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Consideration of Post-Partum Management in HIV-Positive Haitian Women: An Analysis of CD4 Decline, Mortality, and Follow-up after Delivery

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Abstract

Background—A previous study at the GHESKIO HIV clinic confirmed that highly active antiretroviral therapy (HAART) prophylaxis reduced mother-to-child transmission (MTCT) and infant mortality in Haiti. This analysis looks at maternal outcomes in this cohort after delivery.

Methods—Records of 508 HIV-positive Haitian women who delivered between 1999–2005 were analyzed. We examined mortality, loss to follow-up, time to death or HAART initiation, and time of decline of CD4 count to 350 cells/microliter.

Results—170 women reached a CD4 200 or developed clinical AIDS and were started on long-term HAART. The median CD4 count at HAART initiation was 178 (IQR 106–227). CD4 decline was stratified by CD4 at delivery to project the mean months to a CD4 of 350. With an initial CD4=350–499 cells/microliter it was 19 months (95% CI 14 - 28) while with a CD4>500 cells/microliter it was 71 months (95% CI 59 - 88). At study close 257 women remained in follow-up with loss to follow up three times less in those on HAART (3.2/100 person-years) than those not on HAART (9.8/100 person-years).

Conclusions—The threshold for starting treatment was often missed in HIV-infected women after delivery. Success of follow-up of women after delivery was favorably influenced by being on HAART. Women with high (>500) initial CD4 counts had a protracted time (5–7 years) before they reach a threshold CD4 count, in contrast to those with CD4<500 cells/μL. Strategies for post-partum treatment of women should be informed by the speed with which they are likely to progress.

Keywords

Haiti; PMTCT; HAART

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Introduction

Apart from sub-Saharan Africa, the Caribbean is the region of the world most affected by HIV/AIDS. Haiti accounts for the majority of the region's current HIV infections^{1, 2}, with an HIV seroprevalence of 2.2% in 2005³. In pregnant women, the mean seroprevalence of HIV in Haiti was 4.4% in 2007⁴. In urban areas it was higher, at a mean of 5.9 %⁴.

Since 2006, the World Health Organization (WHO) has recommended that all HIV-positive expectant mothers in resource-poor settings receive antiretroviral prophylaxis to prevent mother-to-child transmission (MTCT)⁵. More recently, WHO has recommended highly-active antiretroviral therapy (HAART) as a prophylactic regimen for all pregnant women, including those who would not otherwise qualify for treatment for their own health⁶. With more women now receiving HAART as MTCT prophylaxis during pregnancy and breastfeeding, it is important to consider how they should be treated after they have completed their prophylactic regimens.

At the Haitian Group for the Study of Kaposi's Sarcoma and Opportunistic Infections (GHESKIO), a clinic based in Port-au-Prince, researchers have demonstrated that prenatal HAART effectively reduced MTCT of HIV in Port-au-Prince^{7, 8}. These studies were conducted in a cohort of 508 HIV-positive Haitian women who gave birth between 1999 and 2005. Here, we have retrospectively analyzed the follow-up data in this maternal cohort for rates and patterns of loss to follow-up and mortality. We have also modeled the mean time to starting lifelong HAART after receiving HAART prophylaxis, in order to inform optimal post-partum follow-up intervals. We hope that these analyses will help inform an option to continue pregnant women on HAART indefinitely once they have received HAART prophylaxis.

Methods

Study population

The eligible study population was defined as all post-partum HIV-positive women in follow-up at the GHESKIO PMTCT clinic from 1999 to 2005. All women and their children were offered appropriate HIV and post-natal care consistent with the standard of care in Haiti during the study period. The first-line HAART regimen employed during this time for both prophylaxis and treatment was zidovudine, lamivudine and nevirapine. All women were offered family planning services.

Women were excluded for having two or more CD4 counts of less than 200 cells/microliter recorded prior to 27 February 2003, the date that HAART became available at GHESKIO for individuals with a CD4 count below that threshold. This was done in order to control for the limited HIV interventions available in this cohort and health status.

