Prevalence and Factors Associated with Asymptomatic Gonococcal and Chlamydial Infection among US Military Men Infected With the Human Immunodeficiency Virus

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ARTICLE SUMMARY

FOCUS

- Is asymptomatic gonorrhea and chlamydia infection prevalent among US military men?
- If so, are those infections associated with any specific sexual practice or relationship beliefs?

KEY MESSAGES

- Men who have sex with men (MSM) in the US military are at risk for asymptomatic gonorrhea and chlamydia infection, predominantly at extragenital sites.
- Sex with men, anal sex, non-Caucasian ethnicity, age <35 years, and HIV infection for <3 years were all associated with asymptomatic infection.
- Repeal of DADT fostered a change in US military medical culture, allowing clinicians to counsel and screen MSM according to established guidelines.

STRENGTHS

- First comprehensive data set of asymptomatic gonorrhea/chlamydia infection in a US military population
- First study to describe health needs of men who have sex with men in a US military population

WEAKNESSES

- Observational study
- Small n (pilot study)
- Inability to obtain 3 site anatomic screening from all participants

ABSTRACT:

Objectives: *Neisseria gonorrheae* (GC) and *Chlamydia trachomatis* (CT) can facilitate transmission of HIV, and men who have sex with men (MSM) may harbor infections at extragenital sites. Data regarding GC and CT in military populations are lacking. We examined the prevalence and factors associated with asymptomatic GC and CT infection among HIV-infected US military personnel in California.

Methods: Cross-sectional study of asymptomatic men who underwent nucleic acid amplification screening for GC and CT of the pharynx, rectum, and urine. Data on demographics, sexual practices, and HIV variables were collected. Factors associated with infection were analyzed using chi-square tests.

Results: Ninety-nine HIV-positive men were evaluated - 79% MSM, mean age 31 years, 36% Black, and 33% married. Twenty-four percent were infected with either GC or CT. Rectal swabs were positive in 18% for CT and 3% for GC; pharynx swabs were positive in 8% for GC and 2% for CT. Only 1 infection was detected in urine (GC). Anal sex (p=0.04), male partner (OR 7.02, p=0.04), and sex at least once weekly (OR 3.28, p=0.04) were associated with infection. Associated demographic included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001).

Conclusions: We found a high prevalence of extragenital GC/CT infection among HIV-infected military men. Only one infection was detected in the urine, signaling the need for aggressive three site screening of MSM. Clinicians should be aware of high prevalence in order to enhance health through comprehensive STI screening practices.

INTRODUCTION

Neisseria gonorrheae (GC) and *Chlamydia trachomatis* (CT) cause infection in the male urethral, pharyngeal, and rectal mucosa, facilitating transmission of the human immunodeficiency virus (HIV).[1-3] Men who have sex with men (MSM) are at particular risk for harboring these infections at extragenital sites.[4] The United States (US) law, 'don't ask, don't tell' (DADT), allowed gay persons to serve in the military but made it unlawful to reveal his/her sexual orientation and was the cause of separation of nearly 14,000 qualified service members.[5] Although there are several published reports regarding GC/CT infections in MSM, little data exist among US military members.[6-12] This dearth of data is largely a byproduct of DADT which prohibited the recognition and study of MSM health needs; the law was repealed in 2011.

The Naval Medical Center San Diego (NMCSD) is one of three US Navy HIV Evaluation and Treatment Units and provides health care to approximately 575 HIV-infected Department of Defense beneficiaries, approximately half of whom are currently serving on active military duty. Services offered include comprehensive primary and subspecialty health care, mental health services, prevention counseling and health promotion, and HIV and other sexually transmitted infection (STI) screening and management.[13] However, asymptomatic GC/CT screening was not routinely performed in any US Navy medical treatment facility prior to this study. As US Department of Defense beneficiaries, these patients receive open, unrestricted access to care without copayments.

Given the lack of data on asymptomatic GC and CT infection among a US military cohort of HIV-infected men, we conducted a cross-sectional pilot study with the objectives: (1) to describe the prevalence of asymptomatic urethral, pharyngeal, and rectal GC/CT infection in

this population; (2) to describe sexual behaviors, relationship attitudes, and HIV disease attributes among this cohort; and (3) to identify specific factors associated with asymptomatic GC/CT infection.

MATERIALS AND METHODS

Participants and Procedures

All HIV-infected US Navy and Marine Corps members serving on active duty are required to participate in a biannual medical and psychosocial evaluation. Those serving at military bases in the western US and Pacific Basin report to NMCSD for these visits. In order to minimize selection bias, beginning in September 2010, we presented the study to each consecutive military member presenting for required HIV evaluation until we enrolled 100 participants. The study was designed as a pilot to guide design of future research, specifically to establish power calculations required for a full-scale study. No incentive to participation was offered. Those who participated did so to optimize personal sexual health through more thorough STI screening. Inclusion criteria included: male gender, HIV-infected, receiving care at the NMCSD, and having no symptoms referable to the pharynx, urethra, or rectum. Those who voluntarily agreed to participate completed a short questionnaire regarding sexual practices and relationship attitudes. In order to encourage honest responses, the written questionnaire was administered by the clinic's non-military preventive medicine counselor and all responses were confidentially maintained.

Each participant was screened for asymptomatic GC/CT infection of the urethra, pharynx, and rectum using a first-void urine sample and posterior pharyngeal and rectal swabs obtained by their primary HIV provider during their routine, biannual HIV clinic visit. All prevalent infections were appropriately treated. The NMCSD laboratory previously verified the APTIMA Combo2® Assay (Gen-Probe Inc., San Diego, CA) for use in the pharynx and rectum according to Clinical Laboratory Improvement Amendments (CLIA) standards. Medical records were reviewed by an HIV clinician and data regarding demographics, prior STIs, and HIV-related data were collected. The study was approved and waiver of informed consent was granted by the NMCSD Institutional Review Board.

Data Analysis

The data collected (laboratory results, questionnaire responses, and medical record information) were entered into a Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA) database and analyzed with SAS® version 9.2 (SAS Institute, Cary, NC). Prevalence rates were calculated for each type of infection (GC, CT, or both) at each site. The descriptive statistics included for categorical variables were counts and proportions, and means and standard deviations for continuous variables. Chi-square or Fisher's exact tests were performed, as appropriate, to analyze the bivariate relationships between the factors of interest and the outcome defined as being positive for either infection (GC and/or CT in at least one site). Odds ratios (OR), 95% confidence intervals (CI), and *P*-values were reported. *P*-values less than 0.05 were considered statistically significant.

RESULTS

One hundred six consecutive patients were offered participation in the study, six declined, and one hundred were enrolled. One participant was later excluded due to recent treatment of asymptomatic rectal CT infection prior to enrollment. Due to scheduling conflicts and inability of participant to return to the clinic, and despite several attempts to do so, a urine specimen was not collected from 3 participants and rectal/pharyngeal swabs from 12. The cohort (n=99) included 79% who were MSM. The mean age of the cohort was 31 years, and race was self-reported as Black in 36%, Caucasian in 35%, Hispanic in 15%, and other in 13%. Sixty-seven percent were unmarried, and 36% had a previous history of STI. HIV-related characteristics included a mean CD4 count of 609 cells/mm^3, 43% had an HIV viral load <48 copies/μL, 51% were receiving antiretroviral therapy, and the mean time since HIV diagnosis was 63 months. (Table 1)

Twenty-four percent had either GC or CT in at least 1 site. The site with the highest prevalence was the rectum (18.4%), followed by the pharynx (9.2%) and the urethra (1%). Of rectal swabs, 18% were positive for CT and 3% for GC. Of pharynx swabs, 8% were positive for GC and 2% for CT. Only one infection was detected in urine (GC). (Table 2, Figure 1) Eighty-one percent of those with GC/CT infection had a positive screening test at only one site, 19% were positive at two sites, and none were positive at all three sites.

In bivariate analysis, anal sex (p=0.04), having a male partner (OR 7.02, p=0.04), and having sex at least once weekly (OR 3.28, p=0.04) were associated with infection; vaginal sex was protective (OR 0.20, p=0.03). Demographic factors associated with infection included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (Black OR 5.50, p=0.04; Hispanic OR 11.00, p=0.01; other race OR 7.33, p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001). (Table 3, 4)

Only about half of participants reported always using condoms during anal sex, and less than half always required their partner to use condoms during anal sex. During oral sex, less than 15% of participants reported always using condoms and always requiring their partner to use condoms. (Table 4)

With regards to relationship attitudes, 52% of participants reported sexual relations only with a partner in a serious relationship, while 28% disagreed with this statement. Seventy-six percent of participants expected monogamy in a serious relationship, while 14% disagreed with this statement. Twenty-three percent of participants participated in most of their sexual relations with casual friends and 53% disagreed with this statement. None of these beliefs were significantly associated with infection. (Table 4)

DISCUSSION

We found an alarming prevalence of GC/CT infection—nearly twice that of non-military MSM in other large California cities.[7] In fact, our prevalence may represent an underestimate, since some of our patients may have sought screening (and subsequent therapy) at the local county STD clinic prior to their military encounter, due to fear of discipline or discharge.[14 15] We believe there are two important contributors to the high prevalence rates observed: DADT and the first-screen effect.

