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Menstrual cycle phase and single tablet antiretroviral medication adherence in women with HIV

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39

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ABSTRACT

Suboptimal adherence to antiretroviral (ARV) therapy among HIV-infected individuals is associated with increased risk of progression to AIDS and the development of HIV resistance to ARV medications. To examine whether the luteal phase of the menstrual cycle is independently associated with suboptimal adherence to single tablet regimen (STR) ARV medication, data were analyzed from a multicenter cohort study of HIV-infected women who reported regular menstrual cycles and were taking a STR. In a cross-sectional analysis, suboptimal adherence to a STR among women in their follicular phase was compared with suboptimal adherence among women in their luteal phase. In two-way crossover analyses, whereby the same woman was assessed for STR medication adherence in both her follicular and luteal phases, the estimated exact conditional odds of non-adherence to a STR was measured. In adjusted logistic regression analysis of the cross-sectional data (N=327), women with ≤12 years of education were more than 3-times more likely to have suboptimal adherence (OR=3.6, p=0.04) compared to those with >12 years of education. Additionally, women with Center for Epidemiological Studies Depression Scale (CES-D) scores ≥23 were 2.5-times more likely to have suboptimal adherence (OR=2.6, p=0.02) compared to those with CES-D scores <23. In conditional logistic regression analyses of the crossover data (N=184), having childcare responsibilities was associated with greater odds of ≤95% adherence. Menstrual cycle phase was not associated with STR adherence in either the cross-sectional or crossover analyses. The lack of association between phase of the menstrual cycle and adherence to a STR in HIV-infected women means attention can be given to other

10
83more important risk factors for suboptimal adherence, such as depression, level of education, and

84childcare responsibilities.

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86**Keywords:** HIV, medication adherence, menstrual phase, women

87

INTRODUCTION

Suboptimal adherence to antiretroviral (ARV) therapy among HIV-infected individuals is associated with increased risk of progression to AIDS and the development of HIV resistance to ARV medications . Many factors can influence ARV medication non-adherence including medication side-effects, high pill burden, frequent dosing schedules, substance use, depression, stress, food restrictions, lack of social support, and patients' beliefs .

HIV-infected women may be more vulnerable to ARV medication non-adherence than HIV-infected men, due to higher rates of depressive symptoms, partner violence, fear of disclosure, child care responsibilities, and lack of support from interpersonal relationships . Additionally, the hormonal effects of the menstrual cycle may have an impact on taking one's ARV medication as prescribed . These hormonal effects include a change in cognition, mood, and premenstrual symptoms during the luteal phase .

The relationship between fluctuating hormone levels during the menstrual cycle phases and chronic illnesses have been previously explored. In the context of chronic mental illness, schizophrenic patients were found to be at an increased risk of a psychiatric hospitalization after ovulation (in the luteal phase) when estradiol levels are decreasing . Declining levels of estradiol during the luteal phase has also been associated with worsening of other chronic illnesses including systemic lupus erythematosus, multiple sclerosis, asthma, diabetes, and arrhythmia . Thus, in addition to change in cognition, mood, and premenstrual symptoms, HIV disease symptoms may also worsen during the luteal phase and reduce ARV medication adherence.

The newer ARV medications have several advantages over the older drugs, including improved formulations (such as single tablet regimens-STR) and lower levels of adherence

14
110necessary to achieve viral suppression . The lower pill burden, less frequent dosing, and lower
111level of adherence necessary to keep the virus in check are important innovations but these new
112drugs require additional study to understand the remaining barriers (such as the effect of the
113menstrual cycle) to the lower levels of medication adherence.

114 Using a cross-sectional approach, we examined whether the menstrual cycle phase in
115regularly menstruating premenopausal HIV-infected women on a single tablet ARV regimen was
116independently associated with ARV adherence. Based on the literature regarding adverse effects
117of the post-ovulatory menstrual phase on cognition, mood, and symptomatology, we
118hypothesized that HIV-infected women in their follicular phase would report higher 3-day
119adherence to ARV medication than women in their luteal phase, after adjusting for factors
120known to affect medication adherence.

