**HIV Prevention Literature Review III:**

**Prevention of Mother to Child Transmission (PMTCT)**

**& Pediatric HIV in Low- and Low-Middle-Income Countries**

**Draft 2**

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**Acronyms & abbreviations**

ANC Antenatal care

AIDS Acquired immunodeficiency syndrome

ART Antiretroviral treatment

ARV Antiretroviral

CHW Community health worker

CBRHA Community-based reproductive health agents

DMPA Depot-medroxyprogesterone acetate

EBF Exclusive breastfeeding

EID Early infant diagnosis

HAART Highly active anti-retroviral therapy

HIV Human immunodeficiency virus

HCT HIV counseling and testing

HR Hazard ratio

LHW Lay health worker

LTFU Loss to follow-up

M2M Mothers2Mothers program

MCH Mother and child health

MTCT Mother to child transmission

NVP Nevirapine

OR Odds ratio (aOR = adjusted odds ratio)

PMTCT Prevention of mother-to-child transmission

RCT Randomised controlled trial

RR Risk ratio (aRR = adjusted risk ratio)

TBA Traditional birth attendant

UNAIDS Joint United Nations Programme on HIV/AIDS

UNICEF United Nations Children’s Fund

WHO World Health Organization

# Executive Summary

The Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping their Mothers Alive, adopted by the United Nations High Level Meeting on AIDS in 2011, set a goal of reducing the number of new HIV infections among children by 90%, and AIDS-related deaths among pregnant women by 50% (UNAIDS, 2011). Although great strides have been made in reaching these goals, vertical HIV transmission to infants remains unacceptably high in many countries, and attrition along the PMTCT cascade remains high.

A number of studies have identified significant barriers to PMTCT, including individual-level factors (e.g. physical and mental health), factors at the family and social level (e.g. stigma and fear of disclosure of HIV status), and structural factors (e.g. socioeconomic factors, barriers associated with healthcare facilities). Families and male partners play a critical role in supporting women in accessing PMTCT and adhering to treatment, and lack of male support has often been noted. Family and partner support will only become more critical as PMTCT programs transition to initiating HIV-positive pregnant women on immediate and lifelong ART under Option B+.

This review focuses on Prong 2 of PMTCT (family planning for HIV-positive women) and especially on community based approaches to Prong 4 (HIV care, treatment, and support for women and children living with HIV and their families). Interventions were reviewed which addressed seven steps in the PMTCT cascade, starting with initiation of ANC care for all pregnant women and ending with ART adherence for HIV-positive mothers and infants. Interventions were identified which addressed each step of the cascade at the community level (and mostly utilizing community health workers), and most interventions addressed multiple steps. The most frequently targeted step in the PMTCT cascade was HIV testing. Community-based, community health worker-led interventions consistently showed impact on PMTCT indicators, suggesting that such approaches have great potential to further increase PMTCT coverage and decrease vertical HIV transmission.

# Introduction

The Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping their Mothers Alive, adopted by the United Nations High Level Meeting on AIDS in 2011, set a goal of reducing the number of new HIV infections among children by 90%, and AIDS-related deaths among pregnant women by 50% (UNAIDS, 2011). The Global Plan identified 22 priority countries which account for 90% of pregnant women living with HIV globally. All but one (India) are in sub-Saharan Africa. According to UNAIDS’ most recent estimates, in the 21 African priority countries new HIV infections among children decreased 37% from 2009 to 2012, even as 210,000 children were newly infected (UNAIDS, 2013). (Data were not available for India.) Globally, UNAIDS estimates that 4 in 10 pregnant women living with HIV do not receive antiretroviral (ARV) prophylaxis to prevent mother-to-child HIV transmission, and 5 out of 10 at-risk mother-infant pairs do not receive ARVs during breastfeeding to prevent vertical transmission. (UNAIDS, 2013).

Community action, such as community-level efforts against stigma and discrimination and to support women in accessing prevention of mother to child transmission (PMTCT) services, has been recognized as critical to meeting these goals (Sidibé & Goosby, 2012). Community-based approaches to PMTCT have been defined as “strategies and interventions to improve health behaviour and outcomes that are delivered outside of formal health settings including primary, secondary, and tertiary medical facilities” and which “explicitly target community members, their local civil or traditional authorities/leaders or traditional health providers outside the formal sector” (Busza et al., 2012, p. 3).

PMTCT relies on a 4-pronged strategy (UNAIDS, 2011), starting with primary prevention of HIV infection and ending with lifelong care, treatment, and support for mothers and children who are living with HIV (see Figure 1 below). This review will focus on Prong 2 and particularly on community-based support for Prong 4.

**Four prongs** **of PMTCT:**

Prong 1: Primary prevention of HIV infection

**Prong 2: Prevention of unintended pregnancies in women living with HIV**

Prong 3: Prevention of vertical transmission of HIV from women to their infants

**Prong 4: HIV care, treatment and support for women and children living with HIV and their families**

Figure 1: Four Prongs of PMTCT

## The PMTCT Cascade

Effective PMTCT requires a sequence of critical steps, a sequence which is often called the PMTCT cascade. The indicators used to assess the cascade vary somewhat from program to program, and have changed with changes in recommended ARV regimens (for example, the phase-out of single-dose nevirapine prophylaxis in favor of more effective ARV regimens). Based on the available literature, the following PMTCT cascade will be used in this review.

**STEPS OF PMTCT CASCADE:**

1. Initiation of ANC care for pregnant women
2. HIV counseling and testing for pregnant women
3. Enrollment into ART (or pre-ART care) for HIV+ women
4. ARV prophylaxis for HIV+ mothers (if not on ART) and HIV-exposed infants directly after birth
5. Exclusive breastfeeding or replacement feeding for HIV-exposed infants
6. Early infant diagnosis for HIV-exposed infants
7. ART adherence for HIV+ mothers and infants

Figure 2: Steps of PMTCT Cascade

Using the framework of the PMTCT cascade allows for more detailed examination of PMTCT coverage. For example, an analysis of PMTCT coverage and impact in the 21 African priority countries estimated that pediatric infections had decreased from 346,600 to 214,000 between 2009 and 2013, but also provided estimates of ART provision at various points (Adetokunboh & Oluwasanu, 2015). The proportion of pregnant women in these countries receiving ART increased from 33% to 63%, and the proportion of mother-baby pairs who received ART during breastfeeding increased from 11% in 2009 to 51% in 2013 during the same period. In China, significant increases in PMTCT coverage and decreases in vertical transmission were seen after the introduction of PMTCT programs in 2003 (Zeng et al., 2015). In 2011, it was estimated that 90% of pregnant women and 83% of HIV-exposed infants were tested for HIV, and 86% of HIV-diagnosed pregnant women and 90% of HIV-exposed infants received ARV prophylaxis. This resulted in a decreased in vertical transmission from 32% in 2003 to 2% in 2011.

In spite of the gains made in PMTCT, in most contexts loss to follow-up along the PMTCT cascade remains high (Cowan et al., 2015; Marcos, Phelps, & Bachman, 2012). Estimates of adherence and attrition vary, but all studies reviewed agree that PMTCT adherence rates are far from optimal. One meta-analysis of loss to follow-up along the PMTCT cascade found that between 38% and 88% of all women known to be eligible failed to initiate HAART, while in pooled analysis only 43% of those known to be eligible received HAART, and as few as 18% of those who might have been eligible (but were not assessed for eligibility) (Ferguson et al., 2012). Another global meta-analysis found that only 74% of pregnant women achieved optimal ART adherence, and that only 53% of women achieved adequate adherence postpartum, compared to 76% antepartum (Nachega et al., 2012)A third systematic review and meta-analysis of data from 15 countries found that HIV testing uptake at ANC was 94% for opt-out HIV testing, but only 58% for opt-in testing, that coverage of any antiretroviral prophylaxis was 70%, that 62% of eligible pregnant women received ART, and that 64% of HIV-exposed infants received early diagnosis (Wettstein et al., 2012). While higher income countries have generally achieved quite low rates of vertical transmission, Cuba is unique in having completely eliminated mother-to-child transmission of HIV and syphilis, according to the World Health Organization

(World Health Organization, 2015). Cuba’s strategy has included free and early access to prenatal care, HIV and syphilis testing for pregnant women and their partners, lifelong HIV treatment for HIV-positive women (since 2008), ART prophylaxis for HIV-exposed infants, caesarean delivery, and substitution feeding of infants

(Lastre et al., 2014; World Health Organization, 2015).

Lack of PMTCT coverage and adherence results in significant numbers of pediatric HIV infections. The World Health Organization recommends universal HIV treatment for all HIV-infected children under the age of 5, but less than one quarter of children under 5 start ART (according to 2011 estimates), and in 2011 an estimated 230,000 children under the age of 5 died of HIV (UNAIDS, 2013). Although infants born to HIV-positive mothers should be screened at age 4 to 6 weeks for HIV infections, fewer than 1 in 5 infants in resource-limited settings receive this test (Kellerman & Essajee, 2010). Once HIV-positive children are lost to follow-up from the PMTCT system, it is likely that they will not re-enter the healthcare system for some time. Caregivers may not take children for testing or treatment, especially if they do not show signs of illness, and up to one third of HIV-positive infants will not show symptoms of HIV/AIDS until their teens (Ahmed et al., 2013). Active follow-up of those who default from care may be a critical measure, with one meta-analysis showing that HIV-positive infants who were not actively followed up had more than 6 times the risk of dropping out of care (Nduati et al., 2015).

