MEMORANDUM FOR GE
ATTN: COL HANNAH N. WILLIAM

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your journal, entitled Clinical indicators associated with HIV acquisition in the United States Air Force published in Aids Care in accordance with MDWI 41-108, has been approved and assigned local file #16403.

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

Warrior Medics – Mission Ready – Patient Focused
1. TO: CLINICAL RESEARCH
2. FROM: (Author's Name, Rank, Grade, Office Symbol)
   William N Hannah Jr, Col, USAF, MC, 59 MDW/GE
3. GME/GHSE STUDENT: □ YES □ NO
4. PROTOCOL NUMBER: WRAIR #1898

5. PROTOCOL TITLE: (Note: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)
   Epidemiology and Risk Factors for HIV Infection in U.S. Air Force Service Members, 1996-2011

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:
   Clinical indicators associated with HIV acquisition in the United States Air Force

7. FUNDING RECEIVED FOR THIS STUDY? □ YES □ NO
   FUNDING SOURCE: Henry Jackson Foundation (W81XWH-11-2-0174)

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES? □ YES □ NO

9. IS THIS MATERIAL CLASSIFIED? □ YES □ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.? □ YES □ NO
   NOTE: If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

11. MATERIAL IS FOR: □ DOMESTIC RELEASE □ FOREIGN RELEASE
    CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.
    □ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)
    AIDS CARE
    □ 11b. PUBLISHED ABSTRACT (List intended journal.)
    □ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)
    □ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meeting.)
    □ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)

12. HAVE YOUR ATTACHED RESEARCH/TECHNICAL MATERIALS BEEN PREVIOUSLY APPROVED TO BE PUBLISHED/PRESENTED?
    □ YES □ NO
    ASSIGNED FILE #: 16259
    DATE: August 01, 2016

13. EXPECTED DATE WHEN YOU WILL NEED THE CRO TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
    NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).

DATE
December 31, 2016

14. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)
    Hannah Jr, William N, william.n.hannah.mil@mail.mil

15. DUTY PHONE/PAGER NUMBER (210) 539-9477

16. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

   LAST NAME, FIRST NAME AND M.I.   GRADE/RANK   SQUADRON/GROUP/OFFICE SYMBOL   INSTITUTION (If not 59 MDW)
   a. Primary/Corresponding Author
      Hannah Jr, William N
      Col
      59 MDW/GE
      US Military HIV Research
   b. Hakre, Shilpa
   c. Dawson, Peter
   d. Wu, Hao
   e. Peel, Sheila A

17. IS A 502 ISG/IAAC ETHICS REVIEW REQUIRED (JER DOD 5500.07-R)? □ YES □ NO

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 49-401_IP, AND 59 MDW 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

18. AUTHOR'S PRINTED NAME, RANK, GRADE
    William N Hannah Jr, Col, USAF, MC

19. AUTHOR'S SIGNATURE

20. DATE
   November 18, 2016

21. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE
    Woodson S Jones, Dean, SAUSHEC

22. APPROVING AUTHORITY'S SIGNATURE

23. DATE
   November 18, 2016
<table>
<thead>
<tr>
<th>Date Received</th>
<th>Processing Request File Number</th>
<th>Date Reviewed</th>
<th>Assigned Processing Request File Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>November 22, 2016</td>
<td>16403</td>
<td>November 23, 2016</td>
<td></td>
</tr>
</tbody>
</table>

28. Author Contacted for Recommended or Necessary Changes:  
- NO  
- YES If yes, give date.  
- N/A

29. Comments:  
- APPROVED  
- DISAPPROVED

IRB approved exempt study with appropriate disclaimers. Approved.

30. Printed Name, Rank/Grade, Title of Reviewer  
Kevin Kupferer/GS13/Human Research Subject Protection Expert

31. Reviewer Signature  
KUPFERER KEVIN R 1086667270

32. Date  
November 23, 2016

36. Printed Name, Rank/Grade, Title of Reviewer  
37. Reviewer Signature  
38. Date

39. Date Received  
November 23, 2016

41. Comments:  
- APPROVED  
- DISAPPROVED

(In compliance with security and policy review directives.)