121 Additionally, using a within-subject observational two-way crossover design comparing
122follicular to luteal menstrual phase, we also examined whether HIV-infected women reported
123better 3-day adherence to single tablet ARV regimens in the follicular phase compared to the
124luteal phase. We hypothesized that a woman would have higher adherence to single tablet ARV
125medication during her follicular phase than during her luteal phase.

126

127**MATERIALS AND METHODS**

128**Study population**

129 From October 1994 and through March 2013, the longitudinal Women's Interagency HIV
130Study (WIHS) enrolled 4,137 women of whom 3,067 were HIV-infected at entry and an
131additional 23 became HIV-infected during study follow-up. Enrollment occurred at six study

centers in the United States (Chicago, Los Angeles, two in New York city, San Francisco, and Washington DC) and the WIHS methods, baseline characteristics, and participant retention rates have been previously described . Study protocols were approved by the institutional review boards at all sites and informed consent was obtained.

Semi-annually, WIHS participants were interviewed, had blood collected, and underwent a physical examination. Among HIV-infected women, blood was tested for CD4+ lymphocyte counts and HIV RNA levels. At each study visit, women were asked detailed information about their adherence to ARV medication and the date of their last menstrual period. For this investigation, the inclusion criteria were HIV-infected women who reported regular menstrual cycles (no reports of a period at least 3 days early or late in the past 6 months) and taking a single tablet ARV regimen anytime between October 1st 2005 and March 31st 2013 (including participants who were ARV-naïve prior to starting the STR and those who were ARV-exposed). We restricted our analyses to women taking single-tablet ARVs (Trizivir®, Atripla®, Complera®, and Stribild®; Table 1) to minimize the complexity of trying to combine the 3-day adherence measures for each individual drug and to eliminate confounding from complex regimens that may be more difficult to adhere to. Exclusion criteria consisted of women who: 1) were pregnant or breastfeeding, 2) had hysterectomy or oophorectomy, 3) used exogenous hormones, or 4) had irregular menstrual cycles. For this investigation, and to minimize recall bias and match up with the phase of the menstrual cycle, the adherence measure used in the analyses was self-reported ARV adherence in the past 3 days and was asked as follows. “Please indicate on the response card your best guess about how much (DRUG NAME) you have taken in the past 3 days?” There were 20 different response card choices ranging from 0-5% to 96-

18
154100%, in increments of 5%. Photographic medication cards were used to aide in identifying each
155drug used by the participant.
156
157**Study Design**
158 There were two parts to our current study. Part I followed a cross-sectional design where
159the dependent variable was STR adherence and the primary independent variable was the phase
160of the menstrual cycle categorized as either follicular or luteal. The follicular phase was
161determined to be two to 15 days after the last menstrual period and the luteal phase was days 0-1
162or 18 to 35 following the last menstrual period (Figure 1). To avoid misclassification of cycle
163phase, women in between the two phases (days 16-17) of their menstrual cycle were excluded. If
164a woman had multiple visits where she met the inclusion criteria, the data from the most recent
165visit were used for analysis.
166 Part II followed a crossover study where each woman served as her own control. STR
167adherence was evaluated during both the follicular and the luteal phase for the same woman but
168at a different 6-month visit. Women in Part II were a subset of those in Part I and had data
169available during each of the two phases of their menstrual cycle. Once again, if a woman had
170multiple visits where she met the inclusion criteria, the most recent visit was used for analysis.
171
172**Measures**
173 The primary outcome of interest was ARV medication adherence $\leq$95% of the time (yes
174or no). The cutoff of $\leq$95% is a conservative measure of suboptimal adherence since studies
175have reported differing levels of adherence necessary to obtain virologic suppression for the

176different ARV classes as well as within the class of protease inhibitors . Our primary
177independent variable was menstrual cycle phase (follicular or luteal). Other covariates
178considered in the analyses included socio-demographic characteristics (age in years,
179race/ethnicity [African American, Latina, White, and others], interview language [English or
180Spanish], educational attainment, annual household income, place of residence [lives in their
181own apartment or house, yes or no] , employed [yes or no], health insurance status [yes or no],
182gravidity, parity, childcare responsibility [yes or no], and living with partner status [yes or no]),
183behavioral factors (smoking status [current, former, never], number of alcoholic drinks per week,
184and recreational drug use in the past six months [yes or no]), health-related information [self-
185reported health rating on a 5-point scale ranging from 1=excellent to 5=poor] , pregnancy in the
186past 6 months, the Center for Epidemiological Studies Depression Scale [CES-D] score
187dichotomized as either $\geq$23 [the higher symptomatic threshold] or $\geq$16 [the standard cutoff] ,
188body mass index [kg/m^2] categories, waist circumference [cm], self-reports of memory or
189concentration problems [yes or no], prior clinical AIDS diagnosis [yes or no], CD4+ cell
190count/mm^3, and HIV RNA copies/mL) and medication-related information (use of psychiatric
191medication [yes or no] and current number of non-ARV prescription medications).
192

