A descriptive study of outcomes of interventions to prevent mother to child transmission of HIV in two primary health care centres in Lusaka, Zambia.

Chibesa Shichitamba

A dissertation submitted to the University of Zambia in partial fulfillment of the degree of Masters in Public Health

2013

THE UNIVERSITY OF ZAMBIA

COPYRIGHT

Chibesa Shichitamba

2013

CERTIFICATE OF COMPLETION OF DISSERTATION

I,**Chibesa Shichitamba,** do hereby certify that this dissertation is the product of my own work and, in submitting it for my MPH program further attest that it has not been submitted in part or in whole to another University.

Signature: _____ Date_____

I, **Dr C. Kankasa**, having submitted and read this dissertation, am satisfied that this is the original work of the author under whose name it is being presented. I confirm that the work has been completed satisfactorily and is hereby ready for presentation to the examiners.

Supervisor: Dr. C. Kankasa

Supervisor's signature: _____

Date: _____

Head of Department

Signature_____ Date_____

Department of Public Health, School of Medicine, University of Zambia

Declaration

I declare that this dissertation is my own work. It is being submitted for the Master's degree in Public Health at the University of Zambia, Lusaka. It has not been submitted before for any degree or examination at this or any other University.

Signed…….

Student: **Chibesa Shichitamba**

Signed…….

Supervisor: **Dr Chipepo Kankasa**

Signed……

Head of Department of Public Health

Certificate of Approval

This dissertation of Chibesa Shichitamba is approved as fulfilling the requirement for the award of the degree of Masters of Public Health by the University of Zambia.

Examiner – 01

Name: ----------

Signed: ----------

Date: ----------

Examiner – 02

Name: ----------

Signed: ----------

Date: ----------

Examiner – 03

Name: ----------

Signed: ----------

Date: ----------

Head of Department:

Name: ----------

Signed: ----------

Date: ----------

ABSTRACT

Background

Mother-to-child transmission (MTCT) of HIV still remains a major problem worldwide accounting for 90% of the infection in children under the age of fifteen years. In Zambia, Prevention of Mother to Child Transmission (PMTCT) of HIV activities have been carried out for over a decade. Few studies have described the outcome of the interventions. This study, a retrospective observational cohort study, determined whether the PMTCT interventions have been of benefit to HIV exposed children, by reducing HIV vertical transmission.

Method

Data was extracted from the clinical and laboratory records of 534 mother-infant pairs in the MTCT-Plus cohort. Analysis using Pearson Chi –square test for categorical variables, and bivariate and multivariate regression analysis to examine predictors of a positive HIV outcome was done.

Results

A total of 534 infants had their final HIV status established, of which 101 (18.9%) were positive. The proportion of infants with a positive HIV test was much lower in infants where the maternal regimen was Highly Active Antiretroviral Therapy (HAART) at 6.6% (6/91), whilst that of infants where the maternal regimen was single dose nevirapine was 19.9% (74/372).

Conclusion

This study indicates that the Prevention of Mother-to- Child Transmission of HIV treatment interventions in two Lusaka urban clinics appear to have been effective, with the use of HAART regimen for PMTCT having the lowest transmission rate.

TABLE OF CONTENTS

Copyright.....i

Certificate of completion of dissertation.....ii

Declaration……..….....iii

Certificate of approval…..…….…….....iv

Abstract……..……..v

Table of contents…..…….……vii

Dedication……...x

Acknowledgements……..……..…….……...xi

Abbreviations……...……...……..…xii

List of tables..……..……..xiv

CHAPTER ONE…..….....1

1.0 Introduction……..….1

1.1 Problem statement.....4

1.2 Justification for the study.....5

CHAPTER TWO……..……...……..7

2.0 Literature review.....7

2.1 Introduction…….....7

2.2 PMTCT interventions.....8

2.3 PMTCT in Zambia…….....12

CHAPTER THREE……..…...19

3.0 Study objectives.....19

3.1 Research question……...19

3.2 General objective.…….....19

3.2.1Specific objectives.....19

3.3 Study variables…….....20

3.3.1 Main outcome variable.....….....20

3.3.2 Exposure factors…….....20

3.3.3 Possible confounding factors…….....20

CHAPTER FOUR…….....21

4.0 Methodology…….....21

4.1 Study design…….....21

4.2 Study site…….....21

4.3 Study population….....21

4.4 Selection of study population.....22

4.5 Study procedure…….....22

4.6 Data processing and analysis…….....23

4.7 Ethical consideration….....23

4.8 Sample size.....24

4.9 Sampling.....25

CHAPTER FIVE…….....26

5.0 Results.....26

5.1 Description of study population…….....26

5.1.1 Maternal information…….....26

5.1.1 Infant information..... 29

5.2 Transmission rates……...30

5.3 Multivariate analysis predicting positive infant HIV outcome……..32

5.4 Multivariate analysis predicting positive HIV infant or death…….....33

CHAPTER SIX……..…….….35

6.0 Discussion…….……..…….35

6.1 Summary of findings…..…….…….35

6.2 Maternal regimen…….36

6.3Predictors associated with a positive HIV outcome in infants…….……...38

6.4 Limitation of study……...39

6.5 Conclusion and recommendations…….…….....40

References……..42

Appendix 1…….…….…….....49

Appendix 2…….……....51

Appendix 3……..…….…….....52

Appendix 4…….……53

Appendix 5…….……55

Dedication

This work is dedicated to my children Mukela, Chibesa, Mangolwa and Mukata.

To my late mother Mangalita Mpuku Shichitamba who had zeal to have all her nine children educated.

Acknowledgements

I wish to express my sincere gratitude to my supervisors, Professor Seter Siziya and Dr. Chipepo Kankasa for their untiring encouragement and guidance in the course of this research. I acknowledge the guidance of the late Dr. Gavin Silwamba who was one of my supervisors before his untimely demise.

I also wish to thank Dr. Elizabeth Stringer and Michelle Li for assistance rendered.

I am indebted to the Lusaka District Health Management Team and to Chelstone and Mtendere Staff for allowing me to carry out my research.

My gratitude also goes to friends Rokaya Ginwalla and Lois Munthali for encouraging me in the course of this research.

Special thanks to my employers, Ministry of Health for sponsoring my MPH studies.

ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
AZT	Azidothymidine
ART	Anti-retroviral Therapy
CDC	Centre for Disease Control and Prevention USA
DHMT	District Health Management Team
EFV	Efavirenz
FHI	Family Health International
FTC	Emitricitabin
Hb	Haemoglobin
HAART	Highly Active Anti-retroviral Therapy
HIV	Human Immunodeficiency Virus
IATT	Inter Agency Task Team on Prevention
NVP	Nevirapine
NAC	National AIDS Council
MOH	Ministry of Health
MCH	Maternal Child Health
MTCT	Mother to Child Transmission
PMTCT	Prevention of Mother to Child Transmission

RNA	Ribo-Nucleic Acid
Stat	statum
SD	Single Dose
TDF	Tenofovir

μlmicro litre

UNAIDS	Joint United Nations Program on HIV /AIDS
UNICEF	United Nations Children's' Fund
USAID	United States Agency for International Development
WHO	World Health Organization
ZDV	Zidovudine
ZDHS	Zambia Demographic and Health Survey
ZEBS	Zambia Exclusive Breast feeding Study
3TC	Lamivudine

List of Tables

Page

1. Table 1……..28
2. Table 2……..30
3. Table 3……..……..31
4. Table 4…….32
5. Table 5…….34

CHAPTER ONE

1.0 Introduction

The Human Immunodeficiency Virus (HIV) pandemic is one of the most serious problems the world faces today. In 2010, 34 million people were living with HIV, 2.7 million people became infected with the virus, and 1.8 million people died of HIV related causes (UNAIDS 2011). Sub-Saharan Africa had an estimated 1.9 million people become newly infected in 2010.Globally it is estimated that 3.4 million children under the age of 15 years were living with HIV in 2010 (UNAIDS 2011).

Most children acquire the infection through mother-to-child-transmission (MTCT).In the absence of any interventions, the risk of vertical transmission is 15-30 percent in non- breastfeeding populations. Breastfeeding by an infected mother increases the risk by 5-20 percent to a total of 20-40 percent (De Cock et al, 2000).The risk of MTCT can be reduced to less than 2% by evidence based interventions (Thorne, 2005; Dorenbaum et al,2002; Read et al, 2005).

In Zambia it is estimated that about one million people are infected with HIV (National HIV AND AIDS STRATEGIC FRAMEWORK 2006). It is estimated that 39.5% of babies born to HIV positive mothers are infected with the virus (NAC 2002). In 2009, it was estimated that 120,000 children aged 0-14 were living withHIV in Zambia. (UNICEF, 2010)

The HIV crisis has led to increased commitment and support for programs for the prevention of HIV infection in infants and young children. The program for Prevention of Mother to Child Transmission (PMTCT) is a public health program that has been implemented in Zambia

foralmost a decade; with an ultimate goal of preventing HIV infection in infants born to HIV infected mothers.

The Zambia PMTCT program was established in January 1999 by the Ministry of Health. The initial pilot sites were the University Teaching Hospital, Chipata clinic in Lusaka district, Monze Mission Hospital and Kemba Rural Health Centre in Monze District, Mbala District Hospital and Tulemane Health Center in Mbala District. (Kankasa et al, 2002). At inception, the package of care included free voluntary counselling and testing (VCT), screening and treatment of syphilis, anti-retroviral drugs (AZT) prophylaxis for prevention of vertical HIV transmission, infant feeding counselling, infant formula and promotion of male involvement. For anti-retroviral prophylaxis, Zidovudine 300mg twice daily was prescribed from 36 weeks gestation (and later at 34 weeks), and 300mg in labour3 hourly until delivery, or Nevirapine 200mg for the mother (at the onset of labour) and a single dose for the baby at 2milligrams per kilogram body weight within 72 hours of birth.

