ResearchGate

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/283262619

HIV-Infected Ugandan Women on Antiretroviral Therapy Maintain HIV-1 RNA Suppression Across Periconception, Pregnancy, and Postpartum Periods

Article *in* JAIDS Journal of Acquired Immune Deficiency Syndromes · October 2015

DOI: 10.1097/QAI.0000000000000874

CITATIONS
21

READS
68

12 authors, including:



Lynn T Matthews
University of Alabama at Birmingham
72 PUBLICATIONS **1,932** CITATIONS
SEE PROFILE



Angela Kaida
Simon Fraser University
62 PUBLICATIONS **1,955** CITATIONS
SEE PROFILE



Kara Bennett
Bennett Statistical Consulting, Inc
49 PUBLICATIONS **1,322** CITATIONS
SEE PROFILE



Nicholas Musinguzi
Mbarara University of Science & Technology (MUST)
65 PUBLICATIONS **916** CITATIONS
SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Stigma and Food Insecurity View project

Social Analysis of an African Adherence Support Intervention View project

All content following this page was uploaded by Yap Boum II on 31 January 2018.

The user has requested enhancement of the downloaded file.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2017 April 01.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2016 April 1; 71(4): 399–406. doi:10.1097/QAI.0000000000000874.

HIV-infected Ugandan women on antiretroviral therapy maintain HIV-1 RNA suppression across periconception, pregnancy, and postpartum periods

Lynn T Matthews, MD, MPH, MGH,
Center for Global Health and Division of Infectious Disease

Heather B Ribaudo, PhD,
Center for Biostatistics in AIDS Research

Angela Kaida, PhD,
Simon Fraser University, Faculty of Health Sciences

Kara Bennett, MS,
Bennett Statistical Consulting

Nicholas Musinguzi, MA,
Mbarara University of Science and Technology, Mbarara, Uganda

Mark J Siedner, MD, MGH,
Center for Global Health and Division of Infectious Disease

Jerome Kabakyenga, MBChB, PhD,
Mbarara University of Science and Technology, Mbarara, Uganda

PW Hunt, MD,
University of California at San Francisco, Department of Medicine, San Francisco, United States

JN Martin, MD, MPH,
University of California at San Francisco, Department of Medicine, Department of Epidemiology and Biostatistics, San Francisco, United States

Y Boum,
Epicentre Mbarara, Mbarara, Uganda

JE Haberer, MD, MPH, MGH, and
Center for Global Health and Department of General Medicine

David R Bangsberg, MD, MPH, MGH
Global Health, Harvard T.H Chan School of Public Health, Harvard Medical School

Abstract

Background—HIV-infected women risk sexual and perinatal HIV transmission during conception, pregnancy, childbirth, and breastfeeding. We compared HIV-1 RNA suppression and medication adherence across periconception, pregnancy, and postpartum periods, among women on ART in Uganda.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Methods—We analyzed data from women in a prospective cohort study, aged 18-49 years, enrolled at ART initiation and with ≥ 1 pregnancy between 2005-2011. Participants were seen quarterly. The primary exposure of interest was pregnancy period, including periconception (3 quarters prior to pregnancy), pregnancy, postpartum (6 months after pregnancy outcome), or non-pregnancy-related. Regression models using GEE compared the likelihood of HIV-1 RNA ≤400 copies/mL, <80% average adherence based on electronic pill caps (MEMS), and likelihood of 72-hour medication gaps across each time period.

Results—111 women contributed 486 person-years of follow up. Viral suppression was present at 89% of non-pregnant, 97% of periconception, 93% of pregnancy, and 89% of postpartum visits, and was more likely during periconception (aOR 2.15) compared with non-pregnant periods. Average ART adherence was 90% (IQR 70-98%), 93% (IQR 82-98%), 92% (IQR 72-98%) and 92% (IQR 72-97%) during non-pregnant, periconception, pregnant and postpartum periods. Average adherence < 80% was less likely during periconception (aOR 0.68) and 72-hour gaps/90 days were less frequent during periconception (aRR 0.72) and more frequent postpartum (aRR 1.40).

Conclusions—Women with pregnancy were virologically suppressed at most visits, with an increased likelihood of suppression and high adherence during periconception follow-up. Increased frequency of 72-hour gaps suggests a need for increased adherence support during postpartum periods.

Introduction

HIV-infected women who become pregnant risk HIV transmission to sexual partners as well as the fetus. HIV-1 RNA suppression reduces these risks [1, 2] and with updated W.H.O. guidelines, increasing numbers of women are initiating antiretroviral therapy (ART), rather than antiretrovirals (ARVs) as prophylaxis, to both reduce the risk of perinatal transmission and maintain the woman's health [3, 4]. The effectiveness of ART depends on adherence to medication and several studies identify pregnancy and postpartum as periods during which women are at risk for poor adherence to ART.

A recent meta-analysis suggests that women have worse adherence during the postpartum period, however less than half of the analyzed studies included women on ART for their own health and a small minority of the studies included postpartum follow-up [5]. Some data suggest that women on ART for their own health may be more adherent than women taking ARVs for prophylaxis [6], however other studies suggest adherence challenges for this group. Among women initiated on ART during pregnancy in South Africa, 49% of women missed a visit or disengaged from care by six months postpartum [7]. In another South African study, among 896 women with a pregnancy after initiation of ART for her own health (not pregnant at ART initiation), there was an increased risk of non-adherence to ART (measured by <100% adherence by pharmacy refill) during the postpartum period [8]. Early data from Malawi (the first country to adopt the option B+ strategy to reduce perinatal HIV transmission) do not report on adherence or viral suppression but 27% of women who initiated therapy were lost to follow-up at one year [9], and mortality 6-months after initiation of ART is higher than in the pre-Option B+ era [10].

