Decreases in Self-Reported ART Adherence Predict HIV Viremia Among Pregnant and Postpartum South African Women

Tamsin K. Phillips, MPH, Ira B. Wilson, MD, MSc,† Kirsty Brittain, MPH,* Allison Zerbe, MPH,‡ Claude A. Mellins, PhD,§ Robert H. Remien, PhD,§ Catherine Orrell, MD, PhD,‖ Elaine J. Abrams, MD,‡¶ and Landon Myer, MD, PhD**

Introduction: Routine HIV viral load (VL) monitoring is recommended for patients on antiretroviral therapy, but frequent VL testing, required in pregnant and postpartum women, is often not feasible. Self-reported adherence can be valuable, but little is known about its longitudinal characteristics.

Methods: We followed women living with HIV from antiretroviral therapy initiation in pregnancy through 18-month postpartum in Cape Town, South Africa, with repeated measurement of VL and self-reported adherence using a 3-item scale. We used generalized estimating equations [with results presented as odds ratios (ORs) with 95% confidence intervals (CIs)] to investigate the association between viremia and change in adherence over pairs of consecutive visits.

Results: Among 2085 visit pairs from 433 women, a decrease in self-reported adherence relative to the previous visit on any of the 3 self-report items, or the combined scale, was associated with VL >50 and >1000 copies per milliliter. The best-performing thresholds to predict VL >50 copies per milliliter were a single-level decrease on the Likert response item "how good a job did you do at taking your HIV medicines in the way that you were supposed to?" (OR 2.08, 95% CI: 1.48 to 2.91), and a decrease equivalent to ≥5 missed doses or a one-level decrease in score on either of 2 Likert items (OR 1.34, 95% CI: 1.06 to 1.69).

Conclusions: Longitudinal changes in self-reported adherence can help identify patients with viremia. This approach warrants consideration in settings where frequent VL monitoring or other objective adherence measures are not possible.

Key Words: antiretroviral therapy, self-reported adherence, viral load

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INTRODUCTION

Antiretroviral therapy (ART) is the cornerstone of HIV treatment and prevention efforts. Current global guidelines recommend that all individuals living with HIV start lifelong ART as soon as they are diagnosed, thereby improving their long-term health outcomes.[1] HIV transmission during pregnancy, labor and delivery, and breastfeeding can be reduced to below 1% in the presence of suppressive ART.[2] However, optimal ART adherence is essential to achieve sustained viral suppression and to realize the treatment and prevention benefits.

Routine HIV viral load (VL) monitoring is being rolled out globally.[3] VL offers an objective marker of treatment success and a signal for poor adherence and antiretroviral resistance, but even with the push to scale up routine VL monitoring, numerous challenges persist.[3,4] During pregnancy and postpartum, ART adherence is a particular concern due to the added risk of vertical HIV transmission.[5,6] An increased frequency of VL testing is recommended during these periods, but this is not always feasible.[7,8] In low-resource settings where

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From the *Division of Epidemiology and Biostatistics, Centre for Infectious Disease Epidemiology and Research, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa; †Department of Health Services, Policy and Practice, Brown University School of Public Health, Providence, RI; ‡ICAP at Columbia University, Mailman School of Public Health, Columbia University, New York, NY; §HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute, Columbia University, New York, NY; ‖Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine and Department of Medicine, University of Cape Town, Cape Town, South Africa; and ¶Vagelos College of Physicians & Surgeons, Columbia University, New York, NY.

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Correspondence to: Tamsin K. Phillips, MPH, Level 5 Falmouth Building, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa (e-mail: tk.phillips@uct.ac.za).

