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ORIGINAL PAPER

Maternal Motivation to Take Preventive Therapy in Antepartum and Postpartum Among HIV-Positive Pregnant Women in South Africa: A Choice Experiment

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Abstract

HIV-positive pregnant women who are initiated on lifelong antiretroviral therapy (ART) and isoniazid preventive therapy (IPT) have lower adherence rates after delivery. We quantified maternal motivation to take preventive therapy before and after delivery among pregnant women newly diagnosed with HIV. We enrolled pregnant women (≥ 18 years) with a recent HIV diagnosis (< 6 months) at 14 public primary health clinics in Matlosana, South Africa and followed them in the postpartum period. Participants received eight choice tasks comparing two mutually exclusive sub-sets of seven possible benefits related to preventive therapy identified through literature reviews and key informant interviews. Data was analyzed using conditional logit regression in the antepartum versus postpartum periods. Coefficients are reported with 95% confidence intervals (CI). Sixty-five women completed surveys both at enrollment and in the postpartum period. All women were already on ART, while 21 (32%) were receiving IPT at enrollment. The mean CD4 count was 436 (± 246) cells/mm^3. In the antepartum period, preventing HIV transmission to partners was the most important benefit (coefficients (ß) = 0.87, 95% CI 0.64, 1.11), followed by keeping healthy for family (ß = 0.75, 95% CI 0.52, 0.97). Such prioritization significantly decreased in the postpartum period ($p < 0.001$). Compared to other motivators, keeping a high CD4 count was least prioritized in the antepartum period (ß = 0.19, 95% CI − 0.04, 0.43) but was most prioritized in the postpartum period (ß = 0.39, 95% CI 0.21, 0.57). These results highlight that messages on family might be particularly salient in the antepartum period, and keeping CD4 count high in the postpartum period. Understanding maternal motivation may help to design targeted health promotion messages to HIV-positive women around the time of delivery.

Keywords Discrete choice experiment · Isoniazid preventive therapy · Antiretroviral therapy · Pregnant women · South Africa

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Introduction

The World Health Organization set the ambitious target goals of eliminating HIV transmission from mother to child and reducing maternal deaths related to HIV by 2015 [1]. There has been dramatic improvement globally, but 100,000 infants were still infected with HIV, and 20% of pregnant women living with HIV did not receive antiretroviral therapy (ART) in 2015 [2]. It is during antenatal care (ANC) visits that many women first learn that they are infected with HIV and/or tuberculosis (TB). About 37% of women who attended ANC in South Africa were HIV-positive and of these, 23% reported one or more symptom of TB in 2011 [3]. The prevalence of TB in HIV-positive pregnant women is similar to that of the general population, but they might be at aare at an estimated tenfold increased risk of active TB compared to HIV-uninfected pregnant women [4] or men of similar age in sub-Saharan Africa [5].

The South African national guidelines for preventing mother-to-child transmission (PMTCT) recommend that all pregnant and breastfeeding HIV-positive women are initiated on lifelong ART, regardless of CD4 cell counts [6]. If latently infected with TB, up to 36 months of isoniazid preventive therapy (IPT) up to 36 months is recommended. ART not only prevents vertical HIV transmission but also achieves better long-term maternal health outcomes, and IPT can reduce the risk of a patient developing TB by up to 60% among people living with HIV (PLWH) [6–8].

Despite the clear benefit of preventive therapy and freely available drugs at clinics, implementation of these guidelines remains challenging. Many pregnant women are often at an earlier stage of HIV disease without clinical symptoms so they are less likely to be motivated to take ART once they have protected their babies from infection [9]. Recent studies in South Africa showed that up to half of women who initiated ART during pregnancy were lost to follow-up 6 months after delivery [10]. Adherence rates to ART and IPT also significantly drop in the postpartum [11, 12]. In a meta-analysis among sub-Sharan African studies, the proportion of women with adequate adherence for ART (> 80%) reduced from 76% in the antepartum to 53% during the postpartum period [13]. Another study in Lesotho showed that 78.5% of HIV-positive women initiated IPT but only 65% of these women completed the 6-month IPT [14]. Counseling and support systems could be important drivers to retain these women in care after delivery [15–17], but it remains unclear what benefits related to preventive therapy motivate HIV-positive women to take therapies before and after delivery.