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

While much research focuses on adherence and the risks of perinatal transmission during pregnancy and postpartum, HIV-infected women also risk HIV transmission to an uninfected partner during the periconception period. We are unaware of studies evaluating adherence to antiretroviral therapy during the periconception period for women living with HIV.

We compared prevalence of HIV-1 viral suppression measured quarterly and objective medication adherence measured continuously with electronic pill caps across periconception, pregnancy, postpartum, and non-pregnancy-related follow-up periods in a longitudinal cohort of women initiated on ART for their own health with low losses to follow-up, towards estimating risks of sexual and perinatal HIV transmission among HIV-infected women initiated on ART for their own health in Uganda.

Methods

Setting

The Mbarara District of Uganda is located approximately 265 kilometers southwest of the Ugandan capital city of Kampala. Regional adult HIV prevalence is estimated at 10% [11]. The Mbarara University HIV clinic offers comprehensive HIV care services, including ART provided through the Ugandan Ministry of Health with support from the President's Emergency Plan for AIDS Relief (PEPFAR), the Global Fund, and the Family Treatment Fund [12].

Study Participants

Study participants were sampled from the Uganda AIDS Rural Treatment Outcomes (UARTO) cohort study of over 700 HIV-infected adults initiating their first ART regimen at the Mbarara University HIV clinic (NCT01596322). Participants complete quarterly study visits with structured interviews and laboratory testing (CD4+ T cell count and plasma HIV-1 RNA level). For this analysis, we restricted the sample to 18-49 year old women enrolled from June 2005 and followed through September 2011 and with at least one pregnancy.

Measurements

The primary outcome was HIV-1 RNA suppression as measured quarterly. From 2005-2007, plasma HIV-1 RNA levels were assessed using the Roche Amplicor HIV Monitor 1.5 test (Roche, Branchburg, NJ, dynamic range: 400-750,000 copies/ml). In April, 2007, this assay was replaced by the Roche Cobas Taqman HIV-1 test v1.0 (Roche, Branchburg, NJ, dynamic range: 48-10,000,000 copies/ml). HIV-1 RNA level below 400 copies/mL was categorized as suppressed. In the primary analysis, missing HIV-1 RNA data were not included in the analysis.

The primary predictor variable was pregnancy status. Periods of pregnancy were defined based on self-report of pregnancy and pregnancy outcome in structured quarterly interviews. Women were categorized as being pregnant, post-partum (up to 6 months after live birth), periconception (3 quarters prior to first report of pregnancy), or in non-pregnancy-related-follow-up (from one quarter after initiation of therapy up until a first periconception period.)

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

The first quarter after initiation of therapy was censored from analysis in order to allow women time to suppress HIV-1 RNA. Women with second pregnancies prior to one year of postpartum follow-up moved into periconception and/or pregnancy time periods. Women entering the study reported whether they were currently pregnant but did not report on dates of pre-enrollment pregnancy or postpartum status. Thus, no women were counted as postpartum at study entry [Figure 1]. Pregnancies lasting >300 days based on these methods were truncated to end at 300 days. Women who simultaneously reported a new pregnancy and pregnancy outcome since the last visit did not contribute pregnant follow-up time, but could contribute postpartum time.

We also evaluated objective adherence to ART. A subset of enrolled participants were issued a medication event monitoring system (MEMS) electronic pill bottle (Aardex Group, Sion, Switzerland), which records the date and time of each pill bottle opening. Study staff downloaded MEMS data for the preceding observation period at each study visit. We calculated daily adherence in each observation period prior to an HIV-1 RNA measurement (7- 150 days maximum) as the number of doses taken per day divided by the number of doses prescribed in the corresponding ART regimen, with a maximum of 100% if there were more openings than prescribed doses.

Analysis

Baseline characteristics of women in the cohort were described.

The proportion of visits at which women had HIV-1 RNA suppression are described by pregnancy follow-up period. The likelihood of HIV-1 RNA suppression at the different time points was modeled using conditional logistic regression with generalized estimating equations (GEE) and an exchangeable correlation matrix to account for repeated visits. Missing viral load data were censored for 253 of 1612 visits (16% of visits) in the primary analysis.

Average adherence by MEMS cap is described for the four follow-up periods. We used logistic regression with GEE to evaluate the relationship between adherence to at least 80% of prescribed pills and time period [13]. Because treatment interruptions are an independent predictor of virologic treatment failure, Poisson regression with GEE was used to evaluate the frequency of 72 hour gaps/90 days during the time periods [14, 15]. We censored periods of known MEMS device non-usage, including when participants were prescribed medications in blister packs that did not allow for device filling, or when 30 or more days of MEMS non-use was followed by an undetectable HIV-1 RNA measurement (104 / 1828 periods). Patients were censored at the first of: 1) last HIV-1 RNA recorded during MEMS monitoring, 2) death, or 3) study disenrollment (612 /1828 periods).