VLs are infrequent or unavailable, other methods of assessing ART adherence are still required.[9]

Self-reported adherence—which is inexpensive, immediate, and easy to administer—is often used to assess ART adherence in both routine care and research settings. Although validated self-reported adherence measures exist, finding an optimal measure has been a focus of much research.[10–13] Self-reported adherence, which can often overestimate individual medication-taking behavior, measures an individual's perception of their treatment adherence.[10] It may be influenced by various biases such as social desirability or recall bias, and this may vary between individuals depending on their own reference points regarding their medication-taking practices.[11,14,15] Despite these issues, self-reported adherence has often shown a reasonable correlation with VL and other objective markers of adherence, including in low-resource settings.[9,11,16]

Although there have been calls for longitudinal adherence measures to assess changes in ART adherence,[17,18] most studies have only evaluated the association between adherence and VL at a single time point. Longitudinal measures provide an opportunity to examine relative changes in reported adherence that could help to account for individual reporting patterns. Predictors of changes in reported adherence have been explored, but few studies have assessed whether changes in reported adherence are associated with an objective marker such as VL.[19–24] Here, we examined self-reported adherence and VL among women living with HIV over multiple measurement points during and after pregnancy and investigate the association between changes in self-reported adherence and viremia.

METHODS

We conducted a longitudinal analysis of women enrolled into a multiphase implementation science study (the MCH-ART study, ClinicalTrials.gov NCT01933477) that has been described previously.[25] Women were followed from ART initiation during pregnancy for upto 18 months postpartum. Study visits occurred 2–3 times during pregnancy (depending on gestational age), once shortly after delivery and approximately every 3 months thereafter.

Setting

Women were recruited into the parent study between April 2013 and June 2014 when they presented for antenatal care at a large primary care antenatal and obstetric care clinic in Gugulethu, Cape Town, with follow-up through January 2016. This setting is characterized by high levels of poverty and unemployment, and a very high burden of HIV.[26] The local antenatal HIV prevalence was estimated to be 22% in 2015,[27] and all women starting ART received a fixed-dose combination of efavirenz, tenofovir, and emtricitabine.[28]

Measures

Data were collected at study visits, which occurred independently of routine HIV and antenatal care. Interviews were conducted by trained interviewers in the predominant local language, isiXhosa. Demographic characteristics including age, marital status, employment, and timing of HIV diagnosis were collected at the time of enrollment. CD4 cell count and gestational age at presentation for antenatal care were abstracted from routine medical records.

Self-reported adherence was measured using a simple 3-item adherence scale that was developed through a process of rigorous cognitive interviewing and has been validated in the United States.[29–31] It was translated into isiXhosa for use in South Africa, and the cross-sectional validity of the translated individual scale items and the overall scale score were evaluated previously in this setting (Cronbach α = 0.79).[32] The 3 items in the scale (Table 1) include a quantification of missed doses and 2 Likert response scales that ask patients "how good a job did you do taking your medications in the way you were supposed to?" and "how often did you take your medications in the way that you were supposed to?" all with reference to the past 30 days. To analyze the combined scale score, these 3 items were aggregated based on a recoding of each item with equal weighting, to create a score ranging from 0 to 100, with the latter representing the best possible self-reported adherence.

HIV RNA VL, the "gold standard" in our analyses, was measured at each study visit on the same day as the self-reported adherence scale was administered. Separate from routine HIV care services, venous blood was collected and batch tested by the National Health Laboratory Services (Abbott RealTime HIV-1 assay, Abbott Laboratories, Lake Bluff, IL), with results only available at the end of the study period.

Visits

Women were included in analyses from their first suppressed VL after ART initiation (V_0). To minimize potential bias introduced by attrition from the study, we included only women who had at least 4 consecutive study visits after V_0 in primary analyses of self-reported adherence and VL over time (n = 363). Data on trends over time for all women where at least one visit with both an adherence and a VL measure was available after V_0 are presented in Supplemental Digital Content, http://links.lww.com/QAI/B240 (n = 434). We examined changes in self-reported adherence from each visit (V_i) to the next visit (V_{i+1}) among all available visit pairs from initial viral suppression (or from 16 weeks on ART in sensitivity analyses). V_{i+1} was defined as the first visit occurring 1–6 months after V_i. The women and visits included in each analysis are provided in Figure 1A, and the visit pair structure is provided in Figure 1B.

