Successes and challenges of the national programme for the prevention of mother-to-child HIV transmission (PMTCT) in Addis Ababa, Ethiopia

Implementation and impact

Alemnesh Hailemariam Mirkuzie

Thesis submitted in partial fulfilment of the requirements for the degree of Philosophiae Doctor (PhD) at Centre for International Health, Universtiy of Bergen.

Bergen, Norway

2011

Dedication

This thesis is dedicated to mothers all over the world who sacrifice their lives for the better future of their children and to my late step-father, Belachew Abebe.

Table of contents

Acknowledgements

I owe my deepest gratitude to all the mothers and their infants who participated in this study. I would like to thank the PMTCT providers who did all the follow up. Special thanks to the field assistants who conducted the questionnaire interviews, the data entry clerk and Addis Mulu who helped me in data handling.

My sincere appreciation goes to my main supervisor Professor Odd Mørkve and co-supervisors Professor Karen Marie Moland, Dr. Mitike Molla, Professor Sven Gudmund Hinderaker and Professor Anne Åstrøm for their relentless support, encouragement and inspiration throughout my study process. Professor Odd Mørkve has a special place in this work from inception to completion. I appreciate his optimism, academic guidance and wisdom that made me well-grounded and confident with my work. God bless him.

I am grateful to my parents and my siblings for their prayer and unreserved support when I needed it most. My close acquaintance Yetatwork Alemayehu, Etabezahu Alemnayehu, Konjit Alemayehu, Selamawit G/Michael, Ermias, Darmyelesh and Tinsae Folle deserve special mention for their enormous contribution to my success. My gratitude goes to my special friends; Absera Teshome, Mitike Molla, Mercy Karimi Njeru, Nazik M. Nurelhuda, Sally El Tayeb and Susanne Urban who made this PhD journey exciting and enjoyable.

My special thanks to the head of the Centre for International Health Rune Nilsen and CIH administration team; Ingvild Hope, Borgny Kvalnes Lavik, Solfrid Vikøren, Unni Kvernhusvik Sagberg, Linda Karin Forshaw, Jørund Kristoffer Nygård, Therese Marianne Istad, Øyvind

Mørkedal and Ana Veronica Cordova at the Division of Student Affair UIB, for all the facilitation whenever I needed.

It is an honour for me to acknowledge my teachers; Astrid Blystad, Kristian Heggenhougen, Bernt Lindtjørn, Knut Fylkesnes, Bjarne Robberstad, Halvor Sommerfelt, Gunner Kvåle, Charles Karamgi, Ole Bjørn Rekdal and David Sam.

I am heartily thankful to my colleagues and friends; Robert Byamugisha, Ingrid Spjeldnæs, Ferda Gülcan, Zeyede Kebede, Mulu Muleta, Angelina Sijaona, Catherine Kahabuka, Lumbwe Chola, Ingvild Sandoy, Amal Elamin, Nkomba Kayeyi, Mari Skar Manger, Maria Mathisen, Lars Thore Fadnes, Mpundu Makasa, Rahel Manumbu, Elin Hestvik, Marte Jürgensen, Gunn Moss, Joseph Rujumba, Bodil Vaga, Selwa M. Nurelhuda, Erling Svendsen, Solver Mortensen, Fabrice, Nils Gunnar Songstad, Girum Tadesse Tessema, friends at St. Michael church in Bergen, friends at the Ethiopian community in Bergen and to all my friends in Fantoft and in Bergen.

I am indebted to the Centre for International Health, University of Bergen and the Meltzer Foundation for the field work support and Statens Lånekasse for the scholarship throughout the study period. My appreciation goes to the GESOMO, Global Health and the HIV research groups for giving me the opportunity to present my study findings and for their constructive comments.

Lastly, I offer my regards and blessings to all of those who supported me in any respect during the proposal development, field work, data analysis and write up.

Above all, I would like to thank the Almighty God and his beloved Mother Virgin Mary.

Executive summary

Mother-to-child HIV transmission (MTCT) is the main source of HIV infection among children under the age of 15. The majority of these transmissions occur *in utero* and during the intra-partum period and are associated with high rate of mortality in the first year of life. Virtual elimination of peri-natal HIV transmission has become the global target following the availability of highly efficacious prophylactic medications. However, persistent programmatic challenges where the epidemic is most severe are threatening the realization of the target. These challenges include unsolved issues related to HIV testing, ensuring access and adherence to prophylaxis medication, access to safe delivery services, access to infant follow up and partner involvement in PMTCT programmes. This thesis aims at addressing these issues and to assess the impact of the national PMTCT programme in Addis Ababa, the capital of Ethiopia.

The study uses cross-sectional, mixed methods and prospective cohort designs. Retrospective data were collected in 2009 from the national PMTCT programme in Addis Ababa. In the cross-sectional design, 663,603 pregnant mothers attending a national PMTCT programme across the city over a six years period were studied. Trends in PMTCT service utilization were analysed, and the rate of MTCT was assessed in relation to changes in HIV testing policy and changes in prophylactic medication regimen. In the mixed methods design, focus group discussions were conducted first to inform a Theory of Planned Behaviour (TPB) questionnaire. The TPB was applied to explain intended and actual HIV testing. Three thousand and thirty three first time antenatal attendees completed the baseline TPB interviews and 2,928 completed their follow up. The prospective cohort study enrolled 282 HIV-positive mothers. The study assessed the proportions of mothers and infants who adhered to medication recommendations and exposed infants follow up. In the same cohort, the

rate of intra-partum transfers and associated adverse outcomes were assessed among the 228 mothers who reported to have given birth.

In the trend analysis a year by year increase in the proportion of mothers receiving HIV counselling and testing was observed between 2004 and 2009. In parallel with the increased number of mothers receiving HIV testing, the HIV prevalence showed a steady decline. Substantial increase in HIV testing occurred following the shift to routine opt-out approach. The data collected using the mixed methods design following the implementation of opt-out testing approach revealed that intention and type of pre-test counselling/information received were independent, significant determinants of HIV testing. Further analysis showed that the majority of mothers who had low intention to test were also tested. Positive attitude towards HIV testing and approval from social network were significant determinants of intended use of HIV testing.

In the trend analysis the proportions of mothers and infants receiving medication for prophylaxis did not show progress over the years. One year after the shift to routine opt-out approach, only 53% of the mothers and 47% of the infants had received medication. The cohort data further revealed gaps in initiating medication during pregnancy (82%) and ingestion of the medication at birth by mother-infant pairs (68%). Delivering at a health facility was an independent determinant of mother-infant pairs' ingestion of medication at birth.

Overall, 75% of the mothers in the cohort gave birth at emergency obstetric and neonatal care (EmONC) facilities and 42% of them were transferred between facilities during the intra-partum period. Multiple transfers happened to 36% of the mothers due to practical constraints within the health system. Mothers in their second pregnancy were less likely to be transferred than mothers in their first pregnancy. The rate of stillbirths was high. Transferred mothers were about six times more

likely to experience stillbirth than mothers who did not. There was no significant association between stillbirth and syphilis test result, mothers' CD_4 cell count and initiating lifelong ART.

Both the trend and the cohort data showed sub-optimal infant follow up services. A small proportion of the exposed infants were HIV tested. The cumulative HIV infections among babies on single dose nevirapine (sdNVP) regimen who were tested at ≥18 months were 14.9% in 2007. In 2009, among infants on combined ZDV regimen the rates of MTCT were 8.2% and 8.4% at six weeks postpartum in the trend data and in the cohort respectively.

The proportion of partners involved in PMTCT programme remained low. In the cohort the majority of the HIV-positive mothers had disclosed their HIV sero-status to their partner and about one-third of the partners who underwent HIV testing were sero-discordant.

The PMTCT programme has expanded rapidly and has been accompanied by an increased rate of testing. However, the performance of the health system was inadequate in providing subsequent PMTCT services for HIV-positive mothers. Missed opportunities to prophylactic medication uptake, intra-partum care, infant follow up and partner involvement in the PMTCT programme could undermine the effectiveness of the PMTCT programme and negatively impact the survival of exposed infants. This should be a matter of immediate concern and a topic of further research.

List of original papers

Paper I

Mirkuzie AH, Hinderaker SG, Mørkve O. Promising outcomes of a national programme for the prevention of Mother-to-Child HIV transmission in Addis Ababa: a retrospective study. ***BMC Health Services Research.*** 2010; 10:267

Paper II

Mirkuzie AH, Sisay MM, Moland KM, Åstrøm AN. Applying the Theory of Planned Behaviour to explain HIV testing in antenatal settings in Addis Ababa - A cohort study. ***BMC Health Services Research.*** 2011; 11:196

Paper III

Mirkuzie AH, Hinderaker SG, Sisay MM, Moland KM, Mørkve O. Current status of medication adherence and infant follow up in the prevention of mother-to-child HIV transmission programme in Addis Ababa: A cohort study. ***Journal of the International AIDS Society.*** 2011; 14:50

Paper IV

Mirkuzie AH, Hinderaker SG, Sisay MM, Moland KM, Mørkve O. A cohort study on obstetric care for HIV-positive women in Addis Ababa: Intra-partum transfers and associated delays. ***Journal of Public Health and Epidemiology*.** 2011; 3(6): 275-83

Abbreviations and acronyms

AIDS - Acquired immune deficiency syndrome

ANC - Antenatal care

ART - Antiretroviral treatment

ARV - Antiretroviral

CD_4 - Cluster of differentiation 4

CI - Confidence interval

EmONC - Emergency obstetric and neonatal care

FGD - Focus group discussion

FHAPCO - Federal HIV/AIDS prevention and control office

HIV - Human immunodeficiency virus

MDG - Millennium development goal

MOH - Federal ministry of Health

MTCT - Mother-to-child HIV transmission

NVP - Nevirapine

OR - Odds ratio

PBC - Perceived behavioural control

PMTCT - Prevention of mother-to-child HIV transmission

RR - Relative risk

sdNVP - Single dose nevirapine

TPB - Theory of planned behaviour

UNAIDS - Joint United Nations programme on HIV/AIDS

WHO - World health organization

ZDV- Zidovudine

Introduction

Brief overview of the HIV/AIDS epidemic

Since the first AIDS case report in 1981, about 60 million people have been infected with HIV and about 25 million have died of AIDS. Currently, there are about 33.3 million HIV-positive people around the world and about 10% are children under the age of 15 years [1]. This figure includes the 2.6 million new infections that occurred in 2009. The main modes of transmission are sexual contact, mother-to-child, needle sharing and contaminated blood and body fluids. The predominant mode of transmission varies from region to region; in sub- Sahara Africa heterosexual, in Western Europe and the Americas homosexual, and Eastern Europe and Southeast Asia needle sharing [2, 3]. The modes of transmission seem to determine the nature of the epidemic. Heterosexual transmission is largely causing generalized epidemics while needle sharing and heterosexual transmissions are causing concentrated epidemics [1]. A generalized epidemic is characterized by an HIV prevalence among pregnant women in a country exceeding 1% consistently and involving more than specific high risk groups [3].

Most countries in the sub-Saharan region are experiencing a generalized epidemic. The epidemic peaked in the late 1990s. Substantial decline in the HIV/AIDS incidence has been reported in many sub-Sahara African countries since then [1]. The rate of infection in 2009 was down by about 20% in the region compared to 2005. In the same year, 2.2 million people were newly infected with HIV and 1.3 million died of AIDS. In total, about 22.5 million HIV-positive people are living in the region. Of these, over half are women and about 10% are children under the age of 15 years. There are great variations in HIV prevalence within the region. (Fig 1). The southern Africa countries have the highest prevalence; South Africa (17.8%), Botswana (24.8%), Swaziland (25.9%), Zimbabwe

(14.3%) followed by countries in eastern Africa; Kenya (6.3%), Uganda (6.5%), Tanzania (3.4%) and Ethiopia (2.4%). In western Africa, the HIV prevalence is in general lowest but countries like Cameroon (5.3%), Central African Republic (4.7%), Côte d'Ivoire (3.4%), Gabon (5.2%), and Nigeria (3.6%) have higher prevalence [1].

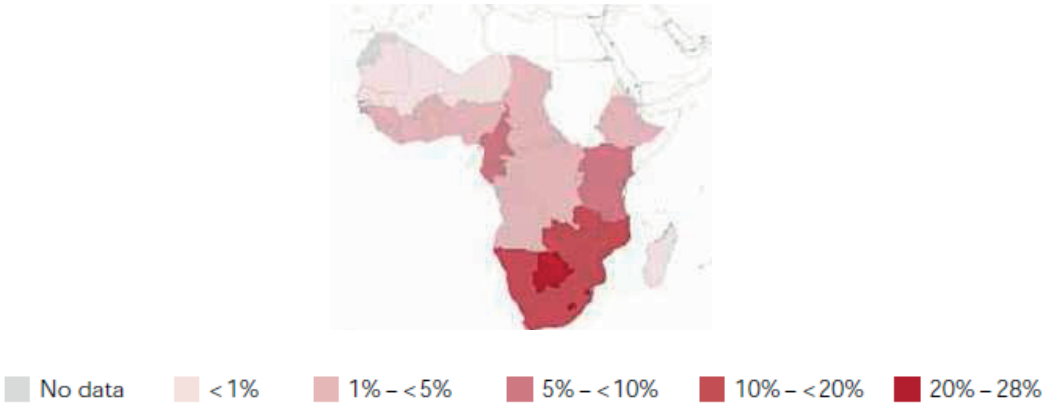


Fig 1: HIV prevalence among adults aged 15-49 years old in sub-Saharan Africa 2009[1]

Although Ethiopia is among the countries having a lower HIV prevalence in the region (2.3%), it is the highest HIV/AIDS burden country next to South Africa because of the large population size [1]. Like in many other sub-Saharan African countries the HIV incidence in Ethiopia has declined by about 25% between 2001 and 2009 [1]. The infection in Ethiopia is still biased towards women and urban populations. The prevalence among women is 1.5 times higher than among men. Urban areas carry the brunt of the epidemic with 7.7% prevalence compared to rural areas with 0.9% prevalence [4]. Addis Ababa, where this work is done has the highest HIV prevalence (9.2 %), and the highest number of HIV infected people (200,000) in the country.

[1] *Joint United Nations programme on HIV/AIDS. UNAIDS report on the global AIDS epidemic 2010.*

In Ethiopia, the antenatal surveillance system has been used since 1989 to assess HIV prevalence trends. This estimate is used as population prevalence proxy to guide HIV prevention efforts. For the surveillance, leftover blood samples collected for routine syphilis testing are used. The samples are unlinked and anonymously collected for a period of three months biannually [5]. Owing to the high HIV prevalence among women, the low antenatal service coverage and the skewed distribution of antenatal surveillance sites in Ethiopia [6, 7], the antenatal HIV prevalence estimates were found to overestimate the population prevalence. In the 2005 Ethiopian demographic and health survey, the HIV prevalence among the general population was 1.4%, whereas it was 3.5% in antenatal sentinel reports [4, 8]. This huge discrepancy called for reconciliation of the two estimates. Subsequently, the national prevalence estimate was adjusted to 2.1% for the year 2007.

Mother-to-child HIV transmission (MTCT)

Mother-to-child HIV transmission was first recognized to be the major source of HIV infection among children under the age of 15 years in the mid-1980s [9]. In 2009 alone, about 360,000 new HIV infections had occurred among children globally; 130,000 in sub-Saharan Africa [1]. There is a declining trend in the occurrence of new infection and AIDS related mortality among children in the region. Although the mortality in 2009 was said to be 20% less compared to 2004, 320,000 children died of AIDS related causes. By 2009, over 14,000 Ethiopian children were estimated to acquire new HIV infections from their mothers and about 4,000 died of AIDS related causes [6]. MTCT can occur during pregnancy, labour, delivery and through breast-feeding [10]. The rate of transmission varies from 20% to 45% [11]. (Table 1). About 5-10% of the infections occur during pregnancy mainly towards the end of the pregnancy.

Table 1: Estimated timing and risk of mother-to-child HIV transmission [1]

Timing	***Rate of MTCT in %***		
	No breast-feeding	**Breast-feeding through 6 months**	**Breast-feeding through 18 to 24 months**
Intra-uterine	5 to 10	5 to10	5 to 10
Intra-partum	10 to 20	10 to 20	10 to 20
Post-partum breast-feeding			
Early (first 2 months)		5 to 10	5 to 10
Late (after 2 months)		1 to 5	5 to 10
Overall	15 to 30	25 to 35	30 to 45

Maternal immunological status and viral load are significant predictors of MTCT [10]. The MTCT is highest during the early and late phase in the natural course of the HIV infection. The early phase of the infection marks high viral replication before the immune system takes control of the replication [12]. (Fig 2). In later phases, due to a compromised immune system, there is a decrease in the cluster of differentiation 4 (CD_4) cell count accompanied by an increase in viral load which favour the risk of MTCT [10]. The other risk factors favouring MTCT include presence of other sexually transmitted infections during pregnancy, uterine infection, invasive obstetric procedures, modes of delivery and infant feeding practices [10, 13-17].

[1] *De Cock et, al.: Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice.*

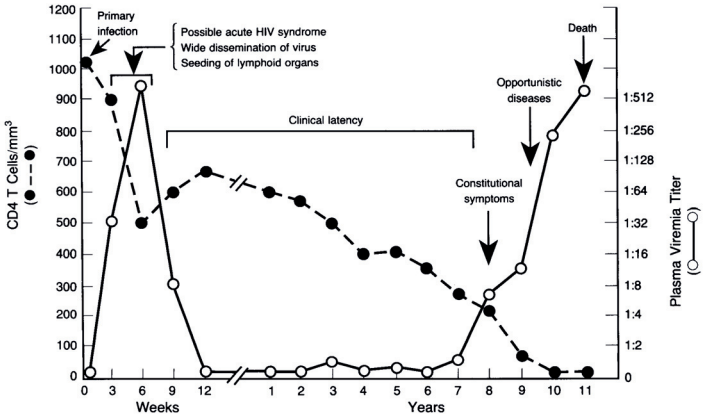


Fig 2: Typical course of HIV infection [1]

Prevention of mother-to-child HIV transmission programmes (PMTCT)

A four pronged comprehensive strategies encompassing primary, secondary and tertiary preventions where mother's and infants' survival are at the core has been proposed for PMTCT. To facilitate implementation of these strategies, guidelines have been developed internationally by the Joint United Nations programme on AIDS (UNAIDS) and the World Health Organization (WHO), and at national levels governments often adapt the international guidelines taking into consideration the local contexts. These prevention strategies are integrated in existing maternal and child health programmes and are implemented mainly under the auspices of the health system. The first prong is HIV prevention among the mothers to be, the second prong is prevention of unintended pregnancies among HIV-positive mothers, the third prong is the prevention of vertical transmission and the fourth prong is provision of treatment, care and support to HIV-positive mothers, their children and family. The effectiveness of the PMTCT programmes is largely dependent on proper

[1] *Pantaleo G. and Fauci A: The immunopathogenesis of human immunodeficiency virus infection.*

implementation and utilization of the recommended services. In industrialized countries, where the recommended services are properly implemented, MTCT is on the verge of elimination, whereas it still represents a threat to child survival in many resource-poor settings [1].

The recent UNAIDS report has created optimism about the success of the PMTCT programmes all over the world [1]. The report highlights 32% reduction in global incidence of MTCT and 24% reduction in the sub-Saharan African region in the past five years largely due to proper implementation of the third and the fourth prongs which are also the main focus of this study. The third prong addressing the prevention of vertical HIV transmission has four major components. These are HIV counselling and testing, provision of prophylactic/therapeutic ARV drugs for mothers and their infants, safe obstetric practices for HIV-positive mothers and infant feeding counselling and support. Moreover, partner involvement in PMTCT and exposed infant follow up are important aspects of the prevention of vertical HIV transmission programmes. All these services are integrated within the continuum of existing maternal and child health care services.

HIV counselling and testing

HIV counselling and testing for PMTCT was first recommended by the Centre for Disease Control in 1985 [9]. The early recommendations were focusing on the then risk groups such as injecting drug users, prostitutes and those with history of sexual transmitted infection. Due to the unavailability of ART prophylaxis at that time, the HIV testing was just to screen out HIV-positive cases for further counselling that could help to reduce MTCT. The HIV testing was offered in an opt-in approach where clients' autonomy and confidentiality were the core principles. It is also referred to as voluntary counselling and testing (VCT) and individual pre- and post-test counselling is part of it. Following the report on the first efficacious ARV prophylactic drug for PMTCT, the Centre for Disease Control revised the HIV counselling and testing recommendations in 1995 [18]. This

revision underscores the need to offer HIV counselling and testing to all antenatal attendees irrespective of their risks. In 2001, the Centre for Disease Control made yet another revision in HIV testing approach [19]. The focus of this revision was to mainstream routine HIV counselling and testing into existing peri-natal care programmes and extending to intra-partum and postpartum testing. Following the revision, the routine HIV testing has been successfully adopted and integrated into the peri-natal care programmes in many industrialized countries.

In 2003, the joint United Nations and WHO set a target to provide free antiretroviral treatment (ART) for three million people living in resource-poor settings by 2005 ('3 by 5 initiative') [20]. Shifting the HIV testing approach from opt-in to routine opt-out in antenatal setting was considered crucial to facilitate women' access to ARV prophylaxis so as to reach the target [21]. Following the WHO recommendations, Botswana, with one of the worst epidemics in the world, became the first country in sub-Saharan Africa to implement the routine opt-out approach [22]. Implementation of routine opt-out approach has brought significant improvement in acceptability of HIV testing with rates of testing increasing from 55% to about 100% [23-27]. Likewise, the rate of HIV testing in Ethiopia has shown significant improvement following the shift to routine opt-out approach [6, 28, 29].

Despite the substantial success in the rate of testing, arguments are still going on about the potential violation of "mothers' autonomy" and insufficiency of the HIV counselling in the routine opt-out approach. Proponents of the routine opt-out approach defended this policy from the perspective of public health. Routine opt-out testing creates opportunities for mothers who otherwise may not test before it is too late [26, 30-32]. This could facilitate access to prophylaxis, treatment, care and support which could ultimately reduce the MTCT and the burden of HIV/AIDS. Offering HIV testing routinely like other antenatal tests can also normalize HIV testing and reduce stigma attached to HIV-positive test results. By contrast, several studies in resource-poor settings show

implementation gaps endangering the effectiveness of the routine opt-out approach [33-35]. According to these studies, several mothers in resource-poor settings for cultural and socio-economic reasons are less empowered to actively opt-out the HIV testing offer. Some mothers may accept testing advice since they fear negative consequences that may affect their subsequent antenatal care, while others they lack awareness of their right to refuse HIV testing. Studies from Tanzania and Kenya show that the pre-test information is in practice less informative with respect to the possibility of opting out, and much emphasis is put to getting the mothers tested [35, 36].

The tension between increasing the rate of testing and the potential violation of ethical principles has dominated the available literature on routine antenatal opt-out testing [26, 30, 35-37]. However, the fundamental behavioural determinants of the routine antenatal HIV testing seem not to be emphasized. Cognitive behavioural theories have been widely applied to HIV preventive behaviours [38-43]. Of these theories, empirical works based on the theory of planned behaviour have shown that the intention to take voluntary HIV counselling and testing is mainly determined by a person's evaluation of the benefits of HIV testing (attitude) and other people's approval or disapproval of the testing (subjective norm) [40, 41]. Hence, identifying behavioural determinants of routine HIV testing and addressing them accordingly could help to bridge the tension between maximizing the rate of testing and respecting the mothers' autonomy.

Antiretroviral (ARV) prophylaxis

In 1994, a multi-centre clinical trial that was conducted in industrialized countries reported the efficacy of the first ARV prophylaxis for PMTCT [44]. In this double blind clinical trial mothers were randomized to receive zidovudine (ZDV) prophylaxis or placebo. ZDV was initiated at 14-34 weeks of gestation to be taken five times daily as intravenous doses during the intra-partum period. Infants were given ZDV syrup six times daily from birth up to six weeks postpartum. An interim

analysis showed a 67.5% reduction in MTCT at the age of 18 months. Eventually ZDV has become the first proven prophylaxis for PMTCT. ZDV is a class of ART called Nucleoside Reverse Transcriptase Inhibitor that can block the action of an HIV enzyme called reverse transcriptase which is necessary for viral replication [45].

However, the complexity and cost of this long course ZDV regimen hampered its potential benefit in resource-poor settings experiencing the highest HIV burden. With the aim to come up with less complex and cheaper ZDV regimen, a clinical trial was conducted in Thailand that enrolled 397 HIV-positive mothers from 1996 to 1997 [46]. ZDV was given to mothers from 36 weeks of gestation twice daily and every three hours during the intra-partum period. The findings showed a 51% reduction in the risk of HIV transmission among infants who were tested at two months postpartum. This simplified short course ZDV has substantially reduced the cost from 800 to 50 United States Dollar [47]. Yet, even the reduced cost was not affordable to many resource-poor settings.

Later, a clinical trial was conducted in Uganda from 1997 to 1999 [48] . The trial enrolled 626 HIV-positive women to assess the efficacy of single dose Nevirapne (sdNVP) regimen. NVP is one of the Non-Neucloside Reverse Transcriptase Inhibitors which prevents the action of reverse transcriptase that helps to translate viral deoxyribonucleic acid to ribonucleic acid [45]. In this trial single-dose NVP was given to mothers to be taken during labour and to infants within 72 hours after birth. All the mothers were advised to exclusively breast feed. The risk of HIV transmission was reduced by 47% at six weeks and by 41% at 18 months [48, 49]. The single-dose NVP regimen has shown comparable efficacy with the short course ZDV regimen. This regimen also provided additional cost saving with better infant survival at 18 months. Consequently, single-dose NVP regimen was scaled up in resource-poor settings.

In the course of implementation, the safety of sdNVP regimen has become a growing concern for two major reasons [10, 50, 51]. First, NVP is associated with liver toxicity [50]. Second, the regimen is prone to drug resistance as it is a mono-therapy and a single point mutation is enough for the NVP to confer drug resistance [10, 51]. To counteract the emergency of drug resistance and to achieve high level of viral suppression, a multi-drug prophylaxis regimen takes hold of the recommendations from 2006.

In the 2006 WHO recommendations, the cut-off point to initiate lifelong ART was CD_4 cell count of less than 200 cells per micro liter [52]. Whilst mothers with CD_4 cell count over 200 cells per micro liter should receive ZDV twice daily from 28 weeks of gestation plus NVP and lamivudine during the intra-partum period and a seven day tail of ZDV and lamivudine during the postpartum. For the infants, ZDV plus sdNVP should be given at birth and a 7 day tail of ZDV. However, if the mothers received the medication for less than one month, the infants' prophylaxis should be extended to one month.

The most recent revision in the WHO guidelines recommends prophylaxis initiation for mothers with a CD_4 count above 350 cells per micro liter, otherwise lifelong ART irrespective of their clinical stage [52]. Several first line recommendations are made available. The choice of appropriate regimen can be made by individual countries depending on their local circumstances. This revision also highlights early initiation of the prophylaxis at 14 weeks gestation and to continue throughout the breast-feeding period. These multidrug extended medication regimens can substantially reduce the MTCT among breast-feeding infants.

Despite availability of various efficacious prophylactic ARV drugs, ensuring the required level of medication utilization and adherence remains challenging especially in resource-poor settings [53,

54]. A report on 16 sub-Sahara African countries shows that over 85% of them have prophylaxis coverage less than 60%, worse still Ethiopia achieved only about 20% coverage (Fig 3). Proper adherence to a given medication regimen is mandatory in order to achieve high and sustained level of viral suppression [55]. Poor adherence could result in sub-optimal viral suppression favouring drug resistance, treatment failures and increase the risk of MTCT.

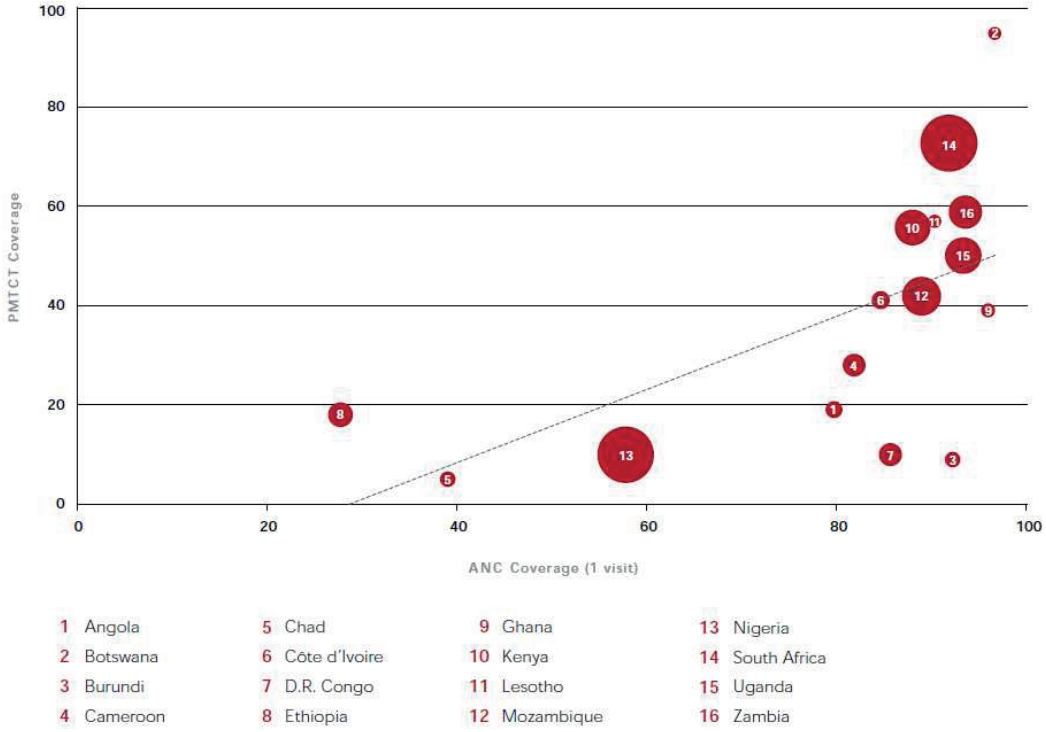


Fig 3: Coverage of antenatal care services and services for PMTCT among women living with in high HIV prevalence countries, size of bubble proportional to HIV-positive pregnant women [1]

[1] *Joint United Nations programme on HIV/AIDS: UNAIDS report on the global AIDS epidemic 2010. Geneva.*

Safe obstetric practices

About 70% of the MTCT in non-breast-feeding infants and about 50% in breast-feeding infants occur during the intra-partum period [11]. The risk of intra-partum transmission increases with intra-partum bleeding, premature rupture of membrane, delayed labour duration after membrane rupture, chorioamnionitis and cervico-vaginal infection [10, 13]. Certain obstetric procedures such as episiotomy and artificial rupture of amniotic membrane are also associated with increased risk of MTCT. Through provision of quality obstetric care at the right time, the risk of intra-partum MTCT can be reduced. Several studies have shown a reduced risk of MTCT in mothers with elective caesarean delivery before the onset of labour [10]. Meta-analysis that compiled over 8,500 patient data from 15 prospective cohort studies conducted between 1985 - 1999 showed a 50% reduced risk of MTCT in the elective caesarean delivery group compared to the group who did not have elective caesarean delivery [56]. Subsequently, caesarean delivery has become the preferred mode of delivery in most industrialized settings. Recent researches however, report no additional benefits of caesarean delivery over spontaneous vaginal delivery if mothers received proper prophylaxis and have a viral load of 400 and less copies/ml [57]. The risks of caesarean delivery seem to outweigh its potential benefit in resource-poor settings. Hence, spontaneous vaginal delivery is for practical and technical reasons still the preferred mode of delivery in those settings.

To ensure the quality of intra-partum obstetric care, both skilled attendant at birth and institutional delivery are considered vital. Institutional delivery not only helps to ensure safe delivery but also facilitates access to prophylaxis medication for HIV-positive mothers and their infants. In Botswana, where almost 100% of all births are attended by skilled health professionals at health facilities, over 95% of infants received the ARV prophylaxis, whereas in Ethiopia with 18% rate of institutional delivery less than 20% of infants received the prophylaxis [1, 28]. On top of its potential contributions for the reduction of MTCT, quality intra-partum obstetric care remains the

best strategy for improving maternal and peri-natal outcomes [58]. In many resource-poor settings, however, the intra-partum obstetric care is often sub-optimal and delayed.

Delay to receive appropriate intra-partum obstetric care can be detrimental to maternal and peri-natal survival [59, 60]. Delays can happen in making decision to seek care ("first delay"), in reaching health facilities ("second delay") and in receiving appropriate care in a health facility ("third delay") [60-62]. Maternal disabilities such as obstetric fistula and incontinence are common consequences of delays in receiving appropriate intra-partum care for obstructed labour [63]. According to studies from resource-poor settings, the "third delay" significantly contributes to maternal morbidity and mortality [59, 64]. In a study from Uganda, about 50% increased risks of peri-natal deaths occurred among mothers who experienced the third delays [62]. Large scale studies have also reported an inverse correlation between stillbirths and the quality and quantity of obstetric care provided during pregnancy and delivery [65, 66]. The lack of prompt attention after reaching facilities is reported to account for about 25% of the intra-partum stillbirths. These delays often indicate poor quality care and can be minimized through improved competence of health professionals, provision of supplies and accountability mechanisms [67].

Infant feeding counselling and support

The MTCT through breast-feeding constitutes 10-15% of the total infections [11]. Mastitis, cracked nipple, inflammation affecting infants oral and gastrointestinal tract can increase the risk of MTCT [17]. Complete avoidance of breast milk eliminates the postnatal transmissions. Exclusive formula feeding is preferred infant feeding method where infant formula is affordable, feasible, acceptable, sustainable and safe (AFASS) [68]. Yet, exclusive formula does not seem practical in resource-poor settings, and can do more harm than good. In those settings, better overall infant survival has been reported among infants receiving exclusive breast-feeding than those receiving exclusive formula,

although the rate of HIV infection seems to be a little bit higher among exclusive breast fed infants. Mixed feeding carries the greatest risk of MTCT [68].

The risk of acquiring HIV also increases with increasing duration of breast-feeding [14, 15, 68-70]. There is 10% additional risk of MTCT for infants receiving breast-feeding for 12 months and 17.5% for those receiving for 18 to 24 months [11]. This has motivated the search for strategies to make breast-feeding safer. Infant feeding recommendations have been continuously updated in line with scientific advances. The most recent recommendations seem to be more accommodating which promotes exclusive breast-feeding up to six months, complementary feeding from six months and to continue breast-feeding up to 12 months given that either the mother or their infant take proper prophylactic medication throughout the breast-feeding period [68].

Exposed infant follow up

Follow up for infants born to HIV-positive mothers is extremely important to improve their survival. Proper infant follow up services provide opportunities for the provision of appropriate infant feeding counselling and support, provision of co-trimoxazole prophylaxis to prevent serious opportunistic infections, for early infant diagnosis and for early initiation of ART for HIV infected infants. It is shown that about 50% of infants who acquire HIV *in utero* and during the intra-partum period die before the first year of life [69, 71-73]. Provision of co-trimoxazole prophylaxis at four to six weeks postpartum can reduce morbidity and mortality among exposed infants by preventing the occurrence of serious opportunistic infections such as pneumocystis pneumonia [71, 74].

Formerly, infant diagnosis was based on antibody testing at the age of 18 months. This antibody test has little survival benefit for those who acquire the infection *in utero* and during the intra-partum period as the majority of these infants could die before they reach 18 months [72]. The high

mortality among infected infants could be prevented through early diagnosis and early initiation of ART. Currently, polymerase chain reaction which detects viral deoxyribonucleic acid is used for early infant diagnosis [72, 73]. The test is done from dried blood spot taken from infants. Despite its potential benefits, exposed infant follow up services are poorly integrated into existing child health programmes. Only 15% exposed infants around the world are tested for HIV [73] while only 22%, 37% and 38% of HIV-positive infants initiated ART in Senegal, Uganda and Cambodia respectively [75].

Partner involvement in PMTCT programme

Partner involvement in PMTCT programme is vital in resource-poor settings, in particular where partners have a significant role in mothers' decision to seek PMTCT services. Most importantly, it could help to reduce the risk of MTCT by preventing new infections among mothers and improve communication between the couples. Mothers can acquire new infection during pregnancy and any time during the breast-feeding period from their partner. Recent sero-conversion is associated with an increased risk of MTCT due to the high viral replication during the early phase of the HIV infection [76]. Moreover, the rate of discordance ranges from 36-85% in Eastern and Southern African region [77]. Recent data show that discordant couples are the newly identified high risk group in Ethiopia [7]. HIV negative partners of the HIV-positive mothers are also at risk of horizontal transmission from their wives.

A review on couple centred counselling shows that partner involvement in HIV testing not only helps to increase disclosure, condom use and uptake of ARV prophylaxis but also contributes to the lower rate of sero-conversion compared to individual counselling [78]. A recent multisite randomized trial demonstrated that early initiation of ART for infected partners can reduce the risk of heterosexual horizontal HIV transmission by 96% compared to delayed ART initiation [79].

Other studies conducted in Botswana, Kenya and Uganda have reported that pre-exposure ARV prophylaxis could significantly reduce the risk of horizontal heterosexual HIV transmission in general and among discordant couples in particular [80-82]. Partner testing and involvement in PMTCT programme can create an opportunity for identifying at risk partners for early initiation of ART or pre-exposure ARV prophylaxis which could ultimately contribute to the success of the HIV prevention efforts.

The PMTCT programme and PMTCT service utilization in Ethiopia

Before the introduction of the PMTCT programme a clinical trial was conducted in three selected public health facilities in Addis Ababa from 2001 to 2003. The trial, is called the Nigat project, which assessed infant feeding among HIV-positive mothers [83]. The findings suggested that adherence to exclusive breast-feeding was poor and that early weaning was common. The free PMTCT programme was launched in 2004. In the first year, 32 health facilities provided the programme across the country. The programme has been scaled up rapidly and by 2010 1,352 health facilities were providing the programme. As the proportions and number of mothers undergoing HIV testing have increased, the HIV prevalence has shown a steady decline [6]. Nonetheless, the proportion of mothers and infants receiving prophylaxis medication remains low with little improvement over the years. (Fig 4).

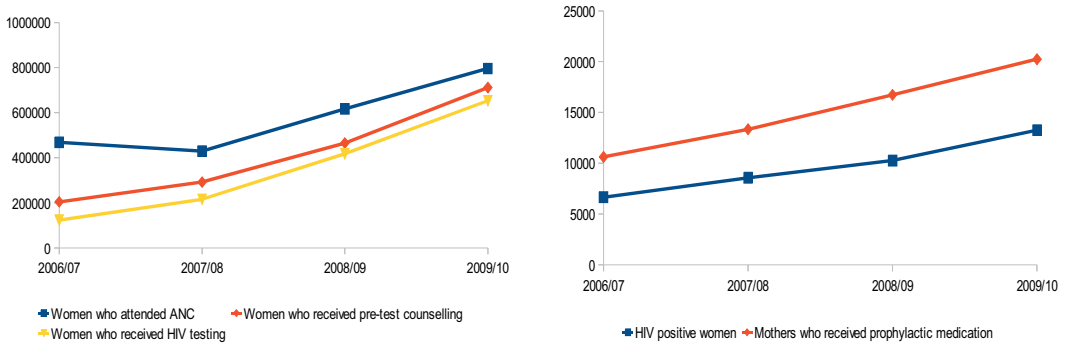


Fig 4: Number of pregnant women attended in PMTCT facilities, who received pre-test counselling and HIV testing between 2006 and 2010 (left) and number of mothers who tested positive and those who received prophylaxis during pregnancy between 2006 and 2010 (right).[1]

Large variation in HIV prevalence and PMTCT service utilization across the nine regions in the country was reported in 2010 [6]. The Southern and Somali regions reported the lowest sero-prevalence (0.8%), whereas Addis Ababa City Council reported the highest prevalence (4.6%). Oromia and Amhara have shown poor achievement in mothers' prophylaxis medication uptake i.e 52% and 41% respectively. By contrast, in Harari 100% and in Beninshangul Gumuz 68% of the mothers received prophylaxis medication. Infant prophylaxis coverage was generally low except in Harari region where 87% of the infants had received prophylaxis at birth. Diredawa is the only City Council where equal number of mothers and infants received prophylaxis.

Federal HIV/AIDS Prevention and Control Office: Annual performance report of multisectoral HIV/ AIDS response 2002 E.C. (2009/2010).

The PMTCT programme and the millennium development goals (MDG)

HIV/AIDS continues to be a threat to health and development especially in resource-poor settings. The PMTCT programmes however, have a great potential in reducing suffering in children and mothers due to HIV. The programmes have a wider scope that can address three of the eights Millennium Development Goals (MDG.). The UN set a target to reduce by two thirds the mortality rate among children under five, to reduce by three quarters the maternal mortality ratio and to halt and begin to reverse the spread of HIV/AIDS [84]. The goals were set based on the 1990 state of health in a country as a reference point to measure progress in 2015. Due to the rapid progression of the HIV epidemic in sub-Saharan Africa in the 1990s, progress towards the health related MDGs has been slow.

In a study from South Africa that used verbal autopsy to determine attributable causes of death, 43% of the deaths among children between one and four years were attributed to HIV/AIDS [85]. Another study also reported 53% mortality among HIV infected children by the age of 18 months, whereas only 4% among non-infected children [69]. In a study from Ethiopia a five fold increase in mortality among women between 33 to 39 years was reported in 2001 compared to 1984 [86]. In the same study the mortality in the age group 25 to 49 years showed a significant year by year increase compared to the five to 14 years old children. By contrast, a study conducted after the introduction of free ART in Ethiopia showed that the mortality among women had declined by about 50% in 2007 compared to 2001 [87]. The majority of the women who initiated lifelong ART are identified in PMTCT programmes. In 2009 about 50% of the HIV-positive mothers' around the world were assessed for their eligibility to initiate ART for their own health in PMTCT programmes and 15% of them had initiated lifelong ART. Successful implementation of a PMTCT programme could save the lives of many children as well as mothers [88]. Friberg and colleague stated that "South Africa has

the potential to reverse trends of increasing child mortality and even shift to being on track to achieving MDG 4 with rapid scale up of PMTCT, a context specific intervention"[67].