Time-updated predictor variables included pregnancy status (primary predictor of interest), asset index via the Filmer Pritchett Index as quintiles [16], unprotected sex, number of sexual partners, primary partner HIV serostatus, HIV serostatus disclosure to primary partner, and time on ART. These items were selected based on expected confounders of adherence. Factors included in the adjusted analysis were those significant at the $p<.05$ level in the unadjusted analysis.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Women were categorized as lost to follow-up upon withdrawal from the study (voluntary or due to moving out of catchment area), death, or when they were not able to be contacted by phone or other tracking.

Sensitivity analyses

Sensitivity analyses for the HIV-1 RNA suppression analyses included (1) treating all missing HIV-1 RNA data as unsuppressed and (2) treating HIV-1 RNA data as missing only when accompanied by a missed visit (e.g. if someone was at the clinic but refused a blood draw, data were censored rather than classified as not virally suppressed).

Data were analyzed with SAS version 9.4 (Cary, NC). Analyses of the MEMS adherence data were performed using Stata 13.0 (Statacorp, College Station, TX, USA).

Ethics

All procedures were approved by institutional review boards at Mbarara University of Science Technology (Mbarara, Uganda), Massachusetts General Hospital/Partners Healthcare (Boston, USA), the University of California, San Francisco. The study was also approved by the Uganda National Council of Science and Technology and the Research Secretariat in the Office of the President.

Results

Among 353 women contributing 1559 person years of follow-up, 111 women with pregnancy contributed 486 person years of follow-up. At baseline, women who experienced pregnancy during follow-up had a median age of 29 years (interquartile range [IQR] 24, 33), CD4 cell count of 165 cells/mm^3 (IQR 90, 145), and 57% (n=38 of those with a primary partner) reported an HIV-infected partner (Table 1). Participants contributed 851 non-pregnancy related follow-up visits, 225 periconception visits, 165 pregnancy visits, and 118 postpartum visits.

Among the women with pregnancy, 5 (5%) were lost to follow-up during the analysis period. Of these five women, two died and the remainder were unable to be tracked.

Viral suppression and pregnancy follow-up period

Among 111 women with pregnancies, HIV-1 RNA suppression was observed at 89% of non-pregnancy follow-up visits (n=851 visits) and 97% of periconception (n=225), 93% of pregnancy (n=165)), and 89% of postpartum (n=118) visits (Figure 2a). In the unadjusted model, the periconception period was associated with an increased odds of viral suppression compared to non-pregnancy related follow-up (OR 2.63, 95% CI 1.44-4.81, p .002). When adjusting for other factors associated with viral suppression (income and time on ART), the periconception period remained associated with an increased likelihood of viral suppression (aOR 2.15, 1.33-3.49, p .002). Viral suppression during pregnancy and postpartum periods were not different than non-pregnancy-related follow-up periods. (Table 2)

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

HIV RNA data were missing at 261 (15%) of visits. These data were censored for the primary analysis. We conducted two sensitivity analyses. In one, all missing HIV-1 RNA data were considered as not suppressed. In a second sensitivity analysis, only missing HIV-1 RNA data accompanied by a missed visit were considered not suppressed. In both analyses, the periconception period remained associated with an increased likelihood of viral suppression. In addition, the postpartum period in these analyses was associated with a reduced likelihood of viral suppression (see Table 2 legend.)

Adherence to daily pill taking by electronic pill caps

For 97 of the 111 participants with pregnancy (87%), MEMS cap data were available to evaluate daily adherence to ART. Average adherence during the time periods was 90% (IQR 70-98%) during non-pregnancy visits (n=604), 93% (IQR 82-98%) during periconception visits (n=252), 92% (IQR 72-98%) during pregnancy visits (n=144), and 88% (IQR 63-97%) during post-partum visits (n=112) (Figure 2b).

The likelihood of average adherence < 80% was decreased during periconception compared to non-pregnancy related follow-up in unadjusted and adjusted analyses (aOR 0.68, 95% CI 0.52-0.91) and was not different during pregnancy and postpartum periods. (Table 3).

There were an average of 0.62, 0.49, 0.67, and 0.95 72 hour gaps/90 day period during non-pregnancy related, periconception, pregnancy, and post-partum periods, respectively. In unadjusted and adjusted analysis, there was a decreased risk of gaps during periconception (aRR 0.72, 95% CI 0.59-0.89) and an increased risk of gaps during postpartum follow up (aRR 1.40, 95% CI 1.13-1.73), both compared to non-pregnancy related follow-up (Table 3). Among 21 women who had at least one 72 hour gap during postpartum follow-up and had an HIV-1 RNA plasma level in the following 12 months, 5 (24%) had at least one detectable HIV-1 RNA level.

Discussion

These data demonstrate that among 111 HIV-infected women initiated on ART for their own health and enrolled in a prospective cohort study with low loss-to-follow-up (5%) in rural Uganda, high rates of HIV-1 RNA suppression were observed throughout periconception (97%), pregnancy (93%), and postpartum periods (89%) visits. In sensitivity analyses, where missing viral load data were characterized as not suppressed, women had a decreased likelihood of suppressed HIV-1 RNA during postpartum follow-up. Daily objective measures indicate that women had an increased risk of 72-hour gaps in pill taking during the postpartum period compared to other non-pregnancy-related follow-up (aRR 1.40, 95% CI 1.13-1.73), however the number of gaps was small (average 0.65, IQR 0-1 for all periods). These data suggest that most women who initiate ART for their own health and remain engaged in care adhere sufficiently to sustain virologic suppression. However, the postpartum period remains a risky time when women may need additional support.