Data collection

Data on these women and their live-born infants had been previously collected through a comprehensive review of the GHESKIO electronic database and paper charts. Methods for data collection and treatment regimens are detailed elsewhere⁷. For the purposes of the present study, data were updated through July 17, 2009, with respect to post-partum mortality, decline in CD4 count, subsequent pregnancy, timing of HAART initiation, and follow-up.

Definitions

CD4 count at delivery—defined as the measurement closest to the date of delivery, drawn within pregnancy or up to 12 weeks post-partum. If there was no CD4 count available during this period, the woman was excluded from analyses requiring this value.

CD4 count at HAART initiation—defined as the CD4 count closest to the date of HAART initiation, within three months before starting HAART. Women with no value in the appropriate time period were excluded from analyses requiring this value.

CD4 count at death—defined as the CD4 count closest to the date of death that was, within 100 days of death. Women with no value in the appropriate time period were excluded from analyses requiring this value.

Active follow-up—women were considered to be in active follow-up at GHESKIO if records reflected that they had been seen at the PMTCT clinic or pharmacy in the year prior to the study close date of 17 July 2009.

HAART initiation—This term is used to refer to initiation of HAART for the woman's own health with anticipation of lifetime therapy. It does not refer to HAART prophylaxis administered by the PMTCT program.

Outcomes analysis

The primary outcomes studied in this cohort were mortality, loss to follow-up, time to death or HAART initiation, and time to decline of CD4 count to 350 cells/microliter. Average time to subsequent pregnancy was also calculated.

Post-partum mortality—In addition to an overall mortality rate, the death rate in the cohort was further calculated for women on HAART from delivery, and for those who never started HAART. We were not able to calculate a meaningful mortality rate for those who started HAART subsequent to delivery because of the greatly varying times to HAART initiation in this group, and the fact that, by definition, they all survived at least long enough to initiate HAART.

Mean and median CD4 counts at time of HAART initiation were compared between the group that died during the study period and the group that did not. Mean and median CD4 counts at death were also calculated for women on and off HAART at death.

Further, women who died were divided into two groups: those who died within 100 days of starting therapy, and those who lived past that point. Mean and median CD4 counts were compared between groups.

Follow-up outcomes—The 473 eligible women were divided into 3 groups: 1) women who died during the study period; 2) women in active follow-up at study close; and 3) women who were seen after delivery but were then later lost to follow-up.

Those who were no longer in active follow-up were further subdivided by reason for leaving GHESKIO: known to have transferred to another care center; known to have declined follow-up but source of subsequent care not known (often because women moved out of the area); and outcome unknown.

Loss to follow-up was quantified per year for only the first three years after delivery, due to a decline in sample size that became impractical for analysis at longer time periods (Tables 1, 2).

Time to HAART initiation or death—The cohort was stratified by CD4 count at delivery into the following groups: <200 cells/ μ L; 200-349 cells/ μ L; 350-499 cells/ μ L; 500 cells/ μ L. The endpoint was defined as HAART initiation or death (Figure 2). Surviving women were censored at study close or if they became pregnant again.

Modeling of time to CD4 $\leq$ 350 cells/microliter—Women were stratified by CD4 at delivery into two groups: 350-499 cells/ μ L and 500 cells/ μ L, and projected time to a decline in CD4 count to 350 cells/ μ L was calculated for each group. The threshold of 350 cells/microliter was chosen because of its current policy relevance, as in 2010 GHESKIO increased its threshold for HAART initiation to this level from the previous one of 200 cells/ μ L.

In the 93 multiparous women in the cohort, projections of decline in CD4 count were restricted to decline between the first delivery and 40 weeks prior to the second delivery, due to uncertainty regarding the effects of HAART or other ART prophylaxis on CD4 count and disease progression during pregnancy.

Time to subsequent pregnancy—Birth rates were calculated for years of follow-up without HAART and years after initiation of HAART. They do not include the delivery at GHESKIO which prompted enrollment into the PMTCT program. We were not able to make a meaningful comparison between the treated and untreated women because of the great variability in time between delivery and HAART initiation.