Adherence and Viral Load Thresholds

To describe the adherence scale score over time, thresholds of 100 versus <100 and ≥ 80 versus <80 were used. In previous work, these cut-offs produced a reasonable balance between sensitivity and specificity.[32] To analyze changes in adherence score from V_i to V_{i+1}, we used a simple approach that could potentially be applied in routine care. We

TABLE 1. Description of Items in the 3-Item Self-Reported Adherence Scale and the Thresholds Used to Assess Change in Adherence Across Visits

Item	Threshold
1. E: In the last 30 days, on how many days did you miss at least one dose of any of your HIV medicines?	Stayed the same
X: Kwintsuku ezi-30 ezidlulileyo, zimini ezingaphi okhe walibala ukutya amchiza akho entsholongwana?	Increased by ≥1 missed dose
Range 0–30	Decreased by ≥1 missed dose
2. E: In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to?	Stayed the same
X: Kwintsuku ezi-30 ezidlulileyo, zimini ezingaphi okhe walibala ukutya amchiza akho entsholongwana?	Increased by ≥1 level
Range "very poor" to "excellent" (1–6)	Decreased by ≥1 level
3. E: In the last 30 days how often did you take your HIV medicines in the way that you were supposed to?	Stayed the same
X: Kwezi ntsuku zi-30 zidlulileyo, kukangaphi usitya amachiza akho entsholongwane ngendlela omele kuwatya ngayo?	Increased by ≥1 level
Range "never" to "always" (1–6)	Decreased by ≥1 level
Combined 3-item scale, range 0–100	Change ≤1 missed dose, both Likert items stayed the same
	Score increased ≥2 missed doses
	Score decreased ≥2 missed doses
	Change ≤4 missed doses, both Likert items stayed the same
	Increased by ≥1 level or ≥5 missed doses on any item
	Decreased by ≥1 level or ≥5 missed doses on any item
	Change ≤9 missed doses or 1 level change in either Likert item
	Increased by ≥2 levels or ≥10 missed doses on any item
	Decreased by ≥2 levels or ≥10 missed doses on any item

E, English; X, isiXhosa.

determined thresholds based on the minimum possible change in each self-reported adherence item. For item 1, reporting missed doses during the past 30 days, we examined a change of a single missed dose. For the other 2 items, 6-level Likert-type responses, a one-level change in response was examined. Larger changes in reported adherence were explored in sensitivity analyses; however, there were very few visit pairs with larger changes, and thus these data are not presented. For the combined scale score, we examined changes ranging from a single missed dose change in item 1 or a one-level change in either of the Likert rating items, through to a change of ≥10 missed doses or ≥2 level change in either of the Likert rating items. All the change thresholds are outlined in Table 1. VL thresholds of >50 and >1000 copies per milliliter were examined based on the South African National ART guideline definitions of suppression and flags for treatment failure.[33]

Analyses

Data were analyzed in Stata v14.0 (Stata Corporation, College Station, TX). Means with SD or medians with interquartile ranges (IQRs) were used to describe continuous variables. Frequencies and proportions were used to describe categorical variables. Regression coefficients (as slopes) with standard error (SE) and χ^2 tests for trend were used to assess trends in reported adherence and VL over time.

Generalized estimating equations with robust SE and exchangeable correlation structures were used to explore the association between changes in reported adherence from V_i to V_{i+1} and VL at V_{i+1}.[13,34] Quasi-likelihood under the independence model criterion, a modification of the Akaike information criterion, was used for model selection.[35] We included baseline self-reported adherence, VL at V_i and time between V_i and V_{i+1} in all models, and examined additional baseline covariates (maternal age, marital status, education, employment, gravidity, gestational age at presentation for antenatal care, timing of diagnosis, and CD4 cell count) that are often available in routine care and have previously been found to be associated with poor adherence or loss of follow-up.[36] We then selected the final adjusted model based on the lowest quasi-likelihood under the independence model criterion. Model results were reported as crude [odds ratio (OR)] and adjusted ORs (aOR) with 95% confidence intervals (CIs).