In November 2001, The Call to Action Program, funded by the Elizabeth Glaser Paediatric AIDS Foundation, was initiated in Lusaka to expand voluntary counselling and testing and Nevirapine availability to all clinics in Lusaka District. Having started in two clinics in 2001, by 2004 the program had expanded to 24 clinics. Currently PMTCT interventions are provided in all primary health care centres in Lusaka.

This retrospective observational cohort study in two of the clinics under Lusaka District describes the outcomes of PMTCT interventions in HIV exposed children;beyond six weeks of age up to the time that a child's final HIV status is established. This status was determined at eighteen months in non-breastfeedingchild or three months after cessation of breastfeeding. The

study highlights whether the PMTCT programis beneficial in reducing transmission of HIV to infants and children as has been observed in other countries.

A study by Stringer et al (2003) assessed the implementation and acceptability of the PMTCT program in Lusaka. Other studies have looked at the integration of PMTCT services into maternal and child health (MCH) services or family planning program (Horizons, 2003). A study by Stringer et al (2003) showed that the use of single dose Nevirapine (SD-NVP) in a prospective cohort in Lusaka had HIV transmission rates at six weeks identical to the landmark HIVNET 012 study in Uganda that had initially demonstrated the efficacy of SD-NVP in an African clinical care setting (Guay et al, 1999).

The study population was a retrospective MTCT-Plus cohort (2002-2007). In 2002, the MTCT-plus Initiative, designed to promote wellness and to improve health care for infected mothers and their children was implemented in two clinics within Lusaka district, namely Chelstone and Mtendere clinic. This initiative was conceived in 2001, as a response to the five point call to action by the then United Nations Secretary (Rabkin and El-Sadr 2003). The initiative was to build on theexperiences of successful PMTCT programs, to create sites where services and high quality HIV care would be linked.

The eligibility into the MTCT-Plus program was limited to a cluster of facilities serving a geographically and socially discrete catchment population. The two centres served as referral centres for these catchment populations. The categories of persons eligible were:

1. Participating woman – any HIV infected woman receiving care at a participating clinic
2. Child of index woman- the child born of the ongoing pregnancy

3. Partner- the father of the index pregnancy (or any partner she is cohabiting with depending on the situation).
4. Additional child- any other child of a participating woman
5. Health care worker- any full time employee of participating clinic.

The HIV infected woman who was or had recently been pregnant was the entry point into this family centred care. The pregnant women were given a single dose of Nevirapine intra-partum. Those women that qualified for HAART were given triple therapy. Babies on delivery were given Nevirapine soon after birth or within 72 hours.

The MTCT-Plus program was implemented from November 2002 to December 2007. Thereafter, all participants were transferred to the current Anti-retroviral (ART) programs in the district clinics. The program enabled a close follow up of all infants born to the HIV infected women in the cohort up until the time when the final HIV status was determined. The HIV final status was confirmed using a rapid antibody test. Those infants found HIV negative were discharged from the program whilst those found positive were followed up until the time of transfer to the HIV care program. This makes the cohort an appropriate population for describing the outcome of thePMTCT interventions. The follow up of the clients was done in such a way as to have the mother infant pair including the spouse if any to be reviewed conveniently at the same time.

1.1 Problem Statement

In the absence of any interventions, approximately 30,000 children of the estimated 475,000 births become infected with HIV yearly in Zambia. Despite integration of the PMTCT activities in our ante-natal clinics, the outcome of these interventions at 18 months of age and beyond has

not been widely described. The MTCT-Plus program did follow up children up to 18 months and beyond. Although data is available for long term follow up, this has not been analysed.

1.2 Justification for the study

Programs for the prevention of HIV infection in infants and young children are gaining increased commitment and support. These programs need continuous monitoring and evaluation in the various settings in which they are implemented to determine their success.

In developed countries, mother to child transmission of HIV has been effectively interrupted by the use of anti-retro viral therapy, elective caesarean section and avoidance of breast feeding.It is worth noting that programs that work well in some settings may fail dismally in others because of differences in the fiscal, socio-economic, demographic, interpersonal and organizational settings in which they are undertaken

In Zambia, PMTCT activities have been carried out for over a decade, however few studies have described the outcome of these interventions. The purpose of the study was to determine whether PMTCT interventions have been of benefit to HIV exposed children, by reducing HIV transmission rates from mother to child.The researcher believes that the results from the MTCT-Plus study will guide the District Health Management Team in the current ART and PMTCT scaling up program, by identifying areas of interventions that require improvement, and thus positively influence planning of PMTCT related activities. The results also give evidence to monitor the progress towards the PMTCT goals, which can be used as a marker of the progress towards attainment of international goals on HIV and AIDS, such as the Millennium Development Goals, to which Zambia is a signatory. In addition, the positive effects, particularly

a marked reduction in vertical transmission, from an in-country perspective will encourage even more HIV positive mothers to accept the interventions.

CHAPTER TWO

2.0 Literature Review

2.1 Introduction

Mother- to-child transmission of HIV remains a major problem worldwide. It is estimated that more than 90% of children living with HIV acquired the virus during pregnancy, birth or breastfeeding- forms of HIV transmission that can be prevented. Rates of transmission have been estimated as follows;

During pregnancy	5-10%
During labour and delivery	10-20%
During breastfeeding	5-20%
Overall without breastfeeding	15-20%
Overall with breastfeeding till 6 months	25-35%
Overall with breastfeeding till 18 to 24 months	30-45%

(Source: de Cock, JAMA (2000).

Risk factors in mother- to- child transmission include a low maternal CD4, high maternal viral load, breastfeeding and vaginal delivery (Mofensen et al 1999, Minkoff et al 1995, Mandelbrot et al1996).

Improvements in child survival have been one of the major targets of development programs during the past decades since 1960. In recent years however, these positive trends have

stagnated, and even reversed especially in many sub-Saharan countries in Africa. This trend has been partly explained by HIV/AIDS. (Walker et al, 2002)

2.2 PMTCT Interventions

The wealth of research on Prevention of Mother to Child Transmission of HIV signifies the magnitude of the problem. In 1994, the first study in the United States among non-breastfed children (Paediatric Aids Clinical Trials Group Protocol 076) demonstrated that with the long regimen of Zidovudine (ZDV), mother to child transmission was reduced by about 67percent (Connor et al, 1994). This regimen consisted of ZDV 100mg five times a day, given to mothers orally between 14 and 36 weeks of pregnancy. During labour ZDV was given by intravenous infusion, and then to infants (2mg/kg) every six hours for six weeks. This regimen was not recommended for developing country because of the complexity and cost.

Since that time, new drugs and drug combinations have been developed. A Centre for Disease Control and Prevention (CDC) sponsored study in Thailand showed a transmission rate of 9.4percent in infants whose mothers' received oral ZDV from 36 weeks gestation through deliveryversus a transmission rate of 18.9percent for infants whose mothers received a placebo. (Shaffer et al 1999)

The UNAIDS PETRA Study in Africa (2002) examined Zidovudine and Lamivudine administration compared with placebo in the prenatal, intra-partum and postnatal periods, and almost all women breastfed their babies. HIV transmission was 9.2percent for those given the anti-retroviral combination therapy.

The National Institute of Health (NIH) sponsored HIV NET 012 study in Uganda compared short course Nevirapine and oral Zidovudine. Nevirapine was administered to the mother as a single dose intrapartum and to the new born at 48-72 hours, while Zidovudine was administered to the mother every 3 hours from the onset of labour through delivery and then to the infant every six hours for one week. Most of the women breast-fed their babies. The HIV transmission was 13.1percent in NVP versus 25.1percent in ZDV group (Guay et al 1999).

Moodley et al (2003) in the SAINT study in South Africa compared Nevirapine monotherapy given in labor and post-partum, including neonatal dose, and a combination of Zidovudine and lamivudine intra-partum dose and seven days post-partum. The results confirmed the HIV NET012 transmission rate of 12.3 percent in the Nevirapine monotherapy, and highlighted the efficacy and safety of short course dual anti-retroviral regimen with a transmission rate of 9.3 percent at eight weeks.

Studies have shown that HAART is associated with the least rate of mother-to-child transmission of HIV. Cooper et al in 2002in a prospective cohort study showed that HAART had the lowest rate of vertical transmission. Ekouevi et al in 2008 in a study in Cote de Ivoire showed that HAART in pregnant African women with advanced HIV disease substantially reduced mother to child transmission. A study in Malawi by Chasela et al in 2010 whose objective was to evaluate the efficacy of a maternal triple antiretroviral regimen or infant NVP prophylaxis for 28 weeks found an HIV-1 transmission risk of 2.9 percent in maternal regimen and 1.7percent in the infant regimen.

In developed countries, other interventions include elective caesarean section, which has been shown to reduce risk of MTCT of HIV by 90 percent in pregnant women with undetectable HIV

RNA, (European collaborative Study, 2005), and the avoidance of breast feeding (Dabis, et al,2004).

Global efforts to fight mother-to-child transmission of HIV began with the launch of the Inter Agency Task Team on Prevention of HIV Transmission in Pregnant Women, Mothers and their Children (IATT), in 1999 by the UNAIDS Secretariat, UNFPA, UNICEF, and WHO. (UNICEF, 2003). The aim of the IATT was to give strong coordinated leadership and guidance to countries for the prevention of mother-to-child transmission of HIV.

The IATT proposed a four pronged approach for the prevention of HIV transmission to pregnant women, mothers and their children:

1. **Primary prevention of HIV in women**

   Avoiding of primary HIV infections in parents to be, will help prevent HIV transmission to infants and young children, as well as help towards other prevention goals. HIV prevention needs to be directed at abroad range of women at risk and their partners. As primary HIV infection during pregnancy and breast feeding poses an increased threat of MTCT, HIV prevention efforts should address the needs of pregnant and lactating women, especially in high prevalence areas. In addition, special effort should be made to prevent future infection among women diagnosed HIV negative especially in ante-natal care settings.

