Association between depressive symptoms, risk factors for sexually transmitted infections, and nongonococcal urethritis

Christopher Hearne

A thesis submitted in partial fulfillment of the requirements for the degree of

Master of Public Health

University of Washington

2016

Committee:

Lisa E. Manhart

Stephen E. Hawes

Program Authorized to Offer Degree:

Public Health – Epidemiology

University of Washington

Abstract

Association between depressive symptoms, risk factors for sexually transmitted infections, and nongonococcal urethritis

Christopher Hearne

Chair of the Supervisory Committee:

Lisa E. Manhart, PhD (chair),
Professor, Epidemiology
Adjunct Professor, Global Health

BACKGROUND: Depressive symptoms and urethritis are common, and may be associated with one another. Severe depression may lead to different risk behaviors than more moderate depression. Therefore individuals with moderate depression may be at increased risk for engaging in certain risk factors and for acquiring nongonococcal urethritis (NGU) compared to individuals with severe depression.

METHODS: This is a retrospective study of 521 men at high-risk for acquiring NGU. Men with and without NGU were given a depression screening instrument and asked about behavioral risk factors for acquiring sexually transmitted infections, including total partners, total new partners, condom use, and history of transactional sex. Poisson regression was used to calculate prevalence ratios for the association between depressive symptoms and behavioral risk factors. Logistic regression was used to calculate odds ratios for the association between depressive symptoms and prevalent NGU.

RESULTS: Compared to men with severe or minimal depressive symptoms, men with moderate depressive symptoms were more likely to have 3 or more sexual partners in the past 60 days, to have 2 or more new sexual partners in the last 60 days, and to report a history of transactional sex. There was no association between condom use and depressive symptoms. There was no association between NGU and depressive symptoms.

CONCLUSIONS: Some behavioral risk factors for acquiring sexually transmitted infections may be more common in men with moderate depressive symptoms, and men with severe depression may have similar behaviors compared to men without depression. This association between depressive symptoms and behavior may not result in increased frequency of NGU in a high-risk population.

BACKGROUND

Depression is the most common mood disorder. It is characterized by low mood and decreased pleasure in activities, and is often accompanied by somatic symptoms including sleep and appetite disturbances [1]. The point prevalence of screening positive for major depression in the United States and Western Europe may be as high as 5% using screening tools like the Comprehensive International Diagnostic Interview (CIDI). The prevalence of ever screening positive for major depression in one's lifetime ranges from 13% to 17% when using depression screening instruments such as the CIDI or the Mini-International Neuropsychiatric Interview (MINI) tool. [2]. Several studies have demonstrated associations between STIs and depressive symptoms. Studies of individuals seeking care at STI clinics have found a high prevalence of probable major depression that ranges from 40 – 50% when using the Center for Epidemiologic Studies Depression Scale (CES-D) and the General Health Questionnaire (GHQ) [3, 4]. A population-based survey in Canada found that individuals with a history of STI were over 50% more likely to screen positive for probable major depression using the CIDI compared to those without a history of STIs [5]. Sexual risk behavior has also been associated with depressive symptoms in diverse populations, including African American female adolescents [6, 7], incarcerated men [8], men who have sex with men (MSM) [9, 10], and heterosexual women [11].

Despite individual studies that have demonstrated associations between STI risk and depression, a meta-analysis failed to demonstrate a significant association between a variety of negative affective states, including depressive symptoms, and either an increase or decrease in sexual risk behaviors [12]. Some have attributed this lack of significant association to weaknesses in the existing literature, including temporal disconnection between depressive symptoms and subsequent risk behaviors, as well as unmeasured moderating variables (such as particular types of events that precipitate depressive symptoms). Crucially, most previous work did not attempt to examine whether the influence of depressive symptoms on prevalent STIs and risk behaviors varied based on the severity of depressive symptoms [12, 13, 14]. Nevertheless, a small number of studies have examined whether individuals with

more severe depression have more behavioral risk factors for acquiring STIs than individuals with moderate depression. These studies observed a linear dose-response relationship between severity of depressive symptoms levels of depression severity and increasing behavioral risk factors in heterosexual African American women [11] and adolescents [1].

Although some health behaviors, including sexual risk behaviors, may exhibit a dose-response association with depression, other associations may be more complex, with higher risk among moderately depressed individuals compared to either those with low levels of depressive symptoms or severe depression [14]. The inverse correlation between severity of depressive symptoms and libido (e.g., more severe depressive symptoms are correlated with lower libido) supports the hypothesis that individuals with moderate depression may engage in more sexual risk behaviors than those with more severe depression [15]. Furthermore, the association between social isolation and major depression suggests a plausible reason why severe levels of depression may reduce the frequency of some high risk sexual behaviors (such as concurrency or anonymous sex) [16].

Sexual risk behaviors can expose men to pathogens that cause reproductive tract disease syndromes. Male urethritis is the most common male reproductive tract syndrome and can be caused by many agents, including *Neisseria gonorrhoeae* and other non-gonococcal etiologies. Recognized causes of non-gonococcal urethritis (NGU) include *Chlamydia trachomatis*, *Mycoplasma genitalium*, *Trichomonas vaginalis*, and occasionally herpes simplex virus and adenovirus [17]. Although the etiology of many cases of NGU remains unknown, some idiopathic cases may be due to unidentified sexually transmitted pathogens. If depressive symptoms are associated with increased sexual risk behavior, they may also be associated with increased risk of NGU.