42. Printed Name, Rank/Grade, Title of Reviewer  
Kevin Linuma, SSgt/E-5, 59 MDW Public Affairs

43. Reviewer Signature  
LINUMA KEVIN MITSU 1269227

44. Date  
November 28, 2016

48. Printed Name, Rank/Grade, Title of Reviewer  
49. Reviewer Signature  
50. Date

Senior Author Notified by Phone of Approval or Disapproval:  
- YES  
- NO  
- COULD NOT BE REACHED  
- LEFT MESSAGE

Comments:  
- APPROVED  
- DISAPPROVED
Clinical indicators associated with HIV acquisition in the United States Air Force

William N. Hannah, Jr. 1, Shilpa Hakre 2,3, Peter Dawson 4, Hao Wu 4, Sheila A. Peel 5, Nelson L. Michael 2, Paul T. Scott 2, Jason F. Okulicz 6

1Department of Medicine, San Antonio Military Medical Center, Fort Sam Houston, TX; Telephone (210) 916-5756; william.n.hannah.mil@mail.mil

2US Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD; Telephone (301) 500-3708; shakre@hivresearch.org, nmichael@hivresearch.org and pscott@hivresearch.org

3Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, MD

4The EMMES Corporation, Rockville, MD; Telephone (301) 251-1161; pdawson@emmes.com and cindyhaowu@gmail.com

5HIV Diagnostics and Reference Laboratory, United States Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD; Telephone (310) 319-2297; speel@hivresearch.org

6Infectious Disease Service, San Antonio Military Medical Center, Fort Sam Houston, TX; Telephone (210) 916-5554; Jason.f.okulicz.mil@mail.mil
Corresponding author:

Jason F. Okulicz, MD
San Antonio Military Medical Center
3551 Roger Brooke Drive, Fort Sam Houston, TX 78234-6200
Phone: (210) 916-5554; Fax (210) 916-5900;
Email: jason.f.okulicz.mil@mail.mil

Funding:

This work was supported by a cooperative agreement (W81XWH-11-2-0174) between the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF) and the US Department of Defense (DoD).

The authors have no financial disclosures to report.

Word Count: 1,497

Disclaimer: The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense or its Components.
Abstract:

Mandatory HIV screening of United States Air Force (USAF) personnel every 2 years effectively identifies incident cases, however testing frequency limits the ability to detect early HIV infection. Identifying clinical indicators of HIV in the USAF population is necessary to develop a supplemental provider-based targeted testing strategy. We conducted a matched case-control study of male active duty USAF personnel with a new HIV diagnosis (n=452) between 1996 and 2011 matched to five randomly selected controls (n=2,176). The relationship between clinical diagnoses, determined by ICD-9 codes, and HIV infection was assessed using conditional logistic regression. In unadjusted analyses of ICD-9 codes ever and within the last 2 years before HIV diagnosis, the conditional odds of HIV infection were greater in those with clinical signs and symptoms of HIV (cOR 5.05, 95% CI 4.00-6.39), mental health diagnoses (cOR 2.61, 95% CI 1.86-3.67), and STI diagnoses (cOR 2.33, 95% CI 1.50-3.60). Compared to those with ≤10 medical encounters in the 2 years prior to HIV diagnosis, individuals with 11-35 medical encounters (cOR 2.19, 95% CI 1.73-2.79) and >35 medical encounters (cOR 4.15, 95% CI 2.69-6.39) had a higher odds of HIV acquisition. In multivariate analyses, clinical signs and symptoms of HIV within the last 2 years of HIV diagnosis (cOR 4.10, 95% CI 3.22-5.22) and ever having a mental health diagnosis (cOR 1.97, 95% CI 1.44-2.70) remained significant (p<0.01). Clinical encounters, particularly those featuring clinical signs and symptoms of HIV or a history of mental health complaints, provide an opportunity for targeted testing as a supplement to mandated testing at 2-year intervals. Provider education to increase HIV testing in persons at risk would enhance early HIV diagnosis and potentially reduce forward transmission in the USAF population.

Key Words: HIV, risk factors, mental health, targeted testing, and USAF
Introduction

The development of a successful human immunodeficiency virus type 1 (HIV-1) prevention program is dependent upon the identification of HIV risk factors in a population and the subsequent testing of at-risk individuals in order to provide effective education to reduce HIV acquisition and transmission. To detect incident cases of HIV, the United States Air Force (USAF) utilizes a system-wide approach with mandated HIV testing for all active duty members approximately every 2 years. Although mandated testing has the benefit of capturing nearly all cases of HIV infection, the testing frequency limits the ability to detect cases early in the course of infection compared with a targeted testing strategy.