DADT likely contributed the most to undiagnosed infection. The American Medical Association posited that this military law compromised the medical care of gay patients serving in the military.[16] Prior to repeal, military healthcare providers often believed they could not ask, document, nor counsel about sexual behaviors or orientations for fear of revealing MSM practices of their patients that they believed would lead to adverse legal action. Therefore, risk would not have been assessed and the need for screening was unknown and did not occur. DADT also prevented patients from providing honest answers or reports of sexual practices, again for fear of adverse legal action. We started our study prior to the repeal because SECNAVINST 5300.30D (the document that governs management of HIV infection in the Navy and Marine Corps) offered protection against adverse action related to information obtained from a medical or epidemiologic interview. Unfortunately, this provision was not well known to military healthcare providers.

Second, our study facilitated the initiation of sexual risk driven screening for GC/CT infection in our healthcare facility. Hence, study data represent the first time many participants were screened for GC/CT infection. First-time screening for a condition may reveal more prevalent cases than subsequent screening, especially in the case of asymptomatic infection, and may

partially explain why we detected higher prevalence than that found in other California cities which may represent subsequent screening data.

Our study also had several important findings regarding HIV-positive men serving in the US military. With regards to sexual practices, most respondents were MSM and engaged in oral, anal (receptive and insertive), and oral-anal sex. As expected, most respondents do not use condoms during oral sex. Surprisingly though was that nearly half of respondents do not always use condoms or require their partners to use condoms during anal sex. Safer sex fatigue, serosorting, and seropositioning may be contributors to low rates of condom use.[17] Regarding relationship attitudes, about half of respondents believe sexual relations should only occur with partners in a serious relationship while approximately one-quarter engage in sex with casual friends. When in a serious relationship, the majority of respondents expect monogamy.

The significant findings noted in our study were not unexpected, however, have not previously been studied or reported in this population. MSM, anal sex, non-Caucasian ethnicity, and younger age were associated with GC/CT and have been identified as STI risk factors in other studies.[18-21] Also, it follows that a person who recently acquired HIV infection or has a history of STI would be at higher risk for GC/CT infection. The increased risk among non-Caucasians may be related to cultural or societal stigma which may prevent an individual from seeking screening services (and need to disclose self-perceived taboo sexual behavior) in a way that DADT likely prevented military MSM from seeking or receiving appropriate screening.

We acknowledge potential limitations of our study: those inherent to an observational design, inability to achieve 100% three site screening from all participants, and small study

population. Although our sample size is small, it is worth noting that trends in our data are similar to trends noted in larger non-military studies of GC/CT infection: most infections were detected at extragenital sites, the majority of rectal infections were due to CT, and the majority of pharyngeal infections were due to GC. Finally, there may have been some reluctance of participants to answer survey questions honestly, although we believe this was minimized by our confidential survey procedures and as reflected by candid responses we did receive.

We have generated the first comprehensive data set of asymptomatic GC/CT infection in a US military population. Although much of what we have learned was assumed to be true, this is the first systematic description and underscores the need for military healthcare providers to screen their MSM population for infection at three anatomic sites. Also, as noted in larger studies, we found that reliance on urine/urethral screening alone will fail to detect the vast majority of asymptomatic infections in an MSM population. Finally, low rates of reported condom use among HIV-positive participants signals the need to enhance safer sex prevention efforts among MSM.

TABLES

Table 1. HIV-infected male demographic characteristics, 2011—San Diego, California (n=99)

HIV variables	
CD4 count mean (SD), cells/mm^3	609 (216)
Suppressed HIV VL (<48 copies/μL)	43%
Receiving ART	51%
Time since HIV diagnosis mean (SD), months	62.8 (59.9)
Demographic variables	
Age	
Mean (SD), years	30.9 (8.2)
<25 years	28%
25-34 years	38%
≥ 35 years	33%
Ethnicity	
Black	36%
Caucasian	35%
Hispanic	15%
Other	13%
Marital Status	
Married	33%
Single	67%
Sexual Practice	
MSM	79%
MSW	21%
Previous STI	
Yes	36%

VL = plasma viral load
ART = antiretroviral therapy
MSM = men who have sex with men
MSW = men who have sex with women
SD = standard deviation
STI = sexually transmitted infection

Table 2. Prevalence of asymptomatic infection by anatomic site, HIV-infected men, 2011—San Diego, California (n=99)*

	Either Infection			CT			GC		
	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate
Overall	20	83	24.1%	17	83	20.5%	8	83	9.6%
Urethra	1	96	1.0%	0	96	0.0%	1	96	1.0%
Rectum	16	87	18.4%	16	87	18.4%	3	87	3.4%
Pharynx	8	87	9.2%	2	87	2.3%	7	87	8.0%

*Some participants did not have screening at all three sites.

Table 3. Survey responses – demographic & sexual practices by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Demographic variables (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Gender of sexual partner(s) (N=98)									
Women only	21	(21.4)	1	(4.8)	20	(26.0)	REF	--	--
Male (MSM)	77	(78.6)	20	(95.2)	57	(74.0)	7.02	1.88, 55.72	0.04
Race/ethnicity (N=99)									0.03
White	35	(35.4)	2	(9.5)	33	(42.3)	REF	--	--
Black	36	(36.4)	9	(42.9)	27	(34.7)	5.50	1.10, 27.64	0.04
Hispanic	15	(15.2)	6	(28.6)	9	(11.5)	11.00	1.89, 64.06	0.01
Other	13	(13.0)	4	(19.0)	9	(11.5)	7.33	1.15, 46.66	0.03
Age (N=99)									
<35 years	66	(66.7)	19	(90.5)	47	(60.3)	6.27	1.36, 28.82	0.02
≥ 35 years	33	(33.3)	2	(9.5)	31	(39.7)	REF	--	--
Previous history of STI (N=99)									
No	63	(63.6)	7	(33.3)	56	(71.8)	REF	--	--
Yes	36	(36.4)	14	(66.7)	22	(28.2)	5.10	1.81, 14.30	0.001
Number of years since HIV diagnosis (N=99)									
> 3 years	57	(57.6)	8	(38.1)	49	(62.8)	REF	--	--
≤ 3 years	42	(42.4)	13	(61.9)	29	(37.2)	2.75	1.02, 7.41	0.04
Sexual practices (N respondents)									
Vaginal sex (N=99)									
No	70	(70.7)	19	(90.5)	51	(65.4)	REF	--	--
Yes	29	(29.3)	2	(9.5)	27	(34.6)	0.20	0.04, 0.92	0.03
Oral sex[b] (N=99)									
No	3	(3.0)	0	(0)	3	(3.8)	REF	--	--
Yes	96	(97.0)	21	(100)	75	(96.2)	--	--	1.00
Anal sex[b] (N=99)									
No	15	(15.2)	0	(0)	15	(19.2)	REF	--	--
Yes	84	(84.8)	21	(100)	63	(80.8)	--	--	0.04
Insertive anal sex (N=80)									
No	15	(18.8)	5	(23.8)	10	(16.9)	1.00	--	--
Yes	65	(81.2)	16	(76.2)	49	(83.1)	0.65	0.19, 2.20	0.52
Receptive anal sex (N=80)									
No	17	(21.3)	2	(9.5)	15	(25.4)	REF	--	--
Yes	63	(78.7)	19	(90.5)	44	(74.6)	3.32	0.67, 15.57	0.21

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.
MSM = men who have sex with men (self-reported).
Oral and oral-anal sex were not significantly associated with infection with p>0.05