Conjoint analysis has been increasingly used as a tool to elicit patients' preferences, allowing them to make choices from sets of hypothetical alternatives, where each alternative is described by several characteristics (i.e. attributes) [18, 19]. We used conjoint analysis to quantitatively measure the relative importance of potential motivators to take preventive therapy among pregnant women with HIV in order to better understand the low uptake of preventive therapy in the postpartum period, and ensure better adherence and retention in care in the long-term.

Methods

Study Participants

This study was conducted in 14 primary care public health clinics in the Dr. Kenneth Kaunda health district in the North West province, South Africa from November 2014 to December 2016. These 14 clinics were selected to utilize the existing study structure of an ongoing cluster randomized trial and enroll a similar population. This trial compares the proportion with known TB infection status and IPT initiation among newly diagnosed HIV patients in clinics using two different diagnostic tests for latent TB infection [20, 21]. Clinics were chosen to cover a range of patient volumes, urban vs rural settings, geographical regions and clinic hours. Patients were eligible for enrollment if they were ≥ 18 years old, newly diagnosed with HIV in the preceding 6 months, currently pregnant and able to demonstrate reading in either English, Xhosa, Setswana or Zulu. We sought to enroll all eligible pregnant women coming to antenatal care services during the study period. All participants gave written informed consent. The study was approved by the institutional review boards at the Johns Hopkins School of Medicine and the University of Witwatersrand.

Study Design

We conducted a longitudinal survey using a conjoint analysis to elicit pregnant mothers' motivation for IPT and ART. Conjoint analysis has been applied to measuring preferences for a wide range of health applications, including HIV prevention [22, 23] and delivery services among women in rural settings [24]. The advantage of conjoint analysis is that it allows us to quantify the degree of preferences (i.e. preference weights) associated with different attributes. One-onto-one in-depth interviews were conducted with 28 HIV-positive patients, 1 female and 1male from each of the 14 participating clinics to elicit patients' perspectives about IPT and ART as part of the parent study [21, 25]. Based on the qualitative interviews with patients and providers, literature review and expert consultations, we determined seven possible benefits of preventive therapy that could matter the most to patients.

We focused on examining positive benefits to inform health promotion messages that could be directly incorporated directly into counseling, clinical consultation and interventions such as SMS text messages [21, 25]. Table 1 shows the seven possible benefits of preventive therapy with example quotes from the qualitative interviews: (1) Keeps me healthy for my family (2) keeps me from giving HIV to my partner (3) keeps my HIV disease under control (4) keeps my CD4 high (5) prevents me from getting sick from infections (6) keeps me healthy and working (7) prevents me from getting TB. These benefits were not selected to be mutually exclusive and may represent similar constructs (i.e. keeping healthy), but we included a specific key term or concept related to perceived benefits of preventive therapy which seemed to be well accepted by patients. For example, previous studies showed that providing CD4 counts results at the time of HIV diagnosis increased the likelihood of ART initiation [26, 27], while counseling messages focusing on a healthy and productive life with ART helped to reduce HIV-related stigma [28]. Also, the concept of preventing TB or other infections may resonate better with patients, compared to keeping them generally healthy.

All conjoint tasks were forced choices (i.e. respondent could not opt out or choose neither option). An example of conjoint tasks is shown in Fig. 1. We used a fractional factorial experiment with an orthogonal main effect design to limit the number of choice tasks required to be answered by respondents out of all 2^7 possible combinations of the seven benefits. Orthogonal main effect design is a simple, statistically efficient and valid design commonly used for discrete choice experiments, and allows for the to estimation ofe coefficients for main effects, assuming that two or higher-level interactions among factors are negligible [29]. The experiment was also balanced such that each benefit and a pair of benefits appeared an equal number of times across eight choice tasks per respondent [30]. Each respondent was asked the same eight choice tasks both at enrollment and the 14 weeks postpartum visit. We pilot-tested the instrument with healthcare providers to refine potential wording and presentation of the instrument.