Given the frequency and clinical implications of NGU, as well as the risk of onward transmission of pathogens to sex partners, it is important to determine if depressive symptoms are associated with increased occurrence of sexual risk behaviors and/or increased risk of STI. To investigate this, we evaluated the association between depressive symptoms and sexual risk behaviors. We also evaluated the

association between depressive symptoms and NGU. Finally, we evaluated whether any relationship between depressive symptoms and sexual risk behaviors or NGU differed depending on severity of the depressive symptoms.

METHODS

Study participants and setting

This is a secondary data analysis of a case control study originally designed to determine if the two Ureaplasma species (*U. urealyticum* – biovar 2 and *U. parvum*) were associated with NGU. The original case control study [18] was nested in a randomized trial of the efficacy of standard therapies for NGU [19]. Both cases and controls were men ≥16 years old or older seeking care at the Public Health Seattle & King County STD Clinic. Individuals who did not speak English or who had active gonococcal infection were excluded. Recruitment occurred from May 2007 to October 2009.

Cases were men with NGU, defined as visible urethral discharge on examination or evidence of urethral inflammation on Gram stain (≥5 polymorphonuclear leukocytes per high-powered field) [19]. Controls were men who were recruited from the waiting room of the STD clinic who had neither urethral discharge on clinical exam nor evidence of urethral inflammation on Gram stain, and who presented to the clinic for reasons other than NGU (e.g., STI/HIV screening, or evaluation and treatment of genital ulcers and warts) [18].

Data collection

All participants received a routine STD examination, which included urine testing for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* using APTIMA Combo 2 assay (Gen-Probe). *Trichomonas vaginalis* was detected using research-only APTIMA TV analyte-specific reagents (Gen-Probe),

Mycoplasma genitalium using an in-house PCR, and Ureaplasmas by broth culture and subsequent species-specific PCR [18].

Additionally, all participants completed a computer-assisted self-interview (CASI), reporting supplemental medical history and risk behaviors, including those related to STI risk. Specifically, respondents reported lifetime history of drug use, lifetime history of transactional sex, number of sexual partners within the past 60 days (total number partners and number of new partners), and condom use in the past 60 days.

The CASI also elicited any self-reported history of a depression diagnosis, and assessed current depressive symptoms using the Center for Epidemiologic Studies Depression Scale 10 (CES-D 10). The CES-D 10 is a condensed version of the CES-D 20 depression screening scale. The original CES-D 20 contains 20 questions about the frequency with which respondents have experienced 9 key symptoms of depression over the past 2 weeks, using a 5-point response scale [20, 21]. The CES-D 10 consists of 10 items that ask respondents to report the extent to which they have experienced depressive symptoms in the past 7 days using a 3-point response scale. A response of 0 indicates that a symptom rarely or never occurs, a response of 1 indicates that the symptom occurs some of the time, a response of 2 indicates that the symptom occurs a moderate amount of the time, and 3 indicates that a symptom occurs every day or almost every day in the past 7 days. Two of the items (which ask if participants are happy and if they are hopeful) are scored inversely, such that higher scores are subtracted from the overall CES-D score. The total CES-D 10 score can range from 0 to 30 and prior assessments demonstrated that a score of 10 or greater on this screening tool correlates highly with a positive screen for major depression, reflecting significant depressive symptoms [22, 23, 24].

Data analysis

In initial analyses of characteristics associated with significant depressive symptoms (e.g., CES-D score ≥10) and characteristics associated with NGU, we used an independent t-test to determine statistical significance of differences in means, the Wilcoxon rank-sum test to evaluate differences in medians and a chi-squared test to evaluate differences in categorical variables. Additionally, we performed a test of trend for the association between significant depressive symptoms and the ordinal categorical variable for education level achieved. In addition to defining significant depressive symptoms as a CES-D score ≥10, we also categorized CES-D 10 scores (which range from 0 – 30) into quartiles to evaluate the presence of a curvilinear relationship between depressive symptoms and sexual risk behavior and/or NGU. The first quartile was comprised of CES-D 10 scores of 0 – 7; the second quartile of scores of 8 – 15; the third quartile included scores 16 – 22, and the fourth quartile included scores 23 – 30.

In univariable analyses, given the relatively high frequency of depressive symptoms, we used Poisson regression with robust standard errors to estimate prevalence ratios and 95% confidence intervals describing the association between sexual risk behavior and depressive symptoms. We used logistic regression to describe the association between NGU and depressive symptoms, maintaining consistency with the original case control study design. We fit eight separate univariable models evaluating the relationship between four behavioral risk factors and two different categorizations of depressive symptoms (≥10 vs. <10 and quartiles). The four behavioral risk factors were condom use (always or sometimes / never), any history of transactional sex (yes / no), new sexual partners (0 – 1 new sexual partners, or ≥2 in the past 60 days), and more sexual partners (0 – 2, or ≥3 total sexual partners in the past 60 days). In the first set of models, individuals with CES-D 10 scores <10 served as the referent category while those in the first quartile (scores 0-7) served as the referent group in the second set of models. We also fit two separate models evaluating the relationship with NGU, employing the same two categorizations of CES-D 10 scores (≥10 vs. <10 and quartiles).

