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Prevention of Mother-to-Child Transmission of HIV in Pregnant Malawian Adolescents

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Prevention of Mother-to-Child Transmission of HIV
in
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by

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DISSERTATION

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Dedication

This dissertation is dedicated to my spouse, Roberta Acker, who offered constant encouragement and day-to-day support of my academic aspirations: I am so very grateful. This work is also dedicated to my doctoral advisor, Dr. Sally Rankin, who not only provided indispensible support and guidance during my doctoral studies, but also fostered my love of global health by opening up numerous opportunities for work and research in Malawi and elsewhere.

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Abstract

Prevention of Mother-to-Child Transmission of HIV

in Pregnant Adolescents in Malawi

Ellen M. Scarr

The HIV/AIDS epidemic is one of the most significant public health challenges of our times. Interventions have slowed the number of deaths from AIDS and allowed those infected to live longer than was previously possible. While most HIV infections continue to be transmitted via heterosexual sex, vertical transmission from mother to child remains the primary cause of pediatric HIV infections. Prevention of mother-to-child transmission (PMTCT) of HIV is a major focus, with rapid scale up of programs designed to initiate antiretroviral therapy (ART) in all pregnant women.

One group of vulnerable pregnant females is adolescents; few studies have included pregnant HIV-infected adolescents. The purpose of this study was to determine HIV prevalence in a population of pregnant adolescents and elicit the barriers and facilitators of the uptake of PMTCT services in those who were HIV-infected.

A mixed methods study was conducted in Blantyre, Malawi. A survey questionnaire sought demographic and reproductive health information; in-depth interviews were conducted with those who revealed their HIV infection. The interview questions sought to elicit the barriers and facilitators of adhering to PMTCT protocols faced by these participants.

The survey questionnaire determined that the study population had an HIV prevalence of 7.8%, higher than in the general Malawian adolescent population. Those who were orphaned and had a history of forced sexual encounter(s) were more likely to be HIV-infected.

The interviews with HIV-infected pregnant adolescents found that all had revealed their HIV status to at least one family member; two who were married had not told their husbands.

All identified the support they received as important to their adherence to ART. Few barriers to adherence were identified: several mentioned the stigmatization of HIV, but such fears did not preclude their adhering to the PMTCT protocols.

As children who were perinatally infected with HIV live into adolescence, pregnancy will become more common in this population. Identifying the characteristics of adolescent pregnancy complicated by HIV allows health care providers to capitalize on the strengths of this population to prevent HIV infection in their children.

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Abbreviations

3TC: Lamivudine
ABC: Abstinence, Be Faithful, Use Condoms
ABC: Abacavir
AIDS: Acquired Immunodeficiency Syndrome
ANOVA: Analysis of Variance
ART: Antiretroviral Therapy
ARV: Antiretroviral
AZT: Azidothymidine (also known as ZDV)
BID: Twice daily
cART: Combination Antiretroviral Therapy
CDC: Centers for Disease Control and Prevention
CHR: Committee on Human Research
CI: Confidence Interval
CIA: Central Intelligence Agency
COMREC: College of Medicine Research and Ethics Committee
CPT: Clotrimoxazole Preventative Therapy
d4T: Stavudine
DHO: District Health Officer
EFV: Efavirenz
FTC: Emtricitabine
GA: Gestational Age
GAIA: Global AIDS Interfaith Alliance
GDP: Gross Domestic Product
HAART: Highly Active Antiretroviral Therapy
HBM: Health Belief Model
HDI: Human Development Index
HHS: Department of Health and Human Services
HIV: Human Immunodeficiency Virus
HIVNET: HIV Prevention Trials Network
HSV: Herpes Simplex Virus
IDU: Injection Drug Use
IKI: Invest in Knowledge Malawi
IUD: Intrauterine Device
KFF: Kaiser Family Foundation
LBW: Low Birth Weight
LMICs: Low- and Middle-Income Countries
LPV/r: Lopinavir Boosted with Ritonavir
MASAF: Malawi Social Action Fund
MHC: Malawi High Commission
MMR: Maternal Mortality Ratio
MOH: Ministry of Health
MTCT: Mother-to-Child Transmission of HIV
NGO: Nongovernmental Organization
NNRTI: Non-nucleoside Reverse Transcriptase Inhibitor

NRTI: Nucleoside Reverse Transcriptase Inhibitor
NSO: National Statistics Office, Malawi
NVP: Nevirapine
OR: Odds Ratio
PACTG: Pediatric AIDS Clinical Trials Group
PCR: Polymerase Chain Reaction
PEPFAR: President's Emergency Plan for AIDS Relief
PETRA: Perinatal Transmission
PFC: Prefrontal Cortex
PI: Protease Inhibitor
PIH: Pregnancy-Induced Hypertension
PMTCT: Prevention of Mother-to-Child Transmission of HIV
PTD: Preterm Delivery
PTL: Preterm Labor
RNA: Ribonucleic Acid
RR: Relative Risk
SAB: Spontaneous Abortion (Miscarriage)
SBA: Skilled Birth Attendant
sd: Single Dose
sdNVP: Single Dose Nevirapine
SMART: Surveillance Monitoring for ART Toxicities
TAB: Therapeutic Abortion
TB: Tuberculosis
TBA: Traditional Birth Attendant
TDF: Tenofovir
TFR: Total Fertility Rate
TPB: Theory of Planned Behavior
TRA: Theory of Reasoned Action
UN: United Nations
UNAIDS: Joint United Nations Programme on HIV/AIDS
UNDP: United Nations Development Program
UNFPA: United Nations Population Fund
UNICEF: United Nations Children's Fund
USAID: United States Agency for International Development
VCT: Voluntary Counseling and Testing
WHO: World Health Organization
WITS: Women and Infants Transmission Study
ZDV: Zidovudine (also known as AZT)
ZVITAMO: Zimbabwe Vitamin A for Mothers and Babies Project

Chapter I: Significance of the Problem

Human immunodeficiency virus (HIV), the causative organism of Acquired Immune Deficiency Syndrome (AIDS), was discovered in 1981 (Broder & Gallo, 1984; Mims et al., 2004), and since that time, HIV has affected millions of people and become one of the most pressing public health concerns of our time. Approximately 36 million persons have died of AIDS since the early 1980s (United States Department of Health and Human Services [HHS], 2013), and an estimated 35.3 million people are currently living with HIV/AIDS (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2013a). While AIDS cases have been reported in every region in the world, 97% of those living with HIV/AIDS reside in low- and middle-income countries (LMICs; Shetty, 2013). Seventy-one percent of those with HIV live in Sub-Saharan Africa, which has been particularly devastated by the disease (UNAIDS, 2013b): one out of every 20 people is living with HIV (World Health Organization [WHO], 2013b), and AIDS is the number one cause of death (Kaiser Family Foundation [KFF], 2013). The relative risk of death from HIV/AIDS in Africa is higher than that of any other region in the world, seven times higher than in wealthier countries (Patton et al., 2009). Factors that continue to perpetuate the epidemic include wealth inequality (Fox, 2012; Magadi, 2013), the biologic susceptibility of women, multiple sexual partners and transactional sex (Uchudi, Magadi, & Mostazir, 2012), gender inequality, lack of educational opportunities, lack of access to care (Rodrigo & Rajapakse, 2010), and lack of awareness of one's HIV infection (Cherutich et al., 2012).

Chapter II: Review of the Literature

A. Introduction

The purpose of this chapter is to review the literature pertaining to HIV infection in adolescents,[i] adolescent pregnancy, pregnancy in HIV-infected adolescents, and prevention of mother-to-child transmission (PMTCT) of HIV by pregnant HIV-infected adolescents. The contextual setting of interest is Malawi, a country in Sub-Saharan Africa with a persistently high HIV prevalence that is pioneering an aggressive PMTCT program to reach all pregnant women infected with HIV.

B. Search Strategy

The HIV epidemic is decidedly complex, with multidimensional determinants including pathophysiological, behavioral, psychosocial and cultural factors that drive the epidemic. Thus, by necessity, this review of the literature demanded a detailed appraisal of the history of the epidemic and evolution of HIV management from the beginning to present day. Accordingly, a large number of search terms were used to conduct the study. A literature search for relevant articles and studies was conducted using PubMed, Cochrane and CINAHL databases. The websites of the WHO, United Nations Children's Fund (UNICEF), HIVInSite, and Malawi Ministry of Health were also searched for relevant material. Search terms included "Human Immunodeficiency Virus," "HIV," "Acquired Immune Deficiency Syndrome," "AIDS," "biology of HIV," "pathophysiology of HIV," "etiology of HIV," "transmission of HIV," "management of HIV," "pediatric HIV," "perinatal transmission of HIV," "prevention of mother-to-child transmission of HIV," "PMTCT," "sexually acquired HIV," "HIV in Africa," "HIV in Sub-Saharan Africa," and "HIV in Malawi."

[i] For the purposes of this paper, an adolescent is defined as a youth between the ages of 13 and 19.

There is a notable dearth of research on specific strategies to prevent mother-to child transmission (MTCT) in pregnant, HIV-infected adolescents. A literature search for relevant articles and studies of adolescent pregnancy and HIV in adolescents was conducted using the aforementioned databases. Search terms, used singly or in combination, included "adolescents," "adolescent pregnancy," "mother-to-child transmission," "MTCT in adolescents," "prevention of mother-to-child transmission in adolescents," "PMTCT and adolescents," and "adolescent pregnancy in Malawi." A thorough review of the literature conducted in 2010-2011 for the author's qualifying examination initially revealed numerous studies related to PMTCT and adolescents, but when examined closely, nearly every study identified by the search enrolled women aged 18 and older, and results specific to the 18 and 19 year old adolescents (versus the older women in the study) were not stratified by age group. Only four articles concerned with PMTCT in HIV-infected adolescents were identified (Birungi, Obare, van der Kwaak, & Namwebya, 2011; Reynolds et al., 2006; Varga & Brooks, 2008a, 2008b). However, only the first two (Birungi et al., 2011; Reynolds et al., 2006) were actually research studies on the use of PMTCT services by pregnant HIV-infected adolescents (the latter was found on the YouthNet[ii] website and was not published in a professional journal); the two publications by Varga and Brooks (2008a, 2008b) were based on a theoretical case study group discussion with adolescents in South Africa. Subsequent literature searches have revealed that only one additional study on PMTCT in adolescents (Horwood, Butler, Haskins, Phakathi, & Rollins, 2013) has been published since the original search was conducted. Thus, this researcher has concluded that PMTCT in pregnant adolescents is an understudied but significant area for research.

[ii] YouthNet was a five-year program funded by the United States Agency for International Development and led by Family Health International.

C. The HIV Epidemic

i. Global HIV

In June of 1981, the first report of what would later be identified as HIV was published in the United States (Centers for Disease Control, 1981): five young homosexual men in Los Angeles had been diagnosed with a rare pneumonia caused by *pneumocystis carinii*. More reports from California and New York followed, identifying a previously unrecognized syndrome characterized by profound immunosuppression, including such conditions as Kaposi's sarcoma, cytomegalovirus, and *Mycobacterium avium* complex; the virus was not identified until 1983 (Fauci, 2008). Initially regarded as a "gay disease," affecting only men who have sex with men, the epidemic soon was recognized as impacting other marginalized groups, including injection drug users, sex workers, and heterosexuals. The first cases in Africa were recognized in 1982, where the illness, called "slim disease" because of the severe wasting that accompanied it, was found to affect both men and women (Serwadda et al., 1985).

While HIV/AIDS had historically been a disease of men who have sex with men in the United States, in other parts of the world women are equally, and in some countries more, affected than men (UNAIDS, 2010b). The feminization of the epidemic is striking. Only 35% of those affected with HIV in the mid-1980s were women (Dworkin & Ehrhardt, 2007); women now account for approximately 52% of persons living with HIV/AIDS globally (KFF, 2013).

HIV/AIDS has now been reported in every country of the world (Central Intelligence Agency [CIA], 2014). The global prevalence peaked in 2000, and has leveled off since 2001 (Bongaarts, Buettner, Heilig, & Pelletier, 2008). The current global prevalence was estimated at 0.8% at the end of 2012 (KFF, 2013).

The United States is the largest donor to the global effort to fight HIV/AIDS, with significant increases in funding in the last decade. In 2011, the U.S. funding represented 59.2% of total international contributions by governments to international AIDS programs (KFF & UNAIDS, 2013). Since 2009, the U.S. has given more than six billion dollars per year to the Global Fund (KFF, 2014). However, funding from global donors has decreased in recent years, and the U.S. president's fiscal year 2014 request is 5% below 2012 levels (KFF, 2014). While LMICs have contributed funds to fight the epidemic in their own countries, there are concerns about the overall slowing of contributions. In 2012, an estimated $18.9 billion dollars funded global HIV programs, far short of the estimated $22 to 24 billion needed for meet the need (KFF & UNAIDS, 2013).

ii. HIV in Sub-Saharan Africa

Sub-Saharan Africa has been disproportionately affected by the HIV epidemic, and continues to be burdened by the majority of new HIV infections (1.6 million in 2012), the majority of children infected with HIV (90% of all pediatric HIV), and the majority of HIV deaths (KFF, 2013; Shetty, 2013). Most HIV transmission in the region occurs via heterosexual sex, although concentrated epidemics are increasingly recognized in men who have sex with men, injection drug users, and sex workers and their clients (Barai et al., 2009; Beyrer et al., 2010; Fay et al., 2011; Papworth et al., 2013; Wolf, Cheng, Kapesa, & Castor, 2013). These are highly stigmatized populations, who face many barriers to accessing care; many do not even know they are infected.

As noted above, women account for 52% of all those living with HIV in the world, but in Sub-Saharan Africa women represent 58% of those infected (KFF, 2013; UNAIDS, 2012b). HIV is now the third most common cause of death in females aged 10 to 24 years, and the

leading cause of death in reproductive-age women (KFF, 2013). Epidemiologic studies in Sub-Saharan Africa have determined that female adolescents and young women are disproportionately affected by HIV/AIDS: young women ages 15 to 24 are up to eight times more likely to be HIV-infected than their male counterparts (UNAIDS, 2010b). Eighty percent of all women in the world with HIV live in Sub-Saharan Africa, while 76% of all 15 to 24 year old HIV-infected females live in Sub-Saharan Africa, mostly in Eastern and Southern Africa (Shetty, 2013; UNAIDS, 2013a). Significantly, HIV prevalence is higher among females than males in nearly every country in Sub-Saharan Africa (UNAIDS, 2010a).

With dramatic increases in funding for HIV/AIDS programs in recent years from the Global Fund to Fight AIDS, Tuberculosis and Malaria, the United States President's Emergency Plan for AIDS Relief (PEPFAR), and other bilateral programs, there have been significant gains in the numbers of HIV-infected persons accessing antiretroviral therapy (ART) in Sub-Saharan Africa. By the end of 2012, an estimated 9.7 million adults and children in LMICs were taking ART as a direct result of this funding (UNAIDS, 2013b). According to the WHO treatment guidelines of 2010, this number represents 61% of those targeted to receive ART by 2015 (WHO, 2010b). However, with the new, expanded WHO treatment guidelines released in 2013, this number represents only 34% of those now eligible to receive ART in LMICs (UNAIDS, 2013b).

This author has spent some time in Malawi, where the AIDS epidemic remains a significant cause of morbidity and mortality. Presented here is background on Malawi to familiarize the reader with the health issues confronting the country.

iii. HIV in Malawi

Malawi is a small, impoverished and under-resourced country located in the south-central region of Sub-Saharan Africa and landlocked by Mozambique, Zambia and Tanzania. Malawi has a population of 16.7 million persons, 65% of whom are under the age of 24: the median age of the population is 17.3 years (CIA, 2014). In Malawi, 74% of the population lives below the national income poverty level: personal income averages $774 US per year (United Nations Development Programme [UNDP], 2013b).

Malawi's Human Development Index (HDI)[iii] of 170 (out of 187) is one of the lowest in the world (HDI 0.418; UNDP, 2013a). Although slowly making improvements in health and other HDI indicators, the country still lags behind the average HDI of all of Sub-Saharan African countries as well as the rest of the world (UNDP, 2013b). Increasingly poor governance and allegations of widespread political corruption, coupled with a heavy reliance on foreign aid, a huge debt burden ($1.23 billion in 2011, 39.3% of gross domestic product [GDP]), a lack of natural resources (e.g., oil, mineral deposits, natural gas), and stagnant economic growth have made Malawi one of the poorest countries in the world (CIA, 2011; Whiteside, 2008). An estimated 85% of the population lives rurally (CIA, 2014; Mizere, 2009), with most people relying on subsistence farming for survival; the largest commercial enterprises, tea plantations and tobacco production, are primarily owned by British and American companies.

Malawi remains one of the countries in Sub-Saharan Africa particularly affected by HIV/AIDS (United States Agency for International Development [USAID], 2010). The first case of HIV in Malawi was diagnosed in 1985 (National Statistics Office [NSO], 2010). HIV prevalence reached its peak in 1999 with an estimated national prevalence of 16.4% (Munthali,

[iii] The Human Development Index is a composite index comprised of life expectancy, educational achievement, and gross national income per capita (UNDP, 2011).

Maleta, Chitonya, & Ndawala, 2009; NSO, 2010). Since that time, HIV prevalence has declined slowly, but today continues to be unacceptably high, at an estimated rate of 11%, ninth highest in the world; 1.1 million Malawians were living with HIV/AIDS in 2012 (Angotti, Dionne, & Gaydosh, 2010; NSO, 2010).

As in other countries in Sub-Saharan Africa, the epidemic in Malawi is feminized. In the years between the 2004 and 2010 Malawi Demographic and Health Surveys, the HIV prevalence rate in the general population fell from 11.8% to 10.6% (NSO, 2010). However, there was minimal decline for women, who have an HIV prevalence rate of 12.9%, compared to an 8.1% prevalence in males (NSO, 2010).

Young Malawian females have been disproportionately infected by HIV. A recent government progress report highlights young women aged 15 to 19, who have an HIV prevalence rate of 4.2%, more than three times that of their male counterparts (Malawi Government, 2012). Similarly, in young people aged 15 to 24, the female HIV prevalence rate is 5.2%, 2.7 times that of males in the same age group (Malawi Government, 2012). Young people age 15 to 24 have the highest rate of new HIV infections in Malawi (Munthali et al., 2006).

The primary mode of HIV transmission in Malawi, as in other countries of Sub-Saharan Africa, is heterosexual transmission. In a report presented to the Malawian National AIDS Commission, Munthali and colleagues (2009) determined that the majority of new infections were occurring via "low risk" or casual heterosexual contact (particularly among youth under the age of 25), and the 2012 progress report continues to identify this as the main source of new infections (Malawi Government, 2012). Drivers of the epidemic in Malawi are no different than those found in other highly impacted countries, and include multiple and concurrent sexual relationships, unprotected sex in discordant couples, low/inconsistent condom use, a very low

uptake of male circumcision (2%), gender inequality and low socioeconomic status of women, a high prevalence of transactional sex, stigmatization of HIV, and late initiation of ART (National AIDS Commission, 2012; UNAIDS, 2013b). In 2012, there were an estimated 55,000 new HIV infections and 46,000 deaths in Malawi (UNAIDS, 2013b).

Although most HIV in Malawi is spread through heterosexual contact, the contribution of maternal-to-child transmission of HIV is not insignificant. In 2011, an estimated 63,500 pregnant women were living with HIV in Malawi (United Nations Children's Fund [UNICEF], 2012b). HIV prevalence rates from antenatal clinic surveillance studies have shown a decrease since the early days of the epidemic, when areas of the country reported HIV prevalence rates as high as 27.6% in pregnant women; in 2010, the median HIV prevalence among all pregnant women was 10.6%, and 5.8% in pregnant adolescents aged 15 to 19 (Malawi Government, 2012). Thus, while improving, perinatal transmission of HIV remains a significant risk in Malawi. Although new pediatric infections have been reduced by at least 50%, 11,000 children in Malawi were infected with HIV through MTCT in 2012 and an estimated 100,000 children are in need of ART for their own health (UNAIDS, 2013b).

Countries with a low HDI, such as Malawi, have been found to have higher rates of maternal and infant mortality, in addition to lower rates of antenatal care and skilled attendance at birth (Alvarez, Gil, Hernández, & Gil, 2009). The word for pregnancy in Chichewa, the primary tribal language of Malawi, is *pakati*, which translates as "the place between life and death" (Jackson, Johnson, Gebreselassie, Kangaude, & Mhango, 2011, p. 133). The translation is telling, as Malawi's maternal mortality ratio (MMR) is one of the highest in the world. Although disputed by health officials in the country, a study published by Hogan et al. (2010) ranked Malawi's MMR as the third highest in the world, at 1140 per 100,000 live births,

surpassed only by Afghanistan and the Central African Republic. A 2013 report by the WHO estimates the MMR in Malawi is 460 per 100,000 births, 24th highest out of 187 countries (CIA, 2014; WHO, 2013c). HIV infection is a major contributor to Malawi's high MMR, as well as to the high child mortality rate, which is 71 per 1000 live births (38th highest in the world; UNICEF, 2013). Maternal mortality is obviously associated with health system factors, but is also strongly correlated with educational and economic factors (Alvarez et al., 2009).

D. Reproductive Health in Malawi

Malawi has a very high total fertility rate among women of all ages. The most recent Malawi Demographic and Health Survey (NSO, 2010) found that an average woman in Malawi has five to six children during her lifetime (total fertility rate [TFR] of 5.7). Significant gender disparities exist in fertility desires: a Strategic Assessment[iv] conducted by the Malawian Ministry of Health in 2009 reported that women would prefer three or four children at most, while men insist on six or more (Jackson et al., 2011). In many countries of the world, including Malawi, a woman's sole purpose in marriage is to produce children (Nalwadda, Mirembe, Byamugisha, & Fexelid, 2010).

The high TFR is not only driven by gender inequality: access to contraception is problematic. The contraceptive prevalence rate in Malawi is only 42%, and only 38% of women who do not want any more children are using a permanent method of contraception (Jacobstein, Curtis, Spieler, & Radloff, 2013; Van Lith, Yahner, & Bakamjian, 2013). While training of community workers to provide contraceptives, including injectables such as DepoProvera®, is increasing slowly, programs experience frequent stock outs, and clinics and health centers are unable to accommodate the tremendous demand for contraceptive services (J. Downing, personal

[iv] A strategic assessment involves participation by a number of multidisciplinary stakeholders in a qualitative process that includes data generation, analysis, development of recommendations, and national dissemination of consensus guidelines (Jackson et al., 2011).

communication, 4/6/11; Health Policy Initiative and DELIVER Project, 2008; WHO, 2011a). In addition, many male partners are reluctant to give consent for a woman's contraceptive use (although a benefit of injectable contraception is that is can be "hidden" from the partner).

The high fertility rate is also a consequence of a lack of information about contraceptives, coupled with pervasive misconceptions about contraception in many parts of the world, and Malawi is no different in this respect. Condoms continue to be associated with promiscuity and HIV prevention, and not pregnancy prevention. Fear of infertility and loss of libido limit interest in contraceptive use, and side effects such as weight gain and irregular bleeding with injectable methods often leads to discontinuation (Jackson et al., 2011; Randrianasolo et al., 2008).

Oral contraceptives are thought to "burn eggs," accumulate in the body and lead to tumors, including cancer, or prevent pregnancy via abortifacient activity (Nalwadda et al., 2010). The risk of uterine perforation by the intrauterine device (IUD), while rare when inserted by a skilled provider, is also a concern.

A cornerstone of the HIV prevention message in many countries, including Malawi, has been "ABC: Abstain, Be faithful, and use Condoms." Yet condom use remains poor. Rumors persist that condoms are porous, allowing for HIV infection, or that the lubricant impregnated in the condom is itself infectious. Many suggest that the condoms have been infected with HIV by whites, to decimate the African population (Williamson, Parkes, Wight, Petticrew, & Hart, 2009). Importantly, condoms are thought to reduce sexual pleasure for men, which greatly reduces a woman's ability to negotiate condom use (Nobelius et al., 2011).

i. Adolescent Reproductive Health

Sub-Saharan Africa has the lowest contraceptive prevalence rate among the major regions of the world (United Nations [UN], 2010; UN, 2013). Contraceptive uptake among

youth 15 to 19 years of age is poor: use of contraception among adolescents in Sub-Saharan Africa, both married and unmarried, ranges from 3% to 49% according to the United Nations (2012). Among married adolescent females in Sub-Saharan Africa who wish to avoid a pregnancy within the next two years, 67% are using no contraception and 12% are using a traditional method (e.g., periodic abstinence, withdrawal, herbal remedies); 42% of sexually active unmarried adolescent females who do not want to become pregnant are using no contraception and 17% are using a traditional method (Guttmacher Institute, 2010). Not surprisingly, contraceptive knowledge is also lacking in adolescents (Bearinger, Sieving, Ferguson, & Sharma, 2007; Nalwadda et al., 2010). Services provided to adolescents are insufficient, including few choices of contraceptives and inadequate counseling on contraceptive methods, use and side effects; judgmental attitudes and denial of services is also common (Nalwadda, Tumwesigye, Faxelid, Byamugisha, & Mirembe, 2011; Odaga, 2012).

In Malawi, only 20.5% of all 15 to 19 year olds reported *ever* using contraception, with injectables, male condoms, and traditional methods most popular; 90% of all 15 to 19 year olds were using no contraception at the time of the survey (NSO, 2010). Among currently married 15 to 19 year old females, only 28.8% were using any type of contraception, likely a reflection on the cultural expectation to bear a child soon after marriage. Of those using a contraceptive method, injectables (e.g., DepoProvera®) were the most commonly used. Among unmarried sexually active adolescents aged 15 to 19, only 31% were using any method of contraception. Male condoms were used by 26.9%, with only 3.1% using injectables; 68.9% of unmarried sexually active adolescent females were using no method of contraception at all (NSO, 2010).

Complicating the matter are restrictive policies that create barriers for unmarried adolescents to access contraception in many countries, as well as frequent supply interruptions of

reversible methods. Even if adolescents wish to use contraception, access to youth-friendly, confidential reproductive health services is limited. Healthcare providers are known to be judgmental, and the ensuing negative interactions between provider and adolescent preclude ongoing adherence to contraceptive services. There are accounts of providers reporting adolescents who come to the clinic for contraceptives to their parents or husbands (Nalwadda et al., 2010). Unmarried adolescents seeking contraception are stigmatized by providers and others as promiscuous or prostitutes. There are limited choices of methods, frequent stock outs, as noted above (making consistent use of any one particular method impossible), and cost can be a burden for an adolescent.

Even with reliable access to contraception, adolescents in both developed and LMICs are less likely to use contraception consistently, because they do not believe they are at risk of pregnancy, have sex on an irregular basis, and lack information about the risks and benefits of various contraceptive methods. A survey of Malawian 15 to 19 year old contraceptive users found that 49.3% discontinued their contraceptive method within 12 months of use; of these, nearly half had an ongoing but unmet need for pregnancy prevention (Blanc, Tsui, Croft, & Trevitt, 2009). A study conducted in the Karonga District of Malawi found that premarital sex was the "norm" in young women, and that adolescent sexual intercourse is often irregular, inconsistent, or unplanned, and thus unprotected (Crampin et al., 2008).

ii. Sexual Education

Despite the need to prevent sexually acquired infections and unwanted pregnancy, and a stated commitment on the part of the Ministry of Health to improving sexual and reproductive health education and services to the youth of Malawi, progress in this area has been slow. Malawi's *Life Skills Curriculum,* tasked with providing HIV education and prevention skills, has

a limited focus and has been only randomly implemented in schools. The program of "youth-friendly services" begun by the health system in 2007 has had very limited success in providing sexual education and contraceptive services to Malawian adolescents (Jackson et al., 2011). Services notoriously lack confidentiality, are often located in clearly marked family planning clinics, and adolescents report that health care providers are judgmental, even scolding, and refuse to provide the requested services such as contraception or even condoms (Jackson et al., 2011). Health care providers create unnecessary barriers for adolescents seeking reproductive health services, including imposed limitations on disbursal of contraceptives based on age or marital status, or requiring parental permission for such services (Mbizvo & Zaidi, 2010).

A cultural norm that exists in many countries, including Malawi, is the lack of communication about sexual and reproductive matters by parents to their children (Kumi-Kyereme, Awusabo-Asare, Biddlecom, & Tanlé, 2007; Rankin, Lindgren, Rankin, & Ng'Oma, 2005). Thus, adolescents rely on peers for information and to establish norms for sexual behaviors among their social circles. Unfortunately, information about contraception, transmission of sexually transmitted infections, and pregnancy risks is often inaccurate or lacking completely. One program that holds promise is "Sisters to Sisters," a peer-education initiative in Malawi, that seeks to empower girls through sexual and reproductive health education, in order to decrease their vulnerability to sexual coercion, unwanted pregnancy, and HIV infection (UNICEF, 2010).

iii. Unwanted Pregnancy and Abortion

Unintended pregnancy occurs in women who have an unmet need for contraception or experience contraceptive failure. In 2012, an estimated 80 million unintended pregnancies occurred in LMICs, 79% of which were in women with an unmet need for contraception (Singh

& Darroch, 2012). Of all unintended pregnancies, 38% result in unplanned births, 12% in miscarriage, and half end in induced abortion (Singh & Darroch, 2012; Singh, Sedgh, & Hussain, 2010).

However, because of legal restrictions and/or a lack of skilled abortion providers, many of these abortions are unsafe. According to the most recent available data (2008), an estimated 43.8 million abortions occur each year, 49% of which are considered to be unsafe[v] (21.6 million; WHO, 2011b). Eighty-six percent of all abortions take place in LMICs, the majority of which are in Africa (Sedgh et al., 2012). Of abortions performed in the developing world, 55% are considered to be unsafe, versus 49% globally (Shah & Åhman, 2012); most worrisome are abortions that take place in Africa, 97% of which are unsafe (Sedgh et al., 2012). Unsafe abortion accounts for 13% of all maternal deaths (WHO, 2011b).

Of the 21.6 million unsafe abortions that occur each year in the world and in Africa, 15% and 22% respectively are in adolescent females ages 15 to 19 (Shah & Åhman, 2012). While the percentage of unsafe abortions in Africa is somewhat higher in the 20-24 year old age group (29%), nonetheless, adolescents are at substantial risk from an estimated 1.4 million unsafe abortions each year (Shah & Åhman, 2012). This high number of abortions speaks to the lack of contraceptive availability and uptake in this vulnerable population.

Abortion is illegal in Malawi, except in cases where a woman's life is at risk (Davis, 2008; Malawi Penal Code, 1930). However, this exception requires spousal consent and the agreement of two obstetricians, and any attempt on the part of a woman to get an abortion in other cases is punishable by seven to 14 years in prison (Jackson et al., 2011). Such laws are an

[v] An unsafe abortion is defined as a "procedure for termination of an unintended pregnancy done either by people lacking the necessary skills or in an environment that does not conform to minimum medical standards, or both" (WHO, 1992; as cited in Grimes et al., 2006, p. 1908).

antiquated carryover from British colonial law, although similar laws in Britain have long since been overturned (Davis, 2008).

In Malawi, researchers estimated that 52% of all pregnancies were unintended (Levandowski et al., 2013). Calculating the number of abortions, safe and unsafe, is difficult, given the illegality in Malawi. However, Levandowski and colleagues (2013) estimated that 67,300 abortions occurred in Malawi in the year of their study, 2009.

Thus, although illegal, abortion is common yet dangerous in Malawi, with unsafe abortions accounting for 18% of Malawi's high MMR (Bruyn & Banda, 2010; Geubbles, 2006; Levandowski et al., 2013). Unmarried adolescents aged 15 to 19 are most likely to seek an abortion; many procedures are performed by unskilled persons and result in infection and hemorrhage (Davis, 2008). In studies of unsafe abortions, up to 40% of hospital admissions are for post-abortion complications (Davis, 2008; Rasch, 2011; Rasch & Kipingili, 2009; Singh, 2006). Clearly, ensuring consistent access to contraception would decrease unwanted pregnancies.

iv. Adolescent Pregnancy

Pregnancy in adolescents, both married and single, is common throughout the world, particularly in LMICs. An estimated 16 million girls aged 15 to 19 give birth each year, accounting for 11% of all births; approximately 95% of these births occur in the poorest countries (WHO, 2011c). Most adolescent pregnancies occur within the context of marriage, with nearly 100% of pregnant adolescents married in Asia and Northern Africa, yet only 70% of pregnant adolescents are married in Sub-Saharan Africa (WHO, 2008). Nalwadda and colleagues (2010) refer to a widening biosocial gap that is occurring in Africa: the decreasing age of puberty and the increasing age of marriage, which puts adolescent females at an increased

risk of pregnancy outside of marriage. While many sexually active adolescents in LMICs are married, the percentage of those married has declined over time, while the prevalence of sexual activity before marriage has increased (Blanc et al., 2009; Walker, 2012).

The population of adolescent females, ages 10 to 17, is projected to increase by 51% in Sub-Saharan Africa from 2010 (75 million) to 2030 (113 million): by that time, 25% of all young women in the world will live in Sub-Saharan Africa (United Nations Population Fund [UNFPA], 2013b). This population growth has significant implications for adolescent pregnancy rates. As a consequence of low contraceptive prevalence, Sub-Saharan Africa has the highest adolescent pregnancy rate in the world (UNFPA, 2013b). In Sub-Saharan Africa approximately 55% of females have given birth before the age of 20, the highest regional rate in the world (Kirchengast, 2009). This figure may actually underestimate the number of adolescents giving birth, as those under the age of 15 who become pregnant are not listed in the majority of statistics (Kirchengast, 2009). The ten countries with the highest adolescent birth rates are Niger, Liberia, Mali, Chad, Afghanistan, Uganda, Malawi, Guinea, Mozambique, and the Central African Republic (Kirchengast, 2009).

Early marriage is not uncommon in Sub-Saharan Africa, as poor families often consider the expense of providing basic necessities for female children, particularly educational fees, as untenable, and encourage/force marriage at an early age (Mbirimtengerenji, 2007). Families are paid a much-needed dowry by the new husband, who then expects his new wife to "prove" her fertility. A newly married young girl assents to bearing a child early in the marriage to confirm her fertility, as well as to secure her relationship with her husband and establish her standing within her community (Mbirimtengerenji, 2007).

Early marriage is common in Malawi, 11th highest in the world, with 48.9% of young women ages 20 to 24 reporting that they were married by the age of 18 (Walker, 2012). And early motherhood ensues: 35% of women in Malawi give birth before the age of 18 (UNPFA, 2013a).

Access to antenatal care is often problematic for adolescents; they may not realize they are pregnant, or don't want to be seen pregnant; some clinics may charge a fee for services, rendering such services too expensive for an adolescent. Thus, late entry to care is not uncommon among pregnant adolescents (as well as pregnant adult women in many LMICs).

The WHO (2002) recommends a minimum of four antenatal visits, with the first visit occurring in the first trimester, preferably before 12 weeks of gestation. The second visit should occur close to 26 weeks (second trimester), with the third and fourth visits in the third trimester (at 32 and 36-38 weeks respectively). However, the most recent *Millennium Development Goals Report* (2013) notes that only 49% of pregnant women in Sub-Saharan Africa received the minimum four antenatal visits. In addition, WHO recommends a post-partum visit, within one week of delivery, to reinforce breastfeeding, provide contraception, and follow-up on issues such as maternal anemia, infant prematurity and contraceptive initiation; however, post-partum visits are rarely done in LMICs (WHO, 2002).

There are few studies on adolescent utilization of antenatal care in the recent literature. An earlier comparative analysis by Magadi, Agwanda and Obare (2007) found that the majority of women in Sub-Saharan Africa entered antenatal care in the second or third trimester, regardless of age. However, adolescents in the study not only were late to enter care, but they also had fewer visits and poorer maternal health than their older counterparts (Magadi et al., 2007). More than 93% of Malawian adolescents (age < 20 years) in this analysis began antenatal

care after the first trimester, and 43% had fewer than four antenatal visits (Magadi et al., 2007). Studies conducted in the United States have also found that some adolescents may not access care at all, or those who do access services may begin care late in their pregnancy with fewer prenatal visits than their adult counterparts (Haeri, Guichard, & Saddlemire, 2009).

In general, women in Sub-Saharan Africa have fewer antenatal visits than women in developed countries: a study involving women from 19 Sub-Saharan countries found approximately 60% had four or fewer antenatal visits, with nearly 20% having two or fewer visits (Nikiéma, Beninguisse, & Haggerty, 2009). The most recent Malawi Demographic and Health Survey found that only 46% of women had the recommended four antenatal visits during pregnancy, and the median gestational age at the first antenatal visit was 5.5 months (results not stratified by age; NSO, 2010). Significantly, 36% of pregnant women initiated antenatal care in the sixth or seventh month (late second/early third trimester) of pregnancy (NSO, 2010).

A recent study by Gross and colleagues (2012) examined the timing of antenatal care initiation and factors that influenced early versus late attendance, comparing adult and adolescent women in Tanzania. The authors found that although 61% of adolescents reported knowing they should begin antenatal care within the first three months of pregnancy, the mean gestational age at the first visit was five months; interestingly, older women in the study initiated care at the same gestational age (Gross, Alba, Glass, Schellenberg, & Obrist, 2012). These findings are in contrast to a number of published studies that have found adolescents initiate antenatal care later than do older women (for example, Cresswell et al., 2013; Magadi et al., 2007; Ochako, Fotso, Ikamari, & Khasakhala, 2011).

An additional concern is that antenatal clinics in LMICs are generally not geared towards providing adolescent-specific care, and often do not treat pregnant adolescents respectfully, with

providers being very judgmental (WHO, 2008). Such issues around access to appropriate care may contribute to poor maternal and infant health. Studies on adolescent pregnancy outcomes have been conflicting, with some finding an increased risk of perinatal complications among adolescent pregnancies, and others finding no associated risks (see the review by Kramer & Lancaster, 2010). Numerous studies have been conducted in the developed world, particularly the United States and Europe, where health care infrastructure and available resources support optimal birth outcomes. However, fewer studies have been conducted in low-resource countries; not only do LMICs lack health care facilities and providers, the high prevalence of anemia and malaria infection in the general population, including young women of reproductive age, confer additional risks for adverse perinatal outcomes. According to research conducted by the WHO's Making Pregnancy Safer program, pregnant young adolescents (under 16 years of age) have a four times higher risk of maternal death than older women, and a 50% higher death rate among their infants (Braine, 2009). Several studies conducted in India, Southeast Asia, and Africa were reviewed and a summary of findings follows.

Studies conducted in India and published in the last four years have consistently found that adolescent pregnancies confer an increased risk of perinatal complications. Kumar, Singh, Pandey, & Bhargava (2007) found that pregnant adolescents aged 14 to 19 had higher rates of pregnancy-induced hypertension (PIH), preterm labor (PTL), preeclampsia and eclampsia, preterm delivery (PTD) and delivered more low birth weight (LBW) infants; there was no difference in the incidence of anemia.[vi] Adolescents aged 17 and younger sustained more adverse outcomes than those aged 18 and 19. Kumar and colleagues postulated that the risks of adverse pregnancy outcomes in adolescents were associated with their young gynecologic age and

[vi] Preterm labor-onset of labor prior to 37 weeks gestation; preterm delivery-delivery before 37 weeks gestation; low birth weight-less than or equal to 2500 grams; anemia-hemoglobin less than 11 g/dL.

competition with the fetus for needed nutrients, as well as psychosocial factors such as having an unplanned and perhaps unwanted pregnancy (Kumar et al., 2007).

Mahavarkar, Madhu & Mule (2008) also studied pregnant adolescents in India and did find a higher risk of anemia, as well as PIH, PTD, and LBW infants, but the adolescents were also more likely to delivery vaginally (spontaneously, without instrumentation) than the older women in their study population. These authors note that the characteristics of the population under study (rural, poor, lacking in education) were likely contributors to the adverse pregnancy outcomes (Mahavarkar et al., 2008).

A more recent study by Sagili and colleagues (2011) studied pregnant adolescents aged 19 and under. Overall, they found less anemia in their study participants, as well as less premature rupture of membranes, and no differences in PIH or LBW infants. However, neither the study by Mahavarkar et al. (2008) nor the study by Sagili et al. (2011) further stratified the ages of the pregnant adolescents, so it is difficult to compare the differences in results. As found by Mahavarkar et al. (2008), more pregnant adolescents in the study by Sagili et al. delivered vaginally, although there was a higher use of episiotomy than in older clients. These authors concluded there was no conclusive evidence of an overall increase in risk with adolescent pregnancy, and suggested that high quality antenatal care (93% of the study participants had "adequate" antenatal care) can help to moderate risks (Sagili et al., 2011).

Mukhopadhyay, Chaudhuri and Paul (2010) studied pregnant 13 to 19 year olds in Eastern India. In addition to the previously noted increased risk of PTD and LBW infants, these researchers found a higher risk of infant complications, including a higher stillbirth rate, more birth asphyxia, and more neonatal deaths within 48 hours of delivery. This population of adolescents also began antenatal care later and had fewer visits. As above, a lack of education

and high levels of poverty, coupled with the lack of antenatal care, was felt to contribute to the poorer outcomes. Studies conducted in Southeast Asia have similar findings to those of the Indian studies above. Adolescents were found to have more PTL and more LBW infants, but fewer surgical or instrument-assisted deliveries (Lao & Ho, 1997, 1998; Omar et al., 2010). Lao and Ho (1997) found that, in China, free care as well as available social support led to favorable outcomes in adolescent pregnancies. Omar and colleagues (2010) confirm the association between adolescent pregnancy outcomes, low education, poverty, and in Malaysia, substance abuse.

There have been several recent studies in Africa on the outcomes of adolescent pregnancy. Kurth and colleagues (2010) cite the lack of outcome studies of adolescent pregnancies in Sub-Saharan Africa, and emphasize that adolescent pregnancy is associated with multiple risks in low-resource countries as compared with high-income settings. They studied pregnant adolescents in Gabon, and found the adolescents had fewer visits resulting in significantly less antenatal care: most adolescents had fewer than three visits. The study group had more malaria parasitemia and more LBW infants, particularly in those under the age of 17. Interestingly, when they corrected for the number of antenatal visits, they found no increased risk of LBW infants, and concluded that adolescent pregnancy (and the inherent lack of antenatal care) was an independent risk factor for delivering a LBW infant in central Africa. The authors also agreed with previous studies that address the anatomic immaturity of the adolescent female, as well as low socioeconomic status and a lack of education, which increase the risks of adverse perinatal outcomes in an adolescent pregnancy (Kurth et al., 2010).

Adeyinka et al. (2010) conducted a study of adolescent pregnancy in Nigeria, a country where 33% of maternal deaths occur in adolescents. They found high rates of PTL, preeclampsia

and eclampsia, LBW and a 22% rate of stillbirth among pregnant adolescents aged 18 and under. The study population also sustained a high rate of obstructed labor, and a 43% rate of cesarean section. The overall complication rate was 44.5% in the adolescent pregnancy group, compared to 22% in the older control group. An additional study in Nigeria also found that children born to adolescent mothers were more likely to die within the first five years of life (Ayotunde, Mary, Melvin, & Faniyi, 2009). Although the literature lacks a large number of studies of adolescent pregnancy outcomes, these studies do suggest that the risk of an adverse outcome is higher in low-resource settings.