These are the first data we are aware of to consider the periconception period, a time of particular risk of sexual transmission to an uninfected partner. These data suggest that women had the highest likelihood of viral suppression and the highest adherence during

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

these periods and therefore periconception risks of sexual transmission to partner were minimal. While qualitative data from this cohort suggest that HIV-infected individuals with uninfected partners are not aware of the concept of antiretroviral treatment as prevention [17], these data suggest excellent adherence and, therefore, a very low risk of periconception transmission. It is unlikely that high adherence to medication is a response to pre-conception counseling as such counseling is rare [18]. These data may reassure healthcare providers whose concerns about periconception transmission may limit counseling about risk reduction in the absence of condom use [19, 20]. These findings are similar to other data from this cohort suggesting a low risk of sexual transmission of HIV [21].

In addition to a risk of loss of viral suppression during 6-month postpartum follow-up observed in the sensitivity analyses, MEMS data suggest an increased risk in gaps in pill-taking during this time. These data are the first to our knowledge to describe objective adherence in the postpartum period among women initiated on ART for their own health. Our results are consistent with prior data evaluating pharmacy refill data, which also demonstrate adherence challenges during postpartum periods, most likely explained by concomitant challenges that women face shortly after childbirth [5-8, 22-25]. These data have important implications given the roll-out of Option B+. Modeling data suggest the cost-effectiveness of the Option B+ strategy, but the benefits are lost if the risk of HIV-1 RNA failure increases by even 2.4% [26]. Early data from Malawi (the first country to adopt option B+) do not report on adherence or viral suppression, but about half of women eligible for ART did not initiate treatment [27] and 27% of women who initiated therapy were lost to follow-up at one year [9]. Roll-out of Option B+ is happening very quickly and is planned or considered for many sub-Saharan African countries[28]. It will be critical to understand and address challenges to adherence in the peripartum period as these programs are implemented to optimize their efficacy and cost-effectiveness.

The high adherence observed even during the vulnerable postpartum period suggests that the simple resources offered to women participating in this cohort may inform future intervention studies. Women who did not attend quarterly visits received a phone call from a research assistant and often offers to help with transport or other barriers to attend clinic. Women who attended quarterly visits received soap, sugar or cooking oil as well as a meal and transport reimbursement. Given the stressors that women face during the postpartum period to provide for herself and her child, these may be very critical tangible supports [29]. Other data suggest that the social support of being part of a cohort of people living with HIV may have also promoted adherence [30]. Finally, some data suggest that electronic monitoring of adherence to pill-taking behavior may promote short-term improvements in adherence over the short term [31, 32].

There are several limitations to this study. As above, women in this cohort are engaged in quarterly visits inclusive of transportation support and attempts to locate them when they do not return for scheduled visits. Thus these women likely face fewer adherence challenges than most women in this setting. Also, women who choose to participate in such a study may differ from the general population. In addition, pregnancy was based on self-report, meaning that pregnancies ending in early miscarriage or termination might not be captured, and the timing of the periconception and pregnancy periods is imperfect, which could lead to

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

misclassification of study periods. However, this misclassification is unlikely to be systematically biased and therefore would bias estimates towards the null. In addition, there were 111 women with pregnancies included in the analysis. For the viral load data, small sample size (visits) may have limited the ability to observe statistically significant associations. Major strengths include the use of objective adherence measurement, use of laboratory-confirmed viral load as an outcome, long follow-up period, and the low late of attrition within the study.

In summary, our data suggest that most women in this setting initiating ART for their own health are sufficiently adherent to maintain high rates of viral suppression during periconception, pregnancy, and postpartum follow-up, with particularly high suppression observed in the periconception period. However, these data also suggest that women experience increased adherence challenges during postpartum periods. Supporting adherence during this critical time may require integration of pediatric care and maternal follow-up care and emphasizing the importance of on-going ART adherence for the maternal health in addition to reducing risks of perinatal transmission. Additional data are required from postpartum women in other settings regarding their specific adherence and suppression experiences and challenges, especially as treatment recommendations and implementation evolve [24, 33, 34]

Acknowledgments

Support: The authors would like to thank UARTO study participants and our research team for contributions to this study. This study was funded by U.S. National Institutes of Health R21HD069194, K23 MH095655, R01MH054907, P30AI027763, U01CA066529, K24 MH87227, K23 MH099916 and R01MH087328; and the Sullivan Family Foundation. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Cohen MS, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011; 365(6):493–505. [PubMed: 21767103]
2. World Health Organization. Programmatic Update: Use of antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. 2012
3. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. WHO; Geneva: 2013.
4. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. 2014
5. Nachega JB, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. AIDS. 2012; 26(16):2039–52. [PubMed: 22951634]
6. Cavallo IK, et al. Predictors of postpartum viral load rebound in a cohort of HIV-infected Brazilian women. Int J Gynaecol Obstet. 2010; 108(2):111–4. [PubMed: 19892340]
7. Phillips T, et al. Disengagement of HIV-positive pregnant and postpartum women from antiretroviral therapy services: a cohort study. J Int AIDS Soc. 2014; 17:19242. [PubMed: 25301494]
8. Henegar CE, et al. Effect of pregnancy and the postpartum period on adherence to antiretroviral therapy among HIV-infected women established on treatment. J Acquir Immune Defic Syndr. 2015; 68(4):477–80. [PubMed: 25559590]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