In multivariable analyses, the following covariates were considered *a priori* for inclusion in the Poisson models and logistic regression models to control for potential confounding: income, education, age, and recreational drug use. Characteristics that changed the effect size between exposure and outcome by 10% or more and were not considered to be in the causal pathway were retained in the final model. Finally, for each multivariable model described above, we performed a test of linear trend using CES-D 10 score quartiles as an ordinal categorical variable to detect whether increasing quartiles of CES-D 10 score were linearly associated with behavioral risk factors or NGU.

RESULTS

Sample Characteristics

Of the 730 men originally enrolled in the parent trial, 200 entered the study prior to the addition of the CES-D 10 assessment and 6 were missing data on depressive symptoms. An additional three individuals had positive nucleic acid amplification tests for *Neisseria gonorrhoeae*, despite the absence of Gram negative intracellular diplococci on Gram stain and were excluded, leaving 521 participants included in these analyses.

Characteristics of men with and without significant depressive symptoms (individuals with CES-D score ≥10 and those with CES-D score <10) are displayed in Table 1. The mean age among men was 33.9 years (SD 10.4) old, 62% were white, and over half had some kind of college degree. Thirty-six percent had significant depressive symptoms as defined by a CES-D 10 score of 10 or greater and 76% had NGU.

Characteristics associated with significant depressive symptoms

In univariable analyses, men with a CES-D 10 score of 10 or more were significantly less likely to report having a college degree (52.2% vs. 62.6%; Table 1). In contrast, neither age nor race differed significantly between men who had clinically important depressive symptom and those who did not. Compared to individuals who did not have significant depressive symptoms, those who had a CES-D 10 score of 10 or greater were significantly more likely to have new sexual partners (37.8% vs. 26.9%), a history of any transactional sex (27.1% vs. 19.2%), and a history of methamphetamine use (23.4% vs. 12.9%), crack cocaine use (21.3% vs. 12.6%), and ecstasy use (41.0% vs. 32.1%). In contrast, individuals with and without significant depressive symptoms did not differ meaningfully in the number of partners or proportion having more sexual partners, consistent condom use, history of receiving money for sex, history of injection drug use, and MSM status.

In multivariable analysis of the association between behavioral risk factors and depressive symptoms, men with significant depressive symptoms (CES-D score 10 or greater) were 36% more likely to report a history of transactional sex (PR 1.36, 95% CI 1.00 – 1.85), after adjustment for race and drug use (Table 2). Men who reported significant depressive symptoms were also 38% more likely to report new partners (PR 1.38, 95% CI 1.06 – 1.80); adjustment for sex, race, education, and age did not change this association meaningfully. However, men who had significant depressive symptoms were not significantly more likely to report inconsistent condom use or more sexual partners, and adjustment for age, sex, drug use, and education did not meaningfully alter these associations.

When depressive symptoms were categorized into quartiles, men in the second quartile of CES-D 10 scores were 53% more likely to report a history of transactional sex compared to those in the first quartile (PR 1.53, 95% CI 1.09 – 2.15), after adjusting for age and drug use. However, men in the third and fourth quartiles did not significantly differ from those in the first quartile. With respect to new sexual partners, again men in the second quartile of CES-D 10 scores were 42% more likely to report new sexual

partners compared to men in the first quartile (PR 1.42, 95% CI 1.07 – 1.89) after adjustment for age and drug use, but there were no significant differences for men in the third and fourth quartiles. In contrast, men in the third quartile of CES-D 10 scores were 37% more likely to report more total sexual partners (≥3 in the past 60 days), after adjustment for race (PR 1.37, 95% CI 1.0 – 1.89), but there were no significant differences for men in the second and fourth quartiles. In contrast, inconsistent condom use was not significantly associated with any of the quartiles of CES-D 10 scores after adjustment for race, sex, education, and drug use.

Linear trend tests demonstrated no significant linear associations between CES-D quartiles and any of the behavioral risk factors ($p>0.05$ for all).

Association between depression and NGU

Characteristics of men with and without NGU are displayed in Table 3. Compared to men without NGU, men with NGU were significantly more likely to be black (33.3% vs. 14.4%) and less likely to have college degree (69.1% vs. 55.5%), but did not differ by age. Men with NGU were also more likely to have had more partners (36.4% vs. 29.3, and less likely to report always using condoms (17.6% vs. 37.5%). However, there were no significant differences between the groups regarding the proportion with new partners, men who have sex with men (MSM) status, any history of transactional sex, and any drug use (injection, methamphetamine, crack cocaine, or ecstasy).

In univariate analysis, NGU cases were more likely than controls to have a CES-D score of 10 or greater (OR 1.35, 95% CI 0.88 – 2.09), but this association was not statistically significant (Table 4). Multivariable adjustment for potential confounders, including age, race, education, and drug use did not meaningfully alter this association, and these characteristics were not included in the model. In multivariable analysis adjusting for race and drug use, men in the second, third, and fourth quartiles of CES-D 10 score were successively more likely to have NGU compared to men in the first quartile.

