this setting. Prior qualitative studies have documented that prominent reasons for care refusal include fear of knowing one’s HIV status, mistrust of the test, stigma associated with institution-supplied infant formula, lack of male partner support, fear of male partner reaction, and negative attitudes of health workers (45-47). Encouragingly, some mothers reported a shift in community attitudes towards HIV – yet this feeling was not shared by all participants.

While this study’s identification of 29 mother-infant pairs not receiving per-guideline PMTCT ARV interventions fulfils a primary objective of the investigation, discussion of the 16 remaining pairs (36%) who did receive per-guideline care is also of interest. In these 16 instances, all mothers and infants were provided with the appropriate ARV regimens according to their eligibility; however, vertical transmission still occurred. These mother-infant pairs serve as true “failures” of PMTCT, especially highlighting the inherent limitations of the AZT/sdNVP regimen. Aetiology of MTCT in these cases is hypothesized to be multifactorial. Firstly, the initiation of ARV prophylaxis (whether AZT or HAART) in pregnancy has no ability to reverse transmissions occurring early in gestation (3). As an estimated 3% of transmissions are thought to occur in-utero prior to 14 weeks gestation, and a further 17% between 14-36 weeks (in non-breastfeeding populations), the prophylactic regimens received by many mothers in this study would not have prevented transmissions occurring at these earlier stages (3). Further, three infants from these 16 mother-infant pairs were mixed-fed, a feeding method well-known to increase the
risk of MTCT (48). Also of importance, while not reported in this study, obstetric practices and/or delivery complications may have contributed to MTCT risk among these mother-infant pairings (49). Finally, the employed study design, involving self-reports of ARV regimens taken and feeding methods may have resulted in the underreporting of MTCT risks such as treatment refusal and mixed-feeding. Mixed-feeding is of concern especially in mothers discontinuing ARV therapy after delivery (i.e., mothers not yet eligible for HAART) (48).

The main limitation of this study is that data were collected only from the perspectives of mothers. This may have allowed for instances of recall bias, particularly surrounding occurrences such as CD4 test results and ARV regimens taken months prior to study conduction. Conducting medical record reviews may have assisted in ensuring accuracy in some of these desired variables; however, many of the participating mothers were not PHRU patients, and thus would not have files available for review onsite. In attempt to minimize this bias, an eligibility criterion was established limiting inclusion to mothers who had delivered recently (on or after December 1, 2008). Furthermore, the use of an interviewer may have created a social-desirability bias, possibly causing underreporting of issues such as participant refusal in PMTCT. To limit this bias, facilitators and interviewers were local women who were not involved in the routine clinical care of the mothers and/or infants.

The data presented here may also be limited due to the participant eligibility criteria. Of note, participating mothers were selected conveniently from just one site in a large urban township, and therefore, these results may not be representative of the experiences of all pregnant HIV-positive women in South Africa. Further, this work only explores the experiences of mothers, and does not account for the
challenges that healthcare staff at PMTCT sites may experience in implementing the evolving national treatment guidelines. Future studies documenting the perspectives and experiences of PMTCT providers in this setting would be of value.

A final important limitation is the fact that the PMTCT evaluation portion of this study was focused solely on ARV regimens. In fact, successful PMTCT involves a comprehensive set of interventions, including not simply the provision of ARVs, but also precautionary measures taken during delivery, and replacement feeding or ARV provision during breastfeeding (26).

Despite these concerns, the collected data are of value as they document the experiences of a group of birthmothers of recently diagnosed HIV-positive infants during the era of PMTCT programmatic scale-up in South Africa. The data presented here provide insight into reasons for possible failures in the PMTCT ARV provision cascade. These data are of timely importance, particularly as additional countries undergo PMTCT scale-up in accordance with the newly released 2010 WHO treatment guidelines for HIV-positive pregnant women in resource-constrained settings (30).

In 2001, the United Nations General Assembly called for a 50% reduction in vertical HIV transmission, alongside 80% PMTCT access globally, by 2010 (50). This goal will remain unmet if individual, structural, and operational factors and barriers continue to hinder access to and uptake of available therapies.
FINAL REMARKS

Encouragingly, it is worth noting that since the time of study conduction, the South African PMTCT guidelines have evolved. Specifically, the earlier provision of AZT has been embraced in the 2010 guideline revision – with recommended initiation from 14, instead of 28, weeks gestation (42). Optimistically, this change will negate the significant MTCT risks of preterm birth documented in this study. The new guidelines also denote pregnant women as a “priority demographic” for rapid HAART initiation at an increased CD4 eligibility cut-off of 350 cells/ml, thereby raising the number of women eligible for the most effective PMTCT ARV intervention.

This evolved PMTCT ARV algorithm, however, is also more complex, as there is an increased variety and frequency of drug administrations at various stages of the provision cascade – possibly lending to additional opportunities for prescription errors, as identified in this study. More rigorous staff training and the introduction of continuous quality control measures are therefore recommended. Furthermore, widespread provision of information and educational materials about PMTCT (over and above counselling), is clearly necessary for all ANC clients.

Finally, the availability of improved PMTCT ARV regimens will have little impact if pregnant women continue to access care late in pregnancy (33). Programs and interventions aiming to diminish barriers to care and encouraging maximal PMTCT uptake and utilization are thus of urgent necessity.
REFERENCE LIST