Table 1 List of seven potential motivations for taking preventive therapy

Motivator	Example quotes*
Keeps me from giving HIV to my partner	"[The doctor] tell me… Start your treatment for HIV because HIV positive is dangerous danger. If you sleep with someone without condom, you're HIV-positive infected that one."
Keeps me healthy and working	"[W]e've got something to help us to keep going."
Keeps me healthy for my family	"This is my life, this one. I want to live for the children. I want to grew up this children." "I have to do this for myself and my children, my kids. I'm still raising them"
Keeps my CD4 high	"I see that it is for my life, I must take it because I see that maybe when I started the treatment that time, maybe my CD4 count will be that, the way it was. But now it goes down, maybe it is because I'm not taking the treatment." "So if I take [ARVs] again for the CD4 count, maybe it will be good then, it will be good"
Keeps my HIV disease under control	"It's good because I want to stay in my life. I want to stay in my life because this ARV is my life." "My [immune] system is so low so that's why I'm taking the ARV."
Prevents me from getting sick from infections	"Yes, it makes me feel good. That infection must not come near to me. They must prevent it before." "I think to prevent it before you are infected is better that way."
Prevents me from getting TB	"I will take it, to prevent the TB, I will take it. Use it." "So I want to prevent TB it's much better. It's better than to get sitting at home and do nothing."

*All quotes were extracted from the qualitative interviews with 28 patients newly diagnosed with HIV in the same 14 clinics

We asked some people with HIV to describe the reasons why they drink medications to prevent disease. In each question, I will show you what two people said, and ask you which person's statements BEST describe the way YOU think about why to take preventive medications.

Person 1:	**Person 2:**
Keeps my CD4 high Keeps my HIV disease under control Keeps me healthy for my family Prevents me from getting TB	Keeps me healthy and working Prevents me from getting sick from infections Keeps me from giving HIV to my partner
□ I am more like this person	□ I am more like this person

Fig. 1 Example of a conjoint analysis task with seven motivators to take preventive therapy among HIV-positive pregnant women

There is no standardized way to calculate sample size required for discrete choice experiments although there are is some published guidances [31, 32]. According to de Bekker-Grob et al. (2015), the a minimum sample size of 57 is required to estimate a parameter of 0.3 or above for our study design at a power of 80% and a 5% significance level when analyzed using multinomial logit.

Statistical Analysis

The data was were analyzed using the a conditional logit model to estimate relative utility (i.e. preference weight) of each potential benefit to take preventive therapy in the antepartum versus postpartum [33–35]. The primary outcome was the choice between two sets of motivators in each given choice task, while the independent variables were a set of seven potential benefits presented in each task. The conditional logit model assumes that all respondents have the same underlying preferences and thate random errors associated with choices are independent and identically distributed (IID) and independent of irrelevant alternatives (IIA). We fitted two separate conditional logit models for each of the antepartum and postpartum periods. An additional model was fitted where both antepartum and postpartum visits and the interaction terms between each benefit and timing of visits were included in one a single model.

We tested two hypotheses: first, whether each of the seven identified benefits are considered as an important motivator for taking preventive therapy among HIV-positive pregnant mothers (i.e. utility associated with the benefit is statistically significant and greater than zero) and second, whether this importance differs in the antepartum versus postpartum periods. Coefficients (referred to as preference weights) are presented with 95% confidence intervals and clustered standard errors to adjust for correlation within individuals. Coefficients can be interpreted to represent patients' utility associated with each benefit (i.e. a higher coefficient means higher utility or value associated with that benefit). The p values for the interaction terms between each benefit and the timing of visits were calculated from the Wald tests to test the statistical difference of the coefficients in the ante- versus postpartum periods. P values < 0.05 were considered significant. All analysis was performed in STATA 13.0.

Results

Participant Characteristics

A total of 72 people pregnant women newly diagnosed with HIV were enrolled and completed the questionnaire. Sixty-five women completed surveys at both baseline and follow-up visit (Table 2). At baseline, the median age was 27 years [Interquartile range (IQR):22–31 years], with average time since initial HIV diagnosis of 51(±75) days. The mean gestational week at enrollment was 18 (±7) weeks. All women were already on ART, and the median CD4 count was 404 (IQR: 228–609) cells/mm^3 and about 30% (n = 19) were on IPT. All participants reported currently having a partner or spouse, but 60% (n = 38) were not living with partners, and 85% (n = 55) were not employed.