193**Statistical Analysis**

194 In part I, we compared the distribution of participant characteristics by menstrual phase
195using contingency tables, and *p* values were calculated using chi-square (when all cells had more
196than 5 observations) or Fisher exact tests (if any cells had less than 5 observations) as
197appropriate. Unadjusted and adjusted logistic regression was used to estimate the odds ratios

(OR) and 95% confidence intervals (CI) for independent variables in relation to ≤95% STR adherence. Logistic regression power calculations were performed using our total sample size and an alpha=0.1. Covariates with $p<0.10$ in unadjusted models were entered into the multivariate model, in addition to menstrual cycle phase (the primary independent variable), for the respective outcomes. The final model fit was assessed using the Hosmer and Lemeshow goodness of fit test.

For part II analyses, exact conditional matched-pair logistic regression was performed to determine the odds ratios and 95% confidence intervals for independent variables to ≤95% STR adherence. In this crossover design, only time varying covariates (covariates that could change from one visit to the next) were assessed in the Part II models since fixed covariates did not change from one visit to the next. Each time varying covariate was evaluated separately while controlling for menstrual cycle phase. All statistical analyses were performed using SAS® software version 9.3 and all reported p-values were two-sided.

RESULTS

Part I - Cross-sectional Design

Three hundred and twenty-seven women met inclusion criteria: 170 in the follicular phase group and 157 in the luteal phase group. The majority of women reported taking Atripla (65%), being 96-100% adherent to their ARV regimen (90%), were >35 years old (83%), were African American (63%), and were not employed (63%). The participants' characteristics were not significantly different for women who had their study visits during their follicular phase compared to women who had their study visits during their luteal phase (Table 2).

In unadjusted analyses for ≤95% adherence to STR ARV (N=34), ≤12 years of education (compared to >12 years, OR=3.38, 95% CI=1.16-9.87) and depressive symptoms (CES-D ≥23, OR=2.63, 95% CI=1.22-5.67) were associated with a higher odds of suboptimal adherence (Table 3). Obesity was marginally associated with suboptimal adherence (OR=1.99, 95% CI=0.94-4.24). Menstrual cycle phase was not associated with STR adherence. When a CES-D score of ≥16 was used (a less restrictive cutoff), depressive symptoms remained significant (OR=2.21, 95% CI=1.07-4.57; data not shown). For this investigation, the power was 76% with a sample size of 327, odds ratio of 0.64, response rate of 10.4%, and alpha of 0.1.

After adjustment for menstrual cycle phase, years of education, CES-D ≥23, and obesity, women with ≤12 years of education were 3.5 times more likely to be non-adherent (95% CI=1.04-12.2) than women with >12 years of education. Additionally, women with CES-D scores ≥23 were more than 2.5 times more likely to be non-adherent (95% CI=1.15-5.90) compared to women with CES-D scores <23. Luteal phase of the menstrual cycle was not significantly associated with suboptimal adherence (OR=0.71, 95% CI=0.33-1.53). The adjusted model fit the data well (chi-square p-value=0.42).

Part II - Crossover Design

We identified a subset of 184 women from Part I who met the inclusion criteria for Part II. Women in Part II were not significantly different from those in only Part I in regards to age, race/ethnicity, education, or language of interview (all p-values >0.05). In addition, there was no difference based on which phase was assessed first (luteal or follicular, p=0.26). In exact conditional regression models adjusted for menstrual phase, having childcare responsibilities was

associated with a greater odds of ≤95% adherence (OR=9.7, 95% CI=1.53-Infinity) however the upper 95% confidence interval included infinity (Table 4). None of the other variables, including the phase of the menstrual cycle, were statistically significant in unadjusted or adjusted models (all p-values >0.05).

