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Longitudinal Trends in Sexual Behaviors with Advancing Age and Menopause Among Women With and Without HIV-1 Infection

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Abstract

We assessed changes in self-reported sexual activity (SA) over 13 years among HIV-infected and uninfected women. The impact of aging and menopause on SA and unprotected anal or vaginal intercourse (UAVI) was examined among women in the Women's Interagency HIV Study (WIHS), stratifying by HIV status and detectable viral load among HIV-infected women. Generalized mixed linear models were fitted for each outcome, adjusted for relevant covariates. HIV-uninfected women evidenced higher levels of SA and UAVI than HIV-infected. The odds of SA declined by 62–64 % per decade of age. The odds of SA in a 6-month interval for women aged 40–57 declined by 18–22 % post-menopause (controlling for age). Among HIV+/detectable women only, the odds of any UAVI decreased by 17 % per decade of age; the odds of UAVI were unchanged pre-menopause, and then decreased by 28 % post-menopause. Elucidating the factors accounting for ongoing unprotected sex among older women should inform interventions.

Keywords

Sexual activity; Sexual risk behaviors; Aging; Menopause; Women's Interagency HIV Study (WIHS)

Introduction

Although sexual activity (SA) continues into older ages among adults in the US [1, 2], there are gender-specific declines in SA with age, along with lower levels of condom use and lower levels of safer sex practice [3–5]. In one national survey, the prevalence of SA for both men and women declined with age, and at all ages women were less likely than men to report SA [1]. From a national probability sample of men and women ages 14–94, the prevalence of vaginal intercourse and condom use for both men and women declined with age [3, 6, 7]. A national survey of men and women over 50 years of age found that 14–17 % reported penile-vaginal intercourse (PVI), and only 20–25 % used condoms during their most recent PVI episode [4]. Another survey of adults ages 50 and older found that only 27 % had ever been tested for HIV; among those tested, 84 % said that their chances of acquiring HIV was "none" [8]. Finally, according to the Centers for Disease Control and Prevention (CDC), the diagnoses of HIV infection occurred at the following rates (per 100,000) in 2011 amongst older age groups: 17.5 (50–54 years of age); 11.4 (55–59 years of age); and 6.9 (60-years of age) [9].

Systematic studies of SA in older HIV-infected adults are sparse, although there is evidence that HIV-infected older adults engage in unprotected intercourse [10–12]. For example, in the Research on Older Adults with HIV (ROAH) study, more than one-third of sexually active older adults with HIV reported engaging in unprotected anal or vaginal intercourse (UAVI), and 18 %reported unprotected sex with a serodiscordant partner [13–15]. Identified risk factors for unprotected sex among older adults with HIV include low levels of

knowledge about HIV transmission, recent substance use, sexual concurrency, partner characteristics (i.e., new, ongoing, casual), unstable housing, loneliness, high CD4 count, and poor psychological well being [11–13, 16–20]. Studies also suggest that safer sex practices among people with suppressed viral load decline since these individuals realize that the risk of transmitting HIV is lower when HIV viral loads are undetectable [21–23].

Little is known about how gender, aging and age-related physical factors such as menopause affect the sexual behaviors of women living with HIV [24–27]. Menopause represents a biological milestone of the aging process; perimenopausal women may experience urogenital changes including vaginal dryness [28] and mucosal thinning, which can both increase HIV acquisition and transmission rates [29]. Postmenopausal women with HIV, like their HIV-uninfected counterparts, may not use condoms as frequently because they no longer require contraception. Although condom use has been shown to decline with age [10, 30, 31], more research is needed to further explore the role of menopause on sexual behavior.

To explore the relationship between aging, SA and UAVI among women with and without HIV-1 infection, this study examined data from the Women's Interagency HIV Study (WIHS), the largest longitudinal cohort study of HIV-infected and uninfected women in the United States. Previous studies from the WIHS have reported that menopausal symptoms do not affect condom use among older women with HIV [32]. In this analysis, we extend this work by examining the relationship of aging, menopause and sexual behavior among HIV-infected and uninfected women over 13 years of follow-up (1998–2011). We posit that older age is associated with a decline in SA and UAVI for both HIV-infected and uninfected women; that women with HIV infection will show a greater decline in sexual behavior as they age as compared to HIV-negative women; and that among HIV-infected women, the impact of age on sexual behavior will be influenced by viral load and menopause status. These findings can be used to help tailor secondary HIV prevention strategies specifically for older heterosexual women with HIV.