Early detection of incident cases is important as individuals who are unaware of HIV infection account for approximately one-third of HIV transmissions in the U.S. (Skarbinski et al., 2015). This can be challenging since several HIV risk factors identified in the general population, including intravenous drug use (IDU) and illicit substance abuse, are mitigated in the US military due to accession standards and mandatory drug testing. Additionally, risk factor identification may be limited by members’ concerns of self-disclosure, stigma of HIV diagnosis, military career impact, and possible disciplinary actions after the repeal of the “Don’t Ask Don’t Tell” policy (Katz, 2010).

There is the potential to identify HIV infection earlier and disrupt forward HIV transmission in approximately 75% of incident cases in the USAF since the majority of cases are identified as a result of mandated screening (Kugbenu, Paulin, Tastad, & Okulicz, 2016). A supplemental targeted testing strategy initiated by providers in clinical settings may be an effective method to improve early HIV diagnosis. It is important to inform providers by ascertaining clinical indicators of HIV infection in the USAF, as well as clinical diagnoses more
common in those with versus without HIV infection. We aim to characterize the clinical indicators associated with HIV infection in order to enhance supplemental provider-directed HIV screening in our population.
Methods

The USAF, in keeping with Department of Defense (DoD) policy, conducts compulsory HIV testing among applicants to USAF service and periodic (every 2 years) and peri-deployment testing among its personnel. In this nested case-control study, the study population consisted of all USAF personnel on active service at any time during the study period, January 1, 1996 through December 31, 2011 who had demographic data available. Among those eligible, all persons with a new HIV diagnosis during the study period were considered cases. Five randomly-selected controls were matched to each case by exact age, length of service (±3 months), sex, race, branch of the military, service component (active duty, National Guard, or Reservists), and HIV test collection date or index date. HIV testing data were obtained from the USAF School of Aerospace Medicine HIV Testing Service and demographic and clinical data were obtained from the Armed Forces Health Surveillance Center (AFHSC). This study was approved by the Walter Reed Army Institute of Research Institutional Review Board.

The relationship between clinical indicators and HIV infection was assessed in univariate analyses using conditional logistic regression. Cases missing a factor were excluded from analysis as were all matched controls and sensitivity analyses did not reveal significant differences in excluded subjects (data not shown). Data for clinical diagnoses were examined by International Classification of Disease, Ninth Revision (ICD-9) diagnostic codes and included sexually transmitted infection (STI) diagnosis, substance abuse, clinical signs and symptoms of HIV infection, clinical HIV syndrome, mental health disorder, psychosocial stressor, headache, sleep disorder, and co-occurring clinical syndromes ever and during the two years before the index date as previously described (Hakre et al., 2011). A final multivariate model for clinical factors was determined using forward and backward iterative stepwise selection of baseline
characteristics and clinical factors occurring prior to HIV diagnosis; a criteria p-value of 0.10 and 0.01 were used to enter and retain factors in the model, respectively. All analyses were performed using SAS version 9.3 (Cary, North Carolina).
Results

A total of 462 incident HIV cases were identified among USAF personnel who served on active duty between January 1, 1996 and December 31, 2011. Due to small numbers, the 10 female cases were removed and all descriptions and analyses are restricted to males (Table 1). In unadjusted analyses within the last 2 years before HIV diagnosis, having clinical signs and symptoms of HIV infection (conditional odds ratio [cOR] 5.05, 95% CI 4.00-6.39), having a clinical syndrome consistent with HIV (cOR 3.02, 95% CI 2.42-3.78), clinical history of a mental health disorder (cOR 2.61, 95% CI 1.86-3.67), or history of a STI (cOR 2.33, 95% CI 1.50-3.60) had significantly higher odds of HIV infection (Table 2). Compared to those with 10 or less medical encounters in the 2 years prior to HIV diagnosis, individuals with 11-35 medical encounters (cOR 2.19, 95% CI 1.73-2.79) and >35 medical encounters (cOR 4.15, 95% CI 2.69-6.39) had a higher odds of HIV acquisition. The most common ICD-9 codes for mental health issue, substance abuse, and STI prior to HIV diagnosis are shown for cases and controls (Figure 1).