9. Tenthani L, et al. Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women (‘Option B+’) in Malawi. AIDS. 2014; 28(4):589–98. [PubMed: 24468999]
10. Kim MH, et al. Implementation and Operational Research: The Impact of Option B+ on the Antenatal PMTCT Cascade in Lilongwe, Malawi. J Acquir Immune Defic Syndr. 2015; 68(5):e77–83. [PubMed: 25585302]
11. Uganda HIV/AIDS Sero-behavioural survey 2004-2005. Ministry of Health (Uganda) and ORC Macro; Calverton, MD: 2006.
12. Geng EH, et al. Diminishing availability of publicly funded slots for antiretroviral initiation among HIV-infected ART-eligible patients in Uganda. PLoS ONE. 2010; 5(11):e14098. [PubMed: 21124842]
13. Nachega JB, et al. Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes. Ann Intern Med. 2007; 146(8):564–73. [PubMed: 17438315]
14. Oyugi JH, et al. Treatment interruptions predict resistance in HIV-positive individuals purchasing fixed-dose combination antiretroviral therapy in Kampala, Uganda. AIDS. 2007; 21(8):965–71. [PubMed: 17457090]
15. Genberg BL, et al. Patterns of antiretroviral therapy adherence and impact on HIV RNA among patients in North America. AIDS. 2012; 26(11):1415–23. [PubMed: 22767342]
16. Filmer D, Pritchett LH. Estimating wealth effects without expenditure data--or tears: an application to educational enrollments in states of India. Demography. 2001; 38(1):115–32. [PubMed: 11227840]
17. Kaida, A., et al. HIVR4P. Cape Town: 2014. Barriers and promoters to uptake of safer conception strategies among HIV-affected couples with fertility intentions in Mbarara, Uganda. Abstract 23.03.
18. Matthews, LT., et al. International AIDS Society/AIDS 2014. Melbourne, Australia: 2014. Barriers and facilitators to provider-initiated assessment of fertility intentions among men and women living with HIV in Uganda Abstract #TUPE125.
19. Matthews LT, et al. Lost Opportunities to Reduce Periconception HIV Transmission: Safer Conception Counseling By South African Providers Addresses Perinatal but not Sexual HIV Transmission. J Acquir Immune Defic Syndr. 2014; 67(Suppl 4):S210–7. [PubMed: 25436820]
20. Matthews, LT., et al. International AIDS Society/AIDS 2014. Melbourne, Australia: 2014. Bariers and facilitators to provider-initiated assessment of fertility intentions among men and women living with HIV in Uganda Abstract #TUPE125.
21. Siedner MJ, et al. Treatment as long-term prevention: sustained reduction in HIV sexual transmission risk with use of antiretroviral therapy in rural Uganda. AIDS. 2014; 28(2):267–71. [PubMed: 24361683]
22. Sha BE, et al. Postpartum viral load rebound in HIV-1-infected women treated with highly active antiretroviral therapy: AIDS Clinical Trials Group Protocol A5150. HIV Clin Trials. 2011; 12(1): 9–23. [PubMed: 21388937]
23. Kilewo C, et al. Prevention of mother-to-child transmission of HIV-1 through breastfeeding by treating mothers with triple antiretroviral therapy in Dar es Salaam, Tanzania: the Mitra Plus study. J Acquir Immune Defic Syndr. 2009; 52(3):406–16. [PubMed: 19730269]
24. Ngarina M, et al. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. BMC Public Health. 2013; 13(1):450. [PubMed: 23647555]
25. Ngarina M, et al. Virologic and immunologic failure, drug resistance and mortality during the first 24 months postpartum among HIV-infected women initiated on antiretroviral therapy for life in the Mitra plus Study, Dar es Salaam, Tanzania. BMC Infect Dis. 2015; 15(1):175. [PubMed: 25886277]
26. Ciaranello AL, et al. Cost-effectiveness of World Health Organization 2010 guidelines for prevention of mother-to-child HIV transmission in Zimbabwe. Clin Infect Dis. 2013; 56(3):430–46. [PubMed: 23204035]
27. Price AJ, et al. Uptake of prevention of mother-to-child-transmission using Option B+ in northern rural Malawi: a retrospective cohort study. Sex Transm Infect. 2014

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

28. Kellerman SE, et al. Beyond prevention of mother-to-child transmission: keeping HIV-exposed and HIV-positive children healthy and alive. AIDS. 2013; 27(Suppl 2):S225–33. [PubMed: 24361632]
29. Matthews, LT., et al. From Option A to B+: Exploring challenges of navigating evolving PMTCT strategies among postpartum women living with HIV in rural Uganda. Abstract MOPEB188. 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015); Vancouver, Canada. 2015.
30. Campbell, J., et al. Social Support Through Observational Trial Participation Among HIV Patients in Southwest Uganda. 10th International Conference on HIV Treatment and Prevention Adherence; Miami, Florida. 2015.
31. Deschamps AE, et al. Use of electronic monitoring induces a 40-day intervention effect in HIV patients. J Acquir Immune Defic Syndr. 2006; 43(2):247–8. [PubMed: 17003672]
32. Sutton S, et al. Does electronic monitoring influence adherence to medication? Randomized controlled trial of measurement reactivity. Ann Behav Med. 2014; 48(3):293–9. [PubMed: 24573909]
33. Buchberg MK, et al. A mixed-methods approach to understanding barriers to postpartum retention in care among low-income, HIV-infected women. AIDS Patient Care STDS. 2015; 29(3):126–32. [PubMed: 25612217]
34. Clouse K, et al. “What they wanted was to give birth; nothing else”: barriers to retention in option B+ HIV care among postpartum women in South Africa. J Acquir Immune Defic Syndr. 2014; 67(1):e12–8. [PubMed: 24977376]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Enroll	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
ART initiation	X	NPR	periC	periC	periC	Preg	Preg	Preg	Post	Post	NPR

Legend:

Q Quarter

X First quarter visits were not considered in order to allow time to suppress HIV-1 virus.