Materials and Methods

Participants

The WIHS is a multicenter, prospective study established in 1993 to investigate HIV disease progression in women in the United States. WIHS participants in this analysis were drawn from six consortia (Washington, DC; San Francisco, CA Bay Area; Los Angeles, CA; Brooklyn, NY; Bronx, NY; and Chicago, IL). The WIHS enrolled women in 1994–95 and 2001–02. Women recruited in the first cohort were either at-risk HIV-uninfected or HIV-infected women. At-risk HIV-uninfected women with self-reported high-risk behaviors, such as injection drug use, having a sexually transmitted disease, having unprotected sex with three or more men or protected sex with more than five men, or having exchanged sex for drugs, money, or shelter were recruited to ensure comparability with the HIV-infected women [33, 34]. In the second wave of recruitment, HIV-infected women with an AIDS-related clinical condition or who acquired HIV perinatally were excluded. Study recruitment and protocols have previously been described [33, 34].

For this study, we examined data from 66,055 WIHS person-visits representing 3,847 women over 13 years of follow-up. We retained 39,812 person-visits, contributed by 1,927 HIV-infected and 742 HIV-uninfected women. We excluded data from participants and visits using a three-phase process that included the following: (1) all visits for all women (17,322 person visits and 764 participants) in the pre-highly active antiretroviral therapy (ART)era (1993–1997); (2) post-event visits for women with a hysterectomy, the removal of either ovary, and visits during which participants reported being pregnant or trying to become pregnant (8,325 person-visits and 328 participants); and (3) HIV-seroconversion (308 person-visits and 18 participants). We excluded all person-visits prior to ART so we could focus on sexual risk behaviors in the ART era. We excluded participants who reported a hysterectomy or an oophorectomy because they may not use condoms as frequently since they no longer require contraception. We also excluded participants who were pregnant or intended on becoming pregnant because most reported unprotected intercourse in order to conceive. In addition, for analyses of menopause, we limited analysis to those visits in which the participants were between 40 and 57 years of age (N = 21,272 visits involving 1,808 women). This age range was selected to reduce the degree of multicollinearity between age and menopause status by constraining age to a menopause-plausible range [35–37].

Study Procedures

WIHS participants complete semiannual study visits in English or Spanish. Each visit includes a standardized, interviewer-administered questionnaire assessing sexual behavior, medical and obstetric/gynecological history, psychosocial factors, and socio-demographics, as well as a physical and gynecological examination. Self-reported measures are selected based on their demonstrated reliability and validity in populations similar to the WIHS. In addition to other tests, blood samples are collected to test for HIV RNA levels. Institutional review boards at each of the study centers approved the study procedures, and informed written consent was obtained from all participants.

Measures

Sexual Behavior—At each study visit, women reported whether they had vaginal or anal sex and the number of vaginal, anal and/or oral sex partners during the past 6 months. UAVI was determined based on assessment of condom use consistency (“always” versus “sometimes” or “never”) for vaginal and anal sex separately. Sexually active women who reported “sometimes” or “never” to either question about condom use were categorized as having UAVI in the past 6 months.

Age and Menopause—After investigation of the functional relationship between age and the outcomes of interest, chronological age was used as a continuous variable. Menopausal status was determined by self-reported vaginal bleeding patterns. Due to irregularities in menstrual cycle patterns, many WIHS participants were not easily categorized via this self-report measure for menopause [38]. For the purpose of this study, we chose a conservative approach for defining the onset of menopause by using self-report data for three consecutive study visits at which no menses were reported during the prior 6 months. Menopause onset

was defined as the date of the second of these three study visits (i.e., 12 months with no menses).