These rates were then used to estimate the average time between pregnancies while off HAART, in order to estimate the interval between courses of PMTCT prophylaxis in multiparous women.

Statistical methods

All incidence rates were calculated using a normal approximation to a Poisson distribution. P-values for comparison of all averages were calculated using a two-tailed t-test assuming equal variance.

For the analysis of time to HAART initiation or death, a Kaplan-Meier survival analysis was used to estimate median months from the first delivery at GHESKIO to the combined endpoint of HAART initiation or death. A log-rank test was used to determine the statistical significance of the difference among the four groups.

A linear mixed model was used to study the change in CD4 counts in untreated women after the first delivery at GHESKIO. To more closely approximate a Gaussian distribution, a log transformation was applied to the longitudinal record of CD4 counts. A linear trend over time was fit for each stratum. Based on the estimated slope coefficients of the trend in each stratum an estimate of the number of months it would take to reach a CD4 count of 350 cells/ μ L was calculated along with approximate 95% confidence intervals.

Ethics

These women had previously signed a written agreement to participate in the provision of services at GHESKIO and to allow the physicians to review their records. The GHESKIO IRB had previously determined review of these records for study purposes to fall within

provision of services. The previous study of the same cohort was approved by the GHESKIO and Weill-Cornell Medical College Institutional Review Boards. The need for informed consent was further evaluated by the Dartmouth College Committee for the Protection of Human Subjects and waived according their criteria^[7].

Results

Cohort description

Five hundred and eight pregnant HIV-infected women were enrolled in GHESKIO's program to limit MTCT between January 1, 1999 and December 31, 2005, at a median age of enrollment of 27 years, interquartile range (IQR) 23-32. Of these 508, 18 were never seen post-partum and were excluded from the analysis. An additional 17 had reached a CD4 count of <200 before the availability of HAART and were therefore excluded for the reasons detailed in the methods. Four hundred and seventy-three women therefore met criteria to enter into this analysis (Figure 1 and Table 1).

Of the 473 who entered into analysis, 160 women were put on HAART, with a total of 515 person-years on HAART. Forty-eight of these were continued on HAART from the time of their delivery for their own health, with the additional 112 put on HAART during their follow-up period.

There were 313 women seen after delivery who had not started on HAART at study close, with a total of 1068 years of follow-up.

Post-partum mortality

Overall mortality in the cohort was 2.8 deaths/100 person-years of follow-up (95% CI: 2.1-3.6). In the women on HAART from delivery, there were 4.0 deaths/100 person-years (95% CI: 0.5-7.6) in the first three years after delivery. In those who never received HAART, mortality was 4.9 deaths/100 person-years (95% CI: 3.2-6.5) during this period.

Eighteen of the 20 women who died after initiating HAART had a CD4 count recorded at HAART initiation. All but one started HAART at a CD4 count below 350 cells/ μ L, with a median CD4 at HAART initiation of 113 cells/ μ L (IQR 54-201). By contrast, the median CD4 at HAART initiation in those who remained in active follow-up as of July 17, 2009 was 180 (IQR 129-229).

Of the 20 given HAART who later died, 11 died within 100 days of starting therapy. The group that died within 100 days had a lower median CD4 at HAART initiation than the group that lived past 100 days: 58 cells/ μ L (IQR 33-126) vs 169 (IQR 100-204). Mean CD4s at HAART initiation were 108 cells/ μ L, SD=113, for the group that lived less than 100 days, and 198 cells/ μ L, SD=147, for the group that lived more than 100 days.

In contrast, the median CD4 count at death for 22 women who never received HAART and had a count recorded within 100 days of death was 140 cells/ μ L (IQR 53-327); the mean CD4 was 216 cells/ μ L, SD=200.

For 8 women on HAART who had a CD4 count within 100 days of death, the median was 140 cells/ μ L (IQR 29-228); the mean was 143 cells/ μ L, SD=121.

Follow-up outcomes

Overall, 257 of the 473 women (52%) followed after delivery, and who had CD4 counts >200 at the date of introduction of HAART at GHESKIO, were alive and in active follow-

up the study close. They had between 3.5 and 10 years of follow-up in the MTCT program (Table 1).