In addition to the risk of poor health outcomes, adolescent pregnancy negatively impacts social and economic status. Adolescent mothers are more likely to drop out of school while pregnant and not return; unmarried pregnant adolescents also risk rejection by their family and partner, and lacking education, have difficulty obtaining or maintaining employment. (Biddlecom, Gregory, Lloyd, & Mensch, 2008; Melvin & Uzoma, 2012).

v. Adolescent Pregnancy in Malawi

After the age of 18, Malawian youth are free to marry; those aged 16 to 18 can marry with parental consent, while the legal age of sexual consent is 13 years (Mizere, 2009). As in other countries, the prevalence of sexual activity before marriage has increased in Malawi. While the median age of first intercourse (coitarche) in Malawian females is 17.2 years, 14.3% of females have begun sexual activity before the age of 15, and higher rates of coitarche are found in those living in rural areas (15%), those with no education (27%) or only primary education (16%), and those among the lowest wealth quintiles (17.7%; Malawi Government, 2012; NSO, 2010).

As noted above, adolescents lack awareness of contraceptive methods; they also lack the skills and empowerment to negotiate for pregnancy prevention or even lack an awareness of susceptibility to pregnancy. Consequently, adolescent pregnancy is common in Malawi. Data from the recent Malawi Demographic and Health Survey in 2010 reported 152 births per 1000 adolescents between the ages of 15 and 19 (NSO, 2010); rates are lower in urban areas (109 births/1000 adolescents) than for rural teens (162 births/1000), although as cited earlier, 85% of the population lives in rural areas (Mizere, 2009). Fertility rates peak between the ages of 20 and 24 (269 births/1000 women), declining thereafter. There has been only a modest decline in fertility rates since the first Malawi Demographic and Health Survey in 1992 (NSO, 2010).

Young women, by means of their gender alone, are susceptible to sexual coercion and/or forced marriages, resulting in sexually transmitted infections and/or unwanted pregnancy. Nearly 10% of girls ages 10 to 14 have experienced sexual violence, while that figure increases to 21% for those 15 to 19 years (NSO, 2010). Eighteen percent of girls under the age of 15 report that their first sexual experience was forced; first sex for 14.3% of girls 15 to 19 was not consensual (NSO, 2010).

In Malawi, only 13.8% of girls complete primary school (compared to 22.3% of boys), and the percentage completing secondary school is less than half that (Abuel-Ealeh et al., 2010). The high dropout rate for girls is linked to early marriage and/or adolescent pregnancy, which often results in an end to educational opportunities (Mbizvo & Zaidi, 2010; NSO, 2010; UNAIDS, 2010c). Until recently, pregnant adolescents in Malawi were forbidden to attend school[vii] (this is a common "rule" in LMICs, including those in Sub-Saharan Africa), and were not allowed to return after delivery. While the law has now changed, allowing girls to return to

[vii] Of note, this "rule" only applies to pregnant females; if a male student impregnates a female, he is not forced to leave school.

school after delivery, many individual schools and/or teachers create unnecessary barriers that inhibit girls from returning to school (Mwansa, 2011).

By the age of 19, 63.5% of adolescent females have begun childbearing (NSO, 2010). As in other LMICs, most adolescent pregnancy in Malawi occurs within marriage or within a partnership. The actual numbers are conflicting: the Malawi Demographic and Health Survey indicates that 20% of females aged 15 to 19 are married (3% in a polygynous marriage), with another 4% in a union (NSO, 2010); a briefing by USAID estimates that approximately 30% of girls aged 15 to 19 are married (Mayzel, Kachala, & Kerner, 2010), and activists against child marriage estimate that 47% of girls are married before age 18 in Malawi (Schmid, 2013).

Once married, societal expectations for children lead to pregnancy soon thereafter. Yet pregnancy has also increased in recent years among unmarried girls. This is attributable to a variety of factors, including poverty, relationships with older men, a push to continue schooling and delay marriage, all coupled with a resulting increase in premarital sex: 40% of 18 and 19 year old unmarried adolescents have had sex (NSO, 2010).

Resulting unplanned pregnancies are associated with a lack of contraceptive use. Of concern, the Malawi Demographic and Health Survey found that only 31% of unmarried sexually active adolescent 15 to 19 year old females were using contraception (NSO, 2010). Among married 15 to 19 year olds, only 28.8% were using any method of contraception (NSO, 2010). Married adolescents have been found to have more frequent unprotected sex as a husband is often anxious to demonstrate both his and her fertility, yet the husbands of adolescent girls are often older, as well as more sexually experienced, and may already have been infected with HIV (Mbizvo & Zaidi, 2010).

As discussed earlier, pregnant adolescents in Sub-Saharan Africa often enter prenatal care at a later gestational age, and have fewer prenatal visits (Birungi et al., 2011; Chaibva, Ehlers, & Roos, 2009; Kurth et al., 2010), although Malawi-specific data on adolescents is lacking. The median gestational age at the first visit of pregnant Malawian women (not stratified by age) is 5.6 months, well beyond the recommendation of the first visit by the end of the first trimester (NSO, 2010). Only 1.6% of Malawian women have a first antenatal visit by 16 weeks, and 36% have their first visit at six or seven months gestation (NSO, 2010). Fewer than half (45%) of Malawian women achieve the WHO recommended minimum of four antenatal visits (WHO, 2002).

While the number of women who deliver with a skilled birth attendant (SBA) present is slowly increasing, as few as 24% of Malawian adolescents deliver with an SBA (Msyamboza et al., 2010). Adolescents in Malawi experience higher rates of postpartum anemia and higher rates of LBW babies. Compared with estimates from a decade earlier, maternal anemia and LBW deliveries are higher now than a decade ago (Msyamboza et al., 2010).

E. Pathophysiology of HIV Transmission

An understanding of HIV pathophysiology, particularly as it relates to HIV in pregnancy and the risk of HIV infection in the fetus/newborn, provides a framework within which to assess the research on PMTCT protocols. Herein is a brief overview of the pathophysiology of HIV transmission and HIV in pregnancy.

HIV is secreted in blood and bodily secretions, including sperm and vaginal fluid. Transmission can occur through sexual intercourse (mucosal contact), exposure to blood and blood products (parenteral contact via transfusion, injection drug use [IDU]), vertical transmission (see below), and breastfeeding. Higher viral loads, such as those associated with

recent seroconversion and/or concomitant infections of the genital mucosa such as genital ulcer diseases (e.g., herpes simplex virus [HSV], syphilis, chancroid) are associated with higher infectivity, more viral shedding, and increased likelihood of transmission (Hollingsworth, Anderson, & Fraser, 2008; Mwapasa et al., 2006; Phiri et al., 2013). Primary HIV infection (the time of seroconversion) has been found to be 26 times more infectious than asymptomatic infection, and late stage infection seven times more infectious: both are periods in which viral load levels are high (Hollingsworth et al., 2008).

i. Sexual Transmission of HIV

Prior studies have found that sexual transmission of the virus from an HIV-infected male to a female is at least twice as efficient as from an infected female to her male partner; an early study done in California determined that male-to-female transmission was eight times more efficient than female-to-male (Padian, Shiboski, Glass, & Vittinghoff, 1997). The discrepancy is thought to be due to a combination of factors, including a greater viral load in semen, a larger amount of male ejaculate, and the greater amount of exposed female epithelial tissue (Campbell et al., 2008). And as noted above, it is well documented that a high plasma viral HIV level increases the risk of transmission from an infected partner (Hollingsworth et al., 2008).

In Sub-Saharan Africa, adolescent girls become infected with HIV through sexual contact with a male partner or husband. Culturally, older males, who are more likely to be HIV-infected, prefer young girls (especially virgins) for sexual partners as they are (initially) less likely to be HIV-infected. A number of studies have looked at whether marriage itself is a risk factor for HIV acquisition; a seminal study by Clark (2004) found that the husbands of married adolescents were more than twice as likely to be HIV-infected than the boyfriends of unmarried adolescent girls (30% vs. 11.5%), and a longitudinal study of serodiscordant couples in Uganda found that

age-disparate marriages were an independent risk factor for HIV acquisition in young women (Biraro et al., 2013). Many adolescent girls marry older men, who may be already infected; the expectation of prompt childbearing from the husband and/or family precludes the use of condoms (Hinden & Fatusi, 2009).

As noted above, forced sex is not uncommon (NSO, 2010), and is unlikely to take place with the use of a condom. Transactional sex is another risk for HIV acquisition: under conditions of poverty, lack of education, young women are forced,[viii] willing, or encouraged by their parents to trade sex for money, clothes, housing and other necessities (Hawkins, Price, & Mussá, 2009; Maganja, Maman, Groves, & Mbwambo, 2007; Mbirimtengerenji, 2007).

While the connection between economic status and HIV is debated in the literature (see Fox, 2012; Gillespie, Kadiyala, & Greener, 2007; Mibirimtengerenji, 2007; Parkhurst, 2010), more authors agree that *for women* in LMICs, poverty, and in particular food insecurity, is often linked to risky behavior for survival (Campbell et al., 2008; Mbirimtengerenji, 2007; Rodrigo & Rajapakse, 2010; Weiser et al., 2011). In addition, early marriage, as seen in many parts of Sub-Saharan Africa, is noted to be associated with poverty (Dahl, 2010; Mbirimtengerenji, 2007; Walker, 2012). In many situations, young women lack the knowledge and negotiation skills necessary to insure safe sexual practices. The situation is underscored by traditions of gender inequality and women's lack of power in society and in relationships, including marriage (Mbirimtengerenji, 2007; Walker, 2012).

Although some studies have been conflicting, others have shown that a particular risk for sexually-acquired HIV in adolescent females is the immaturity of the genital tract (Venkatesh & Cu-Uvin, 2013). With puberty and exposure to estrogen, columnar epithelium begins to recede

[viii] While many authors discuss the difficult life circumstances that force young women to engage in transactional sex, others make the interesting argument that such actions are driven more by a desire for luxury items rather than necessities; for example, see Masvawure, 2010.

into the cervical os, and is replaced with squamous epithelium. The process may take several years to complete, and the presence of cervical ectopy (visibility of the squamocolumnar junction, indicative of columnar epithelium exposure) predisposes to an increased susceptibility to sexually transmitted infections, including HSV and HIV (Leclerc-Madlala, 2008; Venkatesh & Cu-Uvin, 2013).

F. HIV in Pregnancy

i. Mother-to-Child Transmission of HIV

Once infected with HIV, the female can transmit the virus to her sexual partner and, if pregnant, to her fetus or newborn. Worldwide, MTCT of HIV accounts for approximately 90% of HIV infections in children (Ubesie, 2012; Varga & Brooks, 2008a). In 2012 alone, an estimated 260,000 children were infected with HIV through MTCT during the perinatal period or during breastfeeding (UNAIDS, 2013b). Although this represents a significant reduction (52% between 2001 and 2012), MTCT remains a huge burden in the countries most affected (UNAIDS, 2013b). Globally, an estimated 3.3 million children are currently HIV-infected, 88% of whom live in Sub-Saharan Africa (UNAIDS, 2013b). HIV-infected women who become pregnant have a 20-45% chance of transmitting HIV to their infants (WHO, 2010b). However, with the use of ART, the transmission rate can be greatly reduced to less than 2% in non-breastfeeding women, and to less than 5% in breastfeeding women (WHO, 2010b; WHO, 2010c). Thus, prevention of MTCT is a key component in reducing the burden of HIV in Africa. But a pregnant woman's serostatus must first be determined in order for her to receive the appropriate care should she be HIV-infected.

ii. Determining the HIV Status of Pregnant Women in Malawi

Pregnant women who seek antenatal care are encouraged to undergo HIV testing, particularly in countries with high rates of HIV and where MTCT is a substantial risk. HIV testing occurs in two ways: a) the patient seeks HIV testing voluntarily (VCT: voluntary counseling and testing), or b) the provider initiates the testing (as routine testing, part of a diagnostic workup, or through an "opt-out" approach).

In Malawi, HIV testing was first offered in the mid-1990s, primarily in private hospitals and clinics and through research studies. Since 2004, testing has been increasingly accessible, including in district hospitals and many rural clinics. In 2003, the Ministry of Health mandated routine, opt-out HIV testing of all pregnant women (although it was not implemented until 2005 [Weir et al., 2008]), and currently, the national policy is one based on the UNAIDS protocol: all patients will be HIV tested "unless they explicitly refuse" (Angotti et al., 2011). This provider-initiated, opt-out testing has led to 88.5% of pregnant women being tested for HIV while receiving antenatal care (NSO, 2010).

However, a study by Angotti, Dionne, & Gaydosh (2011) conducted in rural Malawi found that HIV testing at antenatal clinics was thought by women to be compulsory in order to obtain antenatal care. One study participant commented that "it is a law to get tested for pregnant women;" another stated "the nurse told us that the government of Malawi has decided to force all the women who are pregnant to be tested for HIV…." (Angotti et al., 2011, p. 310-311). Most of the women interviewed for the study reported they were not given the option to opt-out of testing.

Such perceptions of mandatory testing are problematic for women wishing to access antenatal care but who do not wish to be tested for HIV. The fear of forced testing may lead some women to avoid antenatal care in hospital or district clinics.

Pregnant women who consent to HIV testing and are found to be HIV-infected risk transmitting the virus to the fetus or newborn. An understanding of HIV, its effect on the pregnant woman, and the risks of transmission from mother-to-child are essential to understanding the evidence-based recommendations for PMTCT protocols.

iii. Pathophysiology of HIV in Pregnancy

Pregnancy induces changes in a woman's immune system, irrespective of HIV status. The CD_4 cell count decreases during pregnancy, especially in the third trimester, and the immune response is altered, from cell-mediated to humoral (Grieg, Woods, & Clark, 2011). The latter results in an increased susceptibility to infections, such as *toxoplasmosis* and *listeriosis*. Thus, women who are HIV-infected are at particular risk of transmitting any opportunistic infections, as well as HIV itself, to the fetus. Infections due to *Mycobacterium tuberculosis*, *pneumocystis jirovecii* (formerly *pneumocystis carinii*, PCP), *cytomegalovirus and toxoplasmosis* have been transmitted vertically to the infants of HIV-infected women; what is unclear to date is whether these infections occur in utero, or are a result of exposure during the intrapartum or immediate postpartum period (Greig et al., 2011).

Women who are HIV-infected and become pregnant, or acquire HIV during pregnancy, are at risk of transmitting the virus to their fetus or newborn, either during pregnancy, childbirth, or through breastfeeding (Johri & Ako-Arrey, 2011). Studies conducted early in the epidemic determined the risk of transmission to be between 20% and 45% (Working Group on Mother-to-Infant Transmission of HIV, 1995). Maternal CD_4 count and viral load are key factors in

determining the risk of transmission: women with lower CD_4 counts and higher levels of viremia (higher viral loads) are more likely to transmit the virus (Dorenbaum et al., 2002; Guay et al., 1999; Shapiro et al., 2006). As with other infections, when HIV transmission occurs is not known for certain. It is thought (suggested by fetal autopsies of aborted fetuses) that most transmission occurs near term (37-40 weeks) or during labor and delivery (because of maternal blood transfusions to neonates as well as direct contact with infected secretions in the birth canal); studies have estimated the risk of transmission in utero at 6-23%, 15-65% during labor and delivery, and up to 15% during breastfeeding, but the exact risks are still not clear (Bertolli et al., 1996; De Cock et al., 2000; Guay et al., 1999). It is generally accepted that most transmission does occur during labor/delivery, with breastfeeding conferring a substantial risk as well (Bertolli et al., 1996; Rouzioux et al., 1995).

As has been found in non-pregnant HIV-infected individuals, maternal infection with genital ulcer disease increases the risk of HIV transmission, and thus for pregnant women, MTCT. Antibodies to HSV-2 are common, particularly among HIV-infected women (and men), and infection with HSV-2 increases the rate of HIV transmission in the intrapartum period. In a study conducted by the Zimbabwe Vitamin A for Mothers and Babies Project (ZVITAMBO), 82.5% of the women had HSV-2 antibodies, and the presence of HSV-2 antibodies was associated with an increased risk of intrapartum MTCT (Cowan et al., 2008). Similarly, in a study in the Queen Elizabeth Central Hospital in Blantyre, Malawi, researchers found 8% of HIV-infected pregnant women to be infected with syphilis; 8.7% of the infants born to these women were HIV-infected at birth (indicating intrauterine transmission), and another 17.6% were infected at follow-up (intrapartum or postpartum transmission; Mwapasa et al., 2006).

High HIV viral loads also increase the risk of MTCT. Taha and colleagues (2011) studied 2561 HIV-infected women in Malawi. Those who had recently seroconverted were younger and had had fewer pregnancies than those who had not recently seroconverted. Of the recent seroconverters, there was a 17.8% in-utero transmission rate vs. a 6.7% in-utero transmission rate among women who had not recently converted (Taha et al., 2011). It has been suggested that in-utero transmission may be higher among women who seroconvert during pregnancy, rather than before they become pregnant (Marinda et al., 2011).

G. Prevention of Mother-to-Child Transmission of HIV

Numerous studies of PMTCT interventions have been conducted since the early 1990s, once clinicians and researchers realized that women (rather than just homosexual men) could be infected with HIV and, if pregnant, transmit the virus to the fetus. The studies have attempted to determine the efficacy of various medications, single or in combination, to prevent mother-to-child transmission, although to date the *most* efficacious regimen remains unknown (Shapiro et al., 2010). The following studies reviewed herein were chosen both for their historical or ethical interest, as well as their clinical significance, and are presented in chronological order.

i. Prevention of Mother-to-child Transmission of HIV with Antiretroviral Therapy

Pediatric AIDS Clinical Trials Group (PACTG) 076 (Connor et al., 1994): This study, one of the first published, was conducted in the United States (US) and in France from 1991 to 1993. The purpose of the study was to assess the safety and efficacy of zidovudine (ZDV) in HIV-infected pregnant women (Connor et al., 1994). Four hundred and seventy-seven women were enrolled in the study, and given ZDV 100 mg five times per day from entry into the study (between 14 and 34 weeks of gestation) until the onset of labor. The outcome measure included HIV infection in the infant at 18 months of age. Study results indicated an impressive two-thirds

reduction in HIV transmission from mother to child in the intervention group: HIV prevalence was 25.5% in the control group vs. 8.3% in infants whose mothers had taken ZDV (Connor et al., 1994). The safety of ZDV during pregnancy was established for the mother; infants in the intervention group had statistically significant lower hemoglobin levels at birth. However, by three months of age, the hemoglobin levels were similar between both groups of infants (Connor et al., 1994)

Strengths of this study include its historical impact on the initial management of pregnancies in HIV-infected women, as well as the double-blind, placebo controlled design. Women were enrolled from 59 centers in the US and France; although limited to these two countries, the numerous centers involved speak to the ability to generalize to US and French women. The researchers administered ZDV in the antepartum, intrapartum, and postpartum periods (the latter for the infant only), given the uncertainty of when MTCT occurs. The study was stopped early because the first interim analysis indicated the marked efficacy of ZDV (Siegfried, van der Merwe, Brocklehurst & Sint, 2011), which speaks to the ethics of the study researchers.

The study's weaknesses primarily reflect the lack of information included by the authors in the study report. There is no information given on the number of eligible women who declined participation in the study, so selection bias cannot be assessed. There was a high attrition rate (23.9%), which elicits concerns over study design or characteristics of those who left the study vs. those who continued. However, the authors used survival analysis to appropriately decrease bias from high attrition rates. The cesarean section rate was high (27%) which we now know may have reduced the risk of HIV transmission to the fetus regardless of medication. A single HIV test was used to determine HIV infection in the infants until mid-way

through the study, when current clinical standards led to the use of a second confirmatory test; thus, estimates of HIV infection in the control infant group could be inaccurate. None of the women enrolled in the study breastfed their infants as recommended in developed countries, which limits generalizability to breastfeeding populations, although subsequent studies would examine the efficacy of ART in breastfeeding. And finally, an age cutoff was not listed in the inclusion or exclusion criteria; the mean age of study participants was 25 years, but no information is given as to the range of ages to determine if adolescents were included in the study.

Thai-Centers for Disease Control (CDC) Study (Shaffer et al., 1999): This study took place in two large maternity hospitals in Bangkok, Thailand between 1996 and 1998. The purpose of the study was to determine the efficacy as well as safety of ZDV given from late pregnancy until delivery. Three hundred and ninety-seven women were randomized to the intervention group (300 mg ZDV twice daily [BID] from 36 weeks until onset of labor, once at onset of labor, then every three hours until delivery) or the control group (placebo only, identical tablets taken on same dosing schedule as the intervention group). Inclusion criteria included intention not to breastfeed. No medication was given to the infants.

This study found that ZDV given late in pregnancy and until delivery could reduce HIV transmission to the infant by 50%, to 4.8% in utero and 5.2% in the intrapartum (Shaffer et al., 1999). Although PACTG 076 had demonstrated a somewhat higher efficacy of ZDV to prevent MTCT (66%), availability of and/or feasibility of the regimen in LMICs was limited. In this study, ZDV was given for a shorter period of time than in PACTG 076, with less frequent dosing, used oral rather than intravenous ZDV during labor, and no medication was given to the infants: thus, this regimen was simpler and less costly, yet still resulted in a significant reduction

in HIV transmission (Shaffer et al., 1999). Preliminary results of this trial were announced in early 1998, after which other trials in progress changed control groups from placebo to ZDV (see below).

Strengths of this study include the randomized, double-blind, placebo-controlled design; randomization was accomplished by a permuted block procedure, generated at the CDC, with randomly sized blocks at each hospital site. Study participants, providers, and investigators were all blinded as to study group assignment. The placebo was identical to the study medicine (ZDV) and was dosed exactly the same. Attrition was very low, with a loss to follow-up rate of only 1.2% overall.

A potential study weakness was that only women who intended not to breastfeed were enrolled, which limited generalizability, although breastfeeding by HIV-infected women was strongly discouraged at the time this study was undertaken. Only women 18 years or older were eligible for the study, which also limits generalizability. Adherence was assessed by pill count and patient diary, both of which may be manipulated by a study participant, risking information bias and exposure misclassification. Of note, the risk of HIV transmission in the placebo group in this study was lower than had been previously documented at this hospital (24%; Shaffer et al., 1999) or by the PACTG 076 study (25.5%; Connor et al., 1994). The investigators were unable to ascertain the reason for this lower than expected transmission rate.

HIVNET 012 (Guay et al., 1999): This study from the HIV Prevention Trials Network built on the results of PACTG 076, comparing the safety and efficacy of a short course of ZDV with that of nevirapine (NVP) during labor for the woman and for the first week of life for the infant. Such short course ART was a more viable option for low-resource settings where HIV medications were often not available or in short supply. Conducted in a hospital in Kampala,

Uganda from 1997 to 1999, the researchers randomized 626 women; the study intervention group received a single dose of NVP (sdNVP) 200 mg at the onset of labor, while the control group was given ZDV 600 mg at the onset of labor and 300 mg every three hours thereafter until delivery. Similarly, the infants in the intervention group received a sdNVP syrup (2 mg/kg) within 48 and 72 hours after delivery, while the control group infants were given ZDV 4 mg/kg BID for one week after delivery. The authors hypothesized that the simpler regimen of NVP for mother and infant would be efficacious, given its long half-life (over 60 hours in adults, while the single dose sustains a high blood level for one week in an infant) as compared to ZDV, whose short half-life requires multiple doses (Guay et al., 1999). The authors reported a 47% reduction in the risk of HIV transmission at 14 to 16 weeks, continuing out to an overall 41% reduction in the risk of infection or infant death by 18 months as reported in a follow-up publication (Jackson et al., 2003). These study results led to the adoption of sdNVP for women and infants in many low-resource settings because of its efficacy and simplicity.

Strengths of the HIVNET 012 study included computerized randomization to reduce the risk of bias, the use of sequentially numbered medication packs prepared by a pharmacist reducing allocation bias, and a low overall attrition rate of 2.6% (Guay et al., 1999). Significantly, the women in this study had lower CD_4 counts and higher viral loads than the women in the PACTG 076 study, which supports the efficacy of ART in more immunologically suppressed women. In addition, 99% of the women in this study breastfed their infants, which provided valuable information on the efficacy of ART in preventing postpartum transmission of HIV in the postpartum period. HIV infection in infants was confirmed by multiple tests up to 18 months after birth with the use of both HIV-1 RNA PCR and HIV-1 antibody technology (Jackson et al., 2003).

The study weaknesses included a single hospital site in a large city in Uganda, which may have led to selection bias; refusal of HIV testing by a large number of women who were thus ineligible for the study, which may also have created selection bias; and a lack of blinding to treatment status and outcome among study participants and investigators after randomization. Adherence to medications was assessed by interview, which risks over-reporting of compliance (social desirability effect); pill counts were conducted, although they can be manipulated by study participants. And many unobserved doses of ZDV were given to infants at home during the first week of life, and compliance was not clearly assessed.

The study also had some ethical issues. At the time the study was conducted, it was already established that the risk of HIV transmission in breastfed infants is highest sooner after the initiation of breastfeeding, so the rationale for a single dose of NVP or a one-week course of ZDV could be questioned. Similarly, there were already concerns about sdNVP and the subsequent development of resistance in the infant, yet the infants in the intervention group were given sdNVP, as was the mother. And some studies were already evaluating the use of triple ART for PMTCT; one could argue that this study did provide useful information for limited-resource settings, although if evidence is suggesting that triple ART is more efficacious, one could ask if such studies are ethical. However, the ethics of doing HIV research in resource-limited settings with vulnerable populations has been debated in the literature at length.

PETRA Study (Petra Study Team, 2002): The PETRA study was conducted over three and a half years (1996 to 2000) in Tanzania, South Africa and Uganda. The purpose of the study was to assess the efficacy of short course ZDV and lamivudine (3TC) with the intent of finding an effective multidrug regimen suitable for resource-poor countries; the study design included three arms plus a placebo group, and enrolled a total of 1797 women. PETRA-a participants received

ZDV 300 mg and 3TC 150 mg BID from 36 weeks gestation until labor, ZDV every three hours and 3TC every 12 hours during labor, with a return to BID dosing for one week after delivery. Infants received weight-appropriate doses of ZDV and 3TC for the first week of life. The PETRA-b regimen was ZDV 600 mg and 3TC 150 mg administered at the onset of labor, ZDV and 3TC continued during labor, and then BID dosing for one week after delivery. As in PETRA-a, infants received ZDV and 3TC for one week. PETRA-c medications were the same as PETRA-b, but given only from the onset of labor until delivery, with no medication postpartum. Infants in the PETRA-c group received no medication after birth. The placebo group received no medication, and this arm was discontinued in early 1998 after the publication of other studies demonstrating the reduction in MTCT with ART (Petra Study Team, 2002). The study results were disappointing: the PETRA-a regimen led to a 63% reduction in HIV transmission at four to eight weeks (5.7% rate of infection at six weeks), but this was not sustained at 18 months. Similarly, PETRA-b and PETRA-c had no sustained efficacy at 18 months, with the latter arm not superior to placebo (15.3% infection rate at six weeks, prior to discontinuation of the placebo arm). The study showed very little benefit in reducing infant HIV infection or mortality (Petra Study Team, 2002).

Study strengths include the randomized, double-blind, placebo-controlled design; the five sites from which participants were recruited, which reduces the risk of selection bias; block randomization of subjects; utilization of two HIV tests to confirm infection; and the inclusion of a primarily breastfeeding population of women postpartum.

The research team was only able to enroll 39% of eligible women into the study, which suggests selection bias, and the study suffered a 29.5% attrition rate, also resulting in possible selection bias. Other weaknesses include an over-representation of study participants from

Uganda, with fewer from other study sites, leading to additional concerns of selection bias and generalizability. In addition, women in the placebo group were unmasked when that arm was stopped, and received active treatment; the women and investigators were no longer blinded to these participants.

Most problematic are the ethical concerns of this study design. The results of the PACTG 076 study (Connor et al., 1994) had already been published, as had more recent results from a study conducted in Thailand (Shaffer et al., 1999), both of which clearly demonstrated the efficacy of short course ZDV in reducing the risk of MTCT of HIV. Thus, the use of a placebo group was controversial and seemingly unethical; one could also argue that PETRA-c, in which the infant received no medication, was also questionably ethical. Although this study received approval from the WHO Secretariat Committee on Research Involving Human Subjects as well as the ethics review boards of each study site, the use of a placebo arm raised "an unprecedented and vigorous debate in professional journals" once the study began (Petra Study Team, 2002, p.1185; see also Angell, 1997; Lurie & Wolfe, 1997). The study authors defended the inclusion of a placebo arm, arguing that without the placebo group, errors in the interpretation of the study results would have occurred, with an overestimation of the efficacy of the intrapartum regimens (Petra Study Team, 2002).

PACTG 316 (Dorenbaum et al., 2002): The purpose of this study was to explore whether the addition of sdNVP at the onset of labor coupled with a single dose of NVP syrup for the newborn could further reduce transmission of perinatal HIV among women taking "standard" (at the time) ART, defined by the study authors as any antiretroviral other than a nonnucleoside reverse transcriptase inhibitor (NNRTI). Recommended at a minimum was the PACTG 076 regimen of ZDV 100 mg five times per day from 14 to 34 weeks until the onset of labor (Connor

et al., 1994). The rationale for the study noted that the majority of HIV transmission was thought to occur in the intrapartum period, based on the results of several studies (including Connor et al., 1994; Rouzioux et al., 1995), and so the authors sought to find a supplemental agent for intrapartum use to further reduce MTCT.

This was an international, multicenter study conducted from 1997 to 2000 in the US, Europe, Brazil and the Bahamas. The double-blind study randomized 1270 participants to an intervention arm (sdNVP 200 mg for the mother at the onset of labor in addition to standard ART, with a single dose of NVP syrup [2 mg/kg] for the infant within two to three days of delivery) and a control arm (placebo plus standard ART for the mother, placebo for the infant). The study was discontinued early, as the transmission rates in both arms were too low to meet the study assumption of a 5% transmission rate: HIV infection occurred in 1.4% of the infants in the NVP arm and 1.6% of the infants in the placebo arm. Thirty-four percent of the women underwent an elective cesarean section. The authors concluded that the risk of MTCT was very low when accompanied by standard ART, regular antenatal care, and the availability of elective surgical delivery (Dorenbaum et al., 2002). This study confirmed other contemporary research indicating that the rate of MTCT could be reduced to less than 2% with these measures and suggested that a variety of ART regimens were effective. However, most study participants were enrolled from developed countries rather than resource-limited settings, which limited generalizability.

Study strengths include the randomized design, explicit calculation of study power, and HIV testing of infants at multiple time points. This study was also one of the few to include pregnant HIV-infected adolescents: inclusion criteria specified that females aged 13 years or older (or of legal age to give consent, although this was not specified for the different study sites) were

eligible for enrollment. However, the median age of the study participants was 28 years in both arms, and study results were not stratified by age.

While study participants and providers were blinded to study arm, it is not clear whether the investigators were blinded. There was not enough information given to determine if selection bias was a risk. There was an overall attrition rate of 17.1% (16.3% in the NVP group, 18% in the placebo group) which was not discussed by the authors.

Mashi Study (Shapiro et al., 2006): This purpose of this study was to examine whether the maternal sdNVP dose could be eliminated in women taking ZDV from 34 weeks gestation through delivery. The study was conducted from 2002-2003 in four sites in Botswana, a country with an extremely high HIV prevalence rate; in women screened for inclusion in this study, the HIV prevalence rate was 33.6% (Shapiro et al., 2006). A total of 709 women were enrolled in the study. Women in the intervention arm received ZDV 300 mg BID from 34 weeks and sdNVP at the onset of labor, with supplemental ZDV 300 mg orally every three hours until delivery. Women in the control arm received the same regimen save for a placebo instead of sdNVP at the onset of labor. Infants in both arms received sdNVP within three days of delivery and ZDV 4 mg/kg BID for one month. (Because of the results of the Thai trial [Shaffer et al., 1999] replacement of the placebo with sdNVP for the infants in the control arm was recommended by the study safety and monitoring board and instituted 17 months into the study). Results found no difference in HIV infection in infants at birth or at one month. Of interest however, the study authors found that 45% of randomly sampled women in the study developed at least one resistance mutation after taking a single dose of NVP. The development of NVP resistance after sdNVP had been previously noted and is of concern, as NVP resistance mutations confer

resistance to the entire class of NNRTIs; the high percentage of women who developed resistance in this study was worrisome.

This study had a number of strengths. They enrolled participants from a variety of urban and rural sites within the country, limiting selection bias and increasing generalizability. Participants were assigned to study arms by means of randomized blocks stratified by site, lowering the risk of selection bias. There was a relatively low attrition rate of 7.5%, equally distributed between the two arms of the study. Infants were confirmed to be HIV infected with two tests. Two months after the study began, highly active ART (HAART; triple therapy [ZDV, NVP, and 3TC]) became available in Botswana for women with a CD_4 count less than 200 cells/μL or an AIDS-defining illness. Women in the study who met these criteria were offered HAART, and did not receive sdNVP or placebo at the onset of labor. Although this complicated analyses and made it difficult to assess the possible efficacy of sdNVP in more immunocompromised women, it was an ethical decision.

The study had a few weaknesses. Changing the study design for women eligible for HAART could be considered a study weakness, although the authors analyzed the results both including and excluding infants whose mothers had taken HAART. Multiple analyses were performed, although the *p*-value was not adjusted for multiple testing (e.g., as with the Bonferroni correction). Because all study infants received the same medication regimen (sdNVP and ZDV for one month) after the change in the study design, the researchers were unable to compare the efficacy of infant ART in this study.

Mma Bana (Shapiro et al., 2010): This study, conducted from 2006 to 2008, took place at the same four sites in Botswana by many of the same investigators involved in the Mashi Study (Shapiro et al., 2006). Although the availability of HAART was slowly increasing in low-resource

settings, the most efficacious combination of medications for PMTCT was unknown; the purpose of the study (the Setswana name of which translates to "mother of the baby") was to compare different HAART regimens in a population of HIV-infected pregnant women.

Five hundred and sixty women were enrolled in the study. There were two intervention groups: women with CD_4 counts $\geq$ 200 cells/μL were randomized to either the nucleoside reverse transcriptase inhibitor (NRTI) group (abacavir [ABC] 300 mg, 3TC 150 mg, and ZDV 300mg coformulated as Trizivir,® BID from enrollment between 26 and 34 weeks) or the protease inhibitor (PI) group (lopinavir 400 mg boosted with ritonavir[ix] 100 mg [LPV/r] coformulated as Kaletra,® with ZDV 300 mg and 3TC 150 mg coformulated as Combivir,® both BID from enrollment between 26 and 34 weeks). Medications were continued for both groups until weaning or at six months postpartum, whichever came first. There was also an observational group, women with CD4 counts $\leq$ 200 cells/μL or with an AIDS-defining illness, who received treatment that was the standard of care in Botswana at the time (NVP 200 mg, ZDV 300 mg, and 3TC 150 mg BID); treatment began between 18 and 34 weeks and continued indefinitely. All infants in the study were given sdNVP 6 mg within 72 hours of birth and ZDV 4 mg/kg BID for one month after delivery (Shapiro et al., 2010).

The study results found no difference in HIV transmission rates between the three groups of infants at birth or by six months of age. The overall transmission rate was 1.1%; 2.1% in the NRTI group and 0.4% in the PI group, although the difference in transmission rates between the two groups was not statistically significant (p=0.53). Infants born to mothers in the PI group had higher rates of prematurity (23% vs. 15% in the NRTI group), as had been reported by others; low birth weight was similar in all three groups, while stillbirth was more common in the observation

[ix] Ritonavir is a protease inhibitor used to increase (or "boost") the bioavailability of a second protease inhibitor.

group of women who had lower CD_4 counts and/or AIDS (Shapiro et al., 2010). The study participants also manifested very high rates of virologic suppression regardless of medication regimen (viral loads < 400 copies in more than 90% of women).

Strengths of this study included randomization via permuted blocks stratified according to clinical site and intent to breastfeed as one of the inclusion criteria. Studies that include women who plan to breastfeed have become increasingly important as WHO recommendations regarding infant feeding have changed over time and now encourage exclusive breastfeeding for six months (WHO, UNAIDS, UNFPA, & UNICEF, 2010); it is essential to understand the efficacy of these ART regimens not only during pregnancy but also during breastfeeding. In this study, 91% of women reported exclusive breastfeeding to six months (receiving free formula and food for their infants after weaning until 12 months), and the study confirmed a low rate of MTCT in a breastfeeding population (Shapiro et al., 2010). Another strength of this study was the inclusion of the observational group of more immunosuppressed women receiving standard of care, which provided a third comparison group and demonstrated the efficacy of triple therapy in this population.

The authors conceded that the most important weakness of the study was that it wasn't powered sufficiently to determine any differences between study groups regarding MTCT (Shapiro et al., 2010). Another possible weakness included a lack of information given to assess selection bias. As in other studies, pregnant females 18 and under were excluded from participating in the study; the mean age ranged between 25 and 29 for the three study groups, which may limit generalizability. Mothers were "blinded" to study group but depending on the group were given different numbers of pills, which may well have unblinded them. In addition, adherence was measured by self-report (which is susceptible to recall bias by the participants) and

pill counts (where conceivably, participants could remove and dispose of pills without taking them [e.g., to cover up if they forgot to take them]). There was a high attrition rate in the study: 32.1% in the Trizivir® (NRTI) group and 31.2% in the Kaletra®/Combivir® (PI) group; such attrition bias may have led to inaccurate study results. And because many of the women in the study had higher CD_4 counts and lower viral loads than in other studies, there is limited generalizability of the study results to other populations.

However, this study demonstrated that triple therapy with different combinations of NRTIs or NRTIs/PIs was highly efficacious in preventing HIV infection in the infants of HIV-infected women (<2%). This study was one of the first to demonstrate that continuing HAART from the second trimester of pregnancy through six months of breastfeeding was a valuable option for women in resource-poor countries where safe options to breastfeeding are limited.

Kesho Bora (Kesho Bora Study Group, 2011): This study was conducted between 2005 and 2008 in five sites: one in Burkina Faso, two in Kenya, and two in South Africa. The purpose of Kesho Bora (which means "a better future" in Swahili) was similar to that of the Mma Bana study conducted in nearly the same time frame: to ascertain the safety and efficacy of triple ART, but using a different combination of drugs than Mma Bana. Eight hundred and twenty-four women were randomized to one of two groups. One group (the "triple therapy" group) took 200 mg of LPV boosted with 100 mg of ritonavir (LPV/r), 300 mg of ZDV, and 150 mg of 3TC twice daily from 34 to 36 weeks gestation through six months postpartum. The other group was given ZDV 300 mg BID from 34-36 weeks until delivery, 600 mg of ZDV with a single dose of NVP 200 mg at the onset of labor, and (after study protocols were changed when WHO recommendations were updated) one week of ZDV 300 mg BID and 3TC 150 mg BID after delivery. Infants in both groups were given a dose of NVP syrup (2 mg/kg) within 72 hours of

birth (or up to one week of age). In addition, after the study protocols were updated, all infants also were given ZDV 4 mg/kg BID for one week after delivery. The duration of breastfeeding was approximately 20 weeks for each group, with 77.5% of women ever breastfeeding (but only 44.5% exclusively so by three months).

There was no difference in HIV infections rates in either group of infants at birth or six weeks. However, at one year, 9.5% of the ZDV/sdNVP infants were HIV positive, while 5.4% of infants in the triple therapy group were infected, a 43% reduction in risk of MTCT. There were fewer infant deaths before one year of age in the triple therapy group. Women who received triple therapy had higher CD_4 counts and lower viral loads at delivery and one year postpartum. As had been reported in the literature before, women with lower CD_4 counts and higher viral loads were more likely to transmit HIV to their infants, regardless of medication group. In women who breastfed, HIV transmission rates after delivery were lower in the triple therapy infants than in the ZDV/sdNVP infants (Kesho Bora Study Group, 2011).

Strengths of this study include computer-generated randomization, with participant allocation to group stratified by planned infant feeding method. There was low attrition in the study (6% in the triple therapy arm, 9% in the ZDV/sdNVP arm) and the authors used survival analysis to address even this low attrition rate. In addition, there was intensive follow-up of study participants (91-94% follow-up accomplished). The study took place in five sites in three different countries, which increases generalizability. And as is now the standard, infants were HIV tested on several occasions to confirm infection.

Neither participants nor study investigators were blinded to treatment group, which increased the risk of performance bias and detection bias respectively. The authors don't include a thorough review of study limitations in their discussion section, so it is unclear why no masking

was done. They did mentioned slow recruitment for the study, which limited their ability to detect a difference in infection rates at six weeks, and a concern that the duration of triple therapy may have been too short (median of six weeks) to affect peripartum infection more than what is seen with ZDV/sdNVP.

Interestingly, these authors also mention that it is hard to compare infant mortality rates because those in clinical trials get better care (Kesho Bora Study Group, 2011). Lastly, the medications were stopped at six months of breastfeeding, per the WHO recommendations at the time, so as to not encourage longer breastfeeding, even though the investigators thought it would be preferable to continue as long as women were breastfeeding (which is the current WHO recommendation now [WHO, UNAIDS, UNFPA, & UNICEF, 2010]).

ii. Safety of ART in Pregnancy

As shown in multiple studies, including those reviewed above, the use of ART during pregnancy is efficacious in preventing MTCT of HIV. However, as treatment therapies for HIV-infected pregnant women have progressed from monotherapy (e.g., ZDV) to combination therapy (e.g., HAART), there has also been an emergence of conflicting data suggesting that the use of ART is not without risk. While some studies have found no increased risk of adverse birth outcomes with ART, others have found combination therapy during pregnancy confers a statistically significant risk of adverse birth outcomes, and in particular, preterm delivery (PTD).

Adverse pregnancy outcomes associated with ART in pregnancy were first reported in 1998 by Swiss colleagues, who found a PTD rate of 33% among women taking NRTIs, with and without PIs (Lorenzi et al., 1998). The European Collaborative Study found significant rates of PTD: 16.8% for women on monotherapy (primarily ZDV), 13.4% for those on dual therapy (drugs not specified), and 25.5% for those on HAART (drugs not specified). They also found a

significantly increased risk of severely premature deliveries (< 34 weeks; Thorne, Patel, & Newell, 2004). The risk of PTD was higher in women who initiated therapy before becoming pregnant (Thorne et al., 2004).