Rationale of the study

Virtual elimination of peri-natal HIV transmission has become the global target following the availability of highly efficacious prophylactic medications [89]. However, persistent programmatic challenges where the epidemic is most severe are threatening the realization of the target. These challenges include unsolved issues related to HIV testing, ensuring access and adherence to prophylaxis medication, access to safe delivery services, access to infant follow up and partner involvement in PMTCT programmes. This thesis aims at addressing these issues and to assess the impact of the national PMTCT programme in Addis Ababa and are presented in four papers.

The PMTCT programme in Ethiopia is scaling up rapidly [6, 7, 90]. In the meantime, PMTCT programme implementation strategies have been frequently changing nationally and internationally [21, 52, 68, 71, 73, 91, 92]. However, little has been documented about the national PMTCT programme performance and PMTCT service utilization in general and following policy changes in particular. The impact of the national PMTCT programme in averting new HIV infections has not been assessed. Paper I assessed the trends in PMTCT programme performance across the years and the impact of the programme in terms of averted infections.

Following the introduction of the opt-out approach remarkable achievements in terms of reduced missed opportunities to HIV counselling and testing have been reported from many resource-poor settings including Ethiopia [6, 22-24, 26, 93, 94]. However, several researchers argue against the opt-out approach, that some pregnant mothers are testing despite their lack of intention to test [33, 35, 36]. Nevertheless, there is lack of evidence about the fundamental behavioural factors determining the intended and actual HIV testing among those who tested despite their low intention.

Paper II therefore aimed to identify determinants of intended and actual HIV testing using the Theory of Planned Behaviour (TPB).

In a recent estimate only 54% of the HIV-positive mothers in sub-Saharan Africa receive prophylactic medication during pregnancy [1]. This coverage is far behind the 80% target to achieve virtual elimination of MTCT by 2015. Worse still, there is little progress in prophylactic medication use by mother-infant pairs at birth. This is a critical area that deserves investigation because, unless both mothers and their infants are taking the prophylaxis, the preventive efficacy of the medication will be compromised [95, 96]. Moreover, prophylaxis received by the mothers during pregnancy has been used as a proxy to calculate potential averted infections [1, 6, 28, 52, 89]. This could lead to an overestimation if there is a big gap in prophylaxis received during pregnancy and taking it at birth. The agreement between prophylaxis collection during pregnancy and actual ingestion at birth remains largely unexplored. Exposed infant follow up facilitates access to early infant diagnosis, provision of co-trimoxazole prophylaxis, provision of infant feeding counselling and support and to facilitate access to ART for HIV-positive infants [71-74]. In particular, early infant diagnosis is vital as over 50% of the HIV infected infants die before 1 year of age [71]. Despite its importance little is known about the exposed infant follow up services in Ethiopia. Hence, Paper III assessed adherence to prophylactic medication regimen and infant follow up.

About 50% and 70% of the HIV transmission among breast-feeding and formula feeding infants respectively are occurring towards the end of pregnancy and during the intra-partum period [11]. Optimal obstetric care during the intra-partum period is vital to ensure safe delivery and prophylaxis ingestion by the mothers and their infants. Institutional delivery continues to be an important determinant of ARV prophylaxis ingestion and is associated with low risk of MTCT [97, 98]. In Ethiopia coverage of institutional delivery and ARV prophylaxis is below 20% while poor quality

intra-partum services is commonplace [1, 6, 28]. Nonetheless, little is known about HIV-positive mothers' access to safe obstetric care and possible hindrances to access intra-partum care. Paper IV examined HIV-positive mothers access to obstetric care and outcomes of pregnancy.

Objectives

General objective

To assess performances of the national PMTCT programme and examine potential challenges to the implementation of the PMTCT programme in Addis Ababa.

Specific objectives

1. To examine trends in comprehensive PMTCT service utilization and to assess the rate of MTCT in relation to policy changes.

2. To explain pregnant mothers' intended- and actual HIV testing behaviour using the theory of planned behaviour.

3. To assess adherence to HIV preventive medication regimen and infant follow up.

4. To examine HIV-positive mothers' access to safe obstetric care and pregnancy outcomes.

Methodology

Overviews of the study context

Ethiopia is situated in east Africa sharing borders with Djibouti, Eretria, Kenya, Somalia, Sudan and South Sudan. The country is occupying a total area of 1.1 million square kilometres. The country is divided into nine regional states and two city councils, which are further divided into 801 smaller administrative units (Woredas) [28]. Owing to decentralization of decision making, the administrative units are mandated to do basic planning and political administration including matters related to health since 2002. According to reports, Ethiopia is the second most populous country in Africa next to Nigeria [7]. About 80 million people who are speaking over 80 different languages are living in the country [8]. Women in reproductive age and children under the age of 15 years constitute about two thirds of the population. Eighty five percent of the population are living in rural areas dependent on subsistent farming [99]. The country's economy is relying on agricultural production where coffee remains the major export item. The total share of health budget as a proportion of total budget was about 10% in 2009 [28].

According to the 2007 census, only 42% of the population over 10 year of age are literate; 51% males and 35% females [8]. About two thirds and 60% of the population have access to safe water and safe excreta disposal, respectively [28]. Ethiopia has been implementing a three-tier health service delivery system; the Primary Health Care Units at the bottom of the pyramid, General Hospitals in the middle and Specialized Hospitals on the top of the pyramid [28]. In 1997, the country endorsed a health system reform called Health Sector Development Programme in order to increase the effectiveness of the health system [28]. The reform is a 20 years strategy aimed at achieving improved health and sustainable development.

The primary health service coverage has reached 90% in 2008 following implementation of health extension programme [28]. The health extension programme was launched to achieve universal primary health service coverage in the country. Between 2003 and 2010, the programme had trained and deployed over 30,000 female health cadres to provide basic health services to the rural communities.

Currently, 65.5% of children under one year of age are fully immunized and the under-five child mortality rate has declined to 109/1,000 in 2008 compared to 148/1,000 in 2000 [100]. In 2008, 67.7% of the pregnant mothers attended antenatal care at least once. Although there is some improvement in safe delivery practices compared to the 1990s, it remains the lowest in the world. In 2010 only 18% of the pregnant mothers accessed intra-partum care at health facilities [8]. Of a total of 751 health facilities providing essential obstetric care services across the country only 10% were considered fully functioning (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). Owing to the low coverage and poor quality intra-partum obstetric care, the neonatal and maternal mortality remains high at 39/1,000 live births and 590/100,000 live births respectively [100, 101]. (Table 1).

The available health facilities and the majority of the health manpower are concentrated in the urban areas [28]. About 20% of the health professionals are working in Addis Ababa where less than 5% of the country's population are residing. This has left the majority of the rural population to rely on the health extension workers.

Table 2: Selected health and health related indicators for Ethiopia and for Addis Ababa, estimates from Ministry of Health and United Nation Development Programme[1],[2]

Indicator	**Ethiopia**	**Addis Ababa**
Total population (according to 2007 census)	77,812,236	2,854,462
Life expectancy at birth (in years) - Male (Female)	53.5 (55.4)	54.1(55.8)
Health service coverage (%)	90.0	100
Antenatal service coverage (%)	67.7	111.5
Institutional delivery rate (%)	18.4	62.5
Children fully immunized (%)	65.5	77.6
Access to safe water (%)	66.2	95.0
Access to safe excreta disposal (%)	60.0	76.0
Infant mortality rate per 1,000 live births	77	71
Maternal mortality per 100, 000 live births	590	**NA
Adult HIV prevalence (%)	2.3	8.5
HIV prevalence among pregnant mothers (%)	2.0	4.0
* Health professional to population ratio	1:3030	1:543
Midwife to population ratio	1:56,427	1:11,699

** Health professionals include doctors, nurses, midwives, health officers, **NA- data not available*

The study settings

Addis Ababa is home to about three million culturally and religiously diverse people. The city is administratively divided into 10 sub-cities with varying population sizes. (Fig 5).

[1] *Federal ministry of finance and economic development. Ethiopia: 2010 MDGs report, trends and prospect for meeting MDGs by 2015.*
[2] *Federal Ministry of Health. Health and health related indicators 2008/2009.*

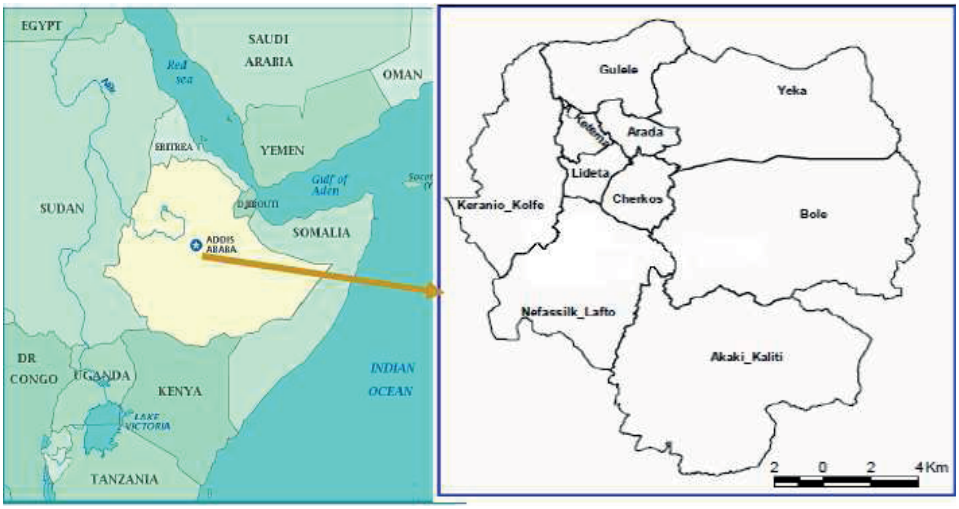


Fig 5: The study area

Of the 54 health facilities providing integrated peri-natal care and PMTCT services across the city about half are public health centres [28]. Despite the proportional distribution of public and private facilities, the public health centres remain the major service providers. These facilities offer antenatal care to 90% of the pregnant mothers, assist 90% institutional deliveries and manage 80% of obstetric complications (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). Emergency Obstetric and Neonatal Care (EmONC) is provided across the city both in private and public facilities. Basic EmONC is provided in the public health centres and hospitals provide comprehensive EmONC. Mothers identified to have serious obstetric complications in the basic EmONC facilities before and after the onset of labour should usually be referred to comprehensive EmONC units. The health services are fairly accessible with a median distance to the nearest referral centre is about five km.

Free PMTCT programme was launched in the city in 2004 in selected public health facilities and from 2007 the programme was expanded to private health facilities [7]. Like most antenatal care

services, PMTCT services were provided free of charge in public health facilities while payments were applied in private health facilities. The services had been offered in accordance with the first national PMTCT guidelines that recommended an opt-in HIV testing approach, sdNVP regimen and rapid antibody testing of infants at the age of 18 months. In 2007, the guidelines were revised and advocated routine opt-out HIV testing approach, combined ZDV regimen and antigen based infant HIV testing at six weeks postpartum. Nonetheless, early recommendations on partner testing irrespective of the mother's HIV status, exposed infant follow up and referral of the mothers for treatment, care and support remained unchanged with renewed emphasis in the revised guidelines [91]. Despite the revisions in the national guidelines that advocate for opt-out approach, the opt-in HIV testing approach remained the standard of practice in private health facilities.

There has been regular monitoring and evaluation of the PMTCT programme in Addis Ababa as part of the national HIV/AIDS prevention and control programme [102]. For monitoring and evaluation a monthly reporting form containing output indicators was distributed to all service outlets by respective sub-city health bureau. The health facilities filled out the reports and sent them to their respective sub-city where the compilation of the reports was taking place. According to the 2010 annual performance report, about 55, 000 pregnant mothers attended PMTCT programmes across the city, 79% tested for HIV and 4.6% were HIV-positive [6]. However, only 53% of the positive mothers and 38% of their infants received ARV prophylaxis. When the actual utilization was compared with the plan, about 77% achievement was reported in HIV testing, whereas only 18% in ARV prophylaxis uptake.

The study designs and data collection procedures

This thesis used cross-sectional, mixed methods and prospective cohort designs. (Table 3). The cross-sectional study compiled six years retrospective PMTCT reports. The mixed methods and the cohort data were collected from mothers who attended 12 public health centres and three private hospitals. A four-to-one public to private ratio was used in selecting the health facilities considering the fact that about 80% to 90% of the pregnant mothers in the city received care from public health facilities. Then individual health facilities were selected on the basis of high client flow and to have representation of all the 10 sub-cities.

Paper I

In total 663,603 antenatal care attendees registered in PMTCT programme across the city were studied. Monthly PMTCT reports were collected from all the 10 sub-cities health bureau in 2009. The reports were also collected from Addis Ababa City Administration Health Bureau and Intra-health (an NGO working on PMTCT) for validation.

Table 3: A summary of the study designs, the data sources, the study participant and the study outcomes in this thesis

Paper	**Study design**	**Study population**	**Study period**	**Main study outcomes**
I - Promising outcomes of a national programme for the prevention of mother-to-child HIV transmission	Cross-sectional retrospective trend analysis	663,603 ANC attendees	2004-2009	• Proportion of mothers tested for HIV • HIV prevalence • Proportion of mother and infants who received prophylaxis • HIV infection among infants • Proportion of partners tested
II - Applying the Theory of Planned Behaviour to explain HIV testing in antenatal settings	Sequential mixed methods	ANC attendees; 27 for FGDs 3033 for questionnaire interviews	January to March 2009	• Intention to test for HIV • Actual HIV testing
III - Current status of medication adherence and infant follow up in the prevention of mother-to-child HIV transmission programme	Prospective cohort study	282 HIV-positive mothers and their infants	January to December 2009	• Proportion of mothers who received prophylaxis during pregnancy • Proportion of mother-infant pairs who ingested prophylaxis at birth • Proportion of infants brought for early infant diagnosis • Rate of MTCT
IV- A cohort study on obstetric care for HIV-positive women in Addis Ababa: Intra-partum transfers and associated delays	Prospective cohort study	282 HIV-positive mothers	January to December 2009	• Proportion of mothers transferred during the intra-partum period • Rate of stillbirth

Paper II

The study on HIV testing behaviour used a sequential exploratory mixed methods design. A mixed methods is an evolving design that combines qualitative and quantitative research methods in the same study in several ways [103]. Combining the two methods enhance the validity of the study by counteracting each other's limitations. In our study the qualitative method played a supportive role for the main quantitative interview. Data were collected at different points within the study in January and February, 2009. The focus group discussions (FGDs) were conducted first to inform the Theory of Planned Behaviour (TPB) questionnaire. According to Creswell and Zhang "In an exploratory sequential design, the intent of the research initially is to explore a construct because it is not adequately addressed in the literature, is poorly measured or conceptualized, or is being studied in a population for which the research questions are unknown. After the initial qualitative exploration, the investigator follows up with a quantitative data collection phase to determine if the qualitative findings can be generalized to a sample of a population" [104].

The TPB was applied to determine intended and actual HIV testing as it is a widely used social cognitive theory in preventive behaviours including HIV [38-40, 105, 106]. The TPB focuses on proximal determinants of behaviours that can easily be targeted in behaviour change intervention [107, 108]. In the TPB, the distal determinants of behaviour are assumed to be mediated through the proximal determinants and are less focused upon. Moreover, the distal determinants including socio-demographic, cultural and environmental factors seem to be difficult to target in behaviour change interventions [108]. The TPB includes perceived behavioural control (PBC) on a level with attitude and subjective norm as predictors of behavioural intention, implying that the three predictors influence subsequent behaviour indirectly through behavioural intention. In turn, intention is the key proximal predictor of behaviour. According to the TPB, behavioural intention is a function of attitude, reflecting a favourable or unfavourable evaluation of the particular behaviour

and subjective norm. The subjective norm refers to the perceived social pressure to perform the behaviour. Perceived behavioural control reflects the ease or difficulty associated with performance (Fig 6). Although numerous empirical works have provided support for the power of TPB in predicting intention and behaviour, there remains a substantial amount of variance that is not explained by the TPB. Variables outside the TPB such as past behaviour and descriptive norms have residual effects on intention and behaviour after the TPB variables have been taken into account [42, 109-111] and they were included in this study. The study was conducted in three phases.

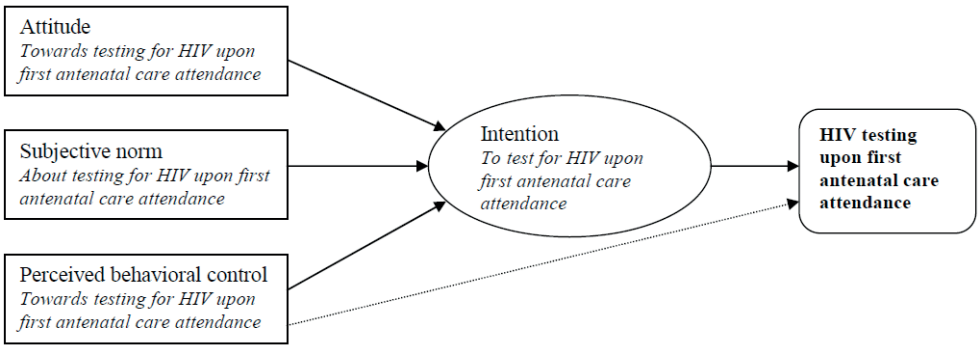


Fig 6: Theory of Planned Behaviour framework applied to predict intended and actual HIV testing

First phase: The focus group discussions

Focus group discussion is a discussion intended to grasp opinions of a group of informants about a topic of interest [112]. In this thesis the FGDs were conducted to capture contextual barriers to HIV testing in antenatal settings to inform the questionnaire interview. A FGD guide was developed in English based on literature review. Then the guide was translated in to Amharic, which is the official language of Ethiopia. Both the principal investigator and the informants were conversant with the language. The questions in the guide were “what factors or circumstances would enable you to test for HIV upon first time antenatal attendance?”, “what factors or circumstances would make it difficult for you to test for HIV upon first time antenatal attendance?” and “ are there any other

issues that come to mind when you think of HIV testing upon first time antenatal attendance?". Three FGDs were conducted with a group of seven, eight and 12 purposefully selected first time antenatal attendees in natural settings. Natural settings here refer to the antenatal clinics. Qualitative research highly valued collection of data in natural settings for deeper understand of research issues [113]. The FDGs were conducted in three different health facilities before the mothers received pre-test counselling. Volunteer mothers who were waiting for antenatal check-up had participated in the discussion. The principal investigator, who has experience in qualitative data collection and analyses, moderated and facilitated all the FGDs. Prior to the discussion the purpose of the study was explained and informed consent was obtained. During the discussions the mothers identified three potential barriers to HIV testing including "scared to test", "concerns about confidentiality" and "fear of disclosing HIV-positive results". Later they were probed as to whether "fear of stigma and/or discrimination", "fear of being chased from home in the case of positive test result" and "fear that they would be denied of proper care" would affect their decision to test. Of the probed questions only "fear of discrimination" was mentioned as a potential barrier to HIV testing. The discussions continued until the point where no new ideas were brought up. Conflicting opinions were brought up for further discussion and consensuses were reached in most of the cases. Notes taken during the FGDs were read before the next FGD to identify emerging themes. No new themes were identified. All the potential barriers identified by the participants were included in the questionnaire and used to measure the concept of perceived behavioural control. None of the FGD participants were included in the subsequent questionnaire interviews.

Based on the findings from the FGDs and following a "manual for constructing a TPB questionnaire in health services researches literatures" [114] a standard TPB questionnaire was developed. In the questionnaire all the constructs including the behaviour of interest (HIV testing) were defined in terms of Target, Action, Context and Time elements. Target here refers to "the

pregnant mothers"; Action refers to "testing"; Context refers to "antenatal settings"; and Time refers to "upon first time attendance".

Second phase: The TPB questionnaire interviews

Prior to actual interviews, the standard TPB questionnaire was first translated into Amharic then back translated to English for validation by a professional translator. Then pre-test interviews were conducted among 100 first time antenatal attendees prior to actual data collection. The pre-test interviews revealed areas that required more clarification. However, none of the pre-tested questionnaires were included in the main study. Mothers who were attending antenatal care for the first time in the current pregnancy in selected health facilities during the study period and who consented to be followed up were included in the study. Known HIV-positive mothers were excluded as they were not eligible for further testing. For the questionnaire interviews 17 college students who had no health related background were recruited to minimize information bias. They were given two days training and all participated in the pre-testing of the questionnaire under close supervision of the principal investigator. The questionnaire interviews were administered before the mothers received pre-test counselling in a face-to-face interview. The interviews were conducted individually in a quiet corner of the antenatal waiting areas. At the end of each day the completed questionnaires were handed to PMTCT counsellors who did the follow up. The study covered 44.3% (3,028) of the eligible mothers. Of these, 1.5% (49) refused to participate while 3,033 completed the questionnaire interviews (Fig 7). Here, intention to test for HIV was the intermediate outcome.

Third phase: The follow up

The follow up from questionnaire interviews to HIV testing took one to five hours. Consequently, the study was considered as a fixed cohort. "In cohort studies on acute disease without induction period and a short time of follow up, like outbreaks, the risk of disease can be estimated directly using the cumulative incidence given a fixed cohort with fixed period of follow up and a low fraction of drop-outs" [115]. The follow up data were collected by the PMTCT counsellors from PMTCT logbooks.

The PMTCT counsellors were routinely conducting the HIV testing and registering whether the mother received pre-test counselling (group or individual), testing, post-test counselling and the HIV test results. These questions were also the variables obtained during the follow up. The registration was done anonymously using the mothers antenatal number as a unique identifier. To be consistent, these unique identifiers were used in the questionnaires. Thirty three PMTCT counsellors were trained on how to collaborate with the field assistants and on how to do the follow up. The principal investigator supervised the counsellors when they obtained follow up data for the first time. Inconsistencies were validated by crosschecking with the mothers' antenatal folder. The study team were checking and collecting the questionnaires every day. Of the 3,033 mothers who completed the TPB interview in the second phase, 2,928 were assessed objectively whether they actually tested for HIV or not during the follow up (Fig 7). The final outcome measured was actual HIV testing.

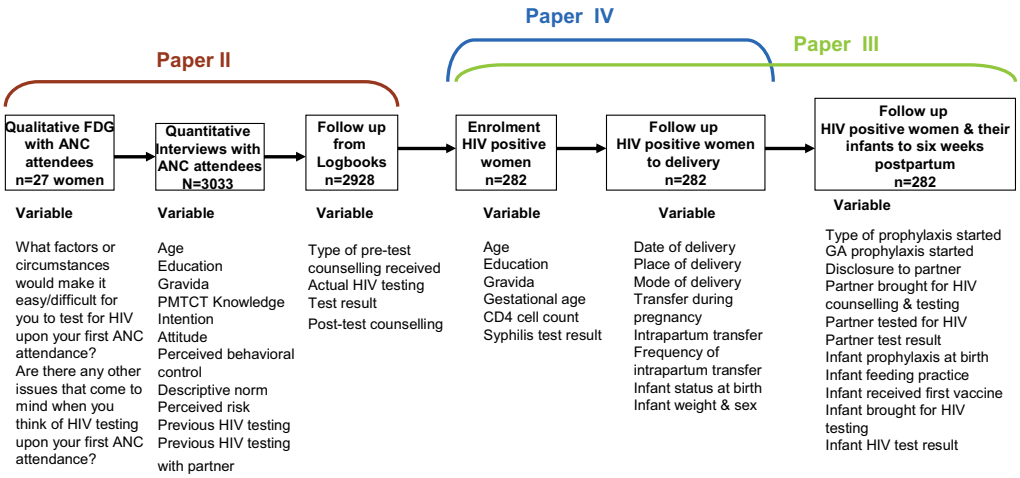


Fig 7: Flow chart of paper I - paper IV, data collection methods, sample sizes and variables

Paper III and IV

Paper III and IV used a general cohort consisting of HIV-positive mothers followed from January to December 2009 (Fig 7). HIV-positive mothers who were attending the PMTCT programme during the study period, those who were attending selected health facilities and those who were willing to be followed up to six weeks postpartum were included. Mothers who were not residing in the city were excluded. Trained PMTCT counsellors collected all the data.

At enrolment, mothers were interviewed using a semi-structured follow up format. To minimize the possibility of having incomplete data and losses to follow up; first, data were obtained from the mothers themselves and from logbooks in the facilities. Second, the follow up schedules of the cohort were made to coincide with the mothers' regular peri-partum visits. These visits were at 28 weeks, 36 weeks, at delivery, six days postpartum and six weeks postpartum. For mothers who were transferred to other health facilities and for those who gave birth at home, follow up data were collected when they came for six days' postpartum care. Reasons for the first transfer were obtained from logbooks at the health centres. Since the reasons for subsequent transfers were not recorded, the mothers were asked directly what was said to them. The cohort enrolled 282 HIV-positive mothers and followed them until six weeks postpartum. Abortion, death of a mother and stillbirth were study endpoints. Mothers were regarded as lost to follow-up when they had not shown up for regular visits and or when it was impossible to trace them.

Study variables

The study variables for paper I obtained from the monthly PMTCT reports were pregnant mothers who received pre-test counselling, HIV testing and post-test counselling; HIV-positive mothers who received prophylaxis medication, infant feeding counselling and those who referred for treatment,

care and support; exposed infants who received prophylaxis medication and those who tested for HIV and number of partners who tested for HIV.

In paper II, the questionnaire interview covered demographic and obstetric information, PMTCT knowledge, perceived risk, TPB variables and questions related to actual HIV testing. (Fig 7 and Annex 5). The TPB variables were assessed in relation to testing for HIV upon first time antenatal care attendance. A five point response scale was used 'very likely' (5) to 'very unlikely' (1),'very certain' (5) to 'very uncertain' (1) and from 'strongly agree' (5) to 'strongly disagree' (1). A sum score was constructed by adding the items corresponding to each variable. The higher the score the more positive the attitude, the stronger the intention, the stronger the subjective norm and the more barriers perceived with respect to HIV testing. For use in a logistic regression model later, perceived barrier and previous HIV testing experiences were dichotomized. Mothers who scored greater than or equal to the mean score were considered to have perceived barriers to test for HIV; otherwise they were considered to have no perceived barriers. Mothers who had HIV testing experience/with partner were grouped as "Yes"; otherwise they were regarded as "No". To assess mothers' knowledge on PMTCT, a list of prevention interventions was presented with a possibility to choose more than one. Accordingly, mothers who chose more than one intervention were considered knowledgeable; otherwise not knowledgeable. Actual HIV testing was assessed objectively through information obtained from the PMTCT logbooks.

Variables collected in paper III and IV are presented in fig 7 and annex 6. Reasons for transfers during the intrapartum period were inquired in an open ended question and later they were coded into three categories: obstetric complications, practical constraints (including lack of bed and lack of electric power supply) and reason not stated.

Sample size considerations

In paper I monthly PMTCT reports from February 2004 to August 2009 were collected from all the sub-cities.

Sample size for the cohort was calculated based on the outcome variable that would give the maximum sample, i.e in a population of about 1,500 HIV-positive pregnant mothers [6], 32% mother-infant pairs' adherence to prophylaxis at birth [54], with a precision of 5%, confidence level of 95% and 10% contingency. Based on this calculation a total of 274 HIV-positive mothers were required for the follow up. To get this number in a city where the estimated HIV prevalence among pregnant mothers was reported to be 7.4%, about 3,000 mothers were required to get tested. However, during the actual data collection the HIV prevalence in the city was found to be 4.6%, much lower than the report. As a result the questionnaire interviews were extended to 5,000. Known HIV-positive mothers who were not eligible for TPB questionnaire interviews were included in the cohort follow up. As a result the mothers enrolled in the cohort study in paper III and IV were 282. In paper II responses from 3,082 mothers interviewed between January and February were analysed in line with the first proposal.

Data analysis

The qualitative data analysis was conducted concurrent with data collection [113]. The notes were translated into English by the principal investigator. Doing the translation helped to get familiarized with the contents of the FGDs. The notes were read and re-read in the initial phase of the data analysis. Then recurring themes were sorted and phrases such as scared to test, fear of disclosure, confidentiality concern and fear of discrimination were used for labelling.

All the quantitative data were double entered in separate datasets in Microsoft Excel spread-sheets. The two datasets were compared for consistencies by creating a check file. The retrospective reports were analysed using Excel Pivotal tables and charts. Prevalence and Relative Risk (RR) were determined and χ^2 test for trend was analysed using the Epicalc 2000 software.

In paper II-IV, after checking the consistencies in the Microsoft Excel programme, data were transferred to SPSS version 17 for analysis. Descriptive statistics and Pearson Chi- Square were done to describe the characteristics of the mothers in the study. Fisher's Exact Tests were used to check baseline differences in demographic, obstetric and other characteristics between mothers who completed their follow up and those who did not when the expected counts in the cells were less than five.

In paper II, internal consistency reliability was conducted using Chronbach's alpha. Pearson's correlation was used to examine bivariate linear relationship between intention and the TPB variables, PMTCT knowledge and previous HIV testing experiences. Multiple linear regression analysis was applied in prediction of intention from TPB and external variables to calculate R^2 and β values, separately for mothers attending private- and public health care facilities and separately for each health centre and hospital. Logistic regression analysis was applied in prediction of actual HIV testing to examine the relative contribution of theoretical and external variables and to assess the fit of the model in terms of Nagelkerke R Square. Despite using a cohort design, Odds Ratio (OR) was used as an effect measure taking into consideration the fixed follow up time, little losses to follow up and the low prevalence of not testing for HIV in antenatal settings. Moreover, under rare disease assumption, the OR may be an acceptable approximation of the risk ratio [116-118]. To examine possible moderation effect of type of pre-test counselling upon the intention-behaviour

relationship, a two way interaction term between intention and type of pre-test counselling was added to the regression model and tested for statistical significance. Sensitivity, specificity and predictive values were calculated to examine the nature of intention-behaviour relationship.

In paper III bivariate analyses were done to identify association between mother-infant pairs ingesting medication at birth and socio-demographic characteristics, obstetric characteristics, CD_4 cell count and gestational age at enrolment, type of prophylaxis initiated, place of delivery, disclosing HIV status, partner involvement in HIV counselling and testing, partner testing and partner test result. Variables with p-value less than 0.05 in the bivariate model were included in the multivariate logistic regression model to control for potential confounding effect. Proportion of exposed infants brought for early infant diagnosis was calculated among live births, while the rate of MTCT was calculated among infants who had documented six weeks HIV test result.

In paper IV, the main outcome variables were transfer during the intra-partum period and rate of stillbirth. The rate of institutional delivery was calculated among mothers enrolled into the study while comparison between transferred and not transferred during the intra-partum period was made for mothers who completed the study. The rate of intra-partum transfers was calculated among mothers who visited health facilities during labour and delivery. The rate of stillbirths was calculated among the total births and stratified by transfer status. As 19% of the mothers were lost to follow up by the time of delivery, sensitivity analyses were done to assess potential biases due to the loss to follow up.

P-values <0.05 were considered significant and 95% confidence interval (CI) was used.

Ethical considerations

The study was reviewed and approved by the Ethical committee of Addis Ababa City Administration Health Bureau in Ethiopia and the Regional Committee for Medical Research Ethics in Western Norway (Annex 1). Study permits from Addis Ababa City Administration Health Bureau and respective sub cities were obtained. Data were collected anonymously to respect mothers' privacy and to ensure confidentiality. Prior to the interviews, information was provided to each mother about the objective of the study, the possibility to withdraw anytime if they did not want to continue and how the data were to be handled after collection (Annex 2). The HIV-positive mothers were followed up by their respective PMTCT counsellors for confidentiality reasons and to avoid unnecessary disclosure. The mothers' antenatal numbers were used as a unique identifier in the questionnaire interviews as well as in the follow up.

Synopsis of the papers

Paper I: Outcomes of a national PMCT programme

This paper examined trends in PMTCT service utilization and assessed the rate of MTCT in relation to policy changes in the national PMTCT programme. A total of 663,603 antenatal care attendees were registered in the PMTCT programme in Addis Ababa between February 2004 and August 2009. The proportion of mothers who received HIV counselling and testing among new antenatal care attendees increased from 50.7% (95% CI 50.2-51.2) in 2007 to 84.5% (95% CI 84.1-84.9) in 2009 following the shift to routine opt-out testing. Nevertheless, in 2009 only 53.7% of the positive mothers and 40.7% of their infants received ARV prophylaxis. The HIV prevalence among antenatal attendees decreased significantly from 10.5% in 2004 to 4.6% in 2009 in parallel to the increased number of mothers being tested. The HIV-positive mothers were over 18 times (RR 18.5, $p<0.0001$) more likely to be referred for treatment, care and support in 2009 than in 2004. The proportion of partners tested for HIV remained extremly low over the years at about 5%, although the absolute number was increasing year by year. Only 10.6% (95% CI 9.9-11.2) of the HIV exposed infants had been tested for HIV. The cumulative probability of HIV infection among babies on sdNVP regimen who were tested at ≥ 18 months was 14.9% (95% CI 9.8-22.1) in 2007, whereas it was 8.2% (95% CI 5.55-11.97) among babies on ZDV regimen who were tested at ≥ 45 days in 2009.

Paper II: Applying the Theory of Planned Behaviour to explain HIV testing

Focusing a cohort of pregnant mothers attending public and private antenatal care facilities, this mixed methods study applied an extended version of the Theory of Planned Behaviour (TPB) to

explain intended- and actual HIV testing. Mothers attending public health facilities were significantly different from mothers attending private health facilities with respect to socio-demographic and obstetric characteristics ($p<0.01$). The TPB explained 9.2% and 16.4% of the variance in intention among public- and private health facility attendees. Intention and perceived barrier explained 2.4% and external variables explained 7% of the total variance in HIV testing. Positive and negative predictive values of intention were 96% and 6% respectively. Across both groups, subjective norm explained substantial amount of variance in intention, followed by attitudes. Mothers intended to test for HIV if they perceived social support and anticipated positive consequences following test performance. Type of counselling did not modify the link between intended and actual HIV testing.

Paper III: Adherence to prophylactic medication regimen and infant follow up

This study assessed the proportions of mothers and infants who adhered to prophylactic medication regimen and the proportions of exposed infants who were followed up in the PMTCT programme. Two hundred and eighty two mothers were enrolled; 10 had an abortion, five changed health facilities, 13 changed address, two died and 10 were lost to follow up for unknown reason. In total 232 (82%, 95% CI 77-86%) mothers initiated medication during pregnancy; 154 (64%) combined ZDV prophylaxis and 78 (33%) lifelong ART. Seven mothers actively refused medication prescription. Only 171 (60%, 95% CI 55-66%) mothers ingested their medication at birth. Among the 228 mothers who reported to have given birth, 217 were singleton live births, two twins live births and nine stillbirths. Of the 221 live births infants (included the two twins) 191 (87%, 95% CI 81-90%) ingested their medication at birth. Of the 219 live births (twin birth were counted once) 148 (68%, 95% CI 61-73%) mother-infant pairs ingested their medication at birth. Mother-infant pairs who were attended in health facilities at birth were more likely (Adjusted OR 6.7 95% CI

2.90-21.65) to ingest their medication than those who were attended at home. By six weeks postpartum, 189 (86%, 95% CI 80-90%) infants received their first pentavalent vaccine but only 115 (52%, 95% CI 45-58%) of them attended early infant diagnosis. Seventy one infants (32%, 95% CI 26-39%) had documented HIV test results and six (8.4%) were HIV-positive. No significant differences were observed among infants receiving different feeding modalities with respect to MTCT. Hundred and sixty mothers (57%) disclosed their HIV-positive status to their partners, 82 partners were involved in HIV counselling and testing, 109 partners reported to be tested and 34 (31%) partners were sero-discordant.

Paper IV: Intra-partum transfer associated delays and pregnancy outcome

This study used the same cohort data as in paper III. Of the 282 mothers enrolled, 211 (75%) mothers gave birth at Emergency Obstetric and Neonatal Care (EmONC) facilities and 17 (6%) at home and 54 women were lost to follow up by the time of delivery (reasons for lost to follow up are presented in paper III). Of the mothers who gave birth at EmONC facilities 42% were transferred between health facilities during the intra-partum period and 36% were transferred twice and more. Sixty four percent of the first time transfers were due to obstetric complications, while all subsequent transfers were due to practical constraints. Lack of bed was the sole reason for transfers from comprehensive EmONC facilities. Mothers in their second pregnancy were less likely (OR 0.3 95% CI 0.2-0.6) to be transferred than mothers in their first pregnancy. The rate of stillbirths was 39/1000 live births. Mothers who were transferred during the intra-partum period were 5.8 times (95% CI 1.2-28.8) more likely to experience stillbirths than those mothers who did not. The rate of stillbirths was not significantly associated with the syphilis test result, the CD_4 count or initiating lifelong ART.

Discussion

Discussions of methods

The study designs

This thesis used cross-sectional, mixed methods and prospective cohort designs. Combining different designs and methods is, from a methodological perspective, considered vital to improve the validity of the findings.

The cross-sectional design was chosen because of its strength to collect large data in a short time period, although this design has its own limitations to make causal and temporal inference. This design was valuable to collect six years retrospective routine PMTCT reports for trend analysis.

The sequential exploratory mixed methods design was valuable in paper II for comprehensive understanding of the behavioural determinants of antenatal HIV testing. Through FGD, context specific barriers were captured and used as a knowledge base to develop the TPB questionnaire. In spite of the stated strengths, conducting mixed methods study was a time consuming endeavour. The follow up part of this study was analysed as a fixed cohort due to short time period between exposure and outcome. The short follow up period reduced loss to follow up. Moreover, in TPB, intention is often considered an unstable measure as things that crop up between intention measure and actual behaviour could influence the initial intention. Having a very short follow up from this perspective is a strength of our study. Yet, from theoretical perspective short follow up does not allow for calculating incidence rates that cohort studies are often praised for [117]. Despite the short time interval between intention measure and actual HIV testing pre-test information/counselling

were given to the mothers after intention measure. This seemed to have influenced most of the low intenders to take HIV testing.

The strength of the prospective cohort design lies in its ability to make causal and temporal inference between exposure and outcome, given that potential systematic and random errors are taken care of [119].

Selection bias

Selection bias is a systematic error resulting from faults in selection of participants [117, 119]. Cohort studies that collect exposure data before the occurrence of an outcome are less likely to experience selection bias. This thesis used general cohort in paper II, III and IV with internal comparison groups. Such cohorts are less vulnerable to systematic error in selection of participants as the internal comparison groups are decided later in the study process. In paper II, all first time antenatal attendees were enrolled while comparison between high and low intenders in actual HIV testing was done later. In paper III and IV, all HIV-positive mothers attending selected health facilities were followed while internal comparison were made during data analysis.

Information bias

Information bias is also called misclassification that occurs when there is error in the information collected about or from the study participants [117, 119]. Misclassification can be differential, if the bias is related to either an exposure or an outcome. Recall bias is one form of information bias more common in studies relying on retrospective information. Despite using retrospective information, recall bias in the present study (paper I) was less likely as the data were obtained from records. However, ensuring data quality and completeness are the major drawbacks of using routine records especially in resource-poor settings where the quality of reports are often questionable [102].

Limiting the study objective to those indicators that could be calculated from the reports and using multiple data sources ensured 93% complete data.

The prospective designs are less prone to recall bias as the potential predictors are recoded at the beginning of the study. However, social desirability bias can happen in prospective studies. Since most of the outcome data in our study were obtained from logbooks and were objective, the risk of social desirability bias was less likely.

The validity and reliability of a study can easily be affected by measurement errors. Validity refers to the ability of the instrument to measure what is supposed to measure, while reliability refers to the stability, consistency and equivalence of measurements taken [113]. To ensure content validity of the questionnaire in paper II, a guide was used to develop a standard TPB questionnaire and to grasp contextual factors FGDs were conducted. The construct validation of the TPB variables showed significant correlation between intention and attitude, intention and subjective norm as proposed in the TPB. Examination of the observed theoretical associations is as much a test of the theory as it's is a test of its validity

The questionnaire reliability was checked through pre-test interviews prior to actual data collection. The internal consistency reliability of a test is widely assessed by Cronbach's alpha coefficient, the coefficient value ranges from 0 to +1, the higher the score the more reliable the instrument is [113]. In paper II, the Cronbach's alpha coefficients were 0.75 for attitude and subjective norm and 0.92 for intention, indicating the high internal consistencies of the constructs. The questionnaire interviews were done by several field assistants. This would have introduced intra-rater and inter-rater variability if not for the intensive calibration procedure done. Polit and Black pointed out that the reliability of observational studies can be enhanced through calibration process [113].

Employing field assistants sharing similar educational background and gender were intended to reduce inter-rater variability. Moreover, the follow up data in paper II, III and IV were collected by experienced PMTCT counsellors who had sufficient knowledge on PMTCT and all of them were well acquainted with most of the questions in the follow up format. Owing to their ample experiences in routine reporting, one day training was considered sufficient for them. However, hiring these counsellors for the follow up could have introduced some sort of social desirability bias to the study. This could be a non-differential misclassification which bias the effect estimate towards the null.

Losses to follow up are potential threats to the validity of cohort studies [101, 113, 117, 119]. Information bias due to loss to follow up is a serious concern in this work. In paper IV, no outcome data (i.e. intra-partum transfer) were available for 19% of the cohort. This would have resulted in differential misclassification if mothers with missing information were different from those for whom outcome was recorded. Analysis of the baseline characteristics did not show any significant difference between mothers who completed their follow up and those who did not for the variables measured. The losses to follow up were anticipated by the fact that HIV/AIDS is still a disease with stigma, the possibility of abortion among mothers enrolled in early pregnancy, the low rate of institutional delivery in the city (44%) and the high reported dropout rate in PMTCT programmes. Hence, we extended our effort in tracing the loss to follow up using several contact points. Moreover, the sensitivity analysis had shown no effects on the findings.

Confounding and interaction

Confounding is a mixing of effect that can lead to erroneous conclusion [117, 119]. Compared to experimental designs where participants are assigned randomly, observational studies relying on natural assignment of participants often encounter confounding. During data collection potential

confounders can be minimized through random allocation, restriction and matching of participants while during data analysis stratification and use of multivariate model can help to control for confounding effect [117, 119]. Most socio-demographic variables can confound observational studies and should be accounted for. Multivariate logistic regression analyses were employed to control for potential confounding effect by including variables with p-value less than 0.2 in bivariate analysis.