The remaining two hundred and sixteen women were censored for the following reasons: 53 died; 32 declined care; 25 transferred care; and the fate of 106 (22% of the cohort) was unknown (lost to follow-up). Follow-up was related to whether the woman was kept on HAART after delivery: 9.8 women were lost per 100 life-years (95% CI: 7.4-12.1) in the group never put on HAART, and 3.2 women were lost per 100 life-years in those who were on HAART from delivery (95% CI 0.1-6.4) (Table 2). This relationship was statistically significant.

The group lost to follow-up and the group in active care did not differ significantly in their median age at enrollment (27 for both), their median time of enrollment in the program (May 2004 and March 2004, respectively) or their CD4 counts at delivery (555, SD=292, and 553, SD= 319, respectively).

Time to HAART initiation or death

The median maternal CD4 count at delivery of the child defining entry into the cohort was 467 (IQR 304-696). The median CD4 count at HAART initiation was 178 (IQR 106-227). When the cohort was stratified by CD4 at delivery, a significant difference ($p<0.0001$) was found in the progression to the combined endpoint of HAART initiation or death (Figure 2). Estimated median HAART-free survival time for women who had a CD4 of <200 cells/ μ L was 7.0 months (IQR 2-13); for CD4 = 200-349 cells/ μ L it was 33 months (IQR 18-49); for CD4 = 350-499 cells/ μ L it was 50 months (IQR 44-57). For CD4 ≥ 500 cells/ μ L, there was no median available because fewer than 50% of women reached the endpoint.

Modeling of time to CD4 ≤ 350 cells/microliter

A model of average CD4 decline in untreated women after delivery of their first child yielded times to a CD4 of 350 cells/ μ L that were significantly different between the groups with the higher CD4s at delivery (CD4 350-499 cells/ μ L and ≥ 500 cells/ μ L) (Figure 3). The group with CD4 counts between 350-499 at delivery could be expected on average to decline to 350 cells/ μ L in 19 (95% CI: 14-28) months from delivery of the index child. The group with CD4 counts ≥ 500 would decline in 71 (95% CI: 59-88) months.

Time to subsequent pregnancy

In spite of the availability of family planning services, 93 of the 473 women had 106 pregnancies and deliveries subsequent to the delivery that established them in the cohort. Seventy-one women (14% of the cohort) had more than one child while not on long-term HAART. The average time between deliveries prior to HAART initiation was 34.3 months (SD=14.4 months). While not on HAART, the women of this cohort gave birth to 5.8 children/100 person-years (95% CI: 4.5-7.1). After starting HAART the treated women gave birth to 5.2 children/100 person-years (95% CI: 3.3-7.2). Five women had more than one child while receiving HAART; nine women had more than one child while not on HAART.

Discussion

Haiti currently recommends prophylactic HAART administration for all HIV-positive pregnant women, regardless of CD4 count, and allowing at least a 6-month post-partum period of HAART prophylaxis for breastfeeding. This approach appears to be appropriate for this population, where 97% of women were found to breastfeed, exclusively or with other foods, in a 2006 demographic and public health survey³. Additionally, the transition in Haiti to a target CD4 of 350 cells/ μ L for long-term, therapeutic HAART initiation in all

HIV-infected individuals further shortens the potential HAART-free interval. In this setting, understanding patterns of mortality on and off HAART after pregnancy, follow-up and success of meeting treatment targets, and the rate at which post-partum women might reasonably be expected to decline in health are all important in formulating new treatment policy for post-partum women. The present study was undertaken in order to shed light on these areas.

