Prevention of Vertical Transmission of HIV in Resource-Limited Countries

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1 Introduction – Global Status of Efforts to Prevent Vertical Transmission of HIV

Prevention of vertical (i.e., mother-to-child) transmission of HIV is essential to reduce significant HIV-related child morbidity and mortality in developing countries. Globally, pediatric infections comprise about 15% of all new HIV infections each year and virtually all pediatric infections can be prevented by eliminating vertical transmission [1]. The World Health Organization (WHO) recommendations (revised in 2006) for prevention of mother-to-child transmission (PMTCT)[1] include a four-pronged comprehensive strategy [2]. Although we acknowledge the critical role that all approaches play in reducing pediatric HIV infection, the focus of this chapter is on strategies that address the third prong: preventing HIV transmission from infected mothers to their infants. Considerable achievements have been made on this front, including many clinical trials demonstrating good efficacy. Yet after more than 10 years of global efforts to prevent vertical HIV transmission, only an estimated 18% of pregnant women in 2007 had access to services designed to interrupt vertical transmission [3].

Ministries of health and supporting partners in resource-limited settings have successfully demonstrated the ability to deliver these services and have learned important lessons about how the implementation of services can be improved. Most of the countries that have been hardest hit by HIV have developed guidelines and strategies to achieve national coverage of appropriate HIV prevention services. WHO publishes global guidance on the provision of services, which often serves as the foundation for these programs and national strategies [2]. WHO, the United Nations Children's Fund (UNICEF), and the Joint United Nations Program on HIV/AIDS (UNAIDS) estimate that in developing countries only 33% of pregnant

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[1] Since submission, the WHO has released revised PMTCT guidelines available at: http://www.who.int/hiv/pub/mtct/advice/en/index.html.

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women with HIV and only 20% of HIV-exposed infants are receiving antiretrovirals (ARVs) for prevention of vertical transmission of HIV [3]. This estimate demonstrates the generally poor coverage of services to prevent vertical transmission for pregnant women with HIV. It is also estimated that only 12% of HIV-positive pregnant women themselves eligible for antiretroviral therapy (ART) receive it [3].

2 Program Experience

The Thailand and Botswana national programs and those of the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) in several countries exemplify what can be achieved. The specific methods employed in the Foundation's programs have been described elsewhere [4, 5].

2.1 Thailand and Botswana National Programs

National programs to prevent vertical HIV transmission in Thailand and Botswana are largely organized and supported by local governments and demonstrate the potential effectiveness and feasibility of interrupting vertical transmission on a national scale with adequate resources [6, 7]. These countries are leading middle- and lower-income countries in successfully implementing national strategies that have been documented to decrease vertical transmission.

2.1.1 Thailand

Successful approaches to reduce vertical transmission have been documented in Thailand [6]. The country reports that 95% of pregnant women attend antenatal care (ANC) and 97% have access to PMTCT services. The vast majority (85%) of deliveries take place in public hospitals and 94% of pregnant women are tested for HIV. The HIV seroprevalence among pregnant women in Thailand is 1.5%, and 70% of HIV-positive women receive ARV prophylaxis to prevent vertical transmission.

The impressive results of Thailand's program from 2001 to 2003 report a total of 2,200 HIV-exposed infants registered in six provinces. There were known outcomes for 1,667: 1,509 (90.5%) were uninfected and 158 (9.5%) were infected [6]. The cohort which is non-breastfeeding was followed for a minimum of 2 years [6]. The observed vertical transmission rates by birth year were 10.3% in 2001, 9.4% in 2002, and 8.6% in 2003 [6]. These rates are reportedly 46–58% lower than before the PMTCT program was initiated, with dramatic decreases in transmission achieved through the provision of 4 weeks of zidovudine (AZT) to mothers during the antepartum period only. The program's successful service coverage and uptake resulted in a final observed transmission rate of less than 9% [6].

2.1.2 Botswana

PMTCT services have been available in every public antenatal care (ANC) clinic in Botswana since 2002. Botswana's national program provides AZT to pregnant women with HIV from 28 weeks' gestation, with single-dose nevirapine (sdNVP) given at the onset of labor for women with CD4 counts >200 cells/mm^3. Women with lower CD4 counts receive ART when eligibility is determined. Botswana also provides free replacement formula feed for HIV-exposed infants. Data from Botswana's national program were presented at the International AIDS Conference in Mexico City in 2008. Among 10,516 HIV-exposed infants who received polymerase chain reaction (PCR) testing to determine their HIV status between October 2006 and November 2007, the vertical transmission rate in mothers who received no prophylaxis was 12% whereas for mothers receiving sdNVP only, transmission was 7%, a 43% reduction [7]. Transmission was lower (0.7%) among mothers who initiated ART prior to pregnancy [7]. Those with low CD4 counts (<200 cells/mm^3) who initiated ART during pregnancy transmitted HIV to their infants at a rate (2.3%) comparable to that (3.3%) of mothers with higher CD4 counts receiving at least 4 weeks of AZT plus sdNVP [7]. Among mothers receiving less than 4 weeks of AZT, the transmission rate was approximately 5% [7].