In order to reduce attrition along the PMTCT cascade, PMTCT services are increasingly being integrated into maternal, newborn, and child health services (Chi, Bolton-Moore, & Holmes, 2013; UNAIDS, 2011). Such an approach has the benefit of streamlining service provision, requiring fewer visits to health care facilities for mothers and babies and promoting adherence and retention in care, and may also reduce stigma (Chi et al., 2013; UNAIDS, 2011). Community-based programs may also reduce drop-out from PMTCT. A 2012 review found 9 examples of programs which were community-based and/or employed community-oriented groups housed in healthcare facilities to improve outcomes along the PMTCT cascade, and which reported statistically significant improvements in PMTCT outcomes (Marcos et al., 2012; UNAIDS, 2013). This review concluded that such interventions were effective in increasing uptake of testing and prevention services and promoting better rates of disclosure and retention. A review of interventions aimed at improving linkages to, or retention in, pre-ART care or initiation of ART documented a number of interventions with “promising results” aimed at integrating ANC care and ART or offering strategies such as home visits to minimize clinic visits (Govindasamy, Meghij, Negussi, Baggaley, & Ford, 2014; UNAIDS, 2013).

## Barriers to PMTCT coverage

Significant barriers to PMTCT uptake have been noted across multiple studies, and even with the provision of fully integrated HIV and ANC services (Sidibé & Goosby, 2012; Washington, Owuor, & Turan, 2015). In a meta-analysis of barriers to uptake of ART for PMTCT in sub-Saharan Africa, Gourlay and colleagues (2013) identify stigma and fear of disclosure of HIV status (to sexual partners, family members, and community members) as the most salient barriers across more than 40 studies. Stigma was mentioned in nearly all qualitative studies examined, and in quantitative studies, non-disclosure of HIV status to partners was associated with lack of ART uptake among HIV-positive pregnant women in several studies (Busza et al., 2012, p. 3; Gourlay, Birdthistle, Mburu, Iorpenda, & Wringe, 2013). In a review of global studies of ART initiation, adherence, and retention among HIV-positive pregnant women, Hodgson et al. (2014) identified very similar factors, including the negative impact of stigma and fear of disclosure of HIV status. Another global meta-analysis found that barriers to optimal adherence for HIV-positive pregnant women included physical, economic, and emotional stress, depression (especially postpartum), alcohol or drug use, and ART pill burden (Nachega et al., 2012; UNAIDS, 2011). Turan and Nyblade, in a review of the impact of HIV-related stigma on PMTCT, concluded that stigma negatively impacts uptake and adherence of each step of the PMTCT cascade (Adetokunboh & Oluwasanu, 2015; Turan & Nyblade, 2013).

Another review which examined barriers to PMTCT and maternal and newborn child health identified four types of barriers: socioeconomic, social norms and knowledge, physiological, and psychological (O hIarlaithe, Grede, de Pee, & Bloem, 2014; Zeng et al., 2015). A study which followed up all PMTCT patients who had dropped out of care at a large ANC clinic in Malawi (constituting 20% of all women in the PMTCT program) found that over half had stopped taking ART, and that the most common reasons for dropping out of care were challenges with travel or transport money (54%), not understanding the ART education provided (10%), being too weak or sick (10%), and experiencing ART side effects (10%) (Cowan et al., 2015; Marcos et al., 2012; Tweya et al., 2014). Although not well studied, the quality of care provided by health care staff may also be a critical determinant of retention in PMTCT. Qualitative investigation in Kisesa, Tanzania found that women seeking PMTCT services perceived power imbalances in favor of health care providers, and often did not understand the information communicated to them by providers, resulting in missed services (Gourlay et al., 2013). Pregnant women also reported being treated disrespectfully by providers, and such negative behavior or the fear of such treatment negatively influenced PMTCT adherence.

The critical step of HIV testing during pregnancy is often overlooked (Bhardwaj, Carter, Aarons, & Chi, 2015; Ferguson et al., 2012). Barriers to testing during pregnancy may including not perceiving risk of HIV, lack of motivation or self-efficacy, poor mental and physical health (Busza et al., 2012; Nachega et al., 2012). Due to intra-family household dynamics, women may lack financial resources to travel to medical facilities or fear violence from their husbands or male partners if they receive an HIV diagnosis (Busza et al., 2012; Wettstein et al., 2012). The support of husbands or partners and others members of family or social networks is associated with women accepting and adhering to ART as well as receiving antenatal care in a health care facility (Busza et al., 2012; UNAIDS, 2013). Conversely, women who feel stigmatized are less likely to be ART adherent (Busza et al., 2012; Kellerman & Essajee, 2010).

A review of linkage, initiation and retention of children in ART found that children who were orphaned, younger, and with more clinically advanced disease were more likely to be lost to follow-up (Ahmed et al., 2013; Phelps et al., 2013). In addition, children were less likely to be receiving ART if their caregivers perceived stigma, did not have the support of male partners, or were ignorant that pediatric ART was available (Nduati et al., 2015; Phelps et al., 2013). HIV-positive babies born to mothers who attended ANC late in pregnancy (at 28 weeks gestation or later) are also less likely to be retained in care (Chetty et al., 2012), perhaps because such women are more likely to have other risk factors associated with infant loss-to-follow-up, such as lack of education and social and partner support.

Humanitarian emergencies such as those caused by natural disasters and conflict can also greatly disrupt access to PMTCT services and ART for mothers and children (UNICEF, 2013). Health services break down and the availability of ART and other essential commodities can be threatened (UNICEF, 2013). UNICEF recommends that HIV prevention, treatment, and care for infants and children should be prioritized in emergency planning. Contingency planning and partnerships between governments, NGOs, and other actors to trace patients and ensure supply chains of essential drugs can be critical in ensuring that ART can continue to be offered in situations of conflict and upheaval (UNICEF, 2013). The Inter-Agency Standing Committee Task Force on HIV, a collaboration of UN agencies and non-governmental organizations, has published guidelines on responding to HIV in humanitarian emergencies (Inter-Agency Standing Committee (IASC), 2010).

## Role of partners and families

The support of husbands or male partners and other family members may be critical to women’s successful participation in ANC and HIV care, including PMTCT programs. A systematic review found that women who had disclosed their HIV status to a spouse and had a spouse involved in their treatment had improved ART initiation, adherence, and retention (Hodgson et al., 2014). A study in Uganda demonstrated the importance of family members for adherence among all women and men initiating ART treatment. Women and men were asked to choose “medicine companions” (MCs) when they initiated ART treatment to support them in adherence, and 20 women and 20 men were interviewed about their experience with MCs (Foster et al., 2010). Two-thirds of married men (66%) chose their wives as their MCs, while only 31% of married women did so, and some felt that a child was more reliable in this role than a husband. Women were most likely to choose a child as their MC. Participants who had disclosed their sero-status to their families generally received reminders from multiple family members. MCs were reported to be most important during the first 3 months, including to provide reminders, but were considered to be less essential after 6 months on ART.

In Uganda, a simple intervention which involved sending an invitation letter to attend ANC (intervention group) or an information leaflet about ANC (control group) to male partners of new ANC attendees was successful in increasing couple attendance at ANC approximately 3-fold in both study arms (Byamugisha et al., 2011), demonstrating that simple measures may be effective in increasing male partner participation in ANC. A qualitative study in Khayelitsha, South Africa, found that pregnant women were eager to have their male partners attend ANC visits with them and that men would attend if invited, with the main barriers to men’s involvement being lack of awareness about the importance of their attendance, and lack of receptiveness to male partners at healthcare facilities (Mohlala, Gregson, & Boily, 2012).

A review of “family-centered” approaches to PMTCT concluded that women with lower levels of family support were more likely to refuse HIV testing, and that “father involvement in PMTCT and family-based testing and care are critically important” (Betancourt, Abrams, McBain, & Fawzi, 2010). A review of interventions aimed at increasing male involvement in PMTCT found that all 13 interventions examined focused on male partner HIV testing, and that offering HIV testing through facilities such as bars and churches resulted in higher uptake than offering testing at healthcare facilities (Sherr & Croome, 2012). The MTCT-Plus program, which operated in 13 sites in sub-Saharan Africa and Southeast Asia, invited HIV-positive pregnant women to enroll themselves, their infants, and their HIV-positive family members in a comprehensive PMTCT and HIV care program. Over 16,000 people were enrolled in the program from 2003 to 2008 (Betancourt et al., 2010). More than two-thirds of women enrolled their HIV-exposed baby or another family member, and HIV diagnosis of infants, ART initiation and retention in the program were high (Abrams, Myer, Rosenfield, & El-Sadr, 2007). In Kenya, male partners of women in a PMTCT program were more than twice as likely to accept couples’ counseling and testing (HIV testing and mutual disclosure) if they were offered HIV testing at a home visit, compared to men who received a written invitation to be tested at a clinic (Osoti et al., 2014). HIV testing of male partners may promote uptake of PMTCT among their female partner (Osoti et al., 2014). In Ivory Coast, men who knew that their wives or partners were HIV-positive and enrolled in a PMTCT program played an active role in supporting their partners to follow guidelines for exclusive breastfeeding and early weaning (Traoré et al., 2009).