2. **Prevention of unintended pregnancy among HIV-infected women**

   Reproductive health (including family planning) services need to be strengthened so that all women, including those that are infected, can make informed decisions about their future reproductive life, including when to seek appropriate support and services to

prevent unintended pregnancies. Most HIV infected women in the developing world do not know their sera-status. Increased availability of counselling and testing services would enable them to obtain essential care and support services, including family planning and reproductive health services, in order that they can make informed decisions about their future reproductive lives.

3. **Interventions to reduce transmission from HIV- infected pregnant and lactating women to their children**

   For HIV positive women who do become pregnant, WHO has identified a package of interventions for the PMTCT. It includes anti-retroviral drug regimens for HIV infected women and their new born, safe obstetric practices,counselling and support for HIV pregnant women on infant feeding options.

4. **Care and support of women, children, and families infected and affected by HIV/AIDS**

   Care and support must be fully integrated into on-going efforts to improve maternal and child health services, and be tailored to the needs of women for safe and effective antenatal, obstetric, and reproductive health services. This also includes sexual and reproductive health interventions for HIV infected women and other care for HIV infected women and their children born.

(Source: WHO, 2007. Prevention of Mother-to-Child Transmission (PMTCT), Briefing Note, page 5)

In December 2005, representatives of Governments, multilateral agencies, development partners, research institutions, civil society, and people living with HIV, assembled as a matter of urgency

at the PMTCT High Level Global Partners' forum in Abuja, Nigeria to take stock and accelerate action to address the prevention of mother-to-child transmission of HIV, which resulted in a Call To Action for the elimination of HIV infection in infants and children and an HIV and AIDs free generation. (WHO, 2007)

Earlier in 2001, the United Nations Assembly Special Session on HIV/AIDS had set the goal of reducing the proportion of infants infected with HIV by 20percent by the year 2005, and by 50percent by the year 2010.

In 2009, the UNAIDS called for a virtual elimination of mother to child transmission of HIV. In November 2010, WHO in collaboration with UNICEF, UNFPA and UNAIDS organized a technical consultation on the Elimination of Mother to Child Transmission of HIV. The main purpose of the consultation was to provide technical and operational guidance on the goal of MTCT elimination within a framework of support to achieve the Millennium Development Goals (MDGs) by 2015. (WHO, 2010) MDG Goal 6, target 6A aims to have halted by 2015 and began to reverse the spread of HIV/AIDs.

2.3 PMTCT Interventions in Zambia

In Zambia, there have been studies that have measured the feasibility of scaling up single dose Nevirapine as a PMTCT intervention (Stringer et al, 2003).

The study by Stringer reviewed a Nevirapine based peri-natal HIV program initiated in Lusaka in November 2001. Five of the nine delivery centres were targeted. The 'opt-in' approach was used. After group counselling was done, individual counselling followed and those women who expressed interest in the HIV test were tested following signing of a consent form. A 200mg

Nevirapine tablet was given to the positive woman who had completed 26 weeks of gestation, with instruction to ingest the same at the inception of labour.

The study showed that Prevention of Mother to Child Transmission of HIV was feasible and cost effective, however patient attrition and non- adherence represented a major challenge to program success.

The report was only able to give an assumption of infants saved from HIV infection in the program based on knowledge of cumulative transmission rates and expected risk reduction.

Another study in Lusaka by Stringer et al in 2005 looked at the effectiveness of a city wide program to prevent mother to child transmission. This was an anonymous surveillance of newborn cord blood. In the year of the study, there were ten public sector delivery centres in Lusaka, and all participated. All mother- infant pairs delivering during the 12 week surveillance period and who received antenatal care were included in the study.

The main outcome measure was population Nevirapine coverage, defined as the proportion of HIV infected women and HIV exposed infants in the population that ingested Nevirapine. The results showed that out of 2,257 sera-positive mother-infant pairs, only 675 (30percent) received both maternal and neonatal dose of Nevirapine. The surveillance showed that successful peri-natal HIV prevention requires each mother-infant pair to have a successful series of steps from HIV testing through to adherence to prescribed regimen.

Another study by Stringer et al in 2003 looked at the timing of the maternal drug dose and risk of peri natal HIV transmission in the setting of intra-partum and neonatal single dose Nevirapine. In this prospective cohort, 430 HIV infected women had been enrolled; HIV transmission data was

available for 278 women, with 31 infants (11.2percent) infected at 6 weeks. The HIV transmission rate was identical to the 1999 HIVNET 012 trial findings.

The Zambia exclusive breastfeeding (ZEBS) study was designed as a randomized trial evaluating the efficacy of short duration exclusive breastfeeding as a strategy to reduce postnatal HIV transmission, it had HIV free survival at 24 months as a primary outcome (Thea et al 2004).The study showed no net benefit to early breast feeding cessation at 4 months amongst HIV exposed children living in resource limited poor areas, and that exclusive breast feeding in first 4 months significantly reduces HIV transmission.

The primary outcome in this study is the vertical transmission of HIV following PMTCT interventions in both mother and child. The outcome is a means of assessing the impact of the interventions used.

The field of HIV prevention and treatment is very dynamic. In Zambia, from a regimen of a twice a day AZT to single dose Nevirapine to mother and child from inception of PMTCT program, back to a short course of ante-partum Zidovudine beginning at 32 weeks gestation in 2007. In addition, single dose Nevirapinewas still given intra-partum. In 2008, the regimen was modified as shown in Appendix 1. In November 2009, World Health Organization announced new recommendations for preventing mother to child transmission. These included:

- All pregnant women with CD4 counts below 350 or WHO stage 3 or 4 HIV disease should start ART without delay, for life.
- HIV-positive mothers should exclusively breastfeed for the first six months, continued to one year of age if their child is HIV negative or of unknown status, and for at least two

years if their child is also HIV positive, in order to maximize the benefits of breastfeeding.

- Pregnant women who don't need ART for their own health should start taking prophylaxis as soon as possible after week 14 of their pregnancy.
- Either three drugs maternal ART or daily infant prophylaxis should be given throughout the breastfeeding period if the mothers do not need ART for their own health.

The recommendations were later released in July 2010 as 2010 guidelines: "Antiretroviral drugs for treating pregnant women and preventing HIV infections in infants''. The 2010 guidelines refer to two key approaches:

- Lifelong ART for HIV infected women in need of treatment for their own health, which is also safe and effective in reducing mother to child transmission of HIV ,
- Short-term ARV prophylaxis to prevent MTCT during pregnancy, delivery and breastfeeding for HIV infected women not in need of treatment.

Whereas the earlier 2006 guidelines recommended as first line ART regimen Zidovudine (AZT) +Lamivudine (3TC) + Nevirapine (NVP), the 2010 guidelines hadexpanded thenumber of treatment options as first line regimens for pregnant women:

- AZT +3TC +NVP or
- AZT + 3TC + EFV or
- TDF +3TC(or FTC) + NVP or
- TDF + 3TC(or FTC) + EFV

The 2010 guidelines include two options both of which start early in pregnancy at 14 weeks or as soon as possible thereafter.

Option A: Twice daily AZT for the mother from 14 weeks, for the infant prophylaxis with either AZT or Nevirapine for six weeks after birth, if the infant is not breastfeeding. If the infant is breastfeeding, daily NVP infant prophylaxis should be continued for one week after the end of the breastfeeding period.

Option B: A three drug prophylactic regimen for the mother taken during pregnancy and throughout the breastfeeding period, as well as infant prophylaxis for six weeks after birth, whether or not the infant is breastfeeding.

With regard to infant feeding, there are two major changes in the new guidelines from the earlier 2006guidelines:

1. National Health Authorities should decide whether health policies should principally counsel and support HIV positive mothers to either breast feed and receive ARV interventions or avoid all breastfeeding, as the strategy that will most likely give infants the greatest chance of HIV free survival.
2. In settings where national authorities recommend HIV positive mothers to breastfeed and provide ARVS to prevent transmission, mothers should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter, and should continue breastfeeding for the first twelve months of life.

Evidence suggests that with the new guidelines, mother- to- child transmission of HIV could be reduced to less than 5percent in breastfeeding populations, while also providing the best

available treatment for the mother's health. The PMTCT WHO guidelines were first issued in 2000 and revised in 2004, 2006 and 2010. National authorities are advised to choose a national policy based on local circumstances and health system capacity (WHO 2009).

The Ministry of Health in Zambia has updated the guidelines accordingly and has adopted option A of the 2010 guidelines. The recommendations are as follows;

- For HIV positive women from 14 weeks of pregnancy: AZT 300mg twice daily in antenatal period, in labour, 200mg NVP single dose stat at onset and in addition, 150mg of 3TC plus 300mg AZT (combined) , then repeated every 12 hours until delivery. Post natal 3TC 150mg and AZT 300mg twice daily for seven days.
- For HIV positive women presenting in third trimester (36 weeks). AZT 300mg twice daily in antenatal period, in labour, 200mg NVP single dose at onset and in addition, 150mg of 3TC and 300mg AZT, then repeated every 12 hours until delivery. Post natal 3TC 150mg and AZT 300mg twice daily for seven days.
- For HIV positive women who have not received prophylaxis in antenatal period: in labor, 200mg NVP single dose at onset of labour and in addition, 150mg of 3TC plus 300mg AZT, repeated every 12 hours until delivery. Post natal 3TC 150mg and AZT 300mg twice daily for seven days.