2.2 Elizabeth Glaser Pediatric AIDS Foundation Program and Experience

The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has supported programs to prevent vertical transmission and/or to provide care and treatment in 22 countries since 2000.

Most of the countries supported are located in southern and eastern Africa, the regions of the continent with the highest HIV disease burden. Seven countries have continuing programs which no longer require EGPAF support (see Fig. 1; shown in yellow). The programs were originally focused on PMTCT but as they have rapidly grown in size and number, they have also gradually expanded to include a mix of adult and pediatric care and treatment services as well.

Over time, experience and shifts in procedure and policy have improved the uptake of services. At the same time the program has expanded, reaching almost 2 million women during 2003–2005, compared to 250,000 in 2000–2002, and in the years 2006–2008, more than 4.5 million women accessed ANC services in 18 countries. Pregnant women routinely receive HIV counseling, 85% are tested for HIV and at least 80% of HIV-positive pregnant women receive ARV prophylaxis (see Fig. 2). The greatest limitation to preventing even more infections is the level of service coverage achieved to date.

Infant uptake of ARV prophylaxis is consistently lower than maternal ARV uptake. This needs to be understood in order to improve programs further. Frequency of delivery in a facility (or by a skilled birth attendant) varies by country and region but is generally lower than ANC attendance. Infants born at home usually do not

