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## Association between depression and condom use differs by sexual behavior group in patients with HIV

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### Abstract

Identifying a relationship between depression and sexual risk behavior in HIV-infected patients could establish a mechanism to enhance prevention efforts. We conducted a cross-sectional analysis using data from the University of Pennsylvania Center for AIDS Research and used ordinal logistic regression to measure the association between depression and non-condom use. 716 men who have sex with men (MSM), 262 heterosexual men and 277 heterosexual women were included. The association between depression and non-condom use was strongest in heterosexual men with and without HIV-infected regular partners (OR 8.53, 95% CI 1.18–61.89 and OR 2.30, 95% CI 0.99–5.36 respectively), but absent in heterosexual women regardless of partner. Although the OR was low in MSM overall, an association was detected in MSM without HIV-infected regular partners (OR 2.44, 95% CI 1.39 – 4.31). In conclusion, we demonstrated an association between depression and non-condom use driven by heterosexual men and MSM without HIV-infected regular partners. Sexual risk should be addressed when intervening on depressive symptoms in these subgroups.

### Background

Approximately 50,000 new cases of HIV infection are diagnosed per year in the United States despite extensive public health efforts<sup>1</sup>. Since the great majority of transmissions are attributable to sexual contact, the need to target high-risk sexual behavior is clear. The effect of depression on sexual risk behavior is of particular interest given the high prevalence of depression in HIV-infected patients<sup>2</sup>.

Among HIV-uninfected individuals, the weight of the literature suggests that both men who have sex with men (MSM) and heterosexual adolescents and adults with depression are at

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#### Compliance with Ethical Standards:

**Conflict of Interest:** Drs. Cristina Brickman, Chelsea Voytek, David Metzger and Robert Gross have no conflicts of interest to declare.

**Ethical approval:** All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent:** All individuals provided informed consent prior to enrollment with the University of Pennsylvania Center for AIDS Research Clinical Core and completion of a detailed health questionnaire every 6–12 months. We obtained a waiver of informed consent to use de-identified data from this questionnaire specifically for our study purposes.

risk for engaging in high-risk sexual behavior and contracting sexually transmitted infections (STI)<sup>3-7</sup>. In HIV-infected patients, the relationship between depression and sexual risk has been primarily evaluated in MSM where studies also support a positive correlation<sup>8-12</sup>. Comparatively little is known about depression and sexual risk behavior in HIV-infected people who are not MSM. Not all studies, however, have demonstrated an association<sup>13</sup>. A non-linear, inverted U-shape, association has been proposed to account for this: patients with moderate levels of depression may be more likely to engage in high-risk sexual behavior than patients with severe, and presumably more debilitating, depression<sup>5,8,14</sup>.

For example, a recent study of HIV-infected MSM, heterosexual men and women 45 years-old who received motivational telephone interviews to decrease sexual risk behavior detected an association between individuals with moderate depression and non-condom use<sup>15</sup>. Participants with moderate depression also showed greater improvement in risk behavior following motivational interviews compared with participants without depression or with severe depression. However, the relatively small sample size of the study precluded analysis by sexual behavior group, similar to prior studies on depression and sexual risk behavior in non-MSM HIV-infected individuals<sup>16-19</sup>. This approach is problematic given that sexual practices are expected to differ by sexual behavior group and gender.

Our study aimed to define the association between depression and sexual risk behavior among different sexual behavior/gender groups within a large cohort of HIV-infected patients. We hypothesized the presence of a non-linear, inverted U-shaped association such that patients with moderate depression were most likely to engage in high-risk sexual behavior. We further proposed that such an association would be greatest in individuals with a strong incentive to use condoms. Examples include groups at greater risk for HIV transmission like MSM and individuals with HIV-uninfected regular partners and/or casual sex partners.

