Published in final edited form as:

Pediatrics. 2008 April ; 121(4): e787–e793. doi:10.1542/peds.2007-1586.

Association Between Living With Children and Adherence to Highly Active Antiretroviral Therapy in the Women's Interagency HIV Study

Daniel J. Merenstein, MD^a, Michael F. Schneider, MS^b, Christopher Cox, PhD^b, Rebecca Schwartz, PhD^c, Kathleen Weber, BSN^d, Esther Robison, PhD^e, Monica Gandhi, MD, MPH^f, Jean Richardson, DrPH^g, and Michael W. Plankey, PhD^h

^a *Department of Family Medicine, Georgetown University Medical Center, Washington, District of Columbia*

^b *Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland* ^c

State University of New York Downstate Medical Center, Brooklyn, New York ^d *John H. Stroger Hospital of*

Cook County, Chicago, Illinois ^e *Montefiore Medical Center, Bronx, New York* ^f *Department of Medicine,*

University of California, San Francisco, San Francisco, California ^g *Keck School of Medicine, University of*

Southern California, Los Angeles, California ^h *Department of Medicine, Georgetown University Medical Center, Washington, District of Columbia*

Abstract

OBJECTIVE—The purpose of this work was to evaluate whether living with children adversely affects adherence to highly active antiretroviral therapy in HIV-infected women.

PARTICIPANTS AND METHODS—We conducted a prospective cohort study between October 1998 and September 2005. The study outcome was $\geq 95\%$ adherence to highly active antiretroviral therapy evaluated at 5832 semiannual visits among 1366 HIV-infected women in the Women's Interagency HIV Study. The primary exposure defined at the visit immediately before outcome ascertainment was the number of children ≤ 18 years of age reported living in the household.

RESULTS—The percentage of women who reported ≥ 2 children in the household who also reported $\geq 95\%$ adherence ranged from 68% to 75% compared with adherence when either 1 child or no children were reported. Each additional child reported living in the household was associated with a 6% decrease in the odds of $\geq 95\%$ adherence.

CONCLUSION—The impact of living with a child on the ability to take medications by HIV-infected women has not been examined thoroughly. Our data suggest that adherence to highly active antiretroviral therapy is inversely associated with the number of children living in the household.

Keywords

adherence; children; HAART; HIV

What's Known on This Subject

Address correspondence to Daniel J. Merenstein, MD, Georgetown University Medical Center, Department of Family Medicine, 417 Kober Cogan Hall, 3800 Reservoir Rd, NW, Washington, DC 20007. E-mail: djm23@georgetown.edu.

The authors have indicated they have no financial relationships relevant to this article to disclose.

Motherhood potentially places additional stresses on HIV-infected women, because mothers with HIV have been shown to have higher levels of depression, poorer family cohesion, less ability to perform daily functions, and more reliance on their children to perform daily responsibilities.

What This Study Adds

Women living with ≥ 2 children had a trend toward lower rates of adherence than women living without children. Furthermore, we found a consistently decreasing odds of $>95\%$ adherence to highly active antiretroviral therapy as the number of children in the household increased.

Highly active antiretroviral therapy (HAART) has dramatically reduced both the morbidity and mortality among HIV-infected individuals.^{1–4} The evolution of HIV treatment in the developed world has dictated a shift from acute care, in which physicians and patients are most concerned with preventing death or opportunistic infections, to care for a chronic disease with novel considerations.^{5–7}

Optimal adherence to HAART is often difficult to achieve because of factors such as lack of social support, complexity of treatment regimens, and adverse drug effects.^{8–14} Previous studies have also found that no illicit drug use, being white, higher education levels, presence of health insurance, and having a regular primary care provider all positively influence adherence to HAART.^{15–17} Unlike other chronic diseases in which lower adherence rates allow for continued efficacy, greater compliance to HAART is necessary in HIV-infected individuals, because an increased risk of virologic failure has been directly linked to adherence levels $<95\%$.^{10,18,19}