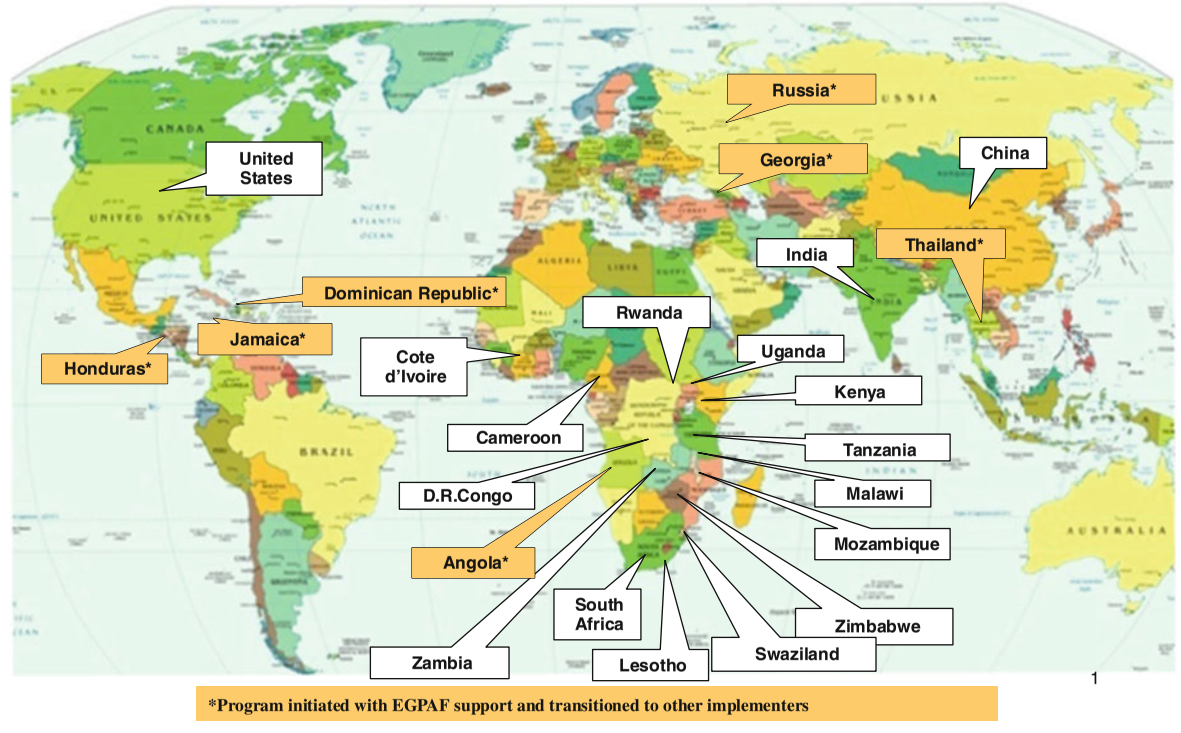

Fig. 1 The Elizabeth Glaser Pediatric AIDS Foundation Global Program Map

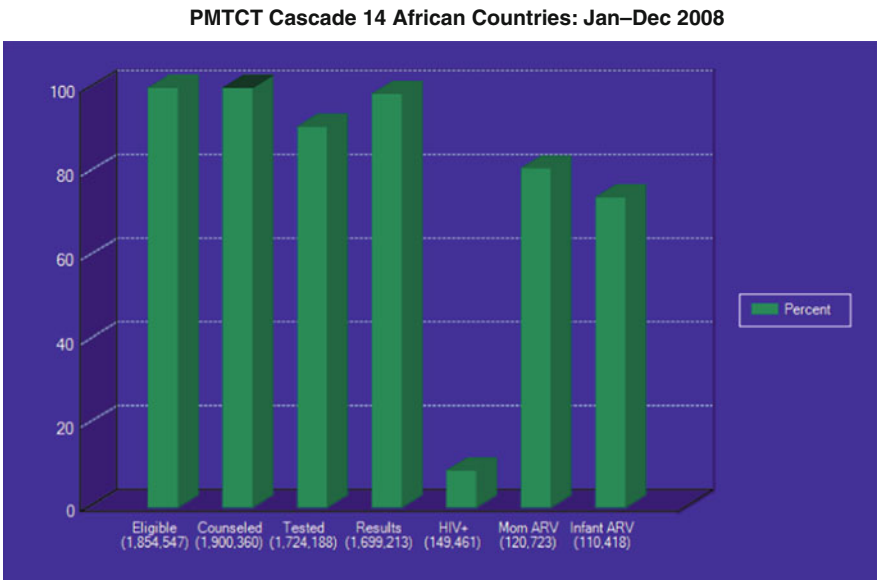

Fig. 2 The Elizabeth Glaser Pediatric AIDS Foundation Africa Program Cascade. ARV, antiretroviral; PMTCT, prevention of mother-to-child transmission. *Source*: EGPAF program data. *Calculation Footnote*: *Mother ARV = sdNVP in ANC + sdNVP in L&D + ANC ART. Infant ARV = sdNVP in ANC + sdNVP in L&D + combination regimen in L&D*

receive ARV prophylaxis. The reported percentage of deliveries taking place in EGPAF-supported health facilities has remained approximately the same over time despite the addition of PMTCT services to these facilities. One must assume that the provision of ARVs for infants is not communicated or is not perceived as sufficient incentive to deliver in a facility or that the general barriers (financial, geographic, logistic, or gender-related) which women face in accessing facilities for delivery have not yet been adequately addressed.

As of December 2008, health facility delivery rates in 17 countries in the program ranged from 28% in Rwanda to 88% in China [8] and were less than 60% in the majority of the African countries [8]. Despite effort to improve the health system infrastructure and quality of maternal and child health (MCH) services for women with HIV, the reality is that almost half of HIV-positive women will not return to deliver their infants in a health facility. Consequently, in many countries, infant ARV prophylaxis is provided in an oral syringe for the mother to take home after her initial ANC visit. Improved uptake is seen using this intervention [4] but increasingly complex combinations of drugs for both mother and infant require programs to evaluate and adapt these approaches.

In Uganda, where roughly 40% of infants are delivered in a health facility, there is roughly 45% uptake of the infant ARV dose. By contrast, in Swaziland, where

75% of infants are delivered in a health facility and where infant ARV prophylaxis is dispensed during the antenatal period, there is close to 100% uptake of the infant dose.

3 Lessons Learned

3.1 Counseling

Counseling for pregnant women initiating antenatal care has evolved from one-on-one pretest counseling toward an approach in which the majority of HIV messages are integrated into a group counseling session. This also covers other important health topics and is intended to be useful to all pregnant women, not just those living with HIV. Posttest counseling continues to be provided one-on-one and is a key opportunity to reinforce HIV prevention messages for all women regardless of their HIV serostatus. Information on exclusive breastfeeding is given to all women as well. For those who are HIV positive, counseling is tailored to provide specific information on future infant feeding choices and should be the point of initiation into longitudinal HIV care, beginning with staging and screening for treatment and enrolment into care.

3.2 Testing

An important early program change was the introduction into antenatal care of rapid HIV tests and their inclusion in national policies [4]. Providing same-day results dramatically improved the percentage of women who received their results and had the opportunity to access ARV prophylaxis and/or continued care and treatment.