Viral Load Suppression—Plasma HIV-1 RNA quantification was performed using the isothermal nucleic acid sequence-based amplification method in laboratories certified by the National Institutes of Health Virology Quality Assurance program, with a lower limit of detection set at 48 copies/milliliters (mL). Presence of detectable plasma HIV-RNA among HIV-infected women was designated as HIV+/detectable, versus HIV +/undetectable in those with non-detectable HIV-RNA. Viral load status was imputed for up to two consecutive visits at which HIV-1 RNA was not recorded if the status at the previous visit was the same for the subsequent visit.

Covariates—At enrollment, WIHS participants provided information about their race/ethnicity (Black, White, Latina, or other), educational attainment (less than high school versus high school or higher), quantity and frequency of drug and alcohol use, symptoms of depression, physical function, and follow-up duration (number of visits since baseline). Depression was assessed using the Center for Epidemiologic Studies-Depression (CES-D) scale [39]; CES-D scores were dichotomized, with ≥16 indicating depressive symptoms [39]. Physical function was assessed with a subscale from the medical outcomes study (MOS) measures [40]. The physical function subscale scores were continuous, ranging from 0 to 100, with 100 representing the highest perceived physical ability [40]. For the purposes of analysis, quintile groups were formed from these scores. Drug use was assessed via self-reported use of crack, cocaine, heroin, or other injection drugs in the previous 6 months (Y/N). Alcohol use was dichotomized as heavy (≥7 drinks/week) versus light/moderate (<7 drinks/week) [41]. In addition to these variables, duration of follow-up was included as covariate in our models.

Statistical Analysis

Justification of the Model—In order to assess the suitability of treating age as a linear predictor of the two outcomes of interest (SA and UAVI), we first constructed logistic regression models to estimate log-odds of each outcome by age category [42]. For these analyses, we stratified age into 5-year groups, starting with ages 18–22 (the youngest participant was 18 years of age). Plots of these age-category-specific log-odds estimates (Fig. 1) were then used to assess the adequacy of using age as a linear predictor in the main regression models. As can be seen in Fig. 1, there was indeed a linear relationship between age and the two outcomes; therefore, in the main analyses, age was included as a continuous variable.

Application of the Model—Descriptive statistics were generated as means and standard deviations (SD), and were stratified by HIV status. Generalized mixed linear models were constructed separately for age as a linear predictor (based upon results of the suitability analysis) and for menopausal status, with predictors of interest including HIV status. Since age and menopausal status are strongly associated, an unconstrained analysis that included both age and menopause as simultaneous predictors would have resulted in multicollinearity. Therefore, we included age as a predictor of interest in an analysis of all

participants, ignoring menopause. In a second analysis, we used menopause as a predictor of interest, controlling for age. In this analysis we avoided the issue of multicollinearity by constraining age to a menopause-plausible range.

The outcomes were modeled as Bernoulli-distributed; a logit link-function was applied. Autocorrelation among observations coming from the same subject on successive visits was modeled as a first-order autoregressive, first-order moving average (ARMA 1, 1) process. Satterthwaite adjustments were made to denominator degrees of freedom. All of the seven plausible covariates (race, education, heavy drinking, current drug use, depression, physical function and follow-up duration) were added to each model. Since only age, menopause and HIV status are considered predictors of interest in this paper, effects of other risk factors appearing in the above list of covariates are not reported. Analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC).

Results

Sample Characteristics

Baseline characteristics of the study population, stratified by HIV status, are shown in Table 1. The majority of the participants were ≥30 years old, Black, had at least a high school education and were premenopausal. HIV-uninfected women were younger ($p<0.0001$). A larger proportion of White and Hispanic women were HIV+/undetectable ($p = 0.0020$) compared to Black women. The majority of participants were sexually active, with the HIV-uninfected women reporting more SA (87 %) than HIV+/detectable (74 %) or HIV+/undetectable (73 %) women ($p < 0.0001$). More than a quarter of the HIV+/detectable (29 %) and HIV+/undetectable (28 %) women reported UAVI. The HIV-uninfected women, however, reported twice (60 %)as much UAVI as did women with HIV ($p < 0.0001$) (see Fig. 2).