  For the exposed infant in the above three recommendations, the breastfeeding infant receives NVP at birth and daily until one week after all exposure to breast milk. In addition, co-trimoxazole is given from six weeks until one week after all exposure to breast milk has ended and is confirmed to be HIV negative. The non-breastfeeding infant

on the other hand receives commercial milk formula, NVP at birth and for six weeks and co-trimoxazole from six weeks until confirmed to be HIV negative.

- For HIV positive women who are on ART or eligible for ART: In antenatal period continue or start ART, continue ART in labour as well as postnatal period. For the exposed infant, the breastfeeding infant receives NVP from birth until six weeks of age. In addition, co-trimoxazole is given from six weeks until one week after all exposure to breast milk has ended and is confirmed to be HIV negative. The non-breastfeeding infant on the other hand receives commercial milk formula, NVP at birth and for six weeks and co-trimoxazole from six weeks until confirmed to be HIV negative. (M.O.H 2010) The details of the regimen are shown in Appendix 1.

The PMTCT program in Zambia has a scale up plan which is called "Virtual elimination of MTCT of HIV and Provision of Care and Treatment of Pediatric HIV. (M.O.H 2010) One of the objectives of this plan is to reduce the vertical transmission of HIV to less than 5 percent by 2015.

The program uses an 'opt-out' approach. The HIV test is routinely recommended and provided to each client. As with any medical procedure, theclient may decline to undertake the test. Evaluating the effectiveness of the interventions is important to determine the success levels in this public health program.

CHAPTER THREE

3.0 Study Objectives

3.1 Research Question

How effective have the Prevention of Mother-to-Child Transmission of HIV treatment interventions been in reducing transmission of HIV in infants and young children at 18 months follow up, in 2 Lusaka urban clinics between 2002 and 2007?

3.2 General Objective

To determine the effectiveness of the PMTCT treatment interventions, in HIV infected women and their children in two selected health centres in Lusaka district (MTCT-Plus cohort) between 2002 and 2007.

3.2.1 Specific Objectives

1. To determine the association between maternal characteristics at enrolment and occurrence of HIV transmission.

2. To determine the association between infant characteristics and occurrence of HIV transmission.

3. To compare the proportions of infants born to HIV infected women that had ingested either single dose Nevirapine for PMTCT or anti-retroviral therapy for treatment, who became infected with HIV in the MTCT plus cohort.

3.3 Study variables

3.3.1 Main outcome variable

Transmission of HIV infection from mother to child was the main outcome measure in this study**.**

3.3.2 Exposure factor

The main exposure measured in the study was the ingestion of either single dose Nevirapine for PMTCT or antiretroviral therapy for treatment where eligible for an HIV positive pregnant woman, and the ingestion of single dose Nevirapine of the infant within 72 hours of birth.

3.3.3 Possible confounding factors

A confounding variable is a variable that is associated with a problem and with a possible cause of the problem. The possible confounders measured in this study were:

- Maternal baseline CD4 count at enrolment
- Maternal educational level and economic status
- Maternal age
- Mode of delivery (spontaneous vaginal delivery/caesarean section)
- Infant feeding options from birth (breastfeeding/formula)

CHAPTER FOUR

4.0 Methodology

4.1 Study design

Thiswas a**r**etrospective observational cohort study**.**

4.2 Study site

The study was carried out in Chelstone and Mtendere primary health care facilities in Lusaka District. These are the clinics that implemented the MTCT-Plus initiative. Chelstone clinic is situated on the eastern part of Lusaka with a catchment population of 95,692. Mtendere clinic is also on the eastern part of Lusaka. It has a catchment population of 64, 669.

4.3 Study population.

Women and their children enrolled in the MTCT-Plus program between 2002 and 2007. Chelstone and Mtendere clinics each serve a geographically and socially discrete catchment population, and receive referrals from smaller health centres within their catchment.

Pregnant women attending antenatal clinic at these centres who were found to be HIV positive were introduced to the MTCT-Plus concept, and those willing to receive care under the program were enrolled. The HIV pregnant women attending antenatal services at the two clinics and their children constitute the target population. This population was selected as they had access to a comprehensive package of PMTCT care which included provision of anti-retroviral therapy. Chelstone and Mtendere clinic at the time of inception of the MTCT-Plus program were the only health centres offering anti-retroviral therapy in addition to PMTCT in a primary care setting,

coupled with active treatment follow up. Follow up of clients was in form of home visits or by phone and this was facilitated by a tracking system as the files were also stored electronically.

4.4 Selection of study population

All the mother-infant pairs in the target population that had accepted to be in the MTCT-Plus program were listed for enrolment. The mother infant pairs with a documented final HIV result were selected for the analysis. The exclusion criterion was those mother-infant pairs in which the infant had no final HIV test result during the course of the study.

4.5 Study procedure

The information relating to the research question was collected through the review of the clinical and laboratory records of the mother-infant pairs. The MTCT-Plus program used standardized forms for each clinical visit. These forms included a screening form, enrolment form and clinical visit form and in addition laboratory forms, which were filled in by the attending health care worker.

The data collected from the maternal forms included age, education attained, employment status, PMTCT regimen and duration, WHO staging and CD4 count at enrollment. The infant data collected included mode of delivery that is whether caesarian section or spontaneous vaginal delivery, breastfeeding data; whether breast fed, or mixed feeding and duration, sex and final HIV status.

Data collection was done in January and early February of 2012, after approval to proceed with the study was granted by the UNZA Research Ethics Committee. Permission to access the client

records was also obtained through the Lusaka District Health Management Team, Ministry of Health.

Two research assistants were engaged in the data collection and a statistician was consulted during data collection and analysis.

4.6 Data Processing and Analysis

The Pearson Chi-square test was used for categorical variables to examine differences in transmission rates by maternal regimen.

Bivariate and multivariate regression analysis was used to identify predictors independently associated with two outcomes: a) positive HIV transmission, and b) positive HIV transmission and death. Crude odds ratios and 95% confidence intervals (95% CIs) were computed using logistic regression models, and adjusted odds ratios and their 95% CIs were generated using generalized estimating equations to account for clustering due to mother infant pairs. The statistical analysis was performed using S.A.S version 9.1.3 (SAS Institute Incorporated Cary, North Carolina)

4.7 Ethical considerations

All clinical records were confidential and continued to be so throughout the study. For analysis, all names were removed and unique numbers designated. No individual patient data is presented. Permission was sought from the UNZA Biomedical Research Ethics Committee. Permission was also sought from the Lusaka DHMT, Ministry of Health to access patient records.

4.8 Sample size

The MTCT-Plus cohort had a total of 534 mother-infant pairs with a documented final HIV result for the infant. This study sought to determine the effectiveness of the PMTCT intervention in the MTCT-Plus cohort. The comparison in vertical HIV transmission to be observed would be made to the expected vertical transmission in the absence of any intervention.

The HIVNET 012 study in Uganda observed a reduction in the transmission rate of 15.8 percent at 18 months.

Ideally, the sample size at 80 percent power and 5 percent significance level is:

$N= (P_1Q_1+P_2Q_2)/ (P_1-P_2) \times f(\alpha, \beta)$ where;

P_1 is expected proportion of vertical transmission of HIV in absence of any intervention which is 40%

P_2 is the expected proportion of vertical transmission of HIV in MTCT-Plus cohort which is 15.8%

Significance level of 5 percent

Power of study (1-β)

Q is 100-P

$N = (40x60+15.8x84.2)/ (40-15.2)^2 \times 7.85$

$3730/ (24.8)^2 \times 7.85$

$3730/585 \times 7.85$

50

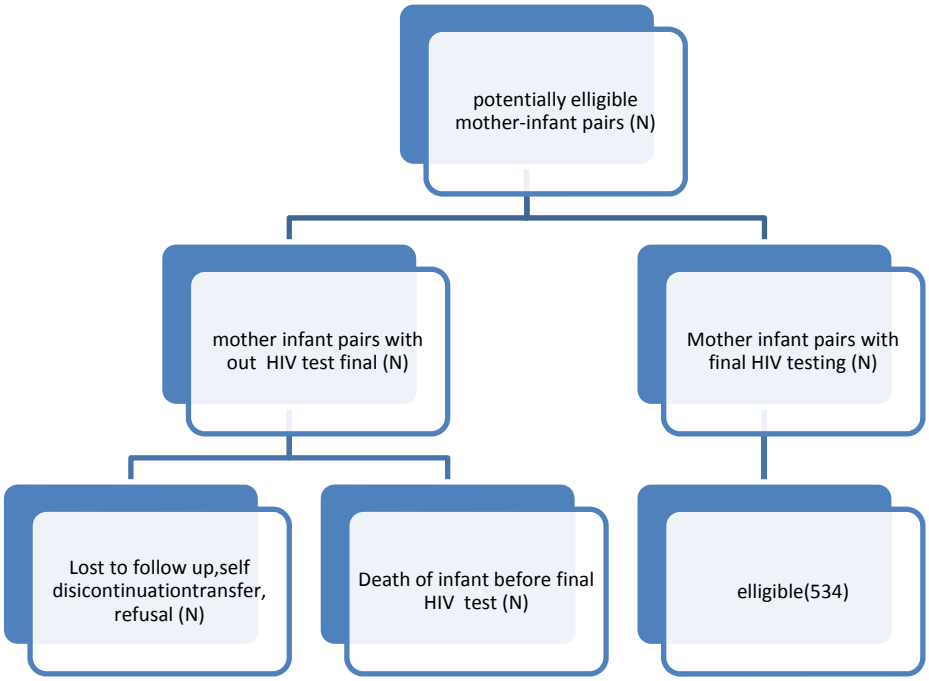
With an expected response rate of 80 percent, then required population is 50/0.8 that is 62.

Considering that the MTCT plus cohort had 534 eligible mother infant pairs, it had been decided to analyze data for the entire group.