## Methods

### Study Population & Design

We conducted a cross-sectional analysis using data from the University of Pennsylvania Center for AIDS Research Clinical Core accrued from September 4, 2007 through April 21, 2014. The Clinical Core maintains information on HIV-infected individuals receiving care at hospitals affiliated with the University of Pennsylvania. Participants complete an extensive questionnaire administered by trained personnel approximately every 6-12 months that includes information on health, mood symptoms and sexual activity. Despite the presence of longitudinal data, we chose a cross-sectional design to measure the association between depression and sexual risk behavior to avoid the erroneous assumption that exposure to depression was equal for all participants at study enrollment. We included all study visits in which participants aged 18 or older reported being sexually active and for which data on depression and sexual behavior was available. Women who did not report sex with men were excluded because of their overall small sample size in our cohort and because of the low risk of sexual HIV transmission in this group<sup>20</sup>. The study protocol was reviewed and approved by the Institutional Review Board of the University of Pennsylvania.

## Measures

Depression was measured using the Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item instrument that is well-recognized and widely used in psychiatric epidemiology to measure depressive symptoms<sup>21</sup>. Responses are graded on a four-point scale with final scores ranging from 0 to 60; scores equal to or greater than 16 are consistent with a clinical diagnosis of depression. We included subjects who answered at least 19 of 20 items and used person-mean imputation to compute the overall scores for subjects with 1 missing item<sup>22</sup>.

Our study questionnaire asked about condom use during any sexual act with two separate questions: the first with a regular sex partner and the second with non-regular sexual partners. We merged data from the above questions to create an item that assessed the frequency of *overall* non-condom use and thus captured any high-risk behavior, the most clinically relevant endpoint. Condom use options consisted of “all of the time”, “most of the time”, “some of the time” and “never” but were condensed into “all of the time”, “some of the time” and “never” because the distinction between “some of the time” and “most of the time” was considered ambiguous. We selected the highest frequency of non-condom use when there was a discrepancy in non-condom use between regular and non-regular sexual partners to capture the behavior most associated with HIV transmission.

Although prior studies have dichotomized non-condom use, we maintained an ordinal variable to better capture the linear or inverted U-shape relationships that we hypothesized would represent the nature of the association between depression and non-condom use. Sensitivity analyses with a dichotomous outcome variable were conducted to compare our results to previous work.

## Statistical Analysis

To compare basic demographics and clinical characteristics, we used Kruskal-Wallis tests for continuous variables and chi-squared analysis for categorical variables.

We used ordinal logistic regression to calculate the odds ratio (OR) between depression and non-condom use. Depression was defined as a CES-D score  $\geq 16$ <sup>21</sup> and we included participants who always used condoms as our analysis reference category. To account for multiple observations within participant, we used generalized linear latent and mixed models (STATA 12.1, gllamm). Odds Ratios (OR) for which the 95% confidence interval (CI) did not include 1.0 were considered statistically significant. Because gllamm does not support traditional approaches to check the proportional odds assumption, we alternatively stratified our analysis by ordinal category (i.e., non-condom use “always to sometimes” and non-condom use “sometimes to never”) to qualitatively compare the magnitudes of these OR.

To evaluate a potential non-linear relationship between depression and condom use, we also used CES-D score as a continuous variable and included a squared term to evaluate the presence of a quadratic relationship. The presence of a significant positive association (OR > 1) between the continuous CES-D score and non-condom use, accompanied by an inverse association (OR < 1) between the square of the CES-D score and non-condom use, would

support the presence of an inverted U-shape relationship in which patients with moderate depression scores are the least likely to use condoms.

### Effect Modification

We decided *a priori* to evaluate the association between depression and non-condom use by sexual behavior/gender subgroup because condom practices differ between these groups<sup>23</sup>. Men who described themselves as gay or bisexual at any visit were termed “MSM” while sexually active men who only reported sex with women were designated “heterosexual men”. For simplicity, heterosexual and/or bisexual women were termed “heterosexual women.”

We further stratified our analysis by the presence or absence of a regular HIV-infected sexual partner to assess whether the association between depression and non-condom use was strongest in subjects with potentially the greatest incentive to use condoms (i.e., those with uninfected partners and thus at risk for transmission events). We did not specifically stratify based on overall HIV status of any partner because our questionnaire did not inquire whether non-regular partners were HIV-infected or not.