Characteristics of the study sample by visits and virologic grouping (detectable vs. undetectable) are shown in Table 1. HIV-uninfected women had the highest levels of alcohol and current drug use (both $p < 0.0001$), the HIV+/undetectable group had the highest occurrence of menopause ($p < 0.0001$) and the HIV+/detectable women had the highest levels of depressive symptoms ($p < 0.0001$). Across visits, there were similar ($p > 0.05$) declines in SA in all groups. SA in HIV+/ detectable women declined to 69 %, in HIV+/undetectable women to 65 %, and SA amongst HIV-uninfected women declined to 70 %. Reported levels of UAVI across all visits also declined over time, although HIV-uninfected women reported significantly ($p < 0.0001$) more UAVI during the 13 years of follow-up than HIV+/detectable or HIV+/undetectable women (54, 25, 22 %, respectively) (see Fig. 2).

Self-Reported Sexual Activity and Age

Adjusted odds ratios (ORs) of any SA by 10-year age increase, stratified by HIV status are shown in Table 2. In a logistic regression model controlling for the aforementioned covariates, we found that for every 10-year age change, the odds of any SA declined by 62 % for HIV+/detectable women, 64 % for HIV+/undetectable women and 62 % for HIV-

women. Differences in SA among virologic groups in terms of age effect were statistically non-significant (F [2, 8858] = 0.37, p = 0.693).

Self-Reported Sexual Activity and Menopausal Status

Adjusted ORs of any SA by menopause, stratified by HIV status, are shown in Table 2. The odds of any SA in a 6-month interval for women aged 40–57 declined by 22 % for HIV+/detectable women, 25 % for HIV+/undetectable women and 18 % for HIV-uninfected women after menopause. These declines were statistically significant only for the women with HIV. Differences in effect of menopause among virologic groups are statistically non-significant (F [2, 12311] = 0.32, p = 0.724).

Self-Reported UAVI and Age

Adjusted ORs of any UAVI by 10-year age change, stratified by HIV status, are shown in Table 2. The ORs for UAVI in a 6 month interval by decade of age, were limited to those visits where there was reported SA (N = 21382 visits or 84 % of original sample of 25,992). The odds of UAVI declined by 17 % for HIV+/detectable women, 9 % for HIV+/undetectable women and 4 % for HIV-uninfected women per decade of age. The decline was only statistically significant for the HIV+/detectable women. Differences among virologic groups in age effect are statistically significant (F [2, 7490] = 3.33, p = 0.036). Pairwise testing yields: HIV+/detectable women versus HIV+/undetectable women (F [1,20296] = 7.84, p = 0.038); HIV+/detectable women versus HIV-uninfected women (F [1,3966] = 3.80, p = 0.051); HIV+/undetectable women versus HIV-uninfected women (F [1,4366] = 0.56, p = 0.454).

Self-Reported UAVI and Menopause (Age 40–57)

Data on UAVI at 6 month intervals for sexually active women aged 40–57 were available for 9906 visits; 83 % of original sample. Adjusted ORs of any UAVI for these women, stratified by HIV status, are shown in Table 2. Odds of UAVI for these women declined by 28 % for HIV+/detectable women and 15 % for HIV+/undetectable women; and odds of UAVI for HIV-uninfected women increased by 4 % after menopause. The decline was only statistically significant for the HIV+/detectable women. Differences in UAVI between virologic groups in terms of the effect of menopause were not statistically significant (F [2, 7088] = 2.32, p = 0.099).

Discussion

Findings from WIHS

We found that older age is associated with an overall decrease in SA and UAVI among both HIV-infected and HIV-uninfected women, after accounting for race/ethnicity, education, heavy drinking, recent drug use, depressive symptoms and physical function. Regardless of HIV status, 65–87 % of the women in this study at baseline and across 13 years of follow-up were sexually active. We found that women with HIV did not show a greater decline in SA as they aged, compared to HIV-uninfected women. We also found that UAVI decreased over time, and HIV-infected women maintained a pattern of reporting less UAVI than HIV-

uninfected women. However, after 13 years of follow-up we found 22–25 % of the HIV-infected women continued to engage in UAVI.