Primary analyses included all women who achieved viral suppression after ART initiation and who had at least one visit with both adherence and VL data available after initial suppression (n = 434; 92% of the total cohort of 471). Sensitivity analyses were conducted including an additional 17 women who did not achieve viral suppression but had adherence and VL measurements after 16 weeks on ART. These results were very similar and are presented in Supplemental Digital Content, http://links.lww.com/QAI/B240.

Ethics

All women included in this analysis provided written informed consent on enrollment into the parent study. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Columbia University Institutional Review Board and the University of Cape Town Human Research Ethics Committee.

RESULTS

Among 471 women followed in the parent cohort, 37 women were excluded from analyses either because they were never observed to reach viral suppression (n = 24), or they did not have at least one visit with adherence and VL measured

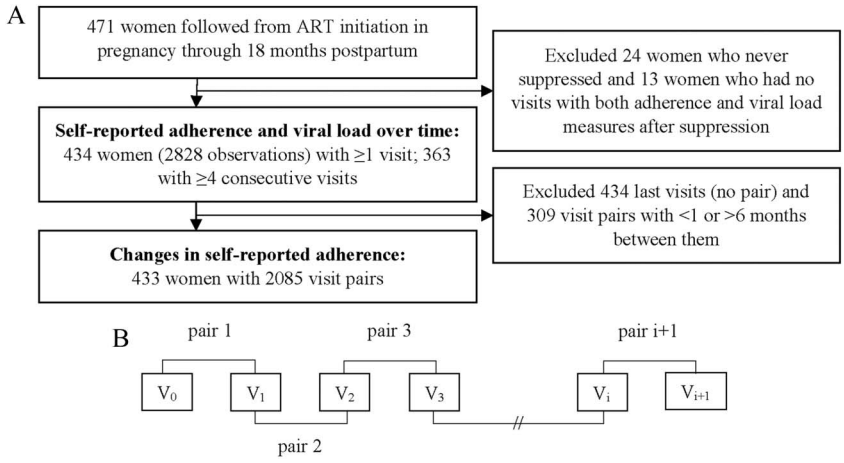

FIGURE 1. A, Flow diagram of patient and visit inclusion and (B) schematic of visit pairs where the first visit (V_0) is the first suppressed visit after ART initiation in pregnancy.

after achieving suppression (n = 13). A total of 2828 visits were available from 434 included women [mean 4 visits per woman after initial viral suppression (range 1–9)]. The median age was 28 years (IQR 25–33), 41% were married or cohabiting, and 56% had been diagnosed with HIV in the incident pregnancy (Table 2). Only 18% were in their first pregnancy, and median gestational age at presentation for antenatal care was 21 weeks (IQR 16–26). Adherence and VL over time were examined among women who had at least 4 consecutive visits after initial suppression (n = 363) to minimize the impact of attrition, as well as among all 434 women. Women excluded were younger, more likely to be in their first pregnancy, presented later for antenatal care and had slightly lower baseline CD4 cell counts compared with the women included (Table 2).

Self-Reported Adherence and Viral Load Over Time

Among women with at least 4 visits after initial suppression (n = 363), the proportion reporting adherence scores ≥80 increased slightly over time (slope 0.024, SE 0.004; χ^2 for trend $P < 0.001$) while the proportion with VLs ≤1000 copies per milliliter decreased (slope −0.028, SE 0.003; χ^2 for trend $P < 0.001$) (Fig. 2). These patterns were consistent when including all 434 women (see Figure 2, Supplemental Digital Content, http://links.lww.com/QAI/B240) and in sensitivity analyses including women who did not suppress after ART initiation (see Figure 3, Supplemental Digital Content, http://links.lww.com/QAI/B240). Although individual fluctuations in reported adherence were observed (see Figure 1, Supplemental Digital Content, http://links.lww.com/QAI/B240), the median reported adherence remained stable over time (see Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B240).