In multivariate analyses, active duty personnel with a clinical syndrome of HIV (cOR 2.23, 95% CI 1.75-2.84) and having clinical signs and symptoms of HIV infection in the prior 2 years (cOR 4.10, 95% CI 3.22-5.22) had higher odds of HIV infection after adjusting for the factors above (Table 3). In addition, ever having a mental health diagnosis (cOR 1.97, 95% CI 1.44-2.70) also remained significant in multivariate analyses.
Discussion

The goal of this study was to identify and assess clinical indicators associated with HIV infection in the USAF. In multivariate analyses in the 2 years prior to HIV diagnosis, five indicators had significantly higher odds of HIV infection: having clinical signs and symptoms of HIV infection, a clinical syndrome consistent with HIV, more frequent medical encounters, clinical history of a mental health disorder and history of a STI. Given that delays in HIV diagnosis are common and opportunities for screening are missed, USAF providers should consider additional targeted HIV screening for patients with these clinical indicators in addition to mandated screening at 2-year intervals.

Numerous studies have demonstrated the clinical association between HIV infection and serious mental health illness, and the prevalence rate of HIV infection in patients with serious mental illness is higher than expected in the general population for the same demographic area (Collins, Holman, Freeman, & Patel, 2006; Kaltenthaler, Pandor, & Wong, 2014; Rosenberg et al., 2001; Wright, Akhtar, Tosh, & Clifton, 2014). Individuals with severe mental illness in the military, however, undergo an extensive evaluation process which ultimately results in separation from active duty for individuals deemed unfit for continued military service. The results of this study suggest that less debilitating forms of mental illness, such as depression, adjustment reactions, and anxiety may also play a contributory role in HIV acquisition in the active duty population. Mental illness has been linked to higher risk sexual activity such as alcohol and drug use, multiple sex partners, engaging in high-risk same-sex sexual activity, lack of condom use, trading sex for drugs or money, and engaging in sex while using psychoactive medications (Kaltenthaler et al., 2014; Meade & Sikkema, 2005; Rosenberg et al., 2001). This
study suggests that providers evaluating individuals with mental health complaints should consider a discussion of HIV risk behaviors and initiate testing if indicated.

In multivariate analyses, clinical syndrome of HIV in the previous 2 years, and having clinical signs and symptoms of HIV infection in the prior 2 years had higher conditional odds of HIV infection after adjusting for other clinical factors. Several studies have been published on missed opportunities in HIV screening in a variety of clinical settings. For example, one study noted that 47% of patients with newly diagnosed HIV infection had had at least 2 prior clinical encounters, with most experiencing HIV-related symptoms in at least one of those visits (Chin, Hicks, Samsa, & McKellar, 2013). A study in South Carolina found that the majority of persons with newly diagnosed HIV had multiple prior health care visits with only 21% likely to prompt a HIV test (Duffus et al., 2009). Thus, in the USAF population, these frequent medical encounters likely represent missed opportunities for HIV testing and education to mitigate possible HIV behavioral risk factors.

Limitations of this study include exclusive use of ICD-9 diagnosis codes as electronic health records were not available for the entire study period. Additionally, many of the clinical diagnoses associated with HIV seroconversion lack specificity and therefore have limited ability to provide explicit screening guidance. Databases do not include sexual risk behavior data which would also inform provider-based supplemental HIV screening in addition to the clinical indicators identified in this study. In conclusion, this study provides important information for USAF providers regarding clinical diagnoses associated with HIV acquisition in the USAF population. Provider education and training initiatives are currently underway to increase HIV testing in persons at risk to enhance early HIV diagnosis and potentially reduce forward transmission in the USAF population.
References