Post-partum mortality

All-cause mortality was not significantly different in HAART and no-HAART groups (Table 2). However, nearly half of the mortality in the group on HAART occurred within 100 days of starting therapy, and mortality was associated with a lower CD4 count at HAART initiation. Recent data from Haiti show that health outcomes are significantly worse when the target for HAART initiation is 200 rather than 350⁹. Other recent studies also strongly suggest that initiation of HAART at lower CD4 counts carries an increased risk of complications of AIDS or death¹⁰⁻¹². Our findings - that mortality in those never put on HAART occurred exclusively in women with a CD4 count <350 cells/ μ L within 100 days of death - are consistent with this literature, and supportive of the decision to increase the CD4 threshold for treatment initiation in Haiti.

In addition, more than 25% of women started HAART at a CD4 count under 106 cells/microliter, well below the target of 200 cells/microliter, in effect during the study period. Though the threshold for treatment is now 350 cells/microliter, the difficulty in beginning treatment at or near the intended CD4 count indicates a need for a follow-up plan specifically targeted at identifying women around the treatment threshold. Findings reported here regarding CD4 progression, if replicable, will help inform this strategy.

A potential relationship was explored between less frequent follow-up intervals and lower CD4 counts at the start of HAART therapy. There was a non-significant trend toward lower CD4s at HAART initiation with longer intervals between the two follow-up visits previous to HAART initiation (data not shown). Clearly, once a patient is seen and documented to be infected, a rigorous follow-up plan must be in place so that they are started on HAART at a time that optimizes their clinical outcomes.

Follow-up

In addition to the late initiation of HAART a higher than anticipated percentage of this cohort was lost to follow-up. It should be noted that being lost to follow-up did not include those who indicated that they had transferred care or declined follow-up. It may have partly represented movement out of or around the country, in which there is now national access to comprehensive HIV treatment. Nevertheless, many of these women had established care for themselves and their children at GHESKIO, and it is concerning that their outcomes are unknown.

The inability to comprehensively follow HIV-infected subjects prior to the need for HAART is not unique to GHESKIO, as shown by the fact that only 46% of HIV-infected South African adults got a repeat CD4 count with a median time between counts of 236 days¹³, and that in another South African study only 15% of people with a CD4 count above 200 returned for the results of their CD4 count¹⁴. Rates of retention as low as 4% at six months have been reported from Malawi for asymptomatic HIV-infected people with higher CD4 counts¹⁵.

The loss to follow-up in these 473 women, overall 16% over three years, is also concerning because it does not mirror findings in another cohort at the same clinic; adults followed while receiving HAART at GHESKIO have been found to have an 8% rate of loss to follow-

up over five years¹⁶. However, when the group is broken down into those either on or off HAART from delivery to study close, the 48 women on HAART continuously had loss to follow-up rates similar to other GHESKIO populations on therapy. These 48 also had better follow-up in the first three years after delivery than those who were not on therapy, to a statistically significant degree (Table 2). Undocumented mortality, family dynamics and misunderstanding of the need to follow up for their own health (rather than just their children's health care) are all possible reasons for the higher rate of loss in those not started on therapy.

The question remains as to whether being placed on therapy was more likely in women who more reliably sought follow-up, or whether being on HAART is a predictor of good follow-up in and of itself. As this could be an important factor in the design of improved follow-up strategies (one of which could be keeping women on HAART indefinitely after delivery regardless of CD4 count). It is an area for future research.

Modeling of CD4 decline

Our analysis shows that timing of CD4 progression to a critical level is predicted by the initial CD4 count. If the CD4 count is above 500, it is unlikely to below the threshold of 350 cells/microliter in less than a year (Figure 3). Therefore, follow-up intervals of one year would be appropriate while the CD4 count is above this level. However, with these longer intervals, other measures will need to be put in place to ensure that women remain in active follow-up.

For women with lower CD4 counts at delivery, a shorter follow-up interval will be necessary to avoid missing the treatment threshold (Figure 3).

When to continue treatment past delivery?

In women whose CD4 counts near delivery are between 350 and 499 cells/ μ L, our data indicates that it would be reasonable to extend treatment indefinitely past pregnancy and breastfeeding. We have found that without treatment these women will progress to a CD4 of less than 350 cells/ μ L by an average of 19 months from delivery (Figure 3).