NPR Non-pregnancy related follow-up. Defined as any visit not associated with periconception, pregnant, or postpartum follow-up.

periC Periconception follow-up. Defined as the 3 quarters prior to first report of pregnancy.

Preg Pregnancy follow-up. Defined as the duration of the woman's pregnancy.

Post Postpartum follow-up. Defined as the 2 quarters postpartum.

Figure 1. Distribution of the 4 time periods for a woman with pregnancy reported at quarter 6

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

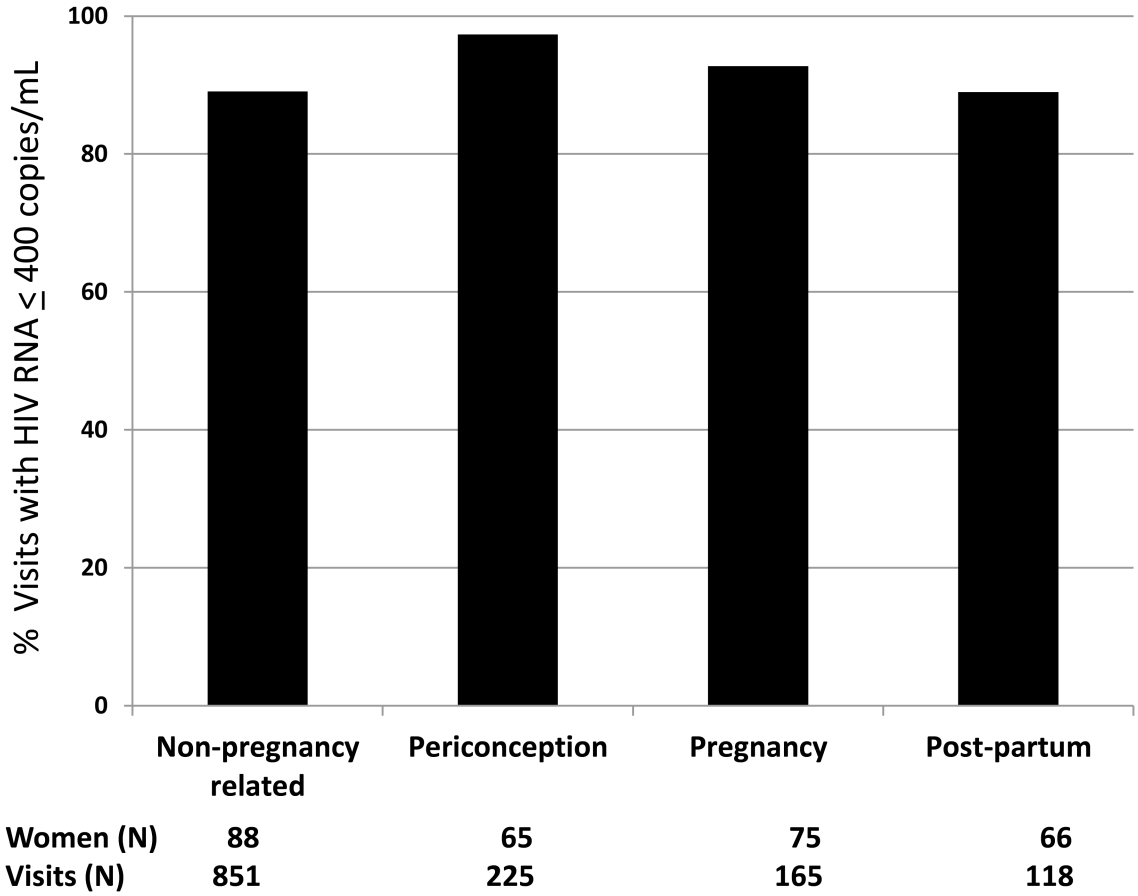


Figure 2a. HIV RNA suppression by follow-up period

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

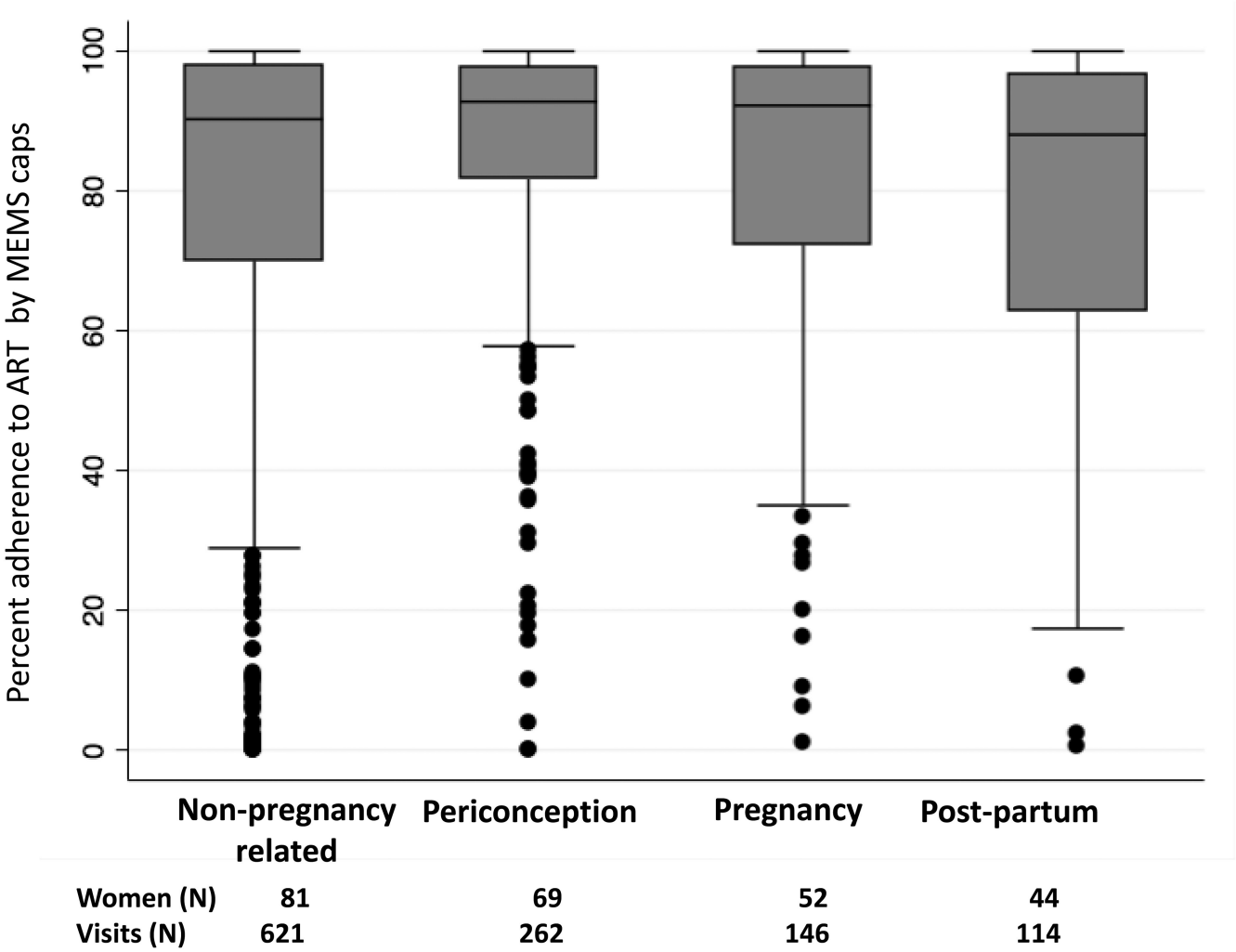


Figure 2b. Adherence to ART by follow-up period

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1
Characteristics of women age 18-49 at cohort enrollment

Variable	All Women (n = 353) (PY f-up = 1559) Median (IQR) or N (%)	Women with pregnancy (n= 111) (PY f-up = 486) Median (IQR) or N (%)	Women without pregnancy (n= 242) (PY f-up = 1073) Median (IQR) or N (%)
Age (years)	32 (27,37)	29 (24,33)	34 (29,38)
CD4 cell count (cells/mm^3)	143 (83,215)	165 (90,245)	133 (80,199)
HIV-1 viral RNA (log10 copies/ml)	4.97 (4.51,5.48)	4.92 (4.45,5.53)	4.98 (4.54,5.46)