Table 4. Survey responses – relationship attitudes & condom use by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Relationship attitudes (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Sexual relationships with >1 partner in the past year (N=99)									
No	39	(39.4)	5	(23.8)	34	(43.6)	REF	--	--
Yes	60	(60.6)	16	(76.2)	44	(56.4)	2.47	0.82, 7.42	0.10
Frequency of sexual activity in the past year (N=99)									
< Once a week	38	(38.4)	4	(19.0)	34	(43.6)	REF	--	--
At least once a week	61	(61.6)	17	(81.0)	44	(56.4)	3.28	1.01, 10.66	0.04
Sexual relations only with partner in a serious relationship (N=99)									0.14
Strongly agree	51	(51.5)	7	(33.3)	44	(56.4)	REF	--	--
Neither agree/disagree	20	(20.2)	5	(23.8)	15	(19.2)	2.10	0.59, 7.60	0.26
Strongly disagree	28	(28.3)	9	(42.9)	19	(24.4)	2.98	0.97, 9.17	0.06
Expect monogamy in a serious relationship (N=99)									0.48
Strongly agree	75	(75.8)	14	(66.7)	61	(78.1)	REF	--	--
Neither agree/disagree	10	(10.1)	3	(14.3)	7	(9.0)	1.87	0.43, 8.14	0.41
Strongly disagree	14	(14.1)	4	(19.0)	10	(12.9)	1.74	0.48, 6.38	0.40
Sexual activities mostly with casual friends (N=99)									0.08
Strongly disagree	52	(53.0)	8	(38.0)	44	(57.2)	REF	--	--
Neither agree/disagree	24	(24.5)	9	(43.0)	15	(19.5)	3.30	1.08, 10.10	0.04
Strongly agree	22	(22.5)	4	(19.0)	18	(23.3)	1.22	0.33, 4.57	0.77
Condom use (N respondents)									
Self-condom use during oral sex (N=92)									
Always	12	(13.0)	4	(20.0)	8	(11.1)	REF	--	--
Do not always	80	(87.0)	16	(80.0)	64	(88.9)	0.50	0.13, 1.87	0.29
Partner-condom use during oral sex (N=90)									
Always	13	(14.4)	4	(19.0)	9	(13.0)	REF	--	--
Do not always	77	(85.6)	17	(81.0)	60	(87.0)	0.64	0.17, 2.34	0.49
Self-condom use during anal sex (N=82)									
Always	42	(51.2)	9	(45.0)	33	(53.2)	REF	--	--
Do not always	40	(48.8)	11	(55.0)	29	(46.8)	1.39	0.51, 3.83	0.52
Partner-condom use during anal sex (N=80)									
Always	37	(46.2)	8	(38.1)	29	(49.2)	REF	--	--
Do not always	43	(53.8)	13	(61.9)	30	(50.8)	1.57	0.57, 4.35	0.38

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.

LICENSE FOR PUBLICATION STATEMENT

CONTRIBUTORSHIP STATEMENT

Robert J. Carpenter contributed to conception and design, acquisition of data, and analysis and interpretation of data, participated in drafting the article or revising it critically for important intellectual content, and was involved in final approval of the version to be published.

All other authors listed contributed to acquisition of data, participated in drafting the article or revising it critically for important intellectual content, and were involved in final approval of the version to be published.

DATA SHARING STATEMENT

No additional data available.

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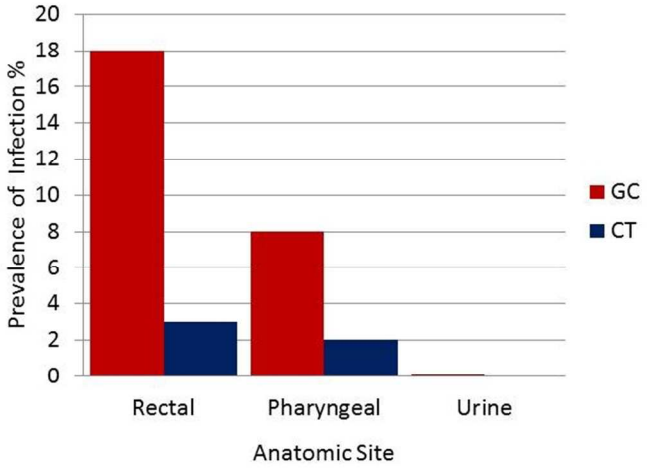

Distribution of asymptomatic gonococcal (GC) and chlamydial (CT) prevalence among HIV-infected men, San Diego, California, 2011
254x190mm (96 x 96 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Incidence and Factors Associated with Asymptomatic Gonococcal and Chlamydial Infection among US Navy and Marine Corps Men Infected With the Human Immunodeficiency Virus

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Title: Incidence and Factors Associated with Asymptomatic Gonococcal and Chlamydial Infection among US Navy and Marine Corps Men Infected With the Human Immunodeficiency Virus

Running Title: HIV and gonococcal/chlamydial infection in US Navy and Marine Corps men

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Key words: HIV, gonorrhea, Chlamydia, military, MSM, "don't ask, don't tell", DADT

Disclosure: The views expressed in this manuscript are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.

ARTICLE SUMMARY

FOCUS

- Is asymptomatic gonorrhea and chlamydia infection prevalent among US military men?
- If so, are those infections associated with any specific sexual practice or relationship beliefs?

KEY MESSAGES

- Men who have sex with men (MSM) in the US military are at risk for asymptomatic gonorrhea and chlamydia infection, predominantly at extragenital sites.
- Sex with men, anal sex, non-Caucasian ethnicity, age <35 years, and HIV infection for <3 years were all associated with asymptomatic infection.
- Repeal of DADT fostered a change in US military medical culture, allowing clinicians to counsel and screen MSM according to established guidelines.

STRENGTHS

- First comprehensive data set of asymptomatic gonorrhea/chlamydia infection in a US military population
- First study to describe health needs of men who have sex with men in a US military population

WEAKNESSES

- Observational study
- Small n (pilot study)
- Inability to obtain 3 site anatomic screening from all participants

ABSTRACT:

Objectives: *Neisseria gonorrheae* (GC) and *Chlamydia trachomatis* (CT) can facilitate transmission of HIV, and men who have sex with men (MSM) may harbor infections at extragenital sites. Data regarding extragenital GC and CT in military populations are lacking. We examined the incidence and factors associated with asymptomatic infection among HIV-infected military personnel.

Methods: Cross-sectional pilot study of asymptomatic men who underwent nucleic acid amplification screening for GC and CT of the pharynx, rectum, and urine at a single military treatment facility in San Diego, CA. Inclusion criteria: male, HIV-infected, Department of Defense beneficiary. Exclusion criteria: any symptom related to urethra, pharynx, or rectum. One participant was also excluded for recent CT treatment. Data on demographics, sexual practices, and HIV variables were collected. Factors associated with infection were analyzed using chi-square tests.

Results: Ninety-nine HIV-positive men were evaluated - 79% MSM, mean age 31 years, 36% Black, and 33% married. Twenty-four percent were infected with either GC or CT. Rectal swabs were positive in 18% for CT and 3% for GC; pharynx swabs were positive in 8% for GC and 2% for CT. Only 1 infection was detected in urine (GC). Anal sex (p=0.04), male partner (OR 7.02, p=0.04), and sex at least once weekly (OR 3.28, p=0.04) were associated with infection. Associated demographic included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001).

Conclusions: We found a high incidence of extragenital GC/CT infection among HIV-infected military men. Only one infection was detected in the urine, signaling the need for aggressive three site screening of MSM. Clinicians should be aware of high incidence in order to enhance health through comprehensive STI screening practices.

INTRODUCTION

Neisseria gonorrheae (GC) and *Chlamydia trachomatis* (CT) cause infection in the male urethral, pharyngeal, and rectal mucosa, facilitating transmission of the human immunodeficiency virus (HIV).[1-3] Men who have sex with men (MSM) are at particular risk for harboring these infections at extragenital sites.[4-10] The United States (US) law, 'don't ask, don't tell' (DADT), allowed gay persons to serve in the military but made it unlawful to reveal his/her sexual orientation and was the cause of separation of nearly 14,000 qualified service members.[11] Although there are several published reports regarding GC/CT infections in MSM, limited data exist among US military members.[7 9 10 12-15] Since 1986, the US military maintains a natural history study of HIV-infected persons and reports of GC/CT in this cohort have been published.[16] Additionally, others have reported on GC/CT in US military men.[17-24] However, these reports fail to represent the full spectrum of GC/CT infection because they only include data from urine/urethra. Extragenital anatomic site data has never been previously captured nor reported by US military studies and, again largely because of DADT, comprehensive sexual practices and behaviors have also never been previously captured nor reported. This dearth of data is largely a byproduct of DADT which prohibited the recognition and study of MSM health needs; the law was repealed in 2011.

The Naval Medical Center San Diego (NMCSD) is one of three US Navy HIV Evaluation and Treatment Units and provides health care to approximately 575 HIV-infected Department of Defense beneficiaries, approximately half of whom are currently serving on active military duty. Services offered include comprehensive primary and subspecialty health care, mental health services, prevention counseling and health promotion, and HIV and other sexually transmitted infection (STI) screening and management.[25] However, three anatomic site

GC/CT screening was not routinely performed in any US Navy medical treatment facility prior to this study. As US Department of Defense beneficiaries, these patients receive open, unrestricted access to care without copayments.