In contrast to many other chronic conditions, HIV affects a younger patient population, and the majority of incident cases in the United States are in black women.^{20–23} Therefore, HIV-infected individuals may have an additional stress in simultaneously caring for children that would not be relevant to older persons living with other chronic diseases. Motherhood potentially places additional stresses on HIV-infected women, because mothers with HIV have been shown to have higher levels of depression, poorer family cohesion, less ability to perform daily functions, and more reliance on their children to perform daily responsibilities.²⁴ Lack of social support in mothers has been associated with nondisclosure of their HIV status, whereas higher levels of stress have been associated with nonadherence.^{25–27} The specifics of the relationship among HIV infection, adherence, and the stress involved in caring for children, however, need to be further elucidated. Using data from the Women's Interagency HIV Study (WIHS), we examined whether HIV-infected women who reported living with children ≤ 18 years of age were less likely to adhere to their HAART regimens, and whether adherence to HAART was associated with the number of children living in the household.

METHODS

The WIHS is a multicenter prospective cohort study established in 1994 to investigate the progression of HIV in women with and at risk for HIV.^{28,29} A total of 3766 women (2791 HIV-infected and 975 HIV-uninfected) were enrolled either in 1994–1995 ($n = 2623$) or 2001–2002 ($n = 1143$) from 6 US locations: New York (Bronx and Brooklyn sites), Chicago, San Francisco, Los Angeles, and Washington, DC. Every 6 months, participants undergo a comprehensive physical examination, provide biological specimens for CD4 cell count and HIV RNA determination, and complete an interviewer-administered questionnaire, which collects data on demographic information, disease characteristics, and specific antiretroviral therapy (ARV) use. An institutional review board at each site approves study protocols and consent forms, and each study participant provides written informed consent at each visit.

Assessment of ARV Use

At each semiannual visit, participants are shown photograph medication cards and are asked the names of specific ARV medications used since their previous visit. The WIHS uses a standard definition of HAART, adapted from the Department of Health and Human Services/Kaiser Panel guidelines.³⁰ Specifically, HAART is defined as any combination of: (1) ≥ 2 nucleoside reverse transcriptase inhibitors (NRTIs) with ≥ 1 protease inhibitor (PI) or ≥ 1 nonnucleoside reverse transcriptase inhibitor (NNRTI) (except for combinations of zidovudine and stavudine with either a PI or NNRTI); (2) 1 NRTI with ≥ 1 PI and ≥ 1 NNRTI; (3) a regimen containing ritonavir and saquinavir in combination with 1 NRTI and no NNRTIs; and (4) an abacavir-containing or tenofovir-containing regimen of ≥ 3 NRTIs in the absence of both PIs and NNRTIs (except for the 3-NRTI regimens consisting of abacavir, tenofovir, and lamivudine or tenofovir, didanosine, and lamivudine). All of the non-HAART combination therapy regimens are classified as combination therapy; use of a single NRTI, PI, or NNRTI is classified as monotherapy.

Outcome Variable

Beginning in October 1998, participants were asked at each visit to indicate how often they had taken their ARV medications as prescribed in the previous 6 months. Participants categorized their level of adherence into 1 of 5 categories: 100% of the time, 95% to 99% of the time, 75% to 94% of the time, $< 75\%$ of the time, or have not taken any of prescribed medications. For our analyses, participants were categorized dichotomously by whether they reported taking antiretroviral medications as prescribed $\geq 95\%$ of the time.¹⁶ Only visits at which participants reported using a HAART regimen at some point since their last visit were included in our analyses; all of the visits at which only no therapy, monotherapy, or non-HAART combination therapy were reported since their last visit were excluded.