However, none of these associations were statistically significant and a test for linear trend was also not statistically significant ($p = 0.27$).

DISCUSSION

We found a large burden of depressive illness in this population, which exceeds the burden described in general population surveys. Approximately one-third of the men in this study met the CES-D 10 threshold for significant depressive symptoms. Men with significant depressive symptoms as defined by a CES-D 10 score of 10 or more were more likely to report a number of risk factors associated with STI acquisition, including a history of transactional sex, certain types of substance use, and two or more new sexual partners in the previous 60 days. Despite this association with increasing sexual risk behaviors, there was no significant association between depressive symptoms defined as a CES-D 10 score ≥10 and NGU.

There was some evidence of a curvilinear relationship between depressive symptoms and sexual risk behavior, but not with NGU. Men with CES-D 10 scores of 8-15 were more likely to report a history of transactional sex as well as new sexual partners compared to men with lower scores, but men with higher scores were not. Men with CES-D 10 scores of 16-22 were more likely to report 3 or more total sexual partners than those with scores of 0-7, but there was no similar increase in the probability of reporting this behavior among men with CES-10 scores of 8-15 or 23-30. We did not observe an association between consistency of condom use and CES-D 10 score.

Two of the four behavioral risk factors (history of transactional sex and ≥2 new sexual partners in the past 60 days) were significantly associated with depressive symptoms when CES-D 10 scores used a binary cut-off of 10 or more to indicate significant depression. When the same risk factors were analyzed in a model using quartiles of possible CES-D 10 scores, participants in either the 2nd CES-D 10 quartile (history of transactional sex, new sexual partners) or the 3rd quartile (more sexual partners) were more likely than those in the 1st quartile to report the risk factor in question. For all three of these risk factors,

those in the 4th quartile of CES-D 10 score, which represents the highest burden of depressive symptoms, were not significantly more likely to report the risk factor in question compared to those in the lowest quartile of CES-D 10 scores. This suggests that relatively moderate depressive symptoms are associated with increased levels of at least some behavioral risk factors for STI acquisition, while individuals with the most severe depressive symptoms are no more likely to exhibit those risk factors than those with the smallest burden of depressive symptoms.

We found a very high prevalence of depressive symptoms in our sample. Significant depression symptoms were reported by 36% of participants in this study. This is substantially higher than studies of community-dwelling adults, which suggest the point prevalence of depression is around 5% [2]. However, other studies have found a similarly large prevalence of depression among individuals seeking care for STIs, ranging as high as 40 – 50% [3, 4]. Several characteristics of this population may predispose to increased prevalence of depressive symptoms. The prevalence of depression tends to decrease with increasing age [25], and our sample was relatively young; more than 50% of participants were under the age of 35. Additionally, substance use is associated with major depressive disorder [26], and in our sample nearly half of the participants reported some type of illicit drug use. Finally, previous work examining the prevalence of depression in the general population used a variety of depression screening instruments other than the CES-D 10 [2, 4], and direct comparison with our sample may be misleading.

We used the CES-D 10 to measure depressive symptoms, which is a screening tool that captures symptoms of major depression. A score of 10 or greater indicates possible major depressive disorder and should prompt a referral for more detailed clinical evaluation, though a cut-point as low as 4 [27] or as high as 12 [28] achieved optimal sensitivity and specificity in older adult populations. However, screening surveys like the CES-D 10 and others cannot on their own be used to diagnose major depressive disorder; this requires a face-to-face interview with a clinician. Therefore it is possible that using a screening tool as a proxy for depression may overestimate the true prevalence of depression in our sample. However, symptoms of depression that fall short of the diagnostic criteria outlined in the

Diagnostic and Statistical Manual V (DSM-5) may produce significant distress and impact other health behaviors [14]. Therefore, using a screening tool may still be an effective way to measure the burden of depressive symptoms, even if the tool cannot provide a means to assess diagnostic criteria for major depressive disorder *per se*.

One possible explanation for the association between some of the behavioral risk factors and depressive symptoms that we observed is that depression may have a dose-dependent disinhibitory effect on sexual risk-taking behavior. Individuals with moderate depressive symptoms (e.g., those in the 2nd or 3rd quartile of possible CES-D 10 scores) may be more prone to risk-taking than those without depression, but individuals with severe depression may adopt behaviors that decrease risk of STI acquisition (such as social isolation, irritability, or co-morbid anxiety symptoms) [12, 13, 14]. This implies that depressive symptoms lead to increases in some behavioral risk factors in a U-shaped pattern. An alternative explanation is that behavioral risk factors themselves generate or exacerbate depressive symptoms. If this were the case, we should expect to see a linear increase in the likelihood of behavioral risk factors for increasing quartiles of CES-D 10, which was not observed in these analyses.