Given the lack of data on asymptomatic GC and CT infection among a US military cohort of HIV-infected men, we conducted a cross-sectional pilot study with the objectives: (1) to describe the incidence of asymptomatic urethral, pharyngeal, and rectal GC/CT infection in this population; (2) to describe sexual behaviors, relationship attitudes, and HIV disease attributes among this cohort; and (3) to identify specific factors associated with asymptomatic GC/CT infection.

MATERIALS AND METHODS

Participants and Procedures

All HIV-infected US Navy and Marine Corps members serving on active duty are required to participate in a biannual medical and psychosocial evaluation. Those serving at military bases in the western US and Pacific Basin report to NMCSD for these visits. In order to minimize selection bias, beginning in September 2010, we presented the study to each consecutive military member presenting for required HIV evaluation until we enrolled 100 participants. The study was designed as a pilot to guide design of future research. No incentive to participation was offered. Those who participated did so to optimize personal sexual health through more thorough STI screening. Inclusion criteria included: male gender, HIV-infected, receiving care at the NMCSD, and having no symptoms referable to the pharynx, urethra, or rectum. Those who voluntarily agreed to participate completed a short questionnaire regarding sexual practices and relationship attitudes. In order to encourage honest responses, the written questionnaire was administered by the clinic's non-military preventive medicine counselor and all responses were confidentially maintained.

Each participant was screened for asymptomatic GC/CT infection of the urethra, pharynx, and rectum using a first-void urine sample and posterior pharyngeal and rectal swabs obtained by their primary HIV provider during their routine, biannual HIV clinic visit. All collected specimens were collected on the day the questionnaire was completed and all infections were appropriately treated. The NMCSD laboratory previously verified the APTIMA Combo2® Assay (Gen-Probe Inc., San Diego, CA) for use in the pharynx and rectum according to Clinical Laboratory Improvement Amendments (CLIA) standards. Medical records were reviewed by an HIV clinician and data regarding demographics, prior STIs, and HIV-related data were collected. The study was approved and waiver of informed consent was granted by the NMCSD Institutional Review Board.

Data Analysis

The data collected (laboratory results, questionnaire responses, and medical record information) were entered into a Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA) database and analyzed with SAS® version 9.2 (SAS Institute, Cary, NC). Incidence rates were calculated for each type of infection (GC, CT, or both) at each site. The descriptive statistics included for categorical variables were counts and proportions, and means and standard deviations for continuous variables. Chi-square or Fisher's exact tests were performed, as appropriate, to analyze the bivariate relationships between the factors of interest and the outcome defined as being positive for either infection (GC and/or CT in at least one site). Odds ratios (OR), 95% confidence intervals (CI), and *P*-values were reported. *P*-values less than 0.05 were considered statistically significant.

RESULTS

One hundred six consecutive patients were offered participation in the study, six declined, and one hundred were enrolled. One participant was later excluded due to recent treatment of asymptomatic rectal CT infection prior to enrollment. Due to scheduling conflicts and inability of participant to return to the clinic, and despite several attempts to do so, a urine specimen was not collected from 3 participants and rectal/pharyngeal swabs from 12. The cohort (n=99) included 79% who were MSM. The mean age of the cohort was 31 years, and race was reported as Black in 36%, Caucasian in 35%, Hispanic in 15%, and other in 13%. Sixty-seven percent were unmarried, and 36% had a previous history of STI. HIV-related characteristics included a mean CD4 count of 609 cells/mm^3, 43% had an HIV viral load <48 copies/μL, 51% were receiving antiretroviral therapy, and the mean time since HIV diagnosis was 63 months. (Table 1)

Twenty-four percent had either GC or CT in at least 1 site. The site with the highest incidence was the rectum (18.4%), followed by the pharynx (9.2%) and the urethra (1%). Of rectal swabs, 18% were positive for CT and 3% for GC. Of pharynx swabs, 8% were positive for GC and 2% for CT. Only one infection was detected in urine (GC). (Table 2) Eighty-one percent of those with GC/CT infection had a positive screening test at only one site, 19% were positive at two sites, and none were positive at all three sites.

In bivariate analysis, anal sex (p=0.04), having a male partner (OR 7.02, p=0.04), and having sex at least once weekly (OR 3.28, p=0.04) were associated with infection; vaginal sex was protective (OR 0.20, p=0.03). Demographic factors associated with infection included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (Black OR 5.50, p=0.04; Hispanic OR 11.00, p=0.01; other race OR 7.33, p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001). (Table 3, 4)

Only about half of participants reported always using condoms during anal sex, and less than half always required their partner to use condoms during anal sex. During oral sex, less than 15% of participants reported always using condoms and always requiring their partner to use condoms. (Table 4)

With regards to relationship attitudes, 52% of participants reported sexual relations only with a partner in a serious relationship, while 28% disagreed with this statement. Seventy-six percent of participants expected monogamy in a serious relationship, while 14% disagreed with this statement. Twenty-three percent of participants participated in most of their sexual relations with casual friends and 53% disagreed with this statement. None of these beliefs were significantly associated with infection. (Table 4)

DISCUSSION

We found an alarming incidence of GC/CT infection—nearly twice that of non-military MSM in other large California cities.[10] In fact, our incidence may represent an underestimate, since some of our patients may seek screening (and subsequent therapy) at the local county STD clinic prior to their military encounter, due to fear of discipline or discharge.[26 27] We believe there are two important contributors to the high incidence rates observed: DADT and the first-screen effect.

DADT likely contributed the most to undiagnosed infection. The American Medical Association posited that this military law compromised the medical care of gay patients serving in the military.[28] Prior to repeal, military healthcare providers often believed they could not ask, document, nor counsel about sexual behaviors or orientations for fear of revealing MSM practices of their patients that they believed would lead to adverse legal action. Therefore, risk would not have been assessed and the need for screening was unknown and did not occur. DADT also prevented patients from providing honest answers or reports of sexual practices, again for fear of adverse legal action. We started our study prior to the repeal because SECNAVINST 5300.30D (the document that governs management of HIV infection in the Navy and Marine Corps) offered protection against adverse action related to information obtained from a medical or epidemiologic interview. Unfortunately, this provision was not well known to military healthcare providers.

Second, our study facilitated the initiation of sexual risk driven screening for GC/CT infection in our healthcare facility. Hence, study data represent the first time most participants were screened for extragenital GC/CT infection. First-time screening for a condition may reveal more incident cases than subsequent screening, especially in the case of asymptomatic

infection, and may partially explain why we detected higher incidence than that found in other California cities which may represent subsequent screening data.

Our study also had several important findings regarding HIV-positive men serving in the US military. With regards to sexual practices, most respondents were MSM and engaged in oral, anal (receptive and insertive), and oral-anal sex. As expected, most respondents do not use condoms during oral sex. Surprisingly though was that nearly half of respondents do not always use condoms or require their partners to use condoms during anal sex. Safer sex fatigue, serosorting, and seropositioning may be contributors to low rates of condom use.[29] Regarding relationship attitudes, about half of respondents believe sexual relations should only occur with partners in a serious relationship while approximately one-quarter engage in sex with casual friends. When in a serious relationship, the majority of respondents expect monogamy.

The significant findings noted in our study were not unexpected. MSM, anal sex, non-Caucasian ethnicity, and younger age were associated with GC/CT and have been identified as STI risk factors in other studies.[16 30-32] Also, it follows that a person who recently acquired HIV infection or has a history of STI would be at higher risk for GC/CT infection. The increased risk among non-Caucasians may be related to cultural or societal stigma which may prevent an individual from seeking screening services (and need to disclose self-perceived taboo sexual behavior) in a way that DADT likely prevented military MSM from seeking or receiving appropriate screening.

We acknowledge potential limitations of our study: those inherent to an observational design, inability to achieve 100% three site screening from all participants, and small study population. Although our sample size is small, it is worth noting that trends in our data are

similar to trends noted in larger non-military studies of GC/CT infection: most infections were detected at extragenital sites, the majority of rectal infections were due to CT, and the majority of pharyngeal infections were due to GC. Finally, there may have been some reluctance of participants to answer survey questions honestly, although we believe this was minimized by our confidential survey procedures and as reflected by candid responses we did receive.

We have generated the first comprehensive data set of asymptomatic GC/CT infection in a US military population. Although much of what we have learned was assumed to be true, this is the first systematic description and underscores the need for military healthcare providers to screen their MSM population for infection at three anatomic sites. Also, as noted in larger studies, we found that reliance on urine/urethral screening alone will fail to detect the vast majority of asymptomatic infections in an MSM population. Finally, low rates of reported condom use among HIV-positive participants signals the need to enhance safer sex prevention efforts among MSM.