Interaction or effect modification is when the association between exposure and outcome varies with the level of a third variable [117]. Like confounding, interaction can also lead to erroneous conclusion and it is necessary to account for its effect during analysis. In paper II, we assessed possible interaction between intentions to test for HIV and the type of pre-test information/ counselling the mothers received. Both intention and type of pre-test counselling can increase the mothers' likelihood of taking an HIV test independent of one another. Possible interaction effect was checked whether actual HIV testing was different among high and low intender depending on the type of pre-test counselling they received. There was no significant interaction between intention and type of pre-test counselling received.

Random error

Random errors can seriously affect the precision of an epidemiologic study and should be minimized [117, 119]. Confidence intervals and p-values are often used to assess the precision of a study in reference to the null hypothesis (the hypothesis of no association between exposure and outcome). Confidence intervals are more informative than p-values as it can indicate both the point estimate and the sample distribution. If the confidence interval includes one, it indicates the lack of association between exposure and outcome. The further the point estimates from one the stronger is the association between the exposure and the outcome. Type I error (α), is when one falsely detects

an association between exposure and outcome in the absence of any association. The common threshold for type one error (p-value) is 5%. Type II (β) error, is when one fails to detect association between exposure and outcome where there is an association. This corresponds to the power of the test with a common threshold value of 80%. This error can be minimized by increasing sample size. In the cohort, the sample size was calculated to achieve a 5% precision, with a 95% confidence level. The sample sizes were sufficient enough to detect association between exposure and main outcomes.

External validity

The external validity of an epidemiological study is concerned with the generalizability of the findings to other populations and/or settings [117, 119]. Measures intended to improve internal validity such as selecting homogenous sample could be counterproductive for ensuring external validity. Some of the potential threats to external validity of observational studies are selection of samples which are not representative of the study population, non-random selection of samples and Hawthorne effect [119]. To ensure representation, in paper I, the entire PMTCT reports from all the 10 sub-cities were collected.

In paper II-IV, although a non-probability sampling was applied in selection of the study sites, attempts were made to improve representation. First, all the sub-cities were included. Second proportional allocation of public and private health facilities depending on the proportion of pregnant mothers being served in those facilities was considered. Third a large proportion of the eligible mothers were included i.e. 44% in paper II and 60% both in paper III and IV. Moreover, less stringent exclusion criteria were used to maximize representation. The lack of consideration of the design effect in determining the sample size could have implied a too limited sample size with lack of statistical power. However, when adjusting for design effect in the statistical analyses- the major

results remained almost unchanged. Still the study may not be representative of the whole nation where the majority of the mothers are living in rural areas with poor access to PMTCT programmes. However, since it was generated from a national programme, lessons learnt herein could benefit the PMTCT programme across the country.

Being a health facility based study, the external validity of the findings could have been limited if over 90% of the mothers were not attending ANC. In paper III and IV, potential Hawthorne effect is a concern due to the training given to the PMTCT counsellors who followed the mothers, the compensation for transport and the follow up care given to the mothers. These could have some positive influence on mothers' adherence to the PMTCT recommendations.

The rate of MTCT was examined based on infants tested for HIV, which could be actually underestimated due to the large loss to follow up. Considering the lack of a system to trace loss to follow up, our findings still highlight the potentially averted infections.

Discussion of the main findings

The PMTCT programme expansion and the declining HIV prevalence

This study showed marked increase in PMTCT programme attendance accompanied by a substantial increase in the proportion of mothers receiving HIV counselling and testing. The HIV prevalence among these mothers has declined steadily paralleling the increased number of mothers tested for HIV and the expansion of the programme. A similar declining trend in HIV prevalence has been observed among the general population and from a sentinel surveillance report in Ethiopia [6, 7]. The declining trend in HIV prevalence can probably be attributed to the expansion of the national PMTCT programme and the inclusion of reports from private facilities where the HIV prevalence among ANC attendees is generally lower than among public facilities attendees. In the sentinel surveillance reports, as the number of sentinel sites increased, the estimated HIV prevalence decreased [7]. More importantly, synergy between the natural progressions of the HIV epidemic, increasing access to ART, behaviour changes among the general population in terms of increased condom use and reduced risky sexual behaviour could have contributed to the decline [6, 8].

Behavioural determinants of routine opt-out HIV testing and issues of informed decision

Our study demonstrates a marked improvement in the rate of HIV testing following the introduction of the routine opt-out approach. Similar successes have been reported from many resource-poor settings that have implemented routine opt-out testing [22, 23, 26, 54]. The present study showed that the majority of mothers had high intention to test upon their first antenatal visit even before they received pre-test counselling. This indicates that HIV testing taking place in antenatal settings has become a common knowledge. A survey conducted in 2004 in Addis Ababa showed that over 75% of the antenatal attendees had knowledge about MTCT/ PMTCT and favourable attitude

towards antenatal HIV testing [120]. In our study mothers intended to test for HIV if they anticipated positive consequences and approval from social network. Consistent with our findings studies about intended use of VCT services also identified attitude and subjective norm to be the strongest predictors [40, 41]. Hence, educational messages to increase mothers' motivation to test should target attitude that mothers hold about the positive consequence of HIV test. Moreover, increasing awareness about the importance of HIV testing to the mothers' wider social network could have positive impact on the mothers' motivation to test.

Despite intention being the strongest independent significant determinant of actual HIV testing, large proportions of non-intenders were tested. The large proportion of low intenders who ended up in testing may be related to more unstable measure of behavioural intention i.e intention might change over time with events that crop up between the assessment of intention and behaviour. In this study the pre-test counselling/information offered to participants probably contributed to a change in mother's initial intention. In this regard the pre-test counselling/information given to the low intenders in particular seem to positively influence them to change their initial lack of intention. The high rate of testing among the low intenders could also be related to poor pre-test information and to the power imbalance between the counsellors and the mothers. Several studies from sub-Saharan Africa have shown that the information given to pregnant mothers in the group pre-test sessions was inadequate and mainly focused on getting the mothers tested without enabling them to opt out if they did not intend to test [35-37]. Several researchers also argue that many mothers in resource-poor settings are less empowered to actively opt-out the testing offer and might accept testing just to conform to the antenatal routines [33, 35, 37]. Here there is a need to come up with strategies to maximize the sensitivity of routine opt-out approach to enhance the mothers' autonomy to make an informed decision. Based on our findings it will be important to create awareness about

the benefit of antenatal HIV testing to motivate non-intenders. So that the fundamental principle of informed consent is not violated and that testing follows an informed choice.

Sub-optimal adherence to prophylactic medication regimen

The present study findings suggested that irrespective of the changes in prophylaxis regimen there was little progress in prophylactic medication utilization over the years. Several empirical works within and outside Ethiopia have also reported sub-optimal utilization of prophylaxis medication. This could be attributed to the lack of tailored strategies to improve adherence to prescribed medication and regular follow up. At the time the " 3 by 5 initiative " was embarked, shifting the HIV testing approach was considered a way forward to recruit those who are eligible for ART [31]. Years of experiences with antenatal routine opt-out testing however, have shown great challenges to ensure access to ARV prophylaxis despite the large proportion of mothers being identified HIV-positive. Although routine testing importantly creates opportunities for mothers who may not have come to know their HIV sero-status otherwise, the poor link between being identified HIV positive and ARV utilization may threaten the justification of the routine testing recommendation.

The study documented that there was progressive and marked decline in adherence to prophylactic medication regimen across the peri-natal period, 82% during pregnancy while 68% at birth by mother-infant pairs. Similar findings have been reported from several Sub-Saharan African countries where the gap between initiating medication during pregnancy and taking it at birth ranges from 10 to 26% [54, 98, 121]. High coverage and quality intra-partum obstetric care could largely account for these differences. In Botswana for instance, 94% of mothers have access to safe institutional delivery and over 90% of HIV-positive mothers received prophylactic medications at birth [97], whereas in Addis Ababa only 44% mothers have access to institutional delivery [122]. Institutional delivery was a significant determinant of mother-infant pairs ingesting medication at

birth, which is in agreement with findings from other resource-poor settings [97, 98]. In many settings including Ethiopia infants are given prophylaxis within 72 hours of birth at the health facility. Infants delivered at home cannot get the prophylactic medication unless they are brought to health facilities. Facilitating access to prophylaxis medication in the case of home birth should be focused upon.

The gaps in receiving medication during pregnancy and mother-infant pairs taking of the drug at birth could undermine the PMTCT programme effectiveness. Optimal efficacy of the medication can be achieved only when mother-infant pairs are taking the medication as prescribed. In a randomized controlled trial conducted in Tanzania, South Africa and Uganda the rate of MTCT was 8.9% where mother-infants pairs received the intra-partum and postpartum prophylaxis doses, whereas the rate was 14.2% where only mothers received the intra-partum dose [95]. Moreover, the proportion of mothers receiving medication during pregnancy is a proxy indicator currently used for measuring PMTCT programme success; hence the gaps could threaten the validity of this indictor. Particularly in resource-poor settings where there are marked gaps in antenatal care and institutional delivery coverage, this indicator could overestimate the PMTCT programme effectiveness.

Challenges to access intra-partum obstetric care and adverse pregnancy outcomes

Safe obstetric practice is an important component of the PMTCT programme due to the high rate of intra-partum MTCT. However, this component has received the least attention from health care actors as well as in the PMTCT literature. The majority (75%) of the mothers in this study visited EmONC facilities for intra-partum care compared to 44% among the general population of mothers. This difference could be due to the promotion of safe obstetric practice for the reduction of MTCT, which may reflect that the message of safe delivery has reached out to the target groups. In addition it is an indication of mothers' high motivation to secure an HIV negative status of their baby.

However, the study project activity (Hawthorne effect) in terms of improved follow up, the compensation for transport and the training given to the study counsellors could have positive influence on the mothers' motivation to seek institutional delivery.

Forty two percent of the mothers who visited basic EmONC facilities for delivery were transferred between EmONC facilities during the intra-partum period. This rate is much higher than the 15% expected rate of referrals due to obstetric complications and the 19% rate of referrals observed in a large scale study from south East Asia [60, 123]. The high rate of transfer in our study indicates that despite the expressed goal of reducing maternal and peri-natal mortality, the health system appeared unable to take advantage of the mothers' motivation for 'safe obstetric care'. Moreover, 36% of the mothers were actually transferred between the EmONC facilities more than once merely due to practical constraints within the health care system. The available EmONC facilities in Addis Ababa are more than the minimum expected standard and are located within five km distance (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). However, shortage of supplies, shortage of skilled professionals and lack of accountability mechanism are common encounters in most of the EmONC facilities across the city. Similar findings have been reported from Tanzania where most of the basic EmONC facilities are functioning poorly in terms of the quality of the services they are expected to provide and this seems to contribute to the excess obstetric complications reported [124, 125].

The presumably undue transfers between facilities delays the mothers in accessing timely intra-partum care. This is likely to increase the risk of MTCT because of prolonged labour duration and missing of the intra-partum prophylactic dose. More importantly, delays to receive appropriate intra-partum care can be detrimental to maternal and peri-natal survival [59, 60]. The rate of stillbirth in our study was 39/1,000 births, much higher than the 21.3 stillbirths per 1,000 births reported for

developing countries [65]. Mothers who were transferred during the intra-partum period were about six times more likely to experience stillbirth than those who were not. In a health facility based study from Uganda delays to receive care at health facilities (to so-called third delay) was responsible for about half of the peri-natal deaths [62].

In the present study the stillbirths were not associated with the mothers CD_4 count, initiating lifelong ART and syphilis test result which further suggests possible health system failure. According to reports, stillbirths occurring during the intra-partum period can largely be attributed to poor quality obstetric care [126]. There is an inverse correlation between the rate of stillbirth and the quality and quantity of obstetric care provided during pregnancy and delivery [65, 66]. In the 2010 MDG countdown report, most of the countries that show slow progress in reducing maternal and neonatal mortality have a poorly functioning health system, Ethiopia is one of them [127, 128]. A recent review concluded that provision of quality basic and comprehensive EmONC can reduce intra-partum stillbirths by about 45% and 75% respectively [58].

Poor exposed infant follow up services and the rate of MTCT

The PMTC guidelines recommend an integrated and comprehensive regular follow up for exposed infants. In the present study however, the infant follow up services were found to be less organized and inconsistent. By six weeks postpartum, large proportions of the exposed infants had received their first pentavalent vaccine but only 52% had received early infant diagnoses. Worse still few of them had documented HIV test result. Poor early infant diagnostic services appeared to be common to many resource-poor settings; 25% in Mozambique [129] and 40% in Kenya [130]. This could create unnecessary missed opportunities to early infant diagnosis. There were obvious deficiencies within the health care system in coordinating and managing the infant follow up services. In most of the study sites, the infant follow up services were scattered all over the health centres often

demanding visits to multiple service points and were available only two or three days per week. In a study by Nyandiko and colleagues in Kenya, the health system was found responsible for the low rate of infant HIV testing [131]. According to Chatterjee and colleague who conducted a study in four countries, health facilities providing integrated optimal infant follow up service are more likely to have infant diagnosis done at the recommended time [75]. The missed opportunities to early infant diagnosis could delay HIV-positive infants in accessing timely treatment and thus negatively impact their chance of survival [132]. Therefore, creating integrated strategies to contain the necessary procedures pertinent for exposed infant follow up at one single point is required for the PMTCT programme to succeed.

Although implementation gaps were obvious, the national PMTCT programme showed promising outcome in terms of averted infections among those who adhered to the programme. All over the study sites the majority of infants were breast fed and the cumulative HIV infection was about 15% among those on sdNVP regimen who tested at ≥18 months. This rate was comparable to the rate of 15.7% MTCT reported in the HIVNET 012 trial among breast fed infants who tested at ≥18 months [49]. In the group that received combined ZDV regimen and was tested at six weeks postpartum the rate of MTCT appeared to be higher in our study compared to the Petra clinical trial and a study from Abidjan [95, 133]. Yet there was overlap in the confidence intervals. Considering the fact that the data in our study were generated from a national programme and the obvious methodological differences with the aforementioned trails, the rate of MTCT observed in the present study indicates some success of the programme. Nevertheless, unaccounted losses to follow up could underestimate the rate of MTCT [134] since less than one quarter of the exposed infants had documented HIV test result. Moreover, the HIV testing done at six weeks postpartum did not account for the possible MTCT through breast-feeding. For further reduction of MTCT among breast-feeding infants, the follow up services for these infants should be well integrated into existing maternal and child health

programmes with clear sense of ownership and accountability from staff involved in the care. Incorporating prophylactic medication throughout the breast-feeding period as per the recent recommendations should also be considered [52].

Low rate of partners involvement in PMTCT programme

Considering all the mothers who have been tested in the PMTCT programme over the years, the rate of partner testing has remained extremely low at a rate of 5%. This is much lower than the 26% partner involvement in a PMTCT programme reported from Uganda [135]. However, a much higher rate of partner testing was observed among the HIV-positive mothers' in the present study. Partner involvement in the PMTCT programme has paramount importance especially among discordant couples. The rate of sero-discordance was 31% in the present study, consistent with findings from the eastern and southern African region, including Ethiopia [7, 77]. Pregnancy increases the risk of horizontal transmission because of mucosal and hormonal changes [136]. Furthermore, mothers with a recent HIV infection are more likely to transmit HIV infection to their babies [76]. Involving partner in PMTCT programme and couple counselling could help to identify at risk individuals living with infected partners for preventive interventions. According to recent reports, early initiation of ART by infected partners and pre-exposure prophylaxis by uninfected partners can substantially reduce the risk of horizontal heterosexual transmission, which could be a compelling reason to improve partner involvement in the PMTCT programme [79-81].

Improving mothers' access to lifelong ART

According to the trend data, an increasing proportion of HIV-positive pregnant mothers were referred for treatment, care and support services year by year. The referral to ART clinics was intended to identify mothers eligible for lifelong ART or those who require ARV prophylaxis using CD_4 cell count as an indicator. According to the 2007 Ethiopian PMTCT guidelines, mothers with CD_4 cell

count of 200 cells per micro liter or less should initiate lifelong ART irrespective of their clinical staging [91]. Over 30% of the mothers in the cohort initiated lifelong ART. This suggests that the PMTCT programme have been increasingly managed to identify those who need treatment for their own health. By doing so, the programme is addressing the most important issues that PMTCT programmes have been criticized for, i.e the lack of sensitivity to the needs of pregnant mothers. Yet, there is a need to further strengthen the link between the PMTCT and the ART programmes to ensure that all HIV-positive pregnant mothers have access to prophylaxis or lifelong treatment.

Conclusions and recommendations

Conclusions

There has been a rapid scaling up of the national PMTCT programme in Addis Ababa accompanied by a substantial increase in the rate of HIV counselling and testing from 2004 to 2009. Paralleling the programme scale up and the increased number of mothers tested, the HIV prevalence has shown a steady decline. The increase in the rate of HIV testing was marked following the shift to routine opt-out HIV testing approach. Data collected following the implementation of routine opt-out testing, however, have shown that some mothers were tested despite their low intention to test. This suggests that in the routine opt-out approach, the mothers' lack of intention to test may not account for the outcome. In order to motivate the low intenders to take HIV testing, one should target the mothers' attitude and subjective norm so that testing follows informed decision.

Missed opportunities to collect prophylactic medication, infant follow-up, safe obstetric care, and partner involvement in HIV testing remained high over the study period. The lack of improvement in medication utilization after the shift to routine opt-out testing should be an issue of serious concern at national and international level as the shift was intended to facilitate access to prophylactic medication. The proportion of mothers who initiated medication during pregnancy was much higher than those mother-infant pairs who ingested the medication at birth. The overall effectiveness of the national PMTCT programme could have been undermined due to these gaps. Optimal efficacy of prophylactic medication can be achieved only when both mother-infant pairs are ingesting it as prescribed. Moreover, the proportion of mother-infant pairs ingesting medication at birth seems to be a more reliable indicator for PMTCT programme planning and evaluation compared to the proxy indicator currently used (i.e the proportion of mothers receiving medication during pregnancy).

Increasing the mothers' access to quality obstetric services is critical to increase adherence to intra-partum medication and to ensure safe delivery. Contrary to the low rate of institutional delivery reported in the city, the majority of the studied mothers did seek intra-partum obstetric care at EmONC facilities. However, the care that the mothers accessed at the health facilities was sub-optimal. Many mothers seemed to be unnecessarily transferred between facilities while in labour. Even worse, some of them were transferred more than once merely due to practical constraints within the health care system. The transfers delayed the mothers in receiving appropriate and timely care. This contributed significantly to the high rate of stillbirth and could have increased the risk of MTCT. The presumably unnecessary transfer reflects the health systems failure to take advantage of the mothers' motivation for "safe obstetric care" and is seriously compromising the mothers' right to appropriate and timely care. Increased attention should be put on this so-called third delay to strengthen safe obstetric care services in the city.

Services pertinent to exposed infants follow up seem to be inconsistent and not well organized, contributing significantly to avoidable missed opportunities. By six weeks postpartum, about 90% of the infants received pentavalent vaccine but only about 50% attended early infant diagnosis and only small proportions had documented HIV test result. This could affect the survival of HIV-positive infants in particular as about 50% of them could die in the first year of life if they do not initiate early ART. In order to maximize the effectiveness of the PMTCT programme and the survival of HIV-positive infants, the health system needs to develop targeted interventions. These interventions must ensure early infant diagnosis and continuity of care and should be integrated within the existing traditional under-five child health services.

The other component of the PMTCT programme that showed low utilization is partner involvement. Partner involvement in the PMTCT programme has been extremely low over the years (about 5%), yet a relatively high proportion of partners of the HIV-positive mothers were involved in the PMTCT programme. One third of the partners were sero-discordant. Hence, to reduce the burden of MTCT it is crucial to involve partners in PMTCT programmes. By doing so partners who are at risk of acquiring new HIV can be identified for pre-exposure prophylaxis. Furthermore, inline with the recent concept of "treatment for prevention", identification of discordant couples could help for early initiation of lifelong ART by the infected partner to prevent both horizontal and vertical transmission.

The impact of the national PMTCT programme seems to be promising when the rate of MTCT is calculated among the tested infants. However, due to the lack of consideration of the lost to follow up, the MTCT reported in the present study could be grossly underestimated.

Recommendations

Considerations for health promotion

Behavioural interventions should be considered to motivate mothers for antenatal HIV testing. These interventions should focus on the positive consequences accruing from the testing. There is a need to target the wider social network of the mother who could possibly exert positive influence on the mother's decision to test. In particular the need for partner involvement in PMTCT programme should be emphasized.

Creating awareness about the need for optimal adherence to PMTCT recommendations should be highlighted using existing information, education and communication channels. There has been wide media coverage about the importance of HIV testing during pregnancy, consequently antenatal HIV testing has become common knowledge. Such effort should be extended to minimize the rate of non-adherence to subsequent PMTCT recommendations.

Considerations for possible health system strengthening

Home delivery was associated with a high risk of mother-infant pairs intra-partum medication non-adherence at birth. Facilitating access to prophylactic medication through provision of the medication to be taken at home in the case of home delivery should be considered as the rate of facility birth in Ethiopia is very low.

Safe obstetric care in a PMTCT programme should attract the attention it deserves from the health care system and health care workers like the other major PMTCT programme components.

The quality of obstetric care services in Addis Ababa should be improved. Especially the basic EmONC facilities that the majority of the city population relies on should be fully functional at all times. This could be done through skill training, provision of supplies and by introducing accountability mechanisms such as audit. Meanwhile, establishing an efficient referral system with reliable ambulance services is essential. Strengthening public-private partnership through innovative mechanisms could also help to reduce the load from public facilities.

A system to trace HIV-positive mothers who default from care should be in place in all health facilities. In this regard lessons can be learnt from ART clinics that used active tracing mechanism for ART defaulters.

The Addis Ababa City Administration Health Bureau and the sub-cities must devise context specific mechanisms to improve the follow up of PMTCT recommendations among HIV-positive mothers and to retain the HIV-positive women in the programme until the follow up is completed.

Considerations for further training

The PMTCT training should emphasize:-

- The need to provide clear information/counselling about the mothers' right to opt-out.

- The need to involve partners in the PMTCT programme with due focus on couple counselling irrespective of the mothers HIV test result.

- Counselling for HIV-positive mothers on medication adherence, safe obstetric care, infant follow up and partner involvement in HIV testing.

- The issue of intra-partum transfers and the "third delay" and the mothers' rights to appropriate and timely care.

Considerations for programme monitoring and for research

The national PMCT report should be used regularly for performance evaluation, to assess changes before and after implementation of any recommendations and to assess the impact of the national PMTCT programme.

The Addis Ababa City Administration Health Bureau, the sub-cities Health Bureau and the health facilities should utilize the monthly reports to evaluate performance and gaps in service provision/utilization.

Further research is imperative to identify and address challenges to ARV prophylaxis adherence, safe obstetric care, infant follow up and partner involvement and challenges to PMTCT programme follow up.

References

1. UNAIDS: *UNAIDS report on the global AIDS epidemic 2010*. Geneva: Joint United Nations programme on HIV/AIDS (UNAIDS); 2010.
2. Buchbinder SP: **HIV Epidemiology and Breakthroughs in Prevention: 30 Years Into the AIDS Epidemic**. *Topics in Antiviral Medicine* 2011, **19**(2).
3. UNAIDS/WHO: **Quality and Coverage of HIV Sentinel Surveillance With a brief History of the HIV/AIDS Epidemic.** In *workshop on HIV/AIDS and Adult Mortality in Developing Countries New York, 8-13 September 2003*. Edited by UNAIDS/WHO. New York; 2003.
4. FMOH: **Single point HIV prevalence estimate: National Consensus Meeting on Single HIV Prevalence Estimation**. Addis Ababa: Federal Ministry of Health; 2007.
5. Bolu O, Anand A, Swartzendruber A, Hladik W, Marum LH, Sheikh AA, Woldu A, Ismail S, Mahomva A, Greby S *et al*: **Utility of antenatal HIV surveillance data to evaluate prevention of mother-to-child HIV transmission programs in resource-limited settings**. *American Journal of Obstetrics and Gynecology* 2007, **197**(3):S17-25.
6. FHAPCO: **Annual Performance Report of Multisectoral HIV/ AIDS Response 2002 E.C. (2009/2010)**. Addis Ababa: Federal HIV/AIDS Prevention and Control Office; 2010.
7. HAPCO/GAMET: **HIV/AIDS in Ethiopia - An Epidemiological Synthesis**. Washington DC: Federal HIV/AIDS Prevention and Control Office and Global HIV/AIDS Monitoring and Evaluation Team; 2008.
8. CSA: **Ethiopia Demographic and Health Survey 2005**. Addis Ababa: Central Statistical Authority; 2006.
9. CDC: **Recommendations for assisting in the prevention of perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus and acquired**

immunodeficiency syndrome. *Morbidity and Mortality Weekly Report* 1985, **34**(48):721-726, 731-722.

10. Lyall EG, Blott M, de Ruiter A, Hawkins D, Mercy D, Mitchla Z, Newell ML, O'Shea S, Smith JR, Sunderland J *et al*: **Guidelines for the management of HIV infection in pregnant women and the prevention of mother-to-child transmission**. *HIV Medicine* 2001, **2**(4):314-334.
11. De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, Alnwick DJ, Rogers M, Shaffer N: **Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice**. *the journal of the American Medical Association* 2000, **283**(9):1175-1182.
12. Giuseppe P, Anthony F: **The immunopathogenesis of human immunodeficiency virus infection**. *New England Journal of Medicine* 1993, **328**(5):327-335.
13. Mandelbrot L, Mayaux MJ, Bongain A, Berrebi A, Moudoub-Jeanpetit Y, Bénifla JL, Ciraru-Vigneron N, Le Chenadec J, Blanche S, Delfraissy JF: **Obstetric factors and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohorts. SEROGEST French Pediatric HIV Infection Study Group**. *American Journal of Obstetrics and Gynecology* 1996, **175**(3):661-667.
14. Becquet R, Bland R, Leroy V, Rollins NC, Ekouevi DK, Coutsoudis A, Dabis F, Coovadia HM, Salamon R, Newell ML: **Duration, pattern of breastfeeding and postnatal transmission of HIV: pooled analysis of individual data from West and South African cohorts**. *PloS One* 2009, **4**(10):e7397.
15. Chasela C, Chen YQ, Fiscus S, Hoffman I, Young A, Valentine M, Emel L, Taha TE, Goldenberg RL, Read JS: **Risk factors for late postnatal transmission of human immunodeficiency virus type 1 in sub-Saharan Africa**. *The Pediatric Infectious Disease Journal* 2008, **27**(3):251-256.

16. Read JS, Newell MK: **Efficacy and safety of cesarean delivery for prevention of mother-to-child transmission of HIV-1**. *Cochrane Database of Systematic Reviews (Online)* 2005(4):CD005479.

17. Gumbo FZ, Duri K, Kandawasvika GQ, Kurewa NE, Mapingure MP, Munjoma MW, Rusakaniko S, Chirenje MZ, Stray-Pedersen B: **Risk factors of HIV vertical transmission in a cohort of women under a PMTCT program at three peri-urban clinics in a resource-poor setting**. *Journal of Perinatology 2010,* **30**(11):717-723.

18. CDC: **U.S. Public Health Service recommendations for human immunodeficiency virus counseling and voluntary testing for pregnant women**. *Morbidity and Mortality Weekly Report* 1995, **44**(RR-7):1-15.

19. CDC: **Revised recommendations for HIV screening of pregnant women**. *Morbidity and Mortality Weekly Report* 2001, **50**(RR-19):63-85.

20. WHO: *Treating 3 million by 2005 : making it happen : the WHO strategy : the WHO and UNAIDS global initiative to provide antiretroviral therapy to 3 million people with HIV/AIDS in developing countries by the end of 2005*. Geneva: World Health Organization; 2003.

21. WHO: *Strategic approaches to the prevention of HIV infection in infants : report of a WHO meeting, Morges, Switzerland, 20-22 March 2002*; 2003.

22. Creek L, Ntumy R, Seipone K, Smith M, Mogodi M, Smit M, Legwaila K, Molokwane I, Tebele G, Mazhani L *et al*: **Successful introduction of routine opt-out HIV testing in antenatal care in Botswana**. *Journal of AIDS* 2007, **45**(1):102-107.

23. Bolu O, Allread V, Creek T, Stringer E, Forna F, Bulterys M, Shaffer N: **Approaches for scaling up human immunodeficiency virus testing and counseling in prevention of mother-to-child human immunodeficiency virus transmission settings in resource-limited countries**. *American Journal of Obstetrics and Gynecology* 2007, **197**(3):S83-89.

24. Chandisarewa W, Stranix-Chibanda L, Chirapa E, Miller A, Simoyi M, Mahomva A, Maldonado Y, Shetty AK: **Routine offer of antenatal HIV testing ("opt-out" approach) to prevent mother-to-child transmission of HIV in urban Zimbabwe**. *Bulletin of the World Health Organization* 2007, **85**(11):843-850.

25. Kwasi T, Mushota K, Prisca K, Rebecca D, Maxmillian B, Catherine T, Diul M: **Increasing uptake of prevention of mother-to-child transmission of HIV services in a resource-limited setting**. *BMC Health Services Research* 2010, **10**(29).

26. Perez F, Zvandaziva C, Engelsmann B, Dabis F: **Acceptability of routine HIV testing ("opt-out") in antenatal services in two rural districts of Zimbabwe**. *Journal of AIDS* 2006, **41**(4):514-520.

27. Byamugisha R, Tylleskar T, Kagawa MN, Onyango S, Karamagi CA, Tumwine JK: **Dramatic and sustained increase in HIV-testing rates among antenatal attendees in Eastern Uganda after a policy change from voluntary counselling and testing to routine counselling and testing for HIV: a retrospective analysis of hospital records, 2002-2009**. *BMC Health Services Research* 2010, **10**:290.

28. FMOH: **Health and health related indicators 2008/2009**. Addis Ababa: Federal Ministry of Health; 2010.

29. Nigatu T, Woldegebriel Y: **Analysis of the Prevention of Mother-to-Child Transmission (PMTCT) Service utilization in Ethiopia: 2006-2010**. *Reproductive health* 2011, **8**:6.

30. Bayer R, Fairchild AL: **Changing the paradigm for HIV testing--the end of exceptionalism**. *New England Journal of Medicine* 2006, **355**(7):647-649.

31. UNAIDS/WHO: **UNAIDS/WHO Policy statement on HIV testing**. Geneva: World Health Organization; 2004.

32. WHO/UNAIDS: **Guidance on provider-initiated HIV testing and counselling in health facilities.** Geneva: World Health Organization; 2007.

33. Njeru MK, Blystad A, Shayo EH, Nyamongo IK, Fylkesnes K: **Practicing provider-initiated HIV testing in high prevalence settings: consent concerns and missed preventive opportunities**. *BMC Health Services Research* 2011, **11**:87.

34. Rennie S, Behets F: **Desperately seeking targets: the ethics of routine HIV testing in low-income countries**. *Bulletin of the World Health Organization* 2006, **84**(1):52-57.

35. Ujiji OA, Rubenson B, Ilako F, Marrone G, Wamalwa D, Wangalwa G, Ekström AM: **Is 'Opt-Out HIV Testing' a real option among pregnant women in rural districts in Kenya?** *BMC Public Health* 2011, **11**:151.

36. Gruskin S, Ahmed S, Ferguson L: **Provider-initiated HIV testing and counseling in health facilities--what does this mean for the health and human rights of pregnant women?** *Developing World Bioethics* 2008, **8**(1):23-32.

37. Were B, Hasunira R: **Routine HIV testing and counselling and access to services for prevention of mother-to child transmission: Experiences of HIV-positive women in Kawempe division, Kampala district, Uganda**. Kampala: HEPS-Uganda; 2010.

38. Astrøm A, Nasir, E: **Predicting intention to treat HIV-infected patients among Tanzanian and Sudanese medical and dental students using the theory of planned behaviour--a cross sectional study**. *BMC Health Services Research* 2009, **9**:213.

39. Fishbein M: **The role of theory in HIV prevention**. *AIDS Care* 2000, **12**(3):273-278.

40. Fogg C, Mawn B: **HIV Screening: Beliefs and Intentions of the Homeless**. *Journal of the Association of Nurses in AIDS Care* 2010, **21**(5):395-407.

41. Kakoko C, Astrøm A, Lugoe L, Lie T: **Predicting intended use of voluntary HIV counselling and testing services among Tanzanian teachers using the theory of planned behaviour**. *Social Science & Medicine* 2006, **63**(4):991-999.

42. Molla M, Astrøm A, Berhane Y: **Applicability of the theory of planned behavior to intended and self-reported condom use in a rural Ethiopian population**. *AIDS Care* 2007, **19**(3):425-431.

43. Bonell C, Imrie J: **Behavioural interventions to prevent HIV infection: rapid evolution, increasing rigour, moderate success**. *British Medical Bulletin* 2001, **58**:155-170.

44. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, VanDyke R, Bey M, Shearer W, Jacobson RL *et al*: **Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group**. *New England Journal of Medicine* 1994, **331**(18):1173-1180.

45. Rathbun RC, Lockhart SM, Stephens JR: **Current HIV treatment guidelines--an overview**. *Current Pharmaceutical Design* 2006, **12**(9):1045-1063.

46. Shaffer N, Chuachoowong R, Mock PA, Bhadrakom C, Siriwasin W, Young NL, Chotpitayasunondh T, Chearskul S, Roongpisuthipong A, Chinayon P *et al*: **Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial.** *Lancet* 1999, **353**(9155):773-780.

47. CDC: **Administration of zidovudine during late pregnancy and delivery to prevent perinatal HIV transmission--Thailand, 1996-1998**. *Morbidity and Mortality Weekly Report* 1998, **47**(8):151-154.

48. Guay LA, Musoke P, Fleming T, Bagenda D, Allen M, Nakabiito C, Sherman J, Bakaki P, Ducar C, Deseyve M *et al*: **Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial**. *Lancet* 1999, **354**(9181):795-802.

49. Jackson JB, Musoke P, Fleming T, Guay LA, Bagenda D, Allen M, Nakabiito C, Sherman J, Bakaki P, Owor M *et al*: **Intrapartum and neonatal single-dose nevirapine compared**

with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: 18-month follow-up of the HIVNET 012 randomised trial. *Lancet* 2003, **362**(9387):859-868.

50. Rivero A, Mira JA, Pineda JA: **Liver toxicity induced by non-nucleoside reverse transcriptase inhibitors**. *The Journal of Antimicrobial Chemotherapy* 2007, **59**(3):342-346.

51. MacIntyre JA: **Controversies in the use of nevirapine for prevention of mother-to-child transmission of HIV**. *Expert Opinion on Pharmacotherapy* 2006, **7**(6):677-685.

52. WHO: **Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access: recommendations for a public health approach. – 2006 version**. Switzerland: World Health Organization; 2006.

53. Ahoua L, Ayikoru H, Gnauck K, Odaru G, Odar E, Ondoa-Onama C, Pinoges L, Balkan S, Olson D, Pujades-Rodríguez M: **Evaluation of a 5-year programme to prevent mother-to-child transmission of HIV infection in Northern Uganda**. *Journal of Tropical Pediatrics* 2010, **56**(1):43-52.

54. Manzi M, Zachariah R, Teck R, Buhendwa L, Kazima J, Bakali E, Firmenich P, Humblet P: **High acceptability of voluntary counselling and HIV-testing but unacceptable loss to follow up in a prevention of mother-to-child HIV transmission programme in rural Malawi: scaling-up requires a different way of acting**. *Tropical Medicine & International Health* 2005, **10**(12):1242-1250.

55. Nachega J, Hislop M, Dowdy D, Chaisson R, Regensberg L, Maartens G: **Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes**. *Annals of Internal Medicine* 2007, **146**(8):564-573.

56. The International Perinatal HIV Group: **The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1--a meta-analysis of 15 prospective cohort studies**. *New England Journal of Medicine* 1999, **340**(13):977-987.

57. Warszawski J, Tubiana R, Le Chenadec J, Blanche S, Teglas JP, Dollfus C, Faye A, Burgard M, Rouzioux C, Mandelbrot L: **Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French Perinatal Cohort**. *AIDS (London, England)* 2008, **22**(2):289-299.

58. Yakoob MY, Ali MA, Ali MU, Imdad A, Lawn JE, van den Broek NR, Bhutta ZA: **The effect of providing skilled birth attendance and emergency obstetric care in preventing stillbirths**. *BMC Public Health* 2011, **11**(3).

59. Ramanathan M: **Addressing the 'third delay' in maternal mortality: need for reform**. *Indian Journal of Medical Ethics* 2009, **6**(4):211-212.

60. WHO/UNDP/UNICEF: *Monitoring emergency obstetric care : a handbook*. Geneva: World Health Organization; 2009.

61. Barnes-Josiah D, Myntti C, Augustin A: **The "three delays" as a framework for examining maternal mortality in Haiti**. *Social science & medicine (1982)* 1998, **46**(8):981-993.

62. Waiswa P, Kallander K, Peterson S, Tomson G, Pariyo GW: **Using the three delays model to understand why newborn babies die in eastern Uganda**. *Tropical Medicine & International Health* 2010, **15**(8):964-972.

63. Ekanem EI, Ekanem AD, Ekabua JE, Etuk SJ, Essiet A: **Review of obstetrics genito-urinary fistulae in the University of Calabar Teaching Hospital Calabar, Nigeria**. *Nigerian Journal of Clinical Practice* 2010, **13**(3):326-330.

64. Samuel H, Fikre E, Yemane B: **Health facility-based maternal death audit in Tigray, Ethiopia**. *Ethiopian Journal of Health Development* 2009, **23**(2):115-119.

65. Goldenberg R, McClure E, Bann C: **The relationship of intrapartum and antepartum stillbirth rates to measures of obstetric care in developed and developing countries**. *Acta Obstetricia et Gynecologica Scandinavica* 2007, **86**(11):1303-1309.

66. McClure EM, Saleem S, Pasha O, Goldenberg RL: **Stillbirth in developing countries: a review of causes, risk factors and prevention strategies**. *The Journal of Maternal-fetal & Neonatal Medicine:* 2009, **22**(3):183-190.

67. Friberg IK, Kinney MV, Lawn JE, Kerber KJ, Odubanjo MO, Bergh AM, Walker N, Weissman E, Chopra M, Black RE *et al*: **Sub-Saharan Africa's mothers, newborns, and children: how many lives could be saved with targeted health interventions?** *PLoS Medicine* 2010, **7**(6):e1000295.

68. WHO: **Guidelines on HIV and infant feeding 2010 Principles and recommendations for infant feeding in the context of HIV and a summary of evidence**. Edited by WHO. Geneva; 2010.

69. Rollins NC, Becquet R, Bland RM, Coutsoudis A, Coovadia HM, Newell ML: **Preventing postnatal mother-to-child transmission of HIV: context matters**. *AIDS* 2009, **23**(6):740.

70. Coovadia HM, Rollins NC, Bland RM, Little K, Coutsoudis A, Bennish ML, Newell ML: **Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study**. *Lancet* 2007, **369**:1107-1116.

71. WHO/UNICEF: *Co-trimoxazole prophylaxis for HIV-exposed and HIV-infected infants and children : practical approaches to implementation and scale up*. Geneva: World Health Organization; 2009.

72. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, Jean-Philippe P, McIntyre JA: **Early antiretroviral therapy and mortality among HIV-infected infants**. *New England Journal of Medicine* 2008, **359**(21):2233-2244.

73. WHO: *WHO recommendations on the diagnosis of HIV infection in infants and children*. Geneva: World Health Organization; 2010.

74. Zachariah R, Harries AD, Luo C, Bachman G, Graham SM: **Scaling-up co-trimoxazole prophylaxis in HIV-exposed and HIV-infected children in high HIV-prevalence countries**. *The Lancet Infectious Diseases* 2007, **7**(10):686-693.

75. Anirban C, Sangeeta T, Robert G, Ndapewa H, Sok P, Charles K, Abdoulaye W, Matthew B, Chewe L, Rene E: **Implementing services for Early Infant Diagnosis (EID) of HIV: A comparative descriptive analysis of national programs in four countries**. *BMC Public Health* 2011, **11**(553).

76. Moses SE, Tosswill J, Sudhanva M, Poulton M, Zuckerman M: **HIV-1 seroconversion during pregnancy resulting in vertical transmission**. *Journal of Clinical Virology* 2008, **41**(2):152-153.

77. Lingappa JR, Lambdin B, Bukusi EA, Ngure K, Kavuma L, Inambao M, Kanweka W, Allen S, Kiarie JN, Makhema J *et al*: **Regional differences in prevalence of HIV-1 discordance in Africa and enrollment of HIV-1 discordant couples into an HIV-1 prevention trial**. *PloS one* 2008, **3**(1):e1411.

78. Desgrées-du-Loû A, Orne-Gliemann J: **Couple-centred testing and counselling for HIV serodiscordant heterosexual couples in sub-Saharan Africa**. *Reproductive Health Matters* 2008, **16**(32):151-161.

79. HPTN052 Protocol Team: **Antiretroviral treatment to prevent the sexual transmission of HIV-1: results from the HPTN 052 multinational randomized controlled trial.** In *proceedings of the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention.* Rome: IAS Conference; 2011.

80. Jared B: **Antiretroviral Pre-Exposure Prophylaxis for HIV-1 prevention among heterosexual African men and women: the Partners PrEP Study.** In *The 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention*. Rome: IAS Conference; 2011.

81. The TDF2 Study Group: **Daily oral antiretroviral use for the prevention of HIV infection in heterosexually active young adults in Botswana: results from the TDF2 study**. In *proceedings of the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention*. Italy: IAS Conference; 2011.

82. Padian NS, McCoy SI, Karim SS, Hasen N, Kim J, Bartos M, Katabira E, Bertozzi SM, Schwartlander B, Cohen MS: **HIV prevention transformed: the new prevention research agenda**. *Lancet* 2011, **378**(9787):269-278.

83. Abashawl A, Gudetta B, Lulseged S, Awano T, Adamu R, Kumbi S, Isehak A, Coberly J, Bedri A, Sweat M, Ruff A: **Breastfeeding (BF) practices of HIV seropositive women in a PMTCT project.** In *proceedings of the 15th International Conference on AIDS 2004; Bangkok, Thailand*; 2004.

84. World-Bank: **The Millennium Development Goals Report 2011**. New York: World bank; 2011.

85. Garrib A, Jaffar S, Knight S, Bradshaw D, Bennish ML: **Rates and causes of child mortality in an area of high HIV prevalence in rural South Africa**. *Tropical Medicine & International Health:* 2006, **11**(12):1841-1848.