Primary Exposure

At each odd-numbered visit, participants were queried on the number of individuals with whom they currently lived and whether they were ≤ 18 years of age. Because of the wording of this study question, we could not ascertain whether the individuals ≤ 18 years of age who were reported to live in the household were necessarily the children of the study participant. Data on the number of children ≤ 18 years of age that the study participant reported at a given odd-numbered semiannual visit were concatenated with adherence data from the even-numbered semiannual visit immediately after the odd-numbered visit to preserve temporality of exposure and outcome. At the 16th semiannual WIHS visit, which occurred between April 2002 and September 2002, data on the number of children ≤ 18 years of age were collected as part of the interview instrument because of new WIHS recruitment. Data on the number of children at visit 16 were, therefore, paired with adherence data from visit 17. For analyses, the number of children living in the household was categorized at each visit into 1 of 5 groups: 0 (referent), 1, 2, 3, and ≥ 4 unless otherwise noted.

Statistical Analyses

The unit of analysis was a visit with adherence levels defined at the current visit and the exposure defined at the preceding visit. The odds of $\geq 95\%$ adherence were compared between different exposure groups over time using logistic regression models with generalized estimating equations to account for the statistical dependence incurred by repeated measures of adherence on the same individual.³¹ For each participant who contributed data to analyses, a continuous time-varying covariate corresponding to the time (in years) after the first visit contributed to analysis was included in all of the univariate regression analyses except in the univariate analysis with age (in which age was treated as a time-varying covariate and date of first visit with adherence data were included as a fixed covariate). All of the adjusted regression

models used to assess the relationship between the number of children and adherence to HAART were adjusted for study site; race (black, Hispanic, white, and other); cohort status (1994–1995 or 2001–2002 enrollment); education (at least high school graduate or less than high school graduate); time-updated values of age (per 10 years); income (less than \$6000, \$6001 to \$12 000, \$12 001 to \$18 000, \$18 001 to 30 000, or >\$30 000); marijuana/hash use; cocaine, crack-cocaine, or heroin use (all self-report since last visit); depression (Center for Epidemiologic Studies Depression Scale [CESD] ≥ 16 or CESD < 16); quality of life score (per 10 points); health insurance status (presence or absence); and CD4 cell count (per 100 cells).³² In adjusted analyses, the date of the first semiannual visit with adherence data was also included as a fixed covariate for each individual.

RESULTS

Of the 2791 WIHS participants who were HIV infected at baseline, 2197 (79%) had a visit between October 1998 and September 2005. Of these 2197 women, 1764 (80%) reported HAART use for ≥ 1 visit between October 1998 and September 2005. Of these 1764 women, 1602 (91%) had a second visit wherein HAART use was reported. These 1602 women reported HAART at a total of 12 334 visits (median number of HAART visits: 7; interquartile range: 5–11).

A total of 177 (11%) of the 1602 WIHS participants who were HIV infected at WIHS enrollment and reported using HAART for ≥ 2 study visits between October 1998 and September 2005 and had nonmissing adherence data also reported being pregnant concurrent with ≥ 1 visit in which HAART was reported and were excluded from all of the analyses. All of the longitudinal data for these 177 women were excluded, because adherence levels have been shown to vary greatly during pregnancy and immediately postpartum.^{33–36} Of the remaining 1425 women, 15 (1%) were excluded because they did not have data available to define the primary exposure of interest at any visit during follow-up. Of the remaining 1410 women, an additional 44 (3%) were excluded because the exposure of interest was not defined at the visit immediately before the visit with adherence data, resulting in a final study population of 1366 women. The 1366 women contributed a total of 5832 on-HAART study visits with both outcome and primary exposure data available. Although the 236 WIHS participants who initiated HAART but were not included in analysis (1366 from 1602 above) were younger, had higher CD4 cell counts, and were less likely to have AIDS at enrollment, they were similar to the 1366 women included with respect to race or ethnicity, level of education attained, income level, health insurance status, drug use, depression, and HIV RNA levels.