Despite an association between depressive symptoms and some behavioral risk factors for acquiring STIs, we did not observe an association between depressive symptoms and NGU. In part, this may be because some cases of NGU may not be caused by sexually transmitted pathogens, but rather other exposures such as non-infectious urethral inflammation, allergic responses, or somatization [17]. Another possible explanation is that factors other than sexual risk behavior may play a role in incident NGU. Contextual factors and sexual networks may play a greater role in the transmission of many STIs, including NGU, than individual risk behaviors. Individuals in high-risk sexual networks are at a relatively greater risk of acquiring STIs compared to individuals in lower risk networks, even given the same level of individual risk behavior [29, 30, 31]. Others have found that socioeconomic factors, including assortative mixing, are stronger predictors of prevalent STI than individual risk behaviors [32]. Our hypothesis is that depressive illness increases sexual risk behavior, which then increases the risk of

acquiring STIs. However, in our high-risk sample, the effect of the sexual network may have overwhelmed the effect that depressive symptoms has on NGU acquisition; this may explain why we observed an association between depressive symptoms and behavioral risk factors, but not between depressive symptoms and NGU.

This study had several strengths and limitations. We examined the association between NGU and depressive symptoms using objectively measured NGU and a well-validated depression screening method. The scoring of the CES-D 10 allowed us to evaluate two different ways of defining depressive symptoms (e.g., binary and categorical), and to test the hypothesis that moderate depressive symptoms increase risk, but minimal and severe symptoms do not (indicating a curvilinear relationship). This study also has several limitations. This study included only men who self-referred to a specialty STI clinic, and results from theses analyses may not accurately reflect the associations between STI behavioral risk factors, NGU, and depressive symptoms seen in lower risk populations. Furthermore, the CES-D 10 does not have a validated cut-off to describe varying severities of depressive symptoms. This study divided the total CES-D 10 scale into quartiles to create cut-offs that may approximate mild, moderate, and severe depressive symptoms, but this framework has not been previously validated. Additionally, the observational design of this study makes it difficult to exclude unmeasured confounding as the cause for observed associations. Given the study design, there is also uncertainty regarding the temporal sequence of events. Therefore, these data should not be used to draw causal conclusions.

In summary, we found evidence that men with significant depressive symptoms are more likely to report certain behavioral risk factors for STI acquisition, including a history of transactional sex and ≥2 new sexual partners in the past 60 days. Additionally, we found that mild or moderate levels of depressive symptoms (but not those with the highest burden of depressive symptoms) were somewhat associated with a history of transactional sex, 2 or more new partners in the previous 60 days, and 3 or more total partners in the previous 60 days. We did not find a significant association between depressive symptoms and inconsistent condom use, nor between depressive symptoms and NGU status. Future research should

seek to evaluate these relationships in less homogeneous populations, to evaluate whether depressive symptoms precede changes in risk behaviors, and to determine if other negative affective states, such as anxiety, possess a similar relationship to depressive illness. Future research should also incorporate more precise measurement of depression, such as clinical diagnostic interviewing with a mental health clinician.

Table 1: Sociodemographic Characteristics and Risk Behaviors Associated with Depressive Symptoms as measured by the CES-D 10 in Men Attending a Public STD Clinic

SOCIODEMOGRAPHIC FACTORS	Total sample N (%) n = 521	CES-D ≥10 N (%) n = 188	CES-D <10 N (%) n = 333	p-value
Age				
<25	120 (23.0)	48 (25.5)	72 (21.6)	0.75
25 – 34	196 (37.6)	69 (36.7)	127 (38.1)	
>45	129 (24.8)	46 (24.5)	83 (24.9)	
Race				
White	305 (62.4)	114 (63.7)	191 (61.6)	0.29
Black	142 (29.0)	46 (25.7)	96 (31.0)	
Other	42 (8.6)	19 (10.6)	23 (7.4)	
Education				
Less than HS	32 (6.2)	16 (8.5)	16 (4.8)	**<0.01**
HS or GED	182 (35.1)	74 (39.4)	108 (32.6)	
2 or 4-year degree	259 (49.9)	84 (44.7)	175 (52.9)	
Graduate or professional	46 (8.9)	14 (7.5)	32 (9.7)	
SEXUAL RISK BEHAVIORS				
≥3 partners in past 60 days	181 (34.7)	71 (37.8)	110 (33.0)	0.28
Mean number partners (±SD)	2.8 (3.9)	3.4 (5.7)	2.5 (2.3)	
Median number partners (range)	2 (0-50)	2 (0-50)	2 (0-20)	
≥2 *new* partners past 60 days [1]	149 (30.6)	66 (37.8)	83 (26.9)	**0.02**
Mean *new* partners (±SD)	1.5 (2.4)	1.9 (±3.2)	1.3 (±1.7)	**0.01**
Condom use in past 60 days [2]				
Always	91 (22.5)	34 (18.1)	57 (22.0)	0.93
Usually	100 (24.5)	34 (18.1)	66 (25.5)	
Sometimes	75 (18.3)	29 (15.4)	46 (17.8)	
Never	143 (35.0)	53 (28.2)	90 (34.8)	
Sex of partners in past 60 days [3]				
MSW	322 (67.2)	109 (63.0)	213 (69.6)	0.14
MSM	157 (32.8)	64 (37.0)	93 (30.4)	
Met partner on internet	218 (41.9)	85 (45.2)	133 (40.1)	0.39
History of transactional sex (ever)	115 (22.1)	51 (27.1)	64 (19.2)	**0.04**
ILLICIT DRUG USE				
Injection drug use (ever)	32 (6.1)	14 (7.5)	18 (5.4)	0.35