86. Sanders EJ, Araya T, Kebede D, Schaap AJ, Nagelkerke ND, Coutinho RA: **Mortality impact of AIDS in Addis Ababa, Ethiopia**. *AIDS* 2003, **17**(8):1209-1216.

87. Reniers G, Araya T, Davey G, Nagelkerke N, Berhane Y, Coutinho R, Sanders EJ: **Steep declines in population-level AIDS mortality following the introduction of antiretroviral therapy in Addis Ababa, Ethiopia**. *AIDS* 2009, **23**(4):511-518.

88. Chopra M, Daviaud E, Pattinson R, Fonn S, Lawn JE: **Saving the lives of South Africa's mothers, babies, and children: can the health system deliver?** *Lancet* 2009, **374**(9692):835-846.

89. UNAIDS: **Virtual elimination of mother-to-child transmission of HIV by 2015 HIV vaccine—a public good to right a global wrong. More than four million HIV-positive people now receiving life-saving treatment**. In *UNAIDS Newsletter. Volume 3*. UNAIDS; 2009.

90. Nigatu T, Woldegebriel Y: **Analysis of the Prevention of Mother-to-Child Transmission (PMTCT) Service utilization in Ethiopia: 2006-2010**. *Reproductive Health*, **8**:6.

91. FHAPCO/FMOH.: **Guidelines for Prevention of Mother-to-Child Transmission of HIV In Ethiopia**. Edited by office of the Federal Ministry of Health. Addis Ababa; 2007.

92. WHO: *Guidelines on HIV and infant feeding 2010: principles and recommendations for infant feeding in the context of HIV and a summary of evidence*. Geneva: World Health Organization; 2010.

93. Kasenga F, Byass P, Emmelin M, Hurtig AK: **The implications of policy changes on the uptake of a PMTCT programme in rural Malawi: first three years of experience**. *Global Health Action* 2009, **2**.

94. Moses A, Zimba C, Kamanga E, Nkhoma J, Maida A, Martinson F, Mofolo I, Joaki G, Muita J, Spensley A *et al*: **Prevention of mother-to-child transmission: program changes and the effect on uptake of the HIVNET 012 regimen in Malawi**. *AIDS* 2008, **22**(1):83-87.

95. Petra Study Team: **Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa, and Uganda (Petra study): a randomised, double-blind, placebo-controlled trial**. *Lancet* 2002, **359**(9313):1178-1186.

96. Volmink J, Siegfried N, Van der Merwe L, Brocklehurst P: **Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection**. *Cochrane Database of Systematic Reviews* 2007(1):CD003510.

97. Albrecht S, Semrau K, Kasonde P, Sinkala M, Kankasa C, Vwalika C, Aldrovandi GM, Thea DM, Kuhn L: **Predictors of nonadherence to single-dose nevirapine therapy for the prevention of mother-to-child HIV transmission**. *Journal of Acquired Immune Deficiency Syndromes* 2006, **41**(1):114-118.

98. Kuonza L, Tshuma C, Shambira G, Tshimanga M: **Non-adherence to the single dose nevirapine regimen for the prevention of mother-to-child transmission of HIV in Bindura town, Zimbabwe: a cross-sectional analytic study**. *BMC Public Health* 2010, **10**:218.

99. Central Statistical Authority: **Summary and statistical report of the 2007 population and housing census: population size by age and sex** Addis Ababa: UNFPA; 2008.

100. UNDP: **International Human Development Indicators**. UNDP; 2008.

101. Ministry of Finance and Economic Development: **Ethiopia: 2010 MDGs report, trends and prospect for meeting MDGs by 2015**. Addis Ababa; 2010.

102. FMOH: **Health Management Information System (HMIS)/Monitoring and Evaluation (M&E); Strategic Plan for Ethiopian Health Sector**. Addis Ababa: Federal Ministry of Health; 2008.

103. Creswell J, Clark V: *Designing and conducting mixed method research* London: Sage 2007.

104. Creswell JW, Zhang W: **The application of mixed methods designs to trauma research**. *Journal of Traumatic Stress* 2009, **22**(6):612-621.

105. Armitage J, Conner M: **Efficacy of the Theory of Planned Behaviour: a meta-analytic review**. *The British Journal of Social Psychology* 2001, **40**(Pt):471-499.

106. Gebreeyesus H, Boer H, Kuiper A: **Using the theory of planned behaviour to understand the motivation to learn about HIV/AIDS prevention among adolescents in Tigray, Ethiopia**. *AIDS Care* 2007, **19**(7):895-900.

107. Ajzen I: **The Theory of Planned Behavior**. *Organizational Behavior and Human Decision Processes* 1991, **50**:179-211.

108. Jessor R, Jessor S (Eds.): *Problem behavior and psychosocial development: a longitudinal study of youth*. New York: Academic Press; 1997.

109. Conner M, Armitage C: **Extending the Theory of Planned Behavior: A Review and Avenues for Further Research**. *Journal of Applied Social Psychology* 1998, **28**(15):1429-1464.

110. Sutton S, McVey D, Glanz A: **A comparative test of the theory of reasoned action and the theory of planned behavior in the prediction of condom use intentions in a national sample of English young people**. *Health Psychology* 1999, **18**(1):72-81.

111. Sheeran P: **Intention—Behavior Relations: A Conceptual and Empirical Review**. *European Review of Social Psychology* 2002, **12**(1).

112. Jenny K (Ed.): *Qualitative research in health care*. Oxford: Blackwell; 2006.

113. Polit DF, Beck CT: *Nursing Research; Principles and Methods*. Seventh edition, London: Lippincott Williams & Wilkins; 2004.

114. Jillian JF, Eccles MP, Marie J, Anne W, Jeremy G, Robbie F, Eileen FSK, Liz S, Debbie B: **Constructing questionnaires based on the theory of planned behaviour: A manual for health services researchers**. Edited by Jillian J Francis MPE, Marie Johnston, Anne Walker, Jeremy Grimshaw, Robbie Foy, Eileen F S Kaner, Liz Smith, Debbie Bonetti. United Kingdom University of Newcastle 2004.

115. Anthony BM, David C, Goff J, Karin B, Pascal W: **Handbook of Epidemiology.** In *Cohort Studies*. Edited by Wolfgang Atrens IP. Berlin: Springer; 2007.

116. Schmidt CO, Kohlmann T: **When to use the odds ratio or the relative risk?** *International Journal of Public Health* 2008, **53**(3):165-167.

117. Kenneth JR, Sander G (Eds.): *Modern Epidemiology* Philadelphia: Lippincott-Raven; 1998.

118. Greenland S: **Interpretation and choice of effect measures in epidemiologic analyses**. *American Journal of Epidemiology* 1987, **125**(5):761-768.

119. Kenneth JR (Ed.): *Epidemiology an Introduction*. Nairobi: Oxford university press; 2002.

120. Solomie J, Telahun T: **Knowledge and attitude towards mother to child transmission of HIV and it's prevention among post natal mothers in Tikur Anbessa and Zewditu Memorial Hospitals, Addis Ababa**. *Ethiopian Journal of Health Development* 2005, **19**(3):211-218.

121. Stringer E, Ekouevi D, Coetzee D, Tih P, Creek T, Stinson K, Giganti M, Welty T, Chintu N, Chi B *et al*: **Coverage of nevirapine-based services to prevent mother-to-child HIV transmission in 4 African countries**. *The Journal of the American Medical Association* 2010, **304**(3):293-302.

122. UNDP: *Human Development Report 2010 : the real wealth of nations ; pathways to human development*. New York: United Nations Development Program; 2010.

123. Lumbiganon P, Laopaiboon M, Gülmezoglu AM, Souza JP, Taneepanichskul S, Ruyan P, Attygalle DE, Shrestha N, Mori R, Nguyen DH *et al*: **Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08**. *Lancet* 2010, **375**(9713):490-499.

124. Olsen ØE, Ndeki S, Norheim OF: **Complicated deliveries, critical care and quality in emergency obstetric care in Northern Tanzania**. *International Journal of Gynaecology and Obstetrics* 2004, **87**(1):98-108.

125. Olsen ØE, Ndeki S, Norheim OF: **Availability, distribution and use of emergency obstetric care in northern Tanzania**. *Health Policy and Planning* 2005, **20**(3):167-175.

126. Mohammad YY, Mahrukh AA, Mohammad UA, Aamer I, Lawn. JE, Nynke VB, Zulfiqar AB: **The effect of providing skilled birth attendance and emergency obstetric care in preventing stillbirths**. *BMC Public Health* 2011, **11**(3).

127. Bhutta ZA, Chopra M, Axelson H, Berman P, Boerma T, Bryce J, Bustreo F, Cavagnero E, Cometto G, Daelmans B *et al*: **Countdown to 2015 decade report (2000-10): taking stock of maternal, newborn, and child survival**. *Lancet* 2010, **375**(9730):2032-2044.

128. Accorsi S, Bilal NK, Farese P, Racalbuto V: **Countdown to 2015: comparing progress towards the achievement of the health Millennium Development Goals in Ethiopia and other sub-Saharan African countries**. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2010, **104**(5):336-342.

129. Cook RE, Ciampa PJ, Sidat M, Blevins M, Burlison J, Davidson MA, Arroz JA, Vergara AE, Vermund SH, Moon TD: **Predictors of successful early infant diagnosis of HIV in a rural district hospital in Zambezia, Mozambique**. *Journal of Acquired Immune Deficiency Syndromes* 2011, **56**(4):e104-109.

130. Azcoaga-Lorenzo A, Ferreyra C, Alvarez A, Palma PP, Velilla E, Del Amo J: **Effectiveness of a PMTCT programme in rural Western Kenya**. *AIDS Care* 2011, **23**(3):274-280.

131. Nyandiko WM, Otieno-Nyunya B, Musick B, Bucher-Yiannoutsos S, Akhaabi P, Lane K, Yiannoutsos CT, Wools-Kaloustian K: **Outcomes of HIV-exposed children in western Kenya: efficacy of prevention of mother to child transmission in a resource-constrained setting**. *Journal of Acquired Immune Deficiency Syndromes* 2010, **54**(1):42-50.

132. Creek T, Tanuri A, Smith M, Seipone K, Smit M, Legwaila K, Motswere C, Maruping M, Nkoane T, Ntumy R *et al*: **Early diagnosis of human immunodeficiency virus in infants using polymerase chain reaction on dried blood spots in Botswana's national program for prevention of mother-to-child transmission**. *The Pediatric Infectious Disease Journal* 2008, **27**(1):22-26.

133. Dabis F, Bequet L, Ekouevi DK, Viho I, Rouet F, Horo A, Sakarovitch C, Becquet R, Fassinou P, Dequae-Merchadou L *et al*: **Field efficacy of zidovudine, lamivudine and**

single-dose nevirapine to prevent peripartum HIV transmission. *AIDS* 2005, **19**(3):309-318.

134. Ahoua L, Ayikoru H, Gnauck K, Odaru G, Odar E, Ondoa-Onama C, Pinoges L, Balkan S, Olson D, Pujades-Rodríguez M: **Evaluation of a 5-year programme to prevent mother-to-child transmission of HIV infection in Northern Uganda**. *Journal of Tropical Pediatrics* 2009, **56**(1):43-52.

135. Byamugisha R, Tumwine JK, Semiyaga N, Tylleskär T: **Determinants of male involvement in the prevention of mother-to-child transmission of HIV programme in Eastern Uganda: a cross-sectional survey**. *Reproductive Health* 2011, **7**:12.

136. Moodley D, Esterhuizen TM, Pather T, Chetty V, Ngaleka L: **High HIV incidence during pregnancy: compelling reason for repeat HIV testing**. *AIDS* 2009, **23**(10):1255-1259.

Annexes

Annex 1: Paper I – IV

I

Mirkuzie et al. BMC Health Services Research 2010, 10:267
http://www.biomedcentral.com/1472-6963/10/267

BMC Health Services Research

RESEARCH ARTICLE Open Access

Promising outcomes of a national programme for the prevention of mother-to-child HIV transmission in Addis Ababa: a retrospective study

Alemnesh H Mirkuzie[1,2*], Sven Gudmund Hinderaker[1], Odd Mørkve[1]

Abstract

Background: Prevention of Mother-to-Child HIV Transmission (PMTCT) is still the most effective intervention in combating new HIV infections. In 2008, revised national PMTCT guidelines that incorporated new policies on HIV counselling and testing, antiretroviral prophylaxis regimen and infant HIV diagnosis came into effect in Ethiopia. In the present study we have examined trends in PMTCT service utilization and assessed the rate of MTCT in relation to policy changes in the national PMTCT programme.

Methods: Reports from February 2004 to August 2009 were reviewed in 10 sub-cities in Addis Ababa, Ethiopia. The data was collected from May to October 2009.

Results: The proportion of women who received HIV counselling and testing among new antenatal care attendees increased from 50.7% (95% CI 50.2-51.2) in 2007 to 84.5% (95% CI 84.1-84.9) in 2009 following the shift to routine opt-out testing. Nevertheless, in 2009 only 53.7% of the positive women and 40.7% of their infants received antiretroviral prophylaxis. The HIV prevalence among antenatal attendees decreased significantly from 10.5% in 2004 to 4.6% in 2009 in parallel to the increased number of women being tested. The HIV positive women were over 18 times (RR 18.5, $p < 0.0001$) more likely to be referred for treatment, care and support in 2009 than in 2004. The proportion of partners tested for HIV decreased by 14% in 2009 compared to 2004, although the absolute number was increasing year by year. Only 10.6% (95% CI 9.9-11.2) of the HIV positive women completed their follow up to infant HIV testing. The cumulative probability of HIV infection among babies on single dose nevirapine regimen who were tested at >=18 months was 15.0% (95% CI 9.8-22.1) in 2007, whereas it was 8.2% (95% CI 5.55-11.97) among babies on Zidovudine regimen who were tested at >=45 days in 2009.

Conclusion: The paper demonstrates trends in PMTCT service utilization in relation to changing policy. There is marked improvement in HIV counselling and testing service utilization, especially after the policy shift to routine opt-out testing. However, despite policy changes, the ARV prophylaxis uptake, the loss to follow up and the partner testing have remained unchanged across the years. This should be a matter of immediate concern and a topic for further research.

Background

Prevention of mother-to-child HIV transmission (PMTCT) is still the most effective intervention in combating new HIV infections [1]. When the possibility of having an efficacious vaccine seems questionable, as reported in a recent vaccine trial, holding on to PMTCT programmes gives some hope [2]. PMTCT is a multifaceted intervention. It is not just a way to stop vertical transmission of HIV but also to provide access to treatment, care and support for women who would otherwise not get the chance to know their HIV status before it is too late [1].

Despite its importance, a PMTCT programme often suffers poor resource allocation that could threaten

* Correspondence: ami048@cih.uib.no
[1]Centre for International Health, University of Bergen, Overlege Danielssens Hus, Årstav. 21, Bergen 5020, Norway
Full list of author information is available at the end of the article

programme success [3]. Globally, the challenges in PMTCT programme implementation combined with ever changing scientific advances call for frequent revisits of policies and strategies. In Ethiopia, the first PMTCT guidelines were developed in 2001, incorporating early recommendations by the WHO on HIV counselling and testing, ARV prophylaxis regimen, infant feeding counselling, infant HIV diagnosis algorithm, partner testing and referring HIV positive pregnant women for treatment, care and support [4]. During the recent years, the WHO has made several policy changes to improve PMTCT programme performance. In 2004, the HIV counselling and testing policy was shifted from client initiated opt-in approach to routine opt-out approach in order to improve women's access to prevention interventions and to contain HIV testing within the standard of care for pregnant women [5]. In 2006, the antiretroviral (ARV) prophylaxis regimen was changed from short course single dose NVP (sdNVP) to a more efficacious multidrug zidovudine (ZDV) regimen [1,6]. The infant feeding recommendation was also revised in 2006, when exclusive breast feeding became the preferred method for the first six months, plus complementary feeding from six months. As alternative feeding method, exclusive formula was recommended if formula was acceptable, feasible, affordable, sustainable and safe (AFASS) [7].

The national PMTCT guidelines were revised in 2007, incorporating the policy changes made by the WHO from 2004 to 2006, while retaining the early recommendations on partner testing [6]. The revised guidelines state that all pregnant women undergoing HIV counselling and testing should be advised to bring their partner for HIV testing [6]. Partner testing and involvement in PMTCT is intended to facilitate the women's coping with their test results, adherence to PMTCT recommendations and to facilitate disclosure [8]. However, the potentials of partner testing in PMTCT settings for the prevention of horizontal transmission of HIV is often neglected. Orne-Gliemann et al. described that the large proportion of new HIV infections is occurring in conjugal relationship [9]. Studies from southern and eastern Africa also reported that the prevalence of HIV sero-discordance is within the range of 36%-85% [3,10]. Pregnant women who were HIV negative in early pregnancy could be at risk of acquiring new infection if they had a positive partner at home, which in turn would increase the risk of mother-to-child HIV transmission (MTCT).

In Ethiopia a Monitoring and Evaluation system for HIV/AIDS (M&E) was first launched in 2003 [11]. The system was established to support and strengthen evidence based performance monitoring for HIV/AIDS related interventions [4]. As part of the M&E system, monthly PMTCT reports have been collected from different service outlets to evaluate the performance of the national PMTCT programme at facility, sub-city and region level since the launching of the programme. However, despite the availability of comprehensive PMTCT reports the impact of the programme has not been documented. In this study we make use of the available monthly PMTCT reports from the launching of the PMTCT programme in 2004 to August 2009 in order to examine trends in PMTCT service utilization and to assess the rate of MTCT in relation to policy changes.

Methods

A retrospective study was conducted from May to October 2009. PMTCT monthly reports from February 2004 to August 2009 were reviewed in all the 10 sub-cities of Addis Ababa. The population of Addis Ababa is around three million, and the city is administratively divided into 10 sub-cities and 99 Kebeles. In 2007, a total of 30 hospitals, 29 health centres and 442 clinics were providing health care services [12]. Of the 58 health facilities offering maternity care services, 81% were providing PMTCT services. In 2007 alone, over 70,000 pregnant women who were eligible for PMTCT services were living in the city. Over 80% of these pregnant women were attending antenatal care services, yet only 33.1% of the deliveries were attended by skilled professionals. Of the 24, 584 pregnant women who received HIV counselling and testing in 2007, 7.2% were HIV positive [12].

The first national PMTCT guidelines were developed in 2001 in preparation to launch a PMTCT programme [4]. In 2004, three years after the development of the first PMTCT guidelines, a free PMTCT programme was launched in selected public health facilities [4]. Initially, only six public health centres were offering PMTCT services across the city. The PMTCT programme continued to expand and from 2007 the programme has been scaled up to private facilities. As of April 2009, of a total of 52 facilities offered PMTCT services, 25 of them being private facilities (unpublished report from Addis Ababa City Administration Health Bureau). All the PMTCT facilities were integrated with Antenatal Care (ANC) service and the majority also provided delivery services.

For the monitoring and evaluation of HIV prevention programmes, a M&E system was established in 2003. As part of the M&E system, the monthly PMTCT reporting started in February 2004 with Addis Ketema sub-city. From July 2005, all the sub-cities reported. The PMTCT reporting format developed by the Ministry of Health includes output indicators. The format has been distributed to all service outlets by respective sub-city health

bureaus. The PMTCT reports were first collected from the log books at the service outlets and then reported to the respective sub-cities by the end of each month. In the sub-cities, the reports from all private and public facilities were compiled and reported to Addis Ababa City Administration Health Bureau. In this study we collected the monthly PMTCT reports from the 10 sub-cities where they compiled data from all service outlets that started reporting at different times.

The first national PMTCT guidelines was revised in July 2007 to accommodate changes in policies made by the WHO from 2004 to 2006 [6]. Until the revised guidelines came into effect in early 2008, the HIV counselling and testing was offered as an opt-in approach [13], and sdNVP was given to positive women during pregnancy and to their infants within 72 hours of birth [14]. The HIV positive pregnant women were advised to feed exclusive formula if AFASS; if not, exclusive breast feeding [15].

According to the revised guidelines, pregnant women attending ANC should be offered HIV counselling and testing routinely as an opt-out approach [5,6]. The HIV positive pregnant women should start ZDV from 28 weeks of gestation plus intrapartum lamivudine and sdNVP followed by ZDV for seven days postpartum. For the infant, ZDV and sdNVP should be given at birth followed by ZDV for seven days if the mother received prophylaxis for at least one month, otherwise the infant should receive ZDV for one month postpartum [1,6,16]. The HIV positive pregnant women should receive infant feeding counselling in accordance with the 2006 WHO infant feeding update [6,7]. Moreover, HIV antigen testing of infants with polymerase chain reaction (PCR) at >= 45 days postpartum replaced the former antibody testing at >=18 months of age [6]. Nonetheless, early recommendations on partner testing, irrespective of the woman's HIV status, and referring HIV positive pregnant women for treatment, care and support remained unchanged with renewed emphasis in the revised guidelines [6].

Data analysis

The reports were entered in Microsoft Excel spreadsheet and analyzed using Pivotal tables and charts. Prevalence and Relative risk (RR) were determined and χ^2 test for trend was analysed using the Epicalc 2000 software. The χ^2 trend tests were used to check whether there was a linear trend in PMTCT service utilization and HIV prevalence across the years and were reported as RR with associated p-values. The χ^2 tests for trend change for all outcome indicators were compared across the years taking 2004 as the reference time. P-value less than 0.05 was considered significant. Proportions are reported with 95% confidence intervals.

The following outcome indicators were analysed:

1) The proportion of women who received pre-test counselling, HIV testing and post-test counselling among new ANC attendees.

2) The proportion of women who tested positive and partners who received HIV testing among the total number of women who tested for HIV.

3) The proportion of women (and babies) who received ARV prophylaxis, infant feeding counselling and who were referred for treatment, care and support among women who tested positive for HIV.

4) The proportion of babies who tested positive among exposed babies tested for HIV.

Ethical consideration

The study was reviewed and approved by the Regional Committee for Medical Research Ethics in Western Norway and the Ethical committee of Addis Ababa Region Health Bureau in Ethiopia. Study permit from Addis Ababa Region Health Bureau and respective sub-cities were obtained.

Results

We obtained 565 PMTCT monthly reports from the 10 sub-cities. In Lideta sub-city three reports were missing and we collected them from the service outlets instead. In 6.5% (37) of the reports information on revisiting ANC attendees was either missing, or new and revisit attendees were not reported separately.

During February, 2004 to August, 2009, a total of 663 603 pregnant women attended ANC in health facilities offering PMTCT programme, and 24.6% (163 635) of them were new attendees. Overall, 135 986 women (new and revisit ANC attendees) and 4.9% (6 664) of their partners received HIV testing and 6.2% (8 467) of the women were HIV positive. Of the tested women, 97.1% (131 992) received post-test counselling. Among the HIV positive women, 42.4% (3 594) received ARV prophylaxis, 41.0% (3 474) were referred for treatment, care and support and 82.8% (7 010) received infant feeding counselling. Among babies born to the HIV positive women, 31.0% (2 621) received ARV prophylaxis and 10.6% (896) were tested for HIV (See Additional file 1: Compiled data from February, 2004 to August, 2009 from the 10 sub-cities).

Trends in HIV counselling and testing

Fig 1 presents the year by year trend in HIV counselling and testing utilization. The proportion of women who received pre-test counselling, testing and post-test counselling among new ANC attendees was 66.3% (95% CI 64.8-67.7) in 2004 based on the reports from the three sub-cities that started reporting in 2004. In 2005, following the PMTCT programme scale up to the rest of the

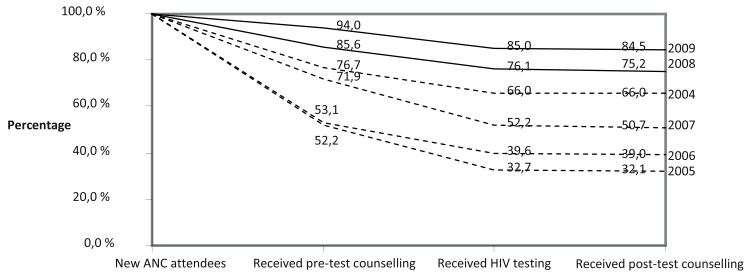


Figure 1 Proportion of women who received pre-test counselling, testing and post-test counselling among new ANC attendees. — In 2004 to 2007 when the HIV testing was offered in an opt-in approach. ___In 2008 and 2009 when the HIV testing was offered routinely in an opt-out approach.

sub-cities, the counselling and testing utilization dropped to 32.1% (95% CI 31.5-32.7). Although the drop appeared to be marked in the three sub-cities that started reporting earlier, those that started later also showed a similar trend. The poor utilization persisted till 2007 when only 50.7% (95% CI 50.2-51.2) of the new attendees received HIV counselling and testing. The PMTCT programme gained momentum in 2008 when the revised guidelines that incorporated routine opt-out testing offer came into effect. Utilization of HIV counselling and testing increased to 84.5% (CI 84.1-84.9) in 2009. The trend in receiving post-test counselling remained stable at high level across the years which imply that almost all the tested women collected their HIV test result (Fig 1).

There were variations across the sub-cities in the proportion of women who had not received pre-test counselling or testing. In 2009, one year following the shift to routine opt-out approach, 12.0%, 18.4%, 19.3%, 14.0%, 14.6% and 27.3% of the women attending ANC in Addis Ketema, Arada, Bole, Kirkos, Lideta and Nifas Silk Lafto sub-city, respectively, did not receive pre-test counselling. Similarly, among women who received pre-test counselling in 2009, 17.3%, 11.3%, 17.0% and 24.8% in Arada, Bole, Gulele and Kirkos sub-cities, respectively, did not receive HIV testing.

HIV testing versus HIV prevalence

Fig 2 presents the overall trends in HIV prevalence among ANC attendees across the years. The HIV prevalence among the total ANC attendees (both new and revisit) who tested for HIV appeared to decline steadily from 10.5% (CI 9.6 -11.5) in 2004 to 4.6% (95% CI 4.3 - 4.8) in 2009 (RR 0.46) in parallel with the increasing number of women testing for HIV. During the same period the trends in HIV prevalence across the sub-cities showed significant decline, except Yeka sub-city where the HIV prevalence actually increased by 17% in 2009 compared to 2004 (RR 1.17, $p < 0.05$) (Table 1).

ARV Prophylaxis uptake

Of the 8 467 HIV positive women, ARV prophylaxis was given to 42.4% (95% CI 41.4-43.5) and to 31.0% (95% CI 30.0-31.0) of their infants. From early 2008, the prophylaxis regimen was shifted from sdNVP to multidrug ZDV regimen. Despite the big difference in the two regimens, the reports did not show marked changes of the trend in prophylactic ARV uptake. In 2004, the ARV prophylaxis uptake by the women and infants was low, but the gap in prophylaxis uptake between the women (24.8%. 95% CI 20.8-29.2) and babies (23.2%. 95% CI 19.3-27.5) was narrow. In 2005 and 2006 an increased proportion of women received prophylaxis, 41.6% (95% CI 39.0-44.3) and 55.0% (95% CI 52.3-57.4) respectively. In 2006 the proportion and number of women who received ARV prophylaxis peaked, yet only 35.1% (95% CI 32.8-37.4) of their infants received prophylaxis, resulting in the widest gap in prophylaxis uptake. In 2007, the prophylaxis uptake by the women and infants dropped to 33.8% (95% CI 31.6-36.1) and 25.4% (95% CI 23.4-27.5), respectively, and the gap narrowed again. The prophylaxis uptake shows an increasing trend since 2008 (Fig 3).

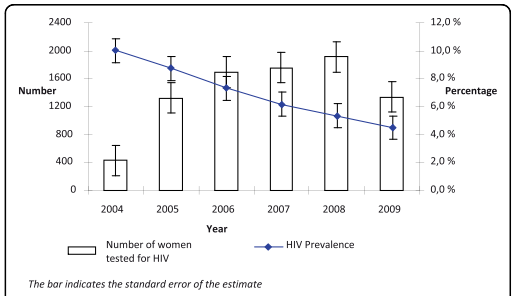


Figure 2 Trends in HIV prevalence among antenatal care attendees tested in PMTCT settings from 2004 to 2009 in Addis Ababa.

Table 1 HIV prevalence among antenatal care attendees who tested for HIV, relative risk and χ^2 for trend test across the years by sub-city

Sub-city	2004		2005		2006		2007		2008		2009		χ^2 trend
	% (n)	RR	% (n)	RR	% (n)	RR	% (n)	RR	% (n)	RR	% (n)	RR	
Addis Ketema	12.8(195)	Ref	11.1(168)	0.99	7.4(170)	0.66	7.8(231)	0.70	4.6(178)	0.41	4.7(130)	0.42	127.3 *
Akaki Kaliti			8.7(99)	Ref	7.0(131)	0.81	6.8(16)	0.78	4.9(136)	0.57	5.3(113)	0.61	22.3 *
Arada			8.9(134)	Ref	8.2(185)	0.92	6.3(159)	0.71	5.9(298)	0.66	3.8(123)	0.43	64.4 *
Bole	8.6(89)	Ref	10.0(112)	1.17	6.8(149)	0.79	5.5(158)	0.64	4.8(171)	0.56	3.2(130)	0.37	105.4*
Gulele			6.7(77)	Ref	6.6(118)	0.98	5.7(156)	0.84	5.0(136)	0.75	4.5(93)	0.67	12.1**
Kirkos			10.2(89)	Ref	9.5(188)	0.93	7.1(162)	0.69	6.8(191)	0.66	4.6(122)	0.44	54.3 *
Kolfe Keraniyo			5.4(67)	Ref	4.9(75)	0.91	2.8(70)	0.51	3.3(73)	0.62	3.7(81)	0.69	7.7‡
Lideta	9.6(148)	Ref	10.2(244)	1.06	6.8(198)	0.71	5.9(228)	0.62	4.8(246)	0.50	4.6(217)	0.48	119.8*
Nifas-silk Lafto			8.0(175)	Ref	7.5(253)	0.93	6.0(232)	0.74	4.6(217)	0.57	4.0(140)	0.49	70.5*
Yeka			7.9(161)	Ref	7.6(228)	0.96	8.2(206)	1.03	9.3(268)	1.17	9.2(193)	1.17	6.2‡

Ref = Reference *P < 0.0001 **P < 0,001 ‡P < 0,01 ‡ ‡ P < 0,05 NB: The denominator for each cell is different

Referral for treatment, care and support

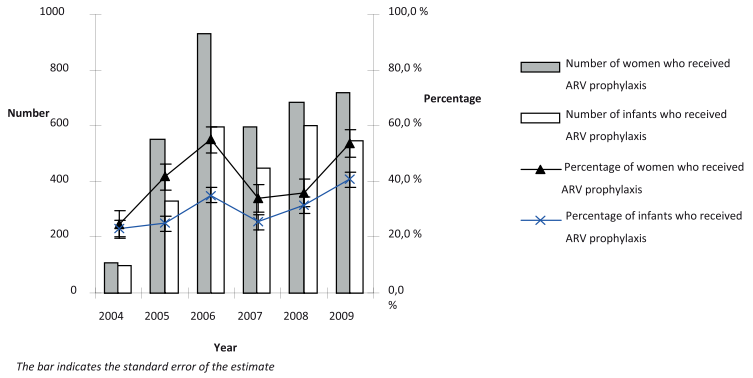
The need for referring HIV positive pregnant women for treatment, care and support gained momentum in response to the 2004-2006 national roadmap to accelerate access to antiretroviral therapy [17] and the launching of the revised PMTCT guidelines [6]. The proportion of HIV positive pregnant women referred for treatment, care and support increased from 3.2% (95% CI 1.9-5.5) in 2004 to 59.9% (95% CI 57.2-62.5) in 2009. In other words, the HIV positive pregnant women in 2009 were over 18 times more likely to be referred for treatment, care and support than their counterparts in 2004 (RR 18.5 X^2 trend p < 0.0001).

Infant feeding counselling

In 2004, when the PMTCT programme was first launched, 58.3% (95% CI 53.5-63.0) of the HIV positive women received infant feeding counselling, compared to 87.3% (95% CI 85.3-89.0) in 2009. The HIV positive women in 2009 had a 50% more chance to receive infant feeding counselling than the positive women in 2004 (RR 1.5, χ^2 trend p < 0.001). Despite the changes in infant feeding recommendation at different times, the report lack information on the kind of infant feeding advice given, infant feeding choice made by the women or pattern of infant feeding.

HIV infection among exposed babies

Overall, only 10.6% (896) (95% CI 9.9-11.2) of the HIV positive women completed their follow up to child HIV testing. The rate of MTCT was evaluated based on the 896 babies tested for HIV during the period 2006-2009. Among the 896 exposed babies 106 were HIV positive. Of the babies on sdNVP regimen who tested at >=18 months with rapid antibody test, 14.3% (95% CI 7.92-24.0) in 2006 and 15.0% (95% CI 9.8-22.1) in 2007 were HIV positive. In 2009, among babies on the multidrug ZDV regimen who tested at >=45 days postpartum with



The bar indicates the standard error of the estimate

Figure 3 Percentage of women and babies who received ARV prophylaxis from 2004 to 2009 in Addis Ababa.

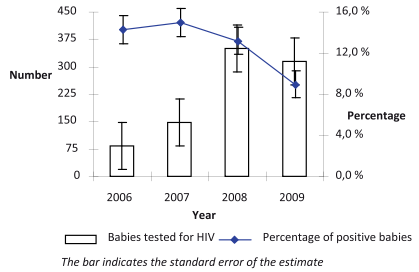


Figure 4 HIV infection among exposed babies tested for HIV from 2006 to 2009 in Addis Ababa.

antigen test using PCR, 8.2% (95% CI 5.55-11.97) were HIV positive (Fig 4).

Partner testing

The overall trend in the proportion of partners tested among women who received HIV testing remained stable at low level i.e 6.4% (95% CI 5.7-7.2) in 2004 and 5.3% (95% CI 5.0-5.5) in 2009. Compared to the women who were tested in 2004, women tested in 2009 were 14% less likely to be tested with their partner (RR 0.86, $p < 0.01$). However, there was an increase in the absolute number of partners tested across the years in parallel with the increased number of women who tested positive. In 2009 the number of partners tested was higher than the number of women who tested positive (Fig 5).

Discussion

In this study we examined trends in PMTCT service utilization and assessed the rate of MTCT in Addis Ababa, Ethiopia. The HIV counselling and testing service utilization improved substantially in 2009 following policy shift to routine opt-out approach. The HIV prevalence appeared to decrease steadily paralleling the increased number of women tested for HIV. Irrespective of policy changes, the uptake of ARV prophylaxis and loss to follow up remained unimproved. Out of the 10.6% (896) exposed babies tested for HIV, the cumulative probability of HIV infection decreased to 15.0% by 2007 among babies on sdNVP regimen tested at >=18 months of age, and to 8.2% by 2009 among infants on ZDV regimen tested at >=45 days of age. The proportion of HIV positive pregnant women referred for treatment, care and support increased eighteen-fold in 2009 compared to 2004. Meanwhile, the proportion of partners tested in the PMTCT setting declined significantly by 14% from 2004 to 2009.

The proportion of women who received HIV counselling and testing among new ANC attendees increased significantly from 50.7% in 2007 to 84.5% in 2009 following the shift to routine opt-out testing. Consistent with our findings, studies from other resource poor settings have revealed significant improvement in HIV testing at ANC from 45% to 99% following the shift to routine opt-out approach [18-20]. Nevertheless, over 10% of the new ANC attendees had not received pretest counselling or testing in 2009. In this regard the opt-out approach, which seems to be robust to maximise HIV testing in many settings [18-20], did not show remarkable success in our study. This could be attributed to two major reasons. First, most of the studies that reported nearly a 100% HIV test acceptance when testing was offered routinely as an opt-out approach, were pilot initiatives [18-20], unlike our study that compiled

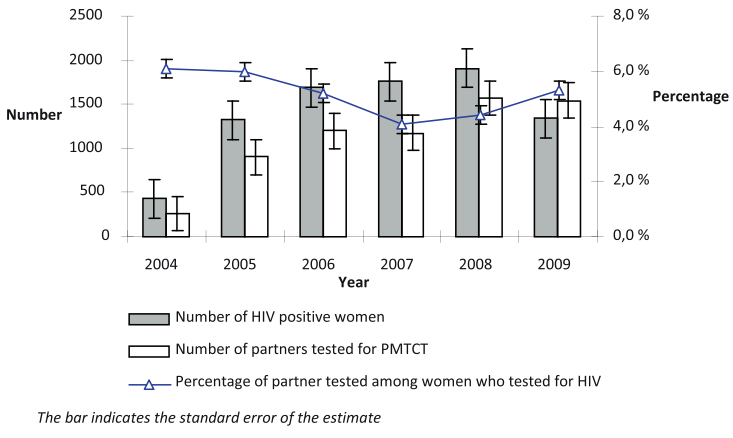


Figure 5 Trends in partner testing in the PMTCT settings from 2004 to 2009 in Addis Ababa.

PMTCT reports from a national programme. In line with our argument, a study in Kenya based on data from 43 PMTCT service outlets reported a 80.6% HIV test acceptance [21]. Second, the expansion of the PMTCT programme to private facilities seem to have contributed to the persistence of a large proportion of women who had not received HIV counselling or testing even after the shift to routine testing. Site factors are reported to be more relevant than participant factors in determining HIV test acceptance in a study from Kenya [21]. In particular, characteristics of the provider appear to be an important determinant for HIV test acceptance. For instance, characteristics of the midwives were found to be an independent determinant for HIV testing uptake in England [22], whereas high test refusal was associated with HIV testing being offered by general practitioners in Canada [21,23]. In almost all the private facilities in Addis Ababa, ANC and HIV testing was offered by physicians who had little or no training on HIV counselling and testing in an opt-in approach. This indicates that there are gaps in the implementation of the routine opt-out testing strategy, particularly in private facilities. On top of that, the utilization of post-test counselling and collection of test result by almost all tested women throughout the years, irrespective of the testing approach employed, implies that the persistent gap in pre-test counselling and HIV testing service utilization could be an evidence of failure of the health system to deliver the programme rather than a failure of the women.

The HIV prevalence among the tested women had reduced by 54% in 2009 compared to the level in 2004, in parallel to the increased number of women being tested. Similar declining trend in HIV prevalence has been observed among adults and from a sentinel surveillance report in Ethiopia. Synergy between the natural progression of the HIV epidemic and behaviour changes among the general population in terms of increased condom use and reduced risky sexual behaviour seem to contribute to the declining prevalence [3,4]. The HIV prevalence estimate in our study was lower than that of the ANC sentinel surveillance report, i.e 6.2% vs 9.3% in 2007/2008 [12]. Consistent with our finding, a study that compiled data from Kenya, Ethiopia, and Zimbabwe for 2005 reported that the HIV prevalence in Ethiopia was 6.4% from PMTCT programme reports and 8.2% from sentinel surveillance reports [24-26]. The two reports, although generated from the same population, have differences in population size and timing of data collection [24-26]. The PMTCT report includes all women who participated in the PMTCT programme all year round. In the sentinel surveillance, leftover blood samples were collected from a smaller number of ANC attendees from selected facilities, often for a period of 3 months biennially.

The decreasing trend in the HIV prevalence estimate across the years could also be attributed to a more representative sample of pregnant women tested for HIV in our study. In other words, the inclusion of more service outlets and therefore reaching out to a large population in our study seems to be more representative, unlike the sentinel surveillance report that relied on reports from a few public facilities. Even in the sentinel surveillance reports, as the number of sentinel sites increased the estimated HIV prevalence declined [4]. More importantly we included reports from private facilities where the HIV prevalence is reported to be lower compared to ANC attendees in public facilities, 2.4% (unpublished report from Addis Ababa City Administration Health Bureau) vs 9.3% [12] respectively in 2007/2008. Moreover, the HIV prevention potential of Highly Active Antiretroviral Therapy (HAART) should not be ignored [27].

Despite the marked increase in HIV testing following the shift to routine opt-out approach, neither the proportion nor the number of women receiving ARV prophylaxis have increased. In 2009, only 53.7% of the women and 40.7% of their babies received ARV prophylaxis. Consistent with our findings, in Addis Ababa, 49.3% of the HIV positive women and 35.3% of their babies received ARV prophylaxis in 2007/2008 [28] and the programme achieved only 30% compared to 80% as the target [12]. Actually, poor ARV prophylaxis uptake is not a new story, even those intervention studies that show almost 100% successes in HIV testing were in short of ARV prophylaxis uptake [18-20]. However, the lack of improvement in ARV prophylaxis utilization following the shift to routine testing is an issue of great concern as the shift to an opt-out approach was primarily intended to increase the proportion of women and infants receiving prophylactic ARV drugs [5]. In the era of routine testing for HIV, the PMTCT programme appears to be an effective screening programme than a prevention programme due to the large number of dropouts after testing. Yet, the gain in HIV testing turnout limits the weakness of the routine opt-out approach in terms of subsequent dropouts and poor adherence to ARV prophylaxis [29]. Currently the availability of potent ARV prophylaxis is changing the landscape, and even mother-to-child HIV transmission through breast feeding has become less of a concern [30]. Yet, still more lives are at stake because of the lack of improvement in uptake of this critical component of the PMTCT programme.

According to Kasenga et al., skilled attendance at birth is an important determinant of ARV prophylaxis uptake that requires thorough consideration [31]. In Addis Ababa, only 30% of the pregnant women had skilled attendance at birth in 2008 [12] corresponding to the

proportion of infants who received ARV prophylaxis [28]. Since infants are given prophylaxis within 72 hours of birth at the health facility, infants delivered at home have less chance to receive ARV prophylaxis than infants delivered in health facilities. An intervention study from Zambia gives some hope that dropouts and non-adherence to ARV prophylaxis could be reduced to zero. This study, which employed multiple interventions, increased the ARV prophylaxis uptake from 29% at baseline to 100% within 3 years [32]. This gives reassurance that the official 80% ARV prophylaxis uptake goal for Ethiopia could be achieved through concerted effort and renewed commitment.