We hope the results of our pilot study will inform and motivate those who design larger, multisite STI clinical trials for the US military. Although our study was small, we can conclude that MSM make up a significant proportion of our HIV-infected population. DADT has been repealed and US Defense Secretary Panetta has mandated extension of military benefits to same sex partners.[33] Therefore, we believe it's also time to include MSM in our military research to enhance overall health.

TABLES

Table 1. HIV-infected male demographic characteristics, 2011—San Diego, California (n=99)

HIV variables	
CD4 count mean (SD), cells/mm^3	609 (216)
Suppressed HIV VL (<48 copies/μL)	43%
Receiving ART	51%
Time since HIV diagnosis mean (SD), months	62.8 (59.9)
Demographic variables	
Age	
Mean (SD), years	30.9 (8.2)
<25 years	28%
25-34 years	38%
≥ 35 years	33%
Ethnicity	
Black	36%
Caucasian	35%
Hispanic	15%
Other	13%
Marital Status	
Married	33%
Single	67%
Sexual Practice	
MSM	79%
MSW	21%
Previous STI	
Yes	36%

VL = plasma viral load
ART = antiretroviral therapy
MSM = men who have sex with men
MSW = men who have sex with women
SD = standard deviation
STI = sexually transmitted infection

Table 2. Prevalence of asymptomatic infection by anatomic site, HIV-infected men, 2011—San Diego, California (n=99)*

	Either Infection			CT			GC		
	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate
Overall	20	83	24.1%	17	83	20.5%	8	83	9.6%
Urethra	1	96	1.0%	0	96	0.0%	1	96	1.0%
Rectum	16	87	18.4%	16	87	18.4%	3	87	3.4%
Pharynx	8	87	9.2%	2	87	2.3%	7	87	8.0%

*Some participants did not have screening at all three sites.

Table 3. Survey responses – demographic & sexual practices by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Demographic variables (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Gender of sexual partner(s) (N=98)									
Women only	21	(21.4)	1	(4.8)	20	(26.0)	REF	--	--
Male (MSM)	77	(78.6)	20	(95.2)	57	(74.0)	7.02	1.88, 55.72	0.04
Race/ethnicity (N=99)									0.03
White	35	(35.4)	2	(9.5)	33	(42.3)	REF	--	--
Black	36	(36.4)	9	(42.9)	27	(34.7)	5.50	1.10, 27.64	0.04
Hispanic	15	(15.2)	6	(28.6)	9	(11.5)	11.00	1.89, 64.06	0.01
Other	13	(13.0)	4	(19.0)	9	(11.5)	7.33	1.15, 46.66	0.03
Age (N=99)									
<35 years	66	(66.7)	19	(90.5)	47	(60.3)	6.27	1.36, 28.82	0.02
≥ 35 years	33	(33.3)	2	(9.5)	31	(39.7)	REF	--	--
Previous history of STI (N=99)									
No	63	(63.6)	7	(33.3)	56	(71.8)	REF	--	--
Yes	36	(36.4)	14	(66.7)	22	(28.2)	5.10	1.81, 14.30	0.001
Number of years since HIV diagnosis (N=99)									
> 3 years	57	(57.6)	8	(38.1)	49	(62.8)	REF	--	--
≤ 3 years	42	(42.4)	13	(61.9)	29	(37.2)	2.75	1.02, 7.41	0.04
Sexual practices (N respondents)									
Vaginal sex (N=99)									
No	70	(70.7)	19	(90.5)	51	(65.4)	REF	--	--
Yes	29	(29.3)	2	(9.5)	27	(34.6)	0.20	0.04, 0.92	0.03
Oral sex[b] (N=99)									
No	3	(3.0)	0	(0)	3	(3.8)	REF	--	--
Yes	96	(97.0)	21	(100)	75	(96.2)	--	--	1.00
Anal sex[b] (N=99)									
No	15	(15.2)	0	(0)	15	(19.2)	REF	--	--
Yes	84	(84.8)	21	(100)	63	(80.8)	--	--	0.04
Insertive anal sex (N=80)									
No	15	(18.8)	5	(23.8)	10	(16.9)	1.00	--	--
Yes	65	(81.2)	16	(76.2)	49	(83.1)	0.65	0.19, 2.20	0.52
Receptive anal sex (N=80)									
No	17	(21.3)	2	(9.5)	15	(25.4)	REF	--	--
Yes	63	(78.7)	19	(90.5)	44	(74.6)	3.32	0.67, 15.57	0.21

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.
MSM = men who have sex with men (self-reported).
Oral and oral-anal sex were not significantly associated with infection with p>0.05

Table 4. Survey responses – relationship attitudes & condom use by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Relationship attitudes (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Sexual relationships with >1 partner in the past year (N=99)									
No	39	(39.4)	5	(23.8)	34	(43.6)	REF	--	--
Yes	60	(60.6)	16	(76.2)	44	(56.4)	2.47	0.82, 7.42	0.10
Frequency of sexual activity in the past year (N=99)									
< Once a week	38	(38.4)	4	(19.0)	34	(43.6)	REF	--	--
At least once a week	61	(61.6)	17	(81.0)	44	(56.4)	3.28	1.01, 10.66	0.04
Sexual relations only with partner in a serious relationship (N=99)									0.14
Strongly agree	51	(51.5)	7	(33.3)	44	(56.4)	REF	--	--
Neither agree/disagree	20	(20.2)	5	(23.8)	15	(19.2)	2.10	0.59, 7.60	0.26
Strongly disagree	28	(28.3)	9	(42.9)	19	(24.4)	2.98	0.97, 9.17	0.06
Expect monogamy in a serious relationship (N=99)									0.48
Strongly agree	75	(75.8)	14	(66.7)	61	(78.1)	REF	--	--
Neither agree/disagree	10	(10.1)	3	(14.3)	7	(9.0)	1.87	0.43, 8.14	0.41
Strongly disagree	14	(14.1)	4	(19.0)	10	(12.9)	1.74	0.48, 6.38	0.40
Sexual activities mostly with casual friends (N=99)									0.08
Strongly disagree	52	(53.0)	8	(38.0)	44	(57.2)	REF	--	--
Neither agree/disagree	24	(24.5)	9	(43.0)	15	(19.5)	3.30	1.08, 10.10	0.04
Strongly agree	22	(22.5)	4	(19.0)	18	(23.3)	1.22	0.33, 4.57	0.77
Condom use (N respondents)									
Self-condom use during oral sex (N=92)									
Always	12	(13.0)	4	(20.0)	8	(11.1)	REF	--	--
Do not always	80	(87.0)	16	(80.0)	64	(88.9)	0.50	0.13, 1.87	0.29
Partner-condom use during oral sex (N=90)									
Always	13	(14.4)	4	(19.0)	9	(13.0)	REF	--	--
Do not always	77	(85.6)	17	(81.0)	60	(87.0)	0.64	0.17, 2.34	0.49
Self-condom use during anal sex (N=82)									
Always	42	(51.2)	9	(45.0)	33	(53.2)	REF	--	--
Do not always	40	(48.8)	11	(55.0)	29	(46.8)	1.39	0.51, 3.83	0.52
Partner-condom use during anal sex (N=80)									
Always	37	(46.2)	8	(38.1)	29	(49.2)	REF	--	--
Do not always	43	(53.8)	13	(61.9)	30	(50.8)	1.57	0.57, 4.35	0.38

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.

LICENSE FOR PUBLICATION STATEMENT

CONTRIBUTORSHIP STATEMENT

Robert J. Carpenter contributed to conception and design, acquisition of data, and analysis and interpretation of data, participated in drafting the article or revising it critically for important intellectual content, and was involved in final approval of the version to be published.

All other authors listed contributed to acquisition of data, participated in drafting the article or revising it critically for important intellectual content, and were involved in final approval of the version to be published.

DATA SHARING STATEMENT

No additional data available.

