

Barriers and Facilitators to Combined ART Initiation in Pregnant Women With HIV: Lessons Learnt From a PMTCT B+ Pilot Program in Swaziland

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Background: In January 2013, Swaziland launched a prevention of mother-to-child transmission of HIV (PMTCT) B+ implementation study in rural Shiselweni. We aimed to identify patient and health service determinants of combined antiretroviral therapy (ART) initiation to help guide national implementation of PMTCT B+.

Methods: This prospective cohort study uses routine data from registers and patient files in the PMTCT B+ pilot zone and a neighboring health zone where PMTCT A was the standard of care. All HIV-positive women not on combined ART at the first antenatal care visit between January 28, 2013 and December 31, 2013 were included.

Results: 399 women from the PMTCT B+ zone and 183 from the PMTCT A zone are included. The overall proportion of women who had not started an antiretroviral intervention before 32 weeks' gestation was lower in the PMTCT A zone (13% vs 25%, $P = 0.003$), yet a higher proportion women with CD4 <350 initiated combined ART in the PMTCT B+ zone (86% vs 74%, $P = 0.032$). Within the PMTCT B+ pilot, initiation rates were highly variable between health facilities; while at patient level, ART initiation was significantly higher among women with CD4 <350 compared with CD4 >350 (80% vs 59%, $P < 0.001$). Among women with CD4 <350, those recorded as newly diagnosed were more likely to initiate combined ART. Although lower educational level and

occupational barriers seemed to hinder combined ART initiation among women with CD4 >350, high proportions of missing socio-demographic data made it impossible to make any firm conclusions to this respect.

Conclusions: This study not only demonstrates challenges in initiating pregnant women on ART, but also identifies opportunities offered by PMTCT B+ for improving treatment initiation among women with lower CD4 counts.

Key Words: PMTCT, antiretroviral therapy, pregnancy, prevention

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INTRODUCTION

The use of antiretroviral drugs for prevention of mother-to-child transmission of HIV (PMTCT) is a well-established element of HIV programming; several studies have shown that mono or combined therapy is effective in protecting the infant from HIV transmission from the mother; reported transmission rates at 6 months after delivery without PMTCT range from 25% to 40%, compared with rates of 1%–8% in PMTCT programs.^{1–3} Since 2010, most countries have implemented 1 of 2 approaches recommended by the World Health Organization (WHO). See Figure S1 (Supplemental Digital Content, <http://links.lww.com/QAI/A628>) for a brief description of these approaches.

In April 2012, the WHO released a programmatic update that defined a new approach to PMTCT (PMTCT B+), whereby lifelong combined antiretroviral therapy (ART) is offered to all pregnant and breastfeeding women with HIV, irrespective of CD4 count or WHO Clinical Stage.⁴ This approach is thought to offer a number of advantages: it is operationally simpler (the same treatment for everyone, no delay when CD4 testing absent); reduced risk of mortality and disease progression (HIV-related and Hepatitis B) associated with treatment interruptions; reduced risk of mother-to-fetus transmission in the next pregnancy from the moment of conception; and reduced risk of transmission to a seronegative partner.^{4,5} Furthermore, it may be beneficial to the health of the mother in the light of emerging evidence on reduced mortality among mothers treated with lifelong ART at CD4 counts above 350.^{6,7}

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Swaziland has a robust PMTCT programme based on the PMTCT Option A approach. Although antenatal HIV prevalence is amongst the highest in the world (37% in 2012),⁸ over 80% of HIV+ pregnant women receive antiretroviral prophylaxis (zidovudine) or combined ART.⁸ Mother-to-child transmission is low at 6 weeks postpartum (2%–3%), although cumulative mother-to-child transmission rates at 18 months remain high at 12%–15%.⁹ Challenges of adherence to nevirapine for the long breastfeeding period (17 months on average), has been suggested as a possible cause.⁹ An additional challenge for HIV care for pregnant women in Swaziland was highlighted in the 2012 Annual PMTCT report from 2012, showing that approximately half of the HIV+ pregnant women eligible for lifelong combined ART according to the national guidelines (CD4 <350 or WHO stages III/IV) were treated with prophylactic therapy only.¹⁰ Failure to initiate lifelong ART puts these women at increased risk of HIV/AIDS-related morbidity and mortality; therefore, there is significant national interest in whether PMTCT B+ can help improve initiation rates among this population. Developing appropriate health messages around PMTCT B+ is particularly challenging, because previous messages declared that if one's CD4 count was greater than 350, they did not need antiretroviral treatment. In Swaziland, zidovudine is often presented to the patient as not being an ART.¹¹ Whether women who were not previously eligible for treatment will initiate combined ART, and what factors influence initiation of combined ART, are important questions for health programmers.