Characteristics of Study Population

Table 1 provides descriptive statistics at the first semiannual visit with adherence data for the study population of 1366 HIV-infected participants. The median age was 40 years, and the majority of women were racial and ethnic minorities, with 53% self-identifying as black and 29% self-identifying as Hispanic. Although only 16% reported a family income greater than \$30 000 per year, 92% of participants reported having health insurance. Thirty-nine percent had ≥ 1 clinical AIDS diagnosis; the median CD4 cell count was 380 cells per mm³, and the median log₁₀ (HIV RNA) was 2.20 copies per mL.

Adherence Levels and Presence of Children

At least 95% adherence to HAART was reported at 76% ($n = 4430$) of all 5832 of the visits. Fifty percent ($n = 684$) of the 1366 women in the study reported $\geq 95\%$ adherence at all of the visits at which they reported HAART. Sixty-six percent ($n = 897$) of the 1366 women reported having ≥ 1 child ≤ 18 years of age living in the household at least once during follow-up; 65%

($n = 583$) of these 897 women reported having children living in the household at all of the visits.

To describe the cross-sectional relationship at each visit between the number of children ≤ 18 years of age reported living in the household and adherence, we calculated the percentage of women with $\geq 95\%$ adherence to HAART stratified by whether ≥ 2 children, 1 child, or no children were reported (Fig 1). Across all of the follow-up visits, the percentage of women who had reported ≥ 2 children in the household, who also reported $\geq 95\%$ adherence, was 72% on average (range: 68%–75%) compared with adherence reported among women who reported either 1 child (average: 76%; range: 71%–82%) or no children (average: 78%; range: 75%–80%). Women who reported ≥ 2 children had lower adherence levels across almost all of the follow-up visits.

Univariate and Multivariate Longitudinal Analyses

To further examine the relationship between the number of children ≤ 18 years of age living in the household and adherence levels, we conducted univariate and multivariate logistic regression analyses. Because we anticipated an inverse relationship between adherence and the number of children, we treated the number of children as a continuous measure in the primary regression analyses. To limit the influence of a small number of visits wherein a relatively large number of children were reported, we categorized the number of children as 0 (referent), 1, 2, 3, and ≥ 4 . Each additional child was associated with a 9% decrease in the odds of $\geq 95\%$ adherence (odds ratio [OR]: 0.91; 95% confidence interval [CI]: 0.85–0.96) in an unadjusted analysis and a 6% decrease in the odds of $\geq 95\%$ adherence (OR: 0.94; 95% CI: 0.88–1.00) in an adjusted analysis that included study site; age; cohort status; race; education; income; marijuana or hash use; cocaine, crack-cocaine, or heroin use; depression; quality of life score; health insurance status; and CD4 cell count (all variables defined as indicated in the “Statistical Analyses”). A similar result was obtained when ≥ 4 children were not combined into 1 group; however, this was not significant (adjusted OR: 0.95; 95% CI: 0.89–1.01). The ORs for the effect of each category of number of children (with report of no children as the reference group) are reported in Table 2, demonstrating a downward trend in adherence in both the unadjusted and adjusted analyses. Although none of the categories was significantly different from the reference group in the adjusted analysis, the overall trend reached borderline statistical significance in the primary analysis (OR: 0.94; $P = .055$).

Consistent with previous research, our results demonstrated that white women had an odds of self-reporting of $\geq 95\%$ adherence levels that were 69% higher than black women. In addition, each 10-year increment in age was associated with a 40% increase in the odds of achieving $\geq 95\%$ adherence. Any report of marijuana use or use of crack, cocaine, or heroin since the previous visit was associated with 26% and 44% lower odds of $\geq 95\%$ HAART adherence, respectively. In addition, we ran a secondary analysis adjusting for whether the women saw a primary care physician, and the results presented in Table 2 were unchanged (data not shown).

DISCUSSION

The importance of family-centered care on children’s health has long been recognized.³⁷ However, the role that the burden of child care plays in the health of parents or caregivers has not been as readily explored. We believe that this relationship is important and that health outcomes can be better predicted by examining the effects of children (and the responsibilities that come with their care) on parental health.