Association Between Changes in Self-Reported Adherence Score and Viral Load

To analyze changes in reported adherence, 2085 visit pairs were available for 433 women [mean 3 visit pairs per woman (range 1–8)]. The average time between V_i and V_{i+1}

TABLE 2. Descriptive Characteristics of Women at the Time of Presentation for Antenatal Care, Presented as n (%) Unless Otherwise Stated

	Included, ≥4 Consecutive Visits After First Viral Suppression	Excluded	Included, ≥1 Visit After First Viral Suppression	Excluded	All Women in the Parent Cohort
No. of women	363 (77)	108 (33)	434 (92)	37 (8)	471
Median age (IQR)	28 (25–33)	27 (23–31)	28 (25–33)	26 (23–30)	28 (24–32)
Age ≤25	95 (26)	42 (39)	121 (28)	16 (43)	137 (29)
Married/cohabiting	152 (42)	41 (38)	178 (41)	15 (41)	193 (41)
Completed secondary school	87 (24)	30 (28)	104 (24)	13 (35)	117 (25)
Employed	143 (39)	41 (38)	169 (39)	15 (41)	184 (39)
First pregnancy	60 (17)	27 (25)	78 (18)	9 (24)	87 (18)
Diagnosed with HIV in this pregnancy	199 (55)	69 (64)	245 (56)	23 (62)	268 (57)
Median CD4 (IQR)	355 (254–544)	327 (214–469)	354 (251–534)	284 (173–456)	354 (248–517)
Median weeks gestation (IQR)	20 (16–25)	24 (19–30)	21 (16–26)	25 (21–31)	21 (16–26)
Median adherence score at first visit on ART	89 (78–94)	89 (78–94)	89 (78–94)	93 (78–94)	89 (78–94)

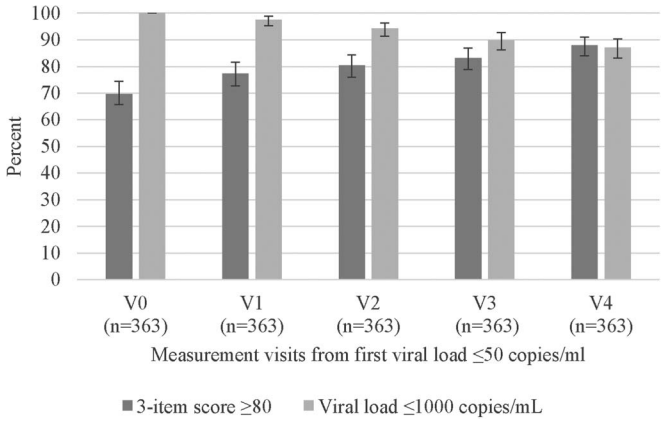

FIGURE 2. The proportion of women with adherence scores ≥80 and HIV viral loads ≤1000 copies per milliliter among 363 women with at least 4 study visits after V_0 (first visit with a viral load ≤50 copies per milliliter after ART initiation during pregnancy). Data are shown from V0 through 4 additional visits (V1–V4).

was 2.4 months (SD 1.1). An adherence score ≥80 was reported at V_i in 81% and at V_{i+1} in 83% of visit pairs. VL at V_i and V_{i+1} was ≤50 copies per milliliter in 89% and 84% of visit pairs, and ≤1000 copies per milliliter in 93% and 89% of visit pairs, respectively. Overall, VL remained below 50 copies per milliliter in most visit pairs. VL declined from >50 to ≤50 copies per milliliter in only 1% of visit pairs and increased from ≤50 to >50 copies per milliliter in 5% of pairs (see Table 2, Supplemental Digital Content, http://links.lww.com/QAI/B240).

The results of univariable generalized estimating equation models predicting VL >50 and >1000 copies per milliliter at V_{i+1}, independent of the VL measure at V_i, are presented in Table 3. Using the change thresholds outlined in Table 1 for a minimum change in each individual item and 3 different change thresholds on the combined scale score, a decrease in score was associated with VL >50 and >1000 copies milliliter. These results persisted in sensitivity analyses that included women who had never suppressed but who had at least 16 weeks on ART (see Table 3, Supplemental Digital Content, http://links.lww.com/QAI/B240). In stratified analyses restricted to visit pairs where the VL at the first visit of the pair (V_i) was ≤50 copies per milliliter (1852 visit pairs), the strength of association increased. However, when restricted to women who already had a raised VL at V_i (126 visit pairs), a change in reported adherence was no longer predictive of having a raised VL at V_{i+1} (Table 3).