Research has also revealed barriers to male involvement in PMTCT. A systematic review of male involvement in PMTCT (with 21 of 24 studies examined coming from sub-Saharan Africa) concluded that ANC and PMTCT were perceived as a woman’s activity, with men’s involvement being seen as unacceptable (Morfaw et al., 2013). Barriers were also identified at the level of health facilities, including long waiting times at ANC clinics and men not being welcomed at PMTCT services. Intra-couple dynamics also contributed to men’s lack of involvement, including lack of communication within the couple, men’s reluctance to be tested for HIV, and women’s fear of domestic violence, stigmatization, or divorce if they involved their husbands in ANC and PMTCT. A PMTCT program in rural Malawi which required that participants disclose their HIV-positive status to their partners was referred to by the community as “the divorce program” due to the frequent negative repercussions of such an approach, including male rejection and abandonment of HIV-positive wives and partners (often accompanied by allegations of infidelity against the HIV-positive women) (Njunga & Blystad, 2010).

## Family planning and PMTCT

Prong 2 of PMTCT calls for reducing unintended pregnancies among HIV-positive women, but a recent review of evidence on the role of family planning in eliminating new pediatric HIV infections concluded that “substantial shortcomings exist” in translating this global policy into practice (Wilcher, Petruney, & Cates, 2013, p. 490). PMTCT programs typically begin within ANC, after a woman is already pregnant, although evidence shows that integrating family planning and HIV services is effective in reducing unintended pregnancies among HIV-positive women (Wilcher et al., 2013). A 2009 review of such integration found 16 studies and 6 types of programs, only 10 of which had published in peer-reviewed publications (Spaulding et al., 2009). Two of these 16 interventions provided integrated family planning and HIV services through community health workers, and one was peer-reviewed and published in the time period included in this review (see Creanga et al. 2007). The review concluded that average study design rigor was low, although positive outcomes were reported in family planning usage. In South Africa, most women who participated in a PMTCT program at public clinics received counseling on family planning postnatally, yet use of contraceptives and condoms were low, and pregnancy desire remained high among HIV-positive women (Peltzer, Chao, & Dana, 2008). A more recent cluster RCT in Kenya found positive results; clinics which were randomized to integrate family planning services into HIV clinics had increased use of effective contraceptive methods (Grossman et al., 2013).

## Effectiveness of community health workers

This review will largely focus on community-based support of PMTCT. The role of community or lay health workers (CHWs/LHWs) in promoting health and providing services (including for HIV) has been extensively studied. A Cochrane review and meta-analyses examined 82 RCTs (55 in high-income countries) of interventions delivered by lay health workers (LHWs) in primary or community health care and intended to improve MCH or management of infectious diseases (Lewin et al., 2010). LHWs were found to be effect in promoting initiation of breastfeeding, including any breastfeeding and exclusive breastfeeding. However, the review found “low quality” evidence that LHWs were effective in reducing child morbidity and child and neonatal mortality. In addition to this quantitative analysis, any qualitative research carried out alongside these trials was also synthesized; such research was available for only 14 of 82 trials, 8 in high-income countries (Glenton, Lewin, & Scheel, 2011). Most qualitative studies found program beneficiaries valued LHWs for the experiences and social background they held in common with beneficiaries, which helped LHWs provide emotional and practical support.

A study of CHWs in Brazil, Ethiopia, Malawi, Namibia, and Uganda found that task-shifting to CHWs with limited training increased access to HIV services, particularly in rural areas and among underserved communities, and that PLHIV’s first contact with the health care system was with a CHW in 39% of cases (Celletti et al., 2010). A systematic review of the role of CHWs in HIV care in sub-Saharan Africa found that CHWs performed a broad range of functions including patient counseling, home-based care, education, adherence support, and livelihood support (Mwai et al., 2013). CHW involvement increased the reach, uptake, and quality of HIV services, increased retention in care, and enhanced the dignity and quality of life of people living with HIV.

In Ethiopia, HIV counseling and testing (HCT) coverage increased from 500,000 to 1.6 million in two years, after CHW were trained to carry out HCT (Celletti et al., 2010). Non-salaried CHWs known as community-based reproductive health agents (CBRHAs) provide the “backbone” of the reproductive health service system in Ethiopia, and a 2007 study found that nearly half of CBRHAs offered integrated family planning and HIV services, including referral for HCT and home-based care for people living with HIV (Creanga, Bradley, Kidanu, Melkamu, & Tsui, 2007). In Namibia, ART initiation and retention was found to increase with CHW involvement (Celletti et al., 2010). Data from three Médecins Sans Frontières clinics in an informal settlement of Nairobi, Kenya found that more than half of HIV-positive patients who were contacted by a social worker (via telephone or an in-person visit) when they missed an appointment returned to the clinic for care, and loss to follow-up among all HIV-positive patients decreased from 21% to 12% over 3 years when such a strategy was adopted (Thomson, Cheti, & Reid, 2011). In a review of data from 9 countries in the Americas, Asia, and Africa, CHWs were found to competently and safely deliver the injectable contraceptive DMPA, leading to increased uptake of family planning among underserved clients (Malarcher et al., 2011).

## Introduction of Option B+

Many African countries, including most of the 21 Global Plan priority countries, have adopted Option B+, which specifies that all HIV-positive pregnant women initiate lifelong ART regardless of CD4 count (Chi et al., 2013). By the end of 2013, the Elizabeth Glaser Pediatric AIDS Foundation reported that in 11 African countries supported by the organization, most programs were reaching at least 50% of HIV-positive women in ANC care with ART (Kieffer et al., 2014). In Malawi, the first country to adopt Option B+, a study in the city of Lilongwe showed that ART use during pregnancy increased and mother to child transmission decreased after the introduction of Option B+ (Kim et al., 2014). However, a nationwide study showed that attrition from Option B+ was high, with 17% of women lost to follow-up within 6 months of initiating lifelong ART (most losses within the first 3 months), and women who initiated lifelong ART during pregnancy having 5 times the odds of being lost to follow-up after an initial clinic visit, compared to women who initiated ART in HIV stage 3/4 or with CD4 count <350 (Tenthani et al., 2014).

Research to date has shown that paradoxically, while Option B+ decreases the number of perinatal infections, it may also increase the number of women who refuse ART or default from care (Bhardwaj et al., 2015). Interruptions in ART can have serious consequences including viral rebound and disease progressions for individuals, and development of viral resistance at the population level (Bhardwaj et al., 2015). In Botswana, the introduction of Option B (early but not universal ART for HIV-positive pregnant women) was found to increase ART uptake but also increase the number of mother-infant pairs receiving no PMTCT intervention at all, resulting in a slights *increase* in mother-to-child transmission (Dryden-Peterson et al., 2015). In Dar es Salaam, Tanzania, a qualitative study found that while some women had positive feelings towards initiating lifelong ART under Option B+, others felt they would lose motivation to continue treatment after their child was protected from HIV infection, feared drug side-effects, and believed that they were not ready to embark on lifelong medication (Ngarina et al., 2014). Also in Dar es Salaam, the same researchers found evidence of loss of motivation to continue ART among post-partum mothers (Ngarina, Popenoe, Kilewo, Biberfeld, & Ekström, 2013). Women eligible for life-long ART showed signs of poor adherence 24 months postnatally, and reported a loss of motivation for ART adherence as well as feelings of hopelessness, a lack of empowerment, and demands of everyday life which interfered with regularly taking medication (Ngarina et al., 2013). These findings highlight the increased need to address retention in care as Options B and B+ are adopted and implemented in Africa and other settings.

# Objectives

The objective of this literature review was to review the evidence for prevention of mother to child transmission of HIV (PMTCT) in low- and middle-income countries, particularly community-based interventions which utilize community health workers, village health committees, and community-based civil society groups (such as faith based organizations and women’s groups).

The central research question addressed by this review is: *What community based interventions and approaches are most successful in preventing mother-to-child transmission of HIV and keeping HIV-positive mothers and children alive in low- and middle-income countries?*

# Methods

A search was carried out using Google Scholar and combinations of the search terms ‘PMTCT’, ‘vertical transmission’, ‘community’, and ‘effectiveness *or* evaluation *or* impact *or* result’. The reference lists of included articles, particularly reviews and meta-analyses, were also searched. Articles from January 2006 through October 2015, which presented findings from community-based interventions which addressed at least one of the steps in the PMTCT cascade (see Figure 2) *or* PMTCT prong 2 (family planning for HIV-positive women), were included. Interventions which assessed other outcomes (such as changes in knowledge regarding PMTCT) but did not assess any of the steps of the PMTCT cascade or PMTCT prong 2 were not included in the review. A few articles which addressed community-based interventions targeting outcomes such as HCT or ART adherence in non-pregnant populations were also included, due to the likely relevance of these findings from pregnant women as well as general populations.

Sources are discussed in the text, as well as presented in the a Table of Sources in the Appendix, according to the steps of the PMTCT cascade. Many interventions addressed multiple outcomes and steps in the PMTCT cascade. In these cases, the interventions are presented according to the first step in the PMTCT cascade targeted by the intervention, or in some cases, according to the main target of the intervention even if earlier steps in the PMTCT cascade were also targeted.