Initially pregnant women were asked if they would like to receive special counseling and testing for HIV. In other words, they had to "opt in." As counseling and testing coverage remained at steady but suboptimal rates, HIV counseling and testing were integrated into routine ANC services and are provided unless women specifically refuse, or "opt out," This "provider-initiated" approach has resulted in substantial increases in the proportion of women receiving counseling and testing in ANC [5].

3.3 ARV Prophylaxis

Provision of ARV prophylaxis in the form of sdNVP to women with HIV and their infants has been the catalyst of most PMTCT services in the countries where EGPAF works. The simplicity of this regimen (one dose for the mother in labor and one dose for the infant within 72 h of delivery), and a donation program that provides NVP for free to PMTCT programs in selected resource-limited countries, has permitted

the initiation of PMTCT services in facilities with no prior ARV experience, including primary care and rural health facilities. In 2006, WHO revised its guidelines to emphasize the use of combination ARV regimens (starting AZT antepartum at 28 weeks' gestation, sdNVP plus AZT/lamivudine (3TC) intrapartum, and AZT/3TC for 7 days postpartum) for pregnant women with HIV who do not yet require ART themselves. These combination regimens have been shown to be more efficacious in preventing vertical transmission and potentially to limit development of viral resistance in the mother to non-nucleoside reverse transcriptase inhibitors (NNRTI) following sdNVP [2].

While most countries have revised their national policies to favor the use of combination regimens, many countries have been slow to roll them out owing to the need for additional training of MCH staff and logistical considerations. EGPAF is supporting ministries of health and other in-country partners to introduce the use of combination regimens at the lowest level including the most remote health centers. They can also be introduced during the initial staff training for new sites. Nevertheless, sdNVP remains an important option as PMTCT services continue to expand at a rate that exceeds the roll-out of the training and systems improvements required for complete coverage of combination regimens.

3.4 Uptake of Maternal and Infant Prophylaxis

Optimally, all pregnant women with HIV not eligible for treatment should be started on AZT during pregnancy (at 28 weeks gestation) and should receive sdNVP during labor when they come to the health facility to deliver. Improvement of maternal uptake of ARV prophylaxis has been achieved by dispensing ARVs at the time of HIV diagnosis rather than waiting for delivery. Optimally, pregnant women should receive at least four prenatal examinations. However, in most of the countries where the Foundation works less than 60% of pregnant women achieve this and the rates can be very low as, for example, in Rwanda where it is only 13% even though 94% come for one ANC visit [8]. Logically, therefore, expectant mothers should receive ARVs when they first come to the ANC clinic. While it is not guaranteed that a woman will actually take the ARVs dispensed, she must have the medication on hand in order to have access to the intervention. Dispensing ARVs at the time of diagnosis has been shown to increase the proportion of women receiving ARVs to about 90% in studies conducted in Tanzania, Cameroon, and Kenya [4]. Despite this, dispensing of ARVs at the first ANC visit is not permitted in many countries. Foundation-supported programs have seen significant improvement in ARV uptake where such policies have been changed [5]. Dispensing is more complicated for combination regimens, as women must return several times to receive longitudinal ARVs (usually AZT) for the remainder of gestation, while NVP and the initial month of AZT can be dispensed at the time of diagnosis. AZT can safely be given from 14 weeks of gestation without increasing viral resistance rates. Despite this some national policies still prohibit giving AZT prior to 28 weeks, thus denying

access to the intervention to women who do not return 12 weeks or less prior to delivery.

3.5 HIV Testing in Labor and Delivery

Ideally, the HIV serostatus of all pregnant women arriving in labor and delivery should be known. However, for a variety of reasons (e.g., not attending ANC, attending ANC that has no PMTCT services, disruption of services), the HIV serostatus of a significant number of women arriving in labor and delivery is unknown. Most, but not all, countries have changed national policies to allow routine HIV counseling and testing in labor and delivery.

Diagnosing a pregnant woman with HIV infection in labor and delivery is far from optimal, especially if combination regimens and/or ART were available to her in the ANC setting, but it still affords an important opportunity to provide ARV prophylaxis to both mother and infant to reduce the risk of vertical transmission. From when the Foundation first began collecting information on HIV testing in labor and delivery in 2005 until December 2008, of the countries that are able to report on HIV status in maternity, 8.6% of more than 4 million women in 18 countries were reported as "HIV status unknown" in labor and delivery. Of these 88.7% were then tested for HIV and 5.4% were found to be HIV positive. Such testing permits access to ARV prophylaxis to this significant group [9].