In January 2013, Médecins sans Frontières (MSF), in collaboration with the Swaziland National AIDS Programme, implemented PMTCT B+ in 1 health zone in the Shiselweni region as a pilot program. In light of the pilot and the WHO guidance recommending PMTCT B+ in settings with high prevalence and high birth rate, the Ministry of Health in Swaziland will roll out PMTCT B+ as national strategy in 2014.¹² This article reports on the early implementation experience of PMTCT B+ in Swaziland, drawing lessons learnt that can guide implementation of this approach nationally, and elsewhere.

METHODS

Design

A prospective cohort study of women found to be HIV-positive (newly diagnosed or known HIV+ status but not already on treatment) at the first antenatal care (ANC), in a health zone implementing PMTCT B+ and a neighboring health zone where PMTCT A is the standard of care.

Setting

Swaziland is a landlocked lower–middle-income country in Southern Africa, with a population of 1.2 million and an HIV prevalence among 18- to 49-year-olds of 31%.¹³ This study is carried out in Shiselweni region, which constitutes 25% of the geographical area of the country and has a relatively poor and rurally located population of 210,000.

Every year, approximately 2000 HIV+ pregnant women access ANC in the region.⁸ Nearly all health care facilities offering ANC in the region are equipped with point-of-care CD4 technology (Alere PimaTM, Waltham, Massachusetts, USA).

In January 2013, PMTCT B+ was introduced as a pilot program in Nhlengano, 1 of 3 health zones in Shiselweni. This study uses routine data from ANC records in all facilities providing PMTCT B+ in Nhlengano zone and all facilities providing PMTCT A in the neighboring health zone of Hlathikhulu (9 facilities per health zone). Prophylactic therapy (zidovudine for the mother, nevirapine for the baby) was offered to women refusing combined ART in the PMTCT B+ zone. At the start of the pilot study, same-day initiation of combined ART was not encouraged. However, after 3 months, it was noted that median time to ART initiation was well over the 1-week target, and a decision was made to adapt the standard operating procedures (SOPs) in favour of same-day initiation for women who were ready. Details of the PMTCT B+ implementation process in Shiselweni and copies of the adapted SOPs are available online (see Information S1 & S2, Supplemental Digital Content, <http://links.lww.com/QAI/A628>).

Participants and Data Collection

Between January 28, 2013 (the start of the pilot study) and December 31, 2013, all women presenting for their first ANC within the study zone who tested HIV+ for the first time, or who already knew their HIV+ status but were not yet on combined ART, were included in the study. Women who were diagnosed HIV+ at subsequent ANC visits by repeat testing were eligible for combined ART within the PMTCT B+ pilot zone but were not included in this study. For the study participants, routine data were collected from the eighteen health structures. Baseline characteristics (the first ANC visit date, maternal age, gestational age at first ANC, CD4 count, WHO clinical stage, and combined ART/zidovudine initiation date) were obtained from ANC registers by MSF data clerks. For women who initiated combined ART, time to ART initiation was calculated as the difference between combined ART initiation date and first ANC date. Women who initiated ART before 32 weeks' gestation were considered to have successfully initiated (for the purposes of PMTCT); for women whose first ANC consultation was 32 weeks or later, initiation was considered successful if it took place within 7 days (the national target for ART initiation in PMTCT programmes). Combined ART initiation was validated with the ART article register, and patient files were retrieved to obtain data on marital status, occupation, educational level, and disclosure status.