We evaluated whether the number of children ≤ 18 years of age living in the home was associated with adherence to HAART by using longitudinal data collected from the WIHS from October 1998 through September 2005. During follow-up, women living with ≥ 2 children

had a trend toward lower rates of adherence than women living without children. Furthermore, in both univariate and multivariate analyses, we found a consistently decreasing odds of $>95\%$ adherence to HAART as the number of children in the household increased. The odds of $\geq 95\%$ HAART adherence associated with no illicit drug use, white race, and older age in the WIHS were similar to those found by other investigators.^{15,16}

It will be particularly important for health care providers to discuss with HIV-infected mothers or caregivers, particularly mothers who have additional stressors such as living in poverty, how child care responsibilities may influence adherence. It may be necessary to establish support systems to alleviate the stress of child care responsibilities among these women based on the trends observed in this analysis.

Our analysis only examined basic stressors that the presence of a child in the household may present. Although the results of the multivariate analyses did not quite reach conventional statistical significance, the CIs and the direction of our estimates suggest association per our a priori hypothesis. Because HIV-infected women are surviving with more productive and active lives and are able to give birth to healthy children, future research needs to delve further into the relationship between child care responsibilities and adherence to medication. We postulate that there is a threshold of stress related to the number of children in the home, age of the child, health of the child, and other familial stressors among women with HIV that, when achieved, may diminish adherence to HAART. This information is important for health care providers, because they can work with treatment teams to erect safety net interventions to improve adherence. Future research should examine the role of social supports around HAART adherence in the context of child caregiving.

Our study has several important limitations. There is no single interview question in the WIHS that confirms that any children ≤ 18 years of age who the participant reports living in the household actually belong to the participant. It is likely that some of these children were not the participants' biological children, but we assumed that the HIV-infected woman in the household was at least partially responsible for caring for the children. In addition, WIHS primarily collects data on the women themselves, and information about the children they report living with them is limited. Thus, data on the age and health status of the children or whether the participants have disclosed their HIV status to the children living in the household are not available. This is potentially important information, because mothers have been reported to approach their HIV status differently according to the age of their children.²⁶ Also, because adherence was self-reported, there is a possibility of misclassification whereby HIV-infected participants, regardless of whether they report children living in the household, tend to overreport adherence rates. There is no reason to believe, however, that the rate of misclassification would be any higher among women without children than among women with children (ie, differential misclassification), and any nondifferential misclassification would bias our estimates of association toward the null.³⁸ In addition, previous WIHS research has shown self-reported adherence to be consistent with objective measures, such as CD4 count, HIV viral load, and self-report of physical functioning.¹⁷ Finally, although our results are consistent with previous adherence research, it is possible that the differences that we observed are because of other unmeasured confounders.

We believe that the number of children living in the household influences adherence to HAART among HIV-infected women. We acknowledge that further exploration of the familial relationship, the age and health status of the children, and HIV-related outcomes are necessary, because the relationship between HIV treatment and maternal health are likely to be tightly linked. To improve adherence in HIV-infected mothers, these relationships will need continued elucidation, and appropriate interventions will need to be investigated.

Acknowledgements

The Women's Interagency HIV Study is funded by the National Institute of Allergy and Infectious Diseases with supplemental funding from the National Cancer Institute and the National Institute on Drug Abuse (grants UO1-AI-35004, UO1-AI-31834, UO1-AI-34994, UO1-AI-34989, UO1-AI-34993, and UO1-AI-42590). Funding is also provided by the National Institute of Child Health and Human Development (grants UO1-HD-32632) and the National Center for Research Resources (grants MO1-RR-00071, MO1-RR-00079, and MO1-RR-00083).

Data in this article were collected by the Women's Interagency HIV Study Collaborative Study Group with centers (Principal Investigators) at New York City/Bronx Consortium (Kathryn Anastos); Brooklyn, NY (Howard Minkoff); Washington DC Metropolitan Consortium (Mary Young); The Connie Wofsy Study Consortium of Northern California (Ruth Greenblatt); Los Angeles County/Southern California Consortium (Alexandra Levine); Chicago Consortium (Mardge Cohen); and Data Coordinating Center (Stephen Gange).