The presence of effect modification was determined by both qualitatively comparing the point estimates of the association between depression and non-condom use before and after stratification, and by likelihood ratio (LR) tests of heterogeneity. P-values  $\leq 0.05$  were considered statistically significant.

### Confounders

Age and race were selected as potential confounders based on clinical relevance.

Our questionnaire did not inquire about non-barrier methods of contraception. We addressed the potential confounding effect of other methods of contraception on the relationship between depression and non-condom use by conducting a separate analysis restricted to older, likely postmenopausal women (age  $> 50$ ) who would be unlikely to require contraception.

We chose not to include viral load as a potential confounder because of concern that it lies within the causal pathway in the relationship between depression and non-condom use. That is, depression may be associated with non-adherence to antiretroviral therapy and a detectable viral load, which may in turn influence a participant’s decision to use condoms. We excluded education level, income, insurance status, heavy alcohol consumption and substance use as potential confounders because of the same concern.

## Results

### Baseline Patient Characteristics

After exclusion of five women who were not sexually active with men, we identified 1348 HIV-infected, sexually active individuals aged 18 or older who contributed 2683 observations. Of these, 93 were excluded due to incomplete data: 27 because of incomplete CES-D scores, 66 because information on sexual behavior was missing. A total of 1255

subjects were thus included, of which 716 were MSM, 262 were heterosexual men and 277 were heterosexual women.

Demographics and clinical characteristics at enrollment are summarized in Table 1. Participants were primarily African American (60%) or Caucasian (32%). HIV-infection was generally well controlled with median CD4 count of 458/mm<sup>3</sup> and undetectable viral load in two-thirds of participants. 28% of participants had CES-D scores consistent with depression: prevalence was highest in HIV-infected women (38%).

### Depression and Non-condom Use

Comparison of the OR among the three sexual behavior subgroups revealed a much stronger association between depression and non-condom use in heterosexual men (adjusted OR 2.83, 95% CI 1.23–6.53), but not for MSM (adjusted OR 1.28, 95% CI 0.83–1.99) or heterosexual women (adjusted OR 1.43, 95% CI 0.75–2.73). Although the LR test for heterogeneity was not significant ( $p=0.26$ ), given the difference in the point estimates among the different sexual behavior groups, we concluded that effect modification by sexual behavior group was present.

While there was no association between depression and non-condom use in MSM with HIV-infected regular partners, a statistically significant association was detected in MSM without HIV-infected regular partners (Table 2). The association between depression and non-condom use was present both in heterosexual men with and without HIV-infected regular partners, while no statistically significant associations were noted in heterosexual women with or without HIV-infected regular partners. Although the LR tests for heterogeneity had  $p$ -values  $> 0.05$  between groups with and without HIV-infected regular partners, in MSM the difference in the absolute value of the OR of the relationship between depression and non-condom use by an HIV-infected regular partner suggested effect modification. Although the point estimates for the OR between depression and non-condom use in heterosexual men differed by HIV-infected regular partner, the wide confidence intervals made it difficult to make conclusions about differences between the groups.

We identified 134 older, likely postmenopausal women (301 visits). Analysis restricted to this group likewise found no statistically significant association between depression and non-condom use (OR 1.33, 95% CI 0.50–3.56 for all older women; OR 2.20, 95% CI 0.24–20.00 for older women with HIV-infected regular partners; OR 1.61, 95% CI 0.51–5.10 for older women without HIV-infected regular partners).

Sensitivity analyses with a dichotomized non-condom use variable revealed an overall decrease in the magnitude of our detected ORs although the direction of the associations and statistical significance were largely maintained (data not shown). Stratifying our analyses by ordinal level (i.e. non-condom use “always to sometimes” and non-condom use “sometimes to never”) did result in qualitatively lower OR when individuals who always use condoms were excluded suggesting that our results may be driven primarily by the transition from “no risk” to “some risk” (data not shown).