According to the findings, an increasing proportion of HIV-positive pregnant women were referred for treatment, care and support services, from 3.2% in 2004 to 59.9% in 2009. The referral is intended for prompt initiation of ARV prophylaxis or treatment for eligible women using CD_4 or lymphocyte count and WHO staging criteria [6]. By doing so, the programme is addressing the most important issues that PMTCT programmes have been criticized for, i.e the lack of sensitivity to the needs of pregnant women. The PMTCT programme is increasingly successful in bridging the gap between prevention and treatment to address the moral and ethical questions raised over the years [1]. The eighteen-fold increase in the proportion of positive pregnant women being referred for treatment, care and support from 2004 to 2009 demonstrates the good will and the potential to integrate new policies and strategies. Yet, more has to be done to ensure that all HIV-positive pregnant women have access to prophylaxis or treatment, care and support.

The ultimate objective of a PMTCT programme is to avert new HIV infections among children. However, only 10.6% (896) of the HIV positive pregnant women completed their follow up to infant HIV testing. The rates of MTCT were therefore assessed based on test result of the 896 babies tested for HIV. In the absence of any PMTCT intervention the cumulative probability of HIV infection among exposed babies aged >=18 months is in the range of 29% to 47% according to a cohort study conducted in an orphanage in Addis Ababa [4]. In our study, the cumulative probability of HIV infection among exposed babies on sdNVP regimen tested at >=18 months was 14.3% in 2006 and 14.9% in 2007. According to the HIVNET 012 randomized trial, sdNVP regimen has a 41% efficacy. In this trial, consistent with our findings, the cumulative probability of infant HIV infection is 15.7% among breast fed infants tested at >=18 months [14]. However, a methodologically similar study from Malawi that compiled monthly reports showed a 15.5% HIV infection rate among infants on sdNVP regimen tested at 6 weeks postpartum without accounting for the breast feeding transmission [33]. Nevertheless, there is a possibility that our estimate could be biased due to the large loss to follow up.

In 2009, 8.2% of the exposed infants on ZDV regimen tested at 45 days were HIV positive. In the Petra clinical trial, multidrug ZDV regimen showed 63% efficacy in reducing MTCT. In this trial the rate of HIV transmission among infants on multidrug ZDV regimen tested at 45 days was 5.7% [16]. Considering the fact that our data are generated from a national PMTCT programme and the obvious methodological difference with the Petra trial, the 8.2% infant infection rate reported in our study indicates the success of the national PMTCT programme among those who completed their follow up to infant HIV testing. A cohort study from similar resource poor settings that evaluated the effectiveness of a PMTCT programme among predominantly formula fed infants on ZDV regimen tested at >=45 days reported a 9.1% cumulative infant HIV infection, higher than the rate of HIV infection reported in our study [34]. However, since the HIV testing was done at >=45 days, those HIV negative infants who continue to breast feed are still at risk of acquiring new infection. In general, the rate of MTCT averted by the national PMTCT programme appears promising among those who adhered to the programme. Nevertheless, the possibility of underestimation cannot be excluded since we lack information on loss to follow up. In line with this limitation, Ahoua et al. found that the cumulative probability of infant HIV infection among tested infants was 8.3%, whereas it was 15.5% when HIV related deaths were included in the analysis [35].

The last, but not least important PMTCT programme outcome indicator examined in our study was partner testing. The proportion of partners tested remained very low with a 14% significant decline in 2009 compared to 2004. A review on couple centred counselling shows that partner involvement in HIV testing not only helps to increase disclosure, condom use and uptake of ARV prophylaxis but also contributes to the lower rate of seroconversion compared to individual counselling [8]. We noted a parallel trend in the number of partners tested with the number of women who tested positive across the years. This indicates that most of the partners who came for HIV testing were those whose wives tested positive. Partner testing in the context of PMTCT seems to facilitate women's coping, yet missing out the important prevention aspect by not advising HIV negative women to bring their partner for testing.

A study from South Africa shows that 3% of the pregnant women who were found to be HIV negative in their first HIV testing during pregnancy became HIV positive in repeat test in late pregnancy, giving a 10.7% incidence per year [36]. This indicates that women are

at risk to acquire new HIV infection from their HIV positive partner anytime during pregnancy and even during breast feeding. In eastern and southern African region, including Ethiopia, 36-85% of HIV positive individuals are believed to live with an HIV negative partner [4,10]. Discordant couples are the newly identified high risk group in Ethiopia, as most infections are occurring within marriage. Because of mucosal and hormonal changes during pregnancy, the HIV incidence is four times higher among pregnant women compared to their non-pregnant counterparts [37]. Meanwhile, women having recent HIV infection are more likely to transmit HIV infection to their babies [36]. Therefore, it is crucial to focus on partner testing and involvement in the PMTCT programme to optimise programme effectiveness. The current strategies in Addis Ababa, that include giving priority for women coming with their partner for testing and sending an invitation home to partner should be encouraged.

One of the limitations of our study is that the rate of MTCT was examined based on infants tested for HIV, which could actually be underestimated due to the large loss to follow up. Considering the lack of a system to trace loss to follow up, our finding still highlights the potentially averted infections. Another limitation is that the PMTCT programme reached out to only 80% of pregnant women due to incomplete ANC attendance [12] and the findings seem not to represent the whole nation, where a high proportion of the population is rural. However, since it was generated from a national programme, lessons learnt herein could benefit the PMTCT programme across the country. We also believe that our findings are generalisable to the big cities where the HIV prevalence is higher.

Retrospective data collected primarily for reporting purposes always have weakness, especially in resource poor settings where the quality of reports are often questionable [11]. By limiting our study objectives to those indicators that could be calculated from the reports we minimized the risk of having incomplete data. We obtained almost all the reports from February 2004 to August 2009 from the 10 sub-cities. To validate our data we checked Addis Ababa City Administration Health Bureau and NGO reports, and our data were found to be consistent. For missing reports we obtained data from log books and reports at service outlets.

Conclusion

Our findings suggest that the proportion of women receiving HIV counselling and testing has increased substantially from 2004 to 2009. The shift in HIV testing approach has further reduced the proportion of women not receiving HIV counselling and testing. However, the lack of improvement in ARV prophylaxis uptake after the shift to routine opt-out testing is an issue of great concern as the shift was intended to facilitate access to ARV prophylaxis. The health system appeared not only to fail to deliver the most critical component of the PMTCT programme, i.e ARV prophylaxis, but also to retain the HIV positive women to complete their follow up. The effectiveness of the national PMTCT programme is questionable as only 10% of the HIV positive women completed their follow up to infant HIV testing. A tracing system for loss to follow up should be in place for measuring the actual impact of the programme. In addition, the sub-cities and the Addis Ababa city Administration Health Bureau must devise a mechanism to increase prophylaxis uptake and to retain the HIV positive women in the programme until the follow up is completed. The counselling Training should emphasize partner testing to ensure that all women tested in PMTCT settings receive counselling on partner testing, irrespective of their HIV status. Further research is imperative to identify and address challenges to ARV prophylaxis uptake, partner testing, referral for treatment, care and support and challenges to follow up. We recommend the health facilities, sub-cities and the City Administration Health Bureaus to utilize the monthly reports to identify gaps in service utilization and to come up with context specific solutions for the realisation of the country's goal of "HIV free generation by 2020".

Additional material

Additional file 1: Compiled monthly PMTCT reports from February, 2004 to August, 2009 for the 10 Sub-cities in Addis Ababa. The table containes monthly PMTCT reports from February, 2004 to August 2009 collected from the 10 sub-cities. Addis Ketema, Bole and Lideta sub-cities started reporting from 2004 while the rest of the sub-cities reported from 2005.

Acknowledgements

This study was financially supported by the Centre for International Health, University of Bergen, the Meltzer Foundation and Statens Lånekasse, Norway. We thank the Addis Ababa City Administration Health Bureau and the health bureaus' in the respective sub-cities for permitting us to collect the reports. Both Addis Ababa City Administration Health Bureau and Intra Health deserve acknowledgement for providing their PMTCT reports for validation. Moreover, we are grateful to Karen Marie Moland for revising the manuscript and to Addis Mulu for transferring the data into a pivotal table and chart format.

Author details

[1]Centre for International Health, University of Bergen, Overlege Danielssens Hus, Årstav. 21, Bergen 5020, Norway. [2]College of Medical and Health Sciences, Department of Nursing and Midwifry, Hawassa University, Awassa, p.o.box 1560, Ethiopia.

Authors' contributions

AHM prepared the study proposal, collected and analyzed the data, interpreted the findings and wrote the manuscript. OM was involved in developing the study proposal, supervising the data collection and revising the manuscript. SGH was involved in developing the study proposal and

revising the manuscript. All authors have read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Received: 9 April 2010 Accepted: 9 September 2010
Published: 9 September 2010

References

1. WHO: **Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access: recommendations for a public health approach.- 2006 version.** WHO: Geneva 2006.
2. Letvin NL: **Virology. Moving forward in HIV vaccine development.** *Science (New York, N.Y.)* 2009, **326(5957)**:1196-8.
3. Potts M, *et al*: **Public health. Reassessing HIV prevention.** *Science (New York, N.Y.)* 2008, **320(5877)**:749-50.
4. HAPCO/GAMET: *HIV/AIDS in Ethiopia - An Epidemiological Synthesis. Washington DC* 2008.
5. UNAIDS/WHO: *UNAIDS/WHO Policy statement on HIV testing* WHO: Geneva 2004.
6. HAPCO/FMOH: *Guidelines For Prevention of Mother-to-Child Transmission of HIV in Ethiopia* MOH: Addis Ababa 2007.
7. WHO, *et al*: *HIV and infant feeding: update based on the technical consultation held on behalf of the Inter-agency Task Team (IATT) on Prevention of HIV infections in pregnant women, Mothers and their Infants, Geneva, 25-27 October 2006* WHO: Geneva 2007, iv, 14 p.
8. Desgrées-du-Loû A, Orne-Gliemann J: **Couple-centred testing and counselling for HIV serodiscordant heterosexual couples in sub-Saharan Africa.** *Reproductive health matters* 2008, **16(32)**:151-61.
9. Orne-Gliemann J, *et al*: **Couple-oriented prenatal HIV counseling for HIV primary prevention: an acceptability study.** *BMC public health* 2010, **10**:197.
10. Lingappa JR, *et al*: **Regional differences in prevalence of HIV-1 discordance in Africa and enrollment of HIV-1 discordant couples into an HIV-1 prevention trial.** *PloS one* 2008, **3(1)**:e1411.
11. FMOH: **Health Managment Information System (HMIS)/Monitoring and Evaluation (M&E); Strategic Plan for Ethiopian Health Sector.** FMOH: Addis Ababa 2008.
12. FMOH: *Health and health related indicators* FMOH: Addis Ababa 2008.
13. CDC: *U.S. Public Health Service Recommendations for Human Immunodeficiency Virus Counseling and Voluntary Testing for Pregnant Women* MMWR 1995, **44(RR-7)**.
14. Jackson JB, *et al*: **Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: 18-month follow-up of the HIVNET 012 randomised trial.** *Lancet* 2003, **362(9387)**:859-68.
15. WHO, *et al*: **HIV and infant feeding: guidelines for decision-makers.** WHO: Geneva 2003, 75.
16. Petra Study Team: **Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa, and Uganda (Petra study): a randomised, double-blind, placebo-controlled trial.** *Lancet* 2002, **359(9313)**:1178-86.
17. FMOH: **Accelarating access to HIV/AIDS treatment in Ethiopia: Road Map for 2004-2006.** FMOH: Addis Ababa 2005.
18. Kasenga F, *et al*: **The implications of policy changes on the uptake of a PMTCT programme in rural Malawi: first three years of experience.** Global health action 2009, **2**.
19. Chandisarewa W, *et al*: **Routine offer of antenatal HIV testing ("opt-out" approach) to prevent mother-to-child transmission of HIV in urban Zimbabwe.** *Bulletin of the World Health Organization* 2007, **85(11)**:843-50.
20. Creek TL, *et al*: **Successful introduction of routine opt-out HIV testing in antenatal care in Botswana.** *Journal of acquired immune deficiency syndromes (1999)* 2007, **45(1)**:102-7.
21. Anand A, *et al*: **Site factors may be more important than participant factors in explaining HIV test acceptance in the prevention of mother-to-child HIV transmission programme in Kenya, 2005.** *Tropical medicine & international health: TM & IH* 2009, **14(10)**:1215-9.
22. Simpson WM, *et al*: **A randomised controlled trial of different approaches to universal antenatal HIV testing: uptake and acceptability and Annex: Antenatal HIV testing - assessment of a routine voluntary approach.** *Health technology assessment (Winchester, England)* 1999, **3(4)**:1-112.
23. Wang FL, *et al*: **Potential factors that may affect acceptance of routine prenatal HIV testing.** *Canadian journal of public health* Revue canadienne de santé publique 2005, **96(1)**:60-4.
24. Fabiani M, *et al*: **Using prevalence data from the programme for the prevention of mother-to-child-transmission for HIV-1 surveillance in North Uganda.** *AIDS (London, England)* 2005, **19(8)**:823-7.
25. Mpairwe H, *et al*: **HIV risk perception and prevalence in a program for prevention of mother-to-child HIV transmission: comparison of women who accept voluntary counseling and testing and those tested anonymously.** *Journal of acquired immune deficiency syndromes (1999)* 2005, **39(3)**:354-8.
26. Bolu O, *et al*: **Utility of antenatal HIV surveillance data to evaluate prevention of mother-to-child HIV transmission programs in resource-limited settings.** *American journal of obstetrics and gynecology* 2007, **197(3)**: S17-25.
27. Cohen J: *17th Conference on Retroviruses and Opportunistic Infections, 16-19 February, San Francisco, CA. Treatment as prevention. Science (New York, N.Y.)* 2010, **327(5970)**:1196-7.
28. HAPCO: *Annual HIV/AIDS Monitoring and Evaluation Report, HAPCO, Editor* MOH: Addis Ababa 2008.
29. Manzi M, *et al*: **High acceptability of voluntary counselling and HIV-testing but unacceptable loss to follow up in a prevention of mother-to-child HIV transmission programme in rural Malawi: scaling-up requires a different way of acting.** *Tropical medicine & international health: TM & IH* 2005, **10(12)**:1242-50.
30. WHO: *New WHO recommendations: Preventing mother-to-child transmission* WHO: Geneva 2009.
31. Kasenga F, Hurtig AK, Emmelin M: **Home deliveries: implications for adherence to nevirapine in a PMTCT programme in rural Malawi.** *AIDS care* 2007, **19(5)**:646-52.
32. Kwasi Torpey MK, Kasonde Prisca, Dirks Rebecca, Bweupe Maxmillian, Thompson Catherine, Mukadi Diul: **Increasing uptake of prevention of mother-to-child transmission of HIV services in a resource-limited setting.** *BMC Health Services Research* 2010, **10(29)**.
33. Moses A, *et al*: **Prevention of mother-to-child transmission: program changes and the effect on uptake of the HIVNET 012 regimen in Malawi.** *AIDS (London, England)* 2008, **22(1)**:83-7.
34. Noel F, *et al*: **Improving outcomes in infants of HIV-infected women in a developing country setting.** *PloS one* 2008, **3(11)**:e3723.
35. Ahoua L, *et al*: **Evaluation of a 5-year programme to prevent mother-to-child transmission of HIV infection in Northern Uganda.** *Journal of tropical pediatrics* 2010, **56(1)**:43-52.
36. Moses SE, *et al*: **HIV-1 seroconversion during pregnancy resulting in vertical transmission.** *Journal of clinical virology: the official publication of the Pan American Society for Clinical Virology* 2008, **41(2)**:152-3.
37. Moodley D, *et al*: **High HIV incidence during pregnancy: compelling reason for repeat HIV testing.** *AIDS (London, England)* 2009, **23(10)**:1255-9.

Pre-publication history
The pre-publication history for this paper can be accessed here:
http://www.biomedcentral.com/1472-6963/10/267/prepub

doi:10.1186/1472-6963-10-267
Cite this article as: Mirkuzie *et al.*: Promising outcomes of a national programme for the prevention of mother-to-child HIV transmission in Addis Ababa: a retrospective study. *BMC Health Services Research* 2010 **10**:267.

II

Mirkuzie et al. BMC Health Services Research 2011, 11:196
http://www.biomedcentral.com/1472-6963/11/196

BMC Health Services Research

RESEARCH ARTICLE Open Access

Applying the theory of planned behaviour to explain HIV testing in antenatal settings in Addis Ababa - a cohort study

Alemnesh H Mirkuzie[1,2*], Mitike M Sisay[3], Karen Marie Moland[4] and Anne N Åstrøm[5]

Abstract

Background: To facilitate access to the prevention of mother-to-child HIV transmission (PMTCT) services, HIV counselling and testing are offered routinely in antenatal care settings. Focusing a cohort of pregnant women attending public and private antenatal care facilities, this study applied an extended version of the Theory of Planned Behaviour (TPB) to explain intended- and actual HIV testing.

Methods: A sequential exploratory mixed methods study was conducted in Addis Ababa in 2009. The study involved first time antenatal attendees from public- and private health care facilities. Three Focus Group Discussions were conducted to inform the TPB questionnaire. A total of 3033 women completed the baseline TPB interviews, including attitudes, subjective norms, perceived behavioural control and intention with respect to HIV testing, whereas 2928 completed actual HIV testing at follow up. Data were analysed using descriptive statistics, Chi-square tests, Fisher's Exact tests, Internal consistency reliability, Pearson's correlation, Linear regression, Logistic regression and using Epidemiological indices. P-values < 0.05 was considered significant and 95% Confidence Interval (CI) was used for the odds ratio.

Results: The TPB explained 9.2% and 16.4% of the variance in intention among public- and private health facility attendees. Intention and perceived barriers explained 2.4% and external variables explained 7% of the total variance in HIV testing. Positive and negative predictive values of intention were 96% and 6% respectively. Across both groups, subjective norm explained a substantial amount of variance in intention, followed by attitudes. Women intended to test for HIV if they perceived social support and anticipated positive consequences following test performance. Type of counselling did not modify the link between intended and actual HIV testing.

Conclusion: The TPB explained substantial amount of variance in intention to test but was less sufficient in explaining actual HIV testing. This low explanatory power of TPB was mainly due to the large proportion of low intenders that ended up being tested contrary to their intention before entering the antenatal clinic. PMTCT programs should strengthen women's intention through social approval and information that testing will provide positive consequences for them. However, women's rights to opt-out should be emphasized in any attempt to improve the PMTCT programs.

Background

Behavioural change interventions such as sexual risk reduction and persistent condom use remain critical HIV prevention strategies, when finding a cure or vaccine against the virus is challenging [1,2]. Being part of the HIV/AIDS prevention strategy, the prevention of mother- to-child HIV transmission (PMTCT) programme aims to curb vertical transmission of HIV from mothers to their infants. Arrays of interventions that are recommended for PMTCT include HIV counselling and testing, antiretroviral (ARV) prophylaxis, safe obstetric practices and safe infant feeding counselling [3]. The HIV counselling and testing intends to screen HIV positive pregnant women for subsequent PMTCT interventions. Until 2004 HIV testing was offered solely in an

* Correspondence: alemmirkuzie@yahoo.com
[1]Centre for International Health, Faculty of Medicine and Dentistry, University of Bergen, Overlege Danielsens Hus, Årstav. 21, Postbox 7804, Bergen 5020, Norway
Full list of author information is available at the end of the article

opt-in approach in resource poor settings. In this approach the testing is initiated by the client and assumed to be voluntary. However, due to some social and structural barriers, acceptability and rate of HIV testing continued to be suboptimal [4,5]. This prompted the WHO to call for a shift in HIV testing approach [6]. Subsequently, routine opt-out HIV testing has become the standard of care for all pregnant women.

Following the implementation of routine opt-out approach a significant improvement in acceptability has been reported with rates of testing ranging from 55% to 100% [4,7-9]. There is however some evidence that the pre-test counselling and the right to opt-out are being compromised. Studies from Kenya and Uganda showed that the information about the possibility to opt-out was not well communicated during the group pre-test counselling [10,11]. Many researchers also argue that most pregnant women in resource poor settings are less empowered and are thus less likely to resist the pressure to comply with the advice given by health professionals in antenatal settings [11-13]. Some women may also get tested against their intention not to do so, believing that testing is a necessary condition to access subsequent care [12,14]. Several researches concerning routine opt-out testing are primarily focused on the tension between increasing the rate of testing and the potential violation of ethical principles [10,11,13,15-17]. Yet, few studies have considered this issue using cognitive-behavioural approach.

According to Jessor (1997), the factors influencing any behaviour, including HIV related behaviour might be ordered along a dimension of conceptual proximity to immediate experience with the particular behaviour [18]. Distal influencing factors including cultural and socio-demographics are largely operating through or are mediated by cognitive processes (proximal determinant) [19]. Taking this point of departure, the more one knows about the cognitive influencing factors of a particular behaviour, the easier it will be to change that behaviour. Being a theory of the proximal cognitive determinants of behaviour, the TPB constitutes a promising theoretical framework for explaining and predicting social behaviours [1] (Figure 1). The theory also seems to constitute a practical tool for the analysis of HIV testing behaviour in antenatal settings and for the identification of barriers and facilitators to change of behaviour.

The TPB includes perceived behavioural control (PBC) on a level with attitude and subjective norm as predictors of behavioural intention, implying that the three predictors influence subsequent behaviour indirectly through behavioural intention (Figure 1). In turn, intention is the key proximal predictor of behaviour. According to the TPB, behavioural intention is a function of attitude, reflecting a favourable or unfavourable evaluation of the particular behaviour and subjective norm. The subjective norm here is referring the perceived social pressure to perform the behaviour. Perceived behavioural control reflects the ease or difficulty associated with performance. Attitudes, subjective norms and perceived behavioural control are underpinned by behavioural, normative and control beliefs, respectively.

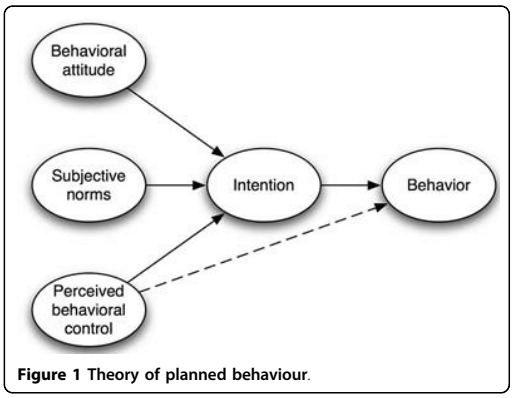


Figure 1 Theory of planned behaviour.

A considerable body of research has confirmed the power of the TPB to predict intentions and behaviours across a range of health behaviours [20]. In a meta-analysis, Armitage and Conner (2001) reported that attitude, subjective norms and PBC accounted for 39% of the variance in intention across 154 applications, whereas intention and PBC accounted for 27% of the variance in behaviours across 63 applications [21]. Nevertheless, some studies have reported the explanatory power of the TPB to be as low as 13% [21] and 7% [22]. Previously, the TPB has been used in sub Saharan African settings to predict HIV preventive behaviours [23-27], mostly in small scaled studies of cross-sectional design. However, the strength of the intention-behaviour relationship in the domain of routine HIV testing using objectively assessed behaviours in prospective studies still remains to be demonstrated.

Empirical works have shown that variables outside the TPB can capture a substantial proportions of variance in explaining intention and behaviour [1,28]. Of these variables past behaviour and descriptive norms had residual effects on intention and behaviour after the TPB variables have been taken into account [26-29]. Descriptive norm here is referring to women's perceptions of what other antenatal attendees (friends, sisters, neighbours...) do with respect to HIV testing. Focusing a cohort of pregnant women attending public and private antenatal care facilities for the first time in their current pregnancy, this study set out to explain intended and actual HIV testing using the extended version of the TPB

framework. According to the TPB, attitudes, subjective norms and perceived behavioural control would predict intended HIV testing, whereas intention and perceived behavioural control would predict actual HIV testing. It was proposed further that the external variables in terms of socio-demographics, descriptive norm, PMTCT knowledge and previous HIV testing experience would add to the explanation of intended- and actual HIV testing beyond the TPB variables. Finally, this study examined whether type of pre-test counselling would modify the strength of the intention behaviour relationship.

Methods

Study settings

The present study was conducted in Addis Ababa, the capital of Ethiopia. The city is administratively divided into 10 sub-cities. The HIV prevalence among adults (15-24 years) in the city is estimated to be 8.8% were the majority of the infections occur through hetro-sexual contact [30]. In total 54 health facilities were providing PMTCT services, where 25 were public health centres. The health services were fairly accessible with a median distance to the nearest referral centre being less than 5 km [31]. About 90% of the pregnant women in the city had antenatal visit at least once and about 90% of these attended public health facilities [30,32]. In 2009 alone 54 698 women attended PMTCT programmes across the city, about 79% received HIV counselling and testing and 4.6% were HIV positive [33].

The first national PMTCT guidelines were developed in 2001 and incorporated an opt-in HIV counselling and testing approach [34]. Two years following the development of the guidelines, PMTCT programmes were launched in selected public health facilities across the country. In 2007, when the PMTCT guidelines were revised, the HIV testing approach shifted from opt-in to routine opt-out [35]. From early 2008, the routine opt-out HIV testing has become the standard of practice in public health facilities [9]. In these facilities, pregnant women were offered HIV testing routinely following an individual or group pre-test counselling free of charge. The PMTCT counsellors attending these women did the HIV testing in the antenatal clinics and the test result often made available in 30 minutes. In private health facilities by contrast, opt-in HIV testing remained the standard of practice since the launching of the PMTCT programmes in 2007. In these facilities, pregnant women received antenatal care by a medical doctor, and were then referred to another room for HIV testing. Pregnant women were paying service charges when they attended private health facilities.

Study design and participants

A sequential exploratory mixed methods study was conducted in January-February, 2009. In this study the qualitative Focus Group Discussions (FGDs) were followed by a prospective cohort study. In a mixed methods design, one of the study designs could have a primary role while the other design has a supportive role [36]. In this study, the cohort was the main design supported by the FGDs. Data were collected in three phases. In the first phase, three FGDs were conducted by the principal investigator in three different health care facilities among first time antenatal attendees. Twenty seven women were selected purposefully for the FGDs. Prior to each FGD all women were explained about the study aim and consents were inquired. During the discussions women were first asked about their demographic and obstetric information then the discussion about HIV testing followed. The questions were "what factors or circumstances would enable you/make it difficult for you to test for HIV upon first time antenatal attendance?", and " are there any other issues that come to mind when you think of HIV testing upon first time antenatal attendance?". The participants identified three potential barriers to HIV testing including "scared to test", "concerns about confidentiality" and "fear of disclosing HIV positive results". The participants were also probed as to whether "fear of stigma and/or discrimination", "fear of being chased from home in the case of positive test result" and "fear that they would be denied of proper care" would affect their decision to test. Of the probed questions only "fear of discrimination" was mentioned as a potential barrier to HIV testing. All the potential barriers identified by the participants were included in the questionnaire and used to measure the concept of perceived behavioural control. None of the FGD participants were included in the subsequent questionnaire interviews.

In the second and the third phase, data were collected from women attending antenatal care in 12 public health centres and three private hospitals. A four-to-one public to private ratio was used in selecting health facilities, considering the fact that over 80% of the pregnant women in the city received care from public health facilities. Then individual health facilities were selected on the bases of high client flow and to have representation of all the 10 sub-cities. The inclusion criteria were attending antenatal care for the first time in the current pregnancy, attending selected health facilities, attending during the study period and consenting to be followed up. Known HIV positive women were excluded as they were not eligible for further testing. The study covered 44.3% of the eligible women attending antenatal care across the city. The cohort used a fixed follow up period.

In the second phase of data collection, a survey was conducted using a pre-tested structured TPB questionnaire to measure the concepts of attitudes, subjective

norms, descriptive norms and behavioural intention. The questionnaire was first translated into Amharic (the official language fluently spoken by all participants) then back translated to English for validation. Two days training was given to 17 field assistants (college students) who participated in pre-testing of the questionnaire under close supervision of the principal investigator. The questionnaire was administered in a face-to-face interview in the maternity waiting area before the women received pre-test counselling. The interviews were conducted in private while the women waited for their turn for antenatal check up one after the other in a quite corner of the waiting areas. For ethical reasons we used the women's antenatal number as a unique identifier in the questionnaire. Completed questionnaires were then handed to PMTCT counsellors providing antenatal care and/or PMTCT services at the end of each day. Among the 3082 women approached, 1.5% (49) refused to participate while 3033 had completed the questionnaire interviews. Intention to test for HIV was the intermediate outcome in the second phase.

In the third phase, the follow up data were collected by the PMTCT counsellors from PMTCT log books. The PMTCT counsellors were routinely conducting the HIV testing and registering whether the woman received pre-test counselling (group or individual), testing, post-test counselling and the HIV test result in the log books. These questions were also included in the questionnaire. The registration was done anonymously using the women antenatal number as a unique identifier. To be consistent, these unique identifiers were used in the questionnaires. Thirty three PMTCT counsellors were trained for two hours on how to collaborate with the field assistants and on how to match each questionnaire with the information obtained from the PMTCT log-books using the unique identifiers and to report inconsistencies. Two hours training were found adequate as they were the ones who did register HIV counselling and testing information routinely in logbooks. Furthermore, the principal investigator supervised them when they obtained follow up information for the first time. Inconsistencies were validated by crosschecking with the woman's antenatal folder. The study team were checking and collecting the questionnaires every day. Of the 3033 women who completed the TPB interview in the second phase, 2928 were assessed objectively whether they actually tested for HIV or not during the follow up (Figure 2). The final outcome measured in this third phase was actual HIV testing.

The study was reviewed and approved by the Ethical committee of Addis Ababa City Administration Health Bureau in Ethiopia and the Regional Committee for Medical Research Ethics in Western Norway. Study permits from Addis Ababa City Administration Health Bureau and respective sub cities were obtained. Informed verbal consent was inquired before each interview.

Study variables

The second phase structured interview covered demographic- and obstetric information, PMTCT knowledge, TPB variables and questions related to previous HIV testing. The TPB variables were assessed in relation to testing for HIV upon first time antenatal care attendance. A five point response scale was used (1) 'very likely' to (5) 'very unlikely', (1) 'very certain' to (5) 'very uncertain' and from (1) 'strongly agree' to (5) 'strongly disagree'. A sum score was constructed by adding the items corresponding to each variable. The higher the score the more positive the attitude, the stronger the intention, the stronger the subjective norm and the more barriers perceived with respect to HIV testing. Intention to test for HIV was assessed using three items; 'I intend/I plan/I want to test for HIV upon first antenatal attendance'. A sum score was constructed by adding the three items. For use in logistic regression model later, intention was dichotomized. Women who scored greater than or equal to the mean score were considered to have high intention; otherwise they were regarded to have low intention. Attitude towards HIV testing was assessed using three items; 'For me, testing for HIV upon my first antenatal attendance is beneficial/right thing to do/bad'. A sum score was constructed by adding the three items. Subjective norm was assessed using four items; 'People who are important to me think that I should test for HIV upon my first antenatal attendance, 'People who are important to me would appreciate that I tested for HIV...', 'My husband agreed that I should test for HIV ...' and 'People who are important to me encouraged me to test for HIV ...'. A sum score was constructed by adding the four items. Descriptive norm was assessed using one item. 'Women who I know and who are important to me would themselves test for HIV upon their first antenatal attendance'. Perceived barrier was assessed using four items; 'For me to test for HIV upon first antenatal attendance is difficult because I feel scared to know the result/I do not want to disclose my HIV status/I suspected that test result will not be kept confidential/People may discriminate me if I found HIV positive'. A sum score was constructed by adding the four items. For use in a logistic regression model later, perceived barrier was dichotomized. Women who scored greater than or equal to the mean score were considered to have perceived barriers to test for HIV; otherwise they were considered to have no perceived barriers.

Previous HIV testing experience was assessed using two questions, i.e 'How many times have you been

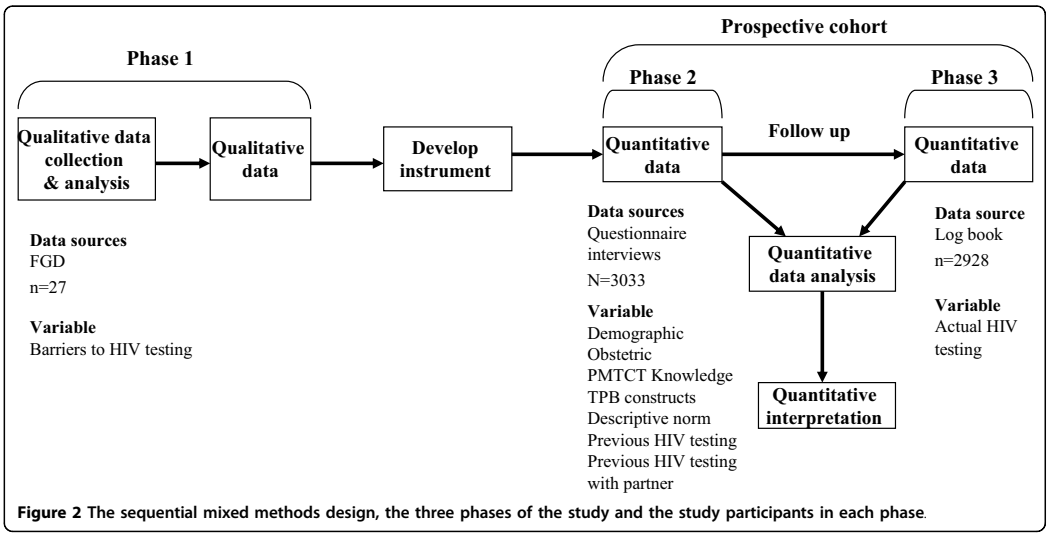


Figure 2 The sequential mixed methods design, the three phases of the study and the study participants in each phase.

tested for HIV?' and 'How many times have you been tested for HIV with your partner' with a response range from 0 to more than 3 times. The correlation between the two measures was less than 0.7. Then we decided not to combine them into a single score but retain them as separate measures. For use in logistic regression model later, previous HIV testing experience was dichotomized. Women who had HIV testing experience/ with partner were grouped as "Yes"; otherwise they were regarded as "No". PMTCT knowledge was assessed using five questions, 'Have you ever heard about mother-to-child HIV transmission?', 'Can an HIV infected mother infect her baby with HIV during pregnancy/delivery/breast feeding?' 'Yes, No and Unsure/I don't know'. Women who said yes were categorized as knowledgeable otherwise not knowledgeable. The fifth question was about the prevention of MTCT; 'What measures do you know for the prevention of mother-to-child HIV transmission?'. A list of prevention interventions was presented with a possibility to choose more than one. Accordingly women who chose more than one interventions were considered knowledgeable; otherwise not knowledgeable. A sum score was constructed from the five items (range 5 to 10). The higher the score the more knowledgeable the woman is.

The third phase actual HIV testing was assessed objectively through information obtained from the PMTCT log books, "What kind of pre-test counselling offered to the woman (individual or group)?", "Did the woman receive HIV testing?", " What was the HIV test result?" and "Did the woman receive post-test counselling?".

Statistical analyses

The quantitative data was double entered in excel spreadsheet and checked for inconsistencies by creating a check file. Then the data was transferred to SPSS version 17 for analysis. Descriptive statistics, Pearson Chi Square tests, were used to describe and to explore baseline differences in socio-demographic, obstetric and other characteristics between women attending public- and private health facilities. Fisher's Exact Tests were used to check baseline differences in demographic, obstetric and other characteristics between women who completed their follow up and those who did not. Internal consistency reliability was conducted using Chronbach's alpha. Pearson's correlation was used to examine bivariate linear relationship between intention and the TPB variables, PMTCT knowledge, descriptive norms and previous HIV testing experiences. Multiple linear regression analysis was applied to explain intention from TPB and external variables to calculate R^2 and β values, separately for women attending private- and public health care facilities and separately for each health centre and hospital. Forward conditional logistic regression analysis was applied to explain actual HIV testing, to examine the relative contribution of the TPB and external variables and to assess the fit of the model in terms of Nagelkerke R^2 and to control for potential confounding effect. Despite using a cohort design, Odds Ratio (OR) was used as an effect measure taking into consideration the fixed follow up time, little losses to follow up and the low prevalence of not tasting for HIV in antenatal settings. "In cohort studies on acute disease without induction period and a short time of follow up, like outbreaks, the risk of disease can be estimated

directly using the cumulative incidence given a fixed cohort with fixed period of follow up and a low fraction of drop-outs" [37]. Moreover, under rare disease assumption, the OR may be an acceptable approximation of the risk ratio [38-40]. To examine possible moderation effect of type of pre-test counselling upon the intention-behaviour relationship, a two way interaction term between intention and type of pre-test counselling was added to the regression model and tested for statistical significance. Sensitivity, specificity and predictive values were calculated to examine the nature of intention-behaviour relationship. P-values < 0.05 was considered significant and for the odds ratio, 95% confidence interval (CI) was used.

Results

Sample profile

Among the 3082 first time antenatal attendees approached, 49 (3.5%) refused to participate in the study, where most of them claimed that they had no time. A total of 3033 women completed questionnaire interviews in the second phase of the data collection. Of these 2928 (96.5%) women completed their follow up to HIV testing in the third phase. Hundred and five women did not complete their follow up, 98 were not given pre-test counselling and 7 did not have complete information regarding pre-test counselling.

Table 1 depicts the characteristics of the participants according to type of health care facility attended. Women attending public facilities were younger than women attending private facilities. The majority of the women (38.7%) attending public health care facilities had education less than 5^{th} grade, whereas 95.7% women attending private health care facilities had education above 9 grade. A total of 73.8% of the women investigated received group pre-test information. The majority (77.1%) of the women attending public health care facilities received group pre-test information, whereas 80.6% of the women attending private health care facilities received individual pre-test counselling.

There was no statistically significant difference between women who completed their follow up and those lost to follow up with respect to age, education, knowledge of PMTCT, previous HIV testing experience and previous HIV testing experience with partner (p > 0.05) (not shown in table).

The TPB variables

Cronbach's alpha for the TPB constructs ranged from 0.75 for attitude and subjective norm to 0.92 for

Table 1 Frequency distribution of women's soci-demographic and obstetric characteristics, PMTCT knowledge and HIV testing experience by public- and private health care facilities

Variable	*Whole sample N = 3033 n (%)*	*Public facilities n = 2751 n (%)*	*Private facilities n = 282 n (%)*	*P-Value*
Age in years				< 0.001
15-24	1444(48.4)	1378(50.9)	66(23.8)	
> 25	1541(51.6)	1330(49.1)	211(76.2)	
Education/grades completed				< 0.001
0 - 4	1061(35.1)	1060(38.7)	1(0.4)	
5 - 8	857(28.4)	846(30.9)	11(3.9)	
> 9	1103(36.5)	834(30.4)	269(95.7)	
Number of pregnancies				< 0.01
1	1524(50.3)	1357(49.3)	167(59.2)	
> 2	1508(49.7)	1393(50.7)	115(40.8)	
PMTCT knowledge				< 0.001
Knowledgeable	2240(76.5)	1987(75.0)	253(91.0)	
Not knowledgeable	687(23.5)	662(25.0)	25(9.0)	
Previous HIV testing experience				< 0.001
Yes	2450(81.0)	2185(79.7)	265(94.0)	
No	575(19.0)	558(20.3)	17(6.0)	
Previous HIV testing experience with partner				< 0.001
Yes	1673(57.2)	1465(55.3)	208(75.6)	
No	1250(42.8)	1183(44.7)	67(24.4)	
Type of pre-test counselling				< 0.001
Group pre-test information	2130(73.8)	2098(77.1)	32(19.4)	
Individual counselling	757(26.2)	624(22.9)	133(80.6)	

intention (Table 2). In general, the women attending both private- and public health care facilities had high intention, favourable attitude, perceived strong normative pressure, and perceived less barriers to undertake HIV testing. There were statistically significant differences between women attending public- and private health care facilities across all theoretical constructs considered ($p < 0.01$), except for descriptive norms. Thus, women attending public health care facilities reported slightly stronger intention, more favourable attitude and stronger perceived normative pressure to undergo HIV testing, compared to their counterparts attending private health care facilities (Table 2).

Explaining intention to test for HIV

The bivariate relationships between intention and the TPB variables, descriptive norm, PMTCT knowledge, previous HIV testing were examined using Pearson's product-moment correlation coefficient, separately for public- and private health care facility attendees (Table 3). Intention was significantly and positively associated with attitude, subjective norm, descriptive norm, PMTCT knowledge, previous HIV testing experience and previous HIV testing experience with partner among public health care facility attendees (the correlation above the diagonal in Table 3). Similarly, intention was significantly and positively associated with attitude, subjective norm and descriptive norm among women attending private health care facility (the correlation below the diagonal in Table 3). By contrast, intention was negatively associated with perceived barrier both in public and private facility attendees, yet the association was not significant among private facility attendees.

All variables that were statistically significantly associated in the bivariate analysis (Table 3) were entered into the multiple linear hierarchical regression models. Among women attending public health care facilities, previous HIV testing experience, previous HIV testing experience with partner and PMTCT knowledge entered in the first step accounted for 2.3% of the variance in intention to test for HIV [$\Delta R^2 = 0.023$, F change = 18.90 (3, 2443), $p < 0.001$]. Previous HIV testing experience ($\beta = 0.056$, $p < 0.05$) and PMTCT knowledge ($\beta = 0.125$, $p < 0.001$) were significantly associated with intention. Entering the TPB variables and descriptive norms in the second step, increased the explained variance with 9.2% [($\Delta R^2 = 0.092$, F change = 63.36 (4, 2439), $p < 0,001$)]. In the final second step, subjective norm ($\beta = 0.20$, $p < 0.001$) had the strongest impact followed in descending order by attitude ($\beta = 0.14$, $p < 0.001$), PMTCT knowledge ($\beta = 0.093$, $p < 0.001$) and descriptive norm ($\beta = 0.08$, $p < 0.001$). Among women attending private health care facilities, PMTCT knowledge ($\beta = 0.08$, $p > 0.05$) entered in the first step accounted for 2.5% variance in intention [($\Delta R^2 = 0.025$, F change = 6.74 (1, 261), $p < 0.01$)]. Entering the TPB components and descriptive norms in the second step increased the explained variance with 16.4% [($\Delta R^2 = 0.164$, F change = 13.0 (4, 257), $p < 0,001$)]. In the final step, the impact of PMTCT knowledge did not remain statistically significant. Subjective norm ($\beta = 0.32$, $p < 0.001$) had the strongest impact followed by attitude ($\beta = 0.125$, $p < 0.05$) (Table 4).