# Findings: Community-based PMTCT interventions

In addition to the articles reviewed in the Introduction, 39 articles reporting on community-based PMTCT interventions were included in this review. These include 16 reviews and meta-analyses (2 of them addressing family planning) and 25 peer-reviewed articles, conference presentations, and reports presenting findings from PMTCT interventions (2 of them addressing family planning). The vast majority of interventions were in sub-Saharan Africa.

One of the most widely implemented and studied applications of community health workers in supporting PMTCT is the Mothers2Mothers program, which is addressed here due to its comprehensive support of PMTCT and its implementation in multiple settings, some of which will be discussed below. Mothers2Mothers originated in South Africa (Teasdale & Besser, 2008), although it has since been implemented in a number of other African countries including Swaziland and Zimbabwe (Malqvist, 2014; Shroufi, Mafara, Saint-Sauveur, Taziwa, & Viñoles, 2013). Mentor Mothers are HIV-positive women who have recently gone through PMTCT themselves and support other mothers in PMTCT access and adherence (Teasdale & Besser, 2008). They are paid professionals (Teasdale & Besser, 2008) who serve as a link between the community and the primary health care system, referring their clients (mothers and children) to health care facilities and working with facilities to trace patients who have defaulted from care (Malqvist, 2014).

Mobile health (mHealth) is another innovative approach to supporting women across the PMTCT cascade. Only one example was identified in the literature of an mHealth program that has been fully implemented and evaluated. In 2010, the Millenium Villages Project in Sauri, Western Kenya adopted the ANC/PMTCT Adherence System, an mHealth tool which used text messages (SMS) to facilitate and coordinate CHW activities around ANC and PMTCT (Mushamiri, Luo, Iiams-Hauser, & Ben Amor, 2015). Prior to this, CHWs had been tasked with supporting pregnant women through the entire PMTCT cascade, but had struggled to provide adequate follow-up and appointment reminders, and the paper-based system used for tracking women was inefficient and prone to error. Under the new mHealth system, CHWs can use SMS to register ANC patients and report health information to a central information system. The mHealth system also provides automated alerts to instruct CHWs to visit pregnant women in their care and remind them of their upcoming ANC appointment. An evaluation of the mHealth system showed that CHWs felt it helped them to track patients more efficiently, that pregnant women felt that CHWs were consistently providing appointment reminders, and that pregnant women served by the mHealth system (HIV-positive and HIV-negative) were more likely to attend ANC visits compared to women not served by the mHealth system. A cluster RCT of the use of mobile phones for the support of PMTCT is also planned in Kenya (Jennings, Ong'ech, Simiyu, Sirengo, & Kassaye, 2013). Qualitative formative research for this trial found that women and men believed that the use of SMS could improve male involvement in PMTCT and couples’ communication, but that issues of privacy and confidentiality were critical, as couples often shared mobile phones. CHWs also believed that an mHealth platform had potential, but emphasized that contact via mobile phone should not replace in-person counseling.

## Initiation of ANC care for pregnant women

The first step in the PMTCT cascade is initiation into ANC care for pregnant women. An intervention in townships of Cape Town, South Africa, increased ANC visits as well as uptake of other PMTCT interventions. Neighborhoods were randomized to receive an intervention of home visits by CHWs (for all mothers, HIV positive and negative) in addition to standard comprehensive healthcare at clinics (le Roux et al., 2013). CHWs had been trained for one month, worked 20 hours per week, and were paid approximately USD$150 per month. They systematically visited every home in their assigned neighborhood, identified pregnant women, and made on average 6 prenatal and 5 postnatal home visits. Pregnant women entered the program at an average 26 weeks pregnancy, and only 2% of women refused participation. A large number (28) of measures of maternal and infant well-being were evaluated, although most did not show significant differences between intervention and control arms for either HIV-positive mothers or all mothers. HIV-positive mothers in the intervention arm were more likely to use one feeding method for 6 months (although not more likely to exclusively breast feed) and avoid birth-related medical complications, and their infants were more likely to receive ART prophylaxis during delivery. The intervention was not associated with greater ART initiation among mothers, attendance at 4 ANC visits, or seeking 6-week infant HIV PCR tests and being notified of results.

## HIV counseling and testing for pregnant women

HIV counseling and testing (HCT) was the step in the PMTCT cascade most frequently targeted by community-based PMTCT interventions. In urban Zimbabwe, a new policy of routine (opt-out) testing was adopted at ANC facilities, and community mobilization activities (including skits) were undertaken by community outreach counselors to increase awareness and acceptance of the new policy (Chandisarewa et al., 2007). HIV testing rates for women presenting for ANC care increased from 65% to 99.9% after the introduction of the new policy, and the proportion of women collecting their HIV results also increased, as did antiretroviral prophylaxis for HIV-positive mother and their infants (Chandisarewa et al., 2007). Women were satisfied with the counseling services, most reported that routine testing was helpful, and HIV-positive women reported low levels of spousal abuse and other adverse consequences.

In Zambia, an intervention to improve PMTCT uptake was introduced at 38 health care facilities, but also included community-based components (Torpey et al., 2010). Lay health workers were trained to conduct HIV testing and lay counselors were trained to support PMTCT services. Traditional and religious leaders were engaged to sensitize communities and increase male partner involvement. At 1-year follow-up there were significant (at p < 0.01) increases in pregnant women who had received HCT and received results (45% to 90%) and in HIV-positive women receiving a complete course of ARV prophylaxis (29% to 66%). Also in Zambia, traditional birth attendants were successfully tasked with administering rapid HIV tests to delivering mothers and nevirapine to mother-infant pairs when the mothers were HIV-positive (single-dose nevirapine to mother and syrup to the infant after birth) (Brennan et al., 2013).

In Free State, South Africa, PMTCT clinics were randomized to receive lay health workers to provide individual support to pregnant women as well as health promotion messages (Stinson et al., 2014). Over 2-year follow-up, the only PMTCT indicator which differed significantly between intervention and control arms was HIV testing at 32 weeks pregnancy among HIV-negative women.

In Kenya, JHPIEGO’s Reaching Every District (RED) approach within an integrated Maternal and Child Health Integrated Program used CHWs to increase PMTCT coverage (Kanyuuru et al., 2015). Communities were tasked with identifying and supporting volunteer CHWs, who served as links between health facilities and the community. They contacted women who missed scheduled appointments, physically traced them if necessary, and engaged partners of pregnant women (regardless of the woman’s HIV status) to encourage male involvement in prenatal care. In addition, communities support the RED program by providing a venue and other resources for monthly community outreaches which included prenatal and postnatal care, EID, HTC, family planning counseling, distribution of family planning commodities, referrals to health facilities, health education, and other services such as growth monitoring of children and immunizations.

In Malawi, the Safeguard the Family program was designed to support Option B+ and strengthen the PMTCT cascade through improvements to health facilities as well as couples’ HTC and male partner involvement and women’s psychosocial support groups (Herce et al., 2015). Over the 3-year project, significant improvements (p < 0.001 ) were seen in HTC uptake (66% to 87%), ART uptake (23% to 96%), infant nevirapine prophylaxis (1% to 100%), and early infant diagnosis via infant DNA PCR (52% to 62%).

In Nigeria, an RCT randomized churches to receive free on-site HIV testing during a church-organized baby shower (intervention arm) or standard referral to ANC care at health facilities (control arm) (Ezeanolue et al., 2015). Churches in both study arms held baby showers once per month at which women were given supplies for a health delivery (including clean razor blades, alcohol, and gloves). Women in both arms were also invited to a reception with baby gifts and refreshments after giving birth, which also allowed for follow-up of women needing post-natal care. Women in the intervention arms received health education and free laboratory tests for HIV as well as five other non-HIV health conditions at the baby shower, while women in the control arm did not. HIV-positive women were referred to a comprehensive HIV program. Women in the intervention churches were no more likely to attend ANC care than women in the control arm, but were significantly more likely to have an HIV test during pregnancy (92% vs. 55%, p < 0.0001).

## Enrollment into ART (or pre-ART care) for HIV-positive women

With the introduction of Option B+, HIV-positive pregnant women are increasingly being initiated onto ART during pregnancy, although a number of older studies pre-date these treatment guidelines. In Kinshasa, Democratic Republic of Congo, maternity facilities which were randomized to receive an HIV-positive volunteer “mother mentor” had 39% increased linkage to HIV care and treatment among pregnant women, compared to control (Edmonds et al., 2012). In Malawi, the *Tingathe*-PMTCT program used dedicated CHWS to link HIV-positive pregnant women to a complete continuum of care, and reduce loss to follow-up (Kim et al., 2012). The program provide opt-out HIV testing, CD4 testing for all newly identified HIV-positive pregnant women, ART initiation for eligible women and PMTCT prophylaxis for those ineligible by CD4 count (before Malawi had adopted Option B+), early infant diagnosis by PCR testing, contrimoxazole preventative therapy, and supplementary nutrition support. Case management was provided by CHWs, who visited women at home and followed them at health facility visits from initial HIV diagnosis until after cessation of breastfeeding and successful ART initiation for infected infants. CHWs were women and men who received 4 weeks of training, earned a small stipend of USD$2.50/day and followed up to a maximum of 50 mother-infant pairs at a time, spending 60% of their time in the community and 40% in the health facility. Impressive retention in the PMTCT cascade was seen over a 24-month evaluation: 98% of HIV-positive were screened for ART eligibility, 73% of eligible women were initiated on ART, 96% of mothers and 98% of infants received ART at delivery, and 81% of infants were tested for HIV by PCR and started cotrimoxazole. Of the 4% of infants who were HIV-positive at first PCR, 84% were enrolled at an ART clinic and 77% were initiated on ART.