Multivariable models were examined for the 2 thresholds with the strongest associations: Item 2 "how good a job did you do at taking your HIV medicines in the way that you were supposed to?" and the combined 3-item scale threshold of a change of one level on either of the Likert items or ≥5 missed doses. A single-level decrease in reported adherence on item 2 remained predictive of having a VL >50 and >1000 copies per milliliter (aOR 2.62, 95% CI: 1.57 to 4.30 and aOR 1.91, 95% CI: 1.15 to 3.17, respectively) in adjusted models (see Table 4, Supplemental Digital Content, http://links.lww.com/QAI/B240). Similarly, a decrease in self-reported adherence score equivalent to ≥5 missed doses or a one-level decrease in score on either item 2 or 3 also remained predictive of VL >50 and >1000 copies per milliliter (aOR 1.62, 95% CI: 1.11 to 2.38 and aOR 1.42, 95% CI: 1.00 to 2.03, respectively). Again, these results were consistent in sensitivity analyses (see Table 5, Supplemental Digital Content, http://links.lww.com/QAI/B240). In all analyses, there was no association between an improvement in reported adherence and odds of viral suppression at V_{i+1}. Increasing age, being married/cohabiting and being employed all independently reduced the odds of having a raised VL, while increasing months on ART, presenting later for antenatal care, having a VL >50 or >1000 copies per milliliter at V_i, and increasing time between Vi and Vi+1, increased the odds of having a VL >50 and >1000 copies per milliliter at V_{i+1} (see Table 4, Supplemental Digital Content, http://links.lww.com/QAI/B240; univariable associations presented in Table 6, Supplemental Digital Content, http://links.lww.com/QAI/B240).

DISCUSSION

In this cohort of women living with HIV who were followed from ART initiation during pregnancy through 18-month postpartum, decreases in self-reported adherence relative to the previous visit were independently predictive of raised VL. Self-reported adherence remained high over repeated follow-up visits, and despite decreases in the proportion of women with viral suppression over time, more than 80% of women attending each visit were virally suppressed.

With a rapidly growing population on ART, routine VL monitoring is recommended at least annually with increased frequency during pregnancy and breastfeeding, but not all settings are able to implement such frequent VL testing.[3,8] Assessing change in reported adherence may provide an interim assessment to flag patients requiring additional intervention between VL measures. The association between reporting decreased adherence and having a raised VL in our cohort was most marked when restricted to visits where the VL at the previous visit was suppressed. When participants had an unsuppressed VL at the first visit of the pair, a decline in reported adherence did not predict viremia. However, in this adherent cohort, there were relatively few such cases, which reduced statistical power to detect these differences. In routine practice, this may be less of a concern as women with any raised VLs should already be flagged for further intervention. One possible application may be to measure change in reported adherence after a suppressed VL as an interim screening tool to prompt adherence counseling or VL testing only among women reporting worse adherence. Further exploration of the utility and application of this approach is warranted in routine care settings where resources limit the frequency of VL testing or other objective adherence measures.

Self-reported adherence measures, although subject to well-documented biases, present the patient's perception of their own adherence behavior, for example, some patients may miss a few doses and report excellent adherence while

TABLE 3. Univariable Generalized Estimating Equation Models for Change in Each Reported Adherence From V_i to V_{i+1} to Predict Viremia >50 and >1000 copies per milliliter at V_{i+1} in all Visit Pairs and Stratified by Viral Load ≤50 or >50 copies per milliliter at V_i.