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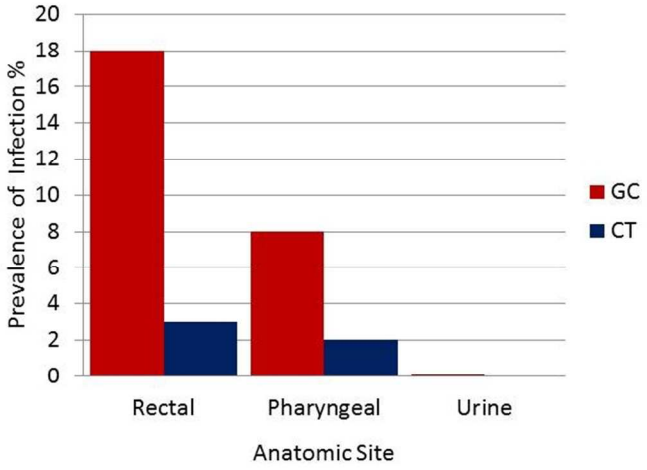

Distribution of asymptomatic gonococcal (GC) and chlamydial (CT) prevalence among HIV-infected men, San Diego, California, 2011
254x190mm (96 x 96 DPI)

Title: ~~Prevalence~~Incidence and Factors Associated with Asymptomatic Gonococcal and Chlamydial Infection among US ~~Military~~ Navy and Marine Corps Men Infected With the Human Immunodeficiency Virus

Running Title: HIV and gonococcal/chlamydial infection in US ~~military members~~Navy and Marine Corps men

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ARTICLE SUMMARY

FOCUS

- Is asymptomatic gonorrhea and chlamydia infection prevalent among US military men?
- If so, are those infections associated with any specific sexual practice or relationship beliefs?

KEY MESSAGES

- Men who have sex with men (MSM) in the US military are at risk for asymptomatic gonorrhea and chlamydia infection, predominantly at extragenital sites.
- Sex with men, anal sex, non-Caucasian ethnicity, age <35 years, and HIV infection for <3 years were all associated with asymptomatic infection.
- Repeal of DADT fostered a change in US military medical culture, allowing clinicians to counsel and screen MSM according to established guidelines.

STRENGTHS

- First comprehensive data set of asymptomatic gonorrhea/chlamydia infection in a US military population
- First study to describe health needs of men who have sex with men in a US military population

WEAKNESSES

- Observational study
- Small n (pilot study)
- Inability to obtain 3 site anatomic screening from all participants

ABSTRACT:

Objectives: *Neisseria gonorrheae* (GC) and *Chlamydia trachomatis* (CT) can facilitate transmission of HIV, and men who have sex with men (MSM) may harbor infections at extragenital sites. Data regarding extragenital GC and CT in military populations are lacking. We examined the ~~prevalence~~incidence and factors associated with asymptomatic ~~GC and CT~~ infection among HIV-infected military personnel.

Methods: Cross-sectional pilot study of asymptomatic men who underwent nucleic acid amplification screening for GC and CT of the pharynx, rectum, and urine at a single military treatment facility in San Diego, CA. Inclusion criteria: male, HIV-infected, Department of Defense beneficiary. Exclusion criteria: any symptom related to urethra, pharynx, or rectum. One participant was also excluded for recent CT treatment. Data on demographics, sexual practices, and HIV variables were collected. Factors associated with infection were analyzed using chi-square tests.

Results: Ninety-nine HIV-positive men were evaluated - 79% MSM, mean age 31 years, 36% Black, and 33% married. Twenty-four percent were infected with either GC or CT. Rectal swabs were positive in 18% for CT and 3% for GC; pharynx swabs were positive in 8% for GC and 2% for CT. Only 1 infection was detected in urine (GC). Anal sex (p=0.04), male partner (OR 7.02, p=0.04), and sex at least once weekly (OR 3.28, p=0.04) were associated with infection. Associated demographic included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001).

Conclusions: We found a high ~~prevalence~~incidence of extragenital GC/CT infection among HIV-infected military men. Only one infection was detected in the urine, signaling the need for aggressive three site screening of MSM. Clinicians should be aware of high ~~prevalence~~incidence in order to enhance health through comprehensive STI screening practices.

INTRODUCTION

Neisseria gonorrheae (GC) and *Chlamydia trachomatis* (CT) cause infection in the male urethral, pharyngeal, and rectal mucosa, facilitating transmission of the human immunodeficiency virus (HIV).[1-3] Men who have sex with men (MSM) are at particular risk for harboring these infections at extragenital sites.[4-10] The United States (US) law, 'don't ask, don't tell' (DADT), allowed gay persons to serve in the military but made it unlawful to reveal his/her sexual orientation and was the cause of separation of nearly 14,000 qualified service members.[11] Although there are several published reports regarding GC/CT infections in MSM, ~~little~~ limited data exist among US military members.[7 9 10 12-15] Since 1986, the US military maintains a natural history study of HIV-infected persons and reports of GC/CT in this cohort have been published.[16] Additionally, others have reported on GC/CT in US military men.[17-24] However, these reports fail to represent the full spectrum of GC/CT infection because they only include data from urine/urethra. Extragenital anatomic site data has never been previously captured nor reported by US military studies and, again largely because of DADT, comprehensive sexual practices and behaviors have also never been previously captured nor reported. This dearth of data is largely a byproduct of DADT which prohibited the recognition and study of MSM health needs; the law was repealed in 2011.

The Naval Medical Center San Diego (NMCSD) is one of three US Navy HIV Evaluation and Treatment Units and provides health care to approximately 575 HIV-infected Department of Defense beneficiaries, approximately half of whom are currently serving on active military duty. Services offered include comprehensive primary and subspecialty health care, mental health services, prevention counseling and health promotion, and HIV and other sexually transmitted infection (STI) screening and management.[25] However, three anatomic site

~~asymptomatic~~ GC/CT screening was not routinely performed in any US Navy medical treatment facility prior to this study. As US Department of Defense beneficiaries, these patients receive open, unrestricted access to care without copayments.

Given the lack of data on asymptomatic GC and CT infection among a US military cohort of HIV-infected men, we conducted a cross-sectional pilot study with the objectives: (1) to describe the ~~prevalence~~incidence of asymptomatic urethral, pharyngeal, and rectal GC/CT infection in this population; (2) to describe sexual behaviors, relationship attitudes, and HIV disease attributes among this cohort; and (3) to identify specific factors associated with asymptomatic GC/CT infection.

MATERIALS AND METHODS

Participants and Procedures

All HIV-infected US Navy and Marine Corps members serving on active duty are required to participate in a biannual medical and psychosocial evaluation. Those serving at military bases in the western US and Pacific Basin report to NMCSD for these visits. In order to minimize selection bias, beginning in September 2010, we presented the study to each consecutive military member presenting for required HIV evaluation until we enrolled 100 participants. The study was designed as a pilot to guide design of future research. No incentive to participation was offered. Those who participated did so to optimize personal sexual health through more thorough STI screening. Inclusion criteria included: male gender, HIV-infected, receiving care at the NMCSD, and having no symptoms referable to the pharynx, urethra, or rectum. Those who voluntarily agreed to participate completed a short questionnaire regarding sexual practices and relationship attitudes. In order to encourage honest responses, the written questionnaire was administered by the clinic's non-military preventive medicine counselor and all responses were confidentially maintained.

Each participant was screened for asymptomatic GC/CT infection of the urethra, pharynx, and rectum using a first-void urine sample and posterior pharyngeal and rectal swabs obtained by their primary HIV provider during their routine, biannual HIV clinic visit. All collected specimens were collected on the day the questionnaire was completed and a~~A~~ll ~~prevalent~~ infections were appropriately treated. The NMCSD laboratory previously verified the APTIMA Combo2® Assay (Gen-Probe Inc., San Diego, CA) for use in the pharynx and rectum according to Clinical Laboratory Improvement Amendments (CLIA) standards. Medical records were reviewed by an HIV clinician and data regarding demographics, prior STIs, and HIV-related data were collected. The study was approved and waiver of informed consent was granted by the NMCSD Institutional Review Board.

Data Analysis

The data collected (laboratory results, questionnaire responses, and medical record information) were entered into a Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA) database and analyzed with SAS® version 9.2 (SAS Institute, Cary, NC). ~~Prevalence~~Incidence rates were calculated for each type of infection (GC, CT, or both) at each site. The descriptive statistics included for categorical variables were counts and proportions, and means and standard deviations for continuous variables. Chi-square or Fisher's exact tests were performed, as appropriate, to analyze the bivariate relationships between the factors of interest and the outcome defined as being positive for either infection (GC and/or CT in at least one site). Odds ratios (OR), 95% confidence intervals (CI), and *P*-values were reported. *P*-values less than 0.05 were considered statistically significant.