Studies from North America have been less conclusive. An early study by the Pediatric AIDS Clinical Trials Group found no increase risk of PTD with ART, although 86% of women in the study were on monotherapy with ZDV (Lambert et al., 2000). The Pediatric Spectrum of HIV Disease study found an overall decrease in the incidence of PTD as therapy progressed from monotherapy to HAART during the study period. However, they did find an association between PTD and HAART that included a PI (Schulte et al., 2007). The Women and Infants Transmission Study (WITS) found an increased risk of PTD in women who started ART in the third trimester that did not contain ZDV, but a decreased risk in those whose regimen contained ZDV (Tuomala et al., 2005).

A concomitant goal of the two seminal ART studies previously discussed (Mma Bana and Kesho Bora) was to ascertain the safety of the studied medication regimens. Both studies found that triple ART during pregnancy and breastfeeding was very efficacious and generally safe. However, the Mma Bana study observed a two-fold increased risk of PTD in the cohort taking HAART that included a PI versus those taking triple NRTI therapy (Shapiro et al., 2010). The Kesha Bora study, which also included PI-based HAART, found no difference in PTD rates (Kesho Bora Study Group, 2011), although the later start (34-36 weeks) of the PI-based HAART might explain the difference in PTD outcomes (e.g., less exposure to medication during pregnancy). There was no difference in the incidence of low or very low birth weight infants in either group (Kesha Bora Study Group, 2011; Shapiro et al., 2010).

In the largest study to date on birth outcomes among HIV-infected women with access to ART, Chen and colleagues (2012) analyzed birth outcomes for more than 33,000 pregnant women in Botswana, of whom 9500 (30%) were HIV-infected. Among HIV-infected women, the rate of PTD was 24% with a median gestational age of 34 weeks. The authors found a 1.2 fold increased risk of PTD for HAART started in the preconception period, while initiating HAART during pregnancy conferred a 1.4 fold increased risk of PTD compared to single dose ZDV. The authors concluded that PTD was associated with the use of a PI-boosted HAART regimen (most often ZDV, 3TC, and LPV/r), either initiated prior to or during pregnancy (Chen et al., 2012). The study also found that women on HAART had a higher rate of stillbirth compared to women on monotherapy, and a higher rate of SGA infants, with women who initiated HAART prior to pregnancy having a higher percentage of SGA infants than those initiating during pregnancy (Chen et al., 2012).

Watts and colleagues (2013) evaluated ART use in the Surveillance Monitoring for ART Toxicities (SMART) network database, and looked specifically at the timing of exposure to combination ART (cART).[x] Of women with first trimester exposure to cART, 21% delivered prematurely, while those with later (second or third trimester initiation) exposure to cART had a PTD rate of 17%. When stratified by class of drug taken, the risk of PTD was associated with PI-containing cART in early pregnancy, but not with an NRTI or NRTI/NNRTI regimen. The risk lost significance in those who initiated therapy at a later gestational age. In addition, severe PTD occurred more often in those with first trimester exposure to PI-containing cART than in

[x] The terminology has recently changed. What previously had been referred to as HAART (highly active antiretroviral therapy) is now referred to as combination antiretroviral therapy (cART). Both terms refer to three or more antiretroviral drugs. For this paper, the term HAART will be used for studies that were done previously, and cART will be used for more recent studies that use the current terminology.

those with later exposure. They concluded that exposure to PI-containing cART in the first trimester of pregnancy may increase the risk of PTD (Watts et al., 2013).

A retrospective analysis published this year by Short and colleagues (2014) looked at PTD in a cohort of 331 women in London, 78% of whom were of African descent. The authors compared multiple ART regimens, including monotherapy with ZDV and PI-based cART. After adjusting for possible confounders (e.g., smoking, drug use, the need for cervical cerclage [indicative of cervical incompetence, a risk for PTD]), the PTD rate in the cohort was 13%; the highest risk was initiation of cART during pregnancy. They also determined a significant association between PTD and PI-based cART. They postulate that the immune reconstitution that occurs with ART initiation alters the body's cytokine environment, such that tolerance of the fetus is reduced, predisposing to PTD (Short, Douglas, Smith, & Taylor, 2014)

As suggested by these studies, it has been proposed that there is a relationship between PIs and PTD. However, the issue is complex and heterogeneous. At the time many of these studies on ART safety were conducted, the guidelines did not recommended starting all pregnant women on ART regardless of CD_4 count or WHO clinical staging as they do currently. Many authors have speculated that, in these earlier studies, women on ART in the first trimester were likely to have more severe HIV disease: PIs were the preferred initial treatment for those with more advanced HIV infection, and severe HIV disease is in itself a risk for PTD and thus served to confound study results (Chougrani, Luton, Matheron, Mandelbrot, & Azria, 2013; Watts et al., 2013).

A study conducted with the French Perinatal Cohort examined the risk of PTD over a 20 year period (Sibiude et al., 2012). With the increasingly complex ART regimens, a steady increase in the PTD rate was observed over four different study periods. In the final phase of the

study, the study authors adjusted for confounders known to increase PTD, such as maternal age, smoking, and CD_4 count as a marker for immunosuppression. They found a PTD rate of 13.6%, more than twice that of the general population (Sibiude et al., 2012). They looked specifically at ART regimens that included a boosted PI (with ritonavir) and a non-boosted PI. The PTD rate was significantly higher in the boosted PI cohort, suggesting that the drug ritonavir, which has complex metabolic and vascular effects, may be implicated in the increased risk of PTD (Sibiude et al., 2012).

There is clearly a need for further studies on the risk of cART and PTD. PTD is associated with a number of confounding variables other than ART use (e.g., maternal age, smoking, drug use), and many of the studies to date have not controlled for these confounders (Chougrani et al., 2013). It would also be interesting to stratify study cohorts by age. As discussed earlier, pregnancy in adolescence is associated with untoward birth outcomes, including PTD. Importantly, adolescents who are taking PI-based cART may be at even further risk, should PIs be determined to have a causal relationship with PTD.

Researchers have been appropriately hesitant to conclusively determine a) if there is a statistically significant association of PTD with the use of cART, and specifically PI-based ART, and b) if the increased risk of PTD seen in some studies is causal. Most authors emphasize the need for more studies to determine the relationship between cART, PI-based regimens, the ritonavir boost and PTD. PIs continue to be used very frequently because of their proven efficacy: in the United States, two of the four recommended first- line ART combinations include a boosted PI, and these recommendations are considered appropriate for pregnant women as well (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2013). The WHO guidelines recommend PIs as an integral part of second line regimens (WHO,

2013a). The results of the Mma Bana study noted above (0.4% rate of MTCT in the group taking a PI-based regimen) highlight the efficacy of PIs in reducing pediatric infections (Shapiro et al., 2010).

Issues regarding the safety of cART in pregnancy remain to be completely understood. However, it is clear that cART has revolutionized HIV treatment, and its use has prevented thousands of pediatric HIV infections by effectively reducing vertical transmission. Experts agree that, at this present time, the benefits of cART outweight the possible risks associate with its use (Chougrani et al., 2013; Kourtis, 2010).

iii. Other Means to Prevent Mother-to-Child Transmission

In addition to ART, two other key interventions shown to reduce the risk of MTCT are cesarean delivery and avoidance of breastfeeding.

Vaginal delivery confers a risk to fetuses as they are exposed to infected vaginal secretions and blood in the birth canal. An analysis of 15 prospective cohort studies by the International Perinatal HIV Group (1999) found that women who had an elective cesarean section lowered the risk of vertical transmission to the infant (odds ratio 0.36-0.47). Even in women receiving ZDV to reduce MTCT, cesarean section further decreased the risk compared to the benefit provided by ZDV alone (International Perinatal HIV Group, 1999). Subsequent studies indicated that elective caesarean delivery, before the onset of labor and/or rupture of membranes, could significantly reduce the risk of MTCT even further (RR 0.17, 95% CI: 0.05-0.55) (Brocklehurst, 2000; Johri & Ako-Arrey, 2011). Thus, in developed countries, cesarean delivery is the recommended mode of delivery for women with a viral load of more than 1000 copies/ml or for those whose viral load is unknown. However, surgical facilities and availability of personnel trained to perform caesarean sections are limited in most areas of Sub-Saharan Africa

(Chigwedere et al., 2008), and the majority of women deliver vaginally. This further underscores the need for access to ART for women in low-resource settings.

Similarly, breastfeeding is not recommended in developed countries, as vertical transmission via breast milk is responsible for 15-20% of MTCT (Bertolli et al., 1996; De Cock et al., 2000; Greig et al., 2011; Guay et al., 1999). In the United States, and other industrialized countries, HIV-infected women are advised to formula-feed their infants. However, in LMICs such as those of Sub-Saharan Africa, where access to potable water is limited, using available water to mix with infant formula powder is hazardous. Studies have compared infant outcomes between formula-fed infants and infants breastfed by HIV-infected mothers. At 18 months, mortality rates were similar, as formula-fed infants died of diarrheal illness (Thior et al., 2006). Given the risks of not breastfeeding in low-resource settings, breastfeeding is recommended by the WHO (2013a).

iv. PMTCT of HIV in Malawi-2010

Essential elements of PMTCT programs include the availability of antenatal HIV testing, access to care, adherence to the ART regimen, and follow-up care for the infant, including ART after birth. In 2010, the WHO revised its guidelines for ART and PMTCT in limited resource settings (WHO, 2010b). With the intent to improve access and ensure provision of evidence-based treatment, the recommendations included earlier initiation of ART and the use of highly active PMTCT regimens, starting at 14 weeks gestational age, continuing through labor and delivery, and extended through the breastfeeding period (WHO, 2010b).

In 2009, more than 80% of Malawian women received sdNVP for PMTCT instead of a more effective ART regimen (UNICEF, 2011). In response to WHO's updated recommendations, the Malawian Ministry of Health developed the first *Malawi Guidelines for*

the Clinical Management of HIV in Children and Adults (Ministry of Health [MOH], 2011). Malawi's strategy for PMTCT began first with the prevention of HIV among parents, as well as the prevention of unintended pregnancies in HIV-infected women. An aggressive ART policy for pregnant HIV-infected women included the initiation of life-long ART for all pregnant and breastfeeding women, without regard to CD_4 count or WHO Clinical Staging Criteria ("Option B+," see discussion below; MOH, 2011).

The standard formulation for ART in Malawi for adults and adolescents age 15 and older was d4T [stavudine] 30 mg/3TC 150 mg/NVP 200 mg (MOH, 2010). However, for pregnant (and breastfeeding) women, the recommended first line therapy was tenofovir (TDF) 300 mg/3TC 300 mg/efavirenz (EFV) 600 mg daily (MOH, 2011). There have been concerns about the potential risk of neural tube defects with EFV in the first trimester, and in the United States we place women who might become pregnant on NVP or a protease inhibitor (e.g., LPV); we do not initiate ART with EFV in pregnant women until the second trimester. In Malawi, the MOH acknowledges the risk of severe toxicity with NVP in women with high CD_4 counts, and thus EFV is preferred. The recommendation was to start TDF/3TC/EFV after 13 weeks gestation; if a woman is already on an EFV-containing regimen pre-conception, there was no need to change therapy (MOH, 2011, p. 40-42).

Patients were advised to take 95% of their medication as ordered in order to avoid developing HIV drug resistant strains (MOH, 2011). Providers were advised to dispense 30 tablets to pregnant women at each visit, and to ascertain adherence at every follow-up (MOH, 2011). This required more antenatal care visits than usual for the HIV-infected pregnant woman.

Other strategies to reduce MTCT in Malawi included the use of a partogram to identify obstructed or prolonged labor in a timely manner; avoidance of artificial rupture of membranes if

possible (except in the case of prolonged labor), frequent vaginal examinations and routine episiotomy; and the umbilical cord should not be "milked" prior to cutting (MOH, 2011, p. 63).

The guidelines also recommend NVP prophylaxis for infants of HIV-infected mothers for six weeks. Ongoing ART for the mother provided protection should breastfeeding continue past six weeks (MOH, 2011). Exclusive breastfeeding was recommended for the first six months of life, unless safe and affordable replacement feeding was available.

Provision of adequate services was slow to reach all pregnant women in need, and even when services were available, a number of barriers existed that prevented women from accessing PMTCT services or constrain them from adhering to the protocols.

v. Barriers to Uptake of PMTCT Services

Early studies on the uptake of PMTCT by pregnant women were confounded to some degree by a lack of available services in Malawi as well as other countries in Sub-Saharan Africa. In 2007, more than one-third of health care facilities in Malawi did not have PMTCT services (van Lettow et al., 2011). In the last few years, there has been a considerable scale-up of PMTCT services available in African countries including Malawi, yet barriers remain and overall uptake of PMTCT services by pregnant women had been suboptimal (Chinkonde, Sundby, & Martinson, 2009; van Lettow et al., 2011).

In a study of women's experiences of PMTCT services and antenatal care in Lilongwe, Malawi, Levy (2009) used an ethnographic research methodology to explore decision making and behaviors. She used individual interviews and focus group discussions, as well as observing clinic flow, health education talks, and group counseling sessions conducted in a clinic where a PMTCT program had been created. Individual interviews were conducted with 34 HIV-infected women (ages not given), six interviews total, the first of which took place after the HIV

diagnosis. Other interviews were scheduled at various times during pregnancy, after the birth, and at the time of infant HIV testing. The focus group discussion participants were 21 other women recruited from a postpartum support group coordinated by the clinic's PMTCT program. The discussions centered around experiences in the PMTCT program and life as experienced by these women with HIV. Key informant interviews were also conducted with nurses and administrative staff associated with the PMTCT clinic, government officials, and aid agencies. The transcripts were thematically coded using a qualitative data analysis program (Levy, 2009).

Study results found that women had many issues and negative experiences within the PMTCT program. Fear for the infant and a feeling of vulnerability to HIV infection prompted many women to be tested, but once positive, they found the program focused more on the health of the fetus/infant than on their health (Levy, 2009). Infrastructure issues were also problematic, with drug shortages, transportation issues, long clinic waiting times, and a lack of coordinated care between the antenatal services and PMTCT services (Levy, 2009).

Duff, Kipp, Wild, Rubaale, & Okech-Ojony (2010) conducted a study to determine the barriers to uptake of and adherence to a PMTCT program in Uganda. This qualitative study used in-depth, face-to-face interviews and focus group discussions with an open-ended question format derived from the literature. Using thematic analysis, the study found that the most significant barriers to PMTCT program uptake and adherence were economic: poverty, transportation costs, cost of food while waiting to be seen in the clinic, the cost of "nutritious" food recommended for those on ART, and economic dependence on husbands who did not support their wives' attendance at the clinic. HIV stigma and fear of disclosure of HIV status were also barriers to accessing care, as were health system factors, including long clinic waiting times and negative interactions with clinic staff (Duff et al., 2010).

Perhaps the most informative study on barriers to PMTCT uptake in Malawi was done by Chinkonde and colleagues (Chinkonde et al., 2009). This was a qualitative study in Lilongwe, Malawi; in-depth interviews were held with married HIV-infected women at four district health centers providing PMTCT services. These women were enrolled in the PMTCT program, and the purpose of the study was to examine reasons for non-adherence to the program. Interview data revealed that fear of disclosure of HIV status and subsequent negative community reactions were a strong deterrent to continued attendance at the clinic. Other PMTCT protocols such as discontinuing breastfeeding at six months and use of formula also were a threat to keeping their HIV status a secret. Women enrolled in PMTCT programs were given food baskets that included soya flour, which many knew was only for HIV-infected women, another source of involuntary HIV disclosure for women (Chinkonde et al., 2009).

Other barriers to adherence were related to inadequate infrastructure and included difficulty getting to the clinic, long waits at the clinic, making appointments that were cancelled once they arrived at the clinic, and unkind, "harsh," and unsupportive staff, including nurses (Chinkonde et al., 2009). Lack of husband support and his refusal to use condoms for further HIV protection were also barriers to adherence (Chinkonde et al., 2009).

A more recent study in the Zomba district of Malawi was conducted prior to changes in ART guidelines, when sdNVP was still the standard of care (van Lettow et al., 2011). The authors found that only 75% of women took the sdNVP at the onset of labor, while only 66% of exposed infants received sdNVP within 72 hours of delivery. There was poor follow-up for infant HIV testing (28%), and most mothers breastfed for 12 months, with some continuing to breastfeed through 18 months. Overall, only 18% of women enrolled in the program followed all recommended strategies for PMTCT (van Lettow et al., 2011). Using semi-structured

interviews and questionnaires, the authors identified barriers to PMTCT uptake and adherence which included an unwillingness to reveal HIV status to others, denial of HIV serostatus, fear of community stigmatization, and lack of spousal support (van Lettow et al., 2011).

Studies in Kenya and South Africa have found similar barriers (Mepham, Zondi, Mbuyazi, Mkhwanazi, & Newell, 2011; Otieno et al., 2010). Fear of disclosure and failure to disclose HIV status to one's partner was strongly correlated with not enrolling or poor adherence to PMTCT, as was fear of stigma, denial of HIV status, and fear of abuse from partner. Personal concerns such as inability to take time off from work to attend clinic, travel away from home, and inability to pay for services were also associated with non-adherence. Interestingly, South African women noted an inability to take medications because other HIV-infected relatives stole them, or they lacked food and/or water with which to take the medications (Mepham et al., 2011). Lack of or misinformation about ART efficacy, inability to understand how to take the medications, fear of medication side effects, and lack of compassionate care were also mentioned by the study participants (Mepham et al., 2011; Otieno et al., 2010).

None of the studies discussed above included pregnant HIV-infected adolescents in their cohorts. As mentioned earlier, four studies were found in an extensive literature search that were specific to pregnant adolescents and PMTCT. Two studies by Varga and Brooks (2008a, 2008b) in South Africa used focus groups with PMTCT clinic staff and community members, including adolescents. HIV infection was not an inclusion criterion; the purpose of the research was to use a case study of an HIV-infected pregnant adolescent to discuss how she might feel, act, and respond to her antenatal care and PMTCT services. The studies found that adolescent barriers to PMTCT uptake were similar to those expressed by adult women: fear of disclosure, fear of rejection by boyfriend/partner, stigma and rejection by her community. The authors suggest that

(unmarried) adolescents are already struggling with the burden of being pregnant, having embarrassed herself and her family; they are already having to deal with the shame and stigma of adolescent pregnancy, and to add having to cope with HIV-infection, medications, and more frequent antenatal visits is too much (Varga & Brooks, 2008a, 2008b).

In an earlier study, Reynolds and colleagues (2006) surveyed pregnant or parenting adolescents who had experience with PMTCT services in Kenya. Barriers to ongoing care included a lack of age-appropriate education: for example, respondents noted that providers did not educate them about the available services nor the benefits of these services, nor did they teach them about condom use or pregnancy prevention for the future (Reynolds et al., 2006). Fear of testing positive, fear of a negative community reaction, and fear of partner anger or rejection all were associated with non-adherence to the PMTCT program. The adolescent participants also mentioned unsympathetic and/or rude health care providers, specifically mentioning nurses, as another barrier (Reynolds et al., 2006).

Another study to include pregnant HIV-infected adolescents was also done in Kenya (Birungi et al., 2011). Although 84% of the 15 to 19 year olds in the study went to at least one antenatal visit, only 67% accessed PMTCT services. The authors note that very few of the participants had four or more visits, and suggest that few antenatal visits precludes the provision of adequate information and education of the need for PMTCT medications and other behaviors (Birungi et al., 2011). The authors suggest that too many HIV services have been geared to pediatric or adult patients, and that there is an urgent need for antenatal care that provides adequate support and education to pregnant HIV-infected adolescents (Birungi et al., 2011).

The strengths of these studies on barriers to PMTCT uptake and adherence are the use of both quantitative and qualitative methods to obtain study data. Methodology in all studies was

fairly sound, with the exception of study bias: most studies obtained their study participants directly from PMTCT clinics or from registers of women who had attended such clinics at some time in the past. There is a risk of selection bias if women have had at least one interaction with the PMTCT clinic. The study by van Lettow et al. (2011) also excluded women who were enrolled at tertiary centers, which likely excluded urban women with higher education and income levels. In studies that examined adherence to infant ART, there was no mechanism to verify that the sdNVP was given or what the feeding method was (e.g., exclusive breastfeeding vs. mixed feeding); the researchers had to rely on maternal recall, which may have overestimated adherence to the protocols. And some studies had to refer women to test centers for infant HIV testing, but had no information as to how many actually complied.

The richness of the qualitative data was most evident in the study by Chinkonde et al. (2009), with many direct quotes from women interviewed to clearly portray the themes identified; unfortunately, no participants were adolescents. The studies by Varga and Brooks (2008a, 2008b) and Reynolds et al. (2006), which involved adolescents, also demonstrated themes with the use of participants' words. Although the study by Birungi et al. (2011) included adolescents and used mixed methods, only the quantitative data were presented in the publication, which incompletely explained the low utilization of PMTCT services by the HIV-infected pregnant adolescents.

vi. Other Barriers to the Uptake and Adherence to PMTCT Protocols

Worldwide, more than 60 million women deliver in non-institutional settings each year, and the vast majority of these births are attended to by traditional birth attendants (TBAs), many of whom are untrained (UNICEF, 2009). Estimates suggest that up to 60% of women in Sub-Saharan Africa deliver in non-institutional settings (primarily their homes) under the care of

TBAs (Stanton, Blanc, Croft, & Choi, 2007). Significantly, studies have shown that care by TBAs and delivery at home are strongly correlated with nonadherence to PMTCT programs (Albrecht, et al., 2006; Delvaux et al., 2009). Research is lacking as to where African adolescents are most likely to deliver.

vii. Malawi's Recent Efforts to Increase PMTCT Coverage

HIV infection in pregnant women has continued to challenge public health interventions, and the goal of eliminating new pediatric HIV infections cannot be attained without effective means of preventing MTCT. Although the number of HIV-infected infants has decreased significantly since the initiation of ART for PMTCT, there were still an estimated 260,000 new pediatric infections via MTCT in 2012 (a decrease from 330,000 pediatric infections in 2011); 90% of these infections were in Sub-Saharan Africa (Ghanotakis, Miller, & Spensley, 2012; UNAIDS, 2012a; UNAIDS, 2013b). ART coverage of HIV-infected pregnant women continued to be unacceptably low, despite some success in improving access: in 2011, only 57% of eligible pregnant women received treatment to prevent MTCT (UNICEF, 2012a). In addition, when earlier guidelines were published in 2006, there was not enough evidence to recommend infant prophylaxis, even in the context of breastfeeding.

In an effort to further expand access to ART for pregnant women and their infants, the WHO released updated guidelines in 2010 for the management of HIV infection in pregnant women, as referred to above (WHO, 2010a).[xi] As had been recommended in earlier guidelines, all pregnant women needing antiretrovirals for their own health (based on a CD_4 count of 350 cells/mm^3 or less or WHO clinical stage 3 or 4 [Tables 1 and 2]) are to start ART as soon as possible and continue ART for life. However, the 2010 guidelines also proposed two new

[xi] Guidelines change fairly often, every two or three years, reflecting new research that provides evidence to further optimize PMTCT management (Shaffer, Abrams, & Becquet, 2014).

options to prevent MTCT in women who do not need ART for themselves (e.g., whose CD_4 count is greater than 350 cells/mm^3 or who are WHO clinical stage 1 or 2):

Option A recommends that the woman start twice daily azidothymidine (AZT) at 14 weeks gestation (or as soon after as possible) and continue throughout pregnancy. At the onset of labor, a single dose of NVP is given, along with the first dose of AZT+3TC (Combivir®), which is continued for seven days postpartum. Infant prophylaxis in breastfed infants requires daily NVP for at least four to six weeks after birth, or until all exposure to breast milk ceases. In infants who are not breastfed, NVP or AZT is given until four to six weeks of age (WHO, 2010a).

Option B advocates triple ART prophylaxis for the mother, starting as early as 14 weeks gestation and continuing until delivery. If she is breastfeeding, she should continue triple ART until one week after the infant is no longer receiving any breast milk. A number of triple ART regimens are recommended, including TDF+3TC (or FTC)+EFV, AZT+3TC+LPV/r, AZT+3TC+ABC, and AZT+3TC+EFV. For the infant, daily NVP or AZT is given until four to six weeks of age, regardless of method of infant feeding (WHO, 2010a). If the mother does not need ART for her own health and she is not in a serodiscordant relationship, she can discontinue ART once any risk of MTCT is gone (e.g., she is no longer breastfeeding).

One of the difficulties in implementing these guidelines in resource-limited settings is the reliance on CD_4 counts to determine whether a woman is a candidate for lifelong treatment or pregnancy prophylaxis with Option A or B. In Malawi, laboratory capacity and infrastructure remain limited, and CD_4 counts are generally available only in larger medical facilities. This reliance on CD_4 counts significantly limited the efforts of the Ministry of Health to increase ART coverage in pregnant women; in 2011, only 35% of eligible pregnant women were receiving

ART (Schouten et al., 2011). In addition, for mothers with high CD_4 counts, Options A and B both result in starting and stopping ART with each subsequent pregnancy (WHO, 2010a). Given the high fertility rate in Malawi, this results in intermittent use of antiretrovirals, which increases the risk of developing drug resistance and jeopardizing the health of the woman.

Thus, in mid-2011 the Ministry of Health developed an innovative modification of Option B called Option B+ (CDC, 2013). Integral to this option is a universal "test and treat" strategy, testing all pregnant women for HIV when they present for antenatal care, and immediate initiation of lifelong ART to all pregnant and breastfeeding women who test positive, regardless of CD_4 count (Table 3). This strategic shift necessitated decentralizing ART administration to all antenatal clinics: in first year of the program, Malawi saw an increase from 303 ART clinics to 641 integrated PMTCT/ART clinics (CDC, 2013). Staff in antenatal clinics were educated on ART counseling and task shifting allowed non-physician staff, including nurses, to initiate ART (CDC, 2013).

Option B+ has dramatically increased ART coverage through PMTCT programs in Malawi. In the year following the rollout of Option B+, the number of pregnant and breastfeeding women on ART expanded from 1,257 to 10,663, a 748% increase (CDC, 2013); PMTCT coverage increased to 60% nationally (Shaffer, Abrams, & Becquet, 2014). The most recent quarterly report from the Malawian Ministry of Health shows that 95% of pregnant women who started on ART did so based on Option B+ guidelines; only 5% of pregnant women who started ART that quarter did so for their own health (MOH, 2012).

The goal of eliminating MTCT of HIV is now thought to be within reach: the benefits of Option B+ include a streamlined approach to initiating treatment, increased access to ART and improved maternal health, prevention of HIV transmission to uninfected partners, prevention of

MTCT in future pregnancies, and a reduction (and possible elimination) of new pediatric HIV infections (CDC, 2013; Gopalappa, Stover, Shaffer, & Mahy, 2014; Landes et al., 2013; Shaffer et al., 2014; van Lettow et al., 2012). Broader ART coverage for HIV-infected mothers reduces maternal mortality, and child survival is known to improve when mothers stay alive (Schouten et al., 2011). A cost-effectiveness analysis found that, while requiring more upfront financial resources (e.g., more HIV test kits, more ART medications, more exposed infant diagnostics and treatment), Option B+ was cost-effective in the long run, saving money by reducing maternal illness/mortality and preventing pediatric infections[xii] (Fasawe et al., 2013). Since Malawi initiated Option B+, a number of other countries have transitioned to Option B+, including Ethiopia, Lesotho, Mozambique, and Haiti (International AIDS Society, 2013; Kellerman et al., 2013).

Importantly, the WHO updated their treatment guidelines in June of 2013, endorsing Option B+ (WHO, 2013a). First-line treatment includes the standard combination of two NRTIs and one NNRTI in a fixed-dose combination pill containing TDF, 3TC (or FTC), and EFV, taken once daily. This combination is recommended for all pregnant women, even those in the first trimester of pregnancy, and also for women who are breastfeeding. Recent studies have found that EFV use early in pregnancy is less likely than previously thought to be associated with an increased risk of birth defects (Ford et al., 2010; WHO, 2013a), while there are persistent concerns about adverse effects (e.g., severe hepatitis, Stevens-Johnson syndrome) with the use of NVP,[xiii] the other main NNRTI option, particularly when used in those with CD_4 counts greater than 250 cells/mm^3 (WHO, 2013a). The first line combination also avoids the common side

[xii] When compared to Option B, the costs and savings of Option B+ were identical, save for the cost of CD_4 testing as required by Option B. Thus, Option B+ is more cost-effective than Option B.

[xiii] The Malawi Ministry of Health does acknowledge that the studies do not *conclusively* show that EFV is completely safe in the first trimester of pregnancy, and propose offering the option of using NVP instead of EFV to non-pregnant women who are planning a future pregnancy (Schouten et al., 2011).

effect of anemia, which is associated with the use of AZT; anemia already complicates many, if not most, pregnancies in Malawi (Schouten et al., 2011). If the combination of TDF, 3TC (or FTC) and EFV is not available, any one of the other ART combinations recommended in Option B is to be used (WHO, 2013a).

Despite its success in dramatically increasing the number of pregnant and breastfeeding women on ART, Option B+ is not without its critics. Coutsoudis and her colleagues, well-known South African physicians and researchers, sparked controversy when they raised ethical, medical and programmatic concerns about Option B+, which they call "extreme" (Coutsoudis et al., 2013). Why should pregnant women be prioritized for treatment over others, males and females alike, especially those with CD_4 counts below 350 cells/mm^3 who are not yet on treatment? What about issues of drug resistance? How can health care systems, already lacking in infrastructure, roll out such an ambitious program? Responses to these concerns supported Malawi's decision to implement Option B+, citing their lack of infrastructure and low enrollment rates in ART, and strongly emphasized that countries need to be able to make their own decisions as to how best to move towards an AIDS-free populace (Goosby, 2013; Schouten et al., 2013)

One critical issue is whether women who receive a positive HIV test result are ready to start ART that same day. The receipt of an HIV diagnosis and the immediate need to make a decision about starting ART is likely overwhelming for many women, and some may agree to start ART without fully considering the implications of such a decision. Tenthani and his colleagues (2014) studied the rate of retention on ART under Option B+ in Malawi. They found that Option B+ patients who initiated ART while pregnant were five times more likely to be lost to follow-up after their initial visit as compared to those who started ART for their own health.

Similarly, women who started ART under Option B+ while breastfeeding (rather than while pregnant) were twice as likely to be lost to follow-up when compared to those who needed ART for their own health. Overall, the loss to follow-up at six months averaged 17%, with a range of 0% to 58% observed in the 540 facilities under study (Tenthani et al., 2014). This is consistent with the loss to follow-up rate disclosed by a Ministry of Health report evaluating Option B+ (16%; MOH, 2012). Tenthani et al. propose that this relatively high loss to follow-up rate may indicate women were resistant to initiating ART under Option B+, perhaps feeling coerced to do so; it is estimated that up to 20% of pregnant or breastfeeding women never start ART after testing positive for HIV, even though medication is provided directly by the clinic (Shaffer et al., 2014). The study by Tenthani et al. also found that women who did not start ART on the same day they received their test results, but started at a later date, had better retention in care. The study authors suggest the some antenatal clinic staff are less prepared to provide ART counseling, and that women who did not receive adequate counseling were not retained in care (Tenthani et al., 2014). These and other concerns need to be carefully studied and evaluated, even while expanded access continues via Option B+.

H. Conclusion

This review of the literature has illustrated the biological, psychosocial, and behavioral complexities of HIV and its effect on maternal and child health. Although effective medications are now available to prolong the lives of those infected with HIV, PMTCT programs are essential to curbing the epidemic and protecting the next generation in the most vulnerable of countries. Particular attention must be paid to HIV in female adolescents, who continue to be at increased risk; while little is known about their uptake and adherence to PMTCT protocols, they

must be engaged in age-appropriate care that addresses their specific concerns and issues, not only to prevent HIV infection in their infants, but also for their own health.

Chapter III: Theoretical Framework

A. The Health Belief Model in the Context of Prevention of Mother-to-Child Transmission of HIV

i. Introduction

As noted in this author's review of the literature, very few studies have examined the uptake and adherence of PMTCT by pregnant, HIV-infected adolescents. While most PMTCT studies do include pregnant women aged 18 and 19 in their sample population, the results are not stratified by age. To date we do not have an understanding of how a pregnant adolescent may differ or be similar to an older pregnant woman who is considering HIV testing and PMTCT uptake.

Essential elements of PMTCT programs include the availability of antenatal HIV testing, access to care, adherence to the ART regimen, and follow-up care for the infant, including ART after birth. Yet despite the scale-up of PMTCT services throughout Sub-Saharan Africa, many pregnant women do not access these programs or adhere to the antiretroviral (ARV) medication regimens (Coffie et al., 2008; Duff et al., 2010; Nassali et al., 2009).

The reasons that women do not access PMTCT programs are multiple and complex. Many women are unaware that they are HIV-infected. They may not recognize the personal behaviors, or the behaviors of their husband or partner, that put them at risk, or they may be afraid to be HIV tested and find out that they are infected. They may not realize that if they are HIV-infected, they have a 25% to 45% risk of transmitting the infection to their infant, either in utero, during labor or delivery, or through breastfeeding (WHO, 2010). They may be unaware that, with the use of ARV medication, the transmission rate can be decreased to less than 5% (WHO, 2010b). They may not wish to disclose their HIV status to a health care provider or birth attendant, fearing a lack of confidentiality. They may not attend a health care facility for

antenatal visits because of transportation issues or competing priorities (e.g., school, work, responsibilities at home), and thus not have access to ART initiated during their pregnancy or to be taken when labor starts. They may not want to take ART if they deliver at home with others present if they have not disclosed their HIV status to their partner, family or birth attendant. They may not wish to give the infant ART medication for the first six weeks of life, because they do not realize that the infant needs ART, or do not want to disclose to others why the infant needs medication. And finally, they may not return to the clinic six weeks after delivery so that the infant ART adherence can be assessed and the infant evaluated in the HIV care clinic for all of the above reasons.

A number of theories were considered to structure a research approach to improving HIV-infected women's adherence to a PMTCT regime. After examination of the HIV and PMTCT literature, the Health Belief Model (HBM) and the Theory of Planned Behavior (TPB) were chosen as the theories for this critique. Both theories provide a useful framework for understanding the complexities and challenges involved in the uptake of PMTCT services by the pregnant woman, both for herself and for her fetus/infant. At the onset, these theories can be used to study the behaviors of the pregnant woman, who must first decide whether or not she will be HIV tested, which would determine her need for a PMTCT program. The second level of applicability of the theories would involve maternal decisions about her own ART use in pregnancy and ART administration to her infant after delivery to prevent transmission of HIV during breastfeeding.

After discussion of each theory, application to HIV testing and PMTCT adherence will be presented, and then each model will be assessed using criteria developed for the critical reflection of theory by Meleis (2007). This section will conclude with an overview of adolescent

developmental theory to illustrate the construct of adolescence, the complexity of understanding adolescence in another culture, and a rationale for the appropriateness of applying these two theories to the pregnant HIV-infected adolescent.

ii. The Health Belief Model

Developed nearly 60 years ago, the HBM was one of the first theories of health behavior (Rimer & Glantz, 2005). The HBM was originally developed by social psychologists Hochbaum, Leventhal, Kegeles and Rosenstock who worked in the United States Public Health Service; they questioned why so few people chose to participate in health prevention screening services (specifically, chest x-rays for tuberculosis [TB] screening) (Rosenstock, 1966/2005; Thalacker, 2010). Adapted from social-psychological theory and further refined by Rosenstock by the time it was published in 1966, the HBM sought to explain health-related behavior, as well as to predict future behaviors (Rosenstock, 1966/2005). The HBM was initially composed of four major components that determine a person's "readiness to act," taking the steps necessary to prevent, screen for, and/or manage disease:

1) Perceived susceptibility: The person believes they are at risk of contracting the disease or developing the health condition.

2) *Perceived severity*: The person believes the disease or health condition has serious health consequences if contracted.

3) *Perceived benefits*: The person believes that undertaking certain actions will reduce their susceptibility to the disease or health condition and its consequences.

4) *Perceived barriers*: The person believes that there are difficulties/barriers to performing the beneficial actions, and must decide if the costs of taking action is outweighed by the benefits of taking action.

In the original model document, Rosenstock (1966/2005) discusses the role of cues to action (where a person is exposed to an environmental cue that supports the perception of susceptibility or supports taking action). This concept was not one of the foundational concepts, as he noted that there wasn't enough research to ascertain its significance, and he commented that such cues (e.g., a poster urging health screening, a recommendation from a provider) may only provide a brief and transient effect on one's health behavior decision making (Rosenstock, 1966/2005). But as subsequent studies supported the need to revise the theory, modifying factors were introduced to the model that included cues to action and self-efficacy. Added to the model in the late 1980s (Rosenstock, Strecher, & Becker, 1988), the concept of self-efficacy was originally developed by Bandura (1977), and is defined as "the conviction that one can successfully execute the behavior required to produce the outcomes" (p.193). Although self-efficacy is an established theory in its own right, the concept of self-efficacy underlies many behavioral theories, including the HBM.

iii. The Health Belief Model and the Uptake of HIV Testing

First, a pregnant woman has to assess her risk of being HIV-infected (*perceived susceptibility*), either as a result of her own behavior(s) or those of her sexual partner(s). For many persons in Sub-Saharan Africa, HIV is still stigmatized as being a disease of prostitutes or those who have been unfaithful to their partners (Thorsen, Sundby, & Martinson, 2008). Women often do not consider themselves to be at risk for HIV if they themselves have not engaged in these behaviors, and do not seek HIV testing. Consequently, many women were not availing themselves of the opportunity to be HIV tested when presenting for antenatal care, and as noted in the earlier review of the literature, many clinics have now initiated provider-initiated, routine

HIV testing for all pregnant women with an "opt-out" option (Njeru, Blystad, Shayo, Nyamongo, & Fylkesnes, 2011).

In considering her risk of HIV-infection, a woman has to consider the consequences of being HIV-infected (*perceived severity*). It would be unusual for a woman living in Sub-Saharan Africa, where HIV has so negatively impacted the quality of life for so many individuals and families and led to the deaths of millions of people, not to comprehend the severity of an HIV infection. The concepts of perceived susceptibility and perceived severity are thought to provide significant motivation for behavioral change (Thalacker, 2010).

In addition to considering the threats of susceptibility and severity, a woman would contemplate the advantages of being HIV tested (*perceived benefits*), such as getting treated if she is infected and before she becomes ill, not transmitting HIV to her sexual partner or fetus, or adopting HIV prevention strategies if she is not infected. In the past, when access to HIV care and ART were not available, the benefit of knowing one's HIV status was debatable. However, now that effective treatment is accessible for many, health care providers and various government health organizations are attempting to reframe HIV testing as a first step to receiving the benefits of care (Levy, 2009).

Similar to assessing perceived benefits, a pregnant woman would also need to consider the disadvantages of being HIV tested (*perceived barriers*), including the ongoing fear and concern for her health that would result from knowing her positive status, and the impact that having a highly stigmatized disease would have on her relationship, family and social support system if disclosed. The concept of perceived barriers has been identified as being the most influential factor for predicting whether or not a particular health-related behavior will occur (Janz & Becker, 1984; Neff & Crawford, 1998). *Cues to action* would likely include

encouragement to be HIV tested by the providers at the facility where she obtains antenatal care, the implementation of routine testing (albeit with the possibility of "opting out") for all pregnant women at antenatal clinics, announcements on the radio emphasizing the need for everyone to "know their status," and other HIV education messages put out through churches, news media, non-governmental organizations (NGOs), and community health workers. And she would have to assess her level of *self-efficacy*, her ability to handle the reality of a positive result and its impact on every aspect of her life, including her ability to prevent transmission of the virus.

iv. The Health Belief Model and Adherence to PMTCT Protocols

After consenting to HIV testing and the confirmation of HIV infection, a pregnant woman should ideally be enrolled in the clinic's PMTCT program as soon as possible and be advised by the appropriate clinic staff of the benefits of ART use during her pregnancy. Recent changes to the clinical management guidelines by the Ministry of Health (MOH) in Malawi (CDC, 2013) support cART for all pregnant women, regardless of CD_4 count or WHO clinical staging criteria. Ideally, this should be initiated upon diagnosis, and as early as 14 weeks gestational age (the beginning of the second trimester), or if a woman presents for care later than 14 weeks, ART should be started as soon as possible, at least within seven days of her positive HIV test (MOH, 2011; WHO, 2010b). Women in their second trimester of pregnancy who test positive for HIV should be started on ART that same day. Medications are continued throughout the pregnancy, during labor, and ideally for the rest of a woman's life. Women who are HIV-infected and present in labor but have not started ART, interrupted ART, or stopped ART require immediate ART initiation (MOH, 2011). In Malawi, the infant should also receive ART (NVP or AZT syrup) for the first four to six weeks of life, regardless of the method of infant feeding. Breastfeeding is the recommended feeding method in Malawi, with exclusive breastfeeding for

six months gradually supplanted by "hygienically prepared foods" after six months, with complete cessation of breastfeeding at 24 months (MOH, 2011, p. 36).

One can imagine the difficulty a pregnant woman experiences upon learning that she is HIV infected, and then having to make decisions about medication therapy for herself during pregnancy, for her infant after delivery, and then for herself on an ongoing basis. Participation in a PMTCT program involves not only compliance with the ART regimen, but also (relatively) more frequent antenatal appointments, issues around disclosure to partner and family members (and possibly to a TBA, depending on where the woman chooses to deliver), and compliance around infant protocols, which includes obtaining and administering the liquid medication to the infant around the clock, adherence to feeding recommendations (exclusive breastfeeding without introduction of solids for six months), and repeated infant testing for HIV.

Application of the HBM is useful in understanding the decision-making process an HIV-infected woman faces regarding PMTCT program participation. The pregnant woman must have some level of perception of the risk that her own HIV infection poses to her unborn infant: she must understand that, at some point in her pregnancy, during labor/delivery or during breastfeeding, the infant may become infected with HIV. This *perceived susceptibility* of transmitting the infection to her infant is thought to be one of the most powerful determinants of a pregnant woman's commitment to participation in a PMTCT program (Levy, 2009); many women who receive an HIV diagnosis do not feel ill, but are motivated to take ARVs during pregnancy to prevent their infants from becoming infected with HIV. Similarly, she must acknowledge that HIV is a potentially life-threatening infection, not only to herself but also to her infant (*perceived severity*), which may serve to strengthen her resolve to adhere to her ART therapy. As noted above, the perception that the infant is susceptible to HIV infection and the

perception that this is severe should (and usually does) serve as significant motivation for enrollment and adherence to a PMTCT program (Levy, 2009).

In considering the difficult options she faces, the HIV-infected pregnant woman should understand that enrollment in and compliance with a PMTCT program can not only provide for an improvement and/or stabilization of her own health status, but also support the health of her unborn child (*perceived benefits*). Access to ART can benefit her by decreasing her viral load, strengthening her immune system, preventing repeated opportunistic infections, and prolonging her life. Reducing the risk of HIV infection in her child to less than 1 in 20 (if she breastfeeds) would likely be perceived as a major benefit that would incentivize adherence to the program (WHO, 2010b).