AtIn the postpartum visits, > 95% all (n = 65) reported that they were still taking ART. Of 65 infants, 1 (1.5%) was confirmed as HIV-positive, 47 (72.3%) were HIV-negative, 4 (6.2%) had indeterminate status, and 13 (20.0%) did not receive PCR tests. Over 90% (n = 61) of participants had ever breastfed their infants, and 67% (n = 41) were still breastfeeding. While 51.5% (n = 33) reported that they received some or a lot of support from friends and family to remind them to take medications, 95.2% (n = 60) reported receiving such support from healthcare providers ($p < 0.001$). Almost everyone (62/65) on ART reported that they were informed about the side effects and reasons to take ART, while 85.7% (12/14) of patients on IPT did so ($p < 0.001$).

Preference Weights in Antepartum Versus Postpartum Period

Preference weights for each of the seven attributes are shown in Table 3. In the antepartum period, pPreventing HIV transmission had the highest coefficient (β = 0.87, 95% CI 0.64, 1.11), followed by keeping healthy for family (β = 0.75, 95% CI 0.52, 0.97), in the antepartum period where positive coefficients represent positive preferences for the motivators. Keeping CD4 high had the lowest coefficient (β = 0.19, 95% CI -0.04, 0.43) (Fig. 2). When the coefficients of the motivators were compared, preventing HIV transmission to a partner had approximately 4.5 times higher utility than keeping CD4 high, and two times higher utility than benefits focused on individual health. Keeping healthy and working and, preventing oneself from getting sick from infections or TB were moderately ranked.

In the postpartum period, the preference weight for keeping CD4 high was the highest (β = 0.41, 95% CI 0.23, 0.59), and associated with more than twice the utility compared to preventing HIV transmission and keeping healthy for family. The preference weights for preventing HIV transmission (β = 0.18, 95% CI 0.00, 0.35) and keeping healthy for family (β = 0.06, 95% CI − 0.12, 0.24) were reduced and no longer significant. Keeping disease under control (β = 0.24, 95% CI 0.06, 0.42) and preventing oneself from getting TB (β = 0.24, 95% CI 0.03, 0.39) were moderately ranked and statistically significant. Compared to the antepartum period, tThe preference weights significantly reduced for preventing HIV transmission ($p < 0.01$) and keeping healthy for family

Table 2 Baseline characteristics among 65 HIV-positive pregnant women who completed the survey, South Africa

	N = 65
Age (years), Median (Q1, Q3)	27 (22, 31)
Time since HIV diagnosis (days), Mean (± SD)	55 ± 51
Gestational weeks, Mean (± SD)	18 ± 7
CD4 cell count (cells/mm^3), Median (Q1, Q3)*	404 (228, 609)
	n (%)
Marital status	
Married	6 (9.4)
Living with partner	20 (31.3)
Not living with partner	38 (59.4)
Employment status	
I work full time	5 (7.7)
I work part time or piece jobs	5 (7.7)
I am not employed	55 (84.6)
Number of adults living in the household	
0–1	24 (36.9)
2+	41 (63.1)
Number of children living in the household	
0–1	55 (84.6)
2+	10 (15.4)
Transportation	
On foot	36 (55.4)
Public taxi or bus	29 (44.6)
TB treatment history	
Yes	4 (6.2)
No	61 (93.8)
Currently on isoniazid preventive therapy	
Yes	19 (29.2)
No	46 (70.8)
Currently on cotrimoxazole preventive therapy	
Yes	4 (6.4)
No	61 (93.6)

Pearson χ^2 test (discrete variables), *t* test (mean comparison for continuous variables) and Mann–Whitney test (median comparison for continuous variables) were used

*Data was available for 48 participants

($p < 0.01$) in the postpartum as well as keeping disease under control ($p = 0.01$) in the postpartum period.

Discussion

Pregnant women newly diagnosed with HIV face the "triple burden" of accepting that they are pregnant, newly diagnosed with HIV, and the need to make the decision to initiate lifelong treatment [36]. We demonstrate that pregnant women initiated on lifelong ART prioritize benefits related to preventive therapy differently in the antepartum versus postpartum periods. We found that HIV-positive pregnant women were most attentive to medication benefits related to social responsibility such as preventing HIV transmission to partners or supporting family during pregnancy. The extent of such prioritization was subdued in the postpartum and keeping high CD4 counts and medication benefits related to their own health were more prioritized. These results provide important insights to help develop and strengthen health promotion messages to pregnant women with HIV around the time of delivery.