4 Modeling Service Coverage

There is a need to enhance and expand geographic coverage (i.e., access to PMTCT services by pregnant women), coverage by the provided services (enhancement of each part of the cascade of services), and coverage with therapy (the proportion of immunocompromised HIV-positive women eligible for therapy who receive it). Achieving significant progress in service coverage, which could avert the majority of the pediatric HIV infections worldwide, will require the full support of national governments as well as adequate and sustained financial resources from donors.

Table 1 illustrates the theoretical success of PMTCT programs in averting HIV infections along the steps of the basic PMTCT cascade. Using a theoretical sample of 100 HIV-positive pregnant women, the table shows the proportions utilizing ANC services, counseled, tested, and receiving ARV prophylaxis based on average uptake percentages in actual EGPAF programs for the stated time intervals. We assume for the purposes of this model that HIV-positive women who do not know their status attend ANC at the same rate as other women. Vertical transmission rates in this model have been calculated for three different scenarios of ARV prophylaxis provision and all are based on the assumption that all women with CD4 counts of <200 cells/mm^3 receive ART. Calculation #1 assumes that all HIV-positive

Table 1 Modeling of effectiveness of interventions to prevent vertical transmission: using a theoretical sample of 100 HIV-positive pregnant women

	2000–2002	Number included in program	Number missed	2003–2005	Number included in program	Number missed	2006–2008	Number included in program	Number missed
Attend ANC 1×percent	90%	90	10	90%	90	10	90%	90	10
Counseled percent	84%	75	25	93%	84	16	100%	90	10
Tested percent	80%	60	40	82%	69	31	89%	80	20
Mom ARV percent	60%	36	64	76%	52	48	82%	66	34
	Expected TR	Number infected	Overall TR		Number infected	Overall TR	Number infected		Overall TR
In absence of ARV	25%	16			12		8.5		
Calculation #1	8%	2.9	18.9%		4.1	16.1%	5.3		13.8%
Calculation #2	3%	1.1	17.1%		1.6	13.6%	2.0		10.5%
Calculation #3	2%	0.7	16.7%		1.0	13%	1.3		9.8%

Source: Barker [10].

ANC, antenatal care; ARV, antiretroviral; TR, transmission rate or total number infected (number infected with no ARV + number infected by calculation 1, 2 or 3 per 100 patients).

women with CD4 counts >200 cells/mm^3 receive sdNVP. Calculation #2 assumes that all HIV-positive women with CD4 counts >200 cells/mm^3 receive 12 weeks of AZT + sdNVP. Calculation #3 assumes that all HIV-positive women, regardless of CD4 count, receive ART. The proportion of women visiting an antenatal clinic at least once during their pregnancy is currently estimated at approximately 90% in Foundation-supported countries, with this proportion varying greatly by country [8]. According to the model, out of a theoretical sample of 100 pregnant women with HIV, 10 will not access any antenatal services.

4.1 2000–2002

Looking at the years 2000–2002 (Table 1), with counseling accessed at a rate of 84%, 75 women with HIV would have been counseled and offered testing, and 60 women (80% of 75 counseled) would have been tested, leaving 40 HIV-infected women (30 who did access antenatal care) with unknown HIV status. If ARVs were given to 60% of women known to be HIV positive, then 36 women out of the original 100 would go on to receive the prophylactic intervention and 64 would not. If there were a vertical transmission rate of 25% for all those who failed to receive ARVs, then of the 64 who missed services, 16 would transmit infection. Depending upon the ARV regimen available, vertical transmission varies from 2 to 8% among the women who receive it. An estimated overall rate of 8% of HIV-positive women receiving sdNVP or ART, depending upon their CD4 count, will transmit the virus to their infants. A combination regimen of AZT plus sdNVP lowers the transmission rate to 3%, and if ART were given to all HIV-positive pregnant women a transmission rate of 2% could be achieved [10]. Adding the instances of transmission among those not accessing the intervention together with transmission instances among those who received the intervention results in overall transmission rates of 16.7–18.9%. Note that this model does not take into account late postpartum transmission from breastfeeding. This model demonstrates that the ARV regimen used has less of an impact on transmission than do increases in the number of women attending ANC and in improvements in uptake of counseling, testing, and delivery of ARVs to all those who come in for services.

4.2 2003–2005

In 2003–2005, ARV prophylaxis was dispensed to approximately half the women eligible to receive it. Of the 48 women who would have missed services according to the model, an estimated 12 mothers would have transmitted HIV to their infants. From 1.0 to 4.1 infants are estimated to become HIV infected among mothers receiving ARV for prophylaxis or therapy, depending upon the ARV regimen. The overall effectiveness of the ARV intervention is calculated with a transmission rate of 13.0–16.1% (see Table 1).