doi:10.1089/apc.2013.0099


doi:10.1089/apc.2008.0193

doi:10.1097/QAI.0b013e31820a7f4d


doi:10.1056/NEJMtp012496

doi:10.1016/j.puhe.2015.11.019


doi:10.1001/jamainternmed.2014.8180

doi:10.1002/14651858.CD009639.pub2
Table 1. Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Case</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number, n</strong></td>
<td>452</td>
<td>2176</td>
<td>2628</td>
</tr>
<tr>
<td><strong>Age at index, median (IQR)</strong>*</td>
<td>27 (23-34)</td>
<td>27 (23-33)</td>
<td>27 (23-33)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>210 (46.5%)</td>
<td>1,025 (47.1%)</td>
<td>1,235 (47.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>35 (7.7%)</td>
<td>155 (7.1%)</td>
<td>190 (7.2%)</td>
</tr>
<tr>
<td>White</td>
<td>207 (45.8%)</td>
<td>996 (45.8%)</td>
<td>1,203 (45.8%)</td>
</tr>
<tr>
<td><strong>Deployment within 2 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 1 deployment</td>
<td>85 (18.8%)</td>
<td>654 (30.1%)</td>
<td>739 (28.1%)</td>
</tr>
<tr>
<td>None</td>
<td>367 (81.2%)</td>
<td>1,522 (69.9%)</td>
<td>1,889 (71.9%)</td>
</tr>
<tr>
<td><strong>Military service time at index, years, median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.5 (3.0-12.0)</td>
<td>6.0 (2.9-11.5)</td>
<td>6.1 (2.9-11.6)</td>
</tr>
<tr>
<td><strong>Marital status at index</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>92 (20.4%)</td>
<td>1,209 (55.6%)</td>
<td>1,301 (46.5%)</td>
</tr>
<tr>
<td>Other</td>
<td>40 (8.9%)</td>
<td>123 (5.7%)</td>
<td>163 (6.2%)</td>
</tr>
<tr>
<td>Single</td>
<td>320 (70.8%)</td>
<td>843 (38.7%)</td>
<td>1,163 (44.3%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0.0%)</td>
<td>1 (0.0%)</td>
<td>1 (0.0%)</td>
</tr>
<tr>
<td><strong>Duty status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Officer</td>
<td>41 (9.1%)</td>
<td>300 (13.8%)</td>
<td>341 (13.0%)</td>
</tr>
<tr>
<td>Enlisted</td>
<td>411 (90.9%)</td>
<td>1,876 (86.2%)</td>
<td>2,287 (87.0%)</td>
</tr>
<tr>
<td><strong>Occupation at index</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Communications/Intelligence</td>
<td>161 (35.6%)</td>
<td>449 (20.6%)</td>
<td>610 (23.2%)</td>
</tr>
<tr>
<td>Engineer</td>
<td>90 (19.9%)</td>
<td>738 (33.9%)</td>
<td>828 (31.5%)</td>
</tr>
<tr>
<td>Healthcare</td>
<td>44 (9.7%)</td>
<td>148 (6.8%)</td>
<td>192 (7.3%)</td>
</tr>
<tr>
<td>Pilot/Aircrew</td>
<td>14 (3.1%)</td>
<td>142 (6.5%)</td>
<td>156 (5.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>143 (31.6%)</td>
<td>699 (32.1%)</td>
<td>842 (32.0%)</td>
</tr>
</tbody>
</table>