It is important to acknowledge that there are many *perceived barriers* to adherence to a PMTCT program that a pregnant woman must consider. A significant, and likely immediate, barrier is fear that confidentiality of her HIV status will not be maintained, and the stigma associated with others knowing her serostatus. Can she access PMTCT services without having to disclose her status to others, or having her status disclosed by others? She must decide whether or not to disclose to her partner that she is HIV infected, and depending on the strength of this relationship, this may expose her to violence, rejection, and/or blame (Ezechi et al., 2009; Mepham et al., 2011). Compliance to medication therapy while trying to maintain confidentiality is another barrier, as it may lead to unwilling or inadvertent disclosure: taking daily ART may be hard to hide from family and friends, and giving medication to a newborn four times per day would likely arouse the suspicions of others (Mepham et al., 2011).

Another perceived barrier might be the ART itself. Studies have shown that many women do not trust that the medications are safe to take, not only for themselves, but also for

their fetuses; the toxicity of some regimens has resulted in a persistent fear that ART has the potential to cause more harm than good to the fetus (McDonald & Kirkman, 2010; Otieno et al., 2010; Reynolds et al., 2006). The idea of taking medication that potentially produces unpleasant and/or harmful side effects is a barrier that a woman may choose not to overcome.

Many clinics providing PMTCT services are clearly designated as the "HIV Clinic" or "PMTCT Clinic," which perpetuates stigmatization of HIV and threatens patient confidentiality when a pregnant woman must obtain care in a setting obviously set apart for HIV-infected patients. Similarly, in countries where one's "medical record" is a self-carried "passport," listing "PMTCT Clinic" and the names of prescribed ARV medications allows anyone reading the passport access to this confidential information, including non-PMTCT providers or family members (R. Masengera, personal communication, 4/25/2011).

The literature also addresses issues of social justice and women who access care for HIV infection. Here, too, in the health care setting, lack of confidentiality and non-consensual disclosure occurs often. HIV-infected women who seek health care are often denigrated by medical, nursing and ancillary staff in the clinical setting (Chinkonde et al., 2009; Kasenga, 2010). Women are judged for being infected, assumed to be "guilty" and their infection a punishment for immoral behavior. Some providers feel that HIV-infected women shouldn't bear children, and treat them accordingly (London, Orner, & Myer, 2008); providers have been known to withhold ART from the infants of HIV-infected women (R. Masengera, personal communication, 4/25/2011). Thus, a woman deciding whether to access PMTCT care may have concerns about provider attitudes towards HIV-infected women. And women who do participate in PMTCT programs are chastised by staff should they not adhere completely to the program protocols (Thorsen et al., 2008).

HIV stigmatization not only affects the infected woman, but also on a larger scale continues to interfere with the success of PMTCT programs. Thorson and colleagues (2008) identified characteristics of PMTCT programs that actually perpetuate stigmatization of HIV. Programs are set up to provide benefits to incentivize HIV-infected women to participate, yet the benefits themselves serve as disclosure of a woman's status. For example, the government of Malawi provided cooking oil and flour to PMTCT participants (as well as others deemed vulnerable) during a food crisis in 2006; women who received such commodities were then recognized by the community as being HIV-infected and were subsequently resented for being given needed commodities and shunned for being HIV-infected (Thorson et al., 2008).

Another potential barrier is accessing appropriate delivery services. Worldwide, more than 60 million women deliver in non-institutional settings each year, and the vast majority of these births are attended to by TBAs, many of whom are untrained (UNICEF, 2009). Estimates suggest that up to 60% of women in Sub-Saharan Africa deliver in non-institutional settings (primarily their homes) under the care of TBAs (Stanton et al., 2007). Significantly, studies have shown that care by TBAs and deliveries at home are strongly correlated with nonadherence to PMTCT programs (Albrecht et al., 2006; Delvaux et al., 2009). TBAs are rarely cognizant of appropriate care and precautions in caring for HIV-infected pregnant women, and most do not have access to ART. Since a woman is likely to choose a TBA in her own community for reasons of proximity, familiarity, and a desire to deliver at home, maintenance of confidentiality by the TBA should the woman disclose her status is likely of great concern.

A last, but important, barrier to acknowledge is the actual reality of accessing PMTCT services. Much of the population in Sub-Saharan Africa lives in rural settings, far from health care clinics, with no available transportation. Regularly scheduled antenatal appointments are

thus often difficult to keep. In addition, some programs require payment for services or medications, which prevents many women from accessing them.

In summary, one can see that the fear and anxiety resulting from considering all possible perceived barriers to accessing PMTCT services could provide a strong incentive for *NOT* enrolling in a PMTCT program. Similarly, once enrolled in a program, a woman encountering barrier after barrier would easily be at risk for nonadherence to the PMTCT protocols and/or leaving the program.

v. Theory Evaluation

Critical evaluation of a theory is essential to determine its usefulness and relevance to research, education, and clinical practice (Chinn & Kramer, 2008). Criteria set forth by Meleis (2007) provides a framework for evaluating the HBM.

Clarity: The HBM outlines a stepwise approach to understanding the factors that lead to (or inhibit) health-related behavioral change. The model as a whole is clearly focused on motivating a person to enact healthy behaviors. The introduction to the model discusses underlying tenets of the model, such as readiness to act, and how the model was developed. The four primary concepts are clearly defined. For example, "perceived susceptibility" is defined as one's belief about his/her chances of getting a health condition. The definitions are succinct, yet unambiguous, and numerous clinical examples provide substantiation.

The relationships between concepts are clear and logically flow from one concept to another (e.g., the initial perceived threat, then perceived benefits coupled with consideration of any perceived barriers). Rosenstock elucidates the theory by using many clinical scenarios; as the theory was developed in response to poor uptake of TB screening, TB is a health condition

used to explicate the concepts (1966/2005). The later addition of modifying concepts (cues to action, self-efficacy) further clarified the theory.

In Rosenstock's original work (1996/2005), he explains the concept of perceived barriers as both factors that might preclude one from taking action, as well as negative consequences of the action once taken. Subsequent authors have focused on one aspect of perceived barriers (usually barriers to taking action) and not the other (e.g., De Paoli, Manongi, & Klepp, 2004; Turner, Hunt, DiBrezzo, & Jones, 2004). This may be a misinterpretation by others of Rosenstock's original tenets, and thus may speak to a need for clarification of this concept.

Consistency: Meleis refers to consistency as the "degree to which congruency exists between the different components of a theory," and notes that there is a degree of overlap between the criteria of clarity and consistency (2007, p. 258). In discussing clarity, it was noted that there is a logical progression from one concept to the next, which provides consistency within the model. There is a clear and understandable relationship or "fit" between each of the concepts. It makes sense that whether or not you think you are at risk for a health condition, what determines any potential behavior change would include how serious the condition is or how severe the consequences would be if you were to acquire the condition. Similarly, while one would logically assess the benefits of a behavioral change to avoid the health risk, one would also consider the negative consequences of such a behavioral change and/or barriers to making the behavioral change. And even after progressing through each step of the HBM process, if one does not have a sense of self-efficacy, lacking the assurance that one has the knowledge, stamina or skills to enact a behavioral change, it is unlikely that behavioral change would be attempted.

Simplicity/complexity: The original HBM contained four clear concepts, based on two classes of variables: those associated with readiness to act (perceived susceptibility and

perceived threat), and those associated with the belief that a behavior will be of an overall benefit to reducing the health-related threat (perceived benefits and perceived barriers) (Rosenstock, 1966/2005). As one of the first theories of health behavior, the simplicity of the HBM allowed for its widespread adoption and utilization by a number of disciplines to predict health behavior. And as an early health theory with diverse applicability, it laid the groundwork for our understanding of what motivates health behavior and served as a foundation for later enhancement of the HBM itself, as well as the development of other health promotion theories, such as self-efficacy theory, social cognitive theory, and the stages of change theory.

It may have been that the original HBM was perhaps "too" simple. As a psychological model, the HBM has been criticized for not taking into account the diverse social, environmental or even economic factors than also contribute to one's decisions regarding health behaviors (Denison, 1996). One could argue that one's own demographics and socio-cultural determinants manifest through each concept of the HBM (e.g., such that being a white, middle-class, well-educated person with health insurance will define one's perceived susceptibility to disease or shape one's evaluation of benefits and barriers), but this assumption would appear to lessen the significant impact these factors could have on health behavior. However, as will be discussed below, the HBM has been shown to be relevant for different demographic and sociocultural populations, including adolescents in LMICs.

As noted earlier, Rosenstock added the concept of self-efficacy to the HBM in the late 1980s, recognizing this as an integral predictor of behavior (Rosenstock et al., 1988). Similarly, the addition of the concept of cues to action, an acknowledgement of the increasing role of media, education and support systems, further enhanced the utility of the model and its efficacy in predicting behavior.

Tautology/Teleology: The HBM avoids the pitfalls of both tautology and teleology. The theory is clear, consistent and simple, without "needless repetition" of concepts throughout that would indicate tautology. Causes of behavioral change (perceived susceptibility, perceived severity, self-efficacy and cues to action) are distinct from consequences of behavioral change (perceived benefits and perceived barriers), thus avoiding teleological problems. In addition, there is strong evidence demonstrating that the HBM is logically coherent.

Diagram: There was no diagrammatic representation of the HBM in Rosenstock's original article (1966/2005). But since that time, numerous representations of the model exist in the literature. The HBM can be visually represented such that this representation further enhances the clarity and comprehension of the theory. While others have created more complex diagrams of the HBM (see Neff & Crawford, 1998), the attached diagram (Strecher & Rosenstock, 1997, adapted by the author) concisely represents the theory concepts, with clear linkages, and includes more recent additions to the theoretical model (Figure 1).

Circle of contagiousness: The HBM has been adopted extensively, serving as the conceptual framework by which a variety of different health-related disciplines (nursing, medicine, psychology, sociology) approach the issue of motivating people to embrace beneficial health behaviors. The literature is replete with extensive evidence of its utility in education, research and practice. As the theory has been adopted by different disciplines, it has been enhanced with additional concepts (e.g., demographics, socioeconomic factors) to improve its accuracy and usefulness.

A search of PubMed for research articles based on the HBM and published in the last few years revealed numerous citations, evidence of the models widespread utility (including Bödecs, Horváth, Szilágyi, Diffellné-Németh, & Sáador, 2010; Brewer et al., 2010; Guvenc, Akyuz, &

Açikel, 2010; Huang, Su, Chien, & Guo, 2010; Mugweni, Ehlers, & Roos, 2008; Noroozi, Jomand, & Tahmasebi, 2010; Ogbuji & Oke, 2010; Parsa & Kandiah, 2010; Temel, Ardahan, & Sesli, 2010; Tenkorang, Rajulton, & Maticka-Tyndaale, 2009; Thornton & Calam, 2010; Tovar, Rayens, Clark & Nguyen, 2010).

An earlier criticism of the HBM was that its usefulness was limited to the United States, or more generally, to developed, industrialized countries. A key assumption of the HBM is that one has the ability to control one's own decisions (Neff & Crawford, 1998), which may preclude other cultures where gender inequities and economic disparities exist, such as in Sub-Saharan Africa. However, researchers have found that the HBM is applicable to different ethnic groups, both in the US and other countries (Adhikari, 1998 [Nepal]; Huang, Su, Chien, & Guo, 2010 [Taiwan]; Lin, Simoni, & Zemon, 2005 [Taiwan]; Mugweni, Ehlers, & Roos, 2008 [Zimbabwe]; Neff & Crawford, 1998 [US]; Noroozi, Jomand, & Tahmasebi, 2010 [Iran]; Ogbuji & Oke, 2010 [Nigeria]; Parsa & Kandiah, 2010 [Malaysia]; Temel, Ardahan, & Sesli, 2010 [Turkey]; Tenkorang, Rajulton, Maticka-Tyndale, 2009 [South Africa]; Thalacker, 2010 [Hmong]).

Researchers have also elucidated the utility of the HBM in various studies related to HIV: Adih and Alexander (1999) studied condom use for HIV prevention in Ghana; Kabiru, Beguy, Crichton, and Zulu (2011) assessed HIV testing among adolescents in Kenya; and Tenkorang, Rajulton, and Maticka-Tyndale used the HBM in their research on perceived HIV risk in South Africa (2008). Also relevant to the topic of PMTCT, Chaibva et al. (2009) looked at adolescent non-utilization of prenatal care, and Mugweni et al. (2008) evaluated non-institutional deliveries; both studies were conducted in Zimbabwe, and both used the HBM as the theoretical underpinning of their research.

Usefulness: As evidenced by the literature search referred to above, the HBM is frequently used as a framework for both research and clinical practice. In addition to the studies just mentioned, the HBM has been used in other specialty areas, including women's practice of self-breast exam and uptake of mammography (Noroozi, Jomand, & Tahmasebi, 2010; Parsa & Kandiah, 2010; Temel, Ardahan, & Sesli, 2010), human papilloma virus vaccination (Brewer et al., 2010), cervical cancer screening (Guvenc, Akyuz, & Açikel, 2010), osteoporosis prevention (Huang, Su, Chien, & Guo, 2010), exercise and weight loss, as well as medication adherence, including in hypertension (Thalacker, 2010). Importantly for the phenomenon of interest to this author, the literature is also replete with examples of the use of the HBM with HIV prevention behaviors and HIV medication adherence (Downing-Matibag & Geisinger, 2009; Ogbuji & Oke, 2010; Oyekale & Oyekale, 2010).

The theory has been tested within different disciplines and in diverse venues. A key issue in its "testability" is the criticism that most HBM research has thus far been done on selected concepts of the model, rather than on the model as a whole (Denison, 1996). Additionally, criticism is aimed at the lack of research addressing the social and environmental factors that determine behavior. These concepts were clearly addressed by Rosenstock (1966/2005) but were not reflected in the original model concepts. While later added to HBM models (Stretcher & Rosenstock, 1997), research validating these concepts is lacking. Although evidence has been presented that recent studies continue to use the HBM as a framework for research, more research needs to be done in this area: as the HBM is studied across socioeconomic classes and in other cultures, the theory will be further legitimized, or appropriate modifications proposed and adopted as needed.

External components: Since the development of the HBM in the 1950s, the world has changed dramatically, from the perspective of health (the impact of the HIV epidemic, the growing disparities in health outcomes between populations), economics (the ongoing recession, the widening gap between rich and poor, governments facing economic collapse) and society (the change in sexual mores, increasing drug use, communication and relationships). Yet the HBM, in its current form, remains relevant and applicable to health behaviors today. It continues to provide a useable framework for professionals to engage patients in behaviors that result in a positive effect on health and well-being. In the opinion of this author, the HBM is an essential theory for consideration when designing health behavior interventions, including those involving the uptake of HIV testing and enrollment in PMTCT services.

B. The Theory of Planned Behavior in the Context of Prevention of Mother-to-Child Transmission of HIV

i. The Theory of Planned Behavior

The origins of the Theory of Planned Behavior (TPB) lie in the Theory of Reasoned Action (TRA), first proposed by Azjen and Fishbein (1980; cited in Sirur et al., 2009); the TPB represents an expansion of the TRA (Azjen, 1991). The primary concept of the TPB is that of *behavioral intention*, which is assumed to be the key factor in determining behavior (Azjen, 1991); three subconcepts are thought to affect behavioral intention:

1) *Behavioral intention*: One's perceived likelihood of carrying out a behavior.
    i. *Behavioral attitude*: One's attitude towards the likelihood of enacting a particular behavior; attitude is thought to be predictive of behavior.
    ii. *Subjective norm*: One's beliefs about how the behavior complies with social norms, how the people whose opinions matter to them feel about the behavior (approval or

disapproval), and how this affects one's motivation to perform (or not perform) the behavior.

iii. *Perceived behavioral control*: One's belief as to whether they have control over a behavior, and whether or not they can exercise that control.

This last subconcept was added when the theory was revised because of the limitations of the TRA when applied to behaviors that were out of one's voluntary control (Azjen, 1991). *Perceived behavioral control* is noted to be similar to Bandura's Theory of Self-Efficacy (Sumintardja et al., 2009), which is also a concept in the HBM.

ii. The Theory of Planned Behavior and the Uptake of HIV Testing

The TPB is a useful model for addressing the issues a pregnant woman faces regarding the uptake of HIV testing. Her *behavioral intention* as to whether or not she will have an HIV test will be determined by her *attitude* towards the testing. Does she believe she is at risk and needs to be tested? If she has the test, what are the possible outcomes and what is her evaluation of what they might mean for her? Would knowing her HIV status be a good thing or a bad thing? What *subjective norms* affect her intention? Have her partner and/or other family members consented to HIV testing? Would they be supportive of her being tested? Is she motivated to be HIV tested to gain their approval? What is her *perceived behavioral control*? Does she feel she is the one to decide to get tested, or must she obtain permission from her partner? If she feels she has the right to decide, does she feel she can make that decision, even in the face of partner opposition? Is she feeling pressured to take the test by a health care provider? As indicated by this last subconcept, the TPB is a useful model when looking at behaviors that necessitate cooperation between one person and another or others (Gu et al., 2009).

iii. The Theory of Planned Behavior and Adherence to PMTCT Protocols

The TPB is a suitable framework for addressing adherence to PMTCT protocols. A pregnant woman's *behavioral intention* as to whether or not she will initiate and comply with ART after a positive HIV test is predicated by her *attitude* towards lifelong medication for herself and, more importantly for most women, her *attitude* towards taking medication to prevent transmission of HIV to her fetus/infant. Here, *attitude* may be determined in part by her knowledge about HIV, her understanding of the risks of HIV transmission during pregnancy and breastfeeding, and perhaps by internalized stigmatization of HIV and fear of personal morbidity and mortality. What *subjective norms* affect her intention? Does she have a partner or family members who are HIV-infected and on ART? Is there someone to whom she could rely on for support? Is her social community one in which those with HIV are supported and cared for, or one where people living with HIV/AIDS (PLWHA) are a target of gossip and avoidance? What is her *perceived behavioral control*? Is she able to decide for herself whether or not to take ART, or are such decisions the purview of her husband/partner? If she makes the decision, can she do so even if she then must endure resistance from her husband/ partner and family members? Does she feel she can reliably adhere to an ART dosing schedule for herself and infant?

iv. Theory Evaluation

The following critique of the TPB will again use criteria set forth by Meleis (2007).

Clarity: The original work by Azjen (1991) is relatively dense and somewhat less readable than that of Rosenstock (1966/2005), but the theory itself is clear with explicit concepts. The TPB is presented in the literature as being comprised of four concepts; this author would postulate that the theory has one main concept (behavioral intention) and that the other concepts presented are in fact subconcepts, which determine the primary concept and subsequently behavior itself. The relationships

between the concepts and subconcepts are clear, such that the subconcepts of attitude, subjective norm and perceived behavioral control can be seen to logically influence behavioral intention.

Consistency: This criterion assesses the congruency between the theory's components. It could be noted that one's attitude towards a behavior may be determined in no small part by one's social relationships, allowing for a significant amount of overlap between the two concepts of attitude and subjective norm. A lack of distinction between these two concepts may reflect a lack of consistency in the defined boundaries of these concepts.

Simplicity/ complexity: The model contains one primary concept and three subconcepts; it is relatively simple rather than overly complex. However, one can make a case of adding more complexity to enhance its predictive capability. As in the HBM, the TPB makes the assumption that all other factors not discretely identified in the model, such as culture and environment, manifest by way of the theoretical concepts and do not independently predict behavioral intent (Rimer & Glanz, 2005). Such an assumption is logical, in that subjective norms and the development of behavioral beliefs can be seen to be a product of one's culture and environment, yet a more definitive inclusion of a socio-cultural concept could strengthen the model. Similarly, although the model addresses behavior that is under one's control, the theory's application could be greatly broadened by addressing behavior that is not under one's volition so that interventions designed for such situations would have a theoretical underpinning.

Tautology/Teleology: Tautology may be a minor issue, with some implied repetition between the constructs associated with one's behavioral beliefs and the influence of subjective norms. Such repetition serves to decrease the clarity of the theory. In the same manner, teleology may be an issue, as separation of cause and consequence is not clearly explicated: are subjective norms a cause of one's

behavioral beliefs? Or is one's assessment of societal and normative beliefs dependent on one's own behavioral beliefs?

Diagram: Azjen (1991) provides a diagram of the TPB that is simple and concise (Figure 2). This visual representation of the TPB serves to clarify understanding and thus application of the theory. The diagram would appear to support this author's assertion that there is one primary concept (intention) and three subconcepts that determine behavioral intention. Bidirectional relationships are highlighted in the diagram, further clarifying conceptual congruence.

Circle of contagiousness: The TPB, while not as widely utilized as the HBM, has certainly been adopted in the professional literature. Here, too, a PubMed search revealed a number of recent articles that use the TPB as the theoretical framework for their studies (Peters & Templin, 2010; Pinto & Ciccolo, 2010; Quinn et al., 2010; Shapiro, Porticella, Jiang, & Gravani, 2010). The TPB has also been used in research conducted with non-US populations (Bryan, Kagee, & Broaddus, 2006 [South Africa]; Buunk-Werkhoven, Dijkstra, & Van Der Schans, 2010 [Netherlands]; Enah, Sommers, Moneyham, Long, & Childs, 2010 [Cameroon]; Gu et al., 2009 [China]; Niven, Nevill, Sayers, & Cullen, 2010 [United Kingdom]).

The TPB has also been utilized as a framework for HIV-related studies conducted in both adolescents and adults in Sub-Saharan Africa. These include studies by Astrøm and Nasir (2009) on HIV treatment in Tanzania and Sudan; Giocos, Kagee, and Swartz' study on planned acceptance of an HIV vaccine by South African adolescents (2007); a study on condom use for HIV prevention in Ethiopia by Molla, Astrøm, and Berhane (2007); and Saal and Kagee's research on ART adherence in South Africa (2011).

Usefulness: Researchers in various disciplines have used the TPB to study physical activity and rehabilitation (McEachan, Sutton, & Myers, 2010; Niven et al., 2010; Pinto & Ciccolo, 2010),

hypertension self-care (Peters & Templin, 2010), research participation (Quinn et al., 2010), oral hygiene (Buunk-Werkhoven et al., 2010), condom use (Bryan et al., 2006; Gu et al., 2009), and HIV prevention (Enah et al., 2010). As noted earlier, the theory is of particular usefulness in addressing behavior that requires cooperation and negotiation between two persons, such as is the case with condom use and other HIV prevention strategies. The theory's usefulness has been established in both the research and clinical practice venues. A meta-analysis done by Albarracin, Johnson, Fishbein, and Muellerleile (2001) determined the utility of the TPB in developing effective behavioral interventions for the prevention of HIV and other sexually transmitted infections. A subsequent analysis by Albarracin and colleagues found the TPB to be relevant to Sub-Saharan Africa, specifically South African marginalized youth, including females (2004).

External components: As was the case with the HBM, the goal of the TPB is to provide a framework for professionals working with individuals, such that decisions around health-related behaviors lead to optimal outcomes. The theory provides the structure to approach the complex issue of personal decision-making as it relates to health. This is congruent with our purpose as health care professions, not only to provide excellent care but also to guide patients in their behavioral decisions.

C. Adolescent Development

Since the late 19th century/early 20th century, adolescence has been recognized in the developed world as a distinct period during which a child transitions to adulthood (Fatusi & Hindin, 2010), a time of profound change in the physical, psychological, and emotional makeup of an individual. But "adolescence" is a sociocultural and psychological construct of industrialized countries, and for many cultures in the developing world, the concept of adolescence doesn't exist: you are a child, and when you begin to develop secondary sexual characteristics at puberty, you are an adult.

While there is now an increasing awareness of the distinct transition period that we call adolescence in LMICs, research studies have primarily focused on the risks and consequences of this time frame (e.g., increasing sexual activity prior to marriage, lack of contraceptive use, unintended pregnancies), rather than considering these behaviors within the context of the neurobiological processes that an adolescent is undergoing.

In the last two decades, neurobiological research, aided by magnetic resonance imaging, has demonstrated the profound brain growth that occurs during adolescence (Weinberger, Elvevåg, & Giedd, 2005). The cells of the brain respond to the hormonal changes of pregnancy (estrogen, progesterone, testosterone), but are also likely influenced by environmental factors such as nutrition, education, infection, and parenting (Dixon-Mueller, 2008), although the extent of this influence is not well delineated as of yet. The limbic structures of the brain are associated with one's socio-emotional development, and are among the first to experience changes associated with the onset of puberty (Keulers, Evers, Stiers, & Jolles, 2010), although full maturation does not occur until later in adolescence. Until these structures mature, adolescents may experience emotional lability and behavioral control issues. The neural connections of the prefrontal cortex (PFC) develop and become more efficient, allowing for the maturation of PFC skills such as impulse control, planning, and organization. These higher order executive functions take longer to develop completely, with associated tasks improving linearly with age (Keulers et al., 2010).

There is a paucity of research on the cognitive, social and emotional development of adolescents in Sub-Saharan Africa. There are certainly studies on adolescents, but the use of the term seems to be based solely on chronologic age, rather than any mention of developmental stage. While there is a slowly increasing awareness of the uniqueness of this transitional time, to

date there is no research to support or refute that the developmental processes of Sub-Saharan African adolescents are any different than those of their peers in more developed countries. Additionally, many external factors that influence adolescent behavior in industrialized countries, such as educational achievement and parental involvement, have been shown to confer similar influence on adolescent behavior in LMICs (Santelli & Melnikas, 2010). The world has seen dramatic changes in the last two decades, changes that continue to evolve and shape our world: technologic advances, ease of communication and access to the internet, increasingly rapid globalization, heightening economic crises, food insecurity, civil unrest and migration. All of these changes have impacted adolescents not only in developed countries, but also those in LMICs. One could argue that adolescents in low- and middle-income countries are transitioning from childhood to adulthood at an accelerated pace than in the past, "catching up" to their Western counterparts, although certainly cultural influences and restraints still exist.

For the purposes of this dissertation, this author has of necessity assumed that a teen-aged girl in Sub-Saharan Africa is no more or less an "adolescent" than her counterpart in the developed world, evidence to the contrary lacking. This paper provides support for utilizing the two theories presented to understand the challenges and decision-making processes facing a pregnant adolescent in Malawi who is HIV-infected.

D. Summary

The theories discussed herein provide a clinically relevant structure for assessing and intervening in the complex issues that determine health-related behavior. Importantly, both theories include concepts that address beliefs, environmental and cultural influence, and self-efficacy/perceived control. Both theories provide an appropriate structural foundation for an intervention aimed at promoting HIV testing and adherence to PMTCT protocols among pregnant women. Numerous

studies have been published that have utilized either the HBM or the TPB as the overarching framework for their research questions, studies that have been conducted in Sub-Saharan Africa and other LMICs, among poor and marginalized populations, including adolescents. As more research is conducted that uses the HBM or the TPB as a theoretical framework, our understanding of the applicability of these theories to diverse populations will continue to grow.

Chapter IV: The Research Study

A. Title of the Research Study

Prevention of Mother-to-Child Transmission of HIV in Pregnant Adolescents in Malawi

B. Purpose of the Study

HIV infection in adolescents and young women remains an important health issue in countries such as Malawi. In addition, HIV infection in females of childbearing age poses a substantial risk of HIV transmission to the fetus/newborn, contributing to more than 90% of infections globally (UNAIDS, 2010b). Yet to date there have been very few studies of adolescent pregnancy in the context of HIV infection or on adolescent PMTCT adherence, even though this is an area of great importance given the high rates of HIV infection in adolescent and young adult females in Sub-Saharan Africa. And specifically, there are have no studies of HIV-infected Malawian adolescents and their uptake of PMTCT services.

Therefore, the purpose of this study was to examine the prevalence of HIV infection amongst a population of pregnant adolescents, ages 19 and younger, receiving antenatal care at the Ndirande Health Centre in Blantyre, Malawi. For those pregnant adolescents found to be HIV-infected, additional data from in-depth interviews was obtained to identify barriers and facilitators to the uptake of PMTCT services.

C. Study Objectives

The objective of the study was to identify barriers and facilitators to the uptake of and adherence to PMTCT protocols among pregnant HIV-infected adolescents, so as to add to the small body of literature in this area. The overriding intent of this study was to provide new knowledge that may assist in the development of adolescent-specific programs for pregnant HIV-infected young women.

The objectives of the study were:

1) *To quantify the HIV prevalence rate among pregnant adolescents at an antenatal clinic in Blantyre, Malawi.*

The rationale for including this objective was to determine the actual HIV prevalence rate among adolescents receiving care at the Ndirande Health Centre. To date, no research has been published that accurately determines the HIV prevalence rate in pregnant Malawian adolescents. The current government estimate is 5.8%, while nursing faculty at the clinic estimate the prevalence to be between 10-12% (M. Chikelepo, personal communication, 7/22/11; Malawi Government, 2012). In addition, determining the HIV prevalence rate in this population of pregnant adolescents serves to contextualize the results from the study.

2) *To quantify the utilization of PMTCT services by pregnant HIV-infected adolescents in an urban Malawian population.*

3) *To quantify the adherence to PMTCT services by pregnant HIV-infected adolescents in an urban Malawian population.*

4) *To identify the barriers and facilitators to adolescent uptake of PMTCT services in urban Malawi.*

D. Research Questions

The specific research questions of this mixed methods study are as follows:

1) What is the HIV prevalence among adolescent females, ages 19 and under, receiving antenatal care at the Ndirande Health Centre?

2) Among pregnant, HIV-infected adolescents receiving antenatal care at the Ndirande Health Centre, what is the rate of the uptake of PMTCT services and the rate of adherence to these services?

3) What are the barriers and facilitators that determine the uptake and adherence to PMTCT services in a population of pregnant, HIV-infected adolescents receiving antenatal care at the Ndirande Health Centre?

E. Study Hypotheses

The specific hypotheses of this mixed methods study were as follows:

Hypothesis #1: The prevalence of HIV infection among pregnant adolescents, ages 15 to 19, receiving antenatal care at the Ndirande Health Center differs from the national HIV prevalence rate of 11%.

Rationale: Specific data on HIV prevalence among pregnant adolescents, ages 19 and under, is lacking. Determination of prevalence rates is be important for tailoring adolescent-specific antenatal care, HIV care, and PMTCT services.

Hypothesis #2: Uptake and adherence to PMTCT services in pregnant HIV-infected adolescents differ from rates of uptake and adherence to PMTCT in pregnant and postpartum HIV-infected adult women as reported in the literature.

Rationale: Numerous studies have examined pregnant women's utilization of various aspects of PMTCT services, including acceptance of HIV counseling and testing, adherence to medication for themselves, provision of medication for their infants and exclusive breastfeeding (Albrecht et al., 2006; Chinkonde et al., 2009; Delvaux et al., 2009; Varga & Brooks, 2008a). But even in studies that include older (e.g., at least 18 years old) pregnant adolescents (Kasenga et al., 2007; Manzi et al., 2005), the results have not been stratified by age group, precluding any understanding of adolescent-specific experiences of PMTCT. While studies suggest that African adolescents have worse experiences when seeking sexual and reproductive health services than do adults (Mashego & Peltzer, 2005; Varga & Brooks, 2008a), research on adolescent

experiences with PMTCT programs is lacking, yet needed.

#3: The barriers expressed by pregnant HIV-infected adolescents to the uptake of and adherence to PMTCT services will differ from the barriers perceived by HIV-infected pregnant adult women as presented in the literature, and these differences are best explored using qualitative methodology.

Rationale: Studies of adult HIV-infected women have elicited many barriers to the utilization of PMTCT services, including fear of positive test results, social stigmatization of HIV, lack of confidentiality, fear of disclosure, lack of spousal support, negative staff attitudes, transportation difficulties, program financial costs, and preference for home delivery (Iwelunmore, Zungu, & Airhihenbuwa, 2010; Kasenga, Byass, Emmelin, & Hurtig, 2009; Manzi et al., 2005; Reynolds et al., 2006; Thorson et al., 2008). Because of a lack of research to date, it is unclear if the barriers to PMTCT program uptake experienced by pregnant HIV-infected adolescents are similar or different. An adolescent's developmental stage, immature prefrontal cortex, sense of invulnerability, influence exerted by the peer group, and lack of knowledge of HIV, pregnancy, and vertical transmission may result in the same or a dissimilar list of barriers to accessing PMTCT services.

Chapter V: Methodology

A. Introduction

Methodology can be understood as the values and ideas that the researcher uses to design and conduct her study: in other words, the "methods" of research (Holloway & Wheeler, 2002). The research method employed should be determined by the research question and study aims, and not predetermined before these have been elucidated, despite one's self-identification as a "quantitative researcher" or "qualitative researcher." Whether one uses a quantitative approach or qualitative approach will depend on the phenomenon of interest, and what method (or mix of methods) is most appropriate for obtaining the desired data to answer the research question.

Given the aims and objectives of this dissertation research study, a mixed methods approach was chosen. Discrete quantitative data was sought to determine HIV prevalence in the study population, while qualitative interviews were conducted to explore the facilitators and barriers to PMTCT protocol adherence. A discussion of mixed methods research follows.

B. Mixed Methods Research

The term "mixed methods" has increasingly been found in the literature, evidence of increasing interest in, popularity of, and respect for this integrative model of research (Bryman, 2006). The method was popularized in the early 20th century through the work of sociologists and cultural anthropologists (Johnson, Onwuegbuzie, & Turner, 2007). These scientists believed that using both quantitative and qualitative research methods was the best way to answer their research questions. Although the use of mixed methods is not a new phenomenon (Brannen, 2009), the use of the terminology is, relatively so (although it may also be referred to as multi-method, mixed research, and mixed methodology; Bryman, 2006). Johnson and colleagues speak to mixed methods as a new research movement, discourse, or paradigm (2007, p. 113).

As defined by the recently published National Institutes of Health report by Creswell and colleagues entitled *Best Practices for Mixed Methods Research in the Health Sciences*, mixed methods research is a methodology that: a) is used for research questions that are complex and thus require multi-level perspectives while maintaining attention to cultural context; b) combines the use of rigorous quantitative methods to determine the scale and frequency of specific constructs and rigorous qualitative methods to identify and comprehend the meaning of these constructs; c) employs several different methods to obtain research data (e.g., questionnaires, biophysical measurements, interviews, focus group discussions); d) designs data collection so that by integrating different methods, the strengths of each are maximized; and e) allows for the conduct of research with attention to philosophical and theoretical perspectives (Creswell et al., 2011, p.4).

The philosophical underpinnings of mixed methods research have been placed between the qualitative Sophists and the quantitative Socrates, yet in reality the philosophy of mixed method research is one of pragmatism, with which it has long been associated (Brannen, 2009; Johnson et al., 2007). Why not seek an expanse of theoretical and/or practical knowledge that comes from a variety of inputs, in order to obtain the most comprehensive and truthful representation of a field of inquiry? The best means to do so is through the use of both quantitative and qualitative research in mixed methods.

Mixed methods are appropriate for research questions or study aims that cannot adequately be studied with either quantitative or qualitative data collection and analysis techniques alone. It is particularly useful for areas of inquiry that have not been previously studied in depth, as a way to generate more specific research questions or facilitate the development of appropriate data collection instruments.

Collins and O'Cathain (2009) refer to mixed methods an "emerging paradigm" (p. 2), and thus the method is defined differently by different researchers. It is important to distinguish the term mixed methods, as intended here to mean the equal and intentional use of both quantitative and qualitative methods to answer a research question, from the different meaning put forth by some researchers. For example, in qualitative research, some authors refer to mixed methods when they have employed two or more different qualitative approaches (e.g., observations and interviews, individual in-depth interviews and focus group discussions) within the same study. In quantitative research, the term mixed methods can be further confused. The use of questionnaires and biophysical measurements in quantitative research can refer to mixed methods. Similarly, expanding a structured questionnaire to include several open-ended (e.g., qualitative) questions or quantifying qualitative data can be construed as a misuse of the original intent of the method, and one can reasonably argue that this is not truly mixed methods research (Bryman, 2006). For the purposes of this dissertation, the discussion of mixed methods refers to the collection of and analysis of both quantitative and qualitative data within the same study.

The key component of mixed methods is that the researcher is using both quantitative and qualitative methods together, collecting both quantitative and qualitative data, to develop the breadth and understanding of the question at hand. Here, one database builds on another. For example, a researcher could use quantitative methodology to determine the prevalence of a particular health condition (e.g., HIV infection in a population of pregnant adolescents) or frequency of behavior (e.g., uptake of and adherence to PMTCT services), and then use qualitative methods to explore, identify, and contextualize experiences and their meanings in the lives of the study participants.

The two types of data are analyzed via their respective analytic techniques, then integrated so as to "maximize the strengths and minimize the weaknesses of each type of data" (Creswell et al., 2011, p. 5). There are several methods by which this integration can be accomplished: merging data, connecting data, and embedding data (Creswell et al., 2011).

Merging data refers to integrating both quantitative data (numerical data) and qualitative data (quotes, text, images) together. Merging data can be accomplished in one of several ways: by combining the data results from both sets of data together in the discussion section of a research report (often the quantitative data is presented first, as is done herein, then the qualitative data to support or explicate [or question] the quantitative results), or by taking qualitative data and convert it into a quantitative form (e.g., by counting the numbers of a particular response or themes). An example would be a study report in which HIV parameters (e.g., CD_4 cell count, viral load, markers of drug resistance) and adherence to ART medication were assessed as continuous and categorical variables, and then data from participant interviews or focus groups presented to understand barriers and facilitators of ART adherence. Creswell and colleagues (2011) also note that merged data can be presented together in a table or graph.

Connecting data refers to a process in which one dataset is used to develop a data collection instrument or tool to collect a second data set (Creswell et al., 2011). For example, quantitative data on sociodemographic characteristics of an HIV-infected population and their adherence to ART could be collected and analyzed, and the results used to guide the development of an interview guide or questions for a focus group exploring reasons for nonadherence.

Embedding data is the third type of data integration, and refers to embedding one dataset, usually one not related to the primary aim of the study, into the "main" dataset to provide

additional clarification or enrichment (Creswell et al., 2011). As an example, a randomized control trial might study two groups of pregnant adolescents, one of which receives routine antenatal care and the other adolescent-focused antenatal care (e.g., peer counseling, group visits, prenatal education adjusted for educational level) to assess any difference in birth outcomes. Embedded within the study could be interviews with participants from each group to assess understanding, preferences, and dislikes.

Greene and colleagues (1989) developed a scheme of five justifications for using mixed methods research:

a) triangulation-to find corroboration and convergence between quantitative and qualitative findings;

b) complementarity-using results from one method to further explicate, illustrate or clarify the results of the other;

c) development-use the results of one method to inform the development of the other method design, such as measurement tools or sampling strategies;

d) initiation-using the question or results of one method to provide a new framework or context for the question or results of the other method; and

e) expansion-broadening the depth and extent of research inquiry through the use of different research methods.

Bryman (2006), building on the work of Greene and colleagues (1989), further elucidated justifications put forth by authors of mixed methods research publications. These additional justifications comprise a more comprehensive list, perhaps as a reflection of the increasing use of mixed methods and support for doing so, and include:

a) triangulation-as above, to enhance and corroborate findings from one method with the other;

b) offset-here, authors note that each method has its strengths and weaknesses, and thus combining them offsets the weaknesses of and exploits the strengths of each;

c) completeness-using both methods brings a more comprehensive assessment to the research question at hand;

d) explanation-one method may be used to explicate the findings of the other method; this is of particular usefulness when one method produces unexpected or contrary results;

e) instrument development-the use of a qualitative research method to develop quantitative measurements or scales. This author would also suggest the converse is also true, in that quantitative results can provide support for the development of qualitative methods (e.g., interview questions, focus group discussion topics);

f) credibility-suggests that the use of both methods strengthens the believability and veracity of the study findings;

g) context-qualitative data provides a context for understanding the relationship between quantitative variables;

h) illustration-the use of qualitative data to elucidate "dry" quantitative findings, which is further enhanced by the use of direct quotes and personal stories obtained through qualitative inquiry;

i) confirm and discover-the use of qualitative data to generate new research questions and hypotheses, and within the same study answer them with quantitative methods;

j) utility or improving the usefulness of findings-this justification refers to the idea that mixed methods research findings will have increased usefulness (e.g., for providers in a clinical setting);

k) diversity of views-this diversity is achieved by combining the researcher's (quantitative) perspective and the participant's (qualitative) perspectives; and

l) enhancement-this refers to the enrichment or augmentation of the findings of one method by collecting further data with the other method (Bryman, 2006).

These reasons for supporting mixed methods underlie the strengths of this approach to research. According to Bryman's review (2006), the most common reasons for the use of a mixed methods approach (either as a rationale for the study design or how the mixed data were actually used) were triangulation, completeness, illustration and enhancement. This would seem to support that a mixed methods approach is most useful for the rigorous study of a topic and provides a breadth of study interpretation not often possible by one method alone.

C. Study Design

The study utilized a mixed methods design, with two phases. The first quantitative phase of data collection was a cross-sectional study, employing a survey questionnaire to obtain socio-demographic information. The second phase of the study used a qualitative methodological approach to determine the barriers and facilitators to adherence to a PMTCT program. To operationalize the qualitative phase of the study, in-depth interviews were conducted with ten HIV-infected pregnant adolescents, who were further queried as to whether or not they had begun taking ART and their adherence to the ART regimen.

D. Study Setting

The two largest cities in the country are Blantyre, the country's financial and commercial center, and Lilongwe, the political capital (populations 856,000 and 821,000 respectively; Index Mundi, 2013). The district of Blantyre comprises the city and surrounding area, with a catchment population of 1.2 million (van Lettow et al., 2012). Blantyre's Queen Elizabeth Central Hospital is the largest hospital in the country, with 1000 beds, and serves as a referral center for all of southern Malawi and the teaching hospital for the country's only medical school (Sawatsky, Parekh, Muula, & Bui, 2014). The district has a total of 28 health care facilities that provide antenatal care and have implemented PMTCT services, including the Ndirande Health Centre where this study was conducted (van Lettow et al., 2012). In 2010, the district of Blantyre saw 42,450 new antenatal visits and nearly 33,000 deliveries in these health care facilities (van Lettow et al., 2012).

There are eight main ethnic tribes in Malawi, the largest of which is the Chewa (Malawi High Commission [MHC], 2012). Each tribe has its own language and dialect, although Chichewa and English are the official languages of the country (MHC, 2012); Chichewa is the common language in Blantyre, and both the survey questionnaires and in-depth interviews were conducted in Chichewa.

Ndirande is a township located in the southwestern zone of Blantyre and notable for its severe poverty, crime, and lack of development (Chillro, 2013). The Ndirande Health Centre, the site of this research, is located at the back of a large dirt lot, littered with garbage and crowded with people milling about and conducting small trade. The Ndirande Health Centre is one of the busiest health centers in Blantyre, with a catchment population of 221,227 (R. Chamanga, personal communication, 2/6/13). There are numerous services offered by the health

center, including HIV testing and counseling, ART, antenatal care and maternity services (the obstetric service delivers an average of 300 babies per month), family planning, youth-friendly health services, an expanded program of immunization, a supplemental feeding program, early infant diagnosis (of HIV), tuberculosis care, and community home-based care (R. Chamanga, personal communication, 2/6/13). In addition, the clinic has a laboratory and a short stay ward, for those awaiting transfer to Queen Elizabeth Central Hospital.