4.9 Sampling

As mentioned earlier, the MTCT-plus initiative was to build on the experiences of successful PMTCT programs. It is this prevailing condition that prompted the purposive selection of the cohort. In this regard, all the mother-infant pairs with a documented final HIV result in the infant were included in the study.

The eligibility flow chart is shown below;



CHAPTER FIVE

5.0Results

5.1 Description of Study Population

5.1.1 Maternal Information

A total of 534 HIV exposed children aged 0 to 9 years at enrolment (November 2002-December 2007) who had a documented final HIV result, and their 465 infected mothers were included in the cohort analysis. The mother-infant pairs' clinical and laboratory data were reviewed in the study. Amongst the 465 mothers, there were 9 sets of twins born, 56 enrolled a second child whilst 4 enrolled a third child. This accounts for the difference between the total infants' number and the total mothers' number (465).

The maternal baseline socio-demographic data, enrolment CD4 count (cells/μl), enrolment haemoglobin level, and Prevention of Mother to Child Transmission (PMTCT) regimen are reported.

The median age of the mothers was 28 years (23.7-31.1). A total of 146 (33.0 percent) mothers had a CD4 count of less than 250 cells per micro litre at enrolment. The median CD4 was 334(IQR: 200-502). Most of the women 372 (80.5 percent) had a WHO staging of I. The median of total pregnancies was 3 (IQR 2-4). At least 217 (46.9 percent) of the mothers lived within 30 minutes of the clinic, and for 201 (43.4 percent), time taken being between 30minutes and an hour. A total of 69 (12.9 percent) women did not take any anti-retroviral regimen. This is explained as follows:

- 7 children were ‘other’ children that were enrolled as part of the MTCT program (that is, not the most recent child/pregnancy) – these did not have any prophylaxis as it may not have been available.
- 15 had said ‘YES’ to receiving PMTCT, but had no details about what kind of PMTCT regimen received (for example, HAART or NVP)
- 41 specifically said ‘NO’ to receiving PMTCT
- 6 had missing or unknown PMTCT status

The description of the maternal characteristics is given in Table 1

Table 1: Description of Cohort -maternal characteristics

MOTHERS (n=465)	**N**	**Value**
Age at enrolment (median, range)	446	27.6 (23.7 – 31.1)
Enrolment CD4 Count (median, IQR)	442	334 (200 – 502)
Enrolment CD4 Count < 250	442	146 (33.0%)
EnrolmentHb (median, IQR)	431	11 (9.9 – 12.1)
EnrolmentHb< 10 g/Dl	431	111 (25.8%)
Enrolment WHO (n, %) I II III IV	462	 372 (80.5%) 54 (11.7%) 32 (6.9%) 4 (0.9%)
Distance from Clinic (n, %) <30 minutes Between 30 and 60 minutes Between 1 and 2 hours 2+ hours	463	 217 (46.9%) 201 (43.4%) 40 (8.6%) 5 (1.1%)
Ever Attended School (n, %)	456	427 (93.6%)
Years of schooling completed (median, IQR)	433	9.0 (7.0 – 10.0)
Employed at Enrolment (n, %)	462	81 (17.5%)
Has Electricity at Home (n, %)	463	223 (48.2%)
Has Piped Water at Home (n, %)	462	116 (25.1%)
Marital Status at Enrolment (n, %) Legally Married Living with a partner Non-married with no partner Widowed	455	 353 (77.6%) 7 (1.5%) 78 (17.1%) 17 (3.7%)
Gravidity (median, IQR)	461	3.0 (2.0 – 4.0)
Parity (median, IQR)	461	2.0 (1.0 – 3.0)
On ARVs at Enrolment (n, %)	464	14 (3.0%)

Abbreviation: IQR, Inter-quartile range;

5.1.2 Infant Information

The transmission of HIV infection from mother to child was the main outcome measure in the study. The final HIV status was determined at 18 months in the non-breastfeeding or three months after cessation of breastfeeding. The feedingpractices were self-reported as well as the infant HIV prophylaxis regimen. A total of 534 infants had their final HIV status established, of which 101 (18.9 percent) were positive. The median time to HIV diagnosis in weeks was 78(IQR: 47-89).

A total of 389 (72.9 percent) of the 534 infants were reported to have received single dose Nevirapine as infant prophylaxis. There were 43 (8.0 percent) infant deaths reported during the period under review, of which 25 were HIV positive. Table 2 gives the descriptive characteristics of the infants in the cohort.

Table 2 Description of cohort infant characteristics

INFANT INFORMATION (n=534)	N	Value
Infant Age in Weeks at Enrolment (median, range)	534	9 (5 – 21)
Infant Gender – Female (n, %)	534	271 (50.8%)
Ever Breastfed at 6 months (n, %))	363	312 (86.0%)
Ever Mixed Fed at 6 months (n, %)	308	113 (36.7%)
Ever Breastfed (all patients, regardless FU time)	519	388 (74.8%)
Ever Mixed Fed (all patients, regardless FU time)	530	206 (38.9%)
Maternal PMTCT Regimen (n, %) sdNVP HAART Other* None	534	 372 (69.7%) 91 (17.0%) 2 (0.4%) 69 (12.9%)
Infant Prophylaxis (n, %) sdNVP Other** None	534	 389 (72.9%) 2 (0.4%) 143 (26.8%)
HIV Positive (Final Result)	534	101 (18.9%)
Time to HIV Diagnosis, weeks (median, IQR)	530	78 (47 – 89)
Deaths	534	43 (8.0%)

*Other Infant Regimen consists of single dose and double dose AZT

**Other Maternal Regimen consists of ante partum AZT, and ante partum AZT/intra-partum NVP

5.2 Transmission rates by maternal regimen

The main exposure measured in the study was the ingestion of either single dose Nevirapine for PMTCT or antiretroviral therapy for treatment where eligible for an HIV positive pregnant woman, and the ingestion of single dose Nevirapine of the infant within 72 hours of delivery. However, some women had a short course of Zidovudine given ante-partum beginning at 32 weeks (or at 28 weeks when regimen was later modified). Six of the infants had both single dose Nevirapine and a short course of Zidovudine.

The majority of the mothers (372, 67.7 percent) took single dose Nevirapine for PMTCT whilst 91 (17.0 percent) were on Highly Active Antiretroviral Therapy (HAART) as they were eligible.

The Pearson Chi-square test was used to examine differences in transmission rates by maternal PMTCT regimen. The proportion of infants with a positive final HIV test whose mothers took single dose Nevirapine was 19.9 percent (74/372), whilst 6 out of 91(6.6 percent) infants whose mothers took HAART had a positive HIV result.

Table 3 shows the proportion of infants with a positive final HIV test in relation to the maternal regimen.

Table 3: Transmission Rates by Maternal Regimen (n=532)

Maternal PMTCT Regimen	Percent of Mothers on Regimen	Positive HIV Test Result (Final)
None	69 (12.9%)	21/69 (30.4%)
SdNVP	372 (67.7%)	74 / 372 (19.9%)
HAART	91 (17.0%)	6/91 (6.6%)

Chi-Square test p-value: 0.0005 note: 2 mothers who were on AZT based regimens are not included

5.3Multivariate analysis predicting positive infant HIV outcome

The results of multivariate analysis predicting a positive HIV outcome are shown in the table below.

Table 4 Multivariate Analysis Predicting Positive Infant HIV Outcome (n=467*)

	Crude OR (95% CI)	AOR^ (95% CI)	p-value (adjusted)
Age			
≥27 years old	1.27 (0.82 – 1.96)	1.25 (0.76 – 2.07)	0.383
< 27 years old	1.00	1.00	--
Education			
Ever Attended School	0.52 (0.24 – 1.12)	0.42 (0.17 – 1.04)	0.062
Never Attended School	1.00	1.00	--
Marital Status			
Married/Partner	0.76 (0.45 – 1.27)	0.72 (0.40 – 1.28)	0.262
Single/Widowed	1.00	1.00	--
Enrolment CD4			
< 250	1.21 (0.76 – 1.93)	1.88 (1.07 – 3.31)	0.029
≥ 250	1.00	1.00	--
Enrolment WHO Stage			
Stages III or IV	1.15 (0.53 – 2.49)	1.08 (0.40 – 2.90)	0.885
Stage I or II	1.00	1.00	--
Maternal PMTCT Regimen			
HAART	0.16 (0.06 – 0.43)	0.16 (0.05 – 0.53)	0.003
sdNVP	0.57 (0.32 – 1.00)	0.77 (0.39 – 1.55)	0.471
None	1.00	1.00	--
Infant Ever Breast Fed (6 mon)			
Yes	0.71 (0.43 – 1.17)	0.54 (0.26 – 1.11)	0.095
No	1.00	1.00	--
Infant Ever Mixed Fed (6 mon)			
Yes	1.12 (0.72 – 1.74)	1.86 (1.02 – 3.41)	0.044
No	1.00	1.00	--
Infant Regimen			
sdNVP	0.71 (0.44 – 1.13)	0.89 (0.50 – 1.60)	0.698
None	1.00	1.00	--

*Number of observations included in the model is 467, due to list wise deletion of missing values
^AOR = Adjusted Odds Ratio adjusting for all variables and for clustering due to mother-infant pairs, 95%CI = 95% Confidence Interval

A CD4 count of less than 250 cells per micro litre was significantly associated with a positive infant HIV outcome (adjusted odds ratio [AOR], 1.88 (1.07-3.31), p-value 0.029). A

maternalPMTCT regimen of HAART was significantly associated with a significant reduction in a positive infant HIV outcome (AOR 0.16[0.05-0.53], p-value 0.003). Where a single dose Nevirapine was taken as the maternal PMTCT regimen, a positive HIV outcome in the infant was less likely (AOR 0.77 [0.39-1.55], p-value 0.471), though this difference was not significant. The transmission rate where the mother did not take any anti retro-viral drug was 30.4 percent (21/69).