Data Analysis

We compared the proportion of eligible patients initiating combined ART in the 2 health zones and the proportion initiating amongst patients with CD4 <350 or WHO Stage III/IV disease. Within the PMTCT B+ zone, we compared characteristics of those who initiated combined ART and those who did not, including a variable indicating

whether the patient attended the first ANC before or after the SOPs were switched in favour of same-day initiation. Pearson χ^2 test was used to test for association between categorical variables, and a nonparametric K-sample median test was used for continuous variables with asymmetrical distributions. In the comparison of ART initiation before and after the implementation of same-day initiation, data from a facility where staff problems led to significant changes in combined ART use during the latter period were excluded to reduce the chance of bias. Socio-demographic characteristics were not available for all patients because of incomplete and inconsistent data recording at facility level. Statistical tests in Tables 1 and 2 are reported excluding missing values.

We also explored the barriers and facilitators to ART initiation in the PMTCT B+ zone using unconditional logistic regression. Adjusted odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated using an unconditional multivariable regression model developed in a stepwise backward manner. Variables that were associated with uptake in univariable analysis with a $P < 0.10$ were considered for

inclusion in the model. Educational level, occupation, marital status, and disclosure status were excluded from multivariable analysis because of the high proportion missing socio-demographic information. Because of effect modification, separate models were evaluated for women with CD4 <350 and women with CD4 >350 . Models were controlled for clustering by health facility. Data entry was carried out using Epidata 3.1, and data analysis used Stata/SE 12 (StataCorp, College Station, TX).

Ethics

Ethical approval for this study was granted by the Scientific and Ethics Committee of the Ministry of Health of Swaziland, and the International Ethics Review Board instituted by MSF. Informed consent for study participation was not solicited from participants, and only routinely collected data were used.

RESULTS

Comparison PMTCT B+ and PMTCT A Health Zones

Five hundred eighty-two women were included in the analysis: 399 (69%) from the PMTCT B+ health zone and 183 (31%) from the PMTCT A health zone. Baseline characteristics of the women are shown in Table 1. Their median age was 25 years [interquartile range (IQR), 22–29 years], the median CD4 was 411 (IQR, 288–558), and the median gestational age at first ANC was 21 weeks (IQR, 17–25). More than half of the women were recorded as newly diagnosed HIV-positive at first ANC consultation. The proportion of newly diagnosed individuals and the proportion of women with CD4 <350 cells per milliliter were higher in PMTCT B+ zone compared with the A zone (64% vs 54%, $P = 0.020$; and 37% vs 29%, $P = 0.033$, respectively). In terms of PMTCT, the proportion of women who had not started any form of antiretroviral intervention (either zidovudine or combined ART) before 32 weeks' gestation was higher in the PMTCT B+ zone, where 98 (25%) women had not initiated combined ART or zidovudine, compared with 23 (13%) in the PMTCT A zone ($P = 0.003$). Amongst the subgroup of women with CD4 counts below 350 cells per milliliter, combined ART initiation was higher in the PMTCT B+ zone [128 (86%) compared with 39 (74%) in the PMTCT A zone ($P = 0.032$)]. The median time to combined ART initiation was 7 days (IQR, 0–28 days) in both zones.

ART Initiation in the PMTCT B+ Zone

The level of combined ART initiation varied significantly between facilities ranging from 38% to 89% ($P = 0.003$, Table 2). Median time to combined ART initiation in the PMTCT B+ zone was 8 days (IQR, 5–31) before implementation of same-day initiation and 0 days (IQR, 1–14 days) ($P < 0.001$) afterward. Although the proportion of pregnant women initiating combined ART did improve slightly with each quarter (Table 2), the overall

TABLE 1. Baseline Characteristics and ART Uptake Among HIV women at First ANC in Nhlanguano and Hlathikhulu Zones, Shiselweni, Jan–Dec 2013

	Nhlanguano Health Zone (PMTCT B+) (N = 399)	Hlathikhulu Health Zone (PMTCT A) (N = 183)	<i>P</i> *
HIV status			
knowledge, N (%)†			
Known status	143 (36)	84 (46)	0.020
Newly diagnosed	254 (64)	98 (54)	
Median age, yrs (IQR)	25 (22–30)	25 (22–29)	0.809
Median Gestational age, wks (IQR)	21 (17–26)	22 (17–26)	0.314
CD4 count, N (%)			
<350	148 (37)	53 (29)	0.033
≥350	201 (50)	110 (60)	
Missing CD4 information	50 (13)	20 (11)	
MTCT prophylaxis, N (%)			
On combined ART at 32 wks' gestation	252 (63)	43 (23)	<0.001
On zidovudine at 32 wks' gestation	49 (12)	117 (64)	
Not on combined ART or zidovudine at 32 wks' gestation	98 (25)	23 (13)	
ART uptake‡ among women CD4 <350, N (%)			
Initiated combined ART	128 (86)	39 (74)	0.032

**P* values shown are from Pearson χ^2 test, except for age, which was from a nonparametric K-sample median test.

†Three individuals had missing information on HIV status knowledge: 2 in the PMTCT B+ zone and 1 in the PMTCT A zone.