Stratified analyses by PMTCT centre showed that, the explained variance in intended HIV testing from the TPB variables and descriptive norm ranged from 7.7% to 32.5%, whereby attitude, subjective norm and descriptive norm explained most of the variance in intention (not shown in table).

Explaining HIV testing behaviour

Of the 2928 women who completed their follow up in phase III, 128 (4.4) did not test for HIV. Table 5 depicts the adjusted odds ratios and 95% CI for actual HIV testing by intention, perceived barriers and the external variables. Socio-demographic and obstetric variables, PMTCT knowledge, previous HIV testing experience and type of pre-test counselling were entered in a first step. In the first step, the chi-square was significant ($\chi^2 = 40.36$ [8], $p < 0.001$) and explained 7% of the variance in actual HIV testing according to Nagelkerke R^2 (0.07, $p < 0.001$). Intention and perceived barrier were entered in the second step and increased the explained variance with 2.4%. The full model containing all variables was statistically significant and explained a total of 9.4% of the variance in HIV testing (Nagelkerke $R^2 = 0.094$, $p < 0.01$). In the final model, women who had over 8 grade of education were less likely to test for HIV compared

Table 2 Descriptive statistics for TPB variables and external variables by public and private health care facility

Construct	*Whole sample, N = 3033*				*Public, n = 2554*		*Private, n = 266*		*P-value*
	α	Items (Range)	Mean	SD	Mean	SD	Mean	SD	
Intention	0.92	3(3-15)	11.1	3.53	11.3	3.50	9.2	3.21	0.000
Attitude	0.75	3(3-15)	13.3	1.43	13.4	1.43	12.3	0.99	0.000
Subjective norm	0.75	4(4-20)	15.1	2.94	15.2	2.98	13.9	2.21	0.000
Descriptive norm		1(1-5)	3.3	1.10	3.3	1.12	3.3	0.88	0.538
Perceived barriers	0.71	4(4-20)	9.2	2.88	9.3	2.97	8.7	1.66	0.002

Table 3 Pearson's correlation between TPB variables and external variables in public and private health care facilities

Variable	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
1. Intention	1	0.20(**)	0.27(**)	0.19(**)	-0.11(**)	0.13(**)	0.11(**)	0.10(**)
2. Attitude	0.24(**)	1	0.19(**)	0.05(**)	-0.15(**)	0.16(**)	0.12(**)	0.07(**)
3. Subjective norm	0.41(**)	0.24(**)	1	0.45(**)	-0.14(**)	0.05(*)	0.09(**)	0.10(**)
4. Descriptive norm	0.26(**)	0.11	0.60(**)	1	-0.18(**)	0.05(**)	0.08(**)	0.09(**)
5. Perceived barrier	-0.01	-0.03	0.12(*)	0.02	1	0.03	-0.12(**)	-0.10(**)
6. PMTCT Knowledge	0.17(**)	0.04	0.20(**)	0.13(*)	-0.03	1	0.13(**)	0.08(**)
7. Previous HIV testing experience	0.08	0.04	-0.00	0.05	-0.23(**)	0.18(**)	1	0.56(**)
8. Previous HIV testing experience with partner	0.04	0.04	-0.01	-0.05	-0.17(**)	0.18(**)	0.52(**)	1

$^{**}p < 0.001$, $^{*}p < 0.05$ (2 tailed)

NB- The correlation above the diagonal is for public health care facility attendees and the one below the diagonal is for private health care facility attendees.

to women with lower level of education. Similarly women who received individual pre-test counselling were 1.85 times [95% CI (1.14, 3.03)] less likely to test for HIV compared to women who received group pre-test information. Moreover, women who had low intention to test for HIV were 2.4 times [95% CI (1.45, 3.85)] less likely to test for HIV compared to their high intending counterparts. To check whether type of pre-test counselling moderated the relationship between intention and actual HIV testing, an interaction term (intention*type of pre-test counselling) was entered in a third step, after controlling for all other variables in the model. This interaction term did not add significantly to the model (Nagelkerkes $R^2 = 0.098$, $P > 0.05$) (Table 5).

Based on cross tabulation of intention and behaviour, epidemiological indices were calculated to examine the nature of the intention -behaviour link. As shown in Table 6, sensitivity was 67% indicating that the majority of the women who tested for HIV had high intention to do so. The specificity of 46% indicated that even women who were not tested had high intention to test. The positive predictive value was 96% indicating that, high intention was a strong predictor of being tested for HIV. The negative predictive value was 6% indicating that, among the women who had low intention the majority of them were tested (Table 6).

Discussion

This study applied an extended version of the TPB framework to explain intended- and actual HIV testing among pregnant women upon their first time antenatal care attendance. The cognitive variables and previous HIV testing experience explained 11.5% and 19% of the variance in intentions to test for HIV among women attending public- and private health care facilities, respectively. As indicated by the significant effect of PMTCT knowledge upon behavioural intention, the TPB appeared less sufficient to account for intended HIV testing in public- than in private health care facility attendees. Nevertheless, most external variables did not maintain their statistical significance when the TPB components were considered, suggesting that the TPB provided a fairly accurate description of the intention formation process related to HIV testing in both groups considered. Compared to recent meta analytical reviews, suggesting a predictive power of 39% in behavioural intentions, the present results indicate a fit below the optimal level [21]. The explained variance in intention from the TPB variables was also lower than what has

Table 4 Intention to test for HIV regressed on previous HIV testing, PMTCT knowledge, TPB variables and descriptive norm

Step	Variable	*Public facility*			*Private facility*		
		β final Step (Sig)	R^2	R^2 Change	β final Step (Sig)	R^2	R^2 Change
Step I	Previous HIV testing experience	0.03(0.14)					
	Previous HIV testing experience with partner	0.14(0.53)					
	PMTCT Knowledge	0.09(0.00)			0.08(0.15)		
			0.023	0.023		0.025	0.025
Step II	Attitudes	0.14(0.00)			0.12(0.03)		
	Subjective norms	0.20(0.00)			0.32(0.00)		
	Descriptive norm	0.08(0.00)			0.07(0.34)		
	Perceived barriers	-0.04(0.07)					
			0.115	0.092		0.19	0.164

Table 5 Actual HIV testing regressed upon TPB and other variables. OR and 95% CI

Variable	*Tested for HIV*			
	No n(%)	**Yes n(%)**	***Step 1 Nagelkerke R^2 = 0.070 OR (95% CI) n = 2586***	***Step 2 Nagelkerke R^2 = 0.094 OR (95% CI) n = 2586***
Age				
15-24	53(3.7)	1366(96.3)	1	
> 25	72(4.9)	1389(95.1)	0.99 (0.58, 1.70)	
Education				
0 - 4	21(2.0)	1032(98.0)	1	1
5 - 8	17(2.0)	833(98.0)	1.08(0.47, 2.46)	1.06(0.46, 2.43)
> 9	87(8.6)	926(91.4)	0.28(0.15, 0.53)	0.29(0.15, 0.56)
PMTCT knowledge				
Knowledgeable	96(4.5)	2053(95.5)	1	
Not knowledgeable	30(4.5)	643(95.5)	0.66(0.38, 1.16)	
Number of pregnancies				
1	71(4.9)	1385(95.1)	1	
> 2	57(3.9)	1414(96.1)	0.94(0.56, 1.58)	
Previous HIV testing experience				
Yes	106(4.5)	2249(95.5)	1	
No	22(3.9)	543(96.1)	0.58(0.28, 1.20)	
Previous HIV testing experience with partner				
Yes	83(5.2)	1522(94.8)	1	
No	38(3.1)	1176(96.9)	1.38(0.75, 2.56)	
Type of pre-test counselling				
Individual counselling	36(4.8)	720(95.2)	1	1
Group pre-test information	46(2.2)	2078(97.8)	1.92(1.18,3.12)	1.85(1.14,3.03)
Intention				
Low	59(6.0)	925(94.0)		1
High	69(3.5)	1875(96.5)		2.38(1.45,3.85)
Perceived barrier				
Yes	27(3.6)	717(96.4)		1
No	101(4.7)	2052(95.3)		1.41(0.83,2.38)

been reported in previous studies from non-occidental settings focusing on voluntary HIV counselling and testing [25], condom use [26] and motivation to learn about HIV/AIDS [24]. Yet, the present figures compare more favourably to TPB studies in other behavioural domains [22,41].

The TPB suggests that changing intentions can be accomplished by influencing attitudes, subjective norms and perceived behavioural control. Thus, to design effective interventions, the relative importance of attitudes, subjective norms and perceived behavioural control in explaining intention becomes vital [1]. As judged from the standardized regression coefficients, this study indicates that the decision to test for HIV upon first time antenatal care attendance was primarily under the control of subjective norms and attitudes, whereas descriptive norms and perceived barriers were less important. This means that pregnant women decided to

Table 6 Levels of intentions and actual HIV testing with associated values of epidemiological indices

Intention	*HIV testing*					*Predictive value*	
	Yes	**No**	**Total**	***Sensitivity***	***Specificity***	**Positive**	**Negative**
High	1875	69	1944	67%	46%	96%	6%
Low	925	59	984				
Total	2800	128	2928				

test for HIV if they perceived a positive normative pressure and if they anticipated more positive than negative personal consequences following testing. In agreement with our finding, in a review that evaluated barriers to HIV testing, perceived benefit of taking an HIV test was an important HIV test promoting factor [42]. This appears to imply that educational messages to increase women's motivation should target attitudinal beliefs women hold about the consequences of HIV testing. Such messages could positively influence their attitudes towards HIV testing, either by changing the strength of beliefs or by introducing new beliefs. In addition messages based on normative pressure might be an effective way to convince pregnant women to test for HIV. In previous studies among Tanzanian school teachers and homeless people in the United States of America, intentions to seek voluntary HIV testing are strongly influenced by attitude and subjective norm [25,43]. In the Ethiopian context, attitude and subjective norms have also been identified to be the strongest predictors of intended condom use among youths [26] and strong predictors of university students' motivation to learn about HIV/AIDS [24]. Moreover, in a meta-analysis of screening attendance generally, subjective norm appeared to be a strong predictor of intentions in the prenatal context. This suggests that decisions made in this context does not only concern the pregnant women, but also husband, the unborn child and significant others [44]. Thus, interventions to improve uptake of PMTCT services should target the family as a whole rather than focusing only on the individual pregnant women. In this regard partner involvement in HIV testing might be an important strategy to be strengthened particularly to manage fear of disclosure, one of the salient barriers identified in the FGDs.

Actual HIV testing was significantly associated with intention; however this was not the case with perceived barriers (Table 5). The significant intention-behaviour link is in accordance with the proposition from the TPB [1]. Our finding is also consistent with findings from a review and meta-analysis on screening attendance that reported intentions to be the strongest predictor of participation in screening [1,44,45]. In general, the power of the TPB in explaining actual HIV testing was weak, accounting for only 2.4% of the total variance in HIV testing. Various factors could explain this weak association. First, it could be due to the low variability in the data, where 95.2% of the women being tested. Second, there could be some shared variances being lost due to measurement discordance [21], as the TPB variables were self reported whilst the HIV testing was assessed objectively. Third, it could be attributed to a more unstable measure of behavioural intention. Although the internal consistency reliability of intention was satisfactory, this is a measure of on the spot reliability. What is important is that intention might change across time since events crop up as the time between the assessment of intention and behaviour increases. In this study the time interval between measuring intention and actual HIV testing was short but pre-test counselling/information offered to participants probably contributed to a change in women's initial intention not to test. Finally, the cognitive determinants seem unable to take account of the full range of variables that could affect the behavioural outcome, including routines of the facilities and the asymmetric power relationship between PMTCT providers and the antenatal attendees.

As demonstrated by the epidemiological indices in Table 6, a possible reason for the intention behaviour gap was a large proportion of non-intenders who actually tested or the very low proportion of true negatives (only 6%). In a previous study of physical activity, false positives (inclined abstainers) were identified to be the most important cause of the gap between intended exercise and actual exercise behaviour [46]. It was also shown that women who attended individual pre-test counselling were 1.85 times less likely to test for HIV compared to women who attended group pre-test information (Table 5). Gruskin, et al., (2008) pointed out that insufficient pre-test information given to women in a routine opt-out approach is detrimental to ensuring informed consent as well as to coping with a positive HIV test. More studies from Sub-Saharan Africa revealed that the information given to pregnant women in the group pre-test sessions was inadequate and, mainly focused on getting the women tested without enabling them to opt out if they did not intend to test [10,11,13]. From a practical point of view, the present analysis suggests that in order to promote HIV testing at first time antenatal visiting, it will be important to motivate non-intenders but also to focus on women who have positive intentions but still do not test for HIV. In addition it is important to ensure that the fundamental principle of informed consent is not violated and that testing follows an informed choice.

To our knowledge this is the first study that applied the TPB to explain intention and actual HIV testing in antenatal care settings. One of the strengths of the study is the use of mixed methods where the qualitative FGDs had informed the quantitative questionnaire. Since all the interviews were conducted at health care facilities using a face-to-face interview, the possibility of social desirability bias cannot be excluded. There could be a possibility of inter-rater variability as we have used 17 field assistants. To minimize the inter-rater variability, field assistants having similar educational level were recruited and trained as a group for two days. In addition, all field assistants participated in pretesting of the

questionnaire under close supervision of the principal investigator. A further strength of the study was that, the actual HIV testing behaviour of the participants was obtained objectively from PMTCT log books.

Conclusions

This study has brought a new prospect to optimize the effectiveness of the routine opt-out HIV testing policy by focusing upon cognitive determinants of intended and actual HIV testing in antenatal settings. According to the findings, pregnant women's intention to test for HIV upon first time antenatal care attendance was based on their normative expectations and the likely consequences following testing, in that order. Thus, women intended to test for HIV if they perceived social support, but also if they anticipated positive consequences accruing from testing. The TPB variables were less sufficient in predicting actual HIV testing, mainly due to a high proportion of non- intenders who completed HIV testing. This suggests that in the routine opt-out testing, women's lack of intention to test may not matter for the end result. Tailored behaviour change communication might be a way forward to facilitate informed and voluntary HIV testing decisions. Attempts aimed at increasing women's motivation to test for HIV should strengthen their intention to do so through informed awareness accompanied with social approval and strengthened conviction that HIV testing will provide mostly positive consequences for them. Women's rights to opt-out from testing should be highlighted and sufficient pre-test information provided to strength PMTCT programs.

List of abbreviations

ARV: Antiretroviral; CI: Confidence Interval; CSA: Central Statistical Authority; GAMET: Global HIV/AIDS Monitoring and Evaluation Team; FGD: Focus Group Discussion; FHAPCO: Federal HIV/AIDS Prevention and Control Office; MOH: Ministry of Health; MTCT: Mother-to-Child HIV Transmission; OR: Odds Ratio; PBC: Perceived Behavioural Control; PMTCT: Prevention of Mother-to-Child HIV Transmission; TPB: Theory of Planned Behaviour; WHO: World Health Organization; UNAIDS: Joint United Nations Programmes on HIV/AIDS; UNDP: United Nations Development Programme.

Acknowledgements

This study was financially supported by the Centre for International Health, University of Bergen, Meltzer foundation and Statens Lånekasse, Norway. We thank the Addis Ababa City Administration Health Bureau and the health bureaus' in the respective sub-cities for facilitating the data collection. Both Addis Ababa City Administration Health Bureau and Intra Health deserve acknowledgement for providing their PMTCT reports for validation. We convey our thanks to Professor Jostein Rise for his comments upon an earlier version of this article. We are also very grateful to all women who participated in the study.

Author details

[1]Centre for International Health, Faculty of Medicine and Dentistry, University of Bergen, Overlege Danielsens Hus, Årstav. 21, Postbox 7804, Bergen 5020, Norway. [2]College of Medical and Health Sciences, Department of Nursing and Midwifry, Hawassa University, Awassa, p.o.box 1560, Ethiopia. [3]Behavioural Sciences Unit, School of Public Health, Collage of Health Sciences, Addis Ababa University, Black Lion Hospital, P.O.Box 9086 Addis Ababa, Ethiopia. [4]Department of Nursing, Bergen University College, Haukelandsbakken 45, Bergen 5009, Norway. [5]Department of Clinical Dentistry, Faculty of Medicine and Dentistry, University of Bergen, Årstav. 17, Bergen 5020, Norway.

Authors' contributions

AHM prepared the study proposal, collected and analyzed the data, interpreted the findings and wrote the manuscript. ANÅ was involved in developing the questionnaire, analyzing the data and revising the manuscript. MMS was involved in training the data collectors, preliminary data analysis and revising the manuscript. KMM was involved in developing the study proposal and revising the manuscript. All authors have read and approved the final manuscript.

Author information

Corresponding author information - AM is from Ethiopia, currently doing her PhD at the Centre for International Health, University of Bergen, Norway.

Competing interests

The authors declare that they have no competing interests.

Received: 15 April 2011 Accepted: 18 August 2011
Published: 18 August 2011

References

1. Ajzen I: **The Theory of Planned Behavior.** *Organizational Behavior and Human Decision Processes* 1991, **50**:179-211.
2. Fishbein M: **The role of theory in HIV prevention.** *AIDS Care* 2000, **12(3)**:273-8.
3. WHO: *Strategic approaches to the prevention of HIV infection in infants: report of a WHO meeting* Morges, Switzerland, 20-22 March 2002; 2003.
4. Bolu O, Allread V, Creek T, Stringer E, Forna F, Bulterys M, Shaffer N: **Approaches for scaling up human immunodeficiency virus testing and counseling in prevention of mother-to-child human immunodeficiency virus transmission settings in resource-limited countries.** *American Journal of Obstetrics and Gynecology* 2007, **197(3)**:S83-9.
5. Deblonde J, De Koker P, Hamers FF, Fontaine J, Luchters S, Temmerman M: **Barriers to HIV testing in Europe: a systematic review.** *European Journal of Public Health* 2010, **20(4)**:422-32.
6. UNAIDS/WHO: *UNAIDS/WHO Policy statement on HIV testing* WHO: Geneva; 2004.
7. Chandisarewa W, Stranix-Chibanda L, Chirapa E, Miller A, Simoyi M, Mahomva A, Maldonado Y, Shetty AK: **Routine offer of antenatal HIV testing ("opt-out" approach) to prevent mother-to-child transmission of HIV in urban Zimbabwe.** *Bulletin of the World Health Organization* 2007, **85(11)**:843-50.
8. Creek L, Ntumy R, Seipone K, Smith M, Mogodi M, Smit M, Legwaila K, Molokwane I, Tebele G, Mazhani L, Shaffer N, Kilmarx H: **Successful introduction of routine opt-out HIV testing in antenatal care in Botswana.** *Journal of AIDS* 2007, **45(1)**:102-7.
9. Mirkuzie A, Hinderaker SG, Mørkve O: **Promising outcomes of a national programme for the prevention of Mother-to-Child HIV transmission in Addis Ababa: a retrospective study.** *BMC Health Services Research* 2010, **10**:267.
10. Were B, Hasunira R: *Routine HIV testing and counselling and access to services for prevention of mother-to child transmission: Experiences of HIV-positive women in Kawempe division, Kampala district, Uganda* Kampala: HEPS-Uganda; 2010.
11. Ujiji OA, Rubenson B, Ilako F, Marrone G, Wamalwa D, Wangalwa G, Ekström AM: **Is 'Opt-Out HIV Testing' a real option among pregnant women in rural districts in Kenya?** *BMC Public Health* 2011, **11**:151.
12. Rennie S, Behets F: **Desperately seeking targets: the ethics of routine HIV testing in low-income countries.** *Bulletin of the World Health Organization* 2006, **84(1)**:52-7.
13. Njeru MK, Blystad A, Shayo EH, Nyamongo IK, Fylkesnes K: **Practicing provider-initiated HIV testing in high prevalence settings: consent concerns and missed preventive opportunities.** *BMC health services research* 2011, **11**:87.
14. Abdool Karim Q, Abdool Karim SS, Coovadia HM, Susser M: **Informed consent for HIV testing in a South African hospital: is it truly informed and truly voluntary?** *American Journal of Public Health* 1998, **88(4)**:637-40.

15. Bayer R, Fairchild AL: **Changing the paradigm for HIV testing–the end of exceptionalism.** *The New England journal of medicine* 2006, **355(7)**:647-9.
16. Perez F, Zvandaziva C, Engelsmann B, Dabis F: **Acceptability of routine HIV testing ("opt-out") in antenatal services in two rural districts of Zimbabwe.** *Journal of AIDS* 2006, **41(4)**:514-20.
17. Gruskin S, Ahmed S, Ferguson L: **Provider-initiated HIV testing and counseling in health facilities–what does this mean for the health and human rights of pregnant women?** *Developing World Bioethics* 2008, **8(1)**:23-32.
18. Jessor R, Jessor SL: *Problem behavior and psychosocial development: a longitudinal study of youth* Academic Press: New York; 1997.
19. Conner M, Norman P: **Predicting health behaviour: A social cognition approach.** In *Predicting Health behaviour.*. Second edition. Edited by: Conner M and Norman. London: Bell and Bain Ltd, Glasgow; 2005:.
20. Dolores A, Blair J, Mark Z: **The influence of attitude on behaviour.** In *The Handbook of Attitudes.* Edited by: Ajzen I. New Jersey, Lawrence Erlbaum Associate; 2005:.
21. Armitage J, Conner M: **Efficacy of the Theory of Planned Behaviour: a meta-analytic review.** *The British Journal of Social Psychology/the British Psychological Society* 2001, **40(Pt)**:471-99.
22. Jamison J, Myers LB: **Peer-group and price influence students drinking along with planned behaviour.** *Alcohol and Alcoholism* 2008, **43(4)**:492-7.
23. Astrøm A, Nasir E: **Predicting intention to treat HIV-infected patients among Tanzanian and Sudanese medical and dental students using the theory of planned behaviour–a cross sectional study.** *BMC health services research* 2009, **9**:213.
24. Gebreeyesus H, Boer H, Kuiper A: **Using the theory of planned behaviour to understand the motivation to learn about HIV/AIDS prevention among adolescents in Tigray, Ethiopia.** *AIDS Care* 2007, **19(7)**:895-900.
25. Kakoko C, Astrøm A, Lugoe L, Lie T: **Predicting intended use of voluntary HIV counselling and testing services among Tanzanian teachers using the theory of planned behaviour.** *Social Science & Medicine* 2006, **63(4)**:991-9.
26. Molla M, Astrøm A, Berhane Y: **Applicability of the theory of planned behavior to intended and self-reported condom use in a rural Ethiopian population.** *AIDS Care* 2007, **19(3)**:425-31.
27. Sutton S, McVey D, Glanz A: **A comparative test of the theory of reasoned action and the theory of planned behavior in the prediction of condom use intentions in a national sample of English young people.** *Health Psychology* 1999, **18(1)**:72-81.
28. Sheeran P: **Intention–Behavior Relations: A Conceptual and Empirical Review.** *European Review of Social Psychology* 2002, **12(1)**.
29. Conner M, Armitage C: **Extending the Theory of Planned Behavior: A Review and Avenues for Further Research.** *Journal of Applied Social Psychology* 1998, **28(15)**:1429-1464.
30. MOH: *Health and health related indicators 2008/2009* Addis Ababa; Ministry of Health; 2010.
31. CSA: *Ethiopia Demographic and Health Survey 2005* Addis Ababa: Central Statistical Authority, CSA; 2006.
32. MOH: *Health and Health related indicators* Addis Ababa: Ministry of Health; 2008.
33. FHAPCO: *Annual Performance Report of Multisectoral HIV/AIDS Response 2002 E.C. (2009/2010)* Addis Ababa: Federal HIV Prevention and Control Office; 2010.
34. HAPCO/GAMET: *HIV/AIDS in Ethiopia - An Epidemiological Synthesis* Washington DC: HAPCO/GAMET; 2008.
35. HAPCO/MOH: *Guidelines for Prevention of Mother-to-Child Transmission of HIV In Ethiopia* Addis Ababa: HAPCO/MOH; 2007.
36. Creswell J, Clark V: *Designing and conducting mixed method research* London: Sage; 2007.
37. Anthony BM, David CG Jr, Karin B, Pascal W: **Cohort Studies.** In *Handbook of Epidemiology.* Edited by: Wolfgang A. Berlin: Springer; 2007:.
38. Schmidt CO, Kohlmann T: **When to use the odds ratio or the relative risk?** *International journal of public health* 2008, **53(3)**:165-7.
39. Rothman KJ: **Cohort studies.** *Modern Epidemiology* Philadelphia: Lippincott-Raven; 1998.
40. Greenland S: **Interpretation and choice of effect measures in epidemiologic analyses.** *American journal of epidemiology* 1987, **125(5)**:761-8.
41. Astrøm A, Kiwanuka S: **Examining intention to control preschool children's sugar snacking: a study of carers in Uganda.** *International Journal of Paediatric dentistry/the British Paedodontic Society [and] the International Association of Dentistry for Children* 2006, **16(1)**:10-8.
42. de Wit JB, Adam PC: **To test or not to test: psychosocial barriers to HIV testing in high-income countries.** *HIV medicine* 2008, **9**:20-2.
43. Fogg C, Mawn B: **HIV Screening: Beliefs and Intentions of the Homeless.** *Journal of the Association of Nurses in AIDS Care* 2010, **21(5)**:395-407.
44. Richard C, David F: **How well do the theory of reasoned action and theory of planned behaviour predict intentions and attendance at screening programmes? A meta-analysis.** *Psychology & Health* 2008, **23(7)**:745-765.
45. Griva F, Anagnostopoulos F, Madoglou S: **Mammography screening and the theory of planned behavior: suggestions toward an extended model of prediction.** *Women & Health* 2009, **49(8)**:662-81.
46. Godin G, Conner M: **Intention-behavior relationship based on epidemiologic indices: an application to physical activity.** *American Journal of Health Promotion* 2008, **22(3)**:180-2.

Pre-publication history
The pre-publication history for this paper can be accessed here:
http://www.biomedcentral.com/1472-6963/11/196/prepub

doi:10.1186/1472-6963-11-196
Cite this article as: Mirkuzie *et al.*: Applying the theory of planned behaviour to explain HIV testing in antenatal settings in Addis Ababa - a cohort study. *BMC Health Services Research* 2011 **11**:196.

III

JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH Open Access

Current status of medication adherence and infant follow up in the prevention of mother to child HIV transmission programme in Addis Ababa: a cohort study

Alemnesh H Mirkuzie[1,2*], Sven Gudmund Hinderaker[1], Mitike Molla Sisay[3], Karen Marie Moland[4] and Odd Mørkve[1]

Abstract

Background: Prevention of mother to child HIV transmission (PMTCT) programmes have great potential to achieve virtual elimination of perinatal HIV transmission provided that PMTCT recommendations are properly followed. This study assessed mothers and infants adherence to medication regimen for PMTCT and the proportions of exposed infants who were followed up in the PMTCT programme.

Methods: A prospective cohort study was conducted among 282 HIV-positive mothers attending 15 health facilities in Addis Ababa, Ethiopia. Descriptive statistics, bivariate and mulitivariate logistic regression analyses were done.

Results: Of 282 mothers enrolled in the cohort, 232 (82%, 95% CI 77-86%) initiated medication during pregnancy, 154 (64%) initiated combined zidovudine (ZDV) prophylaxis regimen while 78 (33%) were initiated lifelong antiretroviral treatment (ART). In total, 171 (60%, 95% CI 55-66%) mothers ingested medication during labour. Of the 221 live born infants (including two sets of twins), 191 (87%, 95% CI 81-90%) ingested ZDV and single-dose nevirapine (sdNVP) at birth. Of the 219 live births (twin births were counted once), 148 (68%, 95% CI 61-73%) mother-infant pairs ingested their medication at birth. Medication ingested by mother-infant pairs at birth was significantly and independently associated with place of delivery. Mother-infant pairs attended in health facilities at birth were more likely (OR 6.7 95% CI 2.90-21.65) to ingest their medication than those who were attended at home. Overall, 189 (86%, 95% CI 80-90%) infants were brought for first pentavalent vaccine and 115 (52%, 95% CI 45-58%) for early infant diagnosis at six-weeks postpartum. Among the infants brought for early diagnosis, 71 (32%, 95% CI 26-39%) had documented HIV test results and six (8.4%) were HIV positive.

Conclusions: We found a progressive decline in medication adherence across the perinatal period. There is a big gap between mediation initiated during pregnancy and actually ingested by the mother-infant pairs at birth. Follow up for HIV-exposed infants seem not to be organized and is inconsistent. In order to maximize effectiveness of the PMTCT programme, the rate of institutional delivery should be increased, the quality of obstetric services should be improved and missed opportunities to exposed infant follow up should be minimized.

* Correspondence: ami048@cih.uib.no
[1]Centre for International Health, University of Bergen, OverlegeDanielssens Hus, Årstav. 21, Bergen 5020, Norway
Full list of author information is available at the end of the article

Background

In 2010, the United Nations reported a declining global incidence of HIV among children under the age of 15 years [1]. Most of the decline happened in sub-Saharan Africa where the epidemic is most severe. Among factors that contributed to the decline, prevention of mother to child HIV transmission (PMTCT) programmes were the most significant, according to this report. Currently, a highly efficacious and safe prophylaxis regimen and/or lifelong antiretroviral treatment (ART) that can reduce mother to child transmission (MTCT) to less than 5% are made available in many resource-poor settings [2]. In those settings, however, ensuring uptake and adherence remains a challenge.

Although prophylactic medication coverage during pregnancy has improved significantly from 15% in 2005 to 68% in 2009 in east and southern Africa, it is still lower than the 80% target [1]. Ethiopia is among the worst-performing countries, with less than 20% prophylaxis coverage [3]. There is big gap in initiating medication during pregnancy and mother-infant pairs ingesting the medication at birth, largely due to progressive defaulting that could undermine the efficacy of the medications [4-8]. A low rate of institutional delivery can largely account for a low rate of prophylaxis ingesting at birth by the mother and infants since medications are often available only in health facilities [3,4,9,10].

The other element of PMTCT programmes showing poor uptake and adherence is follow up of exposed infants. Globally, only 15% of HIV-exposed infants access early infant diagnosis [11]. Studies showed that about 20% of HIV-positive infants die before six months and 35% to 40% die before 12 months [11,12]. Early infant diagnosis is a crucial step to facilitate access to ART, to improve infants' survival and to evaluate the effectiveness of PMTCT programmes [11-13].

In the context of PMTCT, most adherence studies from sub-Saharan Africa focus on a single-dose nevirapine regimen while a combined ZDV regimen, despite its complexities and challenges to adherence, has not been well documented. Moreover, there is a scarcity of research in resource-poor settings related to follow up of exposed infants and the rate of MTCT among exposed infants in programmatic settings. This prospective cohort study was conducted in Addis Ababa to assess: 1) adherence to medication regimen among mothers and infants in a PMTCT programme; 2) the proportion of infants followed up in the PMTCT programmes; and 3) the rate of MTCT at six weeks postpartum.

Methods

The study was conducted in Addis Ababa. The city is the home of about three million culturally and religiously diverse people, and is administratively divided into 10 sub-cities with varying population sizes. In 2009, 54 health facilities were providing integrated perinatal care services, including PMTCT, across the city. Of these, about half were public health centres. Despite the proportional distribution of public and private facilities, the public health centres remained the major providers of perinatal care services, including PMTCT. In public facilities, PMTCT services were provided free of charge. These facilities offered antenatal care to 90% of the pregnant women, conducted 90% of the institutional deliveries and managed 80% of the obstetric complications (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank), [14]. Of the 54,698 pregnant mothers who attended PMTCT programmes across the city, 79% were tested for HIV and 4.6% were HIV positive [3].

Following HIV-positive diagnoses in antenatal clinics, HIV-positive mothers were referred to ART clinics in order to determine their eligibility either for prophylaxis or lifelong ART. The ART clinics provided several services including: 1) collecting blood samples for CD4 cell and lymphocyte count (the blood sample is then sent to a central laboratory); 2) initiating lifelong ART for mothers with CD4 count of 200 cells/mm^3 and less;3) regular monitoring of the mothers' response to ART based on CD4 cell/lymphocyte count; 4) providing adherence counselling using expert patients (HIV-positive volunteer mothers who were trained on adherence); and 5) tracing of ART defaulters (lost to follow up).

Mothers with CD4 counts of 200 cells/mm^3 or more initiated combined ZDV prophylaxis in antenatal clinics. The prophylaxis was initiated at 28 weeks of gestation to be taken twice daily and required monthly refill. The antenatal clinics neither provided adherence counsellors nor traced defaulters. Table 1 shows a summary of the prophylaxis regimen recommended in the revised national PMTCT guidelines.

During the intrapartum period, mothers who initiated prophylaxis were given lamuvudine and sdNVP in addition to ZDV, while those who initiated lifelong ART were required to continue their daily doses. Infants were given ZDV and sdNVP within 72 hours of birth. During the postpartum period, mothers continued taking ZDV for seven days. Infants continued taking ZDV syrup for seven days if their mothers received the medication for one month or more; otherwise the infants took the syrup for one month. Postnatal follow up for exposed infants were recommended at six hours, six days, six weeks, monthly until six months and then every three months until 18 months of age (Table 1). During the six weeks of follow up, the first pentavalent vaccine (haemophilusinfluenzae type B, diphtheria, pertussis, tetanus

Table 1 Medication regimens and infant follow up schedules in the 2007 revised national PMTCT guidelines

Antepartum	*Intrapartum*	*Postpartum*
Mother **If CD4 ≥200 cells/mm^3; *ZDV from 28 weeks of gestation*** **If CD4 < 200 cells/mm^3; *ART***	**Mother** ***ZDV + lamuvudine + single-dose nevirapine*** ***ART*** **Infant** ***ZDV + single-dose nevirapine***	**Mother** ***ZDV + lamuvudine for seven days*** ***ART*** **Infant** ***ZDV for 7 days if mother receives the medication ≥ 4 weeks*** ***ZDV for 1 month if mother receives the medication < 4 weeks***
	Six-hours follow up • ***Routine early postpartum services for mothers and their infants*** • ***Infant feeding counselling***	**Six-days follow-up service** • ***Routine postpartum care for mothers and infants*** • ***Infant feeding counselling*** **Six-weeks follow up services** • ***Routine postpartum care*** • ***Early infant HIV diagnosis using polymerase chain reaction (PCR) from dried blood spot (DBS)*** • ***Cotrimoxazole for infants receiving breast milk for opportunistic infections*** • ***Infant feeding counselling*** • ***First pentavalent vaccine and other routine child health services***

and hepatitis B) and early infant HIV testing were done. The HIV testing was done in a central laboratory using PCR from DBS, which took a minimum of one month.

The study was a health facility-based prospective cohort conducted from January to December 2009 in 12 public health centres and three private hospitals in Addis Ababa. A four-to-one public-to-private ratio was used in selecting health facilities, considering that more than 80% of the pregnant mothers in the city initiated care from public health facilities. Then individual health facilities were selected on the basis of high client flow and to provide representation of all the 10 sub-cities.

In 2009 alone, 1976 pregnant mothers were diagnosed as HIV positive in PMTCT programmes across the city. Of these, approximately 25% were diagnosed in the first quarter of 2009 (January to March) and were eligible for the study taking into consideration the time required for a baby to be six weeks old by completion of the study. Of the 479 mothers diagnosed from January to March across the city and who were eligible for the study, 282 were attending those health facilities selected for our study, and all consented to be followed up (Figure 1).

The study was reviewed and approved by the Ethical Committee of Addis Ababa City Administration Health Bureau in Ethiopia, as well as the Regional Committee for Medical Research Ethics in Western Norway. Study permits from the Addis Ababa City Administration Health Bureau and the respective sub-cities were obtained.

A semi-structured follow-up format was developed in English for data collection. Most of the variables in the format were obtained from PMTCT and exposed infant logbooks and the national PMTCT guidelines, although some were added from reviewed literatures. The inclusion of routinely recorded variables was considered to minimize incomplete information in the case of loss to follow up; it also ensured data quality as the recruited data collectors had experience in doing routine recording. Thirty-three PMTCT counsellors working in antenatal clinics were recruited to collect the data. They were offered half-day training on the follow-up format and on how to do the follow up. Data were collected

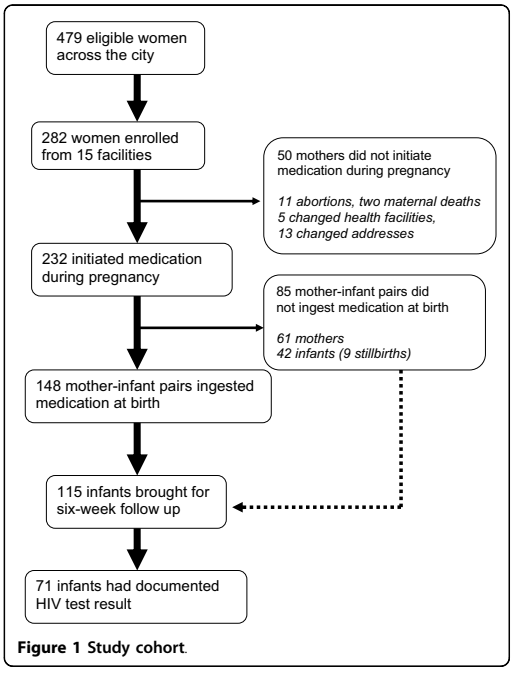


Figure 1 Study cohort.

anonymously using the women's antenatal numbers as their unique identifiers for ethical reasons.

At enrolment, mothers were interviewed on socio-demographic variables, date of HIV testing and gestational age at enrolment. Follow up data were obtained from the mothers themselves and from logbooks in the facilities. The follow-up schedules of the cohort coincided with the women's regular perinatal visits, i.e., at 28 weeks, 36 weeks, at delivery, six days postpartum and six weeks postpartum. The follow-up data at the 28-week visits were CD4 cell count, whether medication was initiated or not, gestational age medication initiated, type of medication initiated (prophylaxis or lifelong ART), disclosing HIV status to partner, and partner involvement in HIV counselling and testing.

At 36 weeks gestation, adherence to medication was assessed using a one-week recall period. Follow-up data at delivery were place of delivery, mode of delivery, mother prophylaxis during labour, infant sex, infant birth weight, infant status at birth, and infant prophylaxis at birth. For mothers who were transferred to other health facilities and for those who gave birth at home, these data were collected when they came for their six-day and six-week postpartum care visits. The follow-up data at six weeks postpartum were about the type of infant feeding practices, first pentavalent vaccination, whether infants were brought in for early infant diagnosis or not, and whether dried blood spot was taken or not. Infant HIV test results were collected from the facilities a minimum of one month following collections of dried blood spot. Study participants were given a small incentive (about US$2) for transport at each visit.

The main study outcomes were the proportions of: 1) mothers initiating medication during pregnancy; 2) mother-infant pairs ingesting medication at birth; 3) infants brought for early infant diagnosis at six weeks postpartum; and 4) infants tested positive at six weeks postpartum. In this study, the term, "initiate", implies the receiving of medication during pregnancy, and "ingest" implies actual swallowing of the drug observed by health professionals or mothers' self reports at birth. "Adherence" implied documented or self-reported initiating/ingesting of the medications and bringing infants for six-week follow up. Analyzing medication initiated by the mothers during pregnancy, we used abortion and death of a mother as study endpoints. Analyzing medication ingested by mother-infant pairs at birth, we used abortion, death of a mother and stillbirth as study endpoints.

The data were double entered in Microsoft Excel and checked for consistencies and then transferred to SPSS version 17 for analysis. Descriptive statistics, bivariate and multivariate logistic regression analyses were done. Variables with p values of less than 0.2 in bivariate analysis were included in the multivariate model to control for potential confounding effects. A p value < 0.05 was considered significant and a 95% confidence interval (CI) was used. The proportions of mothers who initiated medication during pregnancy were calculated among those who were enrolled into the study. The proportions of mother-infant pairs ingesting medication at birth were calculated from live births, and twin births were counted once. The proportions of infants brought for early infant diagnosis at six weeks were calculated from the total live births. The rate of MTCT was calculated among infants with documented HIV test result.

Results

The cohort enrolled a total of 282 HIV-positive pregnant women. Of these, 11 mothers had abortions, two were transferred out, and two died (one while pregnant and the other one after birth). In total, 217 mothers had live births of single infants and two mothers had live birth of twins (Figure 1).

Table 2 shows the demographic and obstetric characteristics of the mothers enrolled in the study. The median age of the mothers was 25 years and the median schooling completed was Grade 7. The majority of the mothers were pregnant for the second time. The median gestational age during enrolment was 21 weeks. The mothers had a median CD4 count of 310 cells/mm^3. In total, 160 (57%) disclosed their HIV-positive status to their partners, 82 partners were involved in HIV counselling and testing, 109 partners reported to be tested, and 75 (69%) partners were HIV positive. By six weeks postpartum, 151 (74%) infants were receiving exclusive breastfeeding, 49 (24%) were receiving exclusive formula feeding, and four (2%) were receiving mixed feeding.

Of the 282 mothers enrolled, 232 (82%, 95% CI 77-86%) initiated medication during pregnancy. Of these, 154 (64%) initiated ZDV prophylaxis and 78 (33%) lifelong ART, while 50 (17.7%) did not initiate any medication during pregnancy. Among the 50 mothers who did not initiate medication, seven (14%) actively refused the medication prescriptions and 11 (22%) had abortions, five changed health facilities, 13 changed their addresses, two were transferred out, two died, and no reasons were given for 10 mothers. The changes in health facilities and addresses were common among mothers who got to know their HIV status for the first time. These mothers often went to other health facilities to confirm their HIV status and to follow PMTCT programme where they would not be recognized. Two mothers were found registered in two health facilities with the intention of obtaining support from both places.