This is one of the first studies to quantify relative utility of ART and IPT as perceived by women initiated on lifelong therapy during pregnancy. We observed that the relative utility related to preventing HIV transmission or supporting family was much higher in the antepartum period. Every participant in this study was tested for HIV and received

Table 3 Coefficients from conditional logistic regression among 65 HIV-positive women in the antepartum versus postpartum periods

Benefits related to preventive therapy	Antepartum		Postpartum		p value[†]
	Coefficient (SE)	95% CI	Coefficient (SE)	95% CI	
Preventing HIV transmission	0.87 (0.14)**	(0.59, 1.15)	0.20 (0.09)*	(0.03, 0.38)	< 0.01
Keeping healthy and working	0.41 (0.11)**	(0.19, 0.63)	0.10 (0.09)	(−0.07, 0.27)	0.02
Keeping healthy for family	0.75 (0.15)**	(0.45, 1.04)	0.05 (0.08)	(−0.09, 0.20)	< 0.01
Keeping CD4 high	0.19 (0.10)	(−0.01, 0.40)	0.41 (0.10)**	(0.22, 0.59)	0.13
Keeping disease under control	0.67 (0.11)**	(0.46, 0.87)	0.24 (0.10)*	(0.04, 0.44)	0.01
Preventing infections	0.40 (0.12)**	(0.16, 0.64)	0.03 (0.10)	(−0.16, 0.22)	0.02
Preventing TB	0.44 (0.11)**	(0.23, 0.66)	0.21 (0.08)**	(0.05, 0.38)	0.10

*P values from Wald tests are reported: p value < 0.05

**p-value < 0.01

[†]P-values were estimated from the model where both antepartum and postpartum visits and the interaction terms between each benefit and timing of visits (postpartum vs. antepartum) were fitted in one model

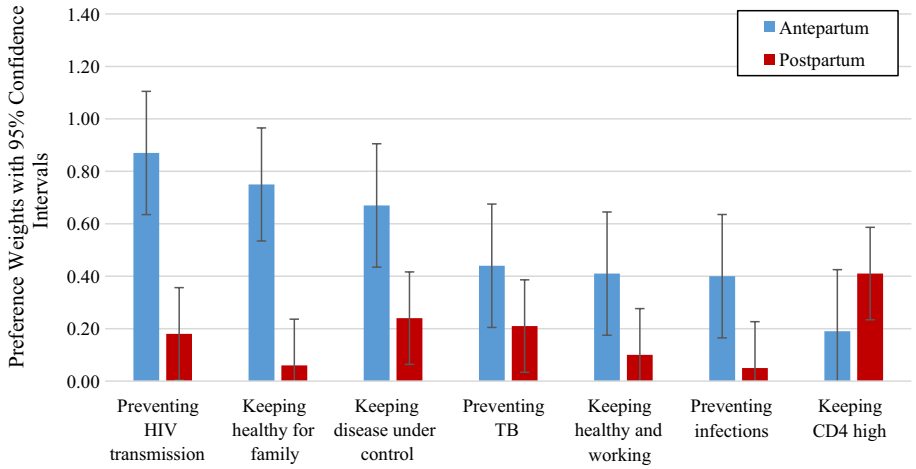

Fig. 2 Preference weights estimated from conditional logit estimates for seven motivators to take preventive therapy among 65 HIV-positive pregnant women in South Africa in the antepartum versus postpartum period. The bar range represents 95% confidence interval for the preference weights

ART during pregnancy. Several quantitative studies have reported that women initiating ART during pregnancy have a strong motivation to take medications to prevent HIV transmission to their infants and then they have fallen out of care as they perceive their own health as relatively less unimportant compared to delivering healthy infants [9, 36]. Providing care for children and family was also considered as an important motivator for women to remain healthy during pregnancy [37]. Our results also underscore that it is crucial to understand and support the social roles of HIV-positive pregnant women.

There was no clear ranking among different benefits in the postpartum period, and the relative utility gain for most benefits significantly decreased compared to in the antepartum. There are a few possible explanations. First, mothers seem to perceive the benefits of preventive therapy for their own health more highly compared to other benefits after delivery. The South African government recommends HIV-positive women initiated on lifelong ART during pregnancy have CD4 counts checked within between 3 and 6 days after delivery in postpartum and continue to receive HIV care and counseling at monthly visits aligned with infant's visits [6]. Almost everyone in the study reported that healthcare providers explained the side effects and benefits of ART and IPT to them during their last clinic visits. Maternal self-reported adherence to ART and IPT in the postpartum was 95% and 92%, respectively, and such rates continued even after termination of breastfeeding, indicating that mothers in our study were likely to continue taking therapy for their own health.