In contrast to most clinics in Malawi where adolescent-specific care is non-existent, the Ndirande Health Centre began providing antenatal care to adolescents every Friday morning in April of 2011. The large group of pregnant adolescents gathers in the central room of the clinic, where they receive education from the nursing staff and other information from "guest" speakers, and are then seen individually for their antenatal visit. All antenatal care is provided by nurses and midwives. The clinic staff has been trained to provide adolescent-appropriate care. The staff has an interest in the welfare of pregnant adolescents, and not only provide antenatal care, but also provide support related to particular life circumstances and encouragement of long term goals, such as returning to school (E. Kapito & R. Chamanga, personal communication, 1/14/14).

The author visited the Ndirande Health Centre in July of 2011 and observed the "teaching" prior to the patients actually being seen. Two women from "Sisters to Sisters," an organization of HIV-infected women who are open about their infection and work to educate other women, were there encouraging the girls (in Chichewa) to get tested and to have safer sex (testing is now "opt-out" in Malawi, although many women think that it is mandatory to be tested in order to receive antenatal care, which is not true). Then a (rather stern) head nurse stood up and (also in Chichewa) talked to the girls about not having sex. To this author's Western orientation, it seemed punitive and not very "youth-friendly" at all (although study

results will reveal that this was not interpreted as such by the clinic attendees). Then the girls got up and stood in line to be weighed and have their blood pressure taken, and were then seen individually for their antenatal visit. Only one male partner was observed among the 45-50 young women being seen that day.

E. Study Approval

Study approval was sought from both the University of California, San Francisco's Committee on Human Research (CHR) and the University of Malawi's College of Medicine Research and Ethics Committee (COMREC). CHR approval was somewhat belabored by a user-unfriendly online application system with multiple glitches that required many in-person consultations with the CHR advisor. Study approval was granted on July 9, 2012 (Appendix A).

Prior to obtaining approval from COMREC, the author was advised that it was necessary to obtain approval to conduct the study at the Ndirande Health Centre from the Director of Health and Social Services for the city of Blantyre, Dr. E. Kanjunjunju, who provides medical supervision of the health center. The study proposal was sent to him and approved on March 20, 2012 (Appendix B). Subsequent approval was also required from Blantyre's District Health Officer (DHO), Dr. E. Nyirenda-Dziwani. A letter was drafted explaining the study proposal and a copy of the study delivered in person by one of the research assistants, Mrs. Rose Chamanga, who explained the purpose of the study and her role as research assistant. Approval was granted by the DHO on July 9, 2012 (Appendix C).

COMREC approval required the author to have CHR approval prior to applying to COMREC, creating a delay of several months in the application process, as this basically required two separate, consecutive application submittals. In addition, COMREC meets once monthly or less often; the committee requested several small clarifications to the original

proposal, with resubmission and approval delayed by the infrequent meetings. Notification of the study approval was conferred via email in December 2012 to the author from Dr. Angela Chimwaza, Dean of Postgraduate Studies and Research at Kamuzu College of Nursing in Blantyre and a former COMREC board member who helped facilitate the application to COMREC (Appendix D). No formal letter of study approval was received from COMREC.

F. Study Sample

Quantitative survey data was collected from a convenience sample of pregnant adolescents, age 19 and younger (the inclusion criteria) who were receiving antenatal care in the Ndirande Health Centre. The sample size was calculated at 84 study participants (two-sided α=0.05, power = 0.80, moderate effect size 0.30); however, since the HIV prevalence rate was unknown in this clinic population and in order to survey enough HIV-infected adolescents (who would then be approached to participate in the qualitative interviews), 102 pregnant adolescents completed the survey questionnaire.

Concurrent with the quantitative data collection, pregnant adolescents who chose to reveal that they were HIV-infected (inclusion criteria) during the survey questionnaire were then asked if they would like to participate in an in-depth interview. Ten subjects consented to participate in an interview.[xiv]

G. Data Collection

i. Data Collection Instruments

A socio-demographic survey questionnaire was developed by the author, based on data reported in the Malawian Demographic and Health Survey (NSO, 2010), and was structured similarly to a Malawian village survey from the Global AIDS Interfaith Alliance (GAIA; E.

[xiv] Of those who participated in the survey questionnaire, eight disclosed that they were HIV-infected. In order to conduct a minimum of ten in-depth interviews, the research assistants obtained consent from two HIV-infected pregnant adolescents (after the initial surveys were completed) who had not completed the questionnaire.

Schell and S. Rankin, personal communication, 2011). Survey questions sought to ascertain demographic information, including markers of wealth and poverty, as well as obstetric, gynecologic and HIV history. While the questionnaire's internal consistency could not be evaluated for reliability because the data sought was not interrelated, the survey's validity is supported by the fact that the Malawian government (and many others) uses some of these same data questions for its Demographic and Health Survey, conducted every four to six years (NSO, 2010). The Demographic and Health Survey program is funded by USAID, and data collected are subjected to rigorous statisitical analysis to ensure that it represents the population under study (NSO, 2010; Rutstein & Rojas, 2006). In addition, guidelines for in-depth interview questions were also developed by the author, based on *a priori* knowledge from published research on barriers and facilitators to PMTCT adherence.

ii. Variables

The survey questionnaire included demographic information (age, marital status, educational level, occupation, living situation, including markers of wealth/poverty such as availability of electricity and water). Sexual history was obtained (age of coitarche, number of sexual partners, contraceptive knowledge and use), as was prior and current obstetric history (parity, prior or current complications, gestational age, gestation age at first antenatal visit, number of antenatal visits, pregnancy experiences at an adolescent-focused antenatal clinic), and HIV awareness (testing history, test result [optional information], knowledge of HIV transmission, HIV prevention).

iii. Data Collection Procedures: Quantitative Data

Two research assistants (Mrs. Rose Chamanga and Mrs. Esnath Kapito), Masters-prepared registered nurses fluent in both Chichewa and English, provided expertise in midwifery

and women's health. The author met with them in Malawi in the summer of 2012 to orient them to the study, including the study purpose and objectives, data collection methodology, and ethical considerations. The survey and interview questions were reviewed in detail to ensure understanding and appropriateness, as were the study consent forms (separate consent forms for the survey questionnaire and interview). Consent forms, survey questions, and interview guidelines were translated into English and back-translated into Chichewa by the two research assistants (Appendices E-L). In lieu of the physical presence of the study author (who lives in the United States), Dr. Angela Chimwaza, who was familiar with the study and personally acquainted with the research assistants, was available for consultation for any issues that might have arisen during data collection, although none did. However, the author was in frequent contact with the research assistants by email during the data collection period (and during data analysis as well).

Data collection took place between January and August 2013. During this time frame, the research assistants attended the weekly Friday adolescent-specific antenatal clinic sessions at Ndirande Health Centre. They approached clinic attendees to see if they would be willing to participate in the demographic survey study; if the clinical attendee was interested, the research assistant would obtain written consent to participate in the study. The survey questionnaires were then completed by the research assistant in an area away from other clinic attendees. No names or any other identifying information was obtained by the research assistants. At the end of the study, each participant received a small token of appreciation for their participation, a bar of soap (a common gift for research study participants in Malawi).

iv. Data Collection Procedures: Qualitative Data

Participants completing the survey questionnaire who disclosed that they were HIV-

infected were asked if they would like to participate in the second phase of the study, an in-depth interview. Qualitative data was collected through these in-depth interviews with ten HIV-infected pregnant adolescents. Once written consent was obtained, the research assistants conducted the interviews (either the same day the survey questionnaire was administered, or at a later clinic visit), using a semi-structured format of questions. Again, no identifying information was obtained from the participants. Interview questions sought to ascertain participant concerns regarding their HIV status in the context of being pregnant, when they were diagnosed and when they began ART, their knowledge of PMTCT efficacy and benefits, and any facilitators and/or barriers they were encountering in adhering to their therapy. Interviews were conducted in Chichewa. Interview data was digitally recorded by the research assistants, who then transcribed the data into English and sent written transcripts via email to the author. Clarification of any points regarding interview data were resolved via email with the research assistants.

H. Data Analysis: Quantitative Data

Completed questionnaires were submitted to Invest in Knowledge Malawi (IKI), an organization building research capacity in Zomba, Malawi. IKI staff coded and inputted the questionnaire data into STATA® statistical analysis software (Version 13.1, StataCorp LP, College Station, TX, USA) and uploaded the deidentified data into a secure cloud environment. Data was then analyzed by the author (Tables 4-26).

Simple frequency rates were used to assess participate demographic characteristics, access to care, sexual and contraceptive history, obstetric history, HIV knowledge and testing, and pregnancy experiences. Data were then analyzed by two dependent variables: the study participants' marital status, to contextualize adolescent pregnancy in this particular cohort, and by HIV status, the primary focus of the study. Univariate analyses were conducted to examine

the association between *marital status* and sociodemographic, sexual and contraceptive history, obstetric history and HIV knowledge. Similarly, *HIV status* and sociodemographic, sexual and contraceptive history, obstetric history and HIV knowledge were examined using univariate analyses. The Wilcoxon (Mann-Whitney) test, a non-parametric analog to the *t-test*, was used to analyze ordinal variables because the study samples under analysis were not normally distributed. In lieu of χ^2 testing, the Fisher's exact test was used to determine relationships between categorical variables, as the expected frequencies of one or more cells was most often under five, given the relatively small sample size of some variables (e.g., those who were HIV-infected). Univariate logistic regression was performed on independent variables found to be significant with the Wilcoxon (Mann-Whitney) and Fisher's exact tests on the dependent variables (marital status and HIV status). Multivariate logistic regression analyses were then conducted using potential covariates whose significance level in univariate analysis and univariate logistic regression was $p \leq 0.05$. Factors were also examined based on *a priori* information from published research. Odds ratios (OR) and confidence intervals (CI) for associations between HIV infection status, marital status, and other relevant variables were determined. The final multivariate logistic regression model by marital status was not statistically significant (p=0.08, McFadden's R^2 0.33; Table 24), but the final multivariate logistic regression model by HIV status was statistically significant ($p<0.0001$, McFadden's R^2 0.43; Table 26). All statistical analyses were performed using STATA® (Version 13.1, StataCorp LP, College Station, TX, USA).

I. Data Analysis: Qualitative Data

The qualitative data was analyzed using the process of thematic analysis, specifically following the six phases of thematic analysis as explicated by Braun and Clarke (2006):

1) *Become familiar with the data*-The transcribed interviews were read and re-read prior to beginning the analysis; memos were written as the interviews were read repeatedly, as part of the process of becoming familiar with emerging patterns and as a way to begin to understand the data;

2) *Generate initial codes*- The author initially developed deductive codes, based on the individual interview questions. These codes represent the original information sought by the in-depth interview process, such as "awareness" (what do they know about preventing the fetus from becoming HIV-infected?), barriers (what challenges do they meet in getting or taking ART?) and facilitators (who and/or what helps them to be compliant with taking their ART?).

3) *Search for themes*-As the initial codes were categorized, the identification of themes began, representing the beginning of data interpretation—the inductive phase of the process. Repeated patterns in responses were identified and grouped accordingly; repeated reading of the data enabled the author to develop more subtle interpretations of the responses. Some of this interpretation was data-driven, meaning that the author's background knowledge of PMTCT in pregnancy and barriers to adherence to ART allowed for identification of subtleties in the responses.

4) *Review themes*-In this phase, themes were reviewed by the author as well as the research assistants. Input from the research assistants was incorporated into the development of themes (as well as the discussion of the study results). Further refinement allowed for the combining of similar themes. Themes that were not repeated in the data (e.g., were expressed by only one participant), while perhaps providing interesting insight, were eliminated.

5) *Define and name themes*-The themes were further explicated and named. The data was again reviewed with the defined themes in mind, to ensure support for and the validity of the themes as identified.

6) *Produce the report*-The presentation of the qualitative data results and analysis from the in-depth interviews follows hereafter.

Of note, many researchers now use qualitative statistical programs developed for the computer, such as NUD*IST,® NVivo,® and atlas.ti.® These programs facilitate coding and theme development, organization of themes, likely ease memoing for most researchers, and assist with data management. However, for the purposes of this dissertation, no statistical software was utilized.

Chapter VI: Quantitative Research Results

This chapter will report the results obtained from the survey questionnaire. First, data will be presented from all of the 102 completed questionnaires. The data includes demographic information, access to antenatal care, sexual and contraceptive history, obstetric history, HIV knowledge and testing, and pregnancy experiences. The data is then reported with marital status as a dependent variable, to provide insight into adolescent pregnancy in Malawi, and finally with HIV status, the phenomenon of interest, as a dependent variable, which provides a context for the qualitative interview data.

A. Survey Questionnaire Results

i. Demographic Information

Data (Table 4) from 102 pregnant adolescents who participated in the survey questionnaire indicate a mean age of 17.8 years (range 15 to 19 years). One-third were orphans, either single (having lost a mother or father) or double (having lost both parents). Two-thirds of the adolescents were married. More than half (52.9%) had some high school education, while 46.1% had an 8th grade education or less. Three-quarters of the participants listed their occupation as "housewife," while another 9.8% were engaged in some type of business endeavor (e.g., hairdresser, selling charcoal, maize or flitters[xv]). Only two participants were still in school, while nearly 11% identified themselves as a "school dropout" or otherwise not working. Most of the participants' husbands or partners were working, primarily as laborers (or in some capacity in the construction business; 23.5%), in business (16.7%) or in sales (13.7%). Interestingly, seven (6.8%) of the study participants did not know what their husband/partner did for work (including two who were married).

[xv] Flitters are a type of pastry popular in Malawi.

As would be expected of a mostly married study cohort, approximately 60% lived with their husbands, while a few others lived with their in-laws. Nearly all others lived with their parents (26.5%) or grandparents (7.8%). Slightly more than half had access to electricity in the home (55.9%). All had access to water, mostly through piped water sold in kiosks by MASAF.[xvi] Only 5.8% had water available in the house.

ii. Access to Antenatal Care

Access to antenatal health care was assessed by asking how far the study participants had to come to the clinic.[xvii] Nearly one quarter of the adolescents (n=24) lived more than two hours from the health center, yet only 10 participants said they took a minibus. Ninety percent of all the study participants indicated they used no other form of transportation other than walking, even those living more than an hour away (Table 5). In the Demographic and Health Survey (NSO, 2010), 55% of 15 to 19 year olds reported that the biggest barrier to accessing care was distance to the nearest clinic.

iii. Sexual and Contraceptive History

More than half (55%) of the 102 study participants had their first sexual encounter at age 16 or younger; six had had sex by the age of 14 (Table 6). The vast majority (95.1%) had only had one sexual partner. As noted earlier in this dissertation, the Malawi Demographic and Health Survey (NSO, 2010) found that nearly 18% of Malawian girls between the ages of 15 and 19 reported that they had experienced sexual violence (14.3% reported that their first sexual encounter was forced; 17.8% reported experiencing some form of sexual violence); in this study

[xvi] MASAF-Malawi Social Action Fund, a community organization involved in water and sanitation projects.
[xvii] Establishing accurate estimates of distance to the clinic was challenging. Some participants responded specifically with the number of minutes or hours it took to get to the clinic, while others mentioned the townships they came from, or just said "near" or "far." Those who responded "near" were included in the "less than one hour" category; those who said "far" were categorized as living more than two hours from the clinic. Specific townships were identified on internet maps (such as Google Maps®) and coded for distance accordingly.

cohort, although none is acceptable, only 7.8% reported a history of forced sex and only one study participant acknowledged having traded sex for money or goods.

Knowledge of contraceptive methods was low, and reflective of the lack of availability of certain options. Eight study participants knew of no contraceptive methods at all; only half had heard of oral contraceptive pills, and even fewer were familiar with injectables, implants or intrauterine devices.

Use of any modern contraceptive method was very low. Forty-five study participants (44.1%) had never used any contraception; of those who had used some type of birth control, 90% reported that method was condoms. Few had used pills (*n*=2) or injectables (*n*=5).

Those who had used contraception were asked why they had discontinued doing so. Nearly half (47.4%) reported that they wished to become pregnant as the reason for discontinuing their contraceptive method. Interestingly, the same number of participants reported that they stopped because their husband or partner did not want them to use contraception.

iv. Obstetric History

At the time of the study, the majority (57.8%) of study participants were in the late second trimester or in the third trimester[xviii] (between 25 and 36 weeks gestational age; no participants were more than 36 weeks pregnant); a third were in the second trimester, with the remaining few in the first trimester (Table 7). Participants were asked how pregnant they were when they first initiated antenatal care. Nearly three-quarters (73.5%) did not begin care until they were in the second trimester of their pregnancy, and nearly 10% began care in the third trimester. As of the date they answered the survey questionnaire, two-thirds of the participants

[xviii] Although not universally standardized, for the purposes of this study the first trimester refers to a gestational age of up to 13 weeks; the second trimester is 14-26 weeks; and the third trimester is 27-40 weeks.

had only had one or two antenatal visits (Figure 3). Only 19.6% had had three visits, despite the majority being in the late second trimester or in the third trimester.

Few study participants related any problems with the current pregnancy. A few (7.9%) noted back or abdominal pains, while ten participants either currently or previously had malaria.

Not surprisingly, more than three-quarters of the study participants were primiparas. Seventeen had been pregnant once before, while six reported two prior pregnancies. Of those who had been pregnant previously, 25% had suffered a miscarriage, and 20.8% revealed they had had a therapeutic abortion.

v. HIV Knowledge and Testing

As could be expected, all of the study participants had heard of HIV before (Table 8). They were all aware that HIV was transmitted via sexual contact. However, only 71.6% were aware that HIV could be transmitted by blood, and only 22.6% knew that mother-to-child transmission was possible. Others mentioned that HIV was spread by razor blades, "dirty" objects (such as dirty dishes or sponges, which is incorrect); only two mentioned breastfeeding as a risk for HIV transmission.

When asked about means by which one could protect oneself from acquiring HIV, the majority (87.3%) knew that using condoms could prevent HIV transmission. Yet only 42.4% agreed that abstinence was protective, and 33.3% knew that avoiding contaminated needles was protective. A few mentioned that wearing protective clothing and gloves could prevent HIV transmission (presumably referring to caring for someone who was ill).

As noted earlier, Malawi has adopted a "test and treat" approach to identifying HIV infections. Not surprisingly, 100% of the participants reported that they had received HIV

counseling, had been offered an HIV test, had taken the HIV test, and received their test results. Of the 102 study participants, eight (7.8%) revealed that their HIV test was positive.

vi. Pregnancy Experiences

Two final questions on the survey were asked to assess the benefits of an adolescent-focused antenatal clinic (Table 9). Study participants were asked, "What is the best thing about coming to antenatal care with other girls your age?" Nearly 60% of respondents noted the peer support provided, as well as describing a "freedom to share" their thoughts and experiences with others like themselves. Also mentioned by 16% was the respectful environment created at the clinic. A number of respondents appreciated the pregnancy-related information the clinic staff provided. A sense of "general encouragement" and specifically encouragement to return to school and continue their education was also mentioned.

Study participants were also asked if there was anything they would change about their antenatal care at the clinic. Nearly all (94%) replied that they were happy with the care and had no suggestions for improvement. A very few suggested the clinic should offer more preventive health care or noted the need for more staff.

B. Survey Questionnaire Results by Marital Status

As noted above, the survey questionnaire data was analyzed by the study participants' marital status. Notably absent in the literature are studies on pregnant adolescents that include sociodemographic information as well as sexual, contraceptive, and obstetric history in the context of marital status.

i. Demographic Information by Marital Status

As expected, the age difference between the single and married study participants was significant (Table 10). One third of the study participants (n=34) were unmarried; their mean

age was 17.4 years. The married study participants had a mean age of 18 years; 69.2% were 18 or 19 years old. (p=0.008). In bivariate logistic regression, unmarried study participants had 0.6 odds of being older (p=0.009, 95% CI 0.392-0.877). There was no difference in orphan status between the two groups.

Years of schooling did not differ significantly between the single and married study participants. Approximately 40% of both single and married adolescents had between five and eight years of schooling, with slightly more than half having between nine and twelve years of school. Literacy was similar in both groups.

There was a significant difference between the study participants' identified occupation. Although single, nearly 60% of this group identified "housewife" as their occupation, versus 82.3% of the married participants. More married participants were in business; more single participants were unemployed and/or school dropouts (p=0.001). Similarly, there was a difference between the occupations of the study participants' husbands or partners. Husbands of the married participants were more likely to be laborers or in construction, in business and in sales, while partners of the single participants were more likely to be students or not working (p<0.001).

The living situation differed between the single and married groups. Obviously, married participants were more likely to live with their husbands, while single participants were more likely to live with their parents or other family members (p< 0.001). There was no difference in availability of electricity or water between the two groups. Interestingly, single participants were 3.8 times more likely to own their own home than married participants (p=0.003, 95% CI 1.58-9.42).

ii. Access to Antenatal Care by Marital Status

There was no difference between the single and married study participants with regard to distance to the clinic (Table 11). The majority of each group lived within one hour of the Ndirande Health Centre. Nor was there a difference in means of transportation to the clinic: nearly everyone walked to the clinic, regardless of distance.

iii. Sexual and Contraceptive History by Marital Status

The married study participants were more likely to have been sexually active by age 16 than unmarried study participants (p=0.025; Table 12). In bivariate logistic regression, unmarried study participants had 2.7 odds of having had sex after the age of 16 (p=0.027, 95% CI 1.122-6.500; Table 23), although this variable lost significance in the final model (Table 24). There was no difference in the number of sexual partners, history of forced sex, or history of transactional sex. Knowledge of contraceptive methods did not vary significantly between the two groups, nor did contraceptive use (or non-use). While not statistically significant, a few married participants had used oral contraceptive pills while no unmarried participants had, and more married participants had used injectables than unmarried. More married participants reported they had stopped their contraceptive method because they desired pregnancy. Interestingly (although not achieving statistical significance), among the unmarried participants, 35.3% reported they stopped contraception because their partner wanted them to, versus 22.1% of married participants.

iv. Obstetric History by Marital Status

Gestational age at the time of the study was not different between the unmarried and married participants (Table 13). Reported gestational age at the time of antenatal care initiation was earlier (less than 12 weeks) for 19.1% of the married participants, versus 11.8% of the

unmarried group. Between 70% and 75% of both groups initiated care between 13 and 24 weeks GA. As might be expected, 17.6% of unmarried participants initiated care in the third trimester, while only 5.9% of married participants did so. The number of antenatal visits to date did not differ significantly between the two groups.

More married participants reported back and abdominal pain complicating their pregnancy than did single participants. More married participants suffered from malaria, while more unmarried participants complained of having diarrhea (p=0.045).

The number of previous pregnancies did not differ significantly between the two groups, nor did the incidence of prior pregnancy complications, including spontaneous abortions. However, more unmarried study participants who had had a previous pregnancy had undergone therapeutic abortions than those who were married (p=0.042); in bivariate logistic regression, unmarried participants had 12.75 odds of having had a therapeutic abortion compared to married participants (p=0.031, 95% CI 1.262-128.78), although this was no longer significant in the final regression model.

v. HIV Knowledge and Testing by Marital Status

As noted earlier, 100% of study participants were aware of HIV, received HIV counseling, agreed to testing, and obtained their HIV test results. Of the eight HIV-infected study participants, three were single and five were married, which was not significantly different (Table 14). There was no statistically significant difference in knowledge of risk factors for HIV transmission or means by which to protect oneself from HIV infection.

vi. Pregnancy Experiences by Marital Status

Nearly three-quarters of both single and married study participants mentioned peer support, freedom to share, and the respectful clinic environment as benefits of receiving

antenatal care in an adolescent clinic. The majority of both groups also reported being happy with the care and had no suggestions for change. Neither reached statistical significance (Table 15).

C. Survey Questionnaire Results by HIV Status

The population of interest of this study is HIV-infected pregnant adolescents. With the purpose of exploring the barriers and facilitators of PMTCT adherence in this population (through in-depth interviews), the analysis of the survey data with HIV status as the dependent variable provides an important contextual background of demographic information, sexual and contraceptive history, obstetric history, and HIV knowledge.

i. Demographic Information by HIV Status

Several demographic variables were statistically significant when analyzed by HIV status (Table 16). As has been reported in the literature, those who were HIV-infected were more likely to be an orphan than those who were HIV uninfected (p=0.016).[xix] In logistic regression models of selected variables, being HIV-infected consistently increased the odds that a study participant would be a single or double orphan (Table 25). In the final multivariate logistic regression model (Table 26), those who were HIV-infected had a 24 odds of being an orphan than those who were HIV uninfected (p=0.009, 95% CI 2.19-267.87).

Study participants who were HIV-infected were less likely to own their own home (p=0.003) and less likely to have electricity in the home (p=0.020). In the logistic regression model (Table 25), those who were HIV-infected had a 10.3 odds of having not having electricity (p=0.032, 95% CI 1.219-87.276).

[xix] Orphan status was analyzed both as a binary (orphan, not an orphan), as well as by specific parental loss (loss of mother, loss of father, loss of both parents). Both analyses were statistically significant (p=0.016 and p=0.018 respectively).

There was no difference in marital status among those who were HIV-infected: approximately two-thirds of both HIV-negative and HIV-positive study participants were married. There was no significant difference between the HIV-negative and HIV-positive study participants in years of education, literacy, occupation (self and husband or partner), living situation, or availability of water.

ii. Access to Antenatal Care by HIV Status

There was no difference between HIV-positive and HIV-negative study participants in regards to access to the clinic (Table 17). The majority of both groups lived within an hour of the clinic and their means of transport to the clinic was walking.

iii. Sexual and Contraceptive History by HIV Status

HIV-infected study participants were more likely to report a history of forced sex than those who were HIV-negative (p=0.015; Table 18); in the bivariate logistic regression model, HIV-positive study participants had a 10.7 odds of having had a forced sexual experience (p=0.006, 95% CI 1.968-57.951; Table 25). Other variables, including number of sexual partners, history of transactional sex, and knowledge, use, and discontinuation of contraceptive methods, were not different between the two groups. Although not statistically significant, nearly half of the HIV-negative study participants had their first sexual encounter by the age of 16, while only a quarter of the HIV-infected participants had had sex by that age.

iv. Obstetric History by HIV Status

There was no statistically significant difference between the HIV-positive and HIV-negative study participants in regards to their obstetric history (Table 19). Gestational age at first antenatal visit, number of antenatal visits, pregnancy problems, number of previous pregnancies, and history of spontaneous or therapeutic abortion were similar between the two groups.

v. HIV Knowledge and Testing by HIV Status

All study participants were counseled and tested for HIV; eight tested positive for the virus. There was no relationship between HIV status and awareness of the risk factors for HIV transmission or ways to protect oneself from HIV, other than avoiding contaminated needles (p=0.049). Although not statistically significant, one-quarter of HIV-negative study participants were aware of MTCT, while none of the HIV-infected participants knew that they were at risk of transmitting the virus to their child (Table 20).

vi. Pregnancy Experiences by HIV Status

Both HIV-infected and HIV-negative study participants expressed similar benefits to engaging in antenatal care in an adolescent-focused clinic, including the peer support and encouragement received (Table 21). Similarly, the majority of both groups reported being happy with the care received and had few suggestions for clinic improvements.

Chapter VII: Qualitative Research Results

i. Characteristics of Study Participants

The age range of the ten study participants in the in-depth interviews was 15 to 19 years old; most participants were 18 or 19 years old. Sixty percent were married at the time of the interview. The majority of the participants were diagnosed with HIV infection at the antenatal clinic. Only one participant had started ART prior to her planned pregnancy; all of the others started ART after becoming pregnant. One adolescent was diagnosed at age 15 in a hospital after an unspecified illness prior to her pregnancy; she was not given ART at that time and didn't start ART until she was five months pregnant and presented for antenatal care at the clinic. Another participant was also diagnosed at 15 years of age in a mobile clinic prior to pregnancy, but didn't start ART until she was eight months pregnant.

ii. Barriers to PMTCT Adherence[xx]

Overall, the interview participants identified few barriers to PMTCT adherence. Only two adolescents, both age 15, mentioned missing appointments (and thus running out of medication). One was at her mother's funeral:

> *Interviewer (I): Do you go to the [clinic] to get ART…?*
> *Participant 1 (P1): No, I haven't gone…for treatment.*
> *I: Why?*
> *P1: Because I had gone to attend my mother's funeral ceremony the date I was supposed to go for resupply of drugs. And the drugs were finished and I didn't go back to the [clinic].*
> *I: Why?*
> *P1: Because I forgot.*

The second participant had a similar story:

> *I: What discourages you from going to receive ART at the [clinic]?*
> *P9: Sometimes I miss appointment date [sic] due to laziness.*

[xx] In the context of this study, "PMTCT adherence" refers to attendance at scheduled antenatal clinic visits and the taking of ART as prescribed.

I: When did you miss your appointment date and why?
P9: I went to the village for the burial ceremony of my grandmother who had passed away. I was supposed to go for resupply of drugs on 10th [sic] but I went there on the 20th so I didn't take any drugs for six days since they were completely finished.

In multiple studies previously reviewed earlier (Chinkonde, et al., 2009; Reynolds, et al., 2006; van Lettow, et al., 2011; Varga & Brooks 2008a), fears of disclosure, stigmatization, and rejection by partner, family and community were an often cited and significant barrier to PMTCT adherence by HIV-infected pregnant adult women. In this study, several interview participants mentioned similar concerns:

I: What discourages you from going to receive ART…?
P5: Sometimes you think that people will see you going for ART and they will know that you have HIV at this age, and naturally you are very concerned and ashamed…

Two of the married adolescents said they had not disclosed their HIV infection to their husbands. As one of them explained:

I: Does your husband know that you are HIV positive?
P3: No.
I: Why didn't you tell him?
P3: I am afraid.
I: Why?
P3: I am afraid if he knows that he will tell his friends.

While not identified as a barrier to PMTCT adherence, one participant did mention finances as a challenge:

P5: …[my husband] does not earn enough money which makes it difficult for me to have good nutrition. Usually, we eat the same type of food with no variety and mostly is [sic] starch and vegetables. Yes, I know a pregnant woman who is also HIV positive needs proteins and fats as well.[xxi]

Interview participants were queried as to any fears or concerns that they might have for their own health or that of their child, as it relates to their HIV-infectivity. Concerns about the

[xxi] Optimal nutrition for HIV-infected persons includes proteins and fats to counteract the rapid oxidation of these nutrients, maintain immune system function, fuel the increased energy requirements associated with HIV, and prevent ART drug toxicity (Grobler, Siegfried, Visser, Mahlungulu, & Volmink, 2013).

safety of the medications for the fetus or themselves, the fear or experience of medication side effects, or worries about being "discovered" taking ART might have been identified as barriers to adherence. Yet no interview participant identified any concerns for their own health; many mentioned that taking ART was a means to staying healthy themselves, a facilitator to PMTCT adherence.

Similarly, many participants stated that had no fears for the health or safety of their child. They expressed their reliance on ART to not only benefit their own health, but also to protect the fetus from HIV:

> *P5: [If you are taking ART] you cannot transmit the virus to the unborn child.*
>
> *P6: With ART, you are able to protect the child from getting the infection from you and in addition, you also get healthy.*

iii. Facilitators of PMTCT Adherence

Several facilitators to PMTCT adherence were identified in the data. These included family support, knowledge and acceptance of one's status.

Most striking in every interview participant's responses was the role that support from one or more family members played in their adherence to the PMTCT program. Every participant identified at least one family member who was aware of her HIV infection, and that the family member/members provided support for her, specifically encouraging her to take her medication as prescribed and attend her antenatal clinic appointments. Of those who were married, all but two said their husbands were aware of their HIV status. Some stated that other siblings were also on ART, which also provided a supportive environment for adherence. In response to the question as to what type of support she has at home, one participant noted:

> *P9: My mother, father, and uncle support me by ensuring that I get the treatment on time, giving me financial and all the support I need such as food,*

clothing...They also encourage me to come to the [clinic] for antenatal care and ART.

A 19 year old study participant who had been diagnosed two years prior to becoming pregnant also noted non-family members as a source of support:

P10: When I discovered my status, the doctor encouraged me to take ART and… even my friends and relatives encourage me.

Another facilitator to PMTCT adherence was knowledge of HIV, ART, and ART's role in preventing transmission to the child. Nearly every study participant mentioned the knowledge they had received at the clinic as helping them adhere to their PMTCT regimen:

I: What encourages you to go to receive treatment at the [clinic]?
P7: They counsel us on the side effects of the drugs such as vomiting and abdominal pains... They also advise us on good nutrition which is important to somebody in my condition.

Other participants noted they were encouraged to attend clinic appointments because:

P5: They counsel us on good nutrition, on the importance of taking the treatment accordingly and compliantly so that the unborn child is protected and the other benefits of taking ART such as leading a healthy life.

P9: They counsel us on drug compliance, and that we should not share drugs with anybody and that we should wait until they are completely finished before we go for re-supply.

In particular, the study participants' understanding of the benefits of ART for themselves and their child were a strong motivator to attend clinic appointments and take their ART regularly.

P3: I don't think I will have any problems taking ART…I will be thinking about my unborn child when taking the drugs.

P5: The benefits [of ART] are that when your immunity was [sic] low, ART will boost that, and it is maintained at high levels which helps the woman to be healthy, and as a result, [the unborn child is protected].

P8: Knowing the benefits of taking this treatment makes me determined to take it.

P9: Right now I do not have any fears because I am on ARV treatment which will help me protect my unborn child from getting HIV and that we both will be healthy.

However, three interview participants did express an understanding that, despite being on ART, there was still the possibility of HIV transmission:

P3: My fear is that I can transmit the virus to my child and I don't want to do that.

P4: I have fears about my unborn child and I hope I don't transmit the virus to the unborn child.

The only participant who identified her pregnancy as planned and who had been on ART for two years prior to becoming pregnant consistently provided the most thoughtful insights to the questions. She demonstrated her understanding of ART:

P10: I have some fears that I can transmit the virus to my unborn child, though with ARV treatment the chances are reduced.

Another theme of note is that of acceptance, as in acceptance of one's HIV infection. Accepting that one is infected and understanding the risks associated with a pregnancy in the context of HIV infection is key to understanding the importance of compliance with ART. Acceptance of one's HIV infection is also an important prelude to disclosure to others who can be a source of support.

I: What encourages you to go to receive treatment at the hospital?
P6: What encourages me is that I have accepted my condition and I know that ARTs [sic] will help me lead a healthy life and also protect my child.

After admitting that she is sometimes afraid to be seen going to the clinic for care and having others realize she is HIV infected, one participant went on to say:

P5: ...but if you have accepted [your HIV status] you are not very worried about [being seen going for ART], rather you focus on getting healthy and protecting the unborn child.

One participant appeared to demonstrate acceptance of her HIV infection and the necessity of taking daily ART by normalizing it:

P2: What encourages me most is that ART is just like any other treatment you can take when you are ill. If you are able to take panadols (e.g., acetaminophen) then you can take ART.

iv. Additional Themes

While not specifically categorized as barriers or facilitators of PMTCT adherence, two additional themes of interest were evident in the participants' responses. The first was regret. Nearly all of the adolescents stated that they would not have become pregnant--"would not have let myself get pregnant"--if they had known they were HIV infected. Unfortunately, since most were diagnosed at the antenatal clinic once they were already pregnant, it was too late.

I: Would you have become pregnant if you had known about your serostatus before you were pregnant?
P4: If I knew that I had HIV I would not have become pregnant…[I am] very sad about it.

P5: …if I knew I had HIV, I would still be using contraceptives so that I don't get pregnant. I would be afraid to transmit the virus to the unborn child.

P6: ...if I knew I had HIV, I would have been very sad and I could not have this pregnancy at all.

Others expressed regret about the timing of the pregnancy, not necessarily that they had become pregnant while HIV infected:

P2: No, if I knew I had HIV I would start on ART first before getting pregnant.

P8: ...if I knew I had HIV, I would not have had this pregnancy at all… let me say that maybe I would have the pregnancy later….so that I could check my immunity first before getting pregnant.

P9: I could have waited until I am on ART before getting pregnant…so that I am sure that my immunity is high and my body is strong before getting pregnant.

Only one study participant, who had been diagnosed two years prior and had been on ART since her diagnosis, discussed the timing of her pregnancy as a deliberate choice:

I: How old were you when you tested HIV positive?
P10: I discovered that I have HIV two years ago when I was 17.

I: How did this happen? Where was this?
P10: We just went to a clinic, with my boyfriend then, to have HIV test and we were both found to be HIV positive. In fact I remember the date, it was on 22nd December, 2011.
I: Were you pregnant at the time?
P10: No, I was not pregnant.
I: So, what happened?
P10: We were both started on ART and a year later we got married and that's when I became pregnant.
I: Did you discuss this, that you wanted a child now?
P10: Yes, we discussed that I should become pregnant now.

Two study participants revealed that the pregnancy was clearly not their choice. Both were married, but had not disclosed their HIV status to their husbands, and it was the husband who wanted them to have a child:

I: So how did you decide to become pregnant?
P1: It's my husband who wanted me to get pregnant.
I: Did he know you have HIV?
P1: No, he does not know that I have HIV.
I: Would you have become pregnant if you had known about your sero-status before you were pregnant?
P1: In fact, when I became pregnant, I knew that I had HIV.

A second respondent had a comparable story:

I: How old were you when you tested HIV positive?
P3: I was 15 years old…
I: And how did this happen?
P3: I went for a test in a mobile clinic.
I: Were you pregnant at the time?
P3: No.
I: So how did you decide to become pregnant?
P3: It's because my boyfriend decided we should be married and it just happened that I got pregnant.
I: So, you knew about your status before you married?
P3: Yes.
I: So after you got married it's your husband who wanted you to get pregnant?
P3: Yes.
I: Does your husband know that you are HIV positive?
P3: No…I am afraid [to tell him].

Chapter VIII: Discussion of Study Results

Given the dearth of research on pregnant adolescents in Malawi and other low- and middle-income countries, the survey questionnaire was designed to identify some of the socio-demographic and health-related characteristics in a population of pregnant adolescents receiving antenatal care in Blantyre. In addition, the survey questionnaire established the prevalence of HIV infection in the study population, and identified HIV-infected participants for the in-depth interviews.

This study cohort was limited to pregnant adolescents between the ages of 15 and 19. The Malawi Demographic and Health Survey reported an HIV prevalence of 4.2% among females aged 15 to 19 years (versus 1.3% in males in that age range; NSO, 2010), while a more recent estimate was 5.8% (Malawi Government, 2012). The Demographic and Health Survey also reported HIV prevalence by age at first sexual encounter: for females who began sexual activity before the age of 16, the HIV prevalence rate was 16.6%; for those who did not have sex until the age of 18 or 19, the HIV prevalence rate was 10.8% (NSO, 2010). Among pregnant women in Malawi (not stratified by age), 10.6% were HIV-infected; the HIV prevalence in this population had been as high as 22.8% in 1998 (NSO, 2010). In this study, the HIV prevalence rate was 7.8%, nearly twice that of all Malawian female adolescents aged 15 to 19 years, but lower than the overall HIV prevalence rate for all pregnant women. Significantly, the HIV prevalence rate in this study cohort is higher than either of the government's recently reported prevalence rates (Malawi Government, 2012; NSO, 2010; See Table 22 for a comparison of this and other study data with data reported in the Malawi Demographic and Health Survey of 2010).

Two-thirds of the study participants were married. Those who were married had a higher mean age than those who were single (18 years versus 17 years). Nearly 60% of the study

participants were 18 or 19 years of age. Only one survey participant was 15 years of age, single and HIV-infected. Data on poor outcomes associated with adolescent pregnancy clearly indicate that younger adolescents are at higher risk, particularly those aged 15 and younger, while HIV itself is a risk for untoward outcomes, including PTD (Adeyinka et al., 2010; Braine, 2009; Kumar et al., 2007; Kurth et al., 2010; Mahavakar et al., 2009). Studies of adult pregnancy often include females over the age of 18, who have not been found to be at age-related risk of pregnancy complications.

Early marriage in common in Malawi, as was noted in the review of the literature above (Walker, 2012). In this cohort of 15 to 19 year olds, the demographic data reveals that two-thirds of the study participants were married, which is consistent with published data on adolescent marriage in Malawi: 75% of females are married by the age of 20 (NSO, 2010). Nearly two-thirds (*n*=5) of the HIV-infected study participants were married; as the in-depth interview data revealed, not all had disclosed their HIV status to their husbands.

Specific data on the incidence of pregnancy among unmarried adolescents in Malawi is lacking. Mayzel et al. (2010) reported that, with the increase in premarital sexual activity among adolescents, there has been an increase in the number of unmarried adolescents who become pregnant. The data obtained in the survey questionnaire reveals that one-third of the study participants were unmarried and pregnant, a somewhat surprisingly high percentage in the context of Malawian culture.

Given the early age of marriage, adolescent pregnancy is not uncommon in Malawi, as noted in the literature review. With a fertility rate of 152 per 1000 females aged 15 to 19, 35% of Malawian adolescents have given birth by the age of 18, with 65% giving birth by the age of 20 (NSO, 2010; UNFPA, 2013a). Adolescent pregnancy is less common in those who have

completed secondary school, and is more likely in those with only primary schooling (NSO, 2010). Adolescent pregnancy is known to interrupt a girl's education, particulary in settings where pregnant girls are forbidden or discouraged from attending school, and many adolescent mothers never return to finish school. More than 90% of Malawian females attend primary school, yet significantly fewer (30.3% in urban areas, 9.1% in rural areas) go on to high school (NSO, 2010). Congruent with the above findings, in this study only 10.8% of the study participants had completed 12 years of schooling (data not shown) and only one participant had completed a post-graduate diploma. It is concerning that 90% of the study participants are unlikely to finish their secondary education, given the challenges of new motherhood. However, study participants mentioned the encouragement provided to them at their antenatal visits, and specifically noted the encouragement by staff to return to school: it is hoped that some, if not many, of these study participants continue their education after their pregnancies.

As has been found in a number of research studies, orphans are at higher risk of HIV infection than their non-orphan counterparts (Odaga, 2012). While a percentage of orphans are infected perinatally (from an infected mother, who may subsequently have died), others who are not infected at birth are still at higher risk of HIV acquisition, due to the socioeconomic and social vulnerabilities associated with orphanhood (Odaga, 2012). Data from the survey questionnaire confirms that those study participants who identified as orphans were more likely to be HIV-infected than those who had not been orphaned: 75% of the study participants who were HIV-infected were orphans, half of whom had lost both parents. However, those who were orphans were no more likely than those who were not to have begun sexual activity at an earlier age, nor have a history of forced sex (data not shown). It is not clear whether the orphans in this study acquired HIV perinatally (although one would expect that they would have been diagnosed

prior to becoming pregnant, either through early infant diagnosis screening or because they developed an HIV-related illness in childhood) or through heterosexual sex. Sadly, all of those who were HIV-infected reported having had only one lifetime sexual partner; if infected through heterosexual sex, it was from the one lifetime partner. In the interviews, two of the participants were afraid to tell their husbands that they were HIV-infected, yet it is very likely that they became infected from their husband (who may or may not know his HIV status).