Two interventions assessing linkage to care for PLHIV in the general population suggest the potential of home visits to support ART initiation. In Uganda, home visits by community support agents, in conjunction with post-test counseling by trained counselors, was successful in increasing uptake of pre-ART care among women and men newly diagnosed with HIV (Muhamadi et al., 2011). In Kenya, newly diagnosed PLHIV who received home visits by HIV-positive “peer navigators” were more likely to enroll in HIV care (Hatcher et al., 2012). Women who had disclosed their HIV status to a partner were more likely to have linked to care, while women who expected a negative response from their partner were less likely to link to care.

## ARV prophylaxis for HIV-positive mothers (if not on ART) and HIV-exposed infants directly after birth

Providing appropriate prophylactic drugs to mothers and babies at delivery is a critical step in PMTCT, and has been a component of many interventions already presented. In addition, an evaluation of the Mothers to Mothers program at three PMTCT facilities in South Africa found that nearly half of HIV-positive pregnant women had had two or more contacts with Mentor Mothers, and that postpartum women had had an average of 6 visits by Mentor Mothers. Women who participated in the Mothers to Mother program were significantly more likely to have taken nevirapine prophylaxis, as well as being more likely to use contraception, practice either exclusive infant formula feeding or exclusive breastfeeding, and have a CD4 test as part of referral to ART services (Teasdale & Besser, 2008). In rural Zimbabwe, volunteer CHWs were utilized to make home visits to women who defaulted from PMTCT programs, and were trained in offering counseling to defaulters (Vogt et al., 2015). This approach was successful in significantly increasing retention in care at the following points in the PMTCT cascade: treatment of infants with nevirapine at 3 days postpartum, cotrimoxazole initiation for infants at 6 weeks postpartum, and HIV diagnosis of infants at 6 weeks postpartum. While no significant decrease was seen in vertical HIV transmission after the introduction of CHW-based defaulter tracing, among fully retained patients, only 2% of newborns were vertically infected.

## Exclusive breastfeeding or replacement feeding for HIV-exposed infants

While many PMTCT interventions did not include a focus on breastfeeding, two interventions targeted exclusive breastfeeding for HIV-positive and HIV-negative mothers. A large trial in Malawi used peer counselors to promote exclusive breastfeeding among all pregnant women in the target communities (Lewycka et al., 2010; 2013). Two interventions were offered together or alone depending on study arm. A community mobilization intervention employed 24 local female facilitators to guide women’s groups through problem identification and prioritization, implementation, and evaluation, with meetings held monthly at village level. An infant feeding and care support intervention utilized 72 volunteer peer counselors to provide advice and support for breastfeeding, birth preparedness, newborn care, and immunization; peer counselors made 5 home visits per woman. In villages where both interventions were offered, women had five times the odds of exclusive breastfeeding, compared to control (Lewycka et al., 2013).

A cluster-randomized trial in Burkina Faso, Uganda, and South Africa also used peer counselors to promote exclusive breastfeeding among pregnant women (regardless of HIV status) who intended to breastfeed (Engebretsen et al., 2014). Pregnant women received counseling during their last trimester of pregnancy and at least 5 post-natal visits in their homes over 6 months. Peer counselors were from the same communities as beneficiaries and received one week of training. Exclusive breastfeeding was almost twice as high in the intervention arm (approximately 80% exclusive breastfeeding at 12 weeks, versus 40%, in Uganda and Burkina Faso). In South Africa no statistically significant differences were seen between intervention and control groups. The intervention was found to be highly acceptable to women, although peer counselors in South Africa were not found to have the same “community belonging” in South Africa as in Burkina Faso and Uganda.

## Early infant diagnosis for HIV-exposed infants

Médecins Sans Frontières supported a Mentor Mother / Mothers2Mothers (M2M) program in Bulawayo, Zimbabwe from 2009 to 2012 which found positive impact on early infant diagnosis (Shroufi et al., 2013). The M2M program involved health education, information on HIV/STI prevention including safer sex, birth planning, infant feeding counseling and support, and HIV adherence counseling. Mentor Mothers worked with healthcare facilities to trace patients who had defaulted from treatment, and spent an average of 6 hours per week with each client. Quantitative data showed that mothers in the M2M program were twice as likely to return for HIV testing of their infants at 6-8 weeks postpartum, compared to mothers not in M2M (99% vs. 49%, p < 0.0005). In-depth interviews with M2M beneficiaries, Mentor Mothers, and family members, and health care staff also suggested that the M2M program had been effective. M2M beneficiaries reported that participation in the program had empowered them, and that Mentor Mothers had often been able to facilitate disclosure of HIV status to male partners. Lack of disclosure to male partners was associated with lack of PMTCT and M2M participation. Mentor Mothers were felt by beneficiaries to be more approachable than health care facility staff, and health care staff reported that the M2M program increased patient retention and adherence.

Another M2M program, known as the *Mamekhaya* program, was piloted and evaluated in Cape Town, South Africa. HIV-positive women attending antenatal care were linked with a Mentor Mother (who provided services similar to those provided by Mentor Mothers in the Zimbabwe M2M program), as well as invited to attend an 8-session cognitive behavioral intervention which consisted of small group sessions led by Mentor Mothers. These sessions incorporated role plays, didactic instruction, group discussions and brainstorming, music, meditation, and goal setting. Topics covered included healthy living, ART adherence, stigma, support, domestic violence, substance abuse, partner testing and disclosure, parenting, and infant-feeding practices. Compared to women at another clinic which served as a control site, participants in the *Mamekhaya* program reported greater social support, reduced depression scores, greater improvements in positive coping, and also had higher knowledge of viral load and CD4 tests and better attendance at follow-up medical visits (Futterman et al., 2010).

## ART adherence for HIV-positive mothers and infants

Few studies have assessed ART adherence over time for HIV-positive mothers or infants. An intervention in Harare, Zimbabwe followed mother-child pairs for five years after birth to study loss to follow-up and mortality (Kurewa et al., 2011). Although the study was not primarily focused on supporting ART adherence, postpartum mothers (regardless of HIV status) were provided with support groups, health education, and trained counselors from the community who followed up after missed medical appointments. During the five-year follow-up CD4 count tests and ART became available in the country. Mortality rates were higher among HIV-positive women compared to HIV-negative women, but loss to follow-up was significantly higher among HIV-negative women (13% among HIV-negative women and 7% among HIV-positive women in the first year), suggesting that the intervention was successful in retaining HIV-positive women in care. Although this study had no control group, the study authors also noted that nevirapine uptake was higher than the national average and that retention was high compared to other African PMTCT programs, although few programs had continued follow-up for more than 2 years.

Although not specifically targeted to HIV-positive mothers and infants, an innovative trial in Uganda proved that ART could be successfully provided outside of health care facilities (Jaffar et al., 2009). Trained field officers visited PLHIV at home every month to deliver ART, monitor participants for signs and symptoms of drug toxicity or disease progression, and provide adherence support. Outcomes (including virological failure) were similar for patients offered ART through this system versus through health care facilities.

## Family planning for HIV-positive women

Despite family planning for HIV-positive women being one of the four prongs of PMTCT, most descriptions of community-based PMTCT programs do not explicitly mention provision of family planning services. An exception is the RED program in Kenya, discussed above, which provided family planning counseling and distribution of family planning commodities as part of an integrated PMTCT / MCH program (Kanyuuru et al., 2015).

# Recommendations

Rapid gains have been made in expanding PMTCT services worldwide and decreasing the vertical transmission of HIV. Yet the continuing unacceptably high rate of new HIV infections among infants demonstrates that significant barriers to PMTCT remain. The findings of this review demonstrate that significant drop-off occurs along the PMTCT cascade. Community action and community-based interventions are critical to ensuring success at every step of the PMTCT cascade and in removing family-level, social and structural barriers to PMTCT access.

Stigma and fear of disclosure of HIV status were identified by multiple studies as serious barriers to PMTCT access for HIV-positive women. While the interventions reviewed did not provide direct evidence of reduction of stigma, it is likely that in many cases reduction of stigma was a critical step in the pathway from community action and support to improved PMTCT outcomes. Many other barriers to PMTCT were also not addressed directly by any intervention reviewed, including economic and emotional stress, poor mental and physical health, and alcohol and drug usage. All of these barriers seem ripe for community-level intervention, including support from faith communities.

O hIarlaithe et al.’s (2014) framework of barriers to PMTCT suggests many gaps in current community-based interventions, as well as opportunities for practical and emotional support of women and infants in need of PMTCT services. Socioeconomic barriers include lack of transportation (or money to pay for transportation) to health care facilities, and while some interventions have addressed this barrier through bringing care to beneficiaries’ communities or homes, certainly more could be done to remove socioeconomic factors as a barrier. Community-based interventions are also well-placed to address barriers of social norms and knowledge, and to help women accept the necessity of ART even if they don’t yet feel ill (what O hIarlaithe et al. label a physiological barrier). Finally, psychological barriers such as stigma, fear, and depression are potent obstacles to care, and are much more likely to be resolved within community-based support systems than in a health facility or medical setting.