This could be that HIV counseling support was well accepted by mothers in this setting. A recent study among HIV-positive women in Ethiopia and Zambia reported that counseling support services were an important driver in maintaining regular clinic visits, while types of clinics or transportation costs were less prioritized in the postpartum period [38]. Similarly, positive attitudes towards treatment and its perceived benefits were reported as the facilitators for adherence to ART and retention in care [39, 40]. Other predictors of disengagement and/or poor adherence in the

postpartum included non-disclosure of HIV status, feeling well, and inadequate knowledge about PMTC [10, 36]. About 80% of our participants had disclosed their HIV status to their partner, potentially contributing to better adherence rates.

Keeping high CD4 counts was associated with the largest utility gain in the postpartum period. Most of the participants had been on ART an average of 2 months at enrollment, but potentially became more familiar with the clinical implications of CD4 counts through repeated HIV counseling and regular clinic visits in the ante- and early postpartum periods. A study among HIV-positive pregnant women in South Africa showed that providing CD4 count results might have helped mothers take their HIV diagnosis more seriously and resulted in improved retention in care and adherence to ART after delivery [36]. Other messages related to individual health benefits, such as preventing infections or keeping them healthy, resulted in similar utility gain. Our study results highlight that counseling in the postpartum period needs to be geared towards communicating CD4 cell counts as well as promoting the benefits of ART and IPT for maternal health.

The South African National Department of Health started the MomConnect program in 2014 for pregnant women to receive weekly messages related to pregnancy and delivery up to 1 year after delivery. It subsequently launched a pilot PMTCT MomConnect program in 2016, targeted at enrollingwith a targeting to enroll all pregnant women and mothers of infants diagnosed with HIV by 2018 to deliver specific messages related to PMTCT [41]. The findings from this study can help to develop targeted messages important to mothers in the ante and postpartum periods in South Africa and similar settings. Further studies are warranted to specify how these health promotion and specific counseling messages could improve clinic attendance and adherence to ART and IPT.

There are several limitations to our study. First, these surveys were done in primary health clinics in a mix of rural and urban areas where regular HIV testing and counseling programs were provided and the disclosure status was quite high. Thus the results reflect such programmatic settings, and can only be generalized to other similar contexts. Second, we did not directly ask about the benefits of preventing HIV transmission to infants, which could be the most important concern for mothers. Preventing HIV transmission to partners may pose similar social responsibility, and factors related to infants were tested in another discrete choice experiment and presented elsewhere [42] [43]. Third, the an objective measure of self-reported adherence to ART, such as viral load suppression, was not available. The self-reported adherence rate could have been overstated, but we used the validated self-reported adherence questionnaire with 4 days of recall, and this short recall period was shown to be well associated with more objective measures [16, 43–45]. We also cannot discount that mothers were paying less attention to the surveys in the postpartum visits and therefore chose more randomly. Given that mothers had already taken the surveys once and were familiar with the choice task, we believe that such bias would have been minimal. In addition, we could not test any effect of potential geographic heterogeneity due to the small number of participants recruited from each clinic. Lastly, the sample size of our study is quite small, and we could not test interactions with other factors like gestational weeks at first ANC visits or number of pregnancies related to lower adherence in the postpartum period [46]. Latent class model or random parameter logit model could not be fitted to account for heterogeneity in preferences across individuals or groups, given the small sample size. Future studies would be needed to examine potential heterogeneity in maternal preferences for preventive therapies.

Conclusion

We observed that prevention of HIV transmission and supporting family members were the most important motivators to for takinge preventive therapy in the antepartum period among HIV-positive pregnant women. Such prioritization diminished in the postpartum period and keeping a high CD4 count became a more important motivator. Understanding maternal motivation may help to design and deliver targeted health promotion messages to HIV-positive women around the time of delivery and to enhance adherence and retention in care after delivery in this setting.

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Author Contributions All authors contributed to design the study. H-YK, CFH, and NM helped to collect the data. H-YK and JFPB performed the data analysis. DK and CT conducted the qualitative interviews. HYK wrote the initial draft of the paper. All authors contributed to read and revised the final manuscript.

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Compliance with Ethical Standards

Conflict of interest The authors declared that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the insti-

tutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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