A majority of married study participants identified their occupation as "housewife," as did most of the single study participants. This is somewhat confusing, at least in the Western context of the word housewife. Although the study participants were asked specifically if they were married, living with a partner, or single (as well as separated, divorced, or widowed), all participants identified themselves as either married or single. It may be that those who were unmarried but identified as housewives may have been in a union and/or living with a partner, but this was not clearly captured by the research assistants.

Most of the study participants' husbands or partners were working, either as a laborer, businessman or salesman. Only three study participants reported their partners were not working at all. Interestingly, nearly 15% of unmarried participants did not know what their partner did for a living, while this was the case for only 3% of married participants. (This author has found this to be true in her own pregnant adolescent patients—unsure of what kind of work the father of their baby does!)

Many of those who identified as housewives did mention outside sources of income (data not shown). This included not only husband/partner salaries, but also many of the study participants received money from a parent or other relative. It is not surprising that this is the case, given the participants' lack of higher education and the low per capita income in Malawi.

In Malawi, 79.8% of the population is reported to have access to an improved source of water for drinking, cooking, and household chores (NSO, 2010). In this study, thanks to piped water from MASAF, public kiosks and community boreholes, 92% of study participants have access to clean water. It may be that the other 8% does as well, but this cannot be determined from the data (e.g., cannot assume that the water from a well or purchased from a neighbor is safe). This near universal access to clean water is congruent with the study setting (the urban and semi-urban environs of Blantyre and the surrounding areas); those in rural areas of the country are much less likely to have access to an improved source of water (NSO, 2010).

Also consistent with the urban/semi-urban setting in which the study participants live is the data on the availability of electricity. Nearly 56% of the study participants had electricity where they lived. In contrast, only 9.1% of the country's population has access to electricity, a figure that is reflective of the fact that the majority of the population lives rurally (NSO, 2010). Interestingly, 87.5% of the HIV-infected study participants did not have electricity (versus 40.4% of HIV-negative study participants), however in logistic regression, the odds of having electricity were greater for HIV-negative participants. As noted above, orphans often face socio-economic challenges as a result of the loss of a parent or parents. As the majority of HIV-infected study participants were orphans, the lack of electricity may be a marker of poverty in these participants.

A rather confounding study result concerns the issue of home ownership. While nearly 70% of all of the study participants rent, when stratified by marital status, 50% of the unmarried participants reported owning their home (versus only 21% of the married participants). Yet 64% of unmarried study participants indicated they live with a parent or parents. The question was

clearly confusing, and some participants likely responded to the question of home ownership as "yes" when in fact, it is their parents who own the home, not the study participant.

In the most recent Malawi Demographic and Health Survey (NSO, 2010), 55% of female adolescents aged 15 to 19 reported that distance to the nearest health facility (whether urban or rural) made it difficult for them to access care. Other studies discussed earlier have found that lack of transportation, or the funds to pay for it, were barriers to accessing PMTCT services (Chinkonde et al., 2009; Duff et al., 2010). In this study, results highlight that for 35% of the study participants, coming to the clinic for antenatal care means a walk of at least an hour, if not two. This is notable, given the clinic's location in Blantyre, the largest city in Malawi. The distance the participants are required to walk and lack of transportation (or funds to pay for it) are likely to contribute to fewer antenatal visits for this population, particularly at the end of pregnancy when a lengthy walk would be more difficult. However, none of those who participated in the in-depth interviews mentioned access to the antenatal clinic as a barrier to coming to their appointments or obtaining ART from the clinic.

Several variables concerning sexual and contraceptive history revealed interesting findings. Married study participants were more likely to have been sexually active by 16 years of age than were unmarried participants. This probably reflects the high rate of early marriage, but may also be an indication that, despite the increase in premarital sexual activity and possible growing acceptance of same, the early onset of sexual activity may put pressure on the female and her partner to get married, especially if a pregnancy ensues.

Fewer than 5% of the study participants had had more than one sexual partner (most of whom had only two lifetime partners; only one study participant had had three partners [data not shown]), which is consistent with Demographic and Health Survey data which reported only

0.7% of 15 to 19 year old females had had two or more partners in the year prior to the survey (NSO, 2010). All eight HIV-infected study participants had only had one lifetime sexual partner; although it isn't possible to determine for certain that each participant was infected with HIV by this one partner, it seems likely that they were. (As noted above, it is unlikely that they were perinatally infected and had survived to adolescence without any HIV-related illnesses or treatment). A history of forced sexual experiences was found in 7.8% of the study participants; it was twice as common in unmarried study participants than married participants and significantly more common in those who were HIV-infected. Unfortunately, as all of the study participants who were HIV-infected had only had one partner, it may have been the experience of forced sex that resulted in pregnancy. Only one study participant (unmarried) revealed a history of engaging in transactional sex, although government reports note that transactional sex continues to be common and contributes to the ongoing HIV epidemic (National AIDS Commission, 2012; Malawi Government, 2012). It may be that study participants were reluctant to reveal a history of transactional sex, which is often highly stigmatized. Conversely, it could be that the exchange of sex for money or gifts from a regular partner is not considered transactional sex by the study participants, but rather an expected "benefit" of dating; this distinction that was not captured by the study questionnaire.

Contraceptive knowledge and use was generally low, reflecting the lack of contraceptive education (nearly 15% of single study participants could not identify any method of contraception), poor contraceptive uptake among adolescents, and limited access to modern methods (past condom use was high [$\geq$ 90%] among all participants who had used any method of contraception, but other methods were infrequently used by the participants). While 41% of married study participants had never used any contraception, this could be an indication of the

desire and cultural norm to become pregnant soon after getting married. However, half of the single study participants had never used any method of contraception, which is unlikely to be a result of desiring pregnancy, and speaks to the difficulty adolescents, particularly unmarried adolescents, have in accessing reliable contraception from health clinics, as noted earlier (Nalwadda et al., 2010). Another interesting result was that, among the single study participants, one third said they stopped using contraception because their partner told them to. Perhaps there was pressure to conceive despite not being married? Among the study participants who were HIV-infected, 37.5% stopped using contraception because their husband or partner told them to. Since the majority of them (83.3%) were using condoms at some point, it is unsettling to think that by discontinuing condom use these study participants not only became pregnant, but also became HIV-infected. Sadly, many of those who were HIV-infected regretted becoming pregnant, once they found out their serostatus.

The study participants' gestational age at the first visit did not differ by HIV status. Although not statistically significant, gestational age at the first visit did differ by marital status. More single study participants initiated antenatal care in the third trimester, while more married study participants initiated care in the first trimester. Following the WHO guidelines, Malawi recommends that the initial antenatal visit be completed in the first trimester, or at least by the end of the 16th week of pregnancy (NSO, 2010). Only 38% of the study participants initiated care by then (data not shown). The WHO guidelines also recommend a minimum of four visits for those with uncomplicated pregnancies: the first visit by 16 weeks, the second visit between 24 and 28 weeks, the third visit at 32 weeks, and the fourth visit at 36 weeks (NSO, 2010; WHO, 2002). A recent study in Kenya found pregnant adolescents unlikely to complete the recommended four antenatal visits (Birungi, Obare, van der Kwaak, & Namwebya, 2011); in

contrast, most of the study participants were on track to meet these visit recommendations (Figure 3), which is encouraging:

A limited number of pregnancy problems were identified by the study participants. More married participants noted abdominal and back pains, although whether these were the benign pains commonly sustained in most pregnancies was not specified by the questionnaire. Other common pregnancy symptoms identified as problems included headaches, vaginal itching, and loss of appetite. Ten percent of the study participants had malaria while pregnant. Overall, HIV-infected study participants did not have significantly more pregnancy problems than those who were not infected.

Nearly 80% of the study participants were primiparas, while 16.8% had been pregnant once before and 5.9% had had two prior pregnancies. Of those who had been pregnant before, six had miscarried and five others had a therapeutic abortion. There was no relationship between HIV status and a history of miscarriage or therapeutic abortion. However, a history of therapeutic abortion was statistically significant among unmarried study participants, which may be a reflection on stigmatization of pregnancy in an unmarried adolescent. As discussed earlier, abortion is illegal in Malawi but not uncommon, and results in significant morbidity and mortality (Davis, 2008; Jackson et al., 2011). It would have been interesting to explore the experiences of these adolescents who had obtained an abortion, including the risks they faced, how they accessed the procedure, and the methods used.

Knowledge of HIV transmission via sexual contact was universally understood. Fewer study participants were aware of HIV transmission through contact with infected blood. Interestingly, fewer than 25% knew that HIV could be passed from mother-to-child; given the public health efforts in Malawi to test all pregnant women for HIV and enroll them in PMTCT

programs, it is somewhat surprising that more study participants weren't aware of this means of transmission. Even more surprising, none of the HIV-infected study participants were aware of MTCT of HIV. In the in-depth interviews, all of the interview participants discussed the benefits of ART and their desire to prevent transmission of the virus to the fetus. It may have been that the survey questionnaires were completed at one antenatal visit, when the HIV-infected participants were tested and given their test results, while the interview may have taken place at a later date, when they had received counseling and education about the importance of ART to prevent MTCT. This discrepant data may be the result of a time lapse between answering the survey questionnaire and participating in the in-depth interview.

As this author has spent much of her professional career providing antenatal care to adolescents in an adolescent-focused clinical setting, it was most rewarding to see the study participants articulate the benefits of such a practice. Contrary to some of the negative findings in the previously discussed published research concerning treatment of adolescents in sexual and reproductive health clinics (Mbizvo & Zaidi, 2010; Reynolds et al., 2006), the study participants appreciated that the staff at the Ndirande Health Centre has created a supportive, respectful environment in which pregnant adolescents receive care.[xxii] The format, with the clinic session beginning with all the patients together, provides an opportunity for every patient to learn together about pregnancy, nutrition, and the importance of education. The group visit allows the patients to ask questions, to learn from each other, and to identify with and support others who are in the same situation as they are. The interview participants clearly articulated the value of the supportive environment, in terms of the education they were receiving about HIV in pregnancy and the benefits of ART to prevent MTCT. The strongly positive feedback on the

[xxii] As noted in the study setting, this author's impression (from a Western point of view) of an educational session at the clinic was very punitive and did not seem supportive. The participants' responses commending the respectful, supportive environment may likely represent a cultural difference in expectations of treatment in such a setting.

adolescent-focused antenatal care provided by the Ndirande Health Centre clearly indicates that it is a model that should be replicated across the country.

The in-depth interviews were conducted to identify barriers and facilitators of PMTCT adherence in this cohort of pregnant HIV-infected adolescents. Encouragingly, few barriers to PMTCT adherence were identified by the interview participants. In previous studies of HIV-infected women, many mention structural and socioeconomic barriers to PMTCT adherence such as cost of services and lack of transportation. The study done in Malawi by Chinkonde and colleagues (2009) found that women also identified difficulty getting to the clinic, long waits at the clinic, and unkind, rude staff as barriers to adherence. No participants in this study mentioned problems with transport; although the clinic is located in an urban township, rather than a rural setting, it draws its clientele from the surrounding urban and suburban area, and some of the study participants walk a long distance to get to the clinic. Nor were long waiting times mentioned as a problem (possibly because the clinic session is structured such that clinic begins with group education and counseling, engaging clinic attendees from the onset of arrival). Reassuringly, no one mentioned any issues with the clinic staff; nearly all mentioned the value of the information they were given by the nurses and no interview participant identified staff behavior as a barrier. In fact, the survey questionnaire participants identified the respectful atmosphere in the clinic as being a valued benefit of obtaining antenatal care there.

Previous studies of adult pregnant women with HIV found barriers to ART adherence included fear of medication side effects, the risk of drug toxicity, and safety concerns for the fetus (McDonald & Kirkman, 2010; Mepham et al., 2011; Otieno et al., 2010; Reynolds et al., 2006). No study participant identified concerns about the medications as a barrier; most only focused on the benefits of taking ART for themselves and their fetus. Only one adolescent

mentioned she'd had some transient dizziness when she first began ART, but that had resolved and did not interfere with her compliance with the medication. No other participants mentioned drug-related issues.

Two of the youngest study participants, both age 15, mentioned missing appointments. Both had been at family funerals in their villages, and were unable to attend their appointments at the clinic. It is understandable and consistent with Malawian customs that they would be required (and expected) to attend, and would want to attend, the funerals of their mother and grandmother. One "forgot" to come back to the clinic for her medication after the funeral, while the other admitted to missing appointments due to "laziness." It is possible that these excuses are indicative of age-related immaturity, although the participant who "forgot" to return to the clinic has not disclosed her status to her husband, and may have difficulty keeping appointments while trying to hide clinic visits from him.

HIV-related stigma is a significant barrier to adherence in many aspects of HIV care. Both internal and external stigma promote shame and secrecy, and can result in avoidance of testing, non-disclosure, perpetuation of HIV transmission, noncompliance with therapy and poor quality of life for those infected (Mbonu, van den Borne, & De Vries, 2009). Studies of HIV-related stigma have identified fears of rejection by one's partner and community as powerful reasons for non-disclosure (Titilope et al., 2011). In the earlier discussion of the Health Belief Model, stigmatization of HIV and fear of involuntary disclosure were identified as *perceived barriers* to PMTCT adherence. Several study participants mention similar concerns. One participant revealed fears that she would be seen going to the PMTCT clinic, and thereby identified as someone with HIV. She admitted to feeling ashamed at this possibility, particularly

as a young person who has acquired HIV. Yet she did not allow these fears to keep her from her appointments.

Two of the interview participants had not disclosed their HIV positivity to their husbands. One clearly states she became pregnant because her husband wanted her to; it is not clear if she, too, wanted to be pregnant. The other said that, after she got married, the pregnancy "just happened." Because their husbands were unaware of their HIV infection, these study participants may have allowed themselves to get pregnant, as to refuse to do so would likely have led to difficulty in the marital relationship, and could have forced the issue of disclosure. One specifically mentions being afraid to tell her husband, for fear that he would tell his friends that she was HIV-infected, an involuntary disclosure that could possibly result in community rejection, and perhaps rejection by her husband. Although neither of these married participants specifically mentioned the fear of abandonment by their husband, this would likely have been a consideration; many studies have found that women have been left by their husbands once they have disclosed their HIV status to them (Madiba & Letsoalo, 2013).

The cultural expectation (and possibly pressure) to have children once one is married likely overrode any fears either of these two participants might have had of being HIV-infected and pregnant. However, this secrecy prompts several concerns. If their husbands are not already HIV-infected (although since the eight HIV-infected interview participants who also completed the survey questionnaire all reported only having one lifetime sexual partner, this seems unlikely), they have been at risk of acquiring HIV unknowingly from their infected wives (a risk that could continue despite viral suppression by ART). It may be that one or both of the young women were infected by having sex with the males who are their husbands, in which case the husbands may not know they themselves are infected and perhaps are eligible for or in need of

treatment. And once the baby is born, protocols require the baby be given ART as well: in Malawi, NVP syrup is given for four to six weeks after birth (assuming the mother is taking ART; if not, ART should be given to the infant until breastfeeding stops), followed by cotrimoxazole preventative therapy (CPT) to avert *pneumocystis jiroveci* pneumonia and other HIV-related illnesses (Interagency Task Team, WHO, & UNICEF, 2013; MOH, 2011). CPT is continued until the infant is confirmed to be HIV negative, after serum tests at 12 and 24 months of age (MOH, 2011). It is difficult to imagine that the father wouldn't at some point become aware that his child was on medication and/or having blood drawn; or, will the mother not give the child prophylaxis or take the child for testing to avoid detection by the father? Will the mother stop taking ART for her own health after delivery to avoid the persistent threat of discovery?

The WHO guidelines recommend exclusive breastfeeding for the first six months of life, with a gradual introduction of solid foods; breastfeeding should continue for twelve months, or until a safe diet can be assured (WHO, 2013a). In Malawi, breastfeeding is the norm, and the median duration of breastfeeding is 24 months (NSO, 2010; Shaffer et al., 2014). A recent study of HIV-infected women in South Africa found that those who had not disclosed their HIV-infection to their partners were more likely not to breastfeed and to lie about the reasons why they weren't adhering to the breastfeeding recommendation (Madiba & Letsoalo, 2013). The interview participants who had not disclosed their HIV status to their husbands are likely to be in a difficult position: breastfeeding and ART for herself and the infant (risk of discovery), breastfeeding and no ART (risk of transmission), or no breastfeeding (risk of discovery, risk of infant malnutrition). These must be extremely difficult decisions for a pregnant adolescent to make.

It has been established that interpersonal violence occurs in relationships affected by HIV. A recent study of HIV-infected women conducted in Uganda, which included some adolescents, found that 36.6% had been the victim of physical and/or sexual abuse (Osinde, Kaye, & Kakaire, 2011). The internalized stigma that results in hiding one's HIV infectivity and the potential risk that exposes one's partner to (e.g., acquisition of HIV) can certainly lead to interpersonal violence; the double threats of discovery and subsequent abuse could lead to untenable stress for the pregnant adolescent.

A number of facilitators of PMTCT adherence were identified by the study participants. Possibly the most reassuring finding of the study was that every participant had revealed their HIV status to someone in her family. The support provided to them in terms of both emotional and physical support is invaluable. Adolescents all over the world need someone to help them develop skills of responsibility, reliability, and perseverance, arguably even more so in the context of HIV infection. Each of these study participants had a family member--husband, parent, grandparent, aunt, uncle or sibling-- who provided some form of support, be that reminders to keep appointments or take medication, providing for adequate nutrition or financial support. Each participant had someone who was aware of her HIV infection and to whom she could rely on for physical and emotional support and encouragement. In the context of the Theory of Planned Behavior presented earlier in this dissertation, where the *subjective norms* and opinions of others contribute to behavioral intention, having a family member who is aware of the participant's HIV status and provides support can significantly impact adherence to PMTCT protocols, including medication adherence and regular attendance at clinic appointments. In contrast to studies of adult pregnant HIV-infected women who had not disclosed their HIV diagnosis to anyone, including their partners, the adolescents in this study had all had the

courage to disclose to at least one family member. It is possible that this may be reflective of a slow trend towards the "normalization" of HIV infection as a chronic illness, manageable with ART.

Another facilitator to PMTCT adherence was the acquisition of knowledge, which was mentioned by every study participant. They expressed their understanding that ART was beneficial to their own health (*perceived benefit*, as postulated by the Health Belief Model), strengthening their immune systems and allowing them to live healthy lives (suggesting an acknowledgement of the *perceived severity* of untreated HIV infection).[xxiii] They also expressed their confidence in the efficacy of ART in preventing HIV in the fetus, and their desire to avoid transmitting the virus to their child clearly motivated them to take the medication and attend their clinic appointments (a second *perceived benefit*). Many mentioned the benefits of going to the clinic in terms of the education they were receiving at their appointments, and how what they learned at the clinic encouraged their ongoing attendance at the clinic. A number of the study participants, however, seemed to express *complete* confidence in the ability of ART to protect their unborn child from HIV, stating that "you cannot transmit" the virus to the fetus if you are taking ART. While combination ART is very effective, there is still a risk (less than 5%) of HIV transmission even with ART (WHO, 2010b). It is not clear that all of the study participants were aware of this small but real risk. Only three participants mentioned that they were still afraid that the child could be infected despite taking ART (the Health Belief Model's *perceived susceptibility*); one expressed the understanding that ART reduces, but does not completely eliminate, the risk of transmission.

[xxiii] The research assistants noted that some of the interview participants felt ART would make them appear "normal," thus avoiding involuntary disclosure of their HIV status to others. However, the transcribed interview data does not support nor deny this observation.

Most likely this is attributable to the fact that the study participants had little understanding of the risks of transmission, since they were only recently diagnosed with HIV. The participants were likely still grieving and coming to terms with their diagnosis coupled with pregnancy. Taking ART may have provided consolation that the fetus would be protected. One participant who was diagnosed two years prior to pregnancy was already taking ART and understood the risk of transmission; if the remaining study participants had been diagnosed before conceiving, perhaps they would have had time to comprehend the risk. The lack of understanding of the risk of transmission may also reflect information given to the participants by the clinic staff (e.g., an emphasis on the efficacy of ART as opposed to addressing the risk of transmission despite ART) to encourage compliance with the medication, or may be indicative of an adolescent's concrete thinking.

The third identified facilitator of PMTCT adherence was acceptance of one's HIV status. As mentioned earlier, most of the study participants received their HIV diagnosis at the antenatal clinic. In the time period between that diagnosis and the study interview, all had undertaken to disclose their infection to a family member, demonstrating an acceptance of the diagnosis and an important prelude to compliance with care. Acceptance of their HIV status allowed the study participants to engage in services, such as initiating ART and attending monthly appointments for antenatal care and medication refills. The support each participant was receiving from one or more family members was also a clear indication of acceptance by the family member(s) of the adolescent's status.

In addition to the identified barriers and facilitators of PMTCT adherence, the study reveals some interesting information about pregnancy in HIV-infected adolescents in Malawi. First, nearly all of the study participants expressed sadness and regret that they were pregnant.

Most said they would not have chosen a pregnancy if they'd known their serostatus; several said they would have at some point chosen to become pregnant, but only after they had been on ART. Because the majority of the interview participants were diagnosed with HIV when they presented for antenatal care, their HIV status obviously did not enter into any decision-making around becoming pregnant. Numerous studies have found judgmental attitudes towards pregnancy in HIV-infected women, even among HIV-infected women themselves (Cooper, et al., 2007; Lawson, Bayly, & Cey, 2013; Myer, Morroni, & Cooper, 2006; Orner, de Bruyn, Harries, & Cooper, 2010; Orner, de Bruyn, & Cooper, 2011). For those who would not have chosen to have children, it may be that internalized stigma has led to this regret. But that others would have become pregnant after being on ART not only shows that these adolescents understand the benefits of ART on their own health prior to pregnancy, but also suggests that attitudes towards childbearing in HIV-infected women may be changing, at least in the younger generation. Regardless, it is unfortunate that there was so much regret expressed over pregnancy, an event that is usually highly desired and anticipated in Malawi.

The majority of adolescents in the study received their HIV diagnosis after becoming pregnant and being tested at the antenatal clinic. This diagnosis would surely cause a great deal of grief and concern for their own health and future, but these adolescents also had to cope with additional concerns for the health of their unborn child. Coupled with any stigma they might be experiencing related to being a pregnant (unmarried in some cases) adolescent, it is plausible that these study participants suffered significant trauma as they entered antenatal care. It is hoped that the nurses at the clinic provided the emotional support that was likely necessary.

In addition, given the regret expressed by many of the participants at being pregnant and HIV infected, or wishing they had known they were infected so as to delay the pregnancy until

they were on treatment, it would appear that public health messages for everyone to get tested and know their status are not reaching a vulnerable population: adolescent girls. This speaks to the need for more outreach to this age group, perhaps in the context of more youth-friendly or adolescent-specific health care settings.

Two of the adolescents who participated in the interviews, both age 15, mentioned that they had received their HIV diagnosis prior to becoming pregnant. They were not put on ART at the time of diagnosis (which may or may not have been appropriate; their immune status at the time is unknown), nor apparently were they given contraceptives or referred for such. Studies have shown that many family planning clinics restrict access to contraception for unmarried women, while other clinics providing care to perinatally HIV-infected adolescents counsel them to abstain from sex rather than providing contraceptives to prevent pregnancy (Birungi et al., 2008; Birungi, Mugisha, Obare & Nyombi, 2009). The HIV management guidelines developed by the Malawian Minsitry of Health recommend that providers of HIV-infected patients assume that anyone aged 15 and older is sexually active, and in order to avoid all unwanted pregnancies, not only offer condoms, but also hormonal contraception (specifically, Depo Provera®) to all women 15 years and older (MOH, 2011). This was a missed opportunity in the care of these two young girls, not only regarding the opportunity to prevent pregnancy, but also in terms of getting them into HIV care. ART is often not available in smaller community clinics (UNICEF, 2012a), and a referral to an HIV Care Clinic for integrated care is recommended (MOH, 2011). It is probable that the mobile clinic where one adolescent was diagnosed wasn't equipped to provide family planning or HIV care, but assuring that an adolescent who receives an HIV diagnosis is engaged in care is obviously important. Similarly, the second adolescent was diagnosed while ill

in the hospital; while it isn't clear from her response that she had an HIV-related illness, the hospital missed an opportunity to provide optimal care and follow-up.

The data showing that ART initiation varied between mid- to late-pregnancy is a notable marker of late entry to care among the study participants, as the Ndirande Health Centre has implemented comprehensive PMTCT services, such that testing and ART initiation occur in the same setting, eliminating the delay often seen between testing, diagnosis and initiation of ART in many settings (UNICEF, 2012a). While the ideal timing for ART initiation in pregnancy isn't clear, Option B+ recommends that all pregnant women be started on ART as soon as possible after diagnosis (UNICEF, 2012a); the slightly older Malawian HIV guidelines endorse initiation by the second trimester (MOH, 2011).

Half of the interview participants were started on ART in the third trimester of their pregnancy. While there have been no studies that have specifically studied the optimal time for starting ART in treatment-naïve pregnant women (Munderi, 2011), in the United States the recommendation is to either begin early in the first trimester or at least by 12 weeks (three months) gestation (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2013). While it is generally accepted that most transmission occurs near term, likely in the ninth month, studies have estimated that the risk of in-utero transmission prior to the onset of labor and delivery may be as high as 23% (Bertolli et al., 1996; De Cock et al., 2000; Guay et al., 1999).

In this study, the average gestational age at the start of ART was six months, with one participant starting ART at eight months. While this may have benefits in terms of the risk of PTD (less exposure to medication during pregnancy, thus a lower risk of PTD), it is suboptimal

in terms of reducing the risk of HIV transmission to the fetus/newborn. Beginning ART in the third trimester may have posed a risk of HIV transmission to the child in these pregnancies.

i. Study Objectives and Study Results

This mixed methods study has provided insight into the sociodemographics of a population of pregnant adolescents in Malawi, identified a higher than previously reported HIV prevalence, and demonstrated few barriers to the adherence to PMTCT protocols. The objectives of this mixed methods study are reiterated below, with author commentary based on the study results.

1) *To quantify the HIV prevalence rate among pregnant adolescents at an antenatal clinic in Blantyre, Malawi*

This objective was successfully met. Of the 102 pregnant adolescents who completed the questionnaire, eight revealed that they were HIV positive (HIV prevalence rate of 7.8%).

2) To quantify the utilization of PMTCT services by pregnant HIV-infected adolescents in an urban Malawian population

3) To quantify the adherence to PMTCT services by pregnant HIV-infected adolescents in an urban Malawian population

These two study objectives were met by information provided in the in-depth interviews. As noted above, of the 102 participants in the demographic survey, eight were HIV-infected (the additional two HIV-infected adolescents who participated in the in-depth interview did not participate in the survey questionnaire). All ten of the pregnant adolescents who were HIV-infected were enrolled in PMTCT services, and were currently taking ART, or were starting the day of the interview (100% uptake).

Assessing adherence to PMTCT services was more difficult, as the interview guidelines did not ask for specific measures of adherence (e.g., how many missed pills per week, gap between refills of medication). Two interviewees did mention an occasion when they ran out of medication and had a lapse in medication adherence. However, the interview participants did voice their understanding of the importance of taking ART as directed, as well as their commitment to doing so.

4) *To identify the barriers and facilitators to adolescent uptake of PMTCT services in urban Malawi*

As discussed above, barriers and facilitators to the uptake and adherence of PMTCT services were identified.

ii. Study Hypotheses and Study Results

Hypothesis #1: The prevalence of HIV infection among pregnant adolescents, ages 15 to 19, receiving antenatal care at the Ndirande Health Centre differs from the national HIV prevalence rate of 11%.

This hypothesis was correct. The prevalence of HIV infection among the study participants was 7.8%. Interestingly, this prevalence is higher than the government estimate of 5.8% for pregnant adolescents aged 15 to 19 years. However, the HIV prevalence in this study cohort is not only lower than the national HIV prevalence rate, it is also lower than the 10.6% HIV prevalence rate of adult pregnant women in Malawi.

Hypothesis #2: Uptake and adherence to PMTCT services in pregnant HIV-infected adolescents differ from rates of uptake and adherence to PMTCT in pregnant HIV-infected adult women as reported in the literature.

This hypothesis was also found to be correct in the context of this study population. Studies of uptake and adherence to PMTCT show a tremendous variability among women; the recent research by Tenthani and colleagues (2014) found as many as 58% of women enrolled in PMTCT programs were lost to follow-up by six months. In this study population, all eight of those who tested positive for HIV were enrolled in the clinic's PMTCT program; while few reported any difficulties adhering to the program medications and appointment schedule, study data did not allow for specific quantification of adherence (see Study Limitations below).

Hypothesis #3: The barriers expressed by pregnant HIV-infected adolescents to the uptake of and adherence to PMTCT services will differ from the barriers perceived by HIV-infected pregnant adult women as presented in the literature, and these differences are best explored using qualitative methodology.

Many of the barriers expressed by pregnant adult women enrolled in PMTCT programs (e.g., negative staff attitudes, transportation difficulties, program financial costs) were not identified as problematic for the study participants. However, other barriers voiced by adult women were also acknowledged by study participants: fear of disclosure (not by staff, but fear of disclosing their serostatus to a husband) and stigmatization of HIV. Regardless of these barriers, they did not impact the study participants' uptake and adherence to the PMTCT protocols.

iii. Study Strengths

The study has several strengths. First, the study provides insight into the characteristics of adolescent pregnancy in a low-income country in Sub-Saharan Africa. There are few studies that specifically explore such a broad range of variables in concert with adolescent pregnancy, and this study provides data on demographics, sexual and reproductive health, and antenatal care and obstetric history, as well as adding to our understanding of HIV knowledge in young

women. The study also provides insight into adolescent pregnancy in Malawi, a country with a majority of young people, early marriage, and a high birth rate among adolescents.

Another strength of this study is its novel contribution to our understanding of adolescent pregnancy in the context of HIV infection. With the increase in population growth among young women of childbearing age, the increase in pediatric HIV infections successfully treated with ART, allowing HIV-infected young girls to survive to adolescence and young adulthood, and the persistently high incidence of new HIV infections in young Africans, there will likely continue to be more HIV-infected adolescents becoming pregnant. This study provides a beginning understanding of HIV-infected adolescents and their capacity to adhere to PMTCT protocols.

Insight into the benefits of an adolescent-focused antenatal clinic is another strength of this study. While clinics that provide antenatal care specifically to pregnant adolescents are not uncommon in the US, the concept is relatively rare in developed countries, including Malawi. The innovative approach of the Ndirande Health Centre and the study participants' evaluation of the care received is extremely positive and shows the benefit of care that is appropriately geared for their age and developmental stage. Providing a supportive, non-judgmental environment and age-appropriate education can contribute to the health and well-being of pregnant HIV-infected adolescents and their infants.

A final strength of this study is its use of mixed methods. The quantitative data provides a background within which to contextualize the qualitative data. The numerous variables examined in the quantitative survey questionnaire allowed for triangulation with the qualitative data obtained in the in-depth interviews, which helped to explicate the experiences of the HIV-infected pregnant adolescents enrolled in the clinic's PMTCT program. For example, that none of the HIV-infected study participants were aware of MTCT of HIV illustrates the need for

education around ART adherence in this population, and the interviews provide support that this education has been undertaken. Satisfaction with the PMTCT services offered by the clinic, noting the support and counseling received, was similar to the overall satisfaction with antenatal services offered by the clinic, a comparison made possible by using mixed methods.

iv. Study Limitations

In the course of conducting the study and subsequently analyzing the data, several study limitations were identified. First, the study was conducted in the largest city in Malawi, and thus the findings may not represent pregnant adolescents in other areas of the country, including the majority of the population that lives in rural areas. Secondly, this was a non-random sample of pregnant adolescents attending an antenatal clinic, and the characteristics of this population are likely different than those pregnant adolescents who do not seek care or who obtain antenatal care from a traditional birth attendant. In addition, there may be have been some participant bias among those who consented to participate in the study; one possible motive could have been the bar of soap that study participants received at the end of their participation.

Another limitation is the possibility of response bias. The survey questionnaire asked a number of sensitive questions related to sexual activity, such as a history of transactional sex. Research has clearly shown that transactional sex is common in Malawi and elsewhere in Sub-Saharan Africa (MacPherson et al., 2012; Maganja et al., 2007; Masvawure, 2010; Stoebenau et al., 2011; Stoebenau et al., 2013; Swidler & Watkins, 2007), yet only one respondent indicated she had received money or goods in exchange for sex. This may reflect response bias, as transactional sex is often equated with prostitution and thus stigmatized. Similarly, few participants admitted to having had an abortion; abortion is illegal in Malawi and yet not

uncommon (Levandowski et al., 2013). Most of the study cohort stated they were primiparas, but a previous abortion may not have been disclosed for fear of admitting to an illegal procedure.

It was hoped that the research assistants would be able to conduct as many as 20 in-depth interviews, to provide a robust amount of qualitative data for analysis. However, the clinic population had a lower-than-expected HIV prevalence rate; while this is encouraging in terms of the HIV epidemic in Malawi and the elimination of pediatric HIV infections, it did not allow for as much qualitative data as had been hoped for.

Several of the questions on the survey were not clearly stated and led to confusing answers. The question of home ownership was likely misinterpreted, such that some of the study participants reported home ownership that was probably attributable to their parents. Similarly, it is unlikely that none of the unmarried study participants was living with her partner, yet all the study participants reportedly answered only "unmarried" or "married" to the question of marital status. An explanation of the optional answers, or perhaps prompting by the research assistants for clarification of the answers might have yielded different results.

In addition, a number of statements made by the study participants could have been explored in more depth. This was likely multifactorial: lack of time on the participant's or research assistant's part, or more likely, a cultural respect for privacy and hesitancy to ask probing questions or seek explanations. It was also likely that, when this author, a novice researcher, oriented the two research assistants to the study and interview guidelines, more explicit directions to follow up on ambiguous or partial information should have been emphasized. For example, some of the participants were only starting antenatal care in the third trimester. What led to the delay? Several participants expressed regret at being pregnant, and stated that if they had known they were infected, they wouldn't have become pregnant. Did they

have access to contraception? Were they using it? Did they try to obtain an abortion? For those whose husbands were unaware of their HIV status, how were they going to adhere to the PMTCT protocols for the newborn without their husbands finding out? Answers to these questions would have given a fuller picture of the challenges and strengths of these study participants.

More specific questions that would answer the third study hypothesis, quantifying the adherence to PMTCT services, should have been included. Questions relating to medication use, compliance with medication schedule, number of pills missed per week and why, gaps between medication refills, would have been valuable and necessary to determine medication adherence.

v. Implications for Nursing

In this study setting, the antenatal care, HIV counseling and testing, and ART initiation and follow-up were all provided by nurses, and the study highlights the ability and efficacy of these nurses. The majority of adolescents receiving care at the Ndirande Health Centre were on track to meet the recommended number of antenatal visits. There was universal uptake of HIV testing, and all of the study participants who were HIV-infected were on ART. As more perinatally HIV-infected young girls survive to adolescence and become pregnant, the role of nurses in providing antenatal and HIV care to this population will continue to grow in importance.

In addition, the study participants were overwhelmingly positive regarding the adolescent-focused care they received. The nurses provided not only direct antenatal care, but also emotional support and encouragement, genuinely caring about these young women. This clinic can serve as a model for other nurse-run clinics, providing care for female and male adolescents with a variety of health care needs.

vi. Areas for Further Research

A number of areas for further research are suggested by the study results. As discussed, two of the married interview participants had not disclosed their HIV status to their husbands. Hiding one's HIV status can lead to non-adherence to ART and clinic appointments, as well as posing significant challenges in providing ART to the infant and having the child undergo HIV testing. While these two interview participants did have others who were aware of their HIV status and were a source of support, it would be interesting to study ongoing PMTCT adherence in adolescents who do not disclose their HIV status to the father of their child.

Interestingly, no interview participant mentioned challenges or problems related to being a pregnant adolescent. While most of the respondents were older adolescents, and many 18 and 19 year old Malawians are married with children, there were younger adolescents in the study, and four of the in-depth interview respondents were not married. As this was primarily a study of HIV in pregnant adolescents, it is likely that the interview questions as written didn't prompt any discussion of other aspects of the pregnancy (e.g., issues related to being a pregnant adolescent) other than those associated with the HIV infection. Did the unmarried adolescents have access to contraception? What barriers to pregnancy prevention did they encounter? Further studies of contraception and pregnancy in adolescents, particularly those who are unmarried, would provide interesting information about the experiences of pregnant adolescents in Malawi.

A study finding of interest was that many of the HIV-infected interview participants expressed regret at being pregnant, stating they would not have become pregnant if they had known their HIV status. Given the small sample size of HIV-infected interview participants, it

would be interesting to study this phenomenon of regret in a larger population of HIV-infected pregnant adolescents.

And lastly, the study does not provide data on the pregnancy outcomes of the study participants. Further research on birth outcomes would contribute to our understanding of adolescent pregnancy in Malawi, and perhaps elsewhere: what pregnancy complications developed, any issues with cephalopelvic disproportion, what the mode of delivery was, and the health of the infants. In particular, it would be useful to study if any of the HIV-infected participants on ART developed premature labor and/or birth, and whether any of the infants born to the HIV-infected adolescents were also HIV-infected.

As discussed in the review of the literature, research on HIV-infection in pregnant adolescents is very limited. Further research into questions such as these will add to our understanding of this vulnerable population.

Appendices

Appendix A: Committee on Human Research Approval Letter,
University of California, San Francisco

Human Research Protection Program
Committee on Human Research
Notification of Expedited Review Approval
Principal Investigator Co-Principal Investigator
Sally H Rankin Ellen M Scarr
Type of Submission: Initial Review Submission Packet
Study Title: Adolescent Uptake of Prevention of Mother-to-Child Transmission of HIV Services in Malawi
IRB #: 12-09125
Reference #: 046097
Committee of Record: San Francisco General Hospital Panel
Study Risk Assignment: Minimal
Approval Date: 07/09/2012 **Expiration Date:** 07/08/2015
Regulatory Determinations Pertaining to this Approval:
This research satisfies the following condition(s) for the involvement of children:
45 CFR 46.404, 21 CFR 50.51: Research not involving greater than minimal risk.
Parental Permission and Assent:
The requirements for permission by parents or guardians is waived under 45 CFR 46.408(c) because the research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects.
The research meets all of the conditions of 45 CFR 46.204 for the involvement of pregnant women or fetuses.
This research is not subject to HIPAA rules.
IRB Comments:
1. In future submissions, such as renewals or modifications, please complete all of the items in the Inclusion of Children in Research section of the application.
2. Please turn in a modification to attach the Malawi IRB approval letter when it becomes available.
All changes to a study must receive CHR approval before they are implemented. Follow the modification request instructions. The only exception to the requirement for prior CHR review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103.b.4, 21 CFR 56.108.a). In such cases, report the actions taken by following these instructions.

Expiration Notice: The iMedRIS system will generate an email notification eight weeks prior to the expiration of this study's approval. However, it is your responsibility to ensure that an application for continuing review approval has been submitted by the required time. In addition, you are required to submit a study closeout report at the completion of the project.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.
For a list of all currently approved documents, follow these steps: Go to My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

San Francisco Veterans Affairs Medical Center (SFVAMC): If the SFVAMC is engaged in this research, you must secure approval of the VA Research & Development Committee in addition to CHR approval and follow all applicable VA and other federal requirements. The CHR website has more information.

Appendix B: Ndirande Health Centre Approval Letter

City of Blantyre

All correspondences to be addressed to:

THE CHIEF EXECUTIVE
TELEPHONE No. 01 870 211
FAX No..(265) 01 870 417/01 870 508
E-mail: bcachief@malawi.net

Ref : ESK/cm

THE SECRETARIAT
TOWN HALL
CIVIC CENTRE
KASUNGU CRESCENT
PRIVATE BAG 67
BLANTYRE
MALAWI

20th March 2012

The Chairman
COMREC
P/Bag 360
Chichiri
Blantyre 3

Dear Sir

PERMISSION TO CONDUCT STUDY AT NDIRANDE CLINIC

I grant Ellen Scarr from the University of California, San Francisco and Dr Angela Chimwaza from Kamuzu College of Nursing permission to conduct a study on pregnant HIV-infected adolescents at the Ndirande Clinic. Adolescent Health, including that of HIV-infected adolescents, is one of the priority areas in maternal health. I hope the findings of the study will assist in improving the care that is provided to this population.

I have gone through the draft proposal which will be submitted to COMREC for approval. The permission has been granted on condition that the proposal satisfies your requirements.

Yours faithfully

Dr ES Kanjunjunju
DIRECTOR OF HEALTH AND SOCIAL SERVICES

Appendix C: District Health Officer Approval Letter

From : The District Health Officer 9th July 2012
P/Bag 66
Blantyre

To : Officer In-charge, Ndirande Health Centre

: Nurse In-charge, Ndirande Health Centre

Dear Sir/Madam,

ADOLESCENT UPTAKE OF PREVENTION OF MOTHER TO-CHILD TRANSMISSION OF HIV SERVICES IN MALAWI

The bearer of this letter, Mrs. Rose Chamanga is a postgraduate student at Kamuzu College of Nursing. She is conducting the study titled as above.

Please assist her accordingly and coordinate to ensure that there is minimal interruption, and delay of antenatal and postnatal services and no deviation from MOH protocols in delivery of care.