RESULTS

One hundred six consecutive patients were offered participation in the study, six declined, and one hundred were enrolled. One participant was later excluded due to recent treatment of asymptomatic rectal CT infection prior to enrollment. Due to scheduling conflicts and inability of participant to return to the clinic, and despite several attempts to do so, a urine specimen was not collected from 3 participants and rectal/pharyngeal swabs from 12. The cohort (n=99) included 79% who were MSM. The mean age of the cohort was 31 years, and race was reported as Black in 36%, Caucasian in 35%, Hispanic in 15%, and other in 13%. Sixty-seven percent were unmarried, and 36% had a previous history of STI. HIV-related characteristics included a mean CD4 count of 609 cells/mm^3, 43% had an HIV viral load <48 copies/µL, 51% were receiving antiretroviral therapy, and the mean time since HIV diagnosis was 63 months. (Table 1)

Twenty-four percent had either GC or CT in at least 1 site. The site with the highest ~~prevalence~~incidence was the rectum (18.4%), followed by the pharynx (9.2%) and the urethra (1%). Of rectal swabs, 18% were positive for CT and 3% for GC. Of pharynx swabs, 8% were positive for GC and 2% for CT. Only one infection was detected in urine (GC). (Table 2) Eighty-one percent of those with GC/CT infection had a positive screening test at only one site, 19% were positive at two sites, and none were positive at all three sites.

In bivariate analysis, anal sex (p=0.04), having a male partner (OR 7.02, p=0.04), and having sex at least once weekly (OR 3.28, p=0.04) were associated with infection; vaginal sex was protective (OR 0.20, p=0.03). Demographic factors associated with infection included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (Black OR 5.50, p=0.04; Hispanic OR 11.00, p=0.01; other race OR 7.33, p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001). (Table 3, 4)

Only about half of participants reported always using condoms during anal sex, and less than half always required their partner to use condoms during anal sex. During oral sex, less than 15% of participants reported always using condoms and always requiring their partner to use condoms. (Table 4)

With regards to relationship attitudes, 52% of participants reported sexual relations only with a partner in a serious relationship, while 28% disagreed with this statement. Seventy-six percent of participants expected monogamy in a serious relationship, while 14% disagreed with this statement. Twenty-three percent of participants participated in most of their sexual relations with casual friends and 53% disagreed with this statement. None of these beliefs were significantly associated with infection. (Table 4)

DISCUSSION

We found an alarming ~~prevalence~~incidence of GC/CT infection—nearly twice that of non-military MSM in other large California cities.[10] In fact, our ~~prevalence~~incidence may represent an underestimate, since some of our patients may seek screening (and subsequent therapy) at the local county STD clinic prior to their military encounter, due to fear of discipline or discharge.[26 27] We believe there are two important contributors to the high ~~prevalence~~incidence rates observed: DADT and the first-screen effect.

DADT likely contributed the most to undiagnosed infection. The American Medical Association posited that this military law compromised the medical care of gay patients serving in the military.[28] Prior to repeal, military healthcare providers often believed they could not ask, document, nor counsel about sexual behaviors or orientations for fear of revealing MSM practices of their patients that they believed would lead to adverse legal action. Therefore, risk would not have been assessed and the need for screening was unknown and did not occur. DADT also prevented patients from providing honest answers or reports of sexual practices, again for fear of adverse legal action. We started our study prior to the repeal because SECNAVINST 5300.30D (the document that governs management of HIV infection in the Navy and Marine Corps) offered protection against adverse action related to information obtained from a medical or epidemiologic interview. Unfortunately, this provision was not well known to military healthcare providers.

Second, our study facilitated the initiation of sexual risk driven screening for GC/CT infection in our healthcare facility. Hence, study data represent the first time most~~many~~ participants were screened for extragenital GC/CT infection. First-time screening for a condition may reveal more ~~prevalent~~ incident cases than subsequent screening, especially in the case of

asymptomatic infection, and may partially explain why we detected higher ~~prevalence~~incidence than that found in other California cities which may represent subsequent screening data.

Our study also had several important findings regarding HIV-positive men serving in the US military. With regards to sexual practices, most respondents were MSM and engaged in oral, anal (receptive and insertive), and oral-anal sex. As expected, most respondents do not use condoms during oral sex. Surprisingly though was that nearly half of respondents do not always use condoms or require their partners to use condoms during anal sex. Safer sex fatigue, serosorting, and seropositioning may be contributors to low rates of condom use.[29] Regarding relationship attitudes, about half of respondents believe sexual relations should only occur with partners in a serious relationship while approximately one-quarter engage in sex with casual friends. When in a serious relationship, the majority of respondents expect monogamy.

The significant findings noted in our study were not unexpected. MSM, anal sex, non-Caucasian ethnicity, and younger age were associated with GC/CT and have been identified as STI risk factors in other studies.[16 30-32] Also, it follows that a person who recently acquired HIV infection or has a history of STI would be at higher risk for GC/CT infection. The increased risk among non-Caucasians may be related to cultural or societal stigma which may prevent an individual from seeking screening services (and need to disclose self-perceived taboo sexual behavior) in a way that DADT likely prevented military MSM from seeking or receiving appropriate screening.

We acknowledge potential limitations of our study: those inherent to an observational design, inability to achieve 100% three site screening from all participants, and small study

population. Although our sample size is small, it is worth noting that trends in our data are similar to trends noted in larger non-military studies of GC/CT infection: most infections were detected at extragenital sites, the majority of rectal infections were due to CT, and the majority of pharyngeal infections were due to GC. Finally, there may have been some reluctance of participants to answer survey questions honestly, although we believe this was minimized by our confidential survey procedures and as reflected by candid responses we did receive.

We have generated the first comprehensive data set of asymptomatic GC/CT infection in a US military population. Although much of what we have learned was assumed to be true, this is the first systematic description and underscores the need for military healthcare providers to screen their MSM population for infection at three anatomic sites. Also, as noted in larger studies, we found that reliance on urine/urethral screening alone will fail to detect the vast majority of asymptomatic infections in an MSM population. Finally, low rates of reported condom use among HIV-positive participants signals the need to enhance safer sex prevention efforts among MSM.

We hope the results of our pilot study will inform and motivate those who design larger, multisite STI clinical trials for the US military. Although our study was small, we can conclude that MSM make up a significant proportion of our HIV-infected population. DADT has been repealed and US Defense Secretary Panetta has mandated extension of military benefits to same sex partners.[33] Therefore, we believe it's also time to include MSM in our military research to enhance overall health.

TABLES

Table 1. HIV-infected male demographic characteristics, 2011—San Diego, California (n=99)

HIV variables	
CD4 count mean (SD), cells/mm^3	609 (216)
Suppressed HIV VL (<48 copies/µL)	43%
Receiving ART	51%
Time since HIV diagnosis mean (SD), months	62.8 (59.9)
Demographic variables	
Age	
Mean (SD), years	30.9 (8.2)
<25 years	28%
25-34 years	38%
≥ 35 years	33%
Ethnicity	
Black	36%
Caucasian	35%
Hispanic	15%
Other	13%
Marital Status	
Married	33%
Single	67%
Sexual Practice	
MSM	79%
MSW	21%
Previous STI	
Yes	36%

VL = plasma viral load
ART = antiretroviral therapy
MSM = men who have sex with men
MSW = men who have sex with women
SD = standard deviation
STI = sexually transmitted infection

Table 2. Prevalence of asymptomatic infection by anatomic site, HIV-infected men, 2011—San Diego, California (n=99)*

	Either Infection			CT			GC		
	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate
Overall	20	83	24.1%	17	83	20.5%	8	83	9.6%
Urethra	1	96	1.0%	0	96	0.0%	1	96	1.0%
Rectum	16	87	18.4%	16	87	18.4%	3	87	3.4%
Pharynx	8	87	9.2%	2	87	2.3%	7	87	8.0%

*Some participants did not have screening at all three sites.

Table 3. Survey responses – demographic & sexual practices by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Demographic variables (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Gender of sexual partner(s) (N=98)									
Women only	21	(21.4)	1	(4.8)	20	(26.0)	REF	--	--
Male (MSM)	77	(78.6)	20	(95.2)	57	(74.0)	7.02	1.88, 55.72	0.04
Race/ethnicity (N=99)									0.03
White	35	(35.4)	2	(9.5)	33	(42.3)	REF	--	--
Black	36	(36.4)	9	(42.9)	27	(34.7)	5.50	1.10, 27.64	0.04
Hispanic	15	(15.2)	6	(28.6)	9	(11.5)	11.00	1.89, 64.06	0.01
Other	13	(13.0)	4	(19.0)	9	(11.5)	7.33	1.15, 46.66	0.03
Age (N=99)									
<35 years	66	(66.7)	19	(90.5)	47	(60.3)	6.27	1.36, 28.82	0.02
≥ 35 years	33	(33.3)	2	(9.5)	31	(39.7)	REF	--	--
Previous history of STI (N=99)									
No	63	(63.6)	7	(33.3)	56	(71.8)	REF	--	--
Yes	36	(36.4)	14	(66.7)	22	(28.2)	5.10	1.81, 14.30	0.001
Number of years since HIV diagnosis (N=99)									
> 3 years	57	(57.6)	8	(38.1)	49	(62.8)	REF	--	--
≤ 3 years	42	(42.4)	13	(61.9)	29	(37.2)	2.75	1.02, 7.41	0.04
Sexual practices (N respondents)									
Vaginal sex (N=99)									
No	70	(70.7)	19	(90.5)	51	(65.4)	REF	--	--
Yes	29	(29.3)	2	(9.5)	27	(34.6)	0.20	0.04, 0.92	0.03
Oral sex[b] (N=99)									
No	3	(3.0)	0	(0)	3	(3.8)	REF	--	--
Yes	96	(97.0)	21	(100)	75	(96.2)	--	--	1.00
Anal sex[b] (N=99)									
No	15	(15.2)	0	(0)	15	(19.2)	REF	--	--
Yes	84	(84.8)	21	(100)	63	(80.8)	--	--	0.04
Insertive anal sex (N=80)									
No	15	(18.8)	5	(23.8)	10	(16.9)	1.00	--	--
Yes	65	(81.2)	16	(76.2)	49	(83.1)	0.65	0.19, 2.20	0.52
Receptive anal sex (N=80)									
No	17	(21.3)	2	(9.5)	15	(25.4)	REF	--	--
Yes	63	(78.7)	19	(90.5)	44	(74.6)	3.32	0.67, 15.57	0.21