DISCUSSION

Understanding the obstacles to attaining high levels of adherence to ARV medication is important among individuals with multiple comorbidities and challenging living situations. In women, it is also important to consider whether hormonal fluctuations contribute to or confound the association with suboptimal medication adherence. However, studying the effect of menstrual cycle phase on medication adherence is difficult because of the need for a large number of subjects, sufficient follow-up time, and the additional information required to disentangle the hormonal influence from other potential confounders.

While a few studies have assessed the effect of the phase of the menstrual cycle on behaviors such as smoking , little is known about the effect of the menstrual cycle phase on medication adherence. One study of 54 HIV-positive women reported no relationship between drug adherence and the weeks of the menstrual cycle, although certain symptoms (feeling sad or depressed) were associated with both the menstrual cycle phase and ARV non-adherence . Another study reported that women with menstrual disorders reported worse ARV adherence .

Our study examined whether the menstrual cycle phase alters adherence to single tablet ARV regimen in a large cohort of regularly menstruating premenopausal HIV-infected women. We did not find an association between the menstrual cycle phase and ARV adherence using

264"within subject" (Part I) and "in-between subject" (Part II) analyses. Less than a college
265education, depressive symptoms, and having childcare responsibilities were significantly and
266negatively associated with single-tablet ARV adherence in women with HIV infection. Of note,
267these three factors have been shown to impede HIV medication adherence in previous studies ,
268and counseling and adherence support should be provided when prescribing ARVs to women
269with these barriers to help them fully adhere to their medication regimen.

270 There are limitations to our findings. Only STRs were included in our analyses and thus
271our study results may not apply to multi-tablet regimens. However, the use of STRs is rapidly
272increasing and the STRs allowed us to have more precise measures of adherence than if we
273included multi-tablet regimens. Another limitation was that most participants reported high
274adherence levels and therefore the number of participants with lower adherence was small, which
275limited our power to detect menstrual phase differences and may limit our ability to generalize
276our results to lesser adhering women. Nonetheless, the study was robust enough to identify
277traditional risk factors for lower medication adherence, such as depression and less education.
278We used self-report for date of last menstrual period and menstrual cycle regularity rather than
279directly measuring hormone levels; however we did exclude women who reported irregular
280cycles and women in the 'wash out phase' (the 2 days between the luteal and follicular phases)
281of their menstrual cycle to reduce the chance of menstrual cycle phase misclassification.
282Similarly, we relied on self-reported adherence and recreational drug use rather than more
283objective measures and self-report may be subject to desirability bias and recall bias. However,
284prior studies in the WIHS found self-reported adherence to be fairly accurate when compared to
285directly measures drug levels in blood and hair and short-term recall should be fairly precise.

Also in the WIHS, self-reported adherence to ARV was predictive of viral suppression and outside of the WIHS, other studies have found self-reported adherence, electronically monitored adherence, and ARV biomarkers in plasma are all correlated with HIV viral suppression . While it is possible that self-reported adherence was overestimated, it is also possible that other factors impact the inability to achieve viral suppression such as prior exposure to other ARV treatment regimens and suboptimal pharmacokinetics (variable absorption, metabolism, or possibly penetration into reservoirs). Another limitation is that we only included women with regular menstrual cycles (to avoid the possibility of cycle phase misclassification) and thus our results may not be applicable to women with irregular menstrual cycles. Finally, WIHS women may not be representative of all HIV-infected women on STRs but are representative of U.S. women living with HIV who reside in large urban cities.

Despite the above mentioned limitations, this study has notable strengths. The WIHS collects comprehensive information on a large number of HIV-infected women in the era of STRs. As such, there are few, if any, studies that can assess risk factors for suboptimal adherence to the newer classes of ARV mediation in hundreds of women. In addition, the frequent assessment (twice a year) of these risk factors means that the measured associations with the outcome are from the past six months and not from a distant time point (such as the baseline visit) which may no longer be accurate. Thus we were able to measure factors, like menstrual cycle phase and depressive symptoms, which contemporarily correspond to their recent medication adherence.