A total of 109 mothers with documented gestation at medication initiation had come for collecting more of

Table 2 Socio-demographic and obstetric characteristics of 282 mothers enrolled into the study

Variable	N = 282 n(%)
Age in years	
15-24	99(35.6)
25-29	111(39.9)
> 30	68(24.5)
Median (IQR)	*25(23-29)*
Education (grades completed)	
0-4	87(31.8)
5-8	98(35.8)
≥ 9	89(32.5)
Median (IQR)	*7(3-10)*
Number of pregnancies	
First	92(33.1)
Second	101(36.3)
Three or more	85(30.6)
Median (IQR)	*2(1-3)*
Gestational age at enrolment	
< 28 weeks	150(65.8)
≥28 weeks	78(34.2)
Median (IQR)	*21(16-28)*
CD4 cell count/mm^3	
< 200	47(26.3)
200-349	55(30.7)
> 349	77(43.0)
Median (IQR)	*310(216-433)*
Disclosed HIV status to partner	
Yes	160(83.8)
No	31(16.2)
Partners involved in HIV counselling and testing	
Yes	82(37.6)
No	136(62.4)
Partners tested for HIV	
Yes	109(49.8)
No	110(50.2)
Partners HIV test result	
Positive	75(68.8)
Negative	34(31.2)

Due to missing values, the numbers may not add up to the total

their medication at 36 weeks. These women were assessed for adherence to prescribed medication using a one-week recall period. Adherence to medication was not significantly different between mothers who initiated prophylaxis and those who initiated lifelong ART (p > 0.05). Of the 77 mothers who initiated ZDV prophylaxis, 55 (68%) never missed a dose, 16 (20%) missed one dose, and 10 (12%) missed more than one dose. Of the 28 mothers who initiated ART, 17 (61%) never missed a dose, six (21%) missed one dose and five (18%) missed more than one dose. No significant associations were observed between receiving medication during pregnancy and socio-demographic and obstetric variables, CD4 cell count, gestational age at enrolment, disclosing HIV status to partner, partner's involvement in HIV counselling and testing, partner's HIV testing and partner's HIV test result (p > 0.05).

Out of the 282 enrolled mothers, 171 (60%, 95% CI 55-66%) had ingested medication during labour. Among mothers who initiated medication during pregnancy 26% did not ingest any medication during labour. In total, 228 mothers were reported to have given birth: 211 (92%) did this at health facilities and 17 (8%) at home. Mothers who gave birth at health facilities were more likely to ingest their medication (77%) than mothers who gave birth at home (53%) (OR 2.94, 95% CI 1.08-8.02). Of the 221 infants born alive (including the two sets of twins), 191 (87%, 95% CI 81-90%) ingested medication at birth.

There was a strong association between medication ingested by the mothers and infants at birth and place of delivery. Infants who were delivered at heath facilities were more likely (OR 13.64, 95% CI 4.64-40.12%) to ingest their medication at birth than those who delivered at home. There was no significant association between mother and infant ingesting medication and demographic variables, obstetric variables, CD4 cell count at enrolment, disclosing HIV status to partner and partner being involved in HIV counselling and testing (p > 0.05).

Of the 219 live births (twin births were counted once), 148 (68%, 95% CI 61-73%) mother-infant pairs ingested the medication at birth. Ingesting the medication by the mother-infant pairs was not significantly associated with education, age, number of pregnancies, gestational age at enrolment, CD4 cell count at enrolment, mode of delivery and disclosing HIV status to partner (Table 3). The likelihood of mother-infant pairs ingesting the medication was much higher among those who had facility birth than home birth (OR 6.7, 95% CI 2.90-21.65).

Staff turnover happened in nine of the 15 (60%) study sites, and those counsellors who were initially recruited were replaced by other counsellors. In all, 174 mothers attended facilities that experienced staff turnover, where 49% of the mother-infant pairs did not ingest their medication at birth. Among the 108 mothers who attended those facilities experiencing no staff turnover, 57% of mother-infant pairs had ingested their medication at birth (p > 0.05).

Among the 221 live births, 189 (86%, 95% CI 80-90%) infants were brought for their first pentavalent vaccine (haemophilusinfluenzae type B, diphtheria, pertussis, tetanus and hepatitis B) and 115 (52%, 95% CI 45-58%) for early infant diagnosis at six weeks postpartum. Among the infants brought for early infant diagnosis,

Table 3 Bivariate and multivariate associations between mother-infant pairs' non adherence to medication at birth and potential determinants

Variable	Mother-infant pairs ingested medication at birth		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	Yes n(%)	No n(%)		
Age in years				
15-24	48(63.2)	28(36.8)	1	
25-29	60(69.8)	26(30.2)	1.35(0.64-2.85)	
≥ 30	37(69.8)	16(30.2)	1.0(0.48-2.11)	
Education (grade completed)				
0-4	38(62.3)	23(37.7)	1	
5-8	55(70.5)	23(29.5)	0.69(0.34-1.41)	
≥9	54(73.0)	20(27.0)	0.61(0.30-1.27)	
Number of pregnancies				
First	48(69.6)	21(30.4)	1	1
Second	59(73.8)	21(26.3)	0.81(0.40-1.66)	0.60(0.27-1.34)
Three or more	39(58.2)	28(41.8)	1.64(0.81-3.32)	1.34(0.62-2.87)
Gestational age at enrolment				
< 28 weeks	78(64.5)	43(35.5)	1	
≥ 28 weeks	47(71.2)	19(28.8)	0.7(0.38-1.40)	
CD4 cell count/mm^3				
≥ 350	49(75.4)	16(24.6)	1	
200-349	31(67.4)	15(32.6)	2.08(0.90-4.80)	
< 200	25(59.5)	17(40.5)	1.48(0.64-3.42)	
Disclosed to partner				
Yes	110(71.9)	43(28.1)	1	
No	19(63.3)	11(36.7)	1.48(0.65-3.37)	
Medication initiated				
ZDV prophylaxis	101(74.8)	34(25.2)	1	1
Lifelong ART	45(63.4)	26(36.6)	1.72(.92-3.19)	1.85(0.96-3.56)
Place of delivery				
Health facility	143(70.8)	59(29.2)	1	1
Home	5(29.4)	12(70.6)	5.82(1.96-17.24)	6.72(2.90-21.65)

Due to missing values, the numbers may not add up to the total

only 71 (32%, 95% CI 26-38%) had documented HIV test results and six (8.4%, 95% CI 4-17%) were HIV positive. The major reasons for not having documented HIV test results were: DBS not collected from infants due to lack of trained staff; DBS tests done, but results not collected from central laboratory doing the PCR test; and misplacing of the test results at the facilities. No significant differences were observed among infants receiving different feeding modalities with respect to MTCT. Four infants (8.2%) were HIV positive among 49 infants who received exclusive breastfeeding, two (9.5%) among 21 infants who received exclusive formula feeding, and none among two infants who received mixed feeding.

Discussion

The PMTCT programme has great potential to achieve virtual elimination of MTCT provided that the recommended interventions are properly followed. Our study showed progressive and marked decline in medication adherence across the perinatal period. Although 82% of the mothers initiated medication during pregnancy, only 68% of the mother-infant pairs ingested the medication at birth. There were unnecessary missed opportunities in exposed infants follow up within the healthcare system. By six weeks postpartum, 86% of the infants received their first pentavalent vaccines, but only 53% were brought for early infant diagnosis. These challenges could seriously undermine the effectiveness of the PMTCT programme, and need thorough consideration.

We found that more than 80% of the mothers initiated medication during pregnancy. This finding compares favourably with several empirical works from Ethiopia and other sub-Sahara African countries [4,9,10,15]. It is also in accordance with the 80% target set by the Joint

United Nations Programme on HIV/AIDS and the World Health Organization to offer prophylactic medication for pregnant mothers in order to halve the MTCT by the year 2015 [16]. Although the proportion of mothers who initiated medication during pregnancy reached the 80% target, only two-thirds of the mother-infant pairs had ingested their medication at birth.

In a large-scale cross-sectional study conducted in four African countries, similar gaps are reported. Among 3196 HIV-positive mothers who gave birth, 2278 (71%) initiated nevirapine during pregnancy while only 1725 (54%) mother-infant pairs had actually taken it when checked for cord blood [15]. By contrast, a clinical trial conducted in Zambia and a study from Botswana reported a more than 90% level of adherence to prophylactic medications [10]. These differences could be attributed to better coverage and quality of intrapartum obstetric care services. In Botswana, 97% of pregnant mothers have access to antenatal care and 94% to safe institutional delivery whereas in Addis Ababa, 90% mothers have access to antenatal care, but only 44% have access to safe institutional delivery [17].

In line with this argument, institutional delivery was a significant determinant of mother-infant pairs ingesting medication at birth in our study. It also reflects the situation in Ethiopia where infant prophylaxis is available only at health facilities, and infants delivered at home have less chance to get medications unless they are brought to health facilities by their parents. Other researchers have also reported the place of delivery to be an important and significant predictor of ingesting medication at birth [9,10].

Nevertheless, 23% of the mothers did not ingest any medication at birth despite giving birth at health facilities. This could indicate possible failure within the healthcare system that put the mothers and their infants at increased risk of MTCT. Staff turnover happened in 60% of the antenatal clinics included in our study, and there is little reason to think that the turnover in labour wards is different. There was higher proportion of non-adherence among those who attended facilities that experienced staff turnover than those who did not attend these facilities, although this difference was not statistically significant. High staff turnover and frequent rotation can create a gap filled by less experienced staff with little or no training in PMTCT/ART. Poor knowledge of PMTCT/ART by staff in delivery wards could possibly reduce mothers' and infants' chance of getting appropriate and timely medications.

Contrary to what is reported by Stringer and colleagues, mother-infant pairs' medication adherence was lower among the group that initiated lifelong ART than those who initiated ZDV prophylaxis [15]. At 36 weeks gestation, more mothers who initiated prophylaxis reported that they had never missed medication in the past week compared with those who initiated lifelong ART. This contrasted with what had been observed in most ART clinics, where they were providing adherence counselling using expert clients, regular follow up, and monitoring and tracing of treatment defaulters.

Studies have also shown that adherence counselling and active tracing mechanisms can improve adherence and treatment outcomes, and can also reduce loss to follow up [18,19]. Alternatively, poor adherence among mothers' who initiated lifelong ART could be a reflection of their poor health status. Sick mothers may not able to get to the health facilities to collect medication for themselves, as well as for their infants. As shown in Table 3, among the group who did not adhere to mother-infant pair medication, 40% of the mothers had CD4 counts of 200 cells/mm^3 or less. This is consistent with a review and research in Ethiopia where a low CD4 cell count is reported to be a significant marker of poor immune status and disease progression [20,21].

Due to the gaps in receiving medication during pregnancy and actual ingesting of the drug by the mother-infant pairs at birth, PMTCT programme effectiveness could be undermined. Compromised efficacy of prophylaxis regimens are reported when the drugs are taken either by the mothers or their infants only. In a double-blind, randomized, placebo-controlled trial conducted in South Africa, Uganda and Tanzania, the rate of MTCT was 8.9% in the group where mothers and infants initiated the intrapartum and postpartum prophylaxis doses, whereas it was 14.2% in the group where mothers, but not their infants, initiated the intrapartum dose [7,8]. Moreover, the proportion of mothers' receiving medication during pregnancy is a proxy indicator currently used for measuring PMTCT programme success; hence the gaps could threaten the validity of this indictor. Particularly in resource-poor settings where there are marked gaps in antenatal care and institutional delivery coverage, this indicator could overestimate PMTCT programme effectiveness. Careful consideration is required in using "the proportion of mothers' receiving medication during pregnancy" as the indicator of PMTCT programme success in these settings.

Our findings suggest that exposed infant follow up was inconsistent and poorly organized, which could negatively impact the success of the PMTCT programme. The 2007 revised PMTC guidelines clearly stated the need for integrated and comprehensive follow-up services for exposed infants [22]. Despite immunization coverage of more than 80% among the HIV-exposed infants, slightly more than 50% of them attended infant follow up at six weeks and less than

one-third had documented HIV test result. This shows lack of integration of HIV care with the under-five child health clinics leading to avoidable missed opportunities.

Consistent with our findings, only 25% of exposed infants were tested for HIV in Mozambique [23]; in Kenya, among 2477 exposed infants, only 40% were tested [5]; and only 59% of babies were tested in Zimbabwe by the age of 15 months [24]. This implies that large missed opportunities are occurring within the health system despite having clear guidelines. In the majority of health facilities, the infant follow-up services were scattered over at least at six service points and were available only two or three days in a week. In a study by Nyandiko and colleagues, the health system was shown to be responsible for the low rate of infant HIV testing [25]. The missed opportunities in infant diagnosis can also delay HIV-positive infants from accessing timely treatment, which is detrimental to their survival [11,13,26]. Therefore, creating integrated strategies to contain the necessary procedures pertinent to exposed infant follow up at one single point within the existing under-five child health clinic could be a way forward for a successful PMTCT programme.

The majority of infants were receiving exclusive breastfeeding and were tested for HIV at six weeks postpartum. The rate of MTCT was 8.4%, which is consistent with the reported rate from a similar study undertaken in Addis Ababa [4]. By contrast, lower rates of MTCT were reported from outside of Ethiopia, 5.7% in the Petra clinical trial and 4.7% in a cohort study for Abidjan among predominantly exclusive breastfed infants tested at six weeks postpartum, but there is an overlap in the confidence intervals [6,7]. The rate of MTCT observed in our study seems to be encouraging compared with the 15-25% MTCT expected at six weeks in the absence of any interventions [27]. Nonetheless, the MTCT reported in our study could be underestimated primarily due to the large proportions of potential non-adherence to medication among the lost-to-follow-up cases.

Secondly, the HIV testing was done at six weeks postpartum and did not account for possible MTCT through breastfeeding. To get further reduction in MTCT among breastfed infants, the 2010 revised guidelines advocates for continuation of mothers' or their infants' medication throughout the breastfeeding period [28]. In this regard, continuous adherence support for extended period can be extremely impotent. This calls for tailored follow-up services integrated into existing maternal and child health programmes with a clear sense of ownership and accountability from staff involved in the care.

One of the limitations of our study is that the rate of MTCT was calculated among infants who completed their follow up to six weeks. This could result in overestimation of the effectiveness the PMTCT programme and also threaten the external validity of the study. Attempts were made to minimize the non-adherence using existing defaulter tracers. Moreover, a qualitative account of mothers' perspectives would have added to the explanation for the loss to follow up. Although the study was conducted as part of a national PMTCT programme and the levels of non-adherence were not different from PMTCT programmes in many sub-Saharan African settings [4,5,23,25,29,30], care should be exercised in generalizing the study findings.

Another limitation is that the internal validity of the study could be affected due to employing several data collectors, but we sought to minimize this risk through the following steps:1) the data collectors were all PMTCT counsellors, who were well acquainted with the issue under study; 2) almost all the variables in the follow-up format were drawn from log books in the facilities used to record routine activities; and 3) all the data collectors were given training.

So far, few cross-sectional studies have reported prophylactic medication coverage in Ethiopia. Our research is the first prospective cohort that has estimated level of non-adherence to PMTCT recommendations and averted infections among HIV-exposed infants. The follow up helped us to identify critical points that many clients are failing in PMTCT programmes.

Conclusions

Despite the large proportion of mothers initiating medication during pregnancy, the majority of them and their infants did not actually ingest the drugs according to the recommendations at birth. This could challenge the overall effectiveness of the national PMTCT programme. The proportion of mother-infant pairs ingesting medication at birth seems to be a more reliable indicator for PMTCT programme planning and evaluation compared with the proxy indicator currently used (i.e., the proportion of mothers receiving medication during pregnancy). Increasing access to quality intrapartum obstetric care services seems to be fundamental to increasing adherence to the recommended medication at birth to reduce MTCT. The focus should also be on increasing the women's awareness on high level adherence to medication regimen for optimal result and removing barriers to institutional delivery.

Meanwhile, facilitating access to medication in the case of home deliveries should also be focused on. Services pertinent to follow up of exposed infants seem to be inconsistent and undeveloped, and might contribute significantly to avoidable missed opportunities and negatively impact the survival of HIV infected infants. Creating a system to contain the necessary procedures for follow up of exposed infants at a single service point

should be considered. Targeted interventions should be developed specifically for HIV-exposed infants within the PMTCT package, which should be integrated within the existing traditional under-five child health services to ensure continuity of care for these children.

Acknowledgements
This study was financially supported by the Centre for International Health, University of Bergen, the Meltzer Foundation and Statens Lånekasse, Norway. We thank the Addis Ababa City Administration Health Bureau and the health bureaus in the respective sub-cities for permitting us to conduct the study. Moreover, we are grateful to all the HIV-positive mothers who participated in the study and to all PMTCT service providers who participated in the data collection.

Author details
[1]Centre for International Health, University of Bergen, OverlegeDanielssens Hus, Årstav. 21, Bergen 5020, Norway. [2]College of Medical and Health Sciences, Department of Nursing and Midwifery, Hawassa University, POBox 1560, Awassa, Ethiopia. [3]School of Public Health, Addis Ababa University, Addis Ababa, Ethiopia. [4]Faculty of Health and Social Sciences, Bergen University College, Department of Nursing, Bergen, Norway.

Authors' contributions
AHM prepared the study proposal, collected and analyzed the data, interpreted the findings and wrote the manuscript. OM was involved in developing the study proposal, supervising the data collection and reviewing the manuscript. SGH was involved in developing the study proposal and reviewing the manuscript. MMS was involved in supervising the data collection and reviewing the manuscript. KMM was involved in developing the study proposal and reviewing the manuscript. All authors have read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Received: 18 May 2011 Accepted: 21 October 2011
Published: 21 October 2011

References

1. UNAIDS: *UNAIDS report on the global AIDS epidemic 2010* Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2010.
2. Kilewo C, Karlsson K, Massawe A, Lyamuya E, Swai A, Mhalu F, Biberfeld G: **Prevention of mother-to-child transmission of HIV-1 through breast-feeding by treating infants prophylactically with lamivudine in Dar es Salaam, Tanzania: the Mitra Study.** *Journal of Acquired Immune Deficiency Syndromes (1999)* 2008, **48(3)**:315-323.
3. FHAPCO: *Annual Performance Report of Multisectoral HIV/AIDS Response 2002 E.C. (2009/2010)* Addis Ababa: Federal HIV/AIDS Prevention and Control Office; 2010.
4. Mirkuzie A, Hinderaker SG, Mørkve O: **Promising outcomes of a national programme for the prevention of Mother-to-Child HIV transmission in Addis Ababa: a retrospective study.** *BMC Health Services Research* 2010, **10.**
5. Azcoaga-Lorenzo A, Ferreyra C, Alvarez A, Palma PP, Velilla E, del Amo J: **Effectiveness of a PMTCT programme in rural Western Kenya.** *AIDS Care* 2011, **23(3)**:274-280.
6. Dabis F, Bequet L, Ekouevi DK, Viho I, Rouet F, Horo A, Sakarovitch C, Becquet R, Fassinou P, Dequae-Merchadou L, Welffens-Ekra C, Rouzioux C, Leroy V: **Field efficacy of zidovudine, lamivudine and single-dose nevirapine to prevent peripartum HIV transmission.** *AIDS* 2005, **19(3)**:309-318.
7. Petra Study Team: **Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa, and Uganda (Petra study): a randomised, double-blind, placebo-controlled trial.** *Lancet* 2002, **359(9313)**:1178-1186.
8. Volmink J, Siegfried NL, Van der Merwe L, Brocklehurst P: **Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection.** *Cochrane Database of Systematic Reviews (Online)* 2007, **1.**
9. Kuonza L, Tshuma CD, Shambira GN, Tshimanga M: **Non-adherence to the single dose nevirapine regimen for the prevention of mother-to-child transmission of HIV in Bindura town, Zimbabwe: a cross-sectional analytic study.** *BMC Public Health* 2010, **10**:218.
10. Albrecht S, Semrau K, Kasonde P, Sinkala M, Kankasa C, Vwalika C, Aldrovandi GM, Thea DM, Kuhn L: **Predictors of nonadherence to single-dose nevirapine therapy for the prevention of mother-to-child HIV transmission.** *Journal of Acquired Immune Deficiency Syndromes* 2006, **41(1)**:114-118.
11. World Health Organization: *WHO recommendations on the diagnosis of HIV infection in infants and children* Geneva: World Health Organization; 2010.
12. Creek TL, Sherman GG, Nkengasong J, Lu L, Finkbeiner T, Fowler MG, Rivadeneira E, Shaffer N: **Infant human immunodeficiency virus diagnosis in resource-limited settings: issues, technologies, and country experiences.** *American Journal of Obstetrics and Gynecology* 2007, **197(3)**: S64-S71.
13. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, Jean-Philippe P, McIntyre JA: **Early antiretroviral therapy and mortality among HIV-infected infants.** *The New England Journal of Medicine* 2008, **359(21)**:2233-2244.
14. MOH: *Health and health related indicators 2008/2009* Addis Ababa: Federal Ministry of Health; 2010.
15. Stringer E, Ekouevi DK, Coetzee D, Tih PM, Creek TL, Stinson K, Giganti MJ, Welty TK, Chintu N, Chi BH, Wilfert CM, Shaffer N, Dabis F, Stringer JS: **Coverage of nevirapine-based services to prevent mother-to-child HIV transmission in 4 African countries.** *The Journal of the American Medical Association* 2010, **304(3)**:293-302.
16. WHO: *PMTCT strategic vision 2010-2015 preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium development goals: moving towards the elimination of paediatric HIV* Geneva: World Health Organization; 2010.
17. UNDP: *Human Development Report 2010: the real wealth of nations; pathways to human development* New York: United Nations Development Program; 2010.
18. Bentz L, Enel P, Dunais B, Durant J, Poizot-Martin I, Tourette-Turgis C, Rebillon M, Le Duff F, Dellamonica P, Pradier C: **Evaluating counseling outcome on adherence to prophylaxis and follow-up after sexual HIV-risk exposure: a randomized controlled trial.** *AIDS Care* 2010, **22(12)**:1509-1516.
19. Igumbor J, Scheepers E, Ebrahim R, Jason A, Grimwood A: **An evaluation of the impact of a community-based adherence support programme on ART outcomes in selected government HIV treatment sites in South Africa.** *AIDS Care* 2011, **23(2)**:231-236.
20. Endale A, Hailu Y, Lindtjørn B: **Predictors of early death in a cohort of Ethiopian patients treated with HAART.** *BMC Infectious Diseases* 2006, **6.**
21. Zeller JM, McCain NL, Swanson B: **Immunological and virological markers of HIV-disease progression.** *The Journal of the Association of Nurses in AIDS Care* 1996, **7(1)**:15-27.
22. HAPCO/FMOH: *Guidelines For Prevention of Mother-to-Child Transmission of HIV In Ethiopia* Addis Ababa: Federal HIV/AIDS Prevention and Control Office/Federal Ministry of Health Editor; 2007.
23. Cook RE, Ciampa PJ, Sidat M, Blevins M, Burlison J, Davidson MA, Arroz JA, Vergara AE, Vermund SH, Moon TD: **Predictors of successful early infant diagnosis of HIV in a rural district hospital in Zambezia, Mozambique.** *Journal of Acquired Immune Deficiency Syndromes* 2011, **56(4)**:104-109.
24. Gumbo FZ, Duri K, Kandawasvika GQ, Kurewa NE, Mapingure MP, Munjoma MW, Rusakaniko S, Chirenje MZ, Stray-Pedersen B: **Risk factors of HIV vertical transmission in a cohort of women under a PMTCT program at three peri-urban clinics in a resource-poor setting.** *Journal Perinatology* 2010, **30(11)**:717-723.
25. Nyandiko W, Otieno-Nyunya B, Musick B, Bucher-Yiannoutsos S, Akhaabi P, Lane K, Yiannoutsos CT, Wools-Kaloustian K: **Outcomes of HIV-exposed children in western Kenya: efficacy of prevention of mother to child transmission in a resource-constrained setting.** *Journal of Acquired Immune Deficiency Syndromes (1999)* 2010, **54(1)**:42-50.

26. Creek T, Tanuri A, Smith M, Seipone K, Smit M, Legwaila K, Motswere C, Maruping M, Nkoane T, Ntumy R, Bile E, Mine M, Lu L, Tebele G, Mazhani L, Davis MK, Roels TH, Kilmarx PH, Shaffer N: **Early diagnosis of human immunodeficiency virus in infants using polymerase chain reaction on dried blood spots in Botswana's national program for prevention of mother-to-child transmission.** *The Pediatric Infectious Disease Journal* 2008, **27(1)**:22-26.
27. De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, Rogers M, Shaffer N: **Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice.** *The Journal of the American Medical Association* 2000, **283(9)**:1175-1182.
28. WHO: *Guidelines on HIV and infant feeding 2010 Principles and recommendations for infant feeding in the context of HIV and a summary of evidence* Geneva: World Health Organization Editor; 2010.
29. Ahoua L, Ayikoru H, Gnauck K, Odaru G, Odar E, Ondoa-Onama C, Pinoges L, Balkan S, Olson D, Pujades-Rodríguez M: **Evaluation of a 5-yearprogramme to prevent mother-to-child transmission of HIV infection inNorthern Uganda.** *Journal of Tropical Pediatrics* 2010, **56(1)**:43-52.
30. Manzi M, Zachariah R, Teck R, Buhendwa L, Kazima J, Bakali E, Firmenich P, Humblet P: **High acceptability of voluntary counselling and HIV-testing but unacceptable loss to follow up in a prevention of mother-to-child HIV transmission programme in rural Malawi: scaling-up requires a different way of acting.** *Tropical Medicine & International Health* 2005, **10(12)**:1242-1250.

doi:10.1186/1758-2652-14-50
Cite this article as: Mirkuzie *et al.*: Current status of medication adherence and infant follow up in the prevention of mother to child HIV transmission programme in Addis Ababa: a cohort study. *Journal of the International AIDS Society* 2011 **14**:50.

IV

Journal of Public Health and Epidemiology Vol. 3(6), pp. 275-283, June 2011
Available online at http://www.academicjournals.org/jphe
ISSN 2141-2316 ©2011 Academic Journals

Full Length Research Paper

A cohort study on obstetric care for HIV positive women in Addis Ababa: Intrapartum transfers and associated delays

Alemnesh H. Mirkuzie[1,2]*, Sven Gudmund Hinderaker[1], Mitike Molla Sisay[3], Karen Marie Moland[4] and Odd Mørkve[1]

[1]Centre for International Health, University of Bergen, Overlege Danielssens Hus, Årstav. 21, Bergen 5020, +47 45070113, Norway.
[2]College of Medical and Health Sciences, Department of Nursing and Midwifery, Hawassa University, Awassa, P. O. Box 1560, Ethiopia.
[3]School of Public Health, Addis Ababa University, Addis Ababa, Ethiopia.
[4]Department of Nursing, Faculty of Health and Social Sciences, Bergen University College, Norway.

Accepted 11 May, 2011

Despite the importance of safe obstetric practice in reducing mother-to-child HIV transmission and adverse perinatal outcomes, little is known about access to intrapartum obstetric care for HIV positive women. A cohort of HIV positive women were followed to assess the rate of intrapartum transfers and associated adverse outcomes in Addis Ababa. Overall, 282 HIV positive pregnant women were followed, 75% gave birth at Emergency Obstetric and Neonatal Care facilities, 42% of them transferred between health facilities during the intrapartum period and 36% were transferred two or more times. Sixty four percent of the first time transfers were due to obstetric complications, while all subsequent transfers were due to practical constraints. Women in their second pregnancy were less likely (OR 0.3 95% CI 0.2-0.6) to be transferred than women in their first pregnancy. Transferred women experienced more stillbirths than women who were not transferred. The rate of stillbirths was not significantly associated with the syphilis test result, the CD_4 count and initiating antiretroviral therapy. There appeared to be serious challenges within the health care system compromising the intrapartum care for our participants and increasing the risk of stillbirth and MTCT. Undue transfers during the intrapartum period should be addressed at all levels of the health care system.

Key words: Delay, EmONC, Ethiopia, intrapartum, MTCT, stillbirth, transfer, PMTCT

INTRODUCTION

Safe obstetric practice is one of the components of the prevention of mother-to-child HIV transmission (PMTCT) programme (Read and Newell, 2005). The rate of MTCT during pregnancy is about 10% while it reaches 20% during the intrapartum period (De Cock et al., 2000). The intrapartum HIV transmission is responsible for about 75% of the HIV infection in non-breast feeding infants and 50% among infants receiving breast feeding for 18 to 24 months (De Cock et al., 2000; Gaillard et al., 2000; Read and Newell, 2005). Certain obstetric procedures during the intrapartum period such as episiotomy and artificial rupture of membrane can increase the risk of mother-to-child HIV transmission (MTCT). The rate of MTCT also increases with increasing duration of labour especially after membrane rupture, indicating the need for prompt attention during the intrapartum period. In obstetric literature, the "three delays" modelis often used

*Corresponding author. E-mail: alemmirkuzie@yahoo.com Tel: 004745070113.

ART, Antiretroviral therapy; **CI,** confidence interval; **DHS,** demographic and health survey; **EmONC,** emergency obstetric and neonatal care; **IQR,** inter quartile range; **MTCT,** mother-to-child HIV transmission; **OR,** odds ratio; **PMTCT,** prevention of mother-to-child HIV transmission.

to explain the non-obstetric causes for poor maternal and perinatal outcomes (Barnes-Josiah et al., 1998; WHO et al., 2009; Waiswa et al., 2010). The "first delay" refers to delay in making decision to seek care, the "second delay" refers to delay in reaching health care facilities and the "third delay" refers to delay in receiving appropriate care after reaching health facility. Studies from resource poor settings show that women often encounter considerable delay in receiving appropriate obstetric care even after reaching a health facility (Coley et al., 2001; WHO et al., 2009). The Interval between admission and treatment often determines the pregnancy outcomes: The shorter the interval the better the outcome and vice versa (WHO et al., 2009). In particular referrals between facilities increase delays that women in labour may not have time for (Ramanathan, 2009; WHO et al., 2009). In resource poor settings, 25% of the stillbirths are caused by prolonged labour and asphyxia, largely a result of lack of prompt attention and poor intrapartum obstetric management (McClure et al., 2009).

In PMTCT programmes, a lot of attention and debate has surrounded medication and infant feeding, while safe obstetric practice despite being an important component of a PMTCT programme has been given less attention. Reviews and Meta analyses have shown that the risk of MTCT is higher in vaginal deliveries compared to elective caesarean deliveries (The International Perinatal HIV Group, 1999; Read and Newell, 2005). Nevertheless, for practical and technical reasons safe vaginal delivery remains the standard of care in many resource poor setting. In these settings including Ethiopia, HIV positive women's access to safe obstetric care and the actual care these women receive have not been well documented. There is also scarcity of evidence showing the relationship between access to intrapartum obstetric care and prenatal outcomes among HIV positive women. Focusing on a cohort of HIV positive women in Addis Ababa, we assessed the rate of institutional delivery, the rate of transfers between health facilities during the intrapartum period and the occurrence of stillbirths.

METHODS

Study setting

The study was conducted in Addis Ababa, the capital of Ethiopia in 2009. Peripartum care including PMTCT and EmONC services were provided both in public and private health facilities across the city (MOH, 2008). The PMTCT services include HIV counselling and testing, provision of antiretroviral prophylaxis/ treatment to women and their babies, safe obstetrics practices and infant feeding counselling. In 2009 alone 54,698 pregnant women attended antenatal care across the city, 43,128 (78.8%) were tested for HIV in PMTCT programmes and 4.6% were HIV positive (FHAPCO, 2010).

According to a report by the ministry of health, 90% of the pregnant women in Addis Ababa had at least one antenatal visit and 44% gave birth at health facilities (MOH, 2008). Basic EmONC was provided in all the public health centres and hospitals provided comprehensive EmONC (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). The signal functions supposed to be provided in basic EmONC include administration of parenteral antibiotics, parenteral uterotonic drugs, parenteral anticonvulsants, manual removal of the placenta and retained products, assisted vaginal delivery and basic neonatal resuscitation. However, according to a report by the Ministry of Health, all the public EmONC facilities in Addis Ababa were missing one or more signal functions to be offered at their level and were only partially functioning. The signal functions in comprehensive EmONC include all the basic EmONC services plus blood transfusion and caesarean section. Women identified to have serious obstetric complications in the basic EmONC facilities before and after the onset of labour should usually be referred to comprehensive EmONC units. In such cases, the woman should be given a referral slip with information about the reasons for the referral, the treatment given and the HIV status of the woman. These formal procedures for referrals are not always followed. In this study, we use the concept 'transfers' to describe situations where the woman is told to seek care at another health facility for obstetric and non-obstetric reasons. Although 33 public and 24 private facilities were providing EmONC services across the city, actual utilization of the services were biased towards public health facilities. Nine out of ten deliveries and 80% of obstetric complications in Addis Ababa were managed in public facilities. The median distance to the nearest referral centre was less than 5 km. Only 47% of the health facilities had ambulance services. The number of skilled staff per 1,000 people is 4.6, compared to the recommended 2.3 staff per 1,000 (WHO, 2005, 2006).

Study design, data collection and data analysis

The data was obtained from a prospective cohort study conducted primarily to assess HIV positive women's adherence to PMTCT recommendations from January to December 2009. Study participants were HIV positive women attending 12 public and three private facilities providing PMTCT and EmONC. We used proportionate allocation in selecting public and private facilities. A ratio 4:1 public to private was used by considering the fact that over 80% of the pregnant women in the city received care from public health facilities. Then individual health facilities were selected on the basis of high client flow and to have representation of all the 10 sub-cities. In 2009 alone, 1,976 pregnant women were diagnosed HIV positive in the PMTCT programmes across the city and approximately 25% were diagnosed in the first quarter of 2009 (January to March). Of the 479 women diagnosed from January to March, 282 (59%) women who consented to be followed up were enrolled in our study. At enrolment, women were interviewed by trained PMTCT counsellors at the respective health facilities, using a structured questionnaire. Follow up data were obtained from the women themselves and from log books in the facilities. For women who were transferred to other health facilities and for those who gave birth at home, follow up data about the delivery were collected when they came for six or 42 days postpartum care. Reasons for transferring the women between health facilities both before and after the onset of labour were inquired in an open ended question. Later these responses were coded into three categories: Obstetric complications, practical constraints (including lack of bed and lack of electric power supply) and reason not stated. Reasons for the first transfer were obtained from log books at the health centres. Since the reasons for subsequent transfers were not recorded, the women were asked directly what was said to them. Study endpoints were abortion, delivery or death of a woman. Women were regarded as lost to follow-up when they had not shown up for regular visits and or we failed to trace them.

The study was reviewed and approved by the Ethical committee of Addis Ababa City Administration Health Bureau in Ethiopia and the Regional Committee for Medical Research Ethics in Western

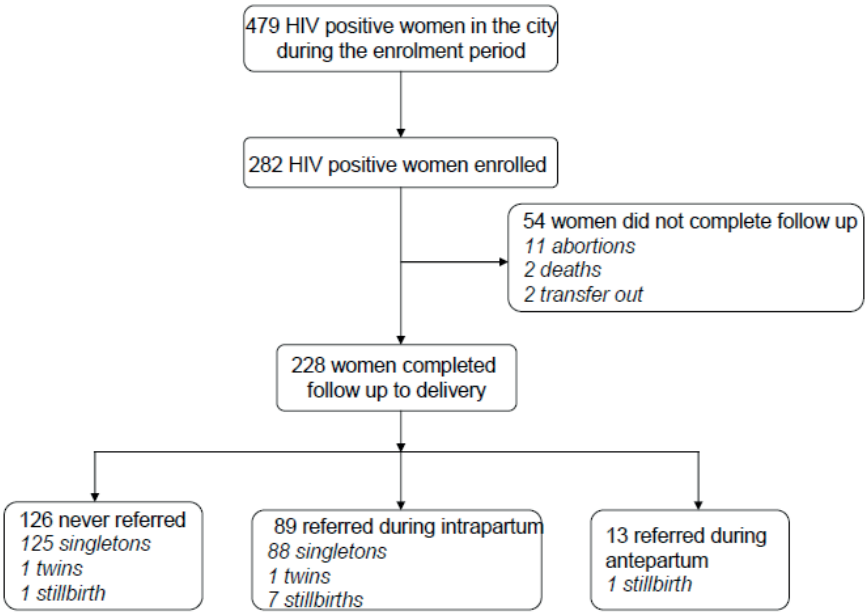


Figure 1. Cohort flow chart.

Norway. Research permits from Addis Ababa City Administration Health Bureau and respective sub cities were obtained. Data were double entered in excel spreadsheet and checked for consistency. Data analyses were done using SPSS version 17. Descriptive statistics and Pearson Chi-Square tests were used to compare baseline characteristics of women who completed their follow up and women who did not. We also used Fisher Exact Test when the expected counts in the cells are less than five. P-values less than 0.05 were considered statistically significant. Odds ratio (OR) with 95% confidence intervals (CI) were used to assess bivariate associations. The rate of institutional delivery was calculated among women enrolled into the study while comparison between transferred and not transferred during the intrapartum period was made only among women who completed the study. The rate of intrapartum transfers was calculated among women who visited health facilities during labour and delivery. The rate of stillbirth was calculated among the total births and stratified by transfer status. Due to the large proportion of women who did not complete their follow up to delivery sensitivity analyses were done to assess potential biases.

RESULTS

Of a total of 282 HIV positive pregnant women, 228 (81%) completed their follow up to delivery. There were 226 singletons and two twin births. Among the 54 women who did not complete their follow up, 11 (20%) had an abortion, 2 (4%) died while pregnant, 2 (4%) were transferred to other health facilities, whereas about the rest 39 (72%) we have no information (Figure 1).Table 1 presents characteristics of the HIV positive women stratified by follow up status. The age range was 15 to 38 years. The median educational status of the women were seventh grade (Inter quartile range (IQR) = 3 to 7). One third (33%) of the women were pregnant for the first time. The majority of the women (66%) were enrolled at 28 weeks of gestation or earlier and had a CD_4 count of 350 and above at enrolment. A total of 214 women were tested for Venereal Disease Research Laboratory (VDRL) and six (2.8%) were reactive for syphilis. There was no statistically significant difference between women who completed their follow up and women who did not with respect to their socio-demographic characteristics, obstetric profiles and CD_4 cell count, gestational age at enrolment and the women syphilis test result (Table 1).

Among the 282 HIV positive women enrolled, 211 (75%, 95% confidence interval (CI) 69.4 to 79.5) gave birth at health facilities. One hundred and two (48%, 95% CI 41.7 to 55.0) women were transferred between health facilities before or after the onset of labour, 89 (42%, 95% CI 35.7 to 48.9) being transferred during the intrapartum period. Of the 72 (34%, 95% CI 28.0 to 40.8) women transferred due to obstetric complications, 58 were transferred during the intrapartum period from basic to comprehensive EmONC facilities. Some of the women had multiple intrapartum transfers. The number of transfers for one woman ranged from one to ten, where 57 (64%) were transferred once, 17 (19%) twice and 15 (17%) were transferred three times or more. All first time intrapartum transfers were from basic EmONC facilities.

Table 1. Baseline characteristics of 282 HIV positive women in Addis Ababa by follow up status.

Variable	Completed follow up		P-value
	Yes = 228	No = 54	
	n (%)	n (%)	
Age			
15-24	79 (35.3)	20 (37.0)	
25-29	91 (40.6)	20 (37.0)	0.89
≥30	54 (24.1)	14 (25.9)	
Median (IQR)	25 (23-29)	25 (22-28)	
Education /grades completed			
0 - 4	65 (29.3)	22 (42.3)	
5 - 8	81 (36.5)	17 (32.7)	0.17
≥9	76 (34.2)	13 (25.0)	
Median (IQR)	8 (4-10)	6 (0-9)	
Number of pregnancy			
1	73 (32.4)	19 (35.8)	
2	84 (37.3)	17 (32.1)	0.77
≥3	68 (30.2)	17 (32.1)	
Median (IQR*)	2 (1-3)	2 (1-3)	
CD_4 cell count at enrolment			0.80
<200	42 (26.3)	5 (26.3)	
200-349	48 (30.0)	7 (36.8)	
≥350	70 (43.8)	7 (36.8)	
Median (IQR)	312 (186-450)	306 (197-512)	
Gestational age at enrolment (weeks)			
≤28	128 (65.3)	22 (68.8)	0.84
>28	68 (34.7)	10 (31.3)	
Median (IQR)	22 (18-28)	18 (14-28)	
Syphilis test (VDRL)			
Reactive	4 (2.0)	2 (7.1)	
Non-reactive	184 (92.9)	24 (85.7)	0.15
Test not done	10 (5.1)	2 (7.1)	

* IQR, Inter quartile range. Due to missing values, the numbers may not add up to the total.

Obstetric complications and practical constraints accounted for 65 and 25% of the reasons for the first time transfers respectively, while all subsequent transfers were due to practical constraints such as lack of bed and lack of electric power supply. Unavailability of bed was the sole reason for transferring labouring women from public comprehensive EmONC facilities to other health facilities. In the case of transfers due to practical constraints, the transfers were made between facilities irrespective of the level of care provided in those facilities and often the women were not given a referral slip but were informed verbally to go to other facilities.

Women in their second pregnancy were less likely to be transferred during the intrapartum period compared to women who were pregnant for the first time (OR 0.3 95% CI 0.2 to 0.6). There was no significant association between being transferred during the intrapartum period and age, education, CD_4 cell count and gestational age at enrolment (Table 2). To account for the 19% of women who did not complete their follow up, sensitivity analyses were performed in two scenarios, (1) considering all these women as transferred during the intrapartum period, and (2) considering all these as not transferred during the intrapartum period. Both scenarios yield similar result to the main analysis.

Of the 193 singleton newborns whose birth weight was

Table 2. Bivariate association between transfer during the intrapartum period and age, education, number of pregnancy, CD_4 cell count and gestational age among 228 HIV positive pregnant women in Addis Ababa.