Recent evidence documents that maternal HAART while breastfeeding for infant prophylaxis will lower MTCT significantly during the post-partum period in resource-poor settings¹⁷⁻²³, and Haiti is therefore currently extending prophylactic HAART to all women out to six months post-partum to allow breastfeeding and considering a policy of continuous HAART after delivery. When these six additional months of HAART are accounted for, the additional HAART that would be administered to women with a CD4 between 350 and 499 cells/ μ L at delivery would average 13 months.

Therefore, because follow-up is poorer in the cohort not receiving HAART (Table 2), and the average time to progression is relatively short, the benefit of the additional HAART administered in terms of improved health outcomes may well outweigh the costs of an extra 13 months of HAART, though this cost-benefit analysis is outside the scope of the current work.

Notably, for women with a CD4 of >500 cells/microliter, the time to a CD4 of 350 cells/microliter is significantly longer (71 months - Figure 3). Therefore, if other studies can identify specific interventions to reduce the rate of loss to follow-up in the group with the highest CD4 count at delivery, a "watch and wait" approach with regards to starting HAART may prove to be safer and more cost-effective in these women than it is in the <500 CD4 group. This is an important area for future research. Recent WHO recommendations have provided the option of continuing all women after delivery on HAART²⁴.

Further, if a woman becomes pregnant a second time before beginning HAART, as 14% of the cohort did, she would begin yet another regime of prophylaxis. With an average birth rate of a child every 3.1 years and, ideally, at least 12 months of HAART per pregnancy (six months before delivery and six months after delivery while breast feeding), a multiparous HIV+ woman would be projected to spend about one third of her time on HAART.

Additionally, the rate of multiparity in these women is evidence of continued heterosexual activity. Treating these women would have the additional benefit, not quantified here, of reducing transmission of the virus to partners in the community²⁵.

Limitations

As a retrospective study, this analysis was limited in its ability to control certain variables that may have affected outcomes or follow-up in the cohort studied. In particular, we were not able to track adherence to HAART therapy or viral loads, without which data the benefits of treatment may not be correctly quantified. As we are suggesting initiation of lifelong HAART particularly if the CD4 count at delivery is <500 cells/microliter, understanding adherence, resistance patterns and viral rebound in this population would be essential before making any true policy recommendation. The benefits of treating over the longer period depend on resistance patterns and any viral rebound, so these will be key measures to evaluate in any prospective trial. However, adherence in this group is probably representative of usual patterns of adherence for this population, so conclusions as to outcomes made here are still informative.

We also acknowledge that in analyses separating women into HAART and no-HAART groups (mortality, subsequent pregnancy, and follow-up outcomes), women never put on long-term HAART may have been healthier than those who were, introducing bias into these analyses. There was a large though not statistically significant difference in average CD4 at delivery between these two groups (Table 1). This study, as a retrospective analysis, was not powered to control for that difference, but it may have affected our reported outcomes.

Additionally, the high number of women with unknown outcomes may result in a bias that we were unable to quantify here. It is unclear from this data whether there are specific risk factors for loss to follow-up that could be addressed, or which would change the conclusions of this study. Also, our definition of loss to follow-up (seen in the year prior to study close) is only a rough indicator of quality of follow-up.

Randomized, prospective studies such as Promise (IMPAACT 1077) are needed to elucidate these issues. Finally, analysis of certain outcomes and relationships between certain variables was limited by small sample size.

Summary and further research

This study begins to address some of the issues that are central to maternal HIV care. In particular, the present analysis provides a model of CD4 decline after delivery, and adds evidence that missing the target CD4 count for starting HAART was common and likely led to excess mortality in this cohort. With a better understanding of determinants of follow-up and confirmation of the CD4 decline curve modeled here, we will be able to better predict in this setting and others how to best maximize the quality of care for post-partum HIV-positive women.

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Figure 1.
Cohort outcomes as of 17 July 2009.

Figure 2.