We also thank Devon Pearce for help preparing this article.

Abbreviations

HAART	highly active antiretroviral therapy
WIHS	Women's Interagency HIV Study
ARV	antiretroviral therapy
NRTI	nucleoside reverse transcriptase inhibitor
PI	protease inhibitor
NNRTI	nonnucleoside reverse transcriptase inhibitor
CESD	Center for Epidemiologic Studies Depression Scale
OR	odds ratio
CI	confidence interval

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FIGURE 1.

The prevalence of $\geq 95\%$ adherence to a HAART regimen stratified by whether the participant reported no children, 1 child, or >1 child of ≤ 18 years of age living in the household at 5832 visits from April 1999 to September 2005 contributed by 1366 HIV-infected participants of the WIHS. X-axis labels correspond with the midpoint of the 6-month interval for each WIHS semiannual study visit. At each time point, data on adherence to HAART are combined with data on the number of children reported from the previous visit. Data on the number of children are only collected at odd-numbered visits (October 1998 to March 1999, October 1999 to March 2000, etc) except for WIHS visit 16, which occurred between April 2002 and September 2002. Data on the number of children for this visit would be seen at the time point labeled January 2003.

TABLE 1

Characteristics of 1366 HIV-Infected Participants of the WIHS at First Semiannual Visit From April 1999 to September 2005 With Adherence Data

Characteristic	Data
Age, median (quartile 1, quartile 3), y	40.0 (34.8, 45.4)
Cohort, <i>n</i> (%)	
1994–1995	979 (72)
2001–20002	387 (28)
Race/ethnicity, <i>n</i> (%)	
Black	718 (53)
Hispanic	400 (29)
White	207 (15)
Other ^a	41 (3)
Completed high school, <i>n</i> (%) ^b	867 (64)
Income, <i>n</i> (%) ^b	
At or less than \$6000	234 (17)
\$6001 to \$12 000	500 (37)
\$12 001 to \$18 000	206 (15)
\$18 001 to \$30 000	207 (15)
More than \$30 000	216 (16)
Have health insurance, <i>n</i> (%)	1256 (92)
Used marijuana/hash, <i>n</i> (%)	225 (16)
Use cocaine, crack-cocaine, or heroin, <i>n</i> (%)	120 (9)
CESD ≥ 16 , <i>n</i> (%) ^b	575 (43)
Quality of life score, median (quartile 1, quartile 3) ^b	68.0 (52.5, 82.7)
Have AIDS, <i>n</i> (%)	539 (39)
CD4 cell count, median (quartile 1, quartile 3), cells per mm ^{3b}	380 (235, 568)
log ₁₀ (HIV RNA), median (quartile 1, quartile 3), copies per mL ^b	2.20 (1.90, 3.71)

If data for a particular variable were missing at the first semiannual visit with adherence data, we used the data, if available at the semiannual visit immediately before this visit.

^a Other category includes Asian/Pacific Islander, Native American/Alaskan, and other.

^b Education was missing for 2 women; income level was missing for 3 women; CESD was missing for 20 women; quality of life score was missing for 18 women; CD4 cell count was missing for 6 women; and log₁₀ (HIV RNA) was missing for 6 women.