CONCLUSIONS

Understanding the barriers to HIV medication adherence among HIV-infected women, especially in the era of improved ARV potency and ease of use, can lead to strategies to maximize adherence and thus the effectiveness of ARV leading to better health outcomes . While the small number of low STR-adhering women may have limited our ability to find significant associations, this is one of the largest studies to evaluate the effect of menstrual cycle phase on medication adherence in HIV-infected women. The lack of association between phase of the menstrual cycle and adherence to ARV in HIV-infected women means attention can be focused on the other more important risk factors for suboptimal adherence, such as depression, level of education, and childcare responsibilities. These findings highlight the need to consider more specific interventions targeted for enhancing and maintaining very high levels of adherence in HIV-infected women.

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Table 1. Multi-class single tablet regimens included in the study.

Brand Name	Active Ingredients	Dosing
Atripla	Efavirenz, Emtricitabine, Tenofovir	Once a day
Complera	Emtricitabine, Rilpivirine, Tenofovir	Once a day
Stribild	Elvitegravir, Cobicistat, Emtricitabine, Tenofovir	Once a day
Trizivir	Abacavir, Lamivudine, Zidovudine	Twice daily

Table 2. Part I participants' characteristics by follicular or luteal phase of the menstrual cycle.

Part I (n= 327)					
Characteristic	**Follicular n=170 (n)**	**(%)**	**Luteal n=157 (n)**	**(%)**	**p-value**
Antiretroviral medication					0.31
Atripla	116	68.24	97	61.78	
Complera	18	10.59	23	14.65	
Stribild	0	0	2	1.27	
Trizivir	36	21.18	35	22.29	
Adherence					0.48
0-85%	8	4.71	5	3.18	
86-95%	13	7.65	8	5.10	
96-100%	149	87.65	144	91.72	
Age group					0.62
<36 years old	26	15.29	31	19.75	
36-40 years old	34	20.00	29	18.47	
41-45 years old	53	31.18	42	26.75	
46-50 years old	46	27.06	40	25.48	
>50 years old	11	6.47	15	9.55	
Race/ethnicity					0.60
non-Hispanic White	13	7.65	12	7.64	
Hispanic White	24	14.12	24	15.29	
African-American	112	65.88	94	59.87	
Other	21	12.35	27	17.20	
Interviewed in Spanish					0.43
no	149	87.65	132	84.62	
yes	21	12.35	24	15.38	
missing	0	.	1	.	
Educational attainment					0.97
< high school	68	40.00	62	39.49	
high school	52	30.59	50	31.85	
college or more	50	29.41	45	28.66	
Annual household income					0.08
<=$12000	86	55.13	67	44.97	
>$12000	70	44.87	82	55.03	
missing	14	.	8	.	

Part I (n= 327)					
Characteristic	**Follicular n=170 (n)**	**(%)**	**Luteal n=157 (n)**	**(%)**	**p-value**
Place of residence					0.92
own place	151	88.82	140	89.17	
other place	19	11.18	17	10.83	
Employed					0.55
no	105	61.76	102	64.97	
yes	65	38.24	55	35.03	
Health insurance					0.52
no	9	5.29	6	3.82	
yes	161	94.71	151	96.18	
Number of pregnancies (gravidity)					0.94
0	9	5.33	8	5.19	
1-3	68	40.24	65	42.21	
4-5	43	25.44	41	26.62	
≥6	49	28.99	40	25.97	
missing	1	.	3	.	
Number of children born (parity)					0.37
0	30	17.65	19	12.10	
1-3	97	57.06	96	61.15	
>3	43	25.29	42	26.75	
Childcare responsibility					0.09
no	75	59.52	59	48.76	
yes	51	40.48	62	51.24	
missing	44	.	36	.	
Partner status					0.46
living with partner	54	34.62	58	38.67	
not living with partner	102	65.38	92	61.33	
missing	14	.	7	.	
Self-reported health rating					0.98
excellent, very good, or good	130	82.28	117	82.39	
fair or poor	28	17.72	25	17.61	
missing	12	.	15	.	
Smoking status					0.65
never	64	37.65	61	38.85	
current	63	37.06	51	32.48	