Community-based approaches might help to address all of these barriers, such as through providing solutions for transportation needs to health care facilities or bringing care to the community (socioeconomic barrier), educating communities about PMTCT or helping to create social norms supportive of women and infants accessing PMTCT (social norm and knowledge barrier), educating women about the need to initiate ART even if they are feeling healthy (physiological barrier), and helping women to overcome stigma, fear, or depression which might keep them from seeking treatment (psychological barriers).

Male partners and families are critical to women’s success in PMTCT, and much more could be done to encourage their active support of the PMTCT process. The research reviewed provided ample evidence of the impact of family support (and especially male partner support), and yielded a number of interventions which have been successful in increasing male HCT and ANC attendance. However, no models were found for interventions which addressed couple dynamics (such as lack of communication or trust) which might lead to men’s lack of support for PMTCT. Such a gap might be filled by community- or church-based interventions.

A wealth of evidence supports the effectiveness of CHWs in health promotion generally, and in supporting PMTCT specifically. Programs such as the Mothers2Mothers program have proven success in supporting HIV-positive women along the PMTCT cascade, and serving as liaisons between the community and health care facilities. The roles, responsibilities, and rewards (including salary) of CHWs varied widely between the studies reviewed, but common ground was seen in that CHWs were nearly always peers who could offer their experience and understanding to clients, and often proved that they could successfully carry out tasks (such as HCT) which have traditionally been confined to healthcare settings. Community-based, CHW-led PMTCT interventions consistently showed impact, and although a number of flat results were also seen in the studies reviewed, no adverse results were recorded. The studies presented here provide multiple examples of successful strategies for greater community engagement in PMTCT services. HCT may be the step in the PMTCT cascade most amenable to community-based support, based on the evidence of consistently strong uptake of HCT across interventions in this review. CHWs also had proven success in partnering with health facilities to support retention in care and trace patients who had defaulted from care.

With the advent of Option B+, the number of women needing support for ART adherence will only increase, as will the challenges of retaining women in care over the long-term. Thus innovative strategies for community-based support are needed more than ever. Notably, only two studies were identified which explicitly partnered with churches or religious leaders, suggesting that faith communities are a resource which remains largely untapped.

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# Appendix: Table of Sources

*Notes:* **Bold type indicates significant results.** Gray cells indicate qualitative research. The term “Africa” is used (for brevity) to refer to sub-Saharan Africa.

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| **Citation** | **Design & population** | **Outcome of interest** | **Country or region** | **Findings**  | **Notes** |
| **Meta-analyses & reviews [16]** |
| Adetokunboh & Oluwasanu 2015 | Review | PMTCT | Africa (21 countries) | Reviewed 39 studies (2011-2015) of PMTCT efforts in 21 priority countries in sub-Saharan Africa. From 2009 to 2013 there was a 42% reduction in new pediatric HIV infections and the 21 priority countries. Challenges included poor adherence to ART, poor linkage between mother-child pairs and postnatal healthcare services, low early infant diagnoses, low pediatric ART coverage, and high unmet need for contraception.  | Article gives country-specific estimates for pediatric HIV infections & maternal deaths for all 21 priority countries. |
| Bhardwaj et al. 2015 | Review | PMTCT | Africa | Reviews recent developments in implementation research across the four prongs of PMTCT. |  |
| Govindasamy et al. 2014 | Systematic review | Linkage to / retention in pre-ART care, initiation of ART for all PLHIV | LMIC | Reviewed 24 studies (2004-2013, 11 from sub-Saharan Africa) describing interventions aimed at improving linkages to or retention in pre-ART care or initiation of ART. Interventions included integration of ART and ANC care for pregnant women, making CD4 count testing and ART initiation home-based or more convenient, behavior interventions and peer support, and food support and other incentives. |  |
| Hodgson et al. 2014 | Systematic review | ART initiation, adherence, and retention for HIV+ pregnant women | Global | Reviewed 34 studies (2008-2014) addressing ART initiation, adherence, and retention among HIV+ pregnant women. Individual-level barrier included poor understanding of HIV/ART/PMTCT. Disclosure to spouse and spousal involvement in treatment were associated with improved initiation, adherence, and retention. Stigma was a major barrier. |  |

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| O hIarlaithe et al. 2014 | Review | PMTCT & maternal & newborn child health | Global | Reviewed 19 studies (6 mostly qualitative, 13 mostly qualitative) addressing barriers to PMTCT & maternal and newborn child health. Identified 4 types of barriers: socioeconomic, social norms & knowledge, physiological, and psychological.  |  |
| Ahmed et al. 2013 | Review | Early infant diagnosis  | Global | Reviews challenges of identifying HIV-infected infants and children, reviews available evidence and guidance, and describes promising strategies for case finding. |  |
| Gourlay et al. 2013 | Systematic review | Barriers to PMTCT | Africa | Reviewed 44 studies (2000-2012) addressing barriers to uptake of ART for PMTCT in sub-Saharan Africa. Key barriers to ART uptake included poor knowledge of HIV/ART/MTCT, lack of education, psychological issues, stigma and fear of disclosure of HIV status, lack of support from partners or communities, preferences for traditional healers and TBAs, and healthy system shortcomings. |  |
| Phelps et al. 2013 | Review | Barriers to linkage, initiation, and retention of children in ART  | Global  | Risk factors for LTFU among HIV+ infants and children include being orphaned, younger age, clinically advanced disease. Caregivers who perceive stigma and do not have the support of male partners are less likely to enrol HIV+ children in ART, or they may be ignorant that such treatment is available.  |  |
| Busza et al. 2012 | Review | PMTCT | Developing countries | Report commissioned by Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) which reviews community-based approaches (in developing countries, 2000 to 2011) to “overcome barriers to PMTCT enrolment, retention, and successful outcomes”.  |  |
| Ferguson et al. 2012 | Systematic review | PMTCT | Global | Reviewed 20 articles (2000-2010, 16/20 from sub-Saharan Africa). Found failure to initiate HAART among 38-88% of known-eligible women (43% in pooled analysis). |  |

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| Marcos et al. 2012 | Review | Community strategies to support PMTCT cascade | Global | Reviewed 27 studies (1990-2011) of approaches that are community-based and/or employ community-oriented groups (housed in healthcare facilities) to improve outcomes along the PMTCT cascade. 9 reported statistically significant improvements in PMTCT outcomes, with 2 occurring exclusively in the community, 4 effectively employing community groups within facilities, and 3 having both community and facility components. These interventions were found to improve knowledge of PMTCT, increase uptake of testing and prevention services, and promote better rates of disclosure and retention. The remaining 18 studies did not report statistically significant results.  |  |
| Nachega et al. 2012 | Systematic review & meta-analysis | ART adherence during pregnancy & postpartum | Global | Reviewed 51 studies (1998-2011) involving >20,000 HIV-infected pregnant women. Studies were from the Americas, Asia, and Africa, with the largest number of studies from a country being from the United States (14). In pooled analysis, 73.5% of pregnant women achieved optimal ART adherence. Adequate adherence was higher antepartum (75.7%) than postpartum (53.0%). Barriers for nonadherence included physical, economic, and emotional stress, depression (especially postpartum), alcohol or drug use, and ART pill burden. |  |
| Malarcher et al. 2011 | Review | Family planning (specifically injectable contraceptive DMPA) | Global | Reviewed 19 studies (1980-2010) of 16 studies in 9 countries of CHW delivery of the injectable contraceptive depot-medroxyprogesterone acetate (DMPA). Appropriately trained CHWs were found to be competent in screening clients, providing safe injections of DMPA, and counseling on side effects, although counseling was generally sub-optimal. Clients and CHWs reported high satisfaction with CHW delivery of DMPA, and community-based provision of DMPA increased uptake of FP. DMPA can be safely provided by appropriately trained and supervised CHWs. |  |

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| Betancourt et al. 2010 | Review | PMTCT | Global | Reviewed 14 studies (1990-2010) of “family-centered” approached to PMTCT. 7 studies addressed extending HCT to the partners of pregnant women attending ANC clinics, 2 studies focused on expending ART to partners and other family members, and 4 studies addressed PMTCT models involving family members.  |  |
| Lewin et al. 2010 | Systematic review & meta-analysis | MCH outcomes or management of infectious diseases | Global | Cochrane systematic review & meta-analysis of RCTs of interventions delivered by lay health workers (LHWs) in primary or community health care and intended to improve MCH or management of infectious diseases. Reviewed 82 studies, 55 conducted in high-income countries. Meta-analysis found evidence of effectiveness of LHWs in promoting initiation of breastfeeding (RR = 1.36, 95% CI = 1.14-1.61), any breastfeeding (RR = 1.24, 95% CI = 1.10-1.39), and exclusive breastfeeding (RR = 2.78, 95% CI = 1.74-4.44). There was “low quality” evidence that LHWs were effective in reducing child morbidity and child and neonatal mortality. |  |
| Spaulding et al. 2009 | Systematic review | FP & HIV program integration | Global | Reviewed 16 studies which integrated FP & HIV programs. 6 types of programs were identified: 1) FP services provided to HCT clients; 2) FP and HCT services provide to MCH clients; 3) FP services provided to PLHIV; 4) CHWs providing integrated FP and HIV services (2 studies); 5) HCT provided to FP clinic clients; 6) HCT and FP services provided to women receiving post-abortion care. Average study design rigor was low, and only 10/16 studies were peer-reviewed. Positive outcomes were reported, and no adverse results. Of the 2/16 studies using CHWs, one was peer-reviewed and in the time period included in this review (see Creanga et al. 2007). |  |