4.3 2006–2008

In 2006–2008 (Table 1), significant improvements were seen in the uptake of services. However, with 10% of all HIV-positive pregnant women not receiving antenatal care, 10% of those counseled not being tested, and 18% of those known to be HIV positive not receiving ARVs, there were 34 out of 100 HIV-positive women who missed the benefit of services. The overall vertical transmission rates were lower for this time period, calculated at 9.8–13.8%, depending upon the ARV regimen used. Again it is noted that successful delivery of services is more influential than the specific regimen used to prevent transmission. Combination regimens are more efficacious, but even with ART administered to every pregnant woman identified as HIV positive (Scenario #3), the model shows that overall transmission rates of less than 9.8% cannot be achieved due to current gaps in service delivery.

5 Effectiveness of Prevention of Vertical Transmission Programs: The PEARL Study

Global goals to reduce vertical transmission are ambitious and appropriate in their scope, yet a lack of clarity and consensus regarding how to monitor the effectiveness of PMTCT programs makes it difficult for policymakers to mount a coordinated response [11]. Some have advocated for the use of population-level "HIV-free child survival" as a gold standard metric to measure the effectiveness of PMTCT programs [11]. A recent CDC-supported study, "PMTCT Effectiveness in Africa: Research and Linkages to Care and Treatment," or "PEARL," measured PMTCT program effectiveness in nonclinical trial settings in Cameroon, Côte d'Ivoire, South Africa, and Zambia [12]. All 43 health centers included in the study offered ongoing PMTCT services that provided a minimum of sdNVP and, in some cases, combination prophylaxis regimens or ART. The study design and assessment of program effectiveness are partially described in a published report preceding the study results [11]. A novel community-survey-based approach was adopted in the hope that it could be implemented widely in developing countries, with only minor modifications required to the existing demographic and health surveys [11].

The study also obtained umbilical cord blood specimens from 28,061 women in delivery to determine their HIV status and to measure the presence of NVP [12, 13]. This method provided a means to document whether dispensed prophylaxis was actually taken [12].

The study documented pervasive gaps in service delivery in representative urban and rural clinics in four countries [12]. Failures were observed at each step of the PMTCT cascade: health facilities failed to test women, provide test results, and dispense NVP and mothers failed to ingest the prophylaxis they were given (see Fig. 3). Service coverage (defined as including dispensing of maternal and infant prophylaxis) across the facilities in four countries was found to be only 50% [12].

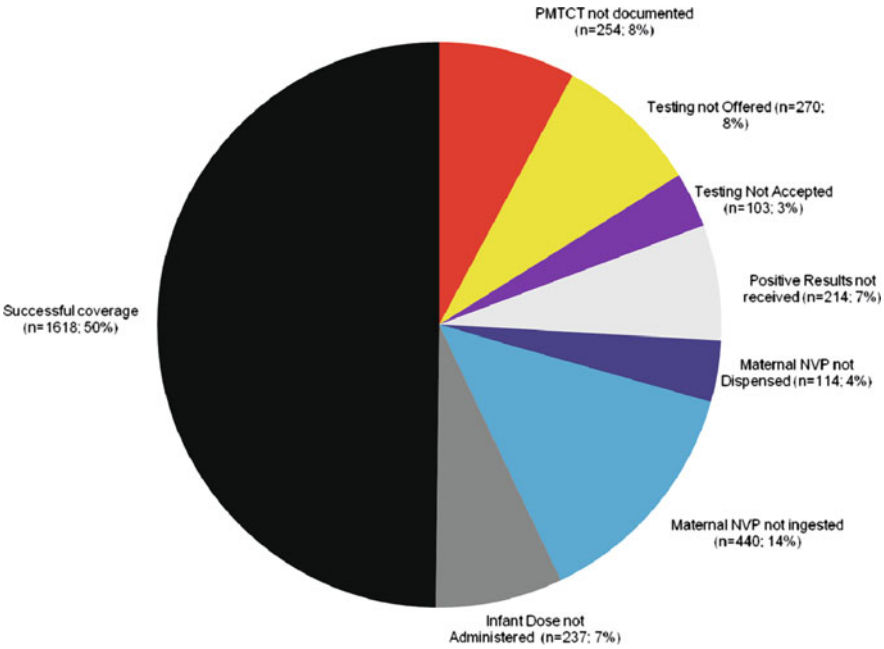

Fig. 3 Results of the PEARL study. PMTCT, prevention of mother-to-child transmission; NVP, nevirapine. *Source*: Stringer [12]

In addition to the functional problems described, women not actually ingesting the ARVs represents an additional barrier that needs to be addressed.