A positive infant outcome was less likely where there was some maternal education (AOR 0.42[0.17-1.004], p-value 0.062), in the married/with partner mothers (AOR 0.72[0.40-1.28], p-value 0.262) though not significant.

A total of 378 (74.8 percent) infants were reported to have ever breastfed, of whom 206 (38.9 percent) were mixed fed. Ever mixed feeding at six months was significantly associated with a positive infant HIV outcome (AOR 1.86[1.02-3.41], p-value 0.044). Single dose Nevirapine in the infant was associated with a reduced risk of positive HIV outcome (AOR 0.89[0.50-1.60], p-value 0.698), but not significant.

5.4 Multivariate analysis predicting positive HIV infant or death.

Multivariate analysis predicting positive HIV infant or death was also done. Although not a stated outcome in the protocol, mortality is of basic public health importance, and therefore predictors of death in the exposed infants are provided. The results were comparable to those predicting positive HIV infant only, with maternal HAART regimen (AOR 0.19[0.06-0.57] P=0.004) and CD4<250 (1.88[1.07-3.31] P=0.029) being significantly associated with the outcome. Maternal education in the mother though not significant, showed a less likelihood of a positive HIV outcome or death (AOR 0.47[0.21-1.06] P=0.069.

However, mixed feeding though being a risk was not significantly associated with the outcome of HIV positive or death (1.53[0.88-2.65] P=0.132) as was observed in the outcome of HIV only. The results are shown in Table 5.

Table 5: Multivariate Analysis predicting Infant HIV Positive or Death (n=467*)

	AOR (95% CI)^	p-value (adjusted)
Maternal Age		
≥27 years old	1.06 (0.66 – 1.69)	0.818
< 27 years old	1.00	--
Education		
Ever Attended School	0.47 (0.21 – 1.06)	0.069
Never Attended School	1.00	--
Enrolment CD4		
< 250	1.84 (1.08 – 3.14)	0.025
≥ 250	1.00	--
Enrolment WHO Stage		
Stages III or IV	0.84 (0.31 – 2.30)	0.737
Stage I or II	1.00	--
Maternal PMTCT Regimen		
HAART	0.19 (0.06 – 0.57)	0.004
sdNVP	0.74 (0.35 – 1.55)	0.417
None	1.00	--
Infant Ever Breast Fed		
Yes	0.60 (0.31 – 1.15)	0.122
No	1.00	--
Infant Ever Mixed Fed		
Yes	1.53 (0.88 – 2.65)	0.132
No	1.00	--
Infant Regimen		
sdNVP	0.89 (0.48 – 1.62)	0.694
None	1.00	--

*Number of observation s included in the model is 467, due to list wise deletion of missing values
^AOR = Adjusted Odds Ratio adjusting for all variables and for clustering due to mother-infant pairs, 95%CI = 95% Confidence Interval

CHAPTER SIX

6.0 Discussion

6.1 Summary of findings

Mother-to-child transmission (MTCT) of HIV still remains a major problem accounting for 90 percent of the infection in children under the age of fifteen years. This study in two Lusaka urban clinics seems to suggest that Prevention of Mother-to-Child Transmission (PMTCT) of HIV treatment interventions appear to have been effective in reducing transmission of HIV to infants and young children. The proportion of infants with a positive HIV test was much lower in infants where the maternal regimen was Highly Active Antiretroviral Therapy (HAART) at 6.6 percent (6/91), whilst that of infants where the maternal regimen was single dose Nevirapine was 19.9 percent (74/372). This result is comparable to studies reported by others. An eighteen (18) month follow up study of the HIVNET 012 randomized trial by Jackson et al in 2003 showed an estimated risk of HIV transmission of 15.7 percent with the use of single dose Nevirapine. The Kesho Bora Study, a multi-centre study in Africa (Kenya, South Africa and Burkina Faso) has shown a cumulative risk of HIV transmission at twelve (12) months in the triple therapy group of 5.6 percent (95 CI 3.4-8.9 percent).

The Women and Infants Transmission Study (WITS), a prospective natural history study in multiple sites in the United States, with an objective to evaluate the impact of different anti-retroviral regimens on perinatal HIV-1 transmission found that protective effect of therapy increased with complexity and duration of regimens. (Cooper et al, 2002)

In the absence of any maternal anti-retroviral regimen, the transmission was 30.4 percent, which is within the range of 30 percent to 45 percent in overall breastfeeding as was reported by De Cock.

In addition to the maternal regimen, this study found maternal CD4 at enrolment of less than 250 cells/micro litre, and mixed feeding in the infant significantly associated with a positive HIV outcome in the infant.

6.2 Maternal regimens

In the study, the use of triple therapy –Highly Active Anti-retro viral Therapy (HAART) was the most effective in reducing transmission of HIV to the infant, with a transmission rate of 6.6 percent (6/91), P=0.0005, a reduction of 83 percent from the expected 39.5 percent in the absence of any interventions. In the MTCT-Plus cohort, HAART was given to women eligible for treatment as part of the PMTCT. The reduction in transmission rate is comparable to the expected reduction in transmission rate in the 2010 PMTCT WHO guidelines of 5percent or less. The use of HAART in PMTCT is one of the most successful public health interventions in recent times. The Kesho Bora Study in five states in Burkina Faso, Kenya and South Africa (2005-2008) showed a transmission rate of 5.4percent with combination therapy. The Mma Bana study in Botswana (2009) showed a very low transmission rate of 1percent with HAART in a breastfeeding population. A study in Cote d'Ivoire (2008) showed a transmission rate of 2.3 percent in pregnant women that were on HAART.

Single dose Nevirapine also showed a reduction in vertical transmission of 49 percent, (19.9 percent [74/372], P=0.0005). These findings are in line with other studies like the HIVNET 012 study in Uganda. In the current PMTCT guidelines, single dose Nevirapine is not recommended. The 19.9 percent transmission is very high considering that the current goal is towards elimination of vertical HIV transmission. It is worth to note however, that historically, single dose nevirapine had become a primary PMTCT tool in resource limited settings; it was cost

effective and also simple to use. However, it soon became apparent that it was associated with resistance issues. Fly et al in a study in 2005 found K103N Nevirapine resistance mutation variants persisting in some women and children for one year or more after the administration of single dose Nevirapine. In another study by Arrive et al 2007, a pooled estimate of Nevirapine resistance prevalence was 35.7 percent in women in 10 study arms, whereas the corresponding prevalence in children was 52.2 percent. This implies the possibility of treatment failure in both women and children on subsequent HAART regimens containing Nevirapine.

The use of single dose Nevirapine in this study, though no longer acceptable was of some benefit when compared to mothers that did not take any anti retro-viral, at all in whom the transmission rate was found to be 30.4 percent, a result as seen by studies done by De Cock.

One of the criteria for eligibility into the MTCT-Plus program was that an HIV infected pregnant woman was attending ante-natal care at the participating clinics. She would thus receive a full package of PMTCT care which included single dose Nevirapine, when not eligible for HAART, with an instruction to ingest the same when in established labour. In the study, 69 (12.9 percent) mothers were reported as not having taken any anti-retroviral drug for PMTCT. A further analysis of this number of mothers showed that 41 denied having received any PMTCT regimen. This raises concern on non-adherence to prescribed counselling and self-administration of PMTCT drugs. A study by Stringer J et al in 2005, to determine the population effectiveness of a city wide perinatal HIV prevention program showed a 32 percent maternal non-adherence to ingestion of prescribed Nevirapine. This study could have shown a lower non adherence as the information was based on self-reporting whereas the study by Stringer was based on an anonymous surveillance of new born cord blood for HIV serology and Nevirapine. However, it

gives an indication of maternal non-adherence being a factor to effectiveness of the program. Temmerman M et al in an observational study in Kenya in 2003 also recommended further qualitative research on the determinants of MCH services coverage and compliance, and the need for improvement in mother-child follow up in order to improve effectiveness of single dose Nevirapine. In another study by Karcher etal 2006 in Tanzania and Uganda observed that directly observed therapy (DOTS) resulted in higher Nevirapine uptake.

6.3 Predictors associated with a Positive HIV outcome in infant

In the study, predictors associated with a positive HIV outcome were a CD4 count of less than 250 cells per micro-litre and mixed feeding in the infant. This is consistent with other studies. A study in France showed a gradual increase in risk of transmission from 15 percent of counts > (greater than) 600 CD4 cells, to 43 percent at counts < (less than) 200 CD4 cells. (Mayaux M J, Blanche S, Rouzioux C et al, 1995). Shapiro, Smeaton and Lockman et al in a study in Botswana found CD4 to be an independent predictor of HIV transmission among others. The HIV RNA viral load is significantly associated with increased risk of transmission as seen in most studies; however thisstudy did not have data on this as HIV RNA was not being done until a later stage of the MTCT-Plus program.

Breast feeding significantly increases the risk of MTCT of HIV substantially (John-Stewart G, et al 2004). Mother-to-child transmission of HIV remains a challenge in resource poor settings. In developing countries, nearly all infants are initially breastfed, and most continue to breast feed until at least six months of age but frequently into the second year of life. (Dabis F et al, 2004). In settings where avoidance of breast feeding is feasible, affordable, and culturally accepted, as

in the United States of America, complete avoidance of breast feeding has been advised since the 1980s. (CDC, 1985)

Zambia is predominantly a breastfeeding population, and hence the need to address breast feeding issues. Mixed feeding in the first 6 months should be discouraged as it has a significant risk associated with HIV transmission as observed in this study.

An observational study in India in 2003 by Phadke M A et al showed an increased risk of hospitalization for replacement fed (animal milk diluted with water) infants born to HIV infected mothers who had received pre-natal ZDV for PMTCT compared to breast fed infants.