HAART-free survival stratified by CD4 at delivery. Combined endpoint is HAART initiation or death, if individuals died prior to starting HAART. Individuals were censored when they had no more datapoints in the GHESKIO record. A univariate Cox model was applied to this data and showed a 3.42% decrease (95% CI: 2.55% - 4.29%) in hazard of death or HAART with every 10 unit increase in CD4 at birth. Sample sizes were: <200 (N=24), 200-349 (N=66), 350-499 (N=105) and 500 (N=191).

Figure 3.

Estimated progression of CD4 count, stratified by CD4 count at delivery. For CD4 at delivery = 350-499: N=96; time to CD4=350 cells/ μ L = 19 months (95%CI=14-28); equation describing model: $\log(\text{CD4}) = 6.1104 - 0.01331 \times \text{Months from birth}$. For CD4 at delivery = 500: N=174; time to CD4=350 cells/ μ L = 71 months (95%CI=59-88); equation describing model: $\log(\text{CD4}) = 6.6421 - 0.01104 \times \text{months from birth}$. Multiparous women are removed from the dataset prior to their second pregnancy while in the cohort.

Table 1
Characteristics of the 473 women who entered into the follow-up analysis

Characteristics of women, by HAART status.

	Never received HAART			On HAART at delivery			Started HAART between first delivery and study close		
Number of women, excluding those never seen in follow-up and those with two CD4 counts <200 prior to HAART availability	313			48			112		
Demographics	Value	Standard deviation	N	Value	Standard deviation	N	Value	Standard deviation	N
Mean CD4 at delivery	618	298	268	218	161	43	479	290	104
Mean CD4 at HAART initiation	-	-	-	184	131	43	200	162	93
Total years of follow-up	1068		313	182		48	620		112
Mean years of follow-up	3.4	2.4	313	3.8	1.6	48	5.5	1.9	112
Total years on HAART	-		-	182		48	333		112
Mean years on HAART	-	-	-	3.8	1.6	48	3.0	2.2	112
Median age at enrollment	27		312	28		48	28		112
Median month/year of first delivery	Nov-03		313	Oct-04		48	Jun-03		112
Number with subsequent pregnancies	58			6			29		
Percent with subsequent pregnancies	19%			13%			26%		
Total follow-up outcomes:									
Deaths		33			5			15	
Transferred		18			2			5	
Declined care		28			2			2	
Lost to follow-up during study period		93			6			7	
Percent lost to follow-up during study period		30%			13%			6.3%	
Three-year follow-up outcomes:									
Deaths		26			5			5	
Transferred		11			1			0	
Declined care		23			2			1	
Lost to follow-up within three years of first delivery		68			4			2	
Percent lost to follow-up within three years of first delivery		22%			8.3%			1.8%	

Table 2
Outcomes in those on HAART from delivery and those who had not received HAART by study closure

Incidence of follow-up outcomes for those never on HAART and those on HAART since delivery, over first three years following first delivery at GHESKIO. (Sample sizes are too small to calculate rates of transfer and declined care for those on HAART at delivery.) *=non-overlapping confidence intervals between groups.

	Overall (Years 1-3 of follow-up)	First year	Second year	Third Year
Life-years				
Never received HAART (N=313)	696	270	230	196
On HAART at delivery (N=48)	124	44	41	39
Loss to follow-up: women lost per 100 life-years (95% confidence interval)				
Never received HAART (N=313)	9.8 (7.4-12.1)*	12.6 (8.4-16.8)*	7.4 (3.9-10.9)	8.7 (4.6-12.8)
On HAART at delivery (N=48)	3.2 (0.1-6.4)*	2.3 (-2.2-6.8)*	2.4 (-2.3-7.2)	5.1 (-2.0-12.1)
Percent lost to follow-up				
Never received HAART (N=313)	22%	11%	6%	8%
On HAART at delivery (N=48)	8%	2%	2%	5%
Mortality: Deaths per 100 life-years (95% confidence interval)				
Never received HAART (N=313)	4.9 (3.2-6.5)	5.5 (2.7-8.2)	6.9 (3.5-10.3)	1.5 (-0.2-3.3)
On HAART at delivery (N=48)	4.0 (0.5-7.6)	9.1 (0.2-18.1)	0	2.5 (-2.4-7.5)