Part I (n= 327)					
Characteristic	**Follicular n=170 (n)**	**(%)**	**Luteal n=157 (n)**	**(%)**	**p-value**
former	43	25.29	45	28.66	
Alcohol use					0.10
none	98	57.99	86	55.13	
1-2 drinks/week	59	34.91	53	33.97	
3-13 drinks/week	11	6.51	9	5.77	
>=14 drinks/week	1	0.59	8	5.13	
missing	1	.	1	.	
Marijuana use					0.58
no	138	81.66	131	83.97	
yes	31	18.34	25	16.03	
missing	1	.	1	.	
Crack use					0.75
no	163	96.45	152	97.44	
yes	6	3.55	4	2.56	
missing	1	.	1	.	
Cocaine use					0.62
no	166	98.22	155	99.36	
yes	3	1.78	1	0.64	
missing	1	.	1	.	
Heroin use					0.22
no	164	97.04	155	99.36	
yes	5	2.96	1	0.64	
missing	1	.	1	.	
Depressive symptoms (CES-D)					0.27
<16	110	65.48	111	71.15	
≥ 16	58	34.52	45	28.85	
missing	2	.	1	.	
Depressive symptoms (CES-D)					0.29
<23	131	77.98	129	82.69	
≥ 23	37	22.02	27	17.31	
missing	2	.	1	.	
Takes psychiatric medication					0.48
no	82	73.87	85	77.98	
yes	29	26.13	24	22.02	
missing	59	.	48	.	

Part I (n= 327)					
Characteristic	**Follicular n=170 (n)**	**(%)**	**Luteal n=157 (n)**	**(%)**	**p-value**
Body Mass Index (kg/m^2)					0.22
Underweight <19.8	3	1.95	7	4.73	
Normal 19.8-26.0	60	38.96	46	31.08	
Overweight 26.1-29.0	24	15.58	19	12.84	
Obese >29.0	67	43.51	76	51.35	
missing	16	.	9	.	
Waist circumference					0.96
≤ 80.0 cm	27	17.42	22	15.49	
80.1-100.0 cm	76	49.03	69	48.59	
100.1-120.0 cm	38	24.52	37	26.06	
>120.0 cm	14	9.03	14	9.86	
missing	15	.	15	.	
Reports memory or concentration problems					0.97
no	154	90.59	142	90.45	
yes	16	9.41	15	9.55	
Current # of non-ART prescription meds					0.15
no other prescription med	44	25.88	45	28.66	
1-2 other prescription meds	45	26.47	54	34.39	
3-5 other prescription meds	52	30.59	32	20.38	
6-18 other prescription meds	29	17.06	26	16.56	
Prior clinical AIDS diagnosis					0.19
no	126	74.12	106	67.52	
yes	44	25.88	51	32.48	
CD4+ count/mm^3					0.98
CD4+ count <200	16	9.70	14	9.15	
CD4+ count 200-499	66	40.00	62	40.52	
CD4+ count ≥500	83	50.30	77	50.33	
missing	5	.	4	.	
HIV RNA copies/mL					0.88
undetectable	116	73.89	106	72.60	
81-3,999 copies	26	16.56	28	19.18	
4,000-49,999 copies	10	6.37	7	4.79	
>49,999 copies	5	3.18	5	3.42	

Part I (n= 327)					
Characteristic	**Follicular n=170 (n)**	**(%)**	**Luteal n=157 (n)**	**(%)**	**p-value**
missing	13	.	11	.	

433**Table 3.** Part I unadjusted and adjusted logistic regression for the odds of ≤95% non-adherence to STR ARV (n=327).
434