In another study by Fawzy A et al 2011, it was found that continued breast feeding is associated with a reduced risk of diarrhoea related morbidity and mortality among uninfected children born to HIV infected mothers, compared to those with early weaning.

Maternal education though not significant was associated with reduced HIV transmission.

6.4 Limitations of the Study

This study was purposively restricted to the catchment population of two health centres in Lusaka where the MTCT-Plus program was being implemented and may not be generalized to the entire Lusaka. However, the population in these two catchment areas is very similar to those in other areas. Information on breast feeding and PMTCT regimen was on self-reported basis.

The method of data collection in the study was the use of existing records. Despite the use of standardized forms in the MTCT-Plus program, there were some uncertainties and inconsistencies within and between records. The results may not be generalized to the entire population as randomization was not used. However, the results give an indication of the success

of the PMTCT interventions and may be used in planning PMTCT activities. The results are expected to be a baseline for further evaluation of PMTCT activities not only in Lusaka but nationwide.

6.5 Conclusion and Recommendations

This study indicates that the Prevention of Mother-to- Child Transmission of HIV treatment interventions in two Lusaka urban clinics appear to have been effective in reducing vertical transmission of HIV. The use of HAART had the lowest reduction in transmission in a breastfeeding population. This is in line with the current PMTCT guidelines, whose goal is to eliminate vertical transmission. In this study HAART was given to the women who were eligible fortreatment, and hence continued ingestion of the same even post-partum.

Single dose Nevirapine, though it reduces the risk of transmission by 49 percent as shown by this study is no longer considered as a PMTCT regimen in the current guidelines. There are areas in the country however, which are very remote where provision of HAART may be a challenge probably due to unavailability of health facilities or trained health care providers. In such an area in the interim, probably a 50 percent reduction in transmission rather than none at all would still be acceptable and probably warrant the use of single dose Nevirapine.

The current PMTCT guidelines have recommendations on infant feeding options. Considering that the body of literature regarding optimal feeding practices has been changing over the years, it is recommended that health care providers be well oriented to avoid confusion and be able to counsel mothers appropriately.

The MTCT-Plus model of family centred care where the mother infant-pairs are reviewed in the same clinic should be encouraged as it makes it easier to follow up the infant right up to the time the final HIV status is determined. The model of care had a deliberate tracking, follow up and monitoring of the women and children post-delivery. In addition, the use of standardized forms enabled the capturing of data which is important in monitoring the impact of the PMTCT interventions.

There is a need for qualitative research on the determinants of compliance to PMTCT interventions to enable a successful program especially as the regimens become more complex.

References

- Arrive E et al 2007. Ghent Group on HIV in women and children. *Int.Journal Epidemiology2007 36(5):1009-1021*
- Centers for Disease Control and Prevention. 1985. Recommendations for assisting in the prevention of peri-natal transmission of human T-lymphotropic virus type III/lymphadenopathy associated virus and acquired immunodeficiency syndrome. MMWR Morbidity Mortality Weekly Report 34: 721-726, 731-732.
- Chasela C S et al 2010. Maternal or infant antiretroviral drugs to reduce HIV-1transmission. *New England J. Med.2010;362:2271-2281*
- Connor E M et al 1994, Reduction of maternal-infant transmission of human immune deficiency virus type 1 with zidovudine treatment. *New England Journal of Medicine; 331:1173-1180*
- Cooper E R et al 2002. Combination anti-retroviral strategies for the treatment of pregnant HIV-1 infected women and prevention of perinatal HIV-1 transmission. *Journal of Acquired Immune Deficiency Syndrome 29:484-494.*
- Dabis F et al 2004. Prevention of HIV transmission through breastfeeding: Strengthening the research agenda. *Journal of Acquired Immune Deficiency Syndrome 2004; 35 (2) 167-168*
- Dabis F et al 2005. Field efficacy of zidovudine, lamivudine and single dose nevirapine to prevent peri-partum HIV transmission. *AIDS 2005:19(3);309-318*
- De Cock K et al 2000.Prevention of mother to child transmission in resource poor countries*. Journal of the American Medical Association, 283(9): 1175-1182*
- De Vincenzi et al 2011. Kesho Bora Study Group. *Lancet Inf.Dis. 2011 11(3):171-180*

- Dorenbaum A et al 2002.Two-dose intra-partum nevirapine and standard antiretroviral therapy to reduce peri-natal HIV transmission. *Journal of the American Medical Association. 288(2):189-198*
- Economic Commission for Africa. Mother to child transmission-plus: *Mitigation Strategies for Africa*. Accessed at http://www.uneca.org on 13/08/07
- Ekouevi et al 2008. HAART-, antiretroviral therapy in pregnant women with advanced HIV disease and pregnancy outcome in Abidjan, Cote d'Ivoire. *AIDS:22(14) 12 September 2008 1815-1820*
- European Collaborative Study 2005. Mother to child transmission of HIV in the era of highly active anti-retroviral therapy. *Clinical Infectious Diseases, 40(3): 458-465.*
- Family Health International 2003. *Baseline AssessmentTools For Pr*eventing *Mother to Child Transmission (PMTCT) of HIV*. Accessed at www.fhi on 21/06/07
- Fawzy A, Arpadi S, Kankasa C et al. Early weaning increases diarrhea morbidity and mortality among uninfected children born to HIV infected mothers in Zambia. J Infectious Diseases 2011
- Flys T et al 2005. Sensitive drug-resistance assays reveal long term persistence of HIV-1 variants with the K103N nevirapine (NVP) resistance mutation in some women and infants after the administration of single dose nevirapine: HIVNET012. *Journal of Infectious Diseases 2005; 192(1):24-29.*
- Guay L et al 1999. Intra-partum and neonatal single dose nevirapine compared with zidovudine for prevention of mother to child transmission of HIV 1 in Kampala, Uganda. *Lancet 1999; 354: 795-802.*

- Gray G. E, Urban M, Cherisich M.F et al. A randomized trial of two post-exposure prophylaxis regimens to reduce mother-to child HIV 1 transmission in infants of untreated mothers. *AIDS 2005; 19(12): 1289-1297.*
- Horizons 2003. Empowering Communities TO Respond To HIV/AIDS.
- Hoffman R, Black V, Technau K et al. Effects of Highly Active Anti-retroviral Therapy Duration and Regimen on Risk for Mother to Child Transmission of HIV in Johannesburg South Africa*. J. Acquired Immune Deficiency Syndrome 2010 May 1:54(1) 35-41*
- Jackson J B et al. Intra-partum and neonatal single dose nevirapine compared with zidovudinefor prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: 18-month follow up of the randomized HIVNET 012 randomised trial. *Lancet 2003; 362 (9387): 859-868*
- John-Stewart G, et al. Breast-feeding and transmission of HIV-1. *J. Acquired Immune Deficiency Syndrome 2004; 35 (2): 196-202*
- Kankasa C et al. *Report on the Rapid assessment of the UN-supportedPMTCT program in Zambia*. UNICEF, 2002.
- Karcher H et al 2006. Outcome of Different Nevirapine Administration Strategies in Preventing Mother-to-child (PMTCT) Programs in Tanzania and Uganda. *Medscape General Medicine. 2006:8(2):12*
- Mandelbrot L et al 1996. Obstetric factors and mother-to-child transmission of human immunodeficiency virus type1: the French peri-natal cohorts. American J. Obstetrics Gynaecology. 175:661-667

- Mayaux M J, Blanche S, Rouzioux C et al, 1995. Maternal factors associated with peri-natal HIV transmission: the French Cohort Study: 7 years of follow up observation. TheFrench Pediatric HIV Study Group. J. *Acquired Immune Deficiency Syndrome Hum. Retroviral. 8:188-194*
- Minkoff, L et al 1995. The relationship of the duration of ruptured membranes to vertical transmission of human immunodeficiency virus. *Am.J.Obstet.Gynaecol. 173:585-589*
- Moodley D et al, 2003. A multi-center randomized controlled trial of nevirapine versus a combination of zidovudine and lamivudine to reduce intra-partum and early post-partum mother-to-child transmission of human immune deficiency virus type 1. *Journal of Infectious Diseases 2003;187 (5): 725-735*
- Mofenson, L et al 1999. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. New England J. Med. 341:385-393
- Ministry of Health 2005. National Protocol Guidelines. Integrated Prevention Mother to Child Transmission Of HIV.
- Ministry of Health 2010. PMTCT 2010 National Protocol Guidelines.
- Millennium Development Goals. http://en.wikipedia.org/wiki/Millenium Development_Goals_Goals, viewed 30th April 2012.
- PETRA Study Team, 2002. Efficacy of three short courses of zidovudine and lamivudine in preventing early and late transmission of HIV 1 from mother to child in Tanzania, South Africa and Uganda. *Lancet 2002:359;1178-1186*

- Phadke M A, Gadgil B, Bharucha et al. Replacement-fed infants born to HIV-infected mothers in India have a hi*gh early post-partum rate* of hospitalization. *J.Nutrition 2003; 133(10):3153-3157*
- Rabkin M and El Sadr W. Saving mothers, saving families; The MTCT-Plus Initiative. WHO 2003. Page 2.
- Read J et al 2005. 'A prospective cohort study of HIV 1 infected pregnant women and their infants in Latin America and the Caribbean' *Conference on Retro-viruses and opportunistic infections Boston, MA, USA22-25 February 2005 (Abstract 790)*
- Rosenfield A et al 2002. The MTCT-Plus program, 'A major initiative to provide treatment and care to HIV infected mothers and their children.' *Paper presented at XIV International conference, July, Barcelona*
- Shapiro R, Smeaton L, Lockman S et al. Risk factors for early and late transmission of HIV via breast feeding among infants born to HIV infectedwomen in a randomized clinical trial in Botswana. *J. Infectious disease 2009;199:1-5*
- Shapiro R et al 2009. A randomized trial comparing highly active antiretroviral therapy regimens for virologic efficacy and the prevention of mother-to-child transmission among breastfeeding women in Botswana. 'MmaBana' Study.*5th IAS conference on HIV Treatment, Pathogenesis and Prevention, Cape Town.*
- Shaffer N et al1999. Randomized placebo controlled trial of short course antenatal zidovudine to reduce perinatal HIV transmission, Bangkok, Thailand. Lancet, 1999;353:773-780