	All Visit Pairs			Pairs with V_i Viral Load ≤50 Copies Per Milliliter		Pairs with V_i Viral Load >50 Copies Per Milliliter	
No. of women	433			428		126	
No. of visit pairs	2085			1852		233	
	No. of visit pairs, N (%)	**To predict VL >50 copies per milliliter**	**To predict VL >1000 copies per milliliter**	**To predict VL >50 copies per milliliter**	**To predict VL >1000 copies per milliliter**	**To predict VL >50 copies per milliliter**	**To predict VL >1000 copies per milliliter**
Change in item 1 (missed dose)							
No change in missed doses	1621 (78)	Ref	Ref	Ref	Ref	Ref	Ref
Increased ≥1 missed dose	223 (11)	0.95 (0.65–1.40)	0.97 (0.62–1.23)	0.96 (0.54–1.71)	1.37 (0.71–2.65)	1.28 (0.51–3.21)	0.85 (0.41–1.76)
Decreased ≥1 missed dose	241 (12)	**1.45 (1.07–1.97)**	**1.41 (1.04–1.93)**	**1.72 (1.11–2.66)**	1.54 (0.84–2.81)	1.87 (0.71–4.92)	1.64 (0.87–3.07)
Change in item 2 (good job)							
No change	1824 (87)	Ref	Ref	Ref	Ref	Ref	Ref
Increased ≥1 level	139 (7)	1.07 (0.70–1.64)	0.93 (0.55–1.58)	0.98 (0.49–1.94)	0.72 (0.26–1.97)	2.36 (0.53–10.52)	1.83 (0.88–3.78)
Decreased ≥1 level	122 (6)	**2.08 (1.48–2.91)**	**1.89 (1.33–2.68)**	**2.30 (1.32–3.99)**	**2.09 (1.03–4.25)**	5.57 (0.80–38.64)	1.85 (0.67–3.93)
Change in item 3 (how often)							
No change	1600 (77)	Ref	Ref	Ref	Ref	Ref	Ref
Increased ≥1 level	240 (12)	0.98 (0.72–1.33)	0.76 (0.51–1.34)	1.23 (0.75–2.00)	1.09 (0.55–2.16)	0.83 (0.33–2.12)	0.61 (0.30–1.23)
Decreased ≥1 level	245 (12)	1.34 (0.98–1.83)	1.10 (0.79–1.54)	**1.72 (1.09–2.71)**	1.73 (0.97–3.09)	1.73 (0.63–4.75)	0.82 (0.43–1.57)
Change in combined score							
No change in missed doses	565 (27)	Ref	Ref	Ref	Ref	Ref	Ref
Increased ≥1 missed dose	784 (38)	1.00 (0.78–1.27)	0.96 (0.73–1.25)	1.08 (0.70–0.66)	1.05 (0.58–1.89)	1.04 (0.45–2.40)	0.94 (0.51–1.76)
Decreased ≥1 missed dose	736 (35)	1.23 (0.98–1.54)	1.22 (0.96–1.55)	**1.53 (1.01–2.31)**	1.72 (0.99–2.97)	1.00 (0.43–2.32)	1.03 (0.57–1.87)
Change ≤4 missed doses	1209 (58)	Ref	Ref	Ref	Ref	Ref	Ref
Increased ≥1 levels or ≥5 missed doses	447 (21)	1.02 (0.78–1.34)	0.95 (0.69–1.30)	1.19 (0.78–1.81)	1.23 (0.42–2.12)	1.21 (0.54–2.72)	1.08 (0.60–1.93)
Decreased ≥1 levels or ≥5 missed doses	429 (21)	**1.34 (1.06–1.69)**	**1.32 (1.05–1.68)**	**1.69 (1.16–2.47)**	**1.71 (1.05–2.78)**	1.19 (0.55–2.57)	1.37 (0.79–2.36)
Change ≤9 missed doses or 1 level	1321 (63)	Ref	Ref	Ref	Ref	Ref	Ref
Increased ≥2 levels or ≥10 missed doses	387 (19)	0.94 (0.72–1.24)	0.87 (0.63–1.21)	1.19 (0.78–1.82)	1.24 (0.71–2.16)	1.28 (0.53–3.11)	1.09 (0.61–1.92)
Decreased ≥2 levels or ≥10 missed doses	377 (18)	**1.29 (1.02–1.63)**	1.28 (0.99–1.65)	**1.65 (1.11–2.45)**	**1.76 (1.07–2.90)**	1.25 (0.56–2.77)	1.22 (0.66–2.24)