‡Uptake of combined ART at any gestational age.

TABLE 2. Clinical and Socio-demographic Characteristics Influencing ART Initiation for PMTCT B+ According to CD4 Count at First ANC Consultation

	Total (N = 399)		CD4 <350 (N = 148)		CD4 ≥350 (N = 201)		CD4 Missing (N = 50)	
	ART Uptake, N (%) [*]	P [†]	ART Uptake, N (%) [*]	P [†]	ART Uptake, N (%) [*]	P [†]	ART Uptake, N (%) [*]	P [†]
Overall	252 (63)		118 (80)		119 (59)		15 (33)	
HIV status knowledge [‡]								
Known status	96 (67)	0.226	48 (87)	0.074	39 (58)	0.792	9 (43)	0.091
Newly diagnosed	155 (61)		69 (75)		80 (60)		6 (21)	
Date of first ANC								
Q1 2013	53 (59)	0.452	23 (77)	0.912	28 (58)	0.425	2 (17)	0.423
Q2 2013	79 (60)		34 (79)		38 (52)		7 (44)	
Q3 2013	78 (67)		44 (80)		31 (63)		3 (23)	
Q4 2013	42 (69)		17 (85)		22 (69)		3 (33)	
Facility								
1	10 (66)	0.003	5 (71)	0.020	4 (57)	0.350	1 (100)	0.559
2	16 (89)		9 (100)		7 (88)		—	
3	8 (38)		2 (40)		6 (40)		0 (0)	
4	22 (73)		10 (91)		12 (67)		0 (0)	
5	16 (67)		7 (88)		8 (62)		1 (33)	
6	122 (69)		61 (85)		58 (62)		3 (25)	
7	23 (59)		7 (88)		11 (69)		5 (33)	
8	23 (44)		14 (67)		6 (35)		3 (21)	
9	12 (55)		3 (43)		7 (58)		2 (67)	
Educational status [§]								
Less than Secondary	90 (70)	0.061	49 (83)	0.454	35 (58)	0.018	6 (67)	0.858
Secondary completed	42 (84)		18 (90)		19 (86)		5 (62)	
Occupation [§]								
Unemployed	86 (83)	0.019	37 (90)	0.319	46 (84)	<0.001	3 (38)	0.027
In paid employment	47 (68)		24 (77)		17 (53)		6 (100)	
Self-employed	8 (89)		5 (100)		3 (100)		0 (0)	
Housewife	3 (42)		3 (75)		0 (0)		0 (0)	
Marital status [§]								
Married	50 (83)	0.115	23 (85)	0.989	23 (82)	0.083	4 (80)	0.457
Single	117 (73)		58 (85)		51 (65)		8 (62)	
Disclosure Status [§]								
Disclosed to family	89 (82)	0.037	40 (93)	0.011	44 (77)	0.111	5 (63)	0.248
Undisclosed to family	41 (68)		19 (70)		15 (60)		7 (88)	

^{*}The percentages shown here are the proportion of women who initiated ART in each subgroup (row percentage). Although the denominator is not shown in this table, it can be deduced, eg, the number of women with a known status 0.63 * 96 = 143 (for total column, the information is also available in Table 1).

[†]P values shown are from Pearson χ^2 test except for age, which was from a nonparametric K-sample median test.

[‡]Two individuals had missing information on HIV status knowledge: one had CD4 <350 and initiated ART, and the other had CD4 >350 and did not initiate ART.