Yours faithfully,

Dr. E. Nyirenda – Dziwani
for : **DISTRICT HEALTH OFFICER**

Telephone: Blantye 01875332 /
01877401
Fax: 01872551
Communication should be addressed to :
The District Health Officer

In reply please quote No. .....
MINISTRY OF HEALTH AND POPULATION
DISTRICT HEALTH OFFICE
P/BAG 66
BLANTYRE
MALAWI

9th July, 2012

Dr. Ellen Scarr
Clinical Professor
University of Califonia
San Francisco

Through : Mrs. Rose Chamanga
Kamuzu College of Nursing
P.O. Box 415
BLANTYRE

Dear Madam,

PERMISSION TO CONDUCT A STUDY "ADOLESCENT UPTAKE OF PREVENTION OF MOTHER TO-CHILD TRANSMISSION OF HIV SERVICES IN MALAWI

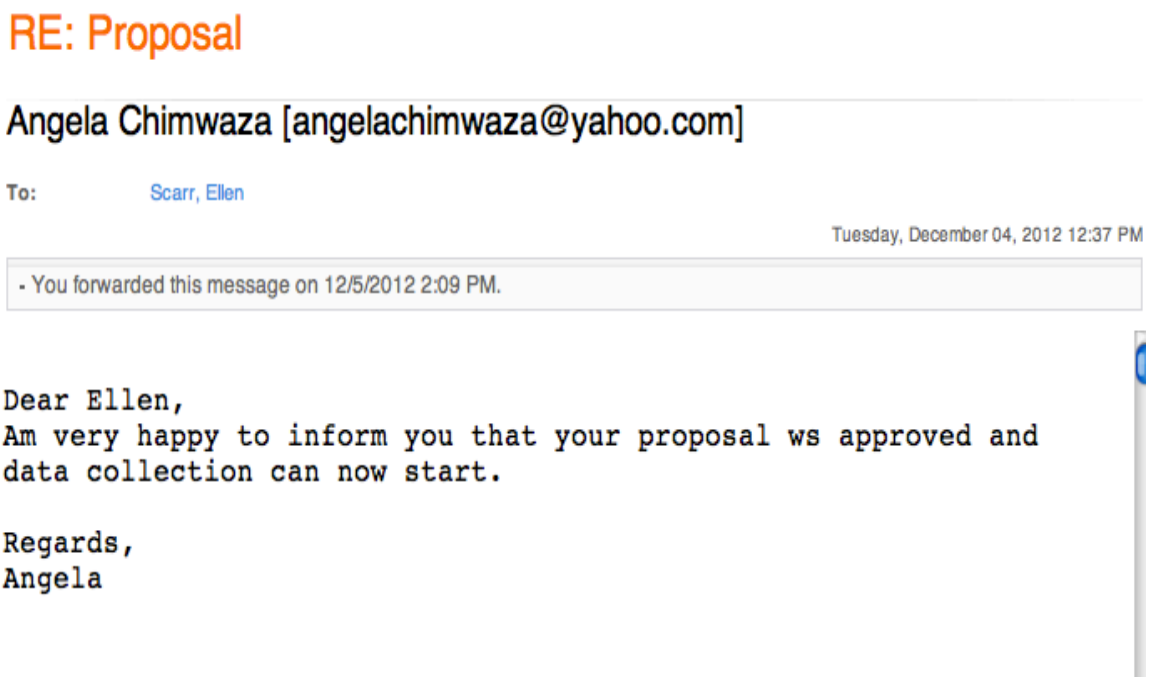
Permission is hereby granted to conduct the above study at Ndirande Health Centre. Please coordinate with the Sister In-Charge and the Officer In-Charge of the Health Centre to ensure that there is no interruption or delay of service provision in ANC and Postnatal clinic.

Also ensure that there is no deviation from the normal protocols of the two clinics.

Yours faithfully,

Dr. E. Nyirenda Dziwani (DMO)
for : **DISTRICT HEALTH OFFICER**

Appendix D: College of Medicine Research and Ethics Committee Approval Email, University of Malawi



RE: Proposal

Angela Chimwaza [angelachimwaza@yahoo.com]

To: Scarr, Ellen

Tuesday, December 04, 2012 12:37 PM

- You forwarded this message on 12/5/2012 2:09 PM.

Dear Ellen,
Am very happy to inform you that your proposal ws approved and data collection can now start.

Regards,
Angela

Appendix E: Study Consent Form, Quantitative Study (English)

University of California, San Francisco
School of Nursing

Research Consent Form
Questionnaire Consent

Adolescent Uptake of Prevention of Mother-to-Child Transmission of HIV Services in Malawi

You are being invited to participate in a research study about adolescent pregnancy in Malawi, and the prevention of mother-to-child transmission (PMTCT) of HIV in those pregnant adolescents who are HIV infected. This study is being conducted by Ellen Scarr, a PhD student from the University of California, San Francisco School of Nursing, and Dr. Angela Chimwaza, faculty at the Kamuzu College of Nursing in Malawi. This study is being conducted as part of Ms. Scarr's doctoral dissertation. The University of Malawi-College of Medicine Research and Ethics Committee and the Committee on Human Research at the University of California, San Francisco have reviewed my request to conduct this project, and approval for the study has been obtained by the clinic Medical Director, Dr. Emmanuel Kanjunjunju.

You are eligible to participate in this study because you are an adolescent who is pregnant and receiving antenatal care at the Ndirande Health Centre. You do not have to be HIV-infected to participate in the study.

There are no known risks if you decide to participate in this research study. There are no costs to you for participating in the study. The information you provide will help us understand the prevalence of HIV in pregnant adolescents and how pregnant adolescents who are HIV-infected use PMTCT services. The questionnaire will take about 20 minutes to complete. The information collected may not benefit you directly, but the information learned in this study should provide more general benefits.

This survey is anonymous. The research assistant will not ask for your name. No one will be able to identify you or your answers, and no one will know whether or not you participated in the study. Should the data be published, no individual information will be disclosed.

Your participation in this study is voluntary. By completing the survey, you are voluntarily agreeing to participate. You are free to decline to answer any particular question you do not wish to answer for any reason.

If you have any questions about the study, please contact Ellen Scarr at ellen.scarr@ucsf.edu or Dr. Angela Chimwaza at angelachimwaza@yahoo.com.

Appendix F: Study Consent Form, Quantitative Study (Chichewa)

University of California, San Francisco
School of Nursing

Research Consent Form
Questionnaire Consent

M'MENE ACHIMATA AKUMALAWI AKUGWIRITSIRA NTCHITO GAWO LIMODZI LA NTCHITO ZA UMOYO LOTHANDIZA KUTETEZA MWANA KUTI ASATENGE KACHILOMBO KA HIV KUCHOKERA KWA MAYI AKE NTHAWI IMENE ALI OYEMBEKEZERA, POBEREKA KOMANSO POYAMWITSA (PMTCT)

Muli kupemphedwa kutenga nawo gawo mu kafukufuku okhudzana ndi kukhala ndi pa thupi (kuyembekezera) kwa achinyamata akuMalawi komanso kuteteza mwana kutenga kachilombo ka HIV koyambitsa matenda a EDZI kuchokela kwa mayi wachinyamata amene ali oyembekezera ndipo anapezeka ndi kachilomboka.

Kafukufukuyu akupangidwa ndi a Ellen Scarr amene akupanga maphunziro a ukachenjede wa unamwino kusukulu ya University of California, San Francisco (UCSF) ya Ku America. Iwo akupanga kafukufukuyu mothandizana ndi a Dr. Angela Chimwaza a Kusukulu ya maphunziro a ukachenjede wa unamwino ya Kamuzu College of Nursing (KCN) yakonkuno ku Malawi. Kafukufukuyu akupangidwa ngati gawo limodzi limene a Ellen Scar akuyenera kukwaniritsa pa maphunziro awo a ukachenjede wa unamwino. Makomiti owunika za kafukufuku opangidwa pa anthu kuno ku Malawi ndiponso ku Amerika anawunika kafukufukuyu ndipo anaona kuti ndi ovemerezeka choncho andipatsa chilolezo choti ndikhonza kucheza nanu ngati mutafuna kutero. Komiti ya kuMalawi imene inawunika kafukufukuyu ndi ya kusukulu ya ukachenjede ya ma Dotolo ya College of Medicine Research and Ethics Committee ndipo ku America inawunika ndi komiti ya kusukulu ya maphunziro a ukachenjede waunamwino ya University of Carlifornia, San Francisco. Kuno kuchipatala cha Ndirande ndapatsidwa chilolezo ndi Mkulu wa a Dotolo a Dr. Emmanuel Kanjunjunju.

Mukuyenerezedwa kutenga nawo gawo mukafukufukuyu chifukwa ndinu wachinyamata amene ali oyembekezera ndipo akulandira chisamaliro cha ku sikelo pano pa Ndirande Health Center. Mudziwenso kuti simukuyenera kuti mukhale ndi kachilombo ka HIV pokhapokha kuti mutenge nawo gawo mukafukufukuyu.

Palibe chiopsezo chinachilichonse ku moyo wanu chodziwika chimene chilipo ngati muvomereze kutenga nawo gawo mukafukufukuyu. Simudzalipilanso kena kalikonse kamba kotenga nawo gawo mukafukufukuyu. Chilichonse chimene mundiuze chikatithandiza kumvesetsa kuti ndi achinyamata oyembekezera angati amene ali ndi kachilombo ka HIV. Izitu zikatithandizanso kumvesetsa za m'mene achinyamata amene ali oyembekezera ndipo anapezeka ndi HIV amagwiritsira ntchito gawo limodzi la ntchito za umoyo lothandiza kuteteza mwana kuti asatenge kachilombo ka HIV kuchokera kwa mayi wake nthawi imene ali oyembekezera, pobereka, komanso poyamwitsa.

Kuchezaku kutitengera pafupifupi mphindi makumi okha basi (20 minutes). Inu sikuti mudzalandira phindu lina lililonse pa inu nokha looneka ndi maso monga ndalama ndi zina zotero kamba koti mwatenga nawo gawo mukafukufukuyu. Koma zimene tiphunzire kuchokera m'mayankho amene mutipatse zikathandiza kuunikiranso kapena kupanganso mapologalamu ena othandiza kuti ntchito yothandiza kuteteza mwana kuti asatenge kachilombo ka HiV kuchokera kwa mayi wake ipite patsogolo.

Mukafukufukuyu sititchula maina a anthu, choncho amene akufunseni mafunso sakufunsani dzina lanu. Apatu zikusonyeza kuti palibe amene adzathe kukuzindikirani inu komanso mayankho anu ndipo palibe amene azadziwe kuti munatenga nawo gawo mukafukufukuyu. Ngati zotsatira za kafukufukuyu zizatsindikizidwe m'abuku ndi mm'alo ena tikukutsimikizirani kuti palibe nkhani zachisinsi komanso zinazilizonse zokhuzana ndi moyo wa wina aliyense atenge nawo gawo mukafukufukuyu zimene zidzalembedwemo.

Kutenga nawo gawo kwanu mukafukufukuyu ndi kongodzipereka chabe kosaumilizidwa. Muli ndi ufulu otha kukana kuvomereza kutenga nawo gawo mukafukufukuyu. Ngati mwavomereza kuti mucheze naye okufunsani mafunso mulinso ndi ufulu wotha kukana kuyankha funso lina lililonse limene simukufuna kuyankha kamba ka zifukwa zina.

Ngati muli ndi mafunso ena alionse okhudzana ndi kafukufukuyu chonde afunseni a Ellen Scarr polemba kalata ya e-mail ku; ellen.scarr@ucsf.edu kapenanso mukhonza kulembera a Dr.Angela Chimwaza ku; angelachimwaza@yahoo.com

Appendix G: Study Consent form, Qualitative Study (English)

University of California, San Francisco
School of Nursing

Research Consent Form
Interview Consent

Adolescent Uptake of Prevention of Mother-to-Child Transmission of HIV Services in Malawi

You are being invited to participate in a research study about adolescent pregnancy in Malawi, and the prevention of mother-to-child transmission (PMTCT) of HIV in those pregnant adolescents who are HIV infected. This study is being conducted by Ellen Scarr, a PhD student from the University of California, San Francisco School of Nursing, and Dr. Angela Chimwaza, faculty at the Kamuzu College of Nursing in Malawi. This study is being conducted as part of Ms. Scarr's doctoral dissertation. The University of Malawi-College of Medicine Research and Ethics Committee and the Committee on Human Research at the University of California, San Francisco have reviewed my request to conduct this project, and approval for the study has been obtained by the clinic Medical Director, Dr. Emmanuel Kanjunjunju.

You are eligible to participate in this study because you are an adolescent who is pregnant, receiving antenatal care at the Ndirande Health Centre, and you have HIV.

There are no known risks if you decide to participate in this research study. There are no costs to you for participating in the study. The information you provide will help us understand the prevalence of HIV in pregnant adolescents and how pregnant adolescents who are HIV-infected use PMTCT services. The interview will take about 45 minutes to complete. The information collected may not benefit you directly, but the information learned in this study should provide more general benefits.

This survey is anonymous. The research assistant will not ask for your name. No one will be able to identify you or your answers, and no one will know whether or not you participated in the study. Should the data be published, no individual information will be disclosed.

Your participation in this study is voluntary. By participating in the interview, you are voluntarily agreeing to participate. You are free to decline to answer any particular question you do not wish to answer for any reason.

If you have any questions about the study, please contact Ellen Scarr at ellen.scarr@ucsf.edu or Dr. Angela Chimwaza at angelachimwaza@yahoo.com.

Appendix H: Study Consent Form, Qualitative Study (Chichewa)

University of California, San Francisco
School of Nursing

Research Consent Form
Interview Consent (Chichewa)

M'MENE ACHINYAMATA AKUMALAWI AKUGWIRITSIRA NTCHITO GAWO LIMODZI LA NTCHITO ZA UMOYO LOTHANDIZA KUTETEZA MWANA KUTI ASATENGE KACHILOMBO KA HIV KUCHOKERA KWA MAYI AKE NTHAWI IMENE ALI OYEMBEKEZERA, POBEREKA KOMANSO POYAMWITSA (PMTCT)

Muli kupemphedwa kutenga nawo gawo mu kafukufuku okhudzana ndi kukhala ndi pa thupi (kuyembekezera) kwa achinyamata akuMalawi komanso kuteteza mwana kuti asatenge kachilombo ka HIV koyambitsa matenda a EDZI kuchokera kwa mayi wake wachinyamata amene ali oyembekezera ndipo anapezeka ndi kachilomboka.

Kafukufukuyu akupangidwa ndi a Ellen Scarr amene akupanga maphunziro a ukachenjede wa unamwino kusukulu ya University of California, San Francisco (UCSF) ya Ku America. Iwo akupanga kafukufukuyu mothandizana ndi a Dr. Angela Chimwaza a Kusukulu ya maphunziro a ukachenjede wa unamwino ya Kamuzu College of Nursing (KCN) yakonkuno ku Malawi. Kafukufukuyu akupangidwa ngati gawo limodzi limene a Ellen Scarr akuyenera kukwaniritsa pa maphunziro awo a ukachenjede wa unamwino. Makomiti owunika za kafukufuku opangidwa pa anthu kuno ku Malawi ndiponso ku Amerika anawunika kafukufukuyu ndipo anaona kuti ndi ovemerezeka, choncho andipatsa chilolezo choti ndikhonza kucheza nanu ngati mutafuna kutero. Komiti ya ku Malawi imene inawunika kafukufukuyu ndi ya kusukulu ya ukachenjede ya ma Dotolo ya College of Medicine Research and Ethics Committee ndipo ku America inawunika ndi komiti ya kusukulu ya maphunziro a ukachenjede waunamwino ya University of Carlifornia, San Francisco. Kuno kuchipatala cha Ndirande ndapatsidwa chilolezo ndi Mkulu wa a Dotolo a Dr. Emmanuel Kanjunjunju.

Mukuyenerezedwa kutenga nawo gawo mukafukufukuyu chifukwa ndinu wachinyamata amene ali oyembekezera ndipo akulandira chisamaliro cha ku sikelo pano pa Ndirande Health Center komanso chifukwa chokuti muli ndi kachilombo ka HIV kamene kamayambitsa matenda a Edzi.

Palibe chiopsezo chinachilichonse ku moyo wanu chodziwika chimene chilipo ngati muvomereze kutenga nawo gawo mukafukufukuyu. Simudzalipilanso kena kalikonse kamba kotenga nawo gawo mukafukufukuyu. Chilichonse chimene mundiuze chikatithandiza kumvesetsa kuti ndi achinyamata oyembekezera angati amene ali ndi kachilombo ka HIV. Izitu zikatithandizanso kumvesetsa za m'mene achinyamata amene ali oyembekezera ndipo anapezeka ndi HIV amagwiritsira ntchito ndondomeko imene inakhazikitsidwa pa nkhani yothandiza kuteteza mwana kutenga kachilombo ka HIV kwa mayi wake nthawi imene ali oyembekezera, pobereka, komanso poyamwitsa.

Kuchezaku kutitengera pafupifupi theka la ola limodzi ndi mphindi khumi ndi zisanu (45 minutes). Inu sikuti mudzalandira phindu lina lililonse pa inu nokha looneka ndi maso monga ndalama ndi zina zotero kamba koti mwatenga nawo gawo mukafukufukuyu. Koma zimene tiphunzire kuchokera m'mayankho amene mutipatse zikathandiza kuunikiranso kapena kupanganso mapologalamu ena othandiza kuti ntchito yothandiza kuteteza mwana kutenga kachilombo ka HiV kuchokera kwa mayi wake ipite patsogolo.

Muyeneranso kudziwa kuti mukafukufukuyu sititchula maina a anthu, choncho amene akukufunsani mafunso sakufunsani dzina lanu. Apatu zikusonyeza kuti palibe amene adzathe kukuzindikirani inu komanso mayankho anu ndipo palibe amene azadziwe kuti munatenga nawo gawo mukafukufukuyu. Ngati zotsatira za kafukufukuyu ziza tsindikizidwe m'abuku ndi mm'alo ena tikukutsimikizirani kuti palibe nkhani zachisinsi komanso zinazilizonse zokhuzana ndi moyo wa wina aliyense atenge nawo gawo mukafukufukuyu zimene zidzalembedwemo.

Kutenga nawo gawo kwanu mukafukufukuyu ndi kongodzipereka chabe kosaumirizidwa. Muli ndi ufulu otha kukana kuvomereza kutenga nawo gawo mukafukufukuyu. Ngati mwavomereza kuti mucheze naye okufunsani mafunso mulinso ndi ufulu wotha kukana kuyankha funso lina lililonse limene simukufuna kuyankha kamba ka zifukwa zina.

Ngati muli ndi mafunso ena alionse okhudzana ndi kafukufukuyu chonde afunseni a Ellen Scarr polemba kalata ya e-mail ku; ellen.scarr@ucsf.edu kapenanso mukhonza kulembera a Dr.Angela Chimwaza ku; angelachimwaza@yahoo.com

Appendix I: Survey Questionnaire, Quantitative Study (English)

Thank you for agreeing to be part of our study. The information that you give us will help us provide better care for other pregnant girls like yourself. I'm going to ask you some questions. The answers are all confidential, and we won't use your name, so no one will know who you are or what your answers were. Please let me know if you don't understand any of the questions, and I will say them another way. Thank you very much for your time. At the end of the survey we will have a small gift for you for your help with the study.

Please ask all questions and circle appropriate answer.	
Section 1: Demographic Information	
1a. What is your age?	13 14 15 16 17 18 19
1b. What is your marital status?	Single Living with Partner Married Separated Divorced Widowed
1c. How many years of school have you completed?	None 1 2 3 4 5 6 7 8 9 10 11 12 University 1 2 3 4 More
1d. Literacy level	Able to read Not able to read
1e. What is your occupation?	Housewife Student Other _____
1f. What is your husband/boyfriend/partner's job?	Specify _____
1g. Living situation:	
i. Availability of electricity	Yes No
ii. Availability of water	In home Well Distance_____
iii. Lives with parents	Yes No
iv. Lives with unmarried partner	Yes No
v. Lives with husband	Yes No
vi. Home ownership	Own Rent Do not pay for housing
vii. Number of rooms in house	1 2 3 4 5 6 More
viii. Other (specify)	
1h. Access to health care:	
i. Distance to clinic from home	Specify _____
ii. What kind of transport do you use?	None (walk) Minibus Bicycle Car Scooter Other_____
1i: Orphan status	Not an orphan Lost mother Lost father Lost both parents
Section 2: Sexual/Contraceptive History	
2a. Age at first sex?	<12 12 13 14 15 16 17 18 19
2b. Number of sexual partners?	1 2 3 4 More than 4
2c. History of forced sex?	Yes No
2d. History of transactional sex?	Yes No
2e. What kind of birth control/contraception methods do you know about?	None Condoms Pills Injectable IUD Other (Specify _____)
2f. What kind(s) of birth control methods have you used in the past?	None Condoms Pills Injectable IUD Other (Specify _____)
2g. Did you have any problems with a birth control method, and if so, what were they?	No problems Too expensive Not available Side effects (Specify _____)

2h. What was the main reason you stopped using birth control?	Never used it Wanted to get pregnant Partner/husband said no Too expensive Not available Side effects (Specify _____)
Section 3: Current Obstetric History	
3a. Estimated due date?	Specify _____
3b. Gestational age today?	_____ Weeks
3c. Gestational age at first antenatal visit?	_____ Weeks
3d. Total number of antenatal visits to date	1 2 3 4 5 6 7 8 More
3e. Have you had any problems with this pregnancy?	Anemia Malaria Preterm Labor Baby not growing well Other (Specify)_____
Section 4: HIV Testing	
4a. Were you counseled about an HIV test?	Yes No
4b. Was an HIV test offered to you?	Yes No
4c. Did you have an HIV test?	Yes No
4d. Did you go back and get your test results?	Yes No
4d. Can you tell me your test result?	Positive Negative
Section 5: Prior Obstetric History	
5a. How many times have you been pregnant before this pregnancy?	None 1 2 3 4 5 More
5b. Have you had a miscarriage before?	Yes No
5c. Have you had an abortion before?	Yes No
5d. Did your previous pregnancy have any complications?	Yes No If yes, what were they? _____ ____
5e. Number of live births?	None 1 2 3 4 5 More
5e. How many children do you have now at home?	None 1 2 3 4 5 More
Section 6: HIV Knowledge	
6a. Have you heard of HIV before?	Yes No
6b. How is HIV spread from one person to another?	Sexual contact Blood From mother to baby Other (Specify _____)
6c. What are some ways that you can protect yourself from HIV?	Don't have sex Use a condom Don't use dirty needles Get tested with a new partner before you have sex Other (Specify_____)
Section 7: Pregnancy Experiences	
7a. What is the best thing about coming for antenatal care with other girls your age?	Specify_____ ____
7b. What, if anything, would you like to change about your antenatal care?	Specify_____ ____

Appendix J: Survey Questionnaire, Quantitative Study (Chichewa)

Mafunso a Mukafukufuku

Zikomo povomera kutenga nawo mbali mu kafukufuku wathu. Zomwe mutifotokozere zitithandiza kuti tipereke chithandizo choyenera kwa atsikana ena oyembekezera monga momwe mulili inumu. Mayankho anu onse azasungidwa mwa chinsisi, ndipo sitidzagwiritsa ntchito dzina lanu, choncho palibe adzakuzindikireni komanso mayankho anu sadzadziwika. Chonde ndidziwitseni ngati simunamvetse funso lirilonse lomwe ndakufunsani.

Chonde funsani mafunso onse ndipo muzunguze pamene pali yankho lolondola.	
Section 1: Demographic Information	
1a. muli ndi zaka zingati?	13 14 15 16 17 18 19
1b. kodi muli pabanja?	Mbeta Kungokhalira limodzi Okwatiwa Kupatukana Kulekana Wamasiye
1c.Mwatha zaka zingati za sukulu?	palibe 1 2 3 4 5 6 7 8 9 10 11 12 Diploma University 1 2 3 4 kuposera
1d. Maphunziro mwafika nawo pati?	mumatha /Simutha kuwerenga
1e. Mumagwira ntchito yanji?	Mayi wa pakhomo/Mwana wa sukulu/ Mlimi/ Zina?_____
1f.Nanga amuna anu/ achibwenzi anu/okhala nawo amagwira ntchito yanji?	Fotokozani _____
1g. Makhalidwe a kunyumba:	
i. Mumakhala ndi ndani ku nyumba kwanu?	Makolo/ Amuna anu / ongokhala naye osati wa pabanja Ana/ Ena (fotokozani) _____
ii.Muli ndi magetsi	Inde / Ayi
iii.muli ndi madzi?	Mnyumba mwanu / Chitsime_____
iv. Nyumba mukukhala ndi yandani?	Yathu/ yalendi/ sitilipira ndalama zanyumba
v. Muli zipinda zingati mnyumba mwanu?	1 2 3 4 5 6 kapena ochulukirapo
vi. Ndalama mumazipeza bwanji pakhomo panu?	Fotokozani_____
vii. Zina (fotokozani)	
1h.Kupeza chithandizo cha za umoyo:	
i. kutalikirana kwa chipatala ndi kunyumba	Fotokozani _____
ii. Mumayenda bwanji kukafika kuchipatala?	Kuyenda pansi/ kukwera Minibasi Njinga/ Galimoto Zina (fotokozani)_____
1i: Ana amasiye	Si wamasiye Amai anamwalira Abambo anamwalira Makolo onse anamwalira
Section 2: Mbiri ya kugonana ndi njira za kulera	
2a. Munayamba kugonana muli ndi zaka zingati?	<12 12 13 14 15 16 17 18 19
2b. Muli ndi anthu angati ogonana nawo?	1 2 3 4 kapena kuchuluka kuposa 4
2c.Munaumirizidwapo kugonedwa?	Inde / Ayi
2d. Munagulitsapo thupi lanu kuti mupeze chithandizo?	Inde / Ayi

2e.Mumadziwa njira ziti zakulera?	Palibe Makondomu Mapilitsi Jakiseni lupu Zina (fotokozani _____)
2f. Mwagwiritsapo ntchito njira ziti zakulera m'mbuyomu?	Palibe Makondomu Mapilitsi Jakiseni IUD Zina(Fotokozani)
2g. Munali ndi bvuto lina liri lonse pogwiritsa ntchito njira za kulera? Ngati ndi choncho, bvuto lake linali lotani?	Panalibe bvuto Kudula kwambiri Sapezeka Zina (Fotokozani)_____
2h. Ndi chifukwa chanji chomwe chinakupangitsani kuti musiye kugwiritsa ntchito njira za kulera?	Sanagwiritsepo ntchito Amafuna kuima mimba Achibwenzi/Amuna awo anakana Ndizodula sizipezeka Kuipa kwa mankhwala (fotokozani _____)
Section 3: Mbiri ya uchembere uno:	
3a. Mukuyembekezeka kuchira liti?	Fotokozani _____
3b. Masiku anu a mimba ndi angati lero?	Milungu _____
3c. Nanga masiku anu a mimba anali angati pamene mumayamba sikelo?	Milungu _____
3d. Mwayendera sikelo kangati pofika lero?	1 2 3 4 5 6 7 8 kapena kuposera apo
3e. Mwakhala ndi bvuto lina liri lonse ndi mimbayi?	Kuchepa magazi Malungo kuyamba matenda mimba yosankhwima Mwana osakula bwino Zina (Fotokozani)_____
Section 4: Kuyezetsa magazi	
4a. Munalankhulidwa za kuyezetsa magazi ku ka chirombo ka HIV?	Inde Ayi
4b. kodi munapatsidwapo mwayi woti muyezetse magazi ku kachirombo ka HIV?	Inde Ayi
4c. Munayezetsa magazi ku HIV?	Inde Ayi
4d. Munabwerera kukatenga zotsatira za magazi anu?	Inde Ayi
4d. Mungandiuze zotsatira za magazi anu?	Mulinako Mulibe
Section 5: Uchembere wa kumbuyoku	
5a.Mwaimapo kangati musanaime mimbayi?	Palibe 1 2 3 4 5 Kapena kuposera apo
5b.Munapititsapo padera?	Inde Ayi
5c. Munachotsapo mimba?	Inde No
5d. Munali ndi bvuto lina liri lonse ndi mimba ya m'mbuyomu?	Yes Ayi Ngati ndi choncho, mabvuto ake anali otani? _____
5e.Mwabereka ana amoyo angati?	Palibe 1 2 3 4 5 Kapena kuposera apo
5e. Nanga panopa muli ndi ana angati ku nyumba?	Palibe 1 2 3 4 5 Kapena kuposera apo

Section 6: Kuzindikira za kachirombo ka HIV	
6a. Munamvapo za kachirombo ka HIV?	Inde Ayi
6b. Kachirombo ka HIV kamafala bwanji?	Pogonana Kudzera m'magazi Kuchoka kwa mayi kupita kwa mwana Zina (Fotokozani _____)
6c. Ndi njira ziti zomwe mungazitetezere ku ka chirombo ka HIV?	Posagonana Pogwiritsa ntchito kondomu Posagwiritsa ntchito masingano onyansa/ ogwiritsidwa ntchito kale Kuyezetsa magazi ndi mnzanu watsopano musanayambe zogonana Zina (Fotokozani_____)
Section 7: Zokumana nazo ndi mimbayi	
7a. Ndi ubwino wanji womwe mukuuwona mukamapezana ndi amnzanu a msinkhu wanu mukabwera ku sikelo?	Fotokozani_____ _____
7b. Mukanakonda atasintha zotani pa chisamaliro chanu cha ku sikelo?	Fotokozani_____ _____

Takukonzerani ka mphatso pokuthokozani chifukwa chotenga nawo mbali pa kafukufuku wathu ameneyu. Zikomo!

Appendix K: Interview Questionnaire, Qualitative Study (English)

Thank you for agreeing to be interviewed for our study. The information that you give us will help us provide better care for other pregnant girls like yourself who have HIV.

I'm going to ask you some questions. The answers are all confidential, and we won't use your name, so no one will ever know who you are or what your answers were. Please let me know **if** you don't understand any of the questions, and I will say them another way.

At the end of the interview, we have a small gift that we will give you to thank you for your help with this study.

Section 1: HIV History
1a. How old were you when you found out you had HIV, and how did you find out?
1b. (If she knew she had HIV before she got pregnant, what were her feelings about having HIV and getting pregnant?)
1c. What are your concerns about having HIV and being pregnant?
Section 2: PMTCT Awareness
2a. Tell me what you know about how you can prevent your baby from getting HIV?
2b. Tell me what you know about programs that treat pregnant girls/women so that the baby doesn't get infected?
2c. What do think are the benefits of taking antiretroviral therapy (ART) in pregnancy?
2d. Do you have any concerns about taking ART during pregnancy?
Section 3: PMTCT Usage
3a. Are you going to a program/clinic for ART, so that the baby won't get HIV?
If she IS NOT going to a PMTCT program, ask these questions:
3b. What made it hard for you to go to a program/clinic for ART?
3c. What would have made it easier for you to go to a program/clinic for ART?
If she IS going to a PMTCT program, ask these questions:
3d. How pregnant were you when you starting going to the program for ART?
3e. Tell me about your experiences at the ART program?
3f. What made it easy for you to go to the program?
3g. What made it hard for you to go to the program?
3h. What makes it easy to take your medicine?
3i. What makes it hard to take your medicine?
3j. Tell me about the people who are the most support for you right now?
Section 4: Pregnancy Experiences
4a. Is there anything else about your pregnancy that you would like me to know?

Appendix L: Interview Questionnaire, Qualitative Study (Chichewa)

Mlozera wa mafunso

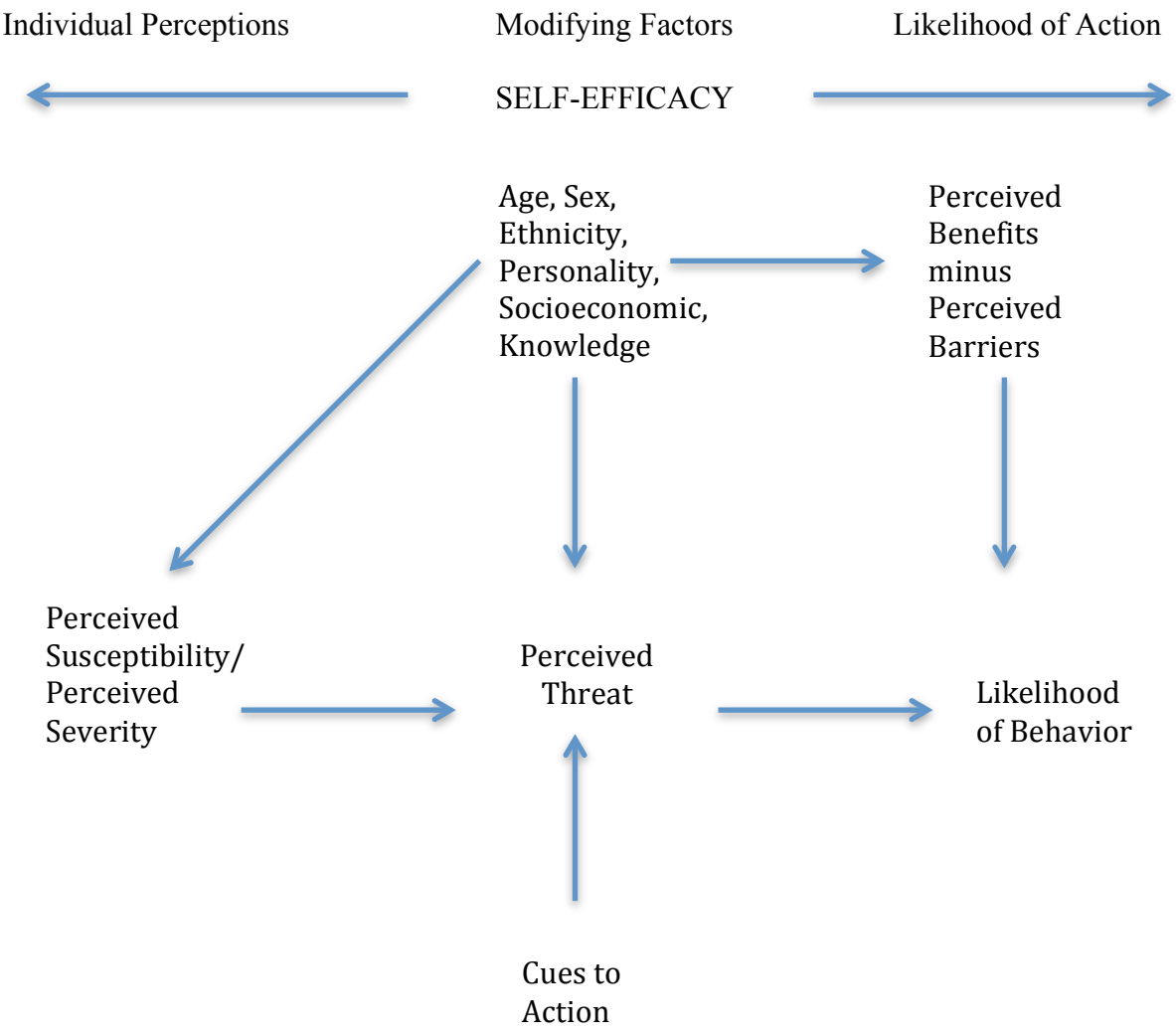
Zikomo povomera kutenga nawo mbali mu kafukufuku wathu.. zomwe mutifotokozere zitithandiza kuti tipereke chithandizo choyenera kwa atsikana ena oyembekezera monga momwe mulili inumu. Mayankho anu onse azasungidwa mwa chinsisi, ndipo sitidzagwiritsa ntchito dzina lanu, choncho palibe adzakuzindikireni komanso mayankho anu sadzadziwika. Chonde ndidziwitseni ngati simunamvetse funso lirilonse lomwe ndakufunsani.

Section 1:Mbiri ya Kachirombo ka HIV
1a. Munali ndi zaka zingati pomwe mumazindikira kuti muli ndi kachilombo ka HIV, ndipo munazindikira bwanji?
1b. (Mukanazindikira kuti muli ndi kachilombo ka HIV musanayime mimba, mumalingalira zotani pa nkhani yokhala ndi kachilombo ka HIV komanso kutenga mimba?)
1c. Nkhawa zanu ndi zotani pamene muli ndi kachilombo ka HIV komanso mimba?
Section 2: Kuteteza mwana ku kachilombo ka HIV kuchokera kwa mayi
2a. Tandiuzani zomwe mukudziwa m'mene mungamutetezere mwana wanu kuti asatenge kachilombo ka HIV?
2b. Tandiuzani mabungwe amene mukuwadziwa amene amathandiza atsikana kapena amayi amene ali ndi mimba kuti mwanayo asatenge kachirombo ka HIV?
2c. Kodi ubwino wokumwa mankhwala owonjezera moyo (ART)kwa mayi woyembekezera ndi wotani?
2d. Muli ndi nkhawa ina iliyonse pa kamwedwe ka mankhwala a ART kwa mayi woyembekezera?
Section 3: Kugwiritsa ntchito chithandizo cha PMTCT
3a. Kodi mukumapita kuchipatala kukalandira chithandizo cha ma ART kuti mwana wanu asatengere ka chirombo ka HIV?
Ngati sakulandira nawo chithandizo cha PMTCT, funsani mafunso awa:
3b. Ndi chiyani chimakulepheretsani kukalandira nawo chithandizo cha ma ART?
3c. Ndi chiyani chikanakupepusirani ulendo okalandira nawo mankhwala a ma ART?
Ngati ali pa chithandizo cha PMTCT, funsani mafunso awa:
3d. Mimba yanu inali yaikulu bwanji pamene mumayamba kulandira mankhwala a ART?
3e. Ndiuzeni zomwe mumakumana nazo kuchipatala pokalandira ma ART?
3f.Ndi chiyani chinakupepusira ulendo wokalandira nawo chithandizo cha ma ART?
3g. Ndi chiyani chinapangitsa kukhala kobvuta kuti mukalandire thandizo la m ART?
3h. Ndi chiyani chimapangitsa kuti kumwa mankhwala kusakhale kokubvutani?
3i.Ndi chiyani chimapangitsa kumwa mankhwala kukhala chinthu chokubvutani?
3j. Tandiuzani anthu amene amakuthandizani pakali pano?
Section 4: Zimene mukukumana nazo ndi mimbayi
4a. Pali china chiri chonse chomwe mudakakonda kundidziwitsa zokhuzana ndi mimbayi?

Takukonzerani ka mphatso pokuthokozani chifukwa chotenga nawo mbali pa kafukufuku wathu ameneyu. Zikomo!

Figures

Figure 1. The Health Belief Model



Adapted from Strecher & Rosenstock, 1997.

Figure 2: The Theory of Planned Behavior

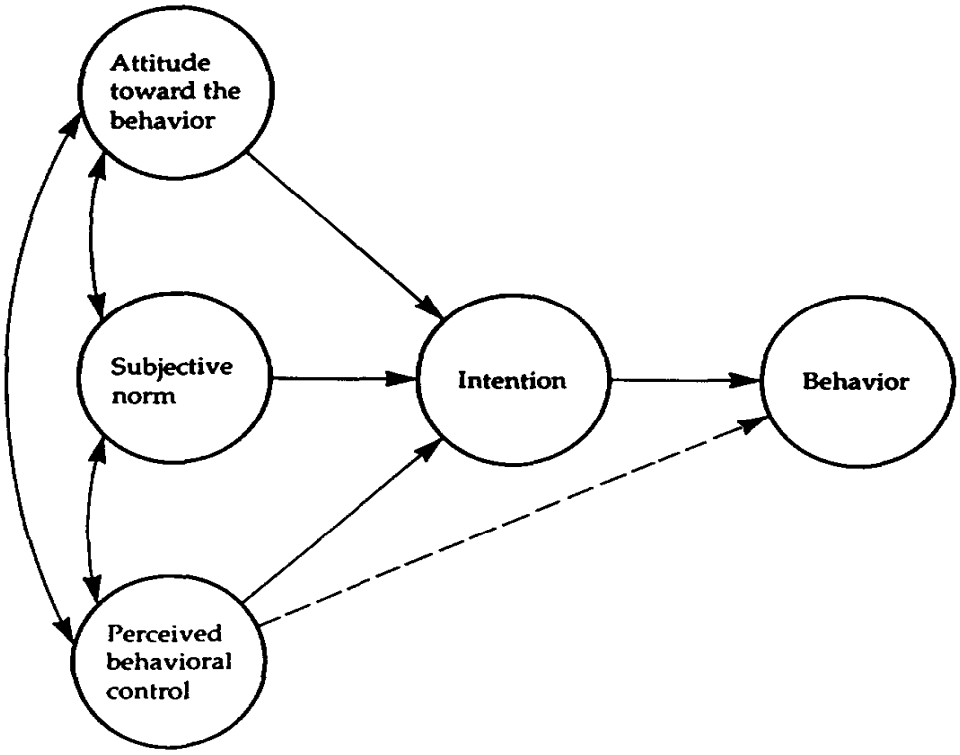


FIG. 1. Theory of planned behavior.

Azjen, I. (1991).