We found that for women aged 40–57, the odds of any SA declined after menopause only for women with HIV. Although the odds ratios for any SA associated with menopause were statistically significant for the women with HIV, we cannot definitively assert that there is any menopause effect among the HIV-uninfected women. We also found that UAVI declined significantly among women ages 40–57 who had a detectable HIV viral load.

Studies of UAVI in HIV-Infected Adults

In a cross-sectional survey of 1,000 older adults with HIV in New York City, 50 % were found to be sexually active and approximately a third reported UAVI, which was significantly associated with loneliness and recent substance use [13, 18]. That study also found that among those who engaged in UAVI, 18 % had unprotected sex with a serodiscordant partner. Other cross-sectional studies have found a prevalence of UAVI of 33 %and 42 %among sexually active older adults with HIV [13, 17, 43]. These findings are considerably higher than those found in this study. Our lower risk estimates might be due to the impact of a larger cohort and a significant duration of follow-up or due to the participants in each of these studies, who represent both men and women.

The decline in SA among older adults could be accounted for by diminishing sexual function. The most commonly reported causes of sexual dysfunction among older women are a lack of interest in sex, failure to achieve orgasm and poor vaginal lubrication [44–47], though poor health, instead of chronological age, may underlie some of these problems. Poor physical and mental health affects sex drive and has been found to be associated with a decline in SA among older adults [48–50]. Postmenopausal women may be less likely to use condoms because they no longer need contraception. Although condom use has been shown to decline with age among women with HIV [30, 31] recent studies found no association with menopause and condom use among women with HIV [31]. More research is needed to explore the role of menopause on sexuality and the sexual behavior of older women [51–55].

Identifying Women at Risk

Our findings demonstrate that there is a proportion of older women with HIV who may benefit from support in maintaining safer sex practices. Future research will be useful to delineate which women are at greatest risk. However, there are a number of plausible psychosocial and interpersonal factors that can be posited, based on research in other populations. Among older adults with HIV, high levels of psychological distress and poor mental health (e.g., depression, loneliness, anxiety, and chronic stress) are common [15, 18, 56–58] and have been well documented in the WIHS cohort [59–65]. Impaired mental health, in turn, has been found to be a determinant of sexual risk behavior among men living with HIV or AIDS [66]. Studies have demonstrated consistent associations between unprotected sex and depression, anxiety [43, 67–69], and loneliness [18]. Older adults with HIV are particularly isolated from supportive social networks and are less likely to disclose their status due to the double stigma of AIDS and ageism, both of which lead to stress and poorer mental health outcomes [70–74]. To compensate for these changes, many older

adults use alcohol, tobacco, and/or illicit drugs which are factors for sexual risk [14, 75–77]. These changing psychosocial and intrapersonal factors highlight the need to understand the context of sexual behavior among older women with HIV.

Limitations

Our study had some limitations. First, only a few sexual risk behavior measures were obtained at each semiannual study visit, limiting our ability to examine additional sexual risk patterns such as partner concurrency and the HIV serostatus of sexual partners. Consequently, we were unable to estimate the risk of potential transmission to sexual partners among women reporting inconsistent condom use. Second, we used self-reported measures to categorize sexual behavior and menopausal status, which involves a possibility of bias and misclassification. Third, participants were recruited from urban sites, so the applicability of our findings to non-urban populations remains unclear. Finally, 96 % of WIHS at the Brooklyn, Bronx and Chicago sites speak English and only 4 % Spanish; therefore, these findings may not represent the sexual behaviors of non-English speaking populations of older women with HIV. Despite these shortcomings, however, we know of no other data set that is able to assess intra-individual changes in sexual risk behaviors among women with HIV from a longitudinal perspective.

Strengths

This study also had several strengths. Exploring sexual behavior among HIV-infected women in a large cohort over time is an innovative area of investigation. To date, there have been few investigations of the relative impact of aging or menopause on SA or UAVI in HIV-infected persons. Our longitudinal analysis allowed us to ascertain the gradual decline in SA and UAVI among HIV-infected women, while the HIV-uninfected women maintained levels of SA and UAVI. This is significant because the HIV-uninfected women in WIHS were matched according to their risk behaviors for HIV. These data suggest that among women at risk for HIV, risk behaviors do not change as women grow older, which points to an urgent need to target HIV prevention messaging to this population.