[§]Socio-demographic details were missing for a high proportion of patients: education (n = 221, 55%), employment (n = 226, 57%), marital status (n = 179, 45%), and disclosure status (n = 232, 58%).

initiation rates remained below the programme target of 80%. The proportion of women initiating combined ART was higher after implementation of same-day initiation and revision of clinical SOPs (60% before, vs 70% after the intervention, $P = 0.045$). Initiation rates were significantly lower among women with higher CD4 counts (59% of women with CD4 >350 initiated combined ART before 32 weeks compared with 80% of women with CD4 <350, $P < 0.001$, OR adjusted for clustering by health facility = 0.37, 95% CI: 0.26 to 0.52). Age did not seem to be associated with initiating combined ART; the median age of the women who started combined ART was 25 (IQR, 22–30) years compared with 24 (IQR, 23–29) years in those who did not start combined ART ($P = 0.494$). The impact of other

patient-level barriers and facilitators of combined ART initiation seemed to be different among the 2 CD4 groups and are described separately in Table 2.

Barriers and Facilitators of ART Initiation Among Women With CD4 >350 in the PMTCT B+ Zone

A large proportion of the women with CD4 >350 had missing information for educational level, occupation, marital status, and disclosure status (119, 59%; 108, 54%; 93, 46%; and 120, 60%, respectively) preventing analysis of the impact of these factors on combined ART initiation with a high degree of validity. However, we observed that among women with

available socio-demographic information and CD4 >350, uptake was significantly higher among women with at least secondary education completed, compared with women with less than secondary education (86% vs 58%, $P = 0.018$, Table 2). Furthermore, women in paid employment had lower initiation rates than those who were unemployed (53% vs 83% respectively, $P < 0.001$).

Barriers and Facilitators of ART Initiation Among Women With CD4 <350 in the PMTCT B+ Zone

There were also high levels of missing socio-demographic information for women with lower CD4 counts (education: 69, 46%; occupation: 67, 45%; marital status: 53, 36%; and disclosure status: 77, 52%). However, in contrast to women with high CD4 counts, among the women with available socio-demographic data, the impact of education, employment, or marital status seemed to be minimal (Table 2). In this group, a higher proportion of women who had disclosed their status to their family initiated ART compared with those who had not disclosed (93% vs 70%, $P = 0.011$). Furthermore, women who knew their HIV+ status before attending their first ANC seemed more likely to start ART for PMTCT compared with women who were newly diagnosed at the ANC appointment, but this did not reach statistical significance (87% vs 75%, $P = 0.074$).

Missing Data

Socio-demographic information (education, employment, and marital status) and disclosure status were obtained from patient files. Two hundred sixty-two (66%) of the women in the study had missing socio-demographic information, and these women were less likely to have started combined ART compared with those with socio-demographic information available (OR, 0.4; 95% CI: 0.2 to 0.6). Furthermore, the disclosure status was not noted for 232 (37%) of the women; similarly, these women were less likely to have started ART compared with those with a disclosure status recorded (OR, 0.3; 95% CI: 0.2 to 0.5).

DISCUSSION

We observed higher rates of initiation of combined ART among pregnant women with CD4 <350 cells per milliliter in the PMTCT B+ setting, relative to a comparable setting where PMTCT A was the standard of care. Because the majority of HIV/AIDS-related morbidity and mortality in pregnancy and the postnatal period occurs in the CD4 <350 group, these findings demonstrate the potential of PMTCT B+ to reduce HIV-related mortality and morbidity.¹⁴ However, it was also noted that fewer women in the PMTCT B+ zone received an antiretroviral treatment before 32 weeks' gestation than those in the PMTCT A zone, which could result in an increased risk of vertical transmission during pregnancy and delivery. Although initiating antiretroviral treatment is no guarantee of adherence, effectiveness of PMTCT B+ must start with

high levels of combined ART uptake. Attention must be paid to reinforcing counseling around benefits of combined ART for PMTCT, and ongoing training and support of health workers is needed to ensure that high rates of initiation are maintained during the transition from PMTCT A to PMTCT B+.