Methamphetamine use (ever)	87 (16.7)	44 (23.4)	43 (12.9)	<**0.01**
Crack cocaine use (ever)	82 (15.7)	40 (21.3)	42 (12.6)	**0.01**
Ecstasy use (ever)	184 (35.3)	77 (41.0)	107 (32.1)	**0.04**

[1] *Male and female*

[2] *For anal and vaginal sex, with male and female sexual partners*

[3] *Only among men that reported insertive sex in the past 60 days; 106 men reported no insertive sex. 42 men reported no insertive sex in past 60 days, or had missing data. 15 men reported insertive sex with both men and women and were included in the MSM category*

Table 2: Multivariable analyses of the Association Between CES-D Score and Selected Behavioral Risk Factors

CES-D 10 Score ≥10	PR (95% CI)	p-value
Inconsistent condom use[1]	0.99 (0.89 – 1.10)	0.88
History of transactional sex[2]	1.36 (1.00 – 1.85)	**0.05**
≥2 *new* SPs in past 60 days[1]	1.38 (1.06 – 1.80)	**0.02**
≥3 SPs in past 60 days[1]	1.14 (0.90 – 1.45)	0.27
CES-D 10 Score, by quartiles	*Inconsistent condom use*[1]	
1st quartile (score 0 – 7)	1.00 (ref)	
2nd quartile (score 8 – 15)	0.95 (0.85 – 1.08)	0.49
3rd quartile (score 16 – 22)	1.05 (0.90 – 1.22)	0.53
4th quartile (score 23 – 30)	1.04 (0.78 – 1.39)	0.76
Linear trend test		0.62
	History of transactional sex[2]	
1st quartile (score 0 – 7)	1.00 (ref)	
2nd quartile (score 8 – 15)	1.53 (1.09 – 2.15)	**0.02**
3rd quartile (score 16 – 22)	1.33 (0.85 – 2.08)	0.22
4th quartile (score 23 – 30)	1.08 (0.44 – 2.65)	0.87
Linear trend test		0.95
	≥2 new SPs in past 60 days[1]	
1st quartile (score 0 – 7)	1.00 (ref)	
2nd quartile (score 8 – 15))	1.42 (1.07 – 1.89)	**0.02**
3rd quartile (score 16 – 22)	0.99 (0.62 – 1.60)	0.99
4th quartile (score 23 – 30)	1.06 (0.45 – 2.50)	0.89
Linear trend test		0.90
	≥3 SPs in past 60 days[3]	
1st quartile (score 0 – 7)	1.00 (ref)	
2nd quartile (score 8 – 15)	0.88 (0.66 – 1.17)	0.37
3rd quartile (score 16 – 22)	1.37 (1.00 – 1.89)	**0.05**
4th quartile (score 23 – 30)	0.63 (0.22 – 1.83)	0.40
Linear trend test		0.57

[1] evaluated race, any drug use, education, and age as potential confounders; point estimates did not change by ≥10%

[2] adjusted for age and any drug use

[3] adjusted for race

PR = prevalence ratio

Table 3: Sociodemographic Characteristics and Risk Behaviors Associated with NGU Status in Men Attending a Public STD Clinic

SOCIODEMOGRAPHIC FACTORS	NGU positive N (%) n = 398	NGU negative N (%) n = 123	p-value
Age			
<25	92 (23.1)	28 (22.8)	0.32
25 – 34	155 (38.9)	41 (33.3)	
35 – 44	91 (22.9)	38 (30.9)	
>45	60 (15.1)	16 (13.0)	
Race			
White	222 (58.7)	83 (74.8)	**<0.01**
Black	126 (33.3)	16 (14.4)	
Other	30 (7.9)	12 (10.8)	
Education			
Less than HS	25 (6.3)	7 (5.7)	**<0.01**
HS or GED	151 (38.1)	31 (25.2)	
2 or 4-year degree	191 (48.2)	68 (55.3)	
Graduate or professional	29 (7.3)	17 (13.8)	
SEXUAL RISK BEHAVIORS			
≥3 partners in past 60 days	145 (36.4)	36 (29.3)	**<0.01**
Number of partners in past 60 days			
Mean number of partners (±SD)	3.0 (3.4)	2.1 (2.0)	**<0.01**
Median number of partners (range)	2 (0-50)	2 (0-10)	**<0.01**
≥2 *new* partners in past 60 days [1]	118 (29.7)	31 (34.8)	0.34
Mean *new* partners (±SD)	1.5 (2.5)	1.4 (1.4)	0.72
Median *new* partners (range)	1 (0-30)	1 (0-9)	0.10
Condom use in past 60 days [2]			
Always	55 (17.6)	36 (37.5)	**<0.01**
Usually	83 (26.5)	17 (17.7)	
Sometimes	61 (19.5)	14 (14.6)	
Never	114 (36.4)	29 (30.2)	
Sex of partners [3]			
MSW	243 (65.9)	79 (71.8)	0.24
MSM	126 (34.2)	31 (28.2)	
Met partner on internet	177 (44.6)	41 (33.3)	**0.03**
History of transactional sex (ever)	87 (21.9)	28 (22.8)	0.83
ILLICIT DRUG USE			