Results are presented as ORs with 95% CIs; statistically significant associations are in bold.

others may miss the same number of doses and report very poor adherence. Assessing a change in reported adherence in an individual over 2 consecutive visits could be a straightforward way for providers to flag emerging adherence problems, relative to each patient's individual reporting. We found that, on average, women with viremia >50 or >1000 copies per milliliter had increased odds of reporting worsening adherence across 2 visits on one or more of the 3 adherence scale items. These findings persisted after adjusting for duration between visits, VL at the previous visit, and other covariates. Previous studies have used similar methods to assess the predictors of changes in reported adherence, but few have linked this change to a biological or objective adherence marker.[21,22,24] The 3 individual scale items examined independently did not all perform equally. The second item, a Likert rating scale of how good a job you did taking your medication in the last 30 days, had the highest point estimates (OR 2.08, 95% CI: 1.48 to 2.91 to detect VL >50 copies per milliliter). An additional benefit of this change in adherence approach is that no adherence score conversions would be required. A provider could, for example, plot a patient's response to each of the 3 questions at each visit. A patient reporting a poorer score on any or a combination of the questions could be flagged for further evaluation and appropriate interventions. Whether longitudinal changes in adherence could be assessed in this way or even using a single item merits testing in other populations and in routine care settings.

Although the strength of this study is the very well-characterized cohort contributing over 2800 visits, it is important to note that there was attrition over time. Women excluded from these analyses were younger, more likely to be in their first pregnancy, presented later for antenatal care, and had lower CD4 cell counts compared with the overall cohort. These characteristics are all potential risk factors for loss to follow-up and poor ART adherence.[36] In pregnant and postpartum women, younger age in particular has been consistently found to predict loss to follow-up and poor adherence.[36,37] By including only the available data, selection bias was introduced, and women at higher risk of poor adherence or viremia are likely to have been excluded. Although this is a limitation, it is equivalent to the selection bias that would be present in the monitoring of ART services in routine care settings. This emphasizes the importance of comprehensive efforts to retain all people living with HIV in ART services.

The longitudinal relationships between changes in self-reported adherence and VL will likely vary depending on the distribution of reported adherence and VL levels in the population being examined, the population sampled (eg, pregnant and postpartum women), and other contextual factors. Here, we studied pregnant and postpartum women from a single site in Cape Town, South Africa. This is likely representative of other urban sites in South Africa and sub-Saharan Africa, but generalizability to other settings and populations should be considered with caution. All adherence and VL measures were taken as part of research study visits, independent of routine HIV care, which may have reduced socially desirable response bias. Language and context translation are complex issues that may have impacted these results. The self-report scale was translated into isiXhosa directly from the questions designed and validated in the United States, and translation could partly explain the differences observed between the individual adherence items. Results may be strengthened by exploring cognitive interviewing approaches in the local language. We studied a population with excellent adherence and high rates of viral suppression for whom, in most cases, adherence could only decrease. It would be important to repeat this analysis in less-adherent populations for whom adherence could both increase and decrease. Finally, we were unable to assess the association between changes in self-reported adherence and an objective adherence marker, such as electronic drug monitoring or drug-level monitoring, which may be better "gold standard" measures of adherence behaviors than VL.

CONCLUSIONS

In this cohort of South African women who initiated ART during pregnancy as part of routine care, self-reporting worse adherence relative to the previous visit on any of 3 simple adherence questions, and specifically, the Likert item asking how good a job you did taking your medications in the way you were supposed to was consistently associated with viremia. These results show that changes in self-reported adherence could provide a simple flag for women at risk for raised VLs. This approach warrants further consideration in the context of monitoring ART adherence in settings with limited access to VL and objective adherence monitoring.

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