6 Importance of Identifying Pregnant Women Eligible for ART

A crucial element in the effort to enhance the overall impact of PMTCT services is to identify pregnant women with HIV who are eligible to receive ART. It is estimated that over 80% of cases of vertical transmission and the same proportion of maternal deaths occur among women with CD4 counts <350 cells/mm^3 [14]. It is likely that as many as 30–50% of women diagnosed with HIV infection in ANC have CD4 counts <350 cells/mm^3 [15]. Treatment of these women could therefore dramatically decrease vertical transmission rates while maintaining maternal health. However, identifying women most in need of treatment remains a challenge, as most ANC sites in resource-limited settings do not have the tools (e.g., CD4 testing, viral load testing) to monitor disease stage.

Ideally, ART eligibility is ascertained at the time of HIV diagnosis through staging performed in ANC and/or by obtaining a CD4 count. Clinical staging is difficult and particularly insensitive during pregnancy, and point-of-service CD4 testing is often unavailable at lower-level clinics. If CD4 testing cannot be performed at the facilities, blood samples must be sent to a central testing facility, and it can take

several days to several weeks for results to be returned to the original clinic. This requires one or more additional ANC visits by the pregnant woman, depending on how long it takes to obtain the test results. Additionally, if the ANC clinic cannot initiate ART, the mother must be referred, and these additional visits and actions required by the woman are critical barriers to her accessing appropriate care. Such logistical barriers are partially responsible for the low proportion of women who are actually screened and staged and eventually enrolled into care or initiated on ART.

Because ANC and other HIV-related services are often provided by different units or facilities that lack common patient information systems to track individual women, following women with HIV identified in ANC and reporting the numbers subsequently enrolled into care and those started on treatment has proven difficult (see Fig. 4). When sites do report these data, it is evident that too few women are receiving ART. At Foundation-supported sites, a very small percentage of HIV-positive women are reported to receive combination therapy (see Fig. 5). This is consistent with UNICEF reports and highlights the need for care providers to focus on improving the identification and treatment of pregnant women eligible for ART.

To improve the identification and initiation of treatment of eligible women on ART, many countries are now moving to integrate ART services into the MCH units [16–18]. For example, in Swaziland, a pregnant woman initiates treatment in MCH and is followed there postpartum until her child is 2 years old, at which point she is then referred to the regular ART clinic. This requires adequate staff in the busy MCH settings who are trained to undertake WHO clinical staging and/or have a process for drawing, tracking, and sending blood samples for CD4 count and are able to interpret results and initiate treatment. Experience has shown that training is not enough, and MCH staff need continued mentoring to provide good quality services [19].

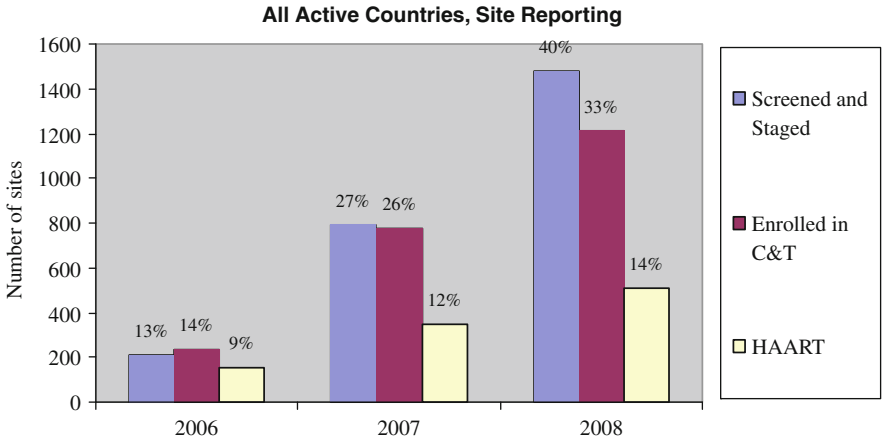

Fig. 4 All active EGPAF country programs, site reporting. *Note*: % refers to proportion of total PMTCT sites. C&T, counseling and testing; HAART, highly active antiretroviral therapy; PMTCT, prevention of mother-to-child transmission. *Source*: EGPAF program data