Injection drug use (ever)	22 (5.5)	10 (8.1)	0.29
Methamphetamine use (ever)	63 (15.8)	24 (20.0)	0.34
Crack cocaine use (ever)	66 (16.6)	16 (13.0)	0.34
Methamphetamine use (ever)	63 (15.8)	24 (20.0)	0.34
Ecstasy use (ever)	142 (35.7)	42 (34.2)	0.76

[1] *Male and female*

[2] *For anal and vaginal sex, with male and female sexual partners*

[3] *Only among men that reported insertive sex in the past 60 days; 106 men reported no insertive sex. 42 men reported no insertive sex in past 60 days, or had missing data. 15 men reported insertive sex with both men and women and were included in the MSM category*

Table 4: Multivariable analyses of the Association Between NGU Status and CES-D Score

	OR (95% CI)	p-value
CES-10 score ≥10[1]	1.35 (0.88 – 2.09)	0.17
CES-D 10 Score, by quartiles[2]		
1st quartile (0 – 7)	1.00 (ref)	
2nd quartile (score 8 – 15)	1.48 (0.91 – 2.40)	0.11
3rd quartile (score 16 – 22)	1.95 (0.90 – 4.21)	0.09
4th quartile (score 23 – 30)	2.20 (0.47 – 10.3)	0.32
Linear trend test		0.27

[1] evaluated race, any drug use, education, and age as potential confounders; point estimates did not change by ≥10%

[2] adjusted for race and any drug use

OR = odds ratio

References

1) Hollon SD, Thase ME, Markowitz JC. (2002). Treatment and prevention of depression. *Psychological science in the public interest*. November;*3*(2):39—77.
2) Cassano P, Fava Maurizio. (2002). Depression and public health: An overview. *Journal of Psychosomatic Research*. October;*53*(4):849-857. doi: http://dx.doi.org/10.1016/S0022-3999(02)00304-5
3) Mo PKH, Gu, J, Lau JTF, You H. (2015). Prevalence and associated factors of mental health problems among monogamous Chinese female patients with sexually transmitted diseases in Hong Kong. *AIDS Care*, *27*(4), 481–488. http://doi.org/http://dx.doi.org/10.1080/09540121.2014.972321
4) Erbelding EJ, Hummel B, Hogan T, Zenilman, J. (2001). High rates of depressive symptoms in STD clinic patients. *Sex Transmitted Disease*, *28*(5), 281–284.
5) Chen Y, Wu J, Yi Q, Huang G, Wong T. (2008). Depression associated with sexually transmitted infection in Canada. *Sexually Transmitted Infections*, *84*(7), 535–40. http://doi.org/10.1136/sti.2007.029306
6) Seth P, Patel SN, Sales JM, DiClemente RJ, Wingood GM, Rose ES. The impact of depressive symptomology on risky sexual behavior and sexual communication among African American female adolescents. *Psychology, Health and Medicine*. 2011 May; 16(3): 346-356. doi:10.1016/j.surg.2006.10.010.
7) Brawner BM, Davis ZM, Fannin EF, Alexander KA. (2012). Clinical depression and condom use attitudes and beliefs among African American adolescent females. *The Journal of the Association of Nurses in AIDS Care. 23*(3), 184–94. http://doi.org/10.1016/j.jana.2011.03.005
8) Khan MR, Kaufman JS, Pence BW, Gaynes BN, Adimora AA, Weir SS, Miller WC. (2009). Depression, sexually transmitted infection, and sexual risk behavior among young adults in the United States. *Archives of Pediatric Adolescent Medicine*, 163(7):644—652. doi: 10.1001/archpediatrics.2009.95
9) Blashill AJ, O'Cleirigh C, Mayer KH, Goshe BM, Safren SA. Body mass index, depression, and sexual transmission risk behaviors among HIV-positive MSM. *AIDS Behavior*. 2012 November;*16*(8):2251-2256. doi: 10.1007/s10461-011-0056-2.
10) De Santis JP, Colin JM, Provencio Vasquez E, McCain GC. (2008). The relationship of depressive symptoms, self-esteem, and sexual behaviors in a predominantly Hispanic sample of men who have sex with men. *American Journal of Men's Health*, *2*(4), 314–21. http://doi.org/10.1177/1557988307312883
11) Holden AE, Shain RN, Miller WB, Piper JM, Perdue ST, Thurman AR, Korte JE. (2008). The influence of depression on sexual risk factor reduction and STD infection in a controlled, randomized trial. *Sexually transmitted disease. 35*(10), 898–904. http://doi.org/10.1097/OLQ.0b013e31817d7a33.
12) Crepaz N, Marks G. (2001). Are negative affective states associated with HIV sexual risk behaviors? A meta-analytic review. *Health Psychology*. *20*(4), 291–299. http://doi.org/10.1037/0278-6133.
13) Kalichman SC, Weinhardt, L. (2001). Negative affect and sexual risk behavior: Comment on Crepaz and Marks (2001). *Health Psychology*, *20*(4), 300–1. http://doi.org/10.1037//0278-6133.20.4.300
14) Simoni JM, Safren SA, Manhart LE, Lyda K, Grossman CI, Rao D, Mimiaga MJ, Wong FY, Catz SL, Blank MB, DiClemente R, Wilson IB. (2011). Challenges in addressing depression in HIV research: Assessment, cultural context, and methods. *AIDS and Behavior*, *15*(2), 376–388. http://doi.org/10.1007/s10461-010-9836-3