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| **Interventions addressing PMTCT cascade [23]** |
| **Citation** | **Design & population** | **Steps in PMTCT cascade targeted*****(see Figure 2)*** | **Country or region** | **Findings**  | **Notes** |
| Ezeanolue et al. 2015 | Cluster RCT, 3002 pregnant women at 40 churches | 1 | 2 |  |  |  |  |  | Nigeria | Healthy Beginnings Initiative: Churches were randomized to receive an intervention of health education and on-site laboratory testing implemented during church-organized baby showers (held once per month, tests offered included HIV and non-HIV conditions) vs. control group of standard referrals to health facilities. There was no difference between study arms in women attending ANC care (79% intervention vs. 80% control) but **women in the intervention group were significantly more likely to have an HIV test (92% vs. 55%, p < 0.0001).** |  |
| Herce et al. 2015 | Serial cross-sectional,  |  | 2 | 3 | 4 |  | 6 |  | Malawi | Safeguard the Family: This program was designed to support Option B+ and to strengthen the PMTCT cascade from HTC through maternal ART initiation and EID. The program included 1) health worker training and mentorship, 2) couples’ HTC and male partner involvement, 3) women’s psychosocial support groups, 4) health and laboratory system strengthening for EID. **Serial cross-sectional data showed increases over the course of the 3-year project in facility-level HTC uptake (66% to 87%), ART (23% to 96%), infant nevirapine prophylaxis (1% to 100%), and EID via infant DNA PCR (52% to 62%) (p < 0.001 for all).** |  |

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| Kanyuuru et al. 2015 | Observational, 33 health facilities + 26 community units | 1 |  |  | 4 |  | 6 |  | Kenya (Bondo District) | JHPIEGO Maternal and Child Health Integrated Program / Reaching Every District (RED): The RED approach was implemented in Bondo District, Kenya to improve PMTCT care with CHWs as the key personnel. **Routine district-level data from pre- and post- implementation showed increases (p < 0.001) in number of women completing 4 prenatal visits (25% to 41%) and proportion of HIV-exposed infants tested by 6 weeks of age (27% to 78%).** |  |
| Mushamiri et al. 2015 | Mixed-methods, health data for 800 pregnant women & qualitative interviews with 20 CHWs & 67 new mothers  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Kenya (Sauri, Western Kenya) | Pregnant women served by an mHealth system were compared to women not served by this system within the same catchment area and in other nearby areas (total n = 800). The mHealth system assisted CHWs in tracking and providing reminders to HIV+ pregnant women in their care to support PMTCT activities at every step of the PMTCT cascade. Women served by the mHealth system (HIV+ and HIV-) went for more ANC visits compared to women in the same catchment area but not served by the mHealth system (aOR = 2.58, 94% CI = 1.10-6.01). Qualitative interviews were also conducted with CHWs and with new mothers about the mHealth system, and found that CHWs felt it helped them to track patients more efficiently, that pregnant women felt that CHWs were consistently providing appointment reminders. |  |
| Vogt et al. 2015 | Retrospective cohort study, 1878 HIV+ pregnant women & their infants |  |  |  | 4 |  | 6 |  | Zimbabwe (Tsholotsho District) | Patient records of 1878 mother-infant pairs in a rural PMTCT program to assess the effects of CHW-based defaulter tracing on the following indicators: vertical transmission 6 weeks postpartum and retention in care at delivery, NVP initiation at 3 days postpartum, cotrimoxazole initiation at 6 weeks postpartum, and EID at 6 weeks postpartum. These indicators were compared before and after the introduction of the CHW-based defaulter tracing program, and **significant differences were found in retention at NVP initiation (aRR = 1.35, 95% CI = 1.28-1.42), cotrimoxazole initiation (aRR = 1.78, 95% CI = 1.58-2.01), and EID (aRR = 2.54, 95% CI = 2.20-2.93)**. Perinatal HIV transmission was not reduced (aRR = 0.72, 95% CI = 0.27-1.96) but among fully retained patients, only 2% of newborns were vertically infected. |  |

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| Engebretsen et al. 2014 | Cluster RCT, 2579 mother-infant pairs (recruited regardless of HIV status) |  |  |  |  |  | 5 |  | South Africa, Uganda, Burkina Faso  | PROMISE-EBF: Mother-infant pairs were randomized to receive intervention of exclusive breastfeeding promotion by peer counselors which included counseling during last trimester of pregnancy and at least 5 post-natal visits over 6 months. **Statistically significant differences were seen in the following behaviors (by country, non significant results not shown), intervention vs control: prelacteal feeds in Burkina Faso & Uganda (11% vs. 36% & 13% vs. 44% respectively); early initiation of breastfeeding (within first hour of life) in Uganda (55% vs. 41%); expressing and discarding of colostrum in Uganda (3% vs. 10%). No statistically significant behavior change was seen in South Africa. Exclusive breastfeeding was almost twice as high in the intervention arm (from ~40% to 80% at 12 weeks in Uganda and Burkina Faso).** The intervention was found to be highly acceptable to women.  |  |
| Stinson et al. 2014 | Cluster RCT, 32 clinics, number of participants unknown | 1 | 2 |  |  |  |  |  | South Africa (Free State) | This cluster RCT randomized 32 clinics to receive LHWs to support pregnant women individually, present health promotion messages, and assist with clinic tasks. Control clinics offered standard PMTCT services. **Over 2-year follow-up, time series analysis showed a significant increase in early ANC presentation, follow-up HIV re-testing at 32 weeks, and PMTCT coverage in both study arms. PMTCT coverage was greater in the intervention site but not significantly so (OR = 1.12, 95% CI = 0.86-1.46). HIV-negative women were more likely to retest at 32 weeks in intervention arm (OR = 1.32, 95% CI = 1.03-1.69).** | Conference presentation only available; not clear which PMTCT indicators were collected in addition to those listed.  |

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| Brennan et al. 2013 | Observational, 280 pregnant women |  | 2 |  | 4 |  |  |  | Zambia | Pilot program in rural Zambia trained traditional birth attendants (TBAs) to administer rapid HIV tests and two-dose NVP prophylaxis (tablet to mother at onset of labor and syrup to infant after delivery). **94% of women with unknown status accepted rapid HIV test and of 16 HIV+ mothers, 13 took NVP prior to birth while 16/16 infants received NVP syrup after birth**.  |  |
| Le Roux et al. 2013 | Cluster RCT, 24 clusters, >1200 mothers including 354 HIV+ mothers | 1 |  | 3 | 4 | 5 | 6 |  | South Africa (Cape Town township) | Philani Intervention Program: 24 neighborhoods were randomized to receive either intervention of home visits by CHWs (for all mothers, HIV positive and negative) plus standard care of comprehensive healthcare at clinics, or standard care only (control arm). 28 measures of maternal and infant well-being were evaluated, and significant overall benefits were found in intervention arm among HIV+ and HIV-negative mothers. **HIV+ mothers in intervention arm were more likely to use one feeding method for 6 months, avoid birth-related medical complications, and their infants were more likely to receive ART prophylaxis during delivery.** The intervention was not associated with greater ART initiation among mothers, attendance at 4 ANC visits, EBF, or infants receiving HIV PCR test (with notification of results) at 6 weeks. Among all mothers, the intervention was associated with consistent condom use, and EBF. |  |