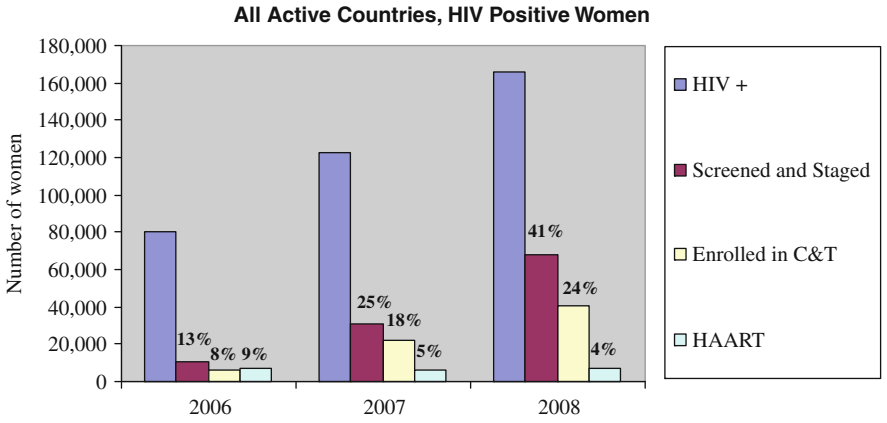

Fig. 5 All active EGPAF country programs, HIV-positive women. *Note*: % refers to proportion of HIV-positive women. C&T, counseling and testing; HAART, highly active antiretroviral therapy. *Source*: EGPAF program data

7 Prevention of Vertical Transmission During Breastfeeding

The finding that HIV can be transmitted from a mother to her infant during breastfeeding has created major dilemmas in resource-limited settings, with an estimated 40% of vertical transmission attributed to breastfeeding in these settings [20]. Improving *HIV-free survival* of infants and children is the ultimate goal of all programs aimed at preventing vertical HIV transmission, yet it has been repeatedly shown that replacement feeding in these settings carries a significant risk of morbidity and mortality for HIV-exposed infants [21, 22]. Improving HIV-free survival of infants must be accomplished while achieving optimal breastfeeding practices. Exclusive breastfeeding for the first 6 months and continued breastfeeding up to 11 months is the single most effective preventive child-survival intervention for all infants [23]. Therefore, HIV-exposed infants should be afforded the same health benefits of exclusive breastfeeding for the first 6 months of life as all other infants.

In the context of HIV, it is imperative that optimal infant and young child feeding practices be ensured. The possibility of reducing postnatal HIV transmission by providing ARVs to the lactating mother or the breastfeeding child has been studied extensively in recent years. It has also been shown that early weaning is not safe in most resource-limited settings. In the PEPI study in Malawi, prolonged ARV prophylaxis administered to the infant was found to reduce postnatal HIV infection significantly [24]. However, early weaning was encouraged, and two-thirds of mothers had stopped breastfeeding after only 9 months postdelivery. Observational data suggest that ART administered to mothers during lactation can reduce transmission of HIV to the infant; additionally, women who require ART for their own health should receive therapy regardless of the vertical transmission prevention benefits. There is a current debate regarding whether mothers with higher CD4 counts should also receive ART during lactation. The recently concluded BAN study in Malawi

demonstrated that both maternal ART and infant NVP administered for 28 weeks were safe and effective in reducing postnatal vertical transmission [25]. The study was not large enough to compare the efficacy of the two regimens. Despite these findings, programs have not yet begun to administer postpartum NVP to infants or ART to mothers routinely regardless of maternal CD4 count, as the feasibility of these interventions still needs to be established.

Based on recent findings, WHO recommends exclusive breastfeeding for the first 6 months of an infant's life and weaning at about 1 year of age [26]. In settings and individual instances in which mothers can safely manage replacement feeding according to the AFASS (acceptable, feasible, affordable, sustainable, and safe) criteria, replacement feeding or early weaning is suggested.

8 Conclusion

Prevention of vertical HIV transmission is of critical importance, yet developing functional programs to deliver badly needed services is a complex undertaking. Low- and middle-income countries, especially those hardest hit by HIV, need to prioritize these services while dedicating appropriate resources to initiate and build sustainable programs. Eliminating pediatric HIV infection is possible, but careful attention must be paid to research establishing the efficacy of various interventions and barriers to their implementation while outlining solutions to guide program implementation.

Access to prevention programs must be expanded for all pregnant women to improve service coverage for women with HIV. Service providers must work hard to optimize each step of the PMTCT cascade in order to improve coverage and thereby achieve optimal outcomes. Focusing on identification and enrollment of women with HIV who are eligible for ART is essential for maternal health and to decrease vertical transmission maximally among this higher-risk group. To achieve significant increases in the HIV-free survival of infants, breastfeeding practices must be optimized, along with ARV regimens shown to be effective in decreasing transmission during the breastfeeding period.

The evolution of the Foundation's PMTCT programs has taught us some important lessons about how these programs can be optimized, but the numerous challenges described indicate that much work remains. However, experience from national programs in Thailand and Botswana shows that it is possible to achieve low transmission rates.

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