15) Mathew RJ. (1982). Sexual dysfunctions in depression. *Archives of Sexual Behavior*. 11(4):323-328.
16) Cornwell E, Waite L. (2009). Social disconnectedness, perceived isolation, and health among older adults. *Journal of Health and Social Behavior*. March;*50*(1):31-48. doi: 10.1177/002214650905000103
17) Martin DH. Management of Sexually Transmitted STDs. In: Holmes K et al, Sexually Transmitted Diseases. 4th edition. Seattle, WA: McGraw-Hill, 2008. Accessed online from University of Washington.
18) Wetmore CM, Manhart LE, Lowens MS, Golden MR, Jensen NL, Whittington WLH, Xet-Mull AM, Astete SG, McFarland NL, McDougal SJ, Totten, PA (2011). Ureaplasma urealyticum is associated with nongonococcal urethritis among men with fewer lifetime sexual partners: A case-control study. *Journal of Infectious Diseases*. *204*(8), 1274–1282. http://doi.org/10.1093/infdis/jir517
19) Manhart LE, Gillespie CW, Lowens MS, Khosropour CM, Colombara DV, Golden MR, Hakhu NR, Thomas KK, Hughes JP, Jensen NL, Totten PA. (2013). Standard treatment regiments for nongonoccocal urethrtitis have similar but declining cure rates: A randomized controlled trial. *Clinical Infectious Diseases*. April;56(7):934—942. doi: 10.1093/cid/cis1022.
20) Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Applied Psychological Measurement. 1977;1:385-401.
21) Eaton WW, Muntaner C, Smith C, Tien A, Ybarra M. Center for Epidemiologic Studies Depression Scale: Review and revision (CESD and CESD-R). In: Maruish ME, ed. The Use of Psychological Testing for Treatment Planning and Outcomes Assessment. 3rd ed. Mahwah, NJ: Lawrence Erlbaum; 2004:363-377.
22) Zhang W, O'Brien N, Forrest JI, Salters KA, Patterson TL, Montaner JSG, Hogg RS, Lima VD. (2012). Validating a shortened depression scale (10 item CES-D) among HIV-positive people in British Columbia, Canada. *PLoS ONE* 7(7): e40793. doi:10.1371/journal.pone.0040793
23) Andresen EM, Malmgren JA, Carter WB, Patrick DL. (1994). Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). *American Journal of Preventative Medicine*, 10(2):77—84.
24) Chang KF, Weng LJ. (2013). Screening for depressive symptoms among older adults in Taiwan: Cutoff of a short form of the Center for Epidemiologic Studies depression scale. *Health*. 5(3A):588–594.
25) Kessler RC, Birnbaum H, Bromet E, Hwang I, Sampson N, Shahly V. (2010). Age differences in major depression: results from the National Comorbidity Survey Replication (NCS-R). *Psychological Medicine*. 40(2):225.
26) Currie SR, Patten SB, Williams JV, Wang J, Beck CA, El-Guebaly N, Maxwell C. (2005). Comorbidity of major depression with substance use disorders. *Canadian Journal of Psychiatry*. 50(10):660—666.
27) Irwin M, Artin KH, Oxman MN. (1999). Screening for depression in the older adult. *Archives of Internal Medicine* 159(August): 1701—1704.
28) Cheng ST, Chan AC. (2005). The Center for Epidemiologic Studies Depression Scale in older Chinese: thresholds for long and short forms. *International Journal of Geriatric Psychiatry*. May 20(5):465—470.
29) Ghani AC, Swinton J, Garnett GP. (1997). The role of sexual partnership networks in the epidemiology of gonorrhea. *Sexually Transmitted Diseases*. *24*(1):45 – 56.
30) Adimora AA, Schoenbach VJ. (2005). Social context, sexual networks, and racial disparities in rates of sexually transmitted infections. *Journal of Infectious Diseases*. 191(supplement 1):S115 – S122.

31) Doherty IA, Padian NS, Marlow C, Aral SO. (2005). Determinants and consequences of sexual networks as they affect the spread of sexually transmitted infections. *Journal of Infectious Diseases*. 191(supplement 1):S42 – S54.
32) Manhart LE, Aral SO, Holmes KK, Critchlow CW, Hughes JP, Whittington WLH, Foxman B. (2004). Influence of study population on the identification of risk factors for sexually transmitted diseases using a case-control design: The example of gonorrhea. *American Journal of Epidemiology*. 160(4):393—402. doi:10.1093/aje/kwh220.