Conclusions

In summary, the decline in SA and UAVI over time among women with and without HIV was dependent on age; however, more than two-thirds of the HIV-infected women in the WIHS were sexually active, and 22 %engaged in UAVI over 13 years of follow-up. The sexual risk behaviors of older women with and without HIV-1 infection are neglected areas of research in part due to the assumptions that as women age they no longer engage in SA or sexual risk behaviors. These findings suggest that as women age they may need additional support for maintaining safer sex practices.

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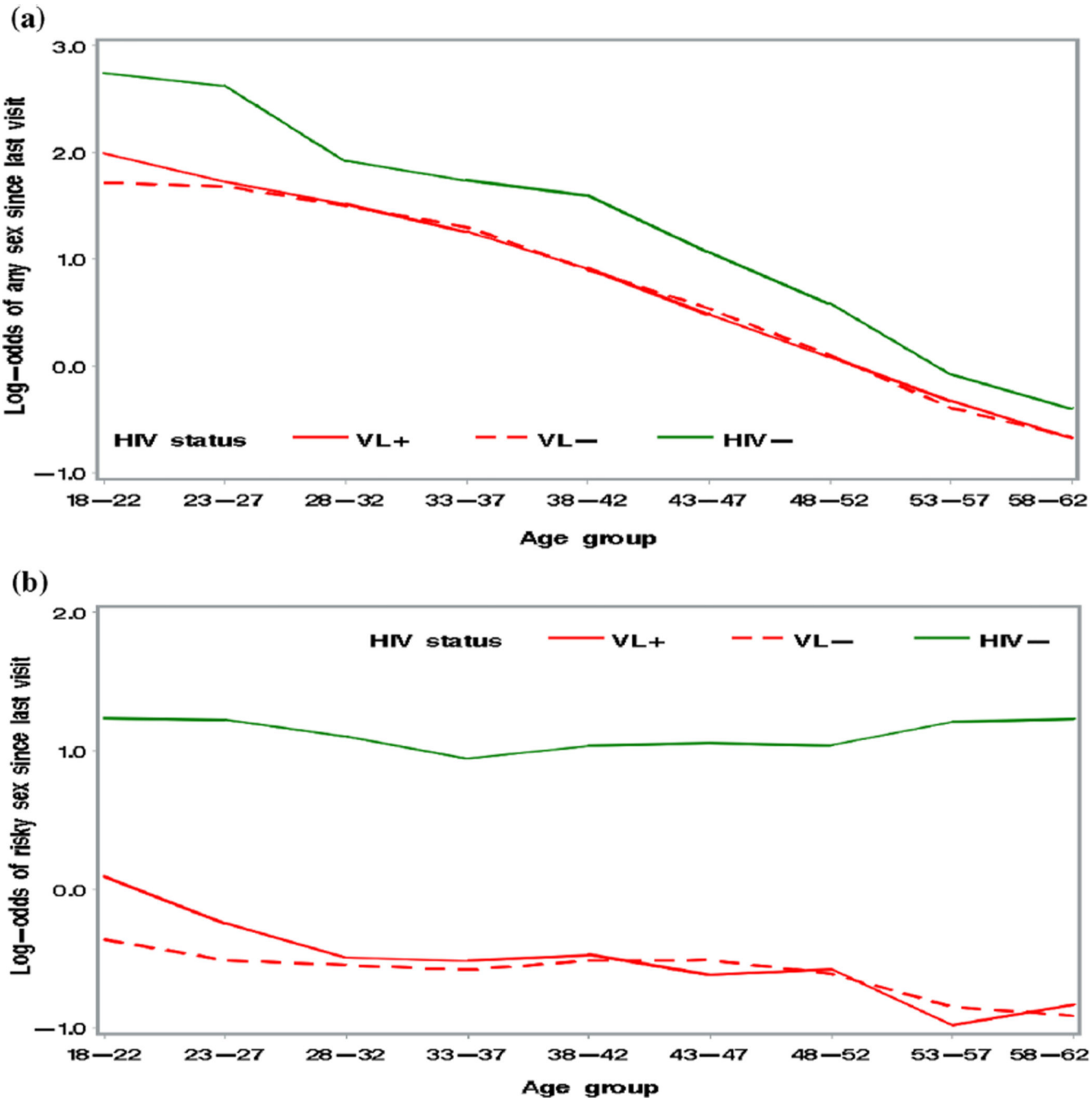

Fig. 1.