Marital status			
Divorced	100 (28%)	22 (20%)	79 (33%)
Married	136 (39%)	67 (60%)	69 (29%)
Never married	26 (7%)	11 (10%)	15 (6%)
Widowed	90 (25%)	11 (10%)	79 (33%)
Asset index (quintiles)			
1st	85 (24%)	29 (27%)	56 (23%)
2nd	74 (22%)	21 (20%)	54 (22%)
3rd	62 (18%)	23 (21%)	39 (16%)
4th	60 (17%)	15 (14%)	45 (19%)
5th	66 (19%)	19 (18%)	47 (20%)
Number of sexual partners in past 3 mos			
0	184 (54%)	32 (30%)	152 (65%)
1	148 (44%)	72 (68%)	76 (33%)
≥ 2	7 (2%)	2 (2%)	5 (2%)
Sex without condoms with ≥1 partner, past 3 mos *	77 (52%)	36 (51%)	41 (53%)
Primary partner HIV status *			
Positive	82 (60%)	38 (57%)	5 (7%)
Negative	16 (12%)	11 (16%)	44 (63%)
Don't know	39 (28%)	18 (27%)	21 (30%)
ART Regimen			
Efavirenz + 2 NRTIs	33 (9%)	13 (12%)	20 (8%)
Nevirapine + 2 NRTIs	296 (84%)	95 (86%)	201 (83%)
Other	2 (1%)	--	2 (1%)
Missing	22 (6%)	3 (3%)	19 (8%)

* These variables only recorded for women reporting at least 1 partner (n=155).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2
HIV-1 viral suppression by pregnancy related follow-up period

(Model limited to 107 women with at least one pregnancy and follow-up visits during periconception, pregnancy and/or postpartum periods.)