Variable	Transferred during the intrapartum period		OR
	Yes =89	No=139	
	n (%)	n (%)	
Age			
15-24	28 (35.4)	51 (64.6)	1
25-29	39 (42.9)	52 (57.1)	1.4 (0.7- 2.5)
≥30	20 (37.0)	34 (63.0)	1.1 (0.5 - 2.2)
Education			
0 – 4	21 (32.3)	44 (67.7)	1
5 – 8	34 (42.0)	47 (58.0)	1.5 (0.8 - 3.0)
≧9	30 (39.5)	46 (60.5)	1.4 (0.7 - 2.7)
Number of pregnancy			
1	39 (53.4)	34 (46.6)	1
2	22 (26.2)	62 (73.8)	0.3 (0.2 - 0.6)
≥3	26 (38.2)	42 (61.8)	0.5 (0.3 - 1.1)
CD_4 cell count			
≥350	29 (41.4)	41 (58.6)	1
200-349	16 (33.3)	32 (66.7)	1.2 (0.5-2.5)
<200	19 (45.2)	23 (54.8)	0.7 (0.3-1.5)
Gestational age (weeks)			
≤28	54 (42.2)	74 (57.8)	1
>28	28 (41.2)	40 (58.8)	1.0 (0.5 - 1.7)

Due to missing values, the numbers may not add up to the total

measured, the median birth weight was 3,000 g (IQR 3,200 to 2,500). No preterm deliveries were reported. Transfer during the intrapartum period was not significantly associated with birth weight. Of the total of nine stillbirths (corresponding to 39 stillbirths per 1,000 births, 95% CI 19.2 to 73.7 per 1,000 births), seven occurred among the women transferred during the intrapartum period, one among the women transferred during the antepartum period and one among the women who were not transferred. Seven stillbirths were among women who were non reactive to VDRL test for syphilis, one among women who did not have VDRL test whereas no still birth among women who were reactive to VDRL test. All the stillbirths were among women who had spontaneous vaginal delivery. Three stillbirths were weighed, and all of them were within the range of 2,500 to 3,900 g. Five stillbirths were registered among women with CD_4 cell count at enrolment of 350 and above and two stillbirths were registered among women with CD_4 cell count at enrolment between 200 and 349. No stillbirth was registered among women with CD_4 cell count less then 200. Two stillbirths were registered among the 73 women who initiated antiretroviral therapy while seven among the 139 women initiated zidovudine prophylaxis (OR = 2.0, 95% CI 0.4 to 5.0).

DISCUSSION

A cohort of HIV positive women was followed to assess the magnitude of intrapartum transfers and its potential adverse outcomes. We identified serious challenges within the health care system compromising the intrapartum care for HIV positive women and increasing the risk of adverse pregnancy outcomes and risk of MTCT. Even though safe obstetric practice has been one of the components of the PMTCT programme in all the study sites, the risk of MTCT due to delays in receiving obstetric care during labour did not seem to be an issue that received sufficient attention in the health care system. Our findings show that the majority of the HIV positive women visited EmONC facilities for delivery. However, a large proportion of them did not receive appropriate obstetric care due to transfers between

health facilities. While, obstetric complications were the major reason for first time transfer, practical constraints were the sole reason for subsequent transfers. Undue transfers leading to the so called "third delay", that is, the delay in receiving appropriate care after reaching a health facility and this may have contributed to an increased risk of stillbirth and MTCT. The HIV disease progression, initiating ART and having a positive syphilis test result seemed not to be related to the risk of stillbirth.

Our findings suggest that delays in receiving appropriate care after arrival at health facility is a common experience among HIV positive women seeking birth care in Addis Ababa. This seems to a considerable extent related to transfers between health facilities during established labour. Overall, 48% of the pregnant women were transferred to other health facilities either before or after the onset of labour, 42% were transferred during the intrapartum period, and 34% were transferred due to obstetric complications. In general, compared to the 19% referrals for complications related to pregnancy and labour reported from a multi country survey across nine Asian countries and the 15% obstetric complications expected to happen during pregnancy, labour, delivery and during the postnatal period, the rate of transfer in our study is high (WHO et al., 2009; Lumbiganon et al., 2010). The risk of intrapartum transfer was lower among women in their second pregnancy than among women who were pregnant for the first time, and this corresponds to a higher risk of obstetric complications such as pre-eclampsia and dystocia among primigravidae (Duckitt and Harrington, 2005).

The high rate of transfer in this study seems to be related to deficiencies within the health care system. In Addis Ababa city where the study was conducted, availability and accessibility of EmONC facilities was not an issue, but access to care and the quality of care provided in those facilities (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). Efficient functioning of a health system can be affected by shortage of supplies, shortage of trained staff, poor competence among available staff and poor staff motivation as well as lack of accountability. Studies from Ethiopia and Tanzania reported that most of the basic EmONC facilities were functioning poorly in terms of the quality of the services they were expected to provide (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). Poor competence among health care providers in basic EmONC facilities may lead to over-diagnosis and failure to handle obstetric complications that could be managed at their level. This argument is supported by the fact that nationally, only 3.3% of the health care workers assisting women in labour had received training in EmONC (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). In their study from Tanzania, Olsen et al. (2004) observed that over-diagnosis was one of the possible reasons for the excess obstetric complications seen in Tanzanian health care facilities. Transfers often cause overburden and fatigue in the already constrained comprehensive EmONC facilities. This in turn affects the quality and quantity of care provided in those facilities and may further increase transfers from comprehensive EmONC facilities. Hence a vicious circle is created. Lack of bed came out as the sole reason for transferring the HIV positive women during the intrapartum period from hospitals. In these comprehensive EmONC facilities, a minimum of 30 to 32 beds including delivery couches are recommended for 1,000 deliveries per year (WHO, 1991), yet the available beds including delivery couches for 1,000 deliveries per year in Addis Ababa were 22, much lower than the minimum requirement (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank; WHO et al., 2009). Therefore, reducing the work load at comprehensive EmONC facilities by limiting unnecessary transfers from basic EmONC facilities and having a functioning referral system with reliable ambulance services are some of the fundamental prerequisites for improved maternal and perinatal outcomes in Addis Ababa.

One can also associate the high rate of transfer to the HIV disease progression of the women. According to studies, asymptomatic HIV-positive women do not have a higher risk of obstetric complications than HIV-negative women and they do not require special obstetric interventions (Bucceri et al., 1997; Coley et al., 2001; Onah et al., 2007). Our finding showed that about 75% of the women had a CD_4 cell count over 200 and they were asymptomatic. It is therefore difficult to attribute the high rate of intrapartum transfer to the HIV disease progression of the women. Furthermore, in a case control study from Nigeria, the rate of caesarean section was not significantly different among HIV positive cases and HIV negative controls, 8.3 vs 11.0% (Onah et al., 2007).

Whatever the reasons for the transfers, they cause delays in receiving appropriate obstetric care. Of the women transferred during the intrapartum period, 36% were actually transferred more than once while in labour. Multiple transfers of a woman will delay provision of the care needed and may be detrimental to maternal and perinatal survival, as some obstetric complications can claim the lives of the women or their babies within a very short time (Ramanathan, 2009; WHO et al., 2009). According to studies from resource poor settings, the "third delay" significantly contributes to maternal morbidity and mortality (Ramanathan, 2009; Samuel, 2009). Maternal disabilities such as obstetric fistula and incontinence are common consequences of delays in receiving appropriate intrapartum obstetric care for obstructed labour (Ekanem et al., 2010). Although there was no maternal death related to intrapartum transfers in our study, the many transferred women may have suffered consequences of the transfers. In a study from Sweden, women who were transferred after the onset of

labour were more stressed of fear of the unknown and more often had a feeling of rejection than those who were not transferred (Wiklund et al., 2002). Some of the practical challenges experienced by the Swedish women were associated with long distance travel and transportation. This problem is even more important in the Ethiopian context where a major barrier to women's health is their low socio-economic status (CSA, 2006). Over 65% of the women in our study had only 8th grade of schooling or lower. The feeling of being rejected may be a major issue to the women in our study, as HIV/AIDS is still a disease with stigma in Ethiopia. This could affect the trust the women have in the health system and may contribute to disruption in the continuity of care. Transfers during the intrapartum period can also put the women at risk of HIV status disclosure through the information provided in the transfer slips. Furthermore, a serious concern is that the delays caused by the transfers can increase the risk of MTCT both because of delayed labour duration and missing the dose of antiretroviral prophylaxis that should be taken during the intrapartum period.

The delays to receive appropriate care due to intra-partum transfers seem to contribute to adverse prenatal outcomes. The overall rate of stillbirth in our study was 39/1,000 births, where the majority of the stillbirths were among women who were transferred during the intrapartum period. Our finding is consistent with the 31.6 stillbirths per 1,000 births reported in the 2005 Ethiopia demographic and health survey (DHS) for Addis Ababa city but higher than the 21.3 stillbirths per 1,000 births reported for developing countries (CSA, 2006; Goldenberg et al., 2007). This could reflect the sub-optimal intrapartum obstetric care that pregnant women are offered in Addis Ababa despite the city being most privileged in terms of availability and accessibility of skilled attendants at birth as well as EmONC facilities. Report has shown that the "third delay" is common in Addis Ababa and a labouring woman waits on average 1.7 h to receive obstetric care after reaching a health facility (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). Similarly, in a health facility based study from Uganda, the "third delay" was responsible for about half of the perinatal deaths (Waiswa et al., 2010).

Although several risk factors are identified for stillbirths, stillbirths occurring during the intrapartum period can largely be attributed to poor quality obstetric care (Mohammad, 2011; Sidra, 2011). Large scale studies reported an inverse correlation between the rate of stillbirth and the quality and quantity of obstetric care provided during pregnancy and delivery (Goldenberg et al., 2007; McClure et al., 2009). For instance, in Nepal, the rate of stillbirth was 54.6/1,000 births with a 9% Skilled attendant at birth, while in Tanzania 29.4/1,000 births with a 35% skilled attendant at birth. Reviews on interventions to improve maternal and newborns outcome reported that about 25% of intrapartum stillbirths can be reduced by providing skilled attendants at birth (Mohammad, 2011; Sidra, 2011). Nonetheless, this does not seem to be the case in our study, despite 75% of the women being given birth at EmONC facilities in the hands of skilled professionals, the rate of stillbirth was unacceptably high. This could reflect the poor functional status of the EmONC service in the city. In support of this argument, a baseline survey conducted to asses the status of EmONC facilities by the ministry of health of Ethiopia revealed that none of the basic EmONC facilities in the Addis Ababa were fully functional (unpublished data, collected by Addis Ababa Fistula Hospital, Ethiopian Road Authority and the World Bank). Similarly, the 2010 countdown report indicated that maternal mortality and neonatal mortality in Ethiopia have not shown promising decline by the fact that interventions for these problems require properly functioning health care system (Bhutta et al., 2010). Provision of quality basic and comprehensive EmONC can reduce intrapartum stillbirths by about 45 and 75% respectively (Mohammad, 2011; Sidra, 2011).

The stillbirths did not seem to be associated with the HIV disease progression in the women, since no stillbirth was reported among women with CD_4 cell count less than 200, but five among women with CD_4 cell count 350 or more. Similarly, the rate of stillbirth among women initiated antiretroviral therapy was also lower than those initiated zidovudine prophylaxes. A study from Tanzania that followed 1,075 HIV positive and 502 HIV negative pregnant women showed no statistical significant difference between HIV positive and HIV negative women with respect to the rate of stillbirth. By contrast, in a study from South Africa that followed 1,449 HIV infected and 1,401 HIV uninfected women, adverse pregnancy outcomes were in general more prevalent among HIV positive women and in particular among those with lower CD_4 cell count (Rollins et al., 2007). Interestingly, no stillbirth was reported among the four women who had positive test result for syphilis. Although we have limitation to make inference due to small sample size, our finding is in accordance with other studies showing that maternal syphilis as a less likely cause of intrapartum stillbirths (Chalumeau et al., 2002; McClure et al., 2009).

The last, but not least important finding of our study was the high rate of institutional deliveries among HIV positive women. In contrast with the low rate of institutional delivery (43.5%) reported among the general female population in the city (MOH, 2008), 75% of the HIV positive women in our study gave birth at health facilities. Various factors could have influenced the HIV positive women's decision to deliver at health facility. Safe obstetric practice has been promoted for the reduction of MTCT since 2004 (Olsenetal., 2005).

The public health message has been that safe delivery among HIV positive women is delivery in health facilities. The high rate of institutional delivery for HIV positive

women in our study reflects that this message has reached out to the target groups. It may also be an indication of women's high motivation to adhere to health workers' advice to secure an HIV negative status of their baby. Moreover, the high rate of institutional delivery may be partly attributed to the study project activities (Hawthorne effect), with improved communication between the women and their PMTCT counsellors and incentives and more focus on the outcome than in routine care.

One of the limitations of the study is that 19% of the women did not complete their follow up. This might threaten the external validity of the study. The fact that HIV/AIDS is still a disease with stigma, the possibility of abortion among women enrolled in early pregnancy, the low rate of institutional delivery in the city (43.5%) (MOH, 2008) and the high reported dropout rate in a national PMTCT programme (Mirkuzie et al., 2010) were taken into account while considering the sample size. During the follow up, substantial effort were made to trace the lost to follow up through telephone, house to house search using existing tracing mechanisms, visiting different hospitals for transferred women, checking ART clinics and the under five clinics. In the analysis, there were no statistical significant differences in the baseline characteristics between women who completed the study and those who did not. Besides, the losses to follow up were not related to the intrapartum transfers and hence less likely to bias our findings. Moreover, the study covered about 60% of the eligible women and we used proportionate allocation to population size when selecting public and private facilities. Hence, we believe that the findings of this study could still be generalized to HIV positive women who attend antenatal care in Addis Ababa. Yet, there could be a Hawthorne effect that increased the rate of institutional delivery. There is no doubt that the study would be stronger if there was an HIV negative comparison, especially to unveil the role of stigma and discrimination in caring for HIV positive women. The reason for not including a comparison group was that the data were drawn from a cohort study set out to assess HIV positive women's adherence to PMTCT recommendations. The possibility of having a historic cohort for comparison was not feasible as the routine information in the delivery logbooks at the facilities do not indicate the women's HIV status for confidentiality reasons.

In conclusion, this study has drawn attention to the problems of safe delivery practices in a PMTCT programme that seem not to attract the attention it deserves from the health care system and health care workers unlike some of the other PMTCT programme components. The study revealed a high rate of institutional delivery among the HIV positive women that may indicate the women's awareness of the importance of institutional delivery to lower the risk of HIV transmission to their babies. However, despite the expressed goal of reducing maternal and perinatal mortality, the health system appeared unable to take advantage of the HIV positive women's motivation for 'safe delivery'. Meanwhile, due to deficiencies within the health care system, the women's right to appropriate care seem to be violated. Over one third of the HIV positive women were transferred during the intrapartum period, and this could partly be due to over-diagnosis of obstetric complications and practical constraints within the health facilities. This delayed the women from receiving timely obstetric care and may have contributed to adverse pregnancy outcomes and increased MTCT. Especially the basic EmONC facilities that the majority of the women relied on, appeared not to be functioning properly, and may have subjected the pregnant women to unnecessary transfers. Improvement in the quality of obstetric care services in Addis Ababa is imperative for the health system to succeed in reducing the rate of stillbirth and the rate of MTCT. The PMTCT training for health workers should also address the issue of intrapartum transfers and the "third delay" so that HIV positive women's access to appropriate and timely intrapartum obstetric care can be ensured.

ACKNOWLEDGEMENTS

This study was financially supported by the Centre for International Health, University of Bergen, the Meltzer Foundation and Statens Lånekasse, Norway. We thank the Addis Ababa City Administration Health Bureau and the health bureaus' in the respective sub-cities for permitting us to conduct the study. Moreover, we are grateful to all the HIV positive women who particiapted in the study and to all PMTCT service providers who particiapted in the data collection.

REFERENCES

Barnes-Josiah D, Myntti C, Augustin A (1998). The "three delays" as a framework for examining maternal mortality in Haiti. Soc. Sci. Med., 46(8): 981-993.

Bhutta ZA, Chopra M, Axelson H, Berman P, Boerma T, Bryce J, Bustreo F, Cavagnero E, Cometto G, Daelmans B, de Francisco A, Fogstad H, Gupta N, Laski L, Lawn J, Maliqi B, Mason E, Pitt C, Requejo J, Starrs A, Victora CG, Wardlaw T (2010). Countdown to 2015 decade report (2000-10): taking stock of maternal, newborn, and child survival. Lancet, 375(9730): 2032-2044.

Bucceri A, Luchini L, Rancilio L, Grossi E, Ferraris G, Rossi G, Vignali M, Parazzini F (1997). Pregnancy outcome among HIV positive and negative intravenous drug users. Eur. J. Obstet. Gynecol. Reprod. Biol., 72(2): 169-174.

Chalumeau M, Bouvier-Colle MH, Breart G (2002). Can clinical risk factors for late stillbirth in West Africa be detected during antenatal care or only during labour? Int. J. Epidemiol., 31(3): 661-668.

Coley JL, Msamanga GI, Fawzi MC, Kaaya S, Hertzmark E, Kapiga S, Spiegelman D, Hunter D, Fawzi WW (2001). The association between maternal HIV-1 infection and pregnancy outcomes in Dar es Salaam, Tanzania. Bjog, 108(11): 1125-1133.

CSA (2006). Ethiopia Demographic and Health Survey 2005. Addis Ababa: Central Statistical Authority.

De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, Alnwick DJ, Rogers M, Shaffer N (2000). Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. Jama, 283(9): 1175-1182.

Duckitt K, Harrington D (2005). Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. Bmj, 330(7491): 565.

Ekanem EI, Ekanem AD, Ekabua JE, Etuk SJ, Essiet A (2010). Review of obstetrics genito-urinary fistulae in the University of Calabar Teaching Hospital Calabar, Nigeria. Niger. J. Clin. Pract., 13(3): 326-330.

FHAPCO (2010). Annual Performance Report of Multisectoral HIV/ AIDS Response 2002 E.C. (2009/2010). Addis Ababa: Federal HIV/AIDS Prevention and Control Office.

Gaillard P, Verhofstede C, Mwanyumba F, Claeys P, Chohan V, Mandaliya K, Bwayo J, Plum J, Temmerman M (2000). Exposure to HIV-1 during delivery and mother-to-child transmission. Aids, 14(15): 2341-2348.

Goldenberg RL, McClure EM, Bann CM (2007). The relationship of intrapartum and antepartum stillbirth rates to measures of obstetric care in developed and developing countries. Acta Obstet. Gynecol. Scand., 86(11): 1303-1309.

Lumbiganon P, Laopaiboon M, Gülmezoglu AM, Souza JP, Taneepanichskul S, Ruyan P, Attygalle DE, Shrestha N, Mori R, Nguyen DH, Hoang TB, Rathavy T, Chuyun K, Cheang K, Festin M, Udomprasertgul V, Germar MJ, Yanqiu G, Roy M, Carroli G, Ba-Thike K, Filatova E, Villar J (2010). Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08. Lancet, 375(9713): 490-499.

McClure EM, Saleem S, Pasha O, Goldenberg RL (2009). Stillbirth in developing countries: a review of causes, risk factors and prevention strategies. J. Matern. Fetal. Neona. Med., 22(3): 183-190.

Mirkuzie AH, Hinderaker SG, Mørkve O (2010). Promising outcomes of a national programme for the prevention of Mother-to-Child HIV transmission in Addis Ababa: a retrospective study. BMC Health Serv. Res., 10: 267

MOH (2008). Health and Health related indicators. Addis Ababa: Ministry of Health.

MOH (2010). Health and Health related indicators. Addis Ababa: Ministry of Health.

Mohammad YY, Mahrukh AA, Mohammad UA, Aamer I, Joy EL, Nynke VB, Zulfiqar AB (2011). The effect of providing skilled birth attendance and emergency obstetric care in preventing stillbirths. BMC Public Health, 11(3).

Olsen ØE, Ndeki S, Norheim OF (2004).Complicated deliveries, critical care and quality in emergency obstetric care in Northern Tanzania. Int. J. Gynaecol. Obstet., 87(1): 98-108.

Olsen ØE, Ndeki S, Norheim OF (2005). Availability, distribution and use of emergency obstetric care in northern Tanzania. Health Policy Plann., 20(3): 167-175.

Onah HE, Obi SN, Agbata TA, Oguanuo TC (2007). Pregnancy outcome in HIV-positive women in Enugu, Nigeria. J. Obstet. Gynaecol., 27(3): 271-274.

Ramanathan M (2009). Addressing the 'third delay' in maternal mortality: need for reform. Indian J. Med. Ethics, 6(4): 211-212.

Read JS, Newell MK (2005). Efficacy and safety of cesarean delivery for prevention of mother-to-child transmission of HIV-1. Cochrane Database Syst. Rev., (4): CD 005479.

Rollins NC, Coovadia HM, Bland RM, Coutsoudis A, Bennish ML, Patel D, Newell ML (2007). Pregnancy outcomes in HIV-infected and uninfected women in rural and urban South Africa. J. Acquir. Immune. Defic. Syndr., 44(3): 321-328.

Samuel H, Fikre E, Yemane B (2009). Health facility-based maternal death audit in Tigray, Ethiopia. Ethiop. J. Health Dev., 23(2): 115-119.

The International Perinatal HIV Group (1999). The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1-a meta-analysis of 15 prospective cohort studies. The New England J. Med., 340(13): 977-987.

Waiswa P, Kallander K, Peterson S, Tomson G, Pariyo GW (2010). Using the three delays model to understand why newborn babies die in eastern Uganda. Trop. Med. Int. Health, 15(8): 964-972.

WHO (1991). Essential elements of obstetric care at first referral level. Geneva: World Health Organization.

WHO (2005). The World Health Report 2005: make every mother and child count. Geneva: World Health Organization.

WHO (2006). The World Health Report 2006 : working together for health. Geneva: World Health Organization.

WHO, UNFPA, UNICEF, AMDD (2009). Monitoring emergency obstetric care : a handbook. Geneva: World Health Organization.

Wiklund I, Matthiesen AS, Klang B, Ransjö-Arvidson AB (2002). A comparative study in Stockholm, Sweden of labour outcome and women's perceptions of being referred in labour. Midwifery, 18(3): 193-199.

Annex 2a: Ethical clearance

UNIVERSITY OF BERGEN
Regional Committee for Medical and Health Research Ethics, Western-Norway

To whom it may concern

Your ref	Our ref	Date
	255.08	17.12.08

Confirmation;

We hereby confirm that the project "Challenges to PMTCT service utilization in Addis Ababa, Ethipoia", by professor Odd Mørkve, Centre for International Health, University of Bergen, is reviewed and approved by the Regional Committee for Medical and Health Research Ethics, Western-Norway (Institutional Review Board).
Our approval is however conditioned upon the following:

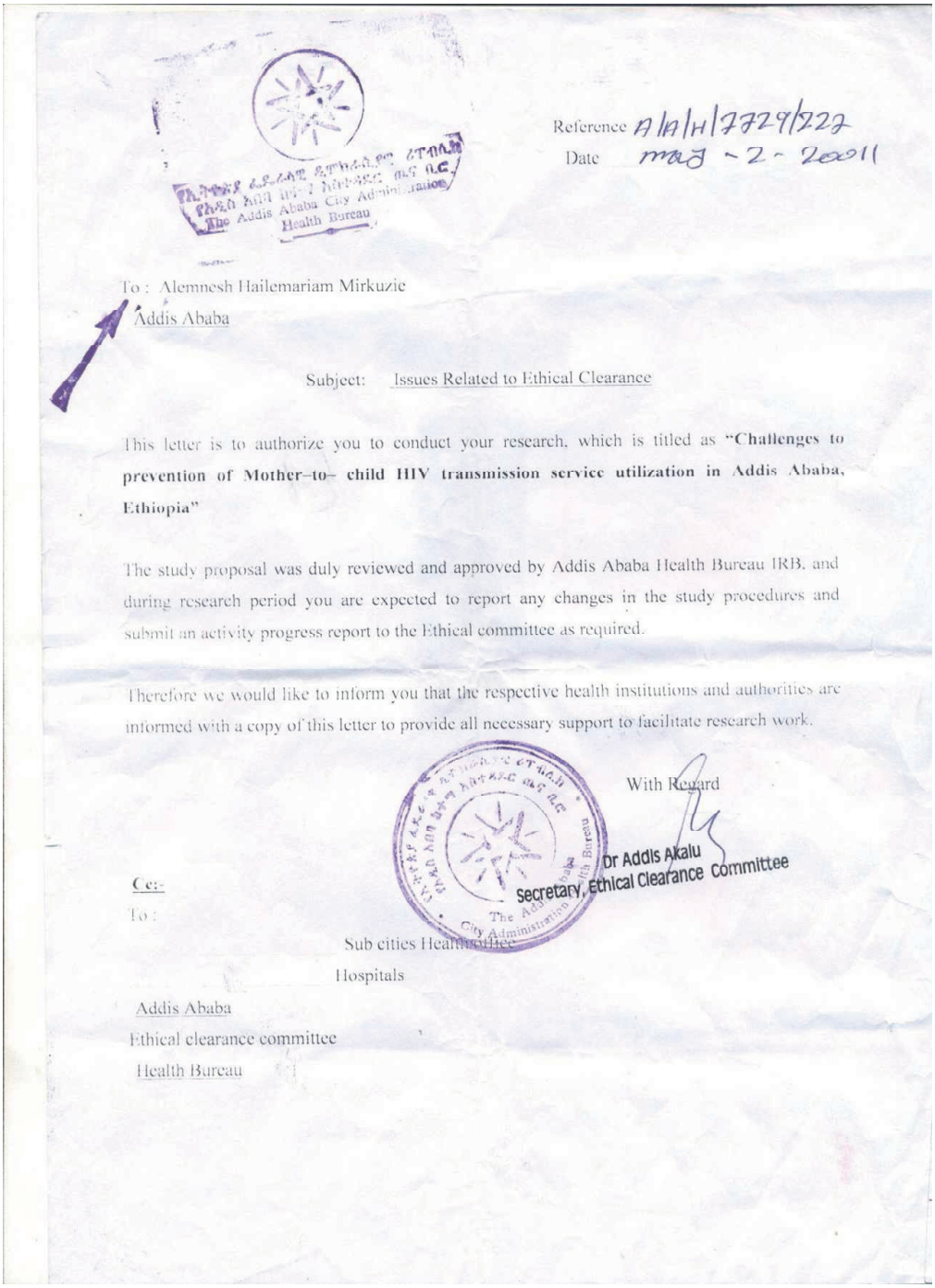
- Interviews are not to be held in the homes of the participants.
- It must me optional for the participants whether or not to answer questions regarding religious affiliation.
- The information letter to the participants must explicitly state that one of the main goals of this project is to facilitate uptake of anti-retroviral prophylaxis among *infants* of mothers with HIV.
- The phrase "I understand" in the consent form must be cut out.

Sincerely yours

Øystein Svindland
Committee secretary

REK VEST
HAUKELAND UNIV. SYKEHUS
Postboks 8704
5020 Bergen

Annex 2b: Ethical clearance



የአዲስ አበባ ከተማ አስተዳደር ጤና ቢሮ
The Addis Ababa City Administration Health Bureau

Reference አ/አ/ጤ/7729/222
Date ማይ -2- 2011

To : Alemnesh Hailemariam Mirkuzie
Addis Ababa

Subject: Issues Related to Ethical Clearance

This letter is to authorize you to conduct your research, which is titled as **"Challenges to prevention of Mother–to– child HIV transmission service utilization in Addis Ababa, Ethiopia"**

The study proposal was duly reviewed and approved by Addis Ababa Health Bureau IRB, and during research period you are expected to report any changes in the study procedures and submit an activity progress report to the Ethical committee as required.

Therefore we would like to inform you that the respective health institutions and authorities are informed with a copy of this letter to provide all necessary support to facilitate research work.

With Regard

Dr Addis Akalu
Secretary, Ethical Clearance Committee

Cc:-
To :
Sub cities Health office
Hospitals
Addis Ababa
Ethical clearance committee
Health Bureau

Annex 3a: Information letter for the questionnaire interview

This is a study conducted by Alemnesh Hailemariam Mirkuzie, a student at the Centre for International Health university of Bergen, Norway and a staff of Hawassa University, Ethiopia. She is currently preparing to carry out field work in connection with her PhD study entitled "Challenges to PMTCT service utilization in Addis Ababa". The aim of this study is to contribute to the prevention of mother to child transmission of HIV efforts, and to elevate the understanding of challenges to successful implementation of the PMTCT programme in Ethiopia. The ultimate goal of the project is to enable HIV-positive women and their infants properly follow the PMTCT recommendations. Therefore, all mothers attending antenatal care for the first time in the index pregnancy are invited to participate.

I would like to ask if you would be willing to participate in this study. I would like to ask you about PMTCT, intention, attitude, subjective norm and perceived barriers to HIV testing and previous HIV testing. The interview will take about half an hour. I would like to emphasise that participation in the study is voluntary and that you can withdraw from the research at any time in the research process without any consequences for you whatsoever. If you decide not to continue the interview at some point, you have the right to do so. If you agree to be interviewed, I will take your antenatal number. Any information you give will be confidential and no one identify you. All identifying information will be removed from this questionnaire and destroyed as soon as all data has been collected.

Annex 3b: Information letter and consent form for HIV-positive mothers to be followed up

This is a study conducted by Alemnesh Hailemariam Mirkuzie, a student at the Centre for International Health university of Bergen, Norway and a staff of Hawassa University, Ethiopia. She is currently preparing to carry out field work in connection with her PhD study entitled "Challenges to PMTCT service utilization in Addis Ababa". The aim of this study is to contribute to the prevention of mother to child transmission of HIV efforts, and to elevate the understanding of challenges to successful implementation of the PMTCT programme in Ethiopia. The ultimate goal of the project is to enable HIV-positive women and their infants to properly follow the PMTCT recommendations. Therefore, all HIV-positive women are invited to participate.

I would like to enrol if you would be willing to participate in this study. I would like to follow you up until six weeks after birth. There will be three follow up visits to be held while you come for your routine antenatal check up, delivery service and six week infant check up. I would like to emphasise that participation in the study is voluntary and that you can withdraw from the research at any time in the research process without any consequences for you whatsoever. If you decide not to continue the interview at some point, you have the right to do so. If you are agreed to be interviewed I will take your antenatal number to facilitate follow up. Any information you give will be confidential and no one identifies you. All identifying information will be removed from this questionnaire and destroyed as soon as all data has been collected.

Finally, if you have any questions please ask either during the interview or afterwards.
The study has been explained to me and I agree to participate. I acknowledge that I can withdraw from the study at any time without any consequences.

Date: _____

Signature (thumb print) of participant:_____

Annex 4: Focus group discussion guide

I- Background information

Name _____

Age _____

Marital status _____

Education _____ (grade completed)

Occupation _____

Number of children _____

II- Barriers to HIV testing upon first antenatal attendance

1. What factors or circumstances would make it difficult for you to test for HIV upon first time antenatal attendance?

2. Are there any other issues that come to mind when you think of HIV testing upon first time antenatal attendance?

Annex 5: Questionnaire

PMTCT site _____ Code Number _____

Part I: Demographic and Socioeconomic characteristics

1. Antenatal care number _____
2. How old are you? _____ years
3. Where is your current address? _____
4. What is your marital status?
    a) Single
    b) Married
    c) Divorced
    d) Widowed
5. What is your religion? If you feel comfortable to answer
    a) Orthodox Christian
    b) Protestant Christian
    c) Muslim
    d) Others, specify _____
6. What is the highest level of education you completed? _____
7. What is the highest level of education your husband completed? _____
8. Where are you working?
    a) Government employee
    b) Petty trading
    c) House wife
    d) Others, specify _____
9. What is your husband's occupation?
10. How much is your family's earning per month? _____Eth. Birr
11. How many people are living in your household (including you)

12. What kind of toilet do you have?
    a) Communal pit latrine
    b) Private pit latrine
    c) Communal water carriage
    d) Private water carriage
    e) Others specify _____

13. Do you have fridge?
    a) Yes
    b) No

Part II: Obstetric characteristics

1. How many pregnancies do you ever had? _____
2. How many deliveries do you ever had? _____
3. How many living children do you have? _____
4. Where did you deliver your last child?
    a) Health institutions
    b) En route to health institution
    c) Home
5. How many months pregnant are you now? _____

Part III: Knowledge about MTCT/PMTCT

1. Pregnant women who are HIV infected transmit HIV to their babies
    a) Always
    b) Sometimes
    c) Not at all
    d) I don't know
2. Can an HIV infected mother infect her baby with HIV during pregnancy?

a) Yes

b) No

a) Unsure

3. Can an HIV infected mother infect her baby with HIV during delivery?

a) Yes

b) No

c) Unsure/I don't know

4. Can an HIV infected mother infect her baby with HIV during breast-feeding?

a) Yes

b) No

c) Unsure/I don't know

5. What preventive measures do you know for MTCT?

a) Anti-retroviral prophylaxis

b) Safe delivery practice

c) Not to breast feed

d) Safe sex practice during pregnancy and throughout the breast-feeding period

Part IV: Predicting intention to use PMTCT services – an application of the TPB

Please rate each statement on the extent to which you agree

The following are statements about whether or not you plan to test for HIV upon your first antenatal care attendance (behavioural intention)

1. I intend to test for HIV upon my first antenatal care attendance

5. Very likely

4. Likely

3. Neither likely nor unlikely

2. Unlikely

1. Very unlikely

2. I plan to test for HIV upon my first antenatal care attendance

5. Strongly agree

4. Agree

3. Neither agree nor disagree

2. Disagree

1. Strongly disagree

3. I want to test for HIV upon my first antenatal care attendance

5. Strongly agree

4. Agree

3. Neither agree nor disagree

2. Disagree

1. Strongly disagree

We would like to know how you feel about testing for HIV at your first antenatal care attendance [attitudes]

4. For me testing for HIV upon my first antenatal care attendance is beneficial

5. Strongly agree

4. Agree

3. Neither agree nor disagree

2. Disagree

1. Strongly disagree

5. For me testing for HIV upon my first antenatal care attendance is the right thing to do

5. Strongly agree

4. Agree

3. Neither agree nor disagree

2. Disagree

1. Strongly disagree

6. For me testing for HIV upon my first antenatal care attendance is bad

5. Strongly agree

4. Agree

3. Neither agrees nor disagrees

2. Disagree

1. Strongly disagree

We would like to know how you think that other people who are important to you (such as husband/parents/ friends/neighbour/counsellors) think about you testing for HIV upon your first antenatal care attendance (subjective norms)

8. People who are important to me think that I should test for HIV upon my first antenatal care attendance

5. Completely true

4. True

3. Neither true nor false

2. False

1. Completely false

9. People who are important to me (husband, parent, neighbour, friends, counsellors) would appreciate that I test for HIV upon my first antenatal care attendance

5. Completely true

4. True

3. Neither true nor false

2. False

1. Completely false

50. My husband agreed that I should test for HIV upon my first antenatal care attendance

5. Completely true

4. True

3. Neither true nor false

2. False

1. Completely false

11. Women who I know and who are important to me would themselves test for HIV upon their fist antenatal care attendance

5. Completely true

4. True

3. Neither true nor false

2. False

1. Completely false

We would like to know how easy or difficult you think it is for you to test for HIV upon your first antenatal care attendance (perceived behavioural control)

12. How easy or difficult do you think it will be for you to test for HIV upon your first antenatal care attendance

5. Very easy

4. Easy

3. Neither easy nor difficult

2. Difficult

1. Very difficult

13. For me to test for HIV upon my first antenatal care attendance is difficult because I feel scared to know the result

5. Completely certain

4. Certain

3. Neither certain nor uncertain

2. Uncertain

1. Completely uncertain

14. For me to test for HIV upon my first antenatal care attendance is difficult because I do not want to disclose my HIV status

5. Completely certain
4. Certain
3. Neither certain nor uncertain
2. Uncertain
1. Completely uncertain

15. For me to test for HIV upon my first antenatal care attendance is difficult because I suspect that test results will not be kept confidential

5. Completely certain
4. Certain
3. Neither certain nor uncertain
2. Uncertain
1. Completely uncertain

16. For me to test for HIV upon my first antenatal care attendance is difficult because people may discriminate me if I found HIV-positive

5. Completely certain
4. Certain
3. Neither certain nor uncertain
2. Uncertain
1. Completely uncertain

Part V: Perceived risk

1. How likely do you think that you are already infected with HIV?

5. Very likely
4. Likely
3. Neither likely nor unlikely

2. Unlikely

1. Very unlikely

2. How likely do you think that you can transmit HIV to your infant?

5. Very likely

5. Likely

3. Neither likely nor unlikely

2. Unlikely

1. Very unlikely

Part VI: Past HIV testing behaviour

1. How many times have you been tested for HIV during the previous years?

1. Four or more times

2. Three times

3. Two times

4. Once

5. Never been tested before

2. How many times have you been tested for HIV with your partner/husband?

1. Four or more times

2. Three times

3. Two times

4. Once

5. Never tested together with my partner/husband

Part VII: Follow up questions to be filled by PMTCT counsellors

1. Did mother receive pre-test counselling/information?

a) Yes

b) No

2. If yes, specify the type

    a) Group pre-test information

    b) Individual pre-test counselling

3. Did the mother tested for HIV?

    a) Yes

    b) No

4. If the mother got tested, what was the test result?

    a) Positive

    b) Negative

5. Did the mother receive post-test counselling?

    a) Yes

    b) No

Annex 6: Follow up format

Follow up format for mothers enrolled in the cohort study Name of PMTCT centre

1. Card number _____

2. Address: Sub - city _____Kebele _____House/telephone number

3. Confidentiality code _____

4. Age _____years

5. Gestational age at enrolment to the study _____weeks

I. Ante-partum data

6. Date of HIV testing _____

7. Date of enrolment to the study _____

8. CD4 count at enrolment _____cells per micro liter

9. VDRL(syphilis test) result

    1) Reactive

    2) Non-reactive

    3) Not done

10. Did the mother initiate prophylaxis at first antenatal visit?

    1) Yes

    2) No

11. Gestational age at prophylaxis initiation _____weeks

12. What kind of prophylaxis regimen did the mother initiate during pregnancy?

    1) Combined Zidovudine

    2) Single dose nevirapine

    3) Lifelong ART

    4) None

13. Which infant feeding options has the mother counselled on?

    1) Exclusive breast-feeding

    2) Exclusive formula feeding

    3) Both

    4) None

14. Was the mother referred for treatment, care and support?

    1) Yes

    2) No

    3) Refused or not applicable

15. Did the mother notify her partner about her HIV status?

    1) Yes

    2) No

16. Did the mother bring her partner for HIV counselling and testing?

    1) Yes

    2) No

17. Has the partner ever tested for HIV?

    1) Yes

    2) No

18. What was partner's HIV test result?

    1) Positive

    2) Negative

II. Prophylaxis adherence at 36 weeks gestation

19. How many doses of prophylaxis medication the mother missed in the last week?

    1) Never missed

    2) One dose

3) Two doses

4) More than two doses

III. Intra-partum data

20. Date of delivery

21. Place of delivery

1) Health institution

2) Home

3) Others (specify) _____

22. Did the mother ingest medication during labour?

1) Yes

2) No

23. What type of prophylaxis medication did she ingest during labour?

1) Zidovudine + lamivudine + single dose nevirapine

2) Zidovudine only

3) Single dose nevirpaine

4) Highly active antiretroviral treatment

5) None

24. Mode of delivery

1) Spontaneous vaginal delivery

2) Caesarean delivery

3) Instrumental delivery

4) Others (specify) _____

25. Was episiotomy performed during delivery?

1) Yes

2) No

26. Was the amniotic membrane ruptured artificially?

    1) Yes

    2) No

27. Infant birth weight _____grams

28. Sex of infant _____

29. What was the infant status at birth?

    1) Live birth

    2) Still birth

30. If the infant was alive, when did the infant ingest the prophylaxis (date)?_____

31. What kind of prophylaxis the infant ingested at birth?

    1) Zidovudine + single dose nevirapine

    2) Single dose nevirapine

    3) None

32. Which infant feeding decision has been made by the mother?

    1) Exclusive breast-feeding

    2) Exclusive formula feeding

    3) Mixed feeding

    4) Others (specify)

IV. Post-partum data

33. Has the mother disclosed her HIV-positive status to her partner?

    1) Yes

    2) No

34. Has the mother ever used condom after knowing her HIV-positive status?

    1) Yes

    2) No

35. If yes for question # 34, how often?

    1) Always

    2) Occasionally

    3) Never

36. Did the mother get transferred between facilities during delivery?

    1) Yes

    2) No

37. If yes to question number 36, how many times she was transferred? _____

38. What was the reason for the transfers? _____

39. How long the mother took the prophylactic medication before birth? _____

40. How long the mother took the prophylactic medication after birth?

41. How long the infant prescribed the prophylactic medication?

42. Which infant feeding practice did the mother report?

    1) Exclusive breast-feeding

    2) Exclusive formula feeding

    3) Mixed feeding

43. If the mother is exclusively breast-feeding, for how long she intends to continue? _____months

44. How was the breast condition of the mother?

    1) Normal

    2) Cracked nipple

    3) Mastitis

    4) Breast abscess

    5) Others (specify)

45. Did the infant ever experienced feeding difficulty?

    1) Yes

    2) No

46. How was the oral condition of the infant?

1) Normal

2) Inflamed (sore)

3) Others (specify) _____

47. Did the infant receive the first pentavalent vaccine at six weeks postpartum?

1) Yes

2) No

48. How many grams the infant weighed at six weeks postpartum? _____grams

49. Was a dried blood spot taken at six weeks for early infant diagnosis?

1) Yes

2) No

3) Mother refused the test

50. If early infant diagnosis was done, what was the test result?

1) Positive

2) Negative

3) No test result available

51. If the infant was HIV negative, did the mother intend to continue breast-feeding after having a negative HIV test result?

1) Yes

2) No

3) Not decided

52. Counsellor remark

_____

_____

Annex 7: Errata

Thesis

Page 1, paragraph 1, line 9 “heterosexual” should read “homosexual”

Page 17 figure 4, the figure to the right, the legend in blue colour “HIV positive women” should read “ Mothers who received prophylactic medication” and the legend in red colour “Mothers who received prophylactic medication” should read “HIV positive women”

Page 44, second paragraph line 9, “39/1000 live births” should read “39/1000 births”

Reference 12, “Giuseppe P, Anthony F” should read “Pantaleo G, Anthony F”

Reference 22, “Creek L, Ntumy R …” should read “Creek TL, Ntumy R…”

Reference 23, “Bolu O, Allread V, Creek T, Stringer E, Forna F, Bulterys M, Shaffer N” should read “Bolu OO, Allread V, Creek TL, Stringer E, Forna F, Bulterys M, Shaffer N”

Reference 114, “Jillian JF, Eccles MP…” should read “Francis JJ, Eccles MP …”

Reference 117, “Kenneth JR, Sander G” should read “Rothman KJ, Greeland S”

Reference 119, “Kenneth JR” should read “Rothman KJ ”

Reference 126, “Mohammad YY, Mahrukh AA, Mohammad UA, Aamer I, Lawn. JE, Nynke VB, Zulfiqar AB” should read “Yakoob MY, Ali MA, Ali MU, Imdad A, Lawn JE, van den Broek NR, Bhutta ZA”

Reference number 58 and 126 are the same