## Non-Linear Relationship between Depression and Non-Condom Use

The use of a continuous CES-D score and the square of a continuous CES-D score to evaluate the relationship between depression and non-condom use yielded no evidence of a non-linear relationship among MSM, heterosexual men or heterosexual women with or without HIV-infected regular partners (data not shown).

## Discussion

The available studies on the relationship between depression and sexual risk behavior in HIV-infected patients focused on MSM<sup>8-13</sup> or did not stratify by sexual behavior group<sup>15-19</sup>, with comparatively little known about HIV-infected heterosexual men and heterosexual women<sup>27-30</sup>. Our study shows clear evidence of an association between depression and non-condom use in a large cohort of HIV-infected patients. The smaller magnitude of the ORs when using a dichotomized non-condom use variable and the absence of a detectable U-shaped relationship supports the presence of a linear association.

This relationship is driven primarily by MSM without HIV-infected regular partners and by all heterosexual men. The only previous study in HIV-infected heterosexual men was limited to men with active intravenous drug use (IVDU)<sup>27</sup>. Of the three studies to comment on depression and sexual risk in HIV-infected women, one was limited by a small sample size<sup>28</sup> and another pooled data from both HIV-infected and HIV-uninfected women<sup>29</sup>. The third study measured depressive symptoms to help characterize the relationship between victimization and condom-use in young HIV-infected women and their “main partners”<sup>30</sup>. While no significant correlation between depression and condom use was identified, the study did not answer the broader question of engaging in sexual risk with others.

Our findings raise the hypothesis that the effect of depression on condom use varies by baseline motivation to use condoms. For example, HIV-infected MSM with HIV-infected regular partners may have less motivation to prevent HIV transmission compared with HIV-infected MSM without HIV-infected regular partners. In comparison, heterosexual men may still be driven to use condoms for contraception irrespective of whether their regular (female) partners have HIV. However, our results for heterosexual men with HIV-infected regular partners should be interpreted with some caution given the small sample size and resulting wide confidence interval of the unadjusted OR. Our questionnaire did not capture HIV status among casual partners; a variable which could have potentially confirmed whether perceived risk of HIV or STI transmission is required among HIV-infected MSM for an association between depression and non-condom use to exist. Yet, our hypothesis remains plausible assuming that HIV-infected MSM are motivated to prevent STI transmission when having sex with both HIV-uninfected regular partners and casual partners of unknown serostatus.

The initial psychosocial models of sexual risk behavior assumed that knowledge or normative perceptions affect sexual behavior in a straightforward, rational fashion: if so, increasing safer sex education and changing perceptive norms among at-risk populations would decrease the spread of HIV<sup>32</sup>. However it has become increasingly clear that less rational factors also play an important role in shaping and determining sexual behavior. The

cognitive escape model suggests that individuals cope with depression by narrowing their attention to immediate pleasurable outcomes to escape awareness of behavioral norms instead of following “rational” or “expected” behavior patterns<sup>32</sup>.

Depression may contribute to non-condom use among HIV-infected patients through both rational and non-rational behavioral factors. Patients with depression commonly experience both general difficulties in concentration and memory coupled with the ability to focus on negative thoughts and to exhibit enhanced recall of negative material<sup>33</sup>. Cognitive deregulation, therefore, could make depressed patients less susceptible to educational materials and/or behavioral interventions that otherwise decrease high-risk behavior in their non-depressed counterparts. From a cognitive escape aspect, patients with depression may be prone to engaging in high-risk sexual behavior as a means of escaping perceived inadequacies or negative feelings about themselves.

Interestingly, our primary analysis found no association between depression and non-condom use in women. This is in contrast to previous studies of HIV-uninfected women, where an association has been noted<sup>6</sup>. Risk factors for HIV acquisition in women include a disadvantaged socioeconomic background, a history of intimate partner violence, and lack of self-efficacy (i.e., the confidence one has in his or her ability to effect change in a specific practice)<sup>34</sup>. These factors may be present at higher rates in women with HIV such that condom use is affected more by depression in their male partners rather than in themselves.