Independent Variable	**Unadjusted OR (95% CI)**	**p-value**	**Adjust OR (95% CI)**	**p-value**
Menstrual Cycle Phase				
Follicular	1.0 (ref)		1.0 (ref)	
Luteal	0.64 (0.31-1.33)	0.23	0.71 (0.33-1.53)	0.38
Atripla	0.74 (0.36-1.53)	0.42		
Age per decade	0.76 (0.43-1.35)	0.36		
Race/ethnicity				
African American	1.0 (ref)			
non-Hispanic White	0.6 (0.13-2.7)	0.51		
Hispanic White	0.46 (0.13-1.59)	0.22		
Other	0.46 (0.13-1.59)	0.22		
Interviewed in Spanish	0.58 (0.17-1.97)	0.38		
≤12 years education	**3.38 (1.16-9.87)**	**0.03**	**3.55 (1.04-12.2)**	**0.04**
Household income <$12,000	0.81 (0.39-1.67)	0.57		
Lives in one's own place	0.53 (0.2-1.39)	0.20		
Employed	0.69 (0.32-1.5)	0.35		
Has health insurance	1.66 (0.21-13)	0.63		
Childcare responsibility	1.11 (0.48-2.53)	0.81		
Living with partner	0.73 (0.33-1.59)	0.43		
Fair or poor self- reported health rating	1.99 (0.86-4.59)	0.11		
Current smoker	1.02 (0.49-2.15)	0.96		
Number of drinks per week				
none	1.0 (ref)			
1-2 drinks	1.32 (0.63-2.77)	0.47		
3 or more drinks	0.68 (0.15-3.11)	0.62		
Crack/cocaine/heroin use	1.24 (0.27-5.69)	0.78		
Marijuana use	1.87 (0.82-4.26)	0.14		

Depressive symptoms (CES-D) ≥ 23	**2.63 (1.22-5.67)**	**0.01**	**2.60 (1.15-5.90)**	**0.02**
Takes psychiatric medications	1.65 (0.59-4.63)	0.34		
BMI >29.0 (obese)	1.99 (0.94-4.24)	0.07	1.90 (0.87-4.16)	0.11
Waist circumference (cm/10)	1.08 (0.86-1.34)	0.53		
Reports memory or concentration problems	1.77 (0.63-4.96)	0.28		
Prior clinical AIDS diagnosis	1.02 (0.47-2.22)	0.96		
CD4+ count/mm^3 <350	1.23 (0.56-2.69)	0.61		
HIV RNA copies/ml >4,000 copies	1.14 (0.45-2.93)	0.78		
Current # of non-ARV prescription medications				
none	1.0 (ref)			
1-2 medications	1.62 (0.61-4.3)	0.34		
3-18 medications	1.42 (0.55-3.63)	0.47		

436**Table 4.** Part II exact conditional logistic regression for the odds of ≤95% non-adherence to STR
437ARV (n=184).
438

Independent Variable	Odds Ratio* (95% CI)	p-value
Menstrual Cycle Phase		
Follicular	1.0 (ref)	
Luteal	1.08 (0.46-2.60)	1.0
Atripla	1.08 (0.06-Infinity)	0.96
Age per decade	2.62 (0.01-649)	0.80
Household income ≤$12,000	0.51 (0.05-3.44)	0.69
Lives in one's own place	1.08 (0.06-Infinity)	0.96
Employed	1.51 (0.18-17.5)	0.99
Has health insurance	0.92 (0.05-Infinity)	1.0
Childcare responsibility	**9.69 (1.53-Infinity)**	**0.04**
Living with partner	0.62 (0.05-5.68)	0.96
Fair or poor self-reported health rating	4.21 (0.40-219)	0.37
Current smoker	1.08 (0.00-20.6)	1.0
Drinks alcohol	1.04 (0.19-5.87)	1.0
Illicit Drug Use		
none	1.0 (ref)	
Crack/cocaine/heroin use	2.36 (0.27-Infinity)	0.52
Marijuana use	0.92 (0.00-17.6)	0.96
Depressive symptoms (CES-D) ≥ 23	1.91 (0.10-108)	1.0
Takes psychiatric medications	1.00 (0-19.0)	1.0
BMI >29.0 (obese)	1.18 (0.06-Infinity)	0.92
Waist circumference (cm/10)	0.84 (0.22-3.09)	0.80
Reports memory or concentration problems	1.04 (0.08-14.43)	1.0
Prior clinical AIDS diagnosis	0.92 (0.01-78.42)	1.0
CD4+ count/mm^3 <350	0.83 (0.05-13.54)	1.0
HIV RNA copies/ml >4,000 copies	0.96 (0.07-13.16)	1.0
Current # of non ARV prescription medications		
none	1.0 (ref)	
1-2 medications	0.47 (0.04-3.94)	0.70
3-18 medications	0.68 (0.04-11.67)	1.0

439
440*All models were adjusted for phase of the menstrual cycle.