- Stringer EM et al. 2003 Prevention of Mother to Child Transmission of HIV on Africa Successes and challenges in scaling up a nevirapine based program in Lusaka Zambia. *AIDS 2003; 17 :1377-1382*
- Stringer JSA et al 2003. Timing of the maternal drug dose and risk of perinatal HIV transmission in the setting of intra-partum and neonatal single dose nevirapine. *AIDS 2003;17 (11): 1659-1665*
- Stringer JSA, et al 2005. Effectiveness of a city wide program to prevent mother-to-child transmission in Lusaka, Zambia. *AIDS 2005;19 (12):1309-1315*
- Stringer E et al 2010. Coverage of Nevirapine Based Services to Prevent Mother-to-Child HIV Transmission in 4 African countries. *JAMA, 2010;304(3)293-302*
- Temmerman M. Mother-to-child HIV transmission in resource poor settings: how to improve coverage*? AIDS 2003;17(8) 1239-1242*
- Thea M et al 2004. Issues in the design of a clinical trial with a behavioral intervention-the Zambia exclusive breastfeeding study. *Control Clinical Trials August: 25(4); 353-365.*
- UNAIDS 2001. *Summary on the Declaration of Commitment on HIV/AIDS.* United Nations General Assembly Special Session on HIV/AIDS 25-27 June 2001.
- UNAIDS/WHO 2006. *AIDS Epidemic Update*
- UNAIDS/WHO 2008. *AIDS Epidemic Update*
- UNAIDS/WHO/UNICEF 2011. Global HIV AIDS Response. Progress Report 2011.
- UNICEF 2003. *Program Recommendations for the Prevention of Mother to childTransmission of HIV*. A Practical Guide For Managers
- UNICEF 2007. Children and AIDS. A Stocktaking Report

- UNICEF 2008. The State of the World's Children. Women and Children-Child Survival
- UNICEF 2010. The State of the World's Children. Child's right
- Walker N et al 2002. Meeting International Goals in child survival and HIV/AIDS *Lancet vol. 360 July 2002*
- WHO/HIV 2002. Prevention of HIV in infants and Young Children.
- WHO 2004. National Guide to Monitoring and evaluating Programs for the Prevention of HIV in Infants and young Children. Accessed at http://www.who/int/hiv/en
- WHO 2006. *Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV infection in Infants in Resource Limited Settings*. Towards Universal access.
- WHO 2007. Prevention of Mother-to-Child Transmission. Briefing note.
- WHO 2008. Kesho Bora study. Accessed at http://www.who.int/reproductive health /publications/rtis on 2nd April 2012
- WHO 2010.New guidance on prevention of mother-to-child transmission of HIV and infant feeding in the context of HIV. 2010 Guidelines: "Antiretroviral drugs for treating pregnant women and preventing HIV infections in infants".
- WHO 2010. *Technical consultation on the Virtual Elimination of Mother-to-Child Transmission of HIV.*
- Zambia Antenatal Clinic Sentinel Surveillance of HIV/SYPILIS Trends 1994-2002
- Zambia Census of Population and Housing 2000
- Zambia Demographic and Health Survey 2001-2002
- Zambia Demographic and Health Survey 2007

APPENDICES

APPENDIX 1

Anti-retroviral Prophylaxis Regimens to Prevent Mother-to-Child Transmission of HIV. 2008

Course	Antenatal	Intra-partum	Postnatal
Recommended for pregnant women presenting at 28weeks pregnancy or earlier. This is preferred regimen	Mother. ZDV 300mg twice a day starting at 28 weeks or as soon as possible.	Mother. 3TC/ZDV(150/300) Start dose of 2 tablets at onset of labor and 1 tablet every 12 hours until delivery. NVP 200mg single dose at onset of labor	Infant. NVP 2mg /kg oral suspension immediately after birth and ZDV 4mg/kg twice a day for 7 days starting immediately after birth. Mother. 3TC/ZDV (150/300) 1 tablet twice a day for 7 days.
Regimen for pregnant women who have received less than 4 weeks of AZT or HAART before delivery		Mother. 3TC/ZDV(150/300) Start dose of 2 tablets at onset of labor and 1 tablet every 12 hours until delivery. NVP 200mg single dose at onset of labor	Infant. NVP 2mg /kg oral suspension immediately after birth and ZDV 4mg/kg twice a day for 28 days starting immediately after birth. Mother. 3TC/ZDV (150/300) 1 tablet twice a day for 7 days.
Regimen for mother who has received no ARV prophylaxis		Mother. 3TC/ZDV(150/300) Start dose of 2 tablets at onset of labor and 1 tablet every 12 hours until delivery. NVP 200mg single dose at onset of labor	Infant. NVP 2mg /kg oral suspension immediately after birth and ZDV 4mg/kg twice a day for 28 days starting immediately after birth. Mother. 3TC/ZDV (150/300) 1 tablet twice a

			day for 7 days
Where combination regimen not available	None	Mother. Single dose NVP 200mg at onset of labor	Infant. NVP 2mg/kg oral suspension immediately after birth
If the mother did not receive any ARVs for prophylaxis and the mother			Infant. NVP 2mg/kg as soon as possible after delivery and ZDV 4mg/kg twice a day for 28 days.

Source: National Protocol Guidelines, Ministry of Health 2008.

APPENDIX 2 **PMTCT PROTOCOL GUIDELINES MOH**

	HIV Positive Women			All Exposed Infants
	Antenatal	**Intrapartum**	**Postnatal**	
For HIV positive women from 14 weeks of pregnancy	AZT 300mg twice daily	NVP 200mg single dose at onset of labour. 3TC 150mg and AZT 300mg stat dose at onset of labour and thereafter repeat every 12 hours until delivery.	3TC 150mg and AZT 300mg twice daily for 7 days.	**Breastfeeding infant:** i. NVP at birth and daily until one week after all exposure to breast milk. ii. Start co-trimoxazole from 6 weeks until a week after all exposure to breast milk has ended and HIV status confirmed negative. **Non-breastfeeding infant:** i. Commercial milk formula. ii. NVP at birth and for 6 weeks. iii. Start co-trimoxazole from 6 weeks until HIV status confirmed negative.
For HIV positive women presenting in 3rd trimester	AZT 300mg twice daily.	NVP 200mg single dose at onset of labour. 3TC 150mg and AZT 300mg stat dose at onset of labour and thereafter repeat every 12 hours until delivery.	3TC 150mg and AZT 300mg twice daily for 7 days.	
For HIV positive women who have not received prophylaxis antenatally		NVP 200mg single dose at onset of labour. 3TC 150mg and AZT 300mg stat dose at onset of labour and thereafter repeat every 12 hours until delivery.	3TC 150mg and AZT 300mg twice daily for 7 days.	
HIV positive women who are on ART or eligible for ART	Continue ART or if eligible start ART	Continue ART	Continue ART	**Breastfeeding infant:** i. NVP from birth until 6 weeks of age. ii. Start co-trimoxazole from 6 weeks until a week after all exposure to breast milk has ended and HIV status confirmed negative. **Non-breastfeeding infant:** i. Commercial milk formula ii. NVP from birth until 6 weeks of age weeks. iii. Start co-trimoxazole from 6 weeks until HIV status confirmed negative.

Adapted from MOH PMTCT GUIDELINES page 14

APPENDIX 3

Detailed budget

Item	Unit cost	Total required	Total cost
Materials/Supplies/Services			
• Reams of paper	K30,000/ream	6	K180,000
• Note books	K8,000 each	4	K32,000
• Printing costs	K850,000	1	K750,000
• Binding proposal summary	K10,000	25	K 250,000
• Binding main proposal	K15,000	5	K75,000
• Binding draft report	K20,000	2	K40,000
• Binding final report	K50,000	4	K200,000
• Pens, pencils	K1,500	8	K12,000
Sub- total			K1,689,000
Layout of final report(Secretarial service)	K500,000	1	K500,000
Research Assistants	K35,000	2x20 days	K1,400,000
Payment of Statistician	K2,500,000	1	K2,500,000
Payment to Ethics committee for submission	K500,000	1	K500,000
Transport for researcher and assistants	K250,000	3	K750,000
Total			K7,339,000
10% contingency			K733,900
Grand Total			K8,072,900

APPENDIX 4

Data collection form

- Study number for maternal- infant pair { }
- Maternal data

  Age in (years) ___ ___

  Education attained ___

  1= no education
  2= Grade 1-7
  3= Grade 8-12
  4= College/University
  9= missing

Economic Status ____

1= no employment

2= Formal employment

3= Informal employment

9= missing

ARV prophylaxis type ____

1=Single dose NVP

2=HAART

If HAART duration in weeks ____

CD4 count at enrolment ____

- Infant data

  Mode of delivery ____

  S= Spontaneous vaginal delivery

  C= Caesarean section

Sex

F= Female

M= Male

Breast feeding

Y= Yes N= No

If breast fed duration

(In months)

Final HIV status

1= positive

2= negative

APPENDIX 5

Gantt chart on study activities

No.	Activity	Jul 2010 to July 2011	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul
1.0	Prepare and submit proposal to graduate forum and Ethics(UNZA)	X												
2.0	Train research assistants					X								
3.0	Data collection and entry							X	X					
4.0	Data analysis								X	X				
5.0	Report writing									X	X			
6.0	Submit draft report											X		
7.0	Submit final report												X	
8.0	Disseminate findings to DHMT													X