Our study has several limitations. As a cross-sectional study we cannot make conclusions about the causality or the long-term associations between depression and sexual risk. While we did not measure the effects of sexual concurrency directly, we considered the association between depression and *any* non-condom use to be clinically relevant and the creation of an endpoint that captured the highest frequency of non-condom use across a variety of settings allowed identification of this risk behavior. In addition, our questionnaires were administered via face-to-face interviews as opposed to audio computer-assisted self-interview software (ACASI) such that answers are vulnerable to reporter bias. However, there is little to suggest that depression affects how patients answer sexual risk questions during face-to-face interviews<sup>35</sup>. The different recall periods between the CES-D questionnaire and non-condom use, which assess symptoms and behavior over the previous week and the previous 6 months respectively, could have resulted in recall bias; if present, we would expect underestimation of past sexual risk behavior which would have decreased the true magnitude of the association between depression and non-condom use. Our study was also done before the widespread use of pre-exposure prophylaxis (PrEP) in HIV-uninfected high-risk individuals. We nevertheless predict that condom use will stay relevant to prevent other STIs and in cases of suboptimal adherence to pre-exposure prophylaxis.

While we could not formally evaluate the proportional odds assumption, our sensitivity analyses suggest that the association between depression and non-condom use may primarily affect the transition from “no risk” to “some risk”. Despite this, we opted to maintain ordinal logistic regression because the overall result (the existence of a clinically important association between depression and non-condom use) was stable across the different models.



We did not adjust for multiple comparisons because we interpreted each subgroup analysis as representing a different hypothesis. Correction for multiple comparisons would not have changed the direction of our ORs or the overall clinical interpretation of the data.

The risk of unmeasured confounders is also potentially present as in all observational studies. Although we were initially concerned about the effect of non-barrier methods of contraception on the association between depression and non-condom use in women, restriction of our data to older women who were unlikely to use condoms for contraception showed no evidence of a confounding effect. Finally, despite our overall large sample size we may have been insufficiently powered to answer certain questions within our smaller subgroup analyses.

In conclusion, we present evidence that HIV-infected patients are vulnerable to the effects of depression on condom use with a stronger association suggested particularly in MSM without regular HIV partners and heterosexual men.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

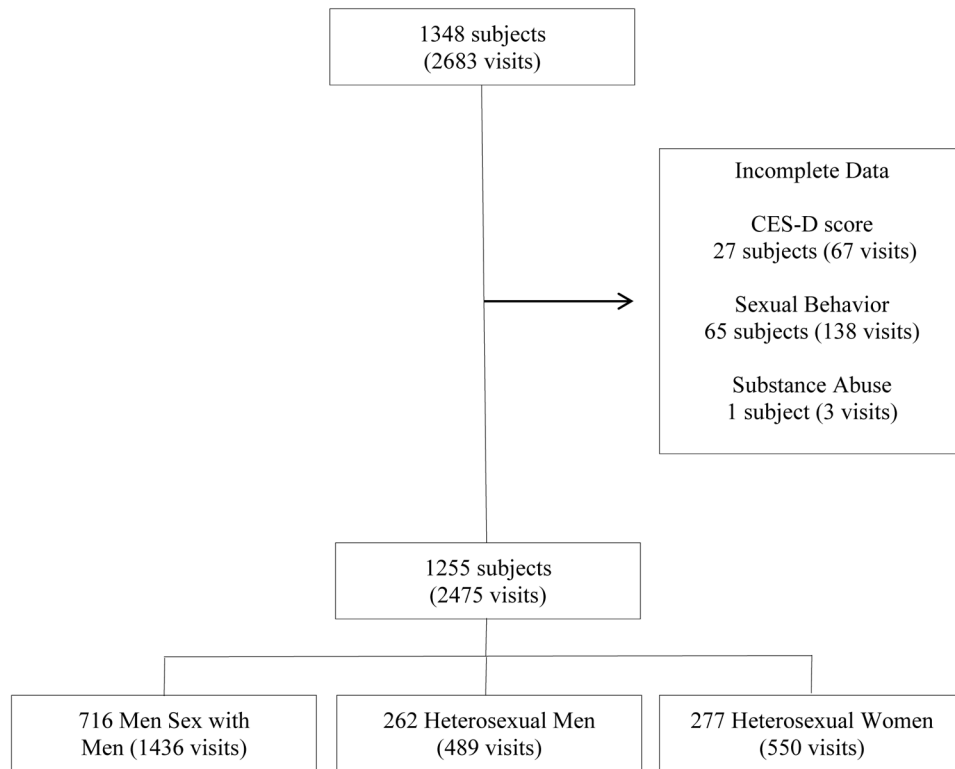
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**Figure 1.**  
Flow Diagram of Study Participants