Linearity of relationship of age to log-odds of sexual behaviors: (**a**) Any sexual activity (SA). (**b**) Any unprotected sexual activity (UAVI) among those sexually active. Age is grouped in 5-year categories beginning with youngest subject in study. *VL+* detectable plasma HIV-RNA, *VL−* non-detectable plasma HIV-RNA, *HIV-* HIV−uninfected

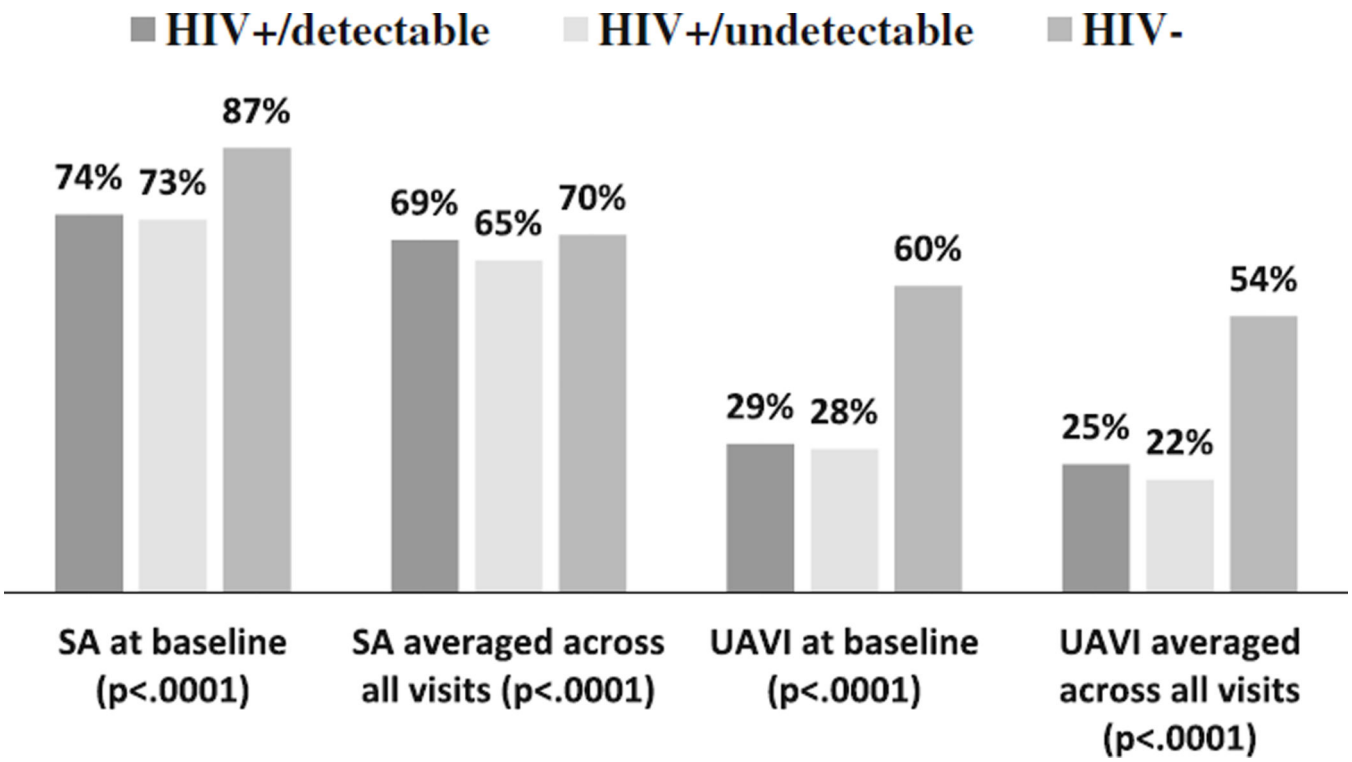

Fig. 2.