The rate of combined ART initiation in the context of the PMTCT B+ pilot program was below 80%, mainly because of lower initiation rates among women with high CD4 counts. However, the levels of ART uptake varied remarkably between different facilities regardless of the CD4 group. Given that this was a new pilot program, it is likely that the level of understanding and acceptance of this new approach varied between facilities, which could explain the varying results observed. This would be expected to improve with time. Although health system barriers have been perceived as barriers for ART initiation for PMTCT in other studies,¹⁵ it should be noted that these findings differ significantly from implementation experiences in Malawi, where much higher rates of ART initiation were described during PMTCT B+ roll-out.¹⁶ This difference in itself suggests that key determinants of combined ART initiation are health system-related. In Malawi, PMTCT B+ was implemented on a nationwide basis; sensitization and mobilization process was led by the Ministry of Health, using all available communication media. By contrast in Swaziland, mass media could not be used to communicate about PMTCT B+, because PMTCT A is still a national strategy. Furthermore, the ongoing availability of prophylactic treatment with zidovudine in Swaziland enables health workers and patients who are skeptical of combined ART to use this "lighter option," often perceived in Swaziland as not being an ART at all.¹¹

It is also important to note that, unlike Malawi, ANC facilities in Shiselweni have point-of-care CD4 testing such that CD4 results are available within 20 minutes of testing. Although not required for combined ART initiation for PMTCT B+, availability of CD4 results may impact both the nurses' and the patients' behavior, given that CD4 level has previously been presented as the principal criterion for ART initiation. Low levels of ART initiation among women with high CD4 counts could reflect the focus of health workers on initiating ART in patients with low CD4 counts, known to be most in need of treatment, in accordance with previous training they have received. Moreover, it could reflect the patients' sense that they are still well and thus can wait to start combined ART, in line with messages previously transmitted by health workers.¹¹

The same-day ART initiation seemed to be an important contributor to the successful introduction of PMTCT B+ in the study zone. Discussions with individual patients (who did and did not initiate combined ART) revealed that many were open to initiate combined ART the same day but were told by the health worker to go back home and think about it.¹¹ However, attention must be paid to treatment education and support when introducing same-day initiation to ensure that attrition rates remain acceptable. Recent findings from Malawi suggest that pregnant women testing HIV-positive and starting ART on the same day are particularly at risk of attrition.¹⁷

The implementation approach and health facility–related factors were the principal but not the sole determinants of ART initiation. Although high levels of missing data made the analysis of the influence of some patient-level factors extremely challenging, it did seem that they varied according to whether the patient’s CD4 level was below or above the threshold for combined ART eligibility (350 cells/mL), used nationally in Swaziland. In those with CD4 counts below 350, nondisclosure of HIV status to family could be a potential barrier to initiation, which has been described in other studies in general HIV+ populations.^{18,19} We also observed higher rates of ART initiation among women with lower CD4 counts who knew they were HIV-positive before coming to ANC. It is possible that the message from previous visits about the need to start ART when the CD4 count was below 350 facilitated combined ART initiation among these women, whereas newly diagnosed women may have needed more time to come to terms with their diagnosis and thus may not have been ready to initiate ART promptly. Interpreting the differences in combined ART uptake according to education, occupation, and marital status is difficult because a large proportion of missing data may have introduced bias into the study. However, among women with available socio-demographic data and higher CD4 counts, initiation rates were the lowest amongst women of a lower education level, which could suggest a barrier in the understanding of the information given during counseling. Similarly, among those with high CD4s and available socio-economic information, initiation rates were lower for women in paid employment (mostly factory workers) compared with unemployed people. This could reflect strict working conditions and a low level of workplace autonomy making it difficult for these women to attend appointments. In light of difficulties interpreting data with a high proportion of missing data, it is worth noting that the observations made here are in line with other studies describing status knowledge, nondisclosure, educational and occupational barriers to ART initiation and adherence.^{20,21}

This study included consecutively recruited women attending ANC facilities in 2 health zones in rural Swaziland. There was an imbalance in the study population such that the intervention zone had more than double the sample size of the comparison zone. Although we recognise that the reduced sample size in the PMTCT A zone reduces the statistical power of the comparisons shown in Table 1, we believe that the impact on our results was minimal. This study was carried out using data available from routine clinical registers and patient files. Approximately 10% of the participants had missing information on CD4 count. This was in part caused by unreliable access to a functioning PIMA machine in 2 of the facilities (1 in each zone) but may also have been due to poor record-keeping in some facilities. We had a higher volume of missing socio-economic information, and because of differences in recording and filing for pre-ART patients in some facilities, these data were less likely to be available for women who did not initiate ART. Hence, missing data were not equally distributed among those initiating and those not initiating ART. This could introduce bias to the study and limit the internal validity of the findings. We might expect those who have complete records to be different from those

with incomplete records (eg, women with complete records may have better access to health care, may be more educated, or may face less work-related barriers). Given these limitations, we urge readers to interpret any of the associations regarding disclosure, educational status, occupation, and marital status with the utmost caution. The issue of missing data highlights the challenge of evaluating programmes using routine data sources, especially in low-resource settings, where a high level of decentralization and task shifting makes detailed comprehensive monitoring and evaluation challenging. Comprehensive recording and data quality should be an important operational concern for national programmes that wish to roll out PMTCT B+.