Figure 3: Antenatal Visits by Gestational Age (Graph)

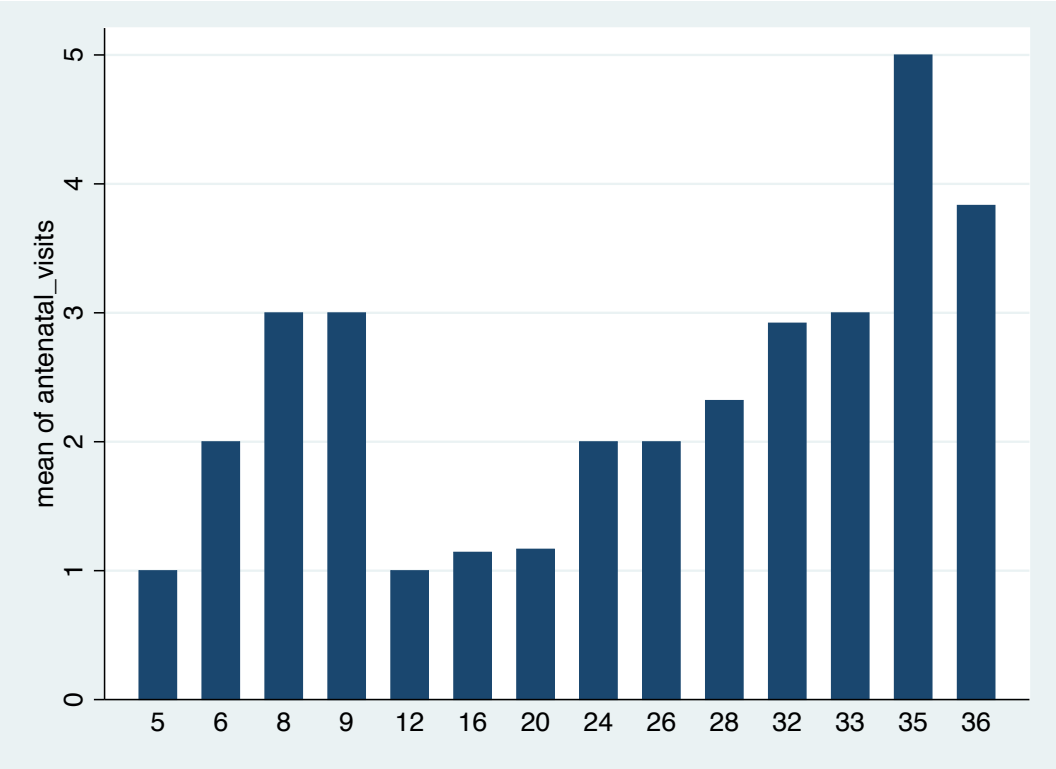


Figure 4: Antenatal Visits by Gestational Age (Detail)

3b. Gestational age today? (weeks)	3d. Total number of antenatal visits to date					
	1	2	3	4	5	Total
5	1	0	0	0	0	1
6	0	1	0	0	0	1
8	0	0	1	0	0	1
9	0	0	1	0	0	1
12	3	0	0	0	0	3
16	6	1	0	0	0	7
20	10	2	0	0	0	12
24	3	11	3	0	0	17
26	0	1	0	0	0	1
28	1	17	5	2	0	25
32	1	9	8	6	0	25
33	0	0	1	0	0	1
35	0	0	0	0	1	1
36	0	1	1	3	0	6
Total	25	43	20	11	1	102

Tables

Table 1: WHO Clinical Staging of HIV-Stages 1, 2 and 3

Stage 1	Asymptomatic
	Persistent generalized lymphadenopathy
Stage 2	Moderate unexplained weight loss (< 10% of body weight)
	Recurrent bacterial upper respiratory infections (current episode plus ≥ one additional episode in the last six months)
	Herpes zoster
	Angular cheilitis (not due to iron or vitamin deficiency)
	Recurrent oral ulcerations (aphthous ulcers; two or more episodes in the last six months)
	Papular pruritic eruption
	Seborrheic dermatitis
	Fungal nail infections (paronychia, onycholysis)
Stage 3	Severe unexplained weight loss (>10% of body weight)
	Unexplained chronic diarrhea for > 1 month
	Unexplained persistent fever for > 1 month (constant or intermittent)
	Oral candidiasis
	Oral hairy leukoplakia
	Pulmonary tuberculosis
	Severe bacterial infection (e.g., pneumonia, empyema, bone or joint infection, bacteremia, severe pelvic inflammatory disease)
	Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis
	Unexplained anemia (< 8 g/dl), neutropenia (< 0.5 x 10^9/l), and /or chronic (> 1 month) thrombocytopenia (< 50 x 10^9/l)

WHO. (2007). *WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.*

Table 2: WHO Clinical Staging of HIV Disease-Stage 4

Stage 4	HIV wasting syndrome (Weight loss > 10%, with obvious wasting or BMI < 18.5, plus either a) unexplained chronic diarrhea for > 1 month, or b) reported fever or night sweats for > 1 month, unresponsive to antimalarials or antibiotics
	Pneumocystis pneumonia
	Recurrent bacterial pneumonia (current episode, plus ≥ one additional episode within the last six months
	Chronic herpes simplex virus infection (orolabial, genital or anorectal) for > one month, or visceral at any site for any duration
	Esophageal candidiasis
	Extrapulmonary tuberculosis
	Kaposi sarcoma
	Cytomegalovirus disease (retina, other organs [excluding liver, spleen, lymph nodes])
	Toxoplasmosis of the central nervous system
	HIV encephalopathy
	Extrapulmonary cryptococcosis
	Disseminated nontuberculous mycobacterial infection
	Progressive multifocal leukoencephalopathy
	Cryptosporidiosis (with diarrhea lasting > one month)
	Chronic isosporiasis
	Disseminated mycosis (coccidioidomycosis, histoplasmosis)
	Recurrent septicemia
	Lymphoma or other solid HIV-associated tumors
	Invasive cervical carcinoma
	Atypical disseminated leishmaniasis
	HIV-associated nephropathy
	HIV-associated cardiomyopathy

WHO. (2007). *WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.*

Table 3: Option A, B, and B+

Antiretroviral Therapy Regimens for the Prevention of Mother-to-Child Transmission of HIV

	Option A	Option B	Option B+
Mother **CD_4 count ≤ 350 cells/mm^3**	Triple ART-Beginning at diagnosis and continuing for life	Triple ART-Beginning at diagnosis and continuing for life	Triple ART-Beginning at diagnosis and continuing for life, regardless of CD_4 count
Mother **CD_4 count > 350 cells/mm^3**	Antepartum: AZT beginning at 14 weeks GA Intrapartum: sdNVP at onset of labor and first dose of AZT/3TC Postpartum: AZT/3TC for 7 days	Triple ART beginning at 14 weeks GA and continuing through delivery (if not breastfeeding); *or* until one week after exposure to all breastmilk has stopped	
Infant	Daily NVP from birth until one week after all breastfeeding stops; *or* until 4-6 weeks of age if not breastfed or if mother is on ART	Daily NVP or AZT from birth until 4-6 weeks of age, regardless of feeding method	

Adapted from *Toolkit. Expanding and simplifying treatment for pregnant women living with HIV: Managing the transition to Option B/B+*. (Interagency Task Team, World Health Organization, & United Nations Children's Fund, 2013).

ART: Antiretroviral therapy
GA: Gestational age
AZT: Azidothymidine
NVP: Nevirapine
sd: Single dose

Table 4: Demographic Characteristics of Study Participants

Study Questionnaire Participants (*n*=102)

Demographic Information	*Frequency (%)*	*Mean (Range)*
Age		17.8 (15-19)
15	1 (1%)	
16	12 (12%)	
17	28 (27.2%)	
18	25 (24.5%)	
19	36 (35.3%)	
Years of Schooling		8.84 (0-13)
0-4	4 (3.9%)	
5-8	43 (42.2%)	
9-12	54 (52.9%)	
Diploma	1 (1%)	
Literacy		
Able to read	97 (95.1%)	
Not able to read	5 (4.9%)	
Marital Status		
Single	34 (33.3%)	
Married	68 (66.7%)	
Occupation		
Housewife	76 (74.5%)	
Nothing/School Dropout	11 (10.7%)	
Business Woman	10 (9.8%)	
Student	2 (1.9%)	
Farming	1 (1%)	
Other	2 (1.9%)	
Partner Occupation		
Laborer/Construction	24 (23.5%)	
Business Man	17 (16.7%)	
Salesman	14 (13.7%)	
Student	13 (12.7%)	
Driver/Transportation	9 (8.8%)	
Mechanic	4 (3.9%)	
Teacher	1 (1%)	
Not working	3 (2.9%)	
Other	10 (9.8%)	
Unknown	7 (6.8%)	
Living Situation		
Lives with Husband	61 (59.8%)	
Lives with Parents	27 (26.5%)	
Lives with Grandparents	8 (7.8%)	
Lives with In-laws	4 (3.9%)	
Lives with Other	2 (1.9%)	

Demographic Information	*Frequency (%)*	*Mean (Range)*
Orphan Status		
Lost Mother	9 (8.8%)	
Lost Father	14 (13.7%)	
Lost Both Parents	11 (10.8%)	
Not an Orphan	68 (66.7%)	
Economic Markers		
Availability of Electricity		
Yes	57 (55.9%)	
No	45 (44.1%)	
Availability of Water		
Public kiosk/MASAF	84 (82.4%)	
In House	6 (5.8%)	
Buys from Neighbor	5 (4.9%)	
Bore hole	4 (3.9%)	
Well	3 (2.9%)	
Home Ownership		
Own	31 (30.4%)	
Rent	71 (69.6%)	

Table 5: Access to Antenatal Care

Study Questionnaire Participants (*n*=102)

	Frequency (%)	*Mean (Range)*
Access to Health Care		
Distance to Clinic		1.6 hours
< 1 hour	66 (64.7%)	
1-2 hours	12 (11.8%)	
> 2 hours	24 (23.5%)	
Transportation		
None (Walk)	92 (90.2%)	
Minibus	10 (9.8%)	

Table 6: Sexual and Contraceptive History

Study Questionnaire Participants (*n*=102)

	Frequency (%)	*Mean*	*St. Dev.*	*Range*
Age at First Sex		16.4	1.33	12-19
12	1 (1%)			
13	2 (1.9%)			
14	3 (2.9%)			
15	15 (14.7%)			
16	35 (34.3%)			
17	25 (24.5%)			
18	16 (15.7%)			
19	5 (4.9%)			
Number of Sexual Partners		1.1	0.32	1-3
1	97 (95.1%)			
2	3 (2.9%)			
3	2 (2%)			
History of Forced Sex				
Yes	8 (7.8%)			
No	94 (92.2%)			
History of Transactional Sex				
Yes	1 (1%)			
No	101 (99%)			
Knowledge of Contraceptive Methods (Multiple responses possible)				
None	8 (7.8%)			
Condoms	78 (83%)			
Pills	47 (50%)			
Injectables	78 (83%)			
IUD	25 (26.6%)			
Other	3 (2.9%)			
Contraceptive Method Use				
None	45 (44.1%)			
Condoms	50 (90.9%)			
Pills	2 (3.4%)			
Injectables	5 (9.1%)			
IUD	0			
Other	0			
Reason for Stopping Contraception				
Never Used It	45 (44.1%)			
Desired Pregnancy	27 (26.5%)			
Husband/Partner Said No	27 (26.5%)			
Side Effects	3 (2.9%)			
Too Expensive	0			

Table 7: Obstetric History

	Frequency (%)	*Mean*	*St. Dev.*	*Range*
Gestational Age (Date of Study)		25.8 weeks	7 weeks	5-36 weeks
≤ 12 weeks	7 (6.9%)			
13-24 weeks	36 (35.3%)			
25-36 weeks	59 (57.8%)			
> 36 weeks	0			
Gestational Age (At 1st Visit)		18.9 weeks	5.9 weeks	4-32 weeks
≤ 12 weeks	17 (16.7%)			
13-24 weeks	75 (73.5%)			
25-36 weeks	10 (9.8%)			
> 36 weeks	0			
Number of Visits (To Date)		2.3	1.1	1-6
1	25 (24.6%)			
2	43 (42.2%)			
3	20 (19.6%)			
4	11 (10.8%)			
5	1 (1%)			
6	2 (2%)			
Pregnancy Problems	*n=101			
None	68 (67.3%)			
Back and/or Abdominal Pain	8 (7.9%)			
Malaria	10 (9.9%)			
Diarrhea	5 (4.9%)			
Other	10 (9.9%)			
Number of Previous Pregnancies				
None	79 (77.4%)			
1	17 (16.7%)			
2	6 (5.9%)			
Complications of Previous Pregnancies *n=23				
No	16 (69.6%)			
Yes	7 (30.4%)			
History of SAB	*n=23			
Yes	6 (26%)			
No	17 (74%)			
History of TAB	*n=23			
Yes	5 (21.7%)			
No	18 (78.3%)			

SAB-Spontaneous abortion
TAB-Therapeutic abortion

Table 8: HIV Testing and Knowledge

	Frequency (%)
Had Heard of HIV Before	
Yes	102 (100%)
Counseled About an HIV Test	
Yes	102 (100%)
No	0
HIV Test Offered	
Yes	102 (100%)
No	0
HIV Test Taken	
Yes	102 (100%)
No	0
HIV Test Results Obtained	
Yes	102 (100%)
No	0
HIV Test Results	
Positive	8 (7.8%)
Negative	94 (92.2%)
Aware of HIV Transmission by:	
Sexual Contact	102 (100%)
Blood	73 (71.6%)
From Mother to Baby	23 (22.6%)
Other	11 (10.8%)
Razor Blades	6 (54.5%0
"Dirty" Objects (Dishes, sponges)	2 (18.2%)
Breastfeeding	2 (18.2%)
Multiple sexual partners	1 (9.1%)
Protection from HIV by:	
Abstinence	43 (42.2%)
Condoms	89 (87.3%)
No Dirty Needles	34 (33.3%)
Get Tested with a New Partner	11 (10.8%)
Other	9 (8.8%)
Monogamy	3 (33.3%)
Protective Clothes/Gloves	3 (33.3%)
Incorrect Answers	3 (33.3%)

Table 9: Pregnancy Experiences at the Ndirande Health Centre

	Frequency (%) *n*=100
Benefits of Adolescent-Centered Antenatal Care	
Peer support/Freedom to Share	59 (59%)
Respectful Environment	16 (16%)
Pregnancy-related Education/Information	9 (9%)
General Encouragement	8 (8%)
Encouragement to Return/Continue Education	6 (6%)
Other	2 (2%)
Suggestions for Clinic	
No Changes/Happy with Care	94 (94%)
Improve facility	1 (1%)
Treat patients with respect	2 (2%)
Offer more preventive health care	2 (2%)
Need more staff	3 (3%)

Table 10: Demographic Characteristics by Marital Status
(With marital status as the dependent variable)

	Single n=34 (%)	*Married n=68 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Mean (Range)	Mean (Range)	Mean (Range)	z score	p-value	p-value
Age	17.4 (15-19)	18.0 (16-19)	17.8 (15-19)	z=-2.651	p=0.008	
15	1 (2.9%)	0	1 (1%)			
16	5 (14.7%	7 (10.3%)	12 (12%)			
17	14 (41.2%)	14 (20.6%)	28 (27.2%)			
18	7 (20.6%)	18 (26.5%)	25 (24.5%)			
19	7 (20.6%)	29 (42.7%)	36 (35.3%)			
Years of Schooling	9.3	8.6	8.8	z=1.396	p=0.163	
0-4	0	4 (5.9%)	4 (3.9%)			
5-8	14 (41.2%)	29 (42.6%)	43 (42.2%)			
9-12	19 (55.9%)	35 (51.5%)	54 (52.9%)			
Diploma	1 (2.9%)	0	1 (1%)			
Literacy						p=0.662
Able to read	33 (97.1%)	64 (94.1%)	97 (95.1%)			
Not able to read	1 (2.9%)	4 (5.9%)	5 (4.9%)			
Occupation						p=0.001
Housewife	20 (58.8%)	56 (82.3%)	76 (74.5%)			
Business Woman	3 (8.8%)	7 (10.3%)	10 (9.8%)			
Student	2 (5.9%)	0	2 (1.9%)			
Farming	0	1 (1.5%)	1 (1%)			
Other	0	2 (2.9%)	2 (1.9%)			
Nothing/ School Dropout	9 (26.5%)	2 (2.9%)	11 (10.7%)			
Partner Occupation						P<0.001
Laborer/Construction	1 (2.9%)	23 (33.8%)	24 (23.5%)			
Business Man	4 (11.8%)	13 (19.1%)	17 (16.7%)			
Salesman	4 (11.8%)	10 (14.7%)	14 (13.7%)			
Student	10 (29.4%)	3 (4.4%)	13 (12.7%)			
Driver/Transport	2 (5.9%)	7 (10.3%)	9 (8.8%)			
Mechanic	2 (5.9%)	2 (2.9%)	4 (3.9%)			
Teacher	0	1 (1.5%)	1 (1%)			
Not working	1 (2.9%)	2 (2.9%)	3 (2.9%)			
Other	5 (14.7%)	5 (7.35%)	10 (9.8%)			
Unknown (by partner)	5 (14.7%)	2 (2.9%)	7 (6.8%)			
Living Situation						P<0.001
Lives with Husband	2 (5.9%)	59 (86.8%)	61 (59.8%)			
Lives with Parents	22 (64.7%)	5 (7.3%)	27 (26.5%)			
Lives with Other	10 (29.4%)	4 (5.9%)	14 (13.7%)			
Orphan Status						p=0.102
Is an Orphan	8 (23.5%)	26 (38.2%)	34 (33.3%)			
Not an Orphan	26 (76.5%)	42 (61.8%)	68 (66.7%)			
Economic Markers						
Availability of Electricity						p=0.679
Yes	18 (52.9%)	39 (57.3%)	57 (55.9%)			
No	16 (47.1%)	29 (42.7%)	45 (44.1%)			

	Single n=34 (%)	*Married n=68 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Mean (Range)	Mean (Range)	Mean (Range)	z score	p-value	p-value
Availability of Water						p=0.847
Public kiosk/ MASAF	23 (67.7%)	49 (72.1%)	84 (82.4%)			
In House	1 (2.9%)	5 (7.4%)1	6 (5.8%)			
Buys from Neighbor	3 (8.8%)		5 (4.9%)			
Bore hole	2 (5.9%)	2 (2.9%)	4 (3.9%)			
Well	1 (2.9%)	2 (2.9%)	3 (2.9%)			
Home Ownership						p=0.003
Own	17 (50%)	14 (20.6%)	31 (30.4%)			
Rent	17 (50%)	54 (79.4%)	71 (69.6%)			

*MASAF-Malawi Social Action Fund (engaged in community projects, including water and sanitation)

Table11: Access to Antenatal by Marital Status

	Single n=34 (%)	*Married n=68 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Access to Health Care						
Distance to Clinic				z=-0.504	p=0.614	
< 1 hour	24 (70.6%)	42 (61.8%)	66 (64.7%)			
1-2 hours	1 (.29%)	11 (16.2%)	12 (11.8%)			
> 2 hours	9 (26.5%)	15 (22%)	24 (23.5%)			
Transportation						p=0.489
None/Walk	32 (94.1%)	60 (88.2%)	92 (90.2%)			
Minibus	2 (5.9%)	8 (11.8%)	10 (9.8%)			

Table 12: Sexual and Contraceptive History by Marital Status

	Single n=34 (%)	*Married n=68 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Age at First Sex				z=2.24	p=0.025	
< 16 years	10 (29.4%)	36 (52.9%)	46 (45.1%)			
> 16 years	24 (70.6%)	32 (47.1%)	56 (54.9%)			
Number of Sexual Partners				z=-0.645	p=0.520	
1	33 (97.1%)	64 (94.1%)	97 (95.1%)			
> 1	1 (1.9%)	4 (5.9%)	5 (4.9%)			
History of Forced Sex						p=0.436
Yes	4 (11.8%)	4 (5.9%)	8 (7.8%)			
No	30 (88.2%)	64 (94.1%)	94 (92.2%)			
History of Transactional Sex						p=0.333
Yes	1 (2.9%)	0	1 (1%)			
No	33 (97.1%)	68 (100%)	101 (99%)			
Knowledge of Contraceptive Methods						
None	5 (14.7%)	3 (4.4%)	8 (7.8%)			p=0.113
Condoms	25 (86.2%)	53 (81.5%)	78 (83%)			p=0.768
Pills	14 (48.3%)	33 (50.8%)	47 (50%)			p=1.000
Injectables	22 (75.9%)	56 (86.2%)	78 (83%)			p=0.244
IUD	7 (24%)	18 (27/7%)	25 (26.6%)			p=0.804
Contraceptive Method Use						
None	17 (50%)	28 (41.2%)	45 (44.1%)			p=0.408
Condoms	16 (94.1%)	34 (89.5%)	50 (90.9%)			p=1.000
Pills	0	2 (5.3%)	2 (3.4%)			p=1.000
Injectables	1 (5.9%)	4 (10.5%)	5 (9.1%)			p=1.000
IUD	0	0	0			-
Reason for Stopping Contraception						p=0.080
Never Used It	17 (50%)	28 (41.2%)	45 (44.1%)			
Desired Pregnancy	4 (11.8%)	23 (33.8%)	27 (26.5%)			
Husband/Partner Said No	12 (35.3%)	15 (22.1%)	27 (26.5%)			
Side Effects	1 (2.9%)	2 (2.9%)	3 (2.9%)			
Too Expensive	0	0	0			

Table 13: Obstetric History by Marital Status

	Single n=34 (%)	*Married n=68 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Gestational Age (Date of Study)				z=1.850	p=0.064	
≤ 12 weeks	1 (2.9%)	6 (8.8%)	7 (6.9%)			
13-24 weeks	10 (29.4%)	26 (38.2%)	36 (35.3%)			
25-36 weeks	23 (67.7%)	36 (52.9%)	59 (57.8%)			
> 36 weeks	0	0	0			
Gestational Age (At first visit)				z=1.839	p=0.060	
≤ 12 weeks	4 (11.8%)	13 (19.1%)	17 (16.7%)			
13-24 weeks	24 (70.1%)	51 (75%)	75 (73.5%)			
25-36 weeks	6 (17.6%)	4 (5.9%)	10 (9.8%)			
> 36 weeks	0	0	0			
Number of Visits to Date				z=0.665	p=0.509	
1	6 (17.6%)	19 (27.9%)	25 (24.6%)			
2	16 (47.1%)	27 (39.7%)	43 (42.2%)			
3	8 (23.5%)	12 (17.6%)	20 (19.6%)			
4	3 (8.8%)	8 (11.8%)	11 (10.8%)			
5	1 (2.9%)	0	1 (1%)			
6	0	2 (2.9%)	2 (2%)			
Pregnancy Problems (n=101)						p=0.045
None	25 (75.8%)	43 (63.2%)	68 (67.3%)			
Back and/or Abdominal Pain	1 (3%)	7 (10.3%)	8 (7.9%)			
Malaria	2 (6.1%)	8 (11.8%)	10 (9.9%)			
Diarrhea	4 (12.1%)	1 (1.5%)	5 (4.9%)			
Other	1 (3%)	9 (13.2%)	10 (9.9%)			
Number of Previous Pregnancies				z=-1.283	p=0.200	
0	29 (85.3%)	50 (73.5%)	79 (77.2%)			
1	3 (8.8%)	14 (20.6%)	17 (16.8%)			
2	2 (5.9%)	4 (5.9%)	6 (5.9%)			
Complications of Previous Pregnancies						p=0.142
Yes	3 (60%)	4 (22.2%)	7 (30.4%)			
No	2 (40%)	14 (77.8%)	16 (69.6%)			
History of Spontaneous Abortion						p=0.280
Yes	0	6 (33.3%)	6 (26%)			
No	5 (100%)	12 (66.7%)	17 (74%)			
History of Therapeutic Abortion						p=0.042
Yes	3 (60%)	2 (11.1%)	5 (21.7%)			
No	2 (40%)	16 (88.9%)	18 (78.3%)			

Table 14: HIV Testing and Knowledge by Marital Status

	Single n=34 (%)	*Married n=68 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Heard of HIV Before				-	-	-
Yes	34 (100%)	68 (100%)	102 (100%)			
Counseled About an HIV Test				-	-	-
Yes	34 (100%)	68 (100%)	102 (100%)			
HIV Test Offered				-	-	-
Yes	34 (100%)	68 (100%)	102 (100%)			
HIV Test Taken				-	-	-
Yes	34 (100%)	68 (100%)	102 (100%)			
HIV Test Results Obtained				-	-	-
Yes	34 (100%)	68 (100%)	102 (100%)			
HIV Test Results						p=1.000
Positive	3 (8.8%)	5 (7.4%)	8 (7.8%)			
Negative	31 (91.2%)	63 (92.6%)	94 (92.2%)			
Aware of HIV Transmission by:						
Sexual Contact	34 (100%)	68 (100%)	102 (100%)			-
Blood	24 (70.6%)	49 (72.1%)	73 (71.6%)			p=1.000
From Mother to Baby	8 (23.5%)	15 (22.1%)	23 (22.6%)			p=1.000
Other	4 (11.8%)	7 (10.3%)	11 (10.8%)			p=1.000
Protection from HIV by:						
Abstinence	14 (41.2%)	29 (42.7%)	43 (42.2%)			p=1.000
Condoms	31 (91.2%)	58 (85.3%)	89 (87.3%)			p=0.536
No Dirty Needles	14 (41.2%)	20 (29.4%)	34 (33.3%)			p=0.269
Get Tested with a New Partner	3 (8.8%)	8 (11.76%)	11 (10.8%)			p=0.748

Table 15: Pregnancy Experiences by Marital Status

	Single n=34 (%)	*Married n=66 (%)*	*All n=100* (%)*	*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	p-value
Benefits of Adolescent-Centered Antenatal Care				p=0.802
Peer support/Freedom to Share	18 (52.9%)	41 (62.1%)	59 (59%)	
Respectful Environment	7 (20.6%)	9 (13.6%)	16 (16%)	
Pregnancy-related Education/Information	4 (11.8%)	5 7.6%)	9 (9%)	
General Encouragement	3 (8.8%)	5 (7.6%)	8 (8%)	
Encouragement to Return/Continue Education	2 (5.9%)	4 (6.1%)	6 (6%)	
Other	0	2 (3%)	2 (2%)	
Suggestions for Clinic				p=0.432
No Changes/Happy with Care	30 (88.2%)	64 (94%)	94 (94%)	
Improve facility	0	1 (1.5%)	1 (1%)	
Treat patients with respect	1 (2.9%)	1 (1.5%)	2 (2%)	
Offer more preventive health care	1 (2.9%)	1 (1.5%)	2 (2%)	
Need more staff	2 (5.9%)	1 (1.5%)	3 (3%)	

Table 16: Demographic Characteristics by HIV Status
(With HIV status as the dependent variable)

	Negative n=94 (%)	*Positive n=8 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Marital Status						p=1.000
Single	31 (33%)	3 (37.5%)	34 (33.3%)			
Married	63 (67%)	5 (62.5%)	68 (66.7%)			
Age	17.8 (16-19)	17.6 (15-19)	17.8 (15-19)	z=0.325	p=0.746	
15	0	1 (12.5%)	1 (1%)			
16	12 (12.8%)	0	12 (12%)			
17	26 (27.7%)	2 (25%)	28 (27.2%)			
18	22 (23.4%)	3 (37.5%)	25 (24.5%)			
19	34 (36.2%)	2 (25%)	36 (35.3%)			
Years of Schooling				z=-0.729	p=0.466	
0-4	4 (4.3%)	0	4 (3.9%)			
5-8	40 (42.6%)	3 (37.5%)	43 (42.2%)			
9-12	49 (52.1%)	5 (62.5%)	54 (52.9%)			
Diploma	1 (1%)	0	1 (1%)			
Literacy						p=0.341
Able to read	90 (95.7%)	7 (87.5%0	97 (95.1%)			
Not able to read	4 (4.3%)	1 (12.5%)	5 (4.9%)			
Occupation						p=0.168
Housewife	71 (75.5%)	5 (62.5%)	76 (74.5%)			
Business Woman	9 (9.6%)	1 (12.5%)	10 (9.8%)			
Student	2 (2.1%)	0	2 (1.9%)			
Farming	0	1 (12.5%)	1 (1%)			
Other	2 (2.1%)	0	2 (1.9%)			
Nothing/ School Dropout	10 10.6%)	1 (12.5%)	11 (10.7%)			

	Negative n=94 (%)	*Positive n=8 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Partner Occupation						p=0.560
Laborer/Construction	22 (23.4%)	2 (25%)	24 (23.5%)			
Business Man	17 (18.1%)	0	17 (16.7%)			
Salesman	12 (12.8%)	2 (25%)	14 (13.7%)			
Student	12 (12.8%)	1 (12.5%)	13 (12.7%)			
Driver/Transport	7 (7.5%)	2 (25%)	9 (8.8%)			
Mechanic	4 (4.3%)	0	4 (3.9%)			
Teacher	1 (1.1%)	0	1 (1%)			
Not working	3 (3.2%)	0	3 (2.9%)			
Other	10 (10.6%)	0	10 (9.8%)			
Unknown (by partner)	6 (6.4%)	1 (12.5%)	7 (6.8%)			
Living Situation						p=0.406
Lives with Husband	57 (60.6%)	4 (50%)	61 (59.8%)			
Lives with Parents	25 (26.6%)	2 (25%)	27 (26.5%)			
Lives with Other	12 (12.8%)	2 (25%)	14 (13.7%)			
Orphan Status (Binary)						p=0.016
Is an Orphan	28 (29.8%)	6 (75%)	34 (33.3%)			
Not an Orphan	66 (70.2%)	2 (25%)	68 (66.7%)			
Orphan Status (Single, double)						p=0.018
Lost Mother	8 (8.5%)	1 (12.5%)	9 (8.8%)			
Lost Father	12 (12.8%)	2 (25%)	14 (13.7%)			
Lost Both Parents	8 (8.5%)	3 (37.5%)	11 (10.8%)			
Not an Orphan	66 (70.2%)	2 (25%)	68 (66.7%)			

	Negative n=94 (%)	*Positive n=8 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Economic Markers						
Availability of Electricity						p=0.020
Yes	56 (59.6%)	1 (12.5%)	57 (55.9%)			
No	38 (40.4%)	7 (87.5%)	45 (44.1%)			
Home Ownership						p=0.003
Yes	30 (31.9%)	1 (12.5%)	31 (30.4%)			
No	64 (68.1%)	7 (87.5%)	71 (69.6%)			
Availability of Water						p=0.84
Public kiosk/ MASAF	80 (85.1%)	4 (50%)	84 (82.4%)			
In House	4 (4.3%)	2 (25%)	6 (5.8%)			
Buys from Neighbor	5 (5.3%)	0	5 (4.9%)			
Bore hole	2 (2.1%)	2 (25%)	4 (3.9%)			
Well	3 (3.2%)	0	3 (2.9%)			

*MASAF-Malawi Social Action Fund (engaged in community projects, including water and sanitation)

Table 17: Access to Antenatal Care by HIV Status

	Negative n=94 (%)	*Positive n=8 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Access to Health Care						
Distance to Clinic				z=1.281	p=0.200	
< 1 hour	59 (62.8%)	7 (87.5%)	66 (64.7%)			
1-2 hours	12 (12.8%)	0	12 (11.8%)			
> 2 hours	23 (24.5%)	1 (12.5%)	24 (23.5%)			
Transportation						p=0.576
None/Walk	85 (90.4%)	7 (87.5%)	92 (90.2%)			
Minibus	9 (9.6%)	1 (12.5%)	10 (9.8%)			

Table 18: Sexual and Contraceptive History by HIV Status

	Negative n=94 (%)	*Positive n=8 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
				z score	p-value	p-value
Age at First Sex				z=1.42	p=0.156	
< 16 years	44 (46.8%)	2 (25%)	46 (45.1%)			
> 16 years	50 (53.2%)	6 (75%)	56 (54.9%)			
Number of Sexual Partners				z=0.666	p=0.506	
1	89 (94.7%)	8 (100%)	97 (95.1%)			
> 1	5 (5.3%)	0	5 (4.9%)			
History of Forced Sex						p=0.015
Yes	5 (5.3%)	3 (37.5%)	8 (7.8%)			
No	89 (94.7%)	5 (62.5%)	94 (92.2%)			
History of Transactional Sex						p=1.000
Yes	1 (1.1%)	0	1 (1%)			
No	93 (98.9%)	8 (100%)	101 (99%)			
Knowledge of Contraceptive Methods						
None	6 (6.4%)	2 (25%)	8 (7.8%)			p=0.119
Condoms	73 (83%)	5 (83.3%)	78 (83%)			p=1.000
Pills	43 (48.9%)	4 (66.7%)	47 (50%)			p=0.677
Injectables	73 (83%)	5 (83.3%)	78 (83%)			p=1.000
IUD	22 (25%)	3 (50%)	25 (26.6%)			p=0.336
Contraceptive Method Use						
None	43 (45.7%)	2 (25%)	45 (44.1%)			p=0.461
Condoms	45 (91.8%)	5 (83.3%)	50 (90.9%)			p=0.452
Pills	1 (2%)	1 (16.7%)	2 (3.4%)			p=0.208
Injectables	4 (8.2%)	1 (16.7%)	5 (9.1%)			p=0.452
IUD	0	0	0			-
Reason for Stopping Contraception						p=0.262
Never Used It	43 (45.7%)	2 (25%)	45 (44.1%)			
Desired Pregnancy	25 (26.6%)	2 (25%)	27 (26.5%)			
Husband/Partner Said No	24 (25.5%)	3 (37.5%)	27 (26.5%)			
Side Effects	2 (2.1%)	1 (12.5%)	3 (2.9%)			
Too Expensive	0	0	0			

Table 19: Obstetric History by HIV Status

	Negative n=94 (%)	*Positive n=8 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Gestational Age (Date of Study)				z=-0.672	p=0.502	
≤ 12 weeks	7 (7.4%)	0	7 (6.9%)			
13-24 weeks	33 (35.1%)	3 (37.5%)	36 (35.3%)			
25-36 weeks	54 (57.4%)	5 (62.5%)	59 (57.8%)			
> 36 weeks	0	0	0			
Gestational Age (At first visit)				z=0.793	p=0.428	
≤ 12 weeks	16 (17%)	1 (12.5%)	17 (16.7%)			
13-24 weeks	69 (73.4%)	6 (75%)	75 (73.5%)			
25-36 weeks	9 (9.6%)	1 (12.5%)	10 (9.8%)			
> 36 weeks	0	0	0			
Number of Visits to Date				z=-0.937	p=0.347	
1	24 (25.5%)	1 (12.5%)	25 (24.6%)			
2	40 (42.6%)	3 (37.5%)	43 (42.2%)			
3	17 (18.1%)	3 (37.5%)	20 (19.6%)			
4	10 (10.6%)	1 (12.5%)	11 (10.8%)			
5	1 (1.1%)	0	1 (1%)			
6	2 (2.1%)	0	2 (2%)			
Pregnancy Problems (n=101)						p=0.494
None	63 (67.7%)	5 (62.5%)	68 (67.3%)			
Back and/or Abdominal Pain	8 (8.6%)	0	8 (7.9%)			
Malaria	9 (9.7%)	1 (12.5%)	10 (9.9%)			
Diarrhea	5 (5.4%)	0	5 (4.9%)			
Other	8 (8.6%)	2 (25%)	10 (9.9%)			
Number of Previous Pregnancies				z=-1.111	p=0.266	
0	74 (78.7%)	5 (62.5%)	79 (77.4%)			
1	16 (17%)	1 (12.5%)	17 (16.7%)			
2	4 (4.3%)	2 (25%)	6 (5.9%)			
Complications of Previous Pregnancies				z=0.615	p=0.538	p=0.526
Yes	6 (28.6%)	1 (50%)	7 (30.4%)			
No	15 (71.4%)	1 (50%)	16 (69.6%)			
History of Spontaneous Abortion						p=1.000
Yes	5 (25%)	1 (33.3%)	6 (26%)			
No	15 (75%)	2 (66.7%)	17 (74%)			
History of Therapeutic Abortion						p=0.521
Yes	4 (20%)	1 (33.3%)	5 (21.7%)			
No	16 (80%)	2 (66.7%)	18 (78.3%)			

Table 20: HIV Testing and Knowledge by HIV Status

	Negative n=94 (%)	*Positive n=8 (%)*	*All n=102 (%)*	*Wilcoxon Mann-Whitney*		*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	z score	p-value	p-value
Heard of HIV Before				-	-	-
Yes	94 (100%)	8 (100%)	102 (100%)			
Counseled About an HIV Test				-	-	-
Yes	94 (100%)	8 (100%)	102 (100%)			
HIV Test Offered				-	-	-
Yes	94 (100%)	8 (100%)	102 (100%)			
HIV Test Taken				-	-	-
Yes	94 (100%)	8 (100%)	102 (100%)			
HIV Test Results Obtained				-	-	-
Yes	94 (100%)	8 (100%)	102 (100%)			
Aware of HIV Transmission by:						
Sexual Contact	94 (100%)	8 (100%)	102 (100%)			-
Blood	68 (72.3%)	5 (62.5%)	73 (71.6%)			p=0.685
From Mother to Baby	23 (24.5%)	0	23 (22.6%)			p=0.193
Other	10 (10.6%)	1 (12.5%)	11 (10.8%)			P=1.000
Protection from HIV by:						
Abstinence	40 (42.6%)	3 (37.5%)	43 (42.2%)			p=1.000
Condoms	82 (87.2%)	7 (87.5%)	89 (87.3%)			p=1.000
No Dirty Needles	34 (36.2%)	0	34 (33.3%)			p=0.049
Get Tested with a New Partner	11 (11.7%)	0	11 (10.8%)			p=0.594

Table 21: Pregnancy Experiences by HIV Status

	Negative n=93 (%)	*Positive n=7 (%)*	*All n=100* (%)*	*Fisher's Exact*
	Median (Range)	Median (Range)	Median (Range)	p-value
Benefits of Adolescent-Centered Antenatal Care				p=0.086
Peer support/Freedom to Share	56 (60.2%)	3 (42.9%)	59 (59%)	
Respectful Environment	15 (16.1%)	1 (14.3%)	16 (16%)	
Pregnancy-related Education/Information	9 (9.7%)	0	9 (9%)	
General Encouragement	5 (5.4%)	3 (42.9%)	8 (8%)	
Encouragement to Return/Continue Education	6 (6.5%)	0	6 (6%)	
Other	2 (2.2%)	0	2 (2%)	
Suggestions for Clinic				p=0.492
No Changes/Happy with Care	87 (92.6%)	7 (87.5%)	94 (92.1%)	
Improve facility	1 (1.1%)	0	1 (1%)	
Treat patients with respect	2 (2.1%)	0	2 (2%)	
Offer more preventive health care	2 (2.1%)	0	2 (2%)	
Need more staff	2 (2.1%)	1 (12.5%)	3 (2.9%)	

Table 22: Comparison-Study Data vs. Malawi Demographic and Health Survey Data (2010)
(Unless otherwise specified, study data and Malawi DHS data are both for females aged 15 to 19 years)

Variable	Study	Malawi DHS
Demographic Information		
Marital Status (% Married)	66.7%	19.5%
Schooling Completed (Median years)	9.0	5.7
None	1%	3.5%
Some Primary	20.6%	59.6%
Completed Primary	24.5%	14%
Some Secondary	42.2%	19.2%
Completed Secondary	10.8%	3.1%
More than Secondary	1%	0.5%
Literacy (% Literate)	95.1%	80.9%
Occupation (% Employed)	14.7%	36.5%
Orphan Status (% who have lost either one or both parents)	33.3%	12.1% [a]
Maternal orphan (Lost mother)	8.8%	3% [a]
Paternal orphan (Lost father)	13.7%	8% [a]
Double orphan (Lost both parents)	10.8%	3% [a]
Availability of Electricity	55.9%	34.7% (Urban) 8.7% (Total)
Availability of Water	100%	92.6% (Urban) 72.7% (Total)
Transportation	90.2% walk to clinic	2% of total population own a car
Sex and Contraception		
Age at First Sex	16.4 years	17.3 years [b]
By age 15	14.7%	18%
By age 18	95.1%	60%
By age 20	100%	80%
Number of Sexual Partners (Mean)	1.1	1.4
History of Forced Sex	7.8%	14.3%
History of Transactional Sex	1%	6.4% [c]
Knowledge of Contraception		
None	7.8%	2%
Condoms	83%	94.7% [d]
Pills	50%	91.1% [d]
Injectables	83%	95.3% [d]
IUD	26.6%	73.8% [d]
Use of Contraception		
None	46.1%	79.5%
Condoms	90.9%	12.5%
Pills	3.4%	1%
Injectables	9.1%	9.2%
IUD	0	0.1%

Variable	Study	Malawi DHS
Obstetric History		
Gestational Age at 1st Antenatal Visit (Median)	5 months	5.6 months
HIV Testing and Knowledge		
HIV Tested	100%	88.5%
HIV Prevalence	7.8%	4.2%
HIV Knowledge-Prevent by:		
Using Condoms	87.3%	68.3%
Monogamy	33.3%	83.2%
Abstinence	42.2%	77.2%
HIV Knowledge-Spread by:		
Mother to Child	22.6%	25%
Breastfeeding	18.2%	85.6%

[a] Total data only available for females ages 15-17, while specific data on orphan type is for any female under the age of 18

[b] Data retrospectively reported by women ages 20-49

[c] Data for males ages 15-24 who had paid for sex; no data in DHS survey on females who engaged in transactional sex

[d] Data on knowledge of specific contraceptive methods from women ages 15-49

Table 23: Bivariate Logistic Regression by Marital Status
(With marital status treated as a dichotomous variable)

Marital Status (Reference: Married)	Odds Ratio	Standard Error	z	P>|z|	95% Confidence Interval	LR X^2 (1)	Prob > X^2
HIV Positive	1.219	0.930	0.26	0.795	0.274-5.435	0.07	0.796
Age	0.586	0.120	-2.60	0.009	0.392-0.877	7.18	0.007
Occupation	1.204	0.098	2.27	0.023	1.026-1.413	5.18	0.023
Lives with	1.099	0.265	0.39	0.695	.685-1.76	0.16	0.692
Own home	3.857	1.757	2.96	0.003	1.58-9.42	9.00	0.003
No Electricity Available	1.195	0.505	0.42	0.672	.523-2.734	0.18	0.673
Orphan	0.768	0.164	-1.23	0.217	0.505-1.168	1.63	0.202
Age at 1st sex >16	2.700	1.210	2.22	0.027	1.122-6.500	5.19	0.023
Hx Forced Sex	0.469	0.347	-1.02	0.306	0.110-2.003	1.03	0.311
Stop contraception	1.038	0.199	0.19	0.846	0.712-1.513	0.04	0.847
Hx TAB	12.75	15.044	2.16	0.031	1.262-128.78	5.05	0.025
Gestational age at 1st visit	1.062	0.040	1.59	0.113	0.986-1.144	2.66	0.103
HIV Positive	1.219	0.930	0.26	0.795	0.274-5.435	0.07	0.796

Table 24: Multivariate Logistic Regression by Marital Status
McFadden's R^2 =0.33
(With marital status treated as a dichotomous variable)

Marital Status (Reference: Married)	Odds Ratio	Standard Error	z	P>|z|	95% Confidence Interval	LR X^2 (3)	Prob > X^2
Age	0.467	0.316	-1.13	0.261	0.124-1.758	6.65	0.084
Occupation	1	.	.	.	.		
Own home	34.118	72.628	1.66	0.097	0.526-2212.68		
Age at 1st sex >16	1	.	.	.	.		
Hx TAB	9.140	14.096	1.43	0.151	0.445-187.789		

Table 25: Bivariate Logistic Regression by HIV Status
(With HIV status treated as a dichotomous variable)

HIV Status (Reference: HIV Negative)	Odds Ratio	Standard Error	z	P>|z|	95% Confidence Interval	LR X^2 (1)	Prob > X^2
Marital Status	0.82	0.625	-0.26	0.795	0.184- 3.655	0.07	0.796
Age	0.85	0.283	0.52	0.686	0.444-1.625	0.25	0.687
Occupation	1.08	0.146	0.53	0.596	0.824-1.403	0.27	0.604
Lives with	1.25	0.326	0.84	0.399	.747- 2.082	0.65	0.419
Own home	0.31	0.333	-1.09	0.276	0.036-2.590	1.53	0.216
No Electricity Available	10.31	11.239	2.14	0.032	1.219-87.276	7.12	0.008
Orphan	7.07	5.99	2.31	0.021	1.344-37.199	6.35	0.012
Age at 1st Sex >16	2.64	2.224	1.15	0.249	0.057-13.757	1.49	0.222
Hx Forced Sex	10.68	9.216	2.74	0.006	1.968-57.951	6.43	0.011
Stopped Contraception	1.61	.433	1.76	0.078	0.948-2.725	2.80	0.094
Hx TAB	2.13	2.858	0.56	0.575	0.152-29.659	0.29	0.588
Gestational age at 1st visit	1.06	0.070	0.81	0.419	0.927-1.201	0.68	0.409

Table 26: Multivariate Logistic Regression by HIV Status
McFadden's $R^2 = 0.43$
(With HIV status treated as a dichotomous variable)

HIV Status (Reference: HIV Negative)	Odds Ratio	Standard Error	z	P>|z|	95% Confidence Interval	LR X^2 (3)	Prob > X^2
No Electricity Available	37.52	055.609	2.45	0.014	2.055-685.15	24.18	<0.0001
Orphan	24.24	29.715	2.60	0.009	2.194-267.87		
Hx Forced Sex	0.03	0.036	-2.72	0.007	0.002-0.366		

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