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| Lewycka et al. 2013 & 2010 | Cluster RCT, 48 clusters with population >185,000 |  |  |  |  | 5 |  |  | Malawi (Mchinji District) | 48 clusters with total population >185,000 were randomized to one of four arms. Arm 1 was a community mobilization intervention which employed 24 local female facilitators to guide women’s groups through problem identification and prioritization, implementation, and evaluation, with meetings held monthly at village level; outcomes of interest were home care, health care seeking behaviors, and maternal & infant mortality. Arm 2 was an infant feeding and care support intervention using 72 peer counselors to provide advice and support for breastfeeding, birth preparedness, newborn care, and immunization; peer counselors made 5 home visits per woman; outcomes of interest were EBF, uptake of HIV-prevention services and infant mortality. Arm 3 had both interventions. Arm 4 had neither intervention. **An intention-to-treat analysis with 3-year follow-up showed decrease of 74% in maternal mortality and of 41% in neonatal mortality in Arm 1 but not Arm 3. In Arm 3 there was an increase in EBF (OR = 5.02, 95% CI = 2.67-9.44).**  |  |
| Shroufi et al. 2013 | Cross-sectional, mixed methods |  |  |  |  | 5 | 6 |  | Zimbabwe (Bulawayo) | Médecins Sans Frontières supported a Mentor Mother / Mothers2Mothers (M2M) program in Bulawayo from 2009 to 2012. M2M involved health education, information on HIV/STI prevention including safer sex, birth planning, infant feeding counseling and support, and HIV adherence counseling. Mentor Mothers worked with healthcare facilities to trace patients who had defaulted from treatment, and spent an average of 6 hours with each client per week. **Quantitative data showed that mothers in the M2M program were twice as likely to return for EID testing at 6-8 weeks, compared to mothers not in M2M (99% vs. 49%, p < 0.0005).** Qualitative data from 84 in-depth interviews with M2M beneficiaries, Mentor Mothers, and family members, and health care staff. M2M beneficiaries reported that it had empowered them, and that Mentor Mothers had often been able to facilitate disclosure to male partners. Lack of disclosure to male partners was associated with lack of PMTCT and M2M participation. Mentor Mothers were felt to be more approachable than health care facility staff. Health care staff reported that the M2M program increased patient retention and adherence. |  |
| Edmonds et al. 2012 | Cluster RCT, 725 HIV+ pregnant women | *Not specified* | Democratic Republic of Congo (Kinshasa) | Maternity facilities in Kinshasa were randomized to receive an HIV+ clinic volunteer (mother mentor) or to control; all sites received enhanced standard of care including PMTCT Option A. **Uptake of HIV care & treatment was greater if the referring maternity had an HIV+ volunteer (HR = 1.39, 95% CI = 1.01-1.91).** | Conference abstract only available |
| Hatcher et al. 2012 | Observational, 808 PLHIV | *Not applicable* | Kenya | Newly diagnosed PLHIV (women and men) received (with consent) a home visit from an HIV+ “peer navigator” who attempted to offer support for enrolling in HIV care. **At 10-month follow-up, HIV+ women who received this home visit were more likely to have enrolled in HIV care (aHR = 1.20, 95% CI = 1.00-1.43) as were HIV+ men (aHR = 1.24, 95% CI = 0.97-1.87).** |  |
| Kim et al. 2012 | Observations, 1688 HIV+ pregnant women |  |  | 3 | 4 |  | 6 | 7 | Malawi (Lilongwe) | *Tingathe-*PMTCT program uses CHW to create a complete continuum of care within PMTCT cascade, with aim of reducing LTFU. **Over 24-month follow-up (2009-2011), 98% of HIV+ pregnant women received a CD4 test, 93.6% received results, and 72.8% of women eligible for ART (pre-Option B+) were initiated on ART. 95.9% of mothers and 97.5% of infants received ART, and 80.7% of infants were tested for HIV by PCR and started cotrimoxazole.** 4.1% of infants were HIV+ at first PCR. Of these, 83.7% were enrolled in ART clinic and 76.7% were initiated on ART. |  |

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| Byamugisha et al. 2011 | RCT, 1060 ANC attendees | 1 |  |  |  |  |  |  | Uganda | 1060 new ANC attendees at a regional referral hospital in Mbale, Uganda were randomized to have their spouses receive an invitation letter to attend ANC (intervention) or an information leaflet about ANC (control). 16% of intervention and 14% of control group attended ANC with their partners (OR = 1.2, 95% CI = 0.8-1.6) and >90% of men who attended an ANC visit in both groups accepted HCT. Although the effect of intervention on both groups was similar, **a simple intervention (sending a letter) increased couple ANC attendance from 5% (observed pre-trial).** |  |
| Kurewa et al. 2011 | Observational, 479 HIV+ mothers with infants & 571 HIV-negative mothers with infants |  |  |  | 4 |  |  | 7 | Zimbabwe | Followed mother-child pairs from national PMTCT program for five years to study loss to follow-up and mortality. Mothers were provided with support groups, health education, and trained counselors from the community who followed up after missed medical appointments. Mortality rates were higher among HIV+ women compared to HIV-negative women, but **LTFU was significantly lower among HIV+ women (13% among HIV-negative women and 7% among HIV+ women in first year,** **p = 0.012 ) suggesting that the intervention was successful in retaining HIV+ women in care.**  |  |
| Muhamadi et al. 2011 | RCT, 400 PLHIV | *Pre-ART care* | Uganda | Newly diagnosed PLHIV (women and men) were randomized to receive an intervention of post-test counseling by staff trained in counseling skills, plus home visits by community support agents to support pre-ART care, or to receive existing standard of care in the control arm (post-test counseling by clinic staff lacking counseling skills). **At 5-month follow-up, individuals in intervention arm were significantly more likely to have been to a health center for clinical check-up (RR = 1.8, 95% CI = 1.4-2.1).** |  |

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| Futterman et al. 2010 | Quasi-experimental,  |  |  | 3 | 4 | 5 | 6 | 7 | South Africa (Cape Town) | *Mamekhaya* / Mothers2Mothers (M2M): Women participating in a M2M intervention at a Cape Town clinic were compared to women attending another ANC clinic in Cape Town. Women in both study arms were received standard PMTCT care and were assessed at baseline and at 6 months postpartum. Compared control, participants in the Mamekhaya program reported greater social support, reduced depression scores, greater improvements in positive coping, and also had higher knowledge of viral load and CD4 tests and better attendance at follow-up medical visits. Women in both arms reported high adherence to PMTCT practices (>90%). |  |
| Torpey et al. 2010 | Prospective, 38 PMTCT sites |  | 2 |  | 4 |  |  |  | Zambia | Zambia Prevention, Care, and Treatment Partnership: Interventions to improve PMTCT uptake were introduced in 38 sites providing PMTCT services. Community-based parts of the intervention included LHWs conducting HIV testing and lay counselors trained to support PMTCT services. Traditional and religious leaders were engaged to sensitize communities and increase male partner involvement. **At 1-year follow-up there were significant (at p < 0.01) increases in pregnant women who had received HCT and received results (45% to 90%) and in HIV+ women receiving a complete course of ARV prophylaxis (29% to 66%).** |  |

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| Jaffar et al. 2009 | Cluster-randomized equivalence trial, 1453 PLHIV |  |  |  |  |  |  | 7 | Uganda | 44 clusters (1453 PLHIV on ART) were randomly assigned to home-based or facility-based care. PLHIV receiving home-based care had trained field officers visit them at home every month to deliver drugs, monitor them for signs and symptoms of drug toxicity or disease progression, and provide adherence support. **At 1-year follow-up, there were no significant differences (at p < 0.05) between intervention and control in virological failure (16% vs. 17%) or mortality rates.** |  |
| Teasdale & Besser 2008 | Cross-sectional |  |  |  | 4 | 5 |  |  |  | Mothers 2 Mothers (M2M) program operated at 155 PMTCT facilities in South Africa and Lesotho by end of 2007. And evaluation at 3 facilities in 2005-2006 found that 60% of patients at those facilities had heard of M2M, and Mentor Mothers had two or more contacts with nearly half of all HIV+ women attending ANC. Postpartum women at the study sites had average 6 visits with Mentor Mothers. In bivariate analysis, **women who had participated in M2M were significantly (at p <0.05) more likely to have taken nevirapine prophylaxis, use contraception, practice either infant formula feeding or EBF, and have a CD4 test.** |  |
| Abrams et al. 2007 | Observational cohort, >12,000 individuals in care (HIV+ pregnant women & their families) | 1 |  |  |  |  |  | 7 | Africa & southeast Asia (13 sites) | MTCT-Plus: HIV+ pregnant women were invited to enroll in MTCT-Plus, a comprehensive PMTCT and HIV care program, along with their infants and other HIV+ family members. **More than 2/3 of women enrolled their HIV-exposed baby or another HIV+ family member, and retention in program was very high. 90% of infants reached 18 months, and of 761 HIV-infected children, 65% were receiving HAART.** |  |

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| Chandisarewa et al. 2007 | Observational, 4551 in ANC care |  | 2 |  | 4 |  |  |  |  | Community counselors were trained to support a new policy of routine (opt-out) HIV testing as part of ANC. **HIV testing of pregnant women increased from the 6 months before the new policy to the 6 months after (65% vs. 99.9%, p < 0.001) as did the number of HIV+ women identified antenatally (p < 0.001). More women collected their HIV test results (p < 0.001). More mother-infant pairs received ARV prophylaxis (p = 0.002).** Women were satisfied with the counseling services, most reported that routine testing was helpful, and HIV+ women reported low levels of spousal abuse and other adverse consequences. |  |
| **Family planning for HIV+ women [2]** |
| Grossman et al. 2013 | Cluster RCT, 18 clinics with >18,000 clinic encounters | Contraceptive use, pregnancy | Kenya | 12 clinics were randomized to integrate FP services into HIV clinics, while 6 clinics were controls (clients desiring FP were referred to FP clinics at the same facility). **At 1-year follow-up, usage of effective contraception methods was higher at intervention clinics (OR = 1.81, 95% CI = 1.24-2.63) while there were no significant differences seen in condom use or pregnancy between intervention and control arms.**  |  |
| Peltzer et al. 2008 | Cross-sectional,758 postnatal women (116 HIV+) | Family planning usage | South Africa | 758 women were interviewed postnatally. Most women had received counseling on safe sex during pregnancy (76% of 116 HIV+ women and 85% of HIV-negative women), but only 66% and 62% respectively had practiced safe sex during pregnancy. Postnatally, almost all women received counseling on family planning, yet use of contraceptives and condoms were low for HIV+ and HIV-negative women. Pregnancy desire was high among HIV+ women, yet lower than for HIV-negative women. |  |