Percent of any SA and UAVI at baseline and averaged across all visits. *HIV+/detectable* detectable plasma HIV-RNA, *HIV+/undetectable* non-detectable plasma HIV-RNA, *HIV-* HIV-uninfected

Table 1

Characteristics of the Study Population at baseline and across study (by) visits

Baseline characteristics	**HIV+/detectable *N* = 1371 *N* (%)**	**HIV+/undetectable *N* = 556 *N* (%)**	**HIV− *N* = 742 *N* (%)**	***p* value**
Age				
18–29	248 (18.1)	111 (20.0)	274 (36.9)	<0.0001
30–39	625 (45.6)	251 (45.1)	282 (38.0)	
40–49	435 (31.7)	156 (28.1)	163 (22.0)	
50–59	56 (4.1)	35 (6.3)	20 (2.7)	
60+	7 (0.5)	3 (0.5)	3 (0.4)	
Race				
White	187 (13.6)	92 (16.6)	97 (13.1)	0.0020
Hispanic	349 (25.5)	184 (33.1)	202 (27.2)	
Black	790 (57.6)	260 (46.8)	414 (55.8)	
Other	45 (3.3)	20 (3.6)	29 (3.9)	
Education				
High school graduate	850 (62.2)	332 (59.8)	478 (65.1)	0.1423
Characteristics across study (by) visits	HIV +/detectable *N* = 16326 *N* (%)	HIV +/undetectable *N* = 12519 *N* (%)	HIV− *N* = 10967 *N* (%)	*p* value
Age				
18–29	1429 (8.8)	689 (5.5)	2150 (19.6)	<0.0001
30–39	5897 (36.1)	3705 (29.6)	3628 (33.1)	
40–49	6547 (40.1)	5440 (43.5)	3686 (33.6)	
50–59	2233 (13.7)	2325 (18.6)	1283 (11.7)	
60+	220 (1.4)	360 (2.9)	220 (2.0)	
Menopausal status				
Yes	2755 (16.9)	2691 (21.5)	1394 (12.7)	<0.0001
Heavy drinking				
Yes	1366 (8.4)	481 (3.9)	1180 (10.8)	<0.0001
Recent drug use				
Yes	4027 (24.9)	1951 (15.7)	3404 (31.2)	<0.0001
CES-D score ≥16				
Yes	5587 (42.1)	3518 (32.1)	3090 (32.4)	<0.0001
Physical Function*	71.1(28.4)	74.2 (27.5)	79.0 (26.1)	<0.001

HIV+/detectable detectable plasma HIV-RNA, *HIV+/undetectable* non-detectable plasma HIV-RNA, *HIV−* HIV-uninfected

* Mean (Standard deviation) calculated

Table 2

Adjusted odds ratios of any sexual activity (SA) and unprotected anal or vaginal intercourse (UAVI) for age and menopause by virologic group

	Number of visits	HIV+/VL+		HIV+/VL−		HIV−		*p* value
		OR	*95 % CI*	*OR*	*95 % CI*	*OR*	*95 % CI*	
Any SA								
Any sex for 10-year age change	*N* = 32,395	0.38	0.34–0.41	0.36	0.33–0.40	0.38	0.33–0.44	0.693
Any sex for menopause controlling for age	*N* = 17,501	0.78	0.68–0.90	0.75	0.64–0.87	0.82	0.65–1.04	0.724
UAVI								
Unprotected sex for 10-year age change	*N* = 21,382	0.83	0.74–0.92	0.91	0.81–1.01	0.96	0.83–1.10	0.036
Unprotected sex for menopause controlling for age	*N* = 9,906	0.72	0.58–0.88	0.85	0.69–1.06	1.04	0.74–1.48	0.099

Analyses of UAVI included only subjects with self-reported sexual activity

All of the seven plausible covariates (race, education, heavy drinking, current drug use, depression, physical function and follow-up duration) were added to each model

HIV+/VL+ detectable plasma HIV-RNA, *HIV+/VL−* non-detectable plasma HIV-RNA, *HIV−* HIV-uninfected

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