**Table 1**

**Baseline Demographics and Clinical Characteristics by Sexual Behavior Subgroup**

	All (N=1255)	Men sex with men (N=716)	Heterosexual Men (N=262)	Heterosexual Women (N=277)	P-value
Age – median (IQR) *	52 (43–60)	52 (40–61)	56 (50–62)	50 (41–56)	<0.01
Visits per subject – median (IQR)	3 (1–4)	3 (1–4)	2 (1–4)	3 (1–4)	0.13
Race – no. (%) **					
- White or Caucasian	398 (32)	326 (46)	42 (16)	30 (11)	<0.01
- Black or African American	755 (60)	331 (46)	199 (76)	225 (81)	
- Other	102 (8)	59 (8)	21 (8)	22 (8)	
CD4 per mm <sup>3</sup> – median (IQR) ***	458 (294–651) n=1188	465 (311–673) n=675	415 (257–618) n=249	458 (287–645) n=264	0.05
Viral Load > 400 copies/ml – no. (%) ***	374 (32) n=1158	205 (31) n=658	63 (26) n=243	106 (41) n=257	<0.01
CES-D 16 – no. (%)	353 (28)	175 (24)	72 (27)	106 (38)	<0.01
Condom Use – no. (%)					
- Never	250 (20)	149 (21)	37 (14)	64 (23)	0.01
- Some of the Time	224 (18)	139 (19)	39 (15)	46 (17)	
- All of the Time	781 (62)	428 (60)	186 (71)	167 (60)	
HIV-infected Regular Partner – no. (%)	362 (29)	233 (33)	61 (23)	68 (25)	<0.01

\* IQR = interquartile range

\*\* Percentages for categorical variables refer to percentage within each sexual behavior subgroup column

\*\*\* The number of participants for each variable is the same as that listed under each sexual subgroup column (N), except for CD4 count and viral load: the number of participants for these two variables is listed within each box (n).

**Table 2**

Association between Depression (CESD-Score &gt;16) and Non-Condom Use

	Odds Ratio (OR) (95% Confidence Interval)			
	All (N=1255)	Men sex with men (N=716)	Heterosexual Men (N=262)	Heterosexual Women (N=277)
<b>Unadjusted OR</b>				
-- HIV-infected regular partner	1.38 (0.65–2.95)	1.23 (0.50–3.02)	<b>8.53 (1.18–61.89)</b>	0.73 (0.06–8.95)
-- No HIV-infected regular partner	<b>2.13 (1.41–3.24)</b>	<b>2.02 (1.15–3.55)</b>	2.30 (0.99–5.36)	1.56 (0.66–3.67)
<b>OR adjusted for age and race</b>				
-- HIV-infected regular partner	1.33 (0.67–2.66)	1.12 (0.53–2.34)	--*	0.90 (0.20–4.08)
-- No HIV-infected regular partner	<b>2.25 (1.49–3.39)</b>	<b>2.43 (1.38–4.30)</b>	<b>2.24 (1.49–3.39)</b>	1.76 (0.79–3.88)

\* model did not converge due to small sample size (n=61)

Bold indicates statistical significance by exclusion of 1.00 from the 95% confidence interval