* Denotes matching factor
<table>
<thead>
<tr>
<th>Group</th>
<th>Condition Ever</th>
<th>Unadjusted Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
<th>Condition in the Last 2 Years</th>
<th>Unadjusted Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case (n=452)</td>
<td>Control (n=2176)</td>
<td></td>
<td></td>
<td></td>
<td>Case (n=452)</td>
<td>Control (n=2176)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STI Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STI History</td>
<td>46 (10.2)</td>
<td>136 (6.3)</td>
<td>1.77</td>
<td>0.0018</td>
<td></td>
<td>31 (6.9)</td>
<td>68 (3.1)</td>
<td>2.33</td>
</tr>
<tr>
<td>No STI History</td>
<td>406 (89.8)</td>
<td>2,040 (93.8)</td>
<td>1.00</td>
<td>0.0018</td>
<td></td>
<td>421 (93.1)</td>
<td>2,108 (96.9)</td>
<td>1.00</td>
</tr>
<tr>
<td>Ulcerative STI History</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcerative STI History</td>
<td>8 (1.8)</td>
<td>31 (1.4)</td>
<td>1.26</td>
<td>0.5654</td>
<td></td>
<td>7 (1.5)</td>
<td>16 (0.7)</td>
<td>2.10</td>
</tr>
<tr>
<td>No Ulcerative STI History</td>
<td>444 (98.2)</td>
<td>2,145 (98.6)</td>
<td>1.00</td>
<td>0.5654</td>
<td></td>
<td>445 (98.5)</td>
<td>2,160 (99.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-Ulcerative STI History</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Ulcerative STI History</td>
<td>39 (8.6)</td>
<td>111 (5.1)</td>
<td>1.83</td>
<td>0.0022</td>
<td></td>
<td>24 (5.3)</td>
<td>55 (2.5)</td>
<td>2.22</td>
</tr>
<tr>
<td>No Non-Ulcerative STI History</td>
<td>413 (91.4)</td>
<td>2,065 (94.9)</td>
<td>1.00</td>
<td>0.0022</td>
<td></td>
<td>428 (94.7)</td>
<td>2,121 (97.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Substance Abuse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substance Abuse History</td>
<td>58 (12.8)</td>
<td>227 (10.4)</td>
<td>1.30</td>
<td>0.1049</td>
<td></td>
<td>44 (9.7)</td>
<td>158 (7.3)</td>
<td>1.41</td>
</tr>
<tr>
<td>No Substance Abuse History</td>
<td>394 (87.2)</td>
<td>1,949 (89.6)</td>
<td>1.00</td>
<td>0.1049</td>
<td></td>
<td>408 (90.3)</td>
<td>2,018 (92.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>Clinical Signs/Symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Signs/Symptoms</td>
<td>316 (69.9)</td>
<td>899 (41.3)</td>
<td>4.75</td>
<td>&lt;0.0001</td>
<td></td>
<td>264 (58.4)</td>
<td>531 (24.4)</td>
<td>5.05</td>
</tr>
<tr>
<td>No Clinical Signs/Symptoms</td>
<td>136 (30.1)</td>
<td>1,277 (58.7)</td>
<td>1.00</td>
<td>&lt;0.0001</td>
<td></td>
<td>188 (41.6)</td>
<td>1,645 (75.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Clinical Syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Syndrome</td>
<td>317 (70.1)</td>
<td>1,176 (54.0)</td>
<td>2.59</td>
<td>&lt;0.0001</td>
<td></td>
<td>250 (55.3)</td>
<td>683 (31.4)</td>
<td>3.02</td>
</tr>
<tr>
<td>No Clinical Syndrome</td>
<td>135 (29.9)</td>
<td>1,000 (46.0)</td>
<td>1.00</td>
<td>&lt;0.0001</td>
<td></td>
<td>202 (44.7)</td>
<td>1,493 (68.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>MH Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MH History</td>
<td>91 (20.1)</td>
<td>203 (9.3)</td>
<td>2.57</td>
<td>&lt;0.0001</td>
<td></td>
<td>58 (12.8)</td>
<td>121 (5.6)</td>
<td>2.61</td>
</tr>
<tr>
<td>No MH History</td>
<td>361 (79.9)</td>
<td>1,973 (90.7)</td>
<td>1.00</td>
<td>&lt;0.0001</td>
<td></td>
<td>394 (87.2)</td>
<td>2,055 (94.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Medical Encounter History</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>10 or less</td>
<td>128 (28.3)</td>
<td>864 (39.7)</td>
<td>1.00</td>
<td>0.0001</td>
<td></td>
<td>221 (48.9)</td>
<td>1,441 (66.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>11 – 35</td>
<td>175 (38.7)</td>
<td>837 (38.5)</td>
<td>2.67</td>
<td>&lt;0.0001</td>
<td></td>
<td>191 (42.3)</td>
<td>662 (30.4)</td>
<td>2.19</td>
</tr>
<tr>
<td>&gt; 35</td>
<td>149 (33.0)</td>
<td>475 (21.8)</td>
<td>5.78</td>
<td>&lt;0.0001</td>
<td></td>
<td>40 (8.8)</td>
<td>73 (3.4)</td>
<td>4.15</td>
</tr>
</tbody>
</table>

CI, confidence interval; STI, Sexually Transmitted Infection; MH, Mental Health
Table 3. Characteristics Retained in Stepwise Multivariate Conditional Logistic Regression Model

<table>
<thead>
<tr>
<th>Clinical Risk Factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental Health Diagnosis Ever</td>
<td>1.97</td>
<td>(1.44, 2.70)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Clinical Syndrome in the Prior 2 Years</td>
<td>2.23</td>
<td>(1.75, 2.84)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Clinical Signs/Symptoms Diagnosis in the Prior 2 Years</td>
<td>4.10</td>
<td>(3.22, 5.22)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Figure 1. Proportion of cases and controls with the most common ICD-9 codes for mental health issue, substance abuse, and STI. A) 311: Depressive disorder not elsewhere classified; 309.0: adjustment disorder with depressed mood; 300.00: Anxiety state unspecified; 309.28: adjustment disorder with mixed anxiety and depressed mood. B) 305.1: nondependent tobacco use disorder; 305.00: nondependent alcohol abuse unspecified drinking behavior; 303.90: other and unspecified alcohol dependence unspecified drinking behavior. C) 099.9: venereal disease unspecified; 078.11: Condyloma acuminatum; 099.41: other nongonococcal urethritis Chlamydia trachomatis; 099.40: other nongonococcal urethritis unspecified.