In conclusion, implementing PMTCT B+ where PMTCT A remains national strategy is challenging but feasible. This study not only demonstrates barriers to initiating pregnant women on combined ART, but also identifies opportunities offered by PMTCT B+ for improving initiation rates among women with lower CD4 counts. Overall, the uptake of combined ART during the first year of Swaziland’s PMTCT B+ pilot was suboptimal, mainly because of poorer initiation rates among women with higher CD4s. The predominant barriers to ART initiation seem to be health service–related, but efforts may still be needed to overcome occupational barriers faced by some women and to ensure that messages about benefits of early ART initiation reach women with lower educational level. Offering same-day initiation for pregnant women who are ready to do so seems to be vital to ensure optimal rates (and timeliness) of ART initiation. These findings will help guide nationwide implementation of PMTCT B+ in Swaziland in 2014 and can be useful for similar, high-prevalence low-resource settings making a switch to PMTCT B+.

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REFERENCES

1. Siegfried N, van der Merwe L, Brocklehurst P, et al. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. *Cochrane Database Syst Rev*. 2011;CD003510.
2. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med*. 1994;331:1173–1180.
3. The Petra Study Team. Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa, and Uganda (Petra study): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2002;359:1178–1186.

4. WHO. *Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants*. WHO, ed. Geneva, Switzerland; 2012.
5. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365:493–505.
6. Hargrove JW, Humphrey JH. Mortality among HIV-positive postpartum women with high CD4 cell counts in Zimbabwe. *AIDS*. 2010;24:F11–F14. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20095074>. Accessed March 16, 2014.
7. Schouten EJ, Jahn A, Midiani D, et al. Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals: time for a public health approach. *Lancet*. 2011;378:282–284.
8. Strategic information Department, Swaziland Ministry of Health. *PMTCT Programme Annual Report 2012*. Mbabane, Swaziland; 2013.
9. Mthethwa N. Swaziland paediatric HIV program overview. Paper presented at: National Paediatric HIV Stakeholders Conference; Mbabane, August 6, 2013.
10. Strategic information Department, Swaziland Ministry of Health. *PMTCT Programme Annual Report 2011*. Mbabane, Swaziland; 2012.
11. Kourline T. Initiation sous traitement antirétroviral des femmes enceintes et allaitantes: Le rôle du personnel soignant et des partenaires. Expérience d'une étude pilote PTME B+ au Swaziland. Poster presented at: AfraVIII; 2014; Montpellier, France.
12. WHO. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection*. World Health Organisation, Geneva, 2013.
13. Swaziland Ministry of Health. *Swaziland HIV Incidence Measurement Survey (SHIMS). First Findings Report*. Mbabane, Swaziland; 2012.
14. WHO. *Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach*. World Health Organisation, Geneva, 2010.
15. Gourlay A, Birdthistle I, Mburu G, et al. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. *J Int AIDS Soc*. 2013;16:1–21.
16. Ministry of Health, Government of Malawi. *Integrated HIV Program Report July–September 2012*. 2012.
17. Tenthani L, Haas AD, Tweya H, et al. Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women ('Option B+') in Malawi. *AIDS*. 2014;28:589–598.
18. Abaynew Y, Deribew A, Deribe K. Factors associated with late presentation to HIV/AIDS care in South Wollo Zone Ethiopia: a case-control study. *AIDS Res Ther*. 2011;8:8.
19. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. *AIDS*. 2012;26:2059–2067.
20. Peltzer K, Pengpid S. Socioeconomic factors in adherence to HIV therapy in low- and middle-income countries. *J Health Popul Nutr*. 2013; 31:150–170.
21. Cherutich P, Kaiser R, Galbraith J, et al. Lack of knowledge of HIV status a major barrier to HIV prevention, care and treatment efforts in Kenya: results from a nationally representative study. *PLoS One*. 2012;7:e36797.