TABLE 2

Analyses of Characteristics Potentially Associated With $\geq 95\%$ Adherence to HAART at 5832 Visits From April 1999 to September 2005
Contributed by 1366 HIV-Infected Participants of the WIHS

Characteristic	No. Person-Visits	No. (%) With $\geq 95\%$ Adherence	Unadjusted OR ^a	95% CI	Adjusted OR ^b	95% CI
No. of children ≤ 18 years of age reported living in the household						
0	2817	2193 (78)	1.00	NA	1.00	NA
1	1402	1073 (77)	0.90	0.76–1.08	0.89	0.73–1.07
2	934	685 (73)	0.78	0.63–0.95	0.85	0.68–1.06
3	402	284 (71)	0.76	0.56–1.02	0.84	0.62–1.12
≥ 4	277	195 (70)	0.70	0.51–0.96	0.77	0.56–1.08
Study site						
1	1188	995 (84)	1.00	NA	1.00	NA
2	1093	753 (69)	0.43	0.33–0.58	0.39	0.29–0.53
3	770	555 (72)	0.49	0.36–0.67	0.47	0.34–0.64
4	1190	975 (82)	0.87	0.65–1.18	0.75	0.55–1.02
5	714	515 (72)	0.53	0.38–0.74	0.50	0.35–0.72
6	877	637 (73)	0.51	0.38–0.70	0.51	0.37–0.70
Age per 10 years	5832	NA	1.22	1.09–1.37	1.40	1.23–1.60
Cohort						
1994–1995	4607	3488 (76)	1.00	NA	1.00	NA
2001–2002	1225	942 (77)	1.12	0.91–1.39	1.63	1.18–2.25
Race or ethnicity						
Black	3000	2164 (72)	1.00	NA	1.00	NA
Hispanic	1669	1311 (79)	1.40	1.15–1.71	1.20	0.96–1.51
White	994	816 (82)	1.77	1.35–2.33	1.69	1.27–2.24
Other	169	139 (82)	1.78	0.97–3.26	1.60	0.86–2.99
Education						
Not completed high school	2043	1542 (75)	1.00	NA	1.00	NA
Completed high school	3787	2887 (76)	1.04	0.87–1.25	1.00	0.83–1.22
Income						
At or less than \$6000	873	646 (74)	1.00	NA	1.00	NA
\$6001 to \$12 000	2073	1558 (75)	1.00	0.84–1.20	0.99	0.81–1.20

Characteristic	No. Person-Visits	No. (%) With ≥95% Adherence	Unadjusted OR ^a	95% CI	Adjusted OR ^b	95% CI
\$12 001 to \$18 000	884	675 (76)	1.05	0.85–1.30	1.07	0.84–1.35
\$18 001 to \$30 000	933	695 (74)	1.02	0.82–1.27	0.98	0.77–1.24
More than \$30 000	1046	839 (80)	1.29	1.00–1.65	1.14	0.86–1.50
Marijuana or hash use						
Reported using	878	608 (69)	0.72	0.59–0.87	0.74	0.60–0.91
No report of using	4932	3805 (77)	1.00	NA	1.00	NA
Crack, cocaine, or heroin use						
Reported using	467	281 (60)	0.55	0.44–0.69	0.56	0.44–0.73
No report of using	5341	4131 (77)	1.00	NA	1.00	NA
Depression						
CESD ≥16	2311	1671 (72)	0.79	0.68–0.90	0.97	0.82–1.15
CESD <16	3342	2631 (79)	1.00	NA	1.00	NA
Quality of life score per 10 points	5621	NA	1.09	1.06–1.13	1.09	1.05–1.14
Health insurance						
No	360	281 (78)	1.00	NA	1.00	NA
Yes	5464	4142 (76)	0.84	0.64–1.12	0.75	0.55–1.01
CD4 cell count per 100 cells	5662	NA	1.07	1.03–1.10	1.06	1.02–1.09

All of the characteristics were evaluated as time varying except for study site, cohort, race, and education. NA indicates not applicable.

^a All of the unadjusted models included a variable representing the time (in years) after the first visit with adherence data. In the unadjusted model with age, we included the date of the first visit with adherence data centered at 2001.0 in the model instead of elapsed time since first visit with adherence.

^b A total of 1320 WHS participants (of 1366 in study population) contributed 5386 visits with complete data and were included in adjusted analysis; 446 person-visits with missing data for ≥1 variable were not included. The date of the first visit with adherence data (centered at 2001.0) was included in adjusted analysis.