Variable	OR (95% CI)	p-value	aOR**	p-value
Periconception follow-up period				
Non-preg follow-up	Reference	Reference	Reference	Reference
Periconception	2.63 (1.44-4.81)	0.002	2.15(1.33,3.49)	0.002
Pregnancy	1.04 (0.63-1.70)	0.890	0.96(0.58,1.58)	0.86
Postpartum	0.91 (0.49-1.71)	0.780	0.84(0.45,1.58)	0.60
Months on treatment				
<12 months	Reference	Reference	Reference	Reference
12-24 months	0.82(0.46,1.45)	0.49	0.82(0.46,1.49)	0.52
≥24 months	0.43(0.21,0.88)	0.02	0.45(0.22,0.95)	0.04
Sex without condoms with >=1 partner, past 3 months *	1.14(0.71,1.84)	0.59		
Number of partners *	0.96(0.63,1.47)	0.85		
Disclosure to partner *				
No	Ref	Ref		
Yes	1.55(0.67,3.56)	0.30		
Not applicable	1.79(0.77,4.17)	0.17		
Partner status *				
HIV-positive	Ref	Ref		
HIV-negative	1.08(0.39,2.97)	0.88		
Don't know status	0.90(0.46,1.79)	0.77		
No partner	1.22(0.73,2.04)	0.45		
Asset index (quintiles)				
1st	Reference	Reference	Reference	Reference
2nd	3.29(1.07,10.17)	0.04	2.53(0.70,9.11)	0.16
3rd	1.15(0.37,3.51)	0.81	0.86(0.24,3.15)	0.82
4th	1.45(0.38,5.54)	0.59	2.18(0.26,18.20)	0.47
5th	1.42(0.35,5.81)	0.63	1.94(0.39,9.70)	0.42

* These variables only recorded for women reporting at least 1 partner.

** Results showed a similar increased likelihood of suppression during the periconception period but also an increase in the odds of suppression during pregnancy in two sensitivity analyses.

a. a. When women missing HIV RNA data were categorized as not suppressed, likelihood of HIV RNA suppression was increased during periconception (aOR 1.81, 95% CI 1.25-2.62, p = .002) and pregnancy (aOR 1.81, 95% CI 1.22-2.70, p = .003) periods, but not during postpartum (aOR 1.59, 95% CI 0.95-2.68, p = .08) all compared to non-pregnancy related follow-up.

b. b. When women missing HIV RNA data were categorized as not suppressed only in the context of a missed visit, the likelihood of suppression was increased during periconception (aOR 1.49, 95% CI 1.01-2.19, p = .04) and pregnancy (aOR 1.80, 95% CI 1.16-2.78, p=.008) visits, but not postpartum (aOR 1.12, 95% CI 0.67-1.88, p = .67) all compared to non-pregnancy related follow-up.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

View publication stats

Table 3

Factors associated with poorer adherence by pregnancy related follow-up period

	Odds of average adherence < 80%				Likelihood of 72 hour gaps/90 days			
Variable	**Univariable OR (95% CI)**	**p-value**	**Multivariable aOR (95% CI)**	**p-value**	**Univariable RR (95% CI)**	**p-value**	**Multivariable aRR (95% CI)**	**p-value**
Periconception follow-up period								
Non-preg follow-up	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Periconception	0.67 (0.50-0.89)	0.005	0.68 (0.52-0.91)	0.01	0.71 (0.59-0.87)	0.001	0.72 (0.59-0.89)	0.002
Pregnancy	1.04 (0.75-1.45)	0.81	0.99 (0.71,1.38)	0.95	0.91 (0.73-1.13)	0.400	0.93(0.74-1.17)	0.53
Postpartum	1.10 (0.77-1.58)	0.61	1.07 (0.74-1.53)	0.73	1.34 (1.08-1.65)	0.007	1.40(1.13-1.73)	0.002
Months on treatment								
<12 months	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
12-24 months	1.09 (0.83-1.43)	0.54	1.09(0.83-1.43)	0.53	1.13 (missing CI)	0.18	1.14 (0.94 – 1.37)	0.18
≥24 months	1.72(1.32-2.24)	<0.001	1.67(1.28-2.19)	<0.001	1.31 (missing CI)	0.002	1.30 (1.07-1.56)	0.005
Sex without condoms with >=1 partner, past 3 months *	0.85(0.65-1.11)	0.23			0.70 (0.58-0.83)	<0.001	0.74 (0.61 – 0.88)	0.001
Number of partners *	0.96 (0.73-1.28)	0.80			0.85 (0.71-1.00)	0.05		
Disclosure to partner *								
Yes	Reference	Reference			Reference	Reference		
No	1.37 (0.77-2.44)	0.29			0.88 (0.59-1.32)	0.53		
Not applicable	1.05 (0.77-1.43)	0.74			1.18 (0.99-1.42)	0.73		
Asset index (quintiles)								
1st	Reference	Reference			Reference	Reference		
2nd	0.53 (0.21-1.35)	0.18			0.82 (0.55-1.24)	0.34		
3rd	0.94 (0.39-2.28)	0.90			0.93 (0.63-1.38)	0.72		
4th	0.78 (0.30-2.04)	0.61			0.70 (0.44-1.12)	0.14		
5th	1.04 (0.42-2.57)	0.93			0.90 (0.59-1.37)	0.61		

* These variables only recorded for women reporting at least 1 partner.