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.
MSM = men who have sex with men (self-reported).
Oral and oral-anal sex were not significantly associated with infection with p>0.05

Table 4. Survey responses – relationship attitudes & condom use by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Relationship attitudes (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Sexual relationships with >1 partner in the past year (N=99)									
No	39	(39.4)	5	(23.8)	34	(43.6)	REF	--	--
Yes	60	(60.6)	16	(76.2)	44	(56.4)	2.47	0.82, 7.42	0.10
Frequency of sexual activity in the past year (N=99)									
< Once a week	38	(38.4)	4	(19.0)	34	(43.6)	REF	--	--
At least once a week	61	(61.6)	17	(81.0)	44	(56.4)	3.28	1.01, 10.66	0.04
Sexual relations only with partner in a serious relationship (N=99)									0.14
Strongly agree	51	(51.5)	7	(33.3)	44	(56.4)	REF	--	--
Neither agree/disagree	20	(20.2)	5	(23.8)	15	(19.2)	2.10	0.59, 7.60	0.26
Strongly disagree	28	(28.3)	9	(42.9)	19	(24.4)	2.98	0.97, 9.17	0.06
Expect monogamy in a serious relationship (N=99)									0.48
Strongly agree	75	(75.8)	14	(66.7)	61	(78.1)	REF	--	--
Neither agree/disagree	10	(10.1)	3	(14.3)	7	(9.0)	1.87	0.43, 8.14	0.41
Strongly disagree	14	(14.1)	4	(19.0)	10	(12.9)	1.74	0.48, 6.38	0.40
Sexual activities mostly with casual friends (N=99)									0.08
Strongly disagree	52	(53.0)	8	(38.0)	44	(57.2)	REF	--	--
Neither agree/disagree	24	(24.5)	9	(43.0)	15	(19.5)	3.30	1.08, 10.10	0.04
Strongly agree	22	(22.5)	4	(19.0)	18	(23.3)	1.22	0.33, 4.57	0.77
Condom use (N respondents)									
Self-condom use during oral sex (N=92)									
Always	12	(13.0)	4	(20.0)	8	(11.1)	REF	--	--
Do not always	80	(87.0)	16	(80.0)	64	(88.9)	0.50	0.13, 1.87	0.29
Partner-condom use during oral sex (N=90)									
Always	13	(14.4)	4	(19.0)	9	(13.0)	REF	--	--
Do not always	77	(85.6)	17	(81.0)	60	(87.0)	0.64	0.17, 2.34	0.49
Self-condom use during anal sex (N=82)									
Always	42	(51.2)	9	(45.0)	33	(53.2)	REF	--	--
Do not always	40	(48.8)	11	(55.0)	29	(46.8)	1.39	0.51, 3.83	0.52
Partner-condom use during anal sex (N=80)									
Always	37	(46.2)	8	(38.1)	29	(49.2)	REF	--	--
Do not always	43	(53.8)	13	(61.9)	30	(50.8)	1.57	0.57, 4.35	0.38

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.

LICENSE FOR PUBLICATION STATEMENT

CONTRIBUTORSHIP STATEMENT

Robert J. Carpenter contributed to conception and design, acquisition of data, and analysis and interpretation of data, participated in drafting the article or revising it critically for important intellectual content, and was involved in final approval of the version to be published.

All other authors listed contributed to acquisition of data, participated in drafting the article or revising it critically for important intellectual content, and were involved in final approval of the version to be published.

DATA SHARING STATEMENT

No additional data available.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Incidence and Factors Associated with Asymptomatic Gonococcal and Chlamydial Infection among US Navy and Marine Corps Men Infected With the Human Immunodeficiency Virus

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ARTICLE SUMMARY

FOCUS

- Is asymptomatic gonorrhea and chlamydia infection prevalent among US military men with HIV?
- If so, are those infections associated with any specific sexual practice or relationship beliefs?

KEY MESSAGES

- Men who have sex with men (MSM) in the US military are at risk for asymptomatic gonorrhea and chlamydia infection, predominantly at extragenital sites.
- Sex with men, anal sex, non-Caucasian ethnicity, age <35 years, and HIV infection for <3 years were all associated with asymptomatic infection.
- Repeal of DADT fostered a change in US military medical culture, allowing clinicians to counsel and screen MSM according to established guidelines.

STRENGTHS

- First comprehensive data set of asymptomatic gonorrhea/chlamydia infection in a male US military population previously infected with HIV.
- First study to describe health needs of men who have sex with men in a US military population.

WEAKNESSES

- Observational study
- Small n (pilot study)
- Inability to obtain 3 site anatomic screening from all participants

ABSTRACT:

Objectives: *Neisseria gonorrheae* (GC) and *Chlamydia trachomatis* (CT) can facilitate transmission of HIV. Men who have sex with men (MSM) may harbor infections at genital and extragenital sites. Data regarding extragenital GC and CT infections in military populations are lacking. We examined the incidence and factors associated with asymptomatic GC and CT infection among this category of HIV-infected military personnel.

Methods: Cross-sectional pilot study of asymptomatic men who underwent nucleic acid amplification screening for GC and CT of the pharynx, rectum, and urine at a single military treatment facility in San Diego, CA. Inclusion criteria: male, HIV-infected, Department of Defense beneficiary. Exclusion criteria: any symptom related to urethra, pharynx, or rectum. One participant was also excluded for recent CT treatment. Data on demographics, sexual practices, and HIV variables were collected. Factors associated with infection were analyzed using chi-square tests.

Results: Ninety-nine HIV-positive men were evaluated - 79% MSM, mean age 31 years, 36% Black, and 33% married. Twenty-four percent were infected with either GC or CT. Rectal swabs were positive in 18% for CT and 3% for GC; pharynx swabs were positive in 8% for GC and 2% for CT. Only 1 infection was detected in urine (GC). Anal sex (p=0.04), male partner (OR 7.02, p=0.04), and sex at least once weekly (OR 3.28, p=0.04) were associated with infection. Associated demographic included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001).

Conclusions: We found a high incidence of extragenital GC/CT infection among HIV-infected military men. Only one infection was detected in the urine, signaling the need for aggressive three site screening of MSM. Clinicians should be aware of high incidence in order to enhance health through comprehensive STI screening practices.

INTRODUCTION

Neisseria gonorrheae (GC) and *Chlamydia trachomatis* (CT) may cause infection in the male urethral, pharyngeal, and rectal mucosa, facilitating transmission of the human immunodeficiency virus (HIV).[1-3] Men who have sex with men (MSM) are at particular risk for harboring these infections at extragenital sites.[4-10] The institution of the United States (US) law, 'don't ask, don't tell' (DADT), allowed gay persons to serve in the military but made it unlawful for a service member to reveal his/her sexual orientation. Until its repeal in 2011, nearly 14,000 qualified service members were separated from the military.[11] Although there are several published reports regarding GC/CT infections in MSM, limited data existed among US military members.[7 9 10 12-15] Since 1986, the US military maintains a natural history study of HIV-infected persons receiving military healthcare and reports of GC/CT infection status in this cohort have been published.[16] Several other reports document GC/CT infections in US military men.[17-24] However, because of the DADT policy these reports could not represent the full spectrum of GC/CT infection in a military MSM population because they only included data from urine/urethra specimens. Presently, extragenital anatomic site data and comprehensive sexual practices and behaviors may now be reported.

The Naval Medical Center San Diego (NMCSD) is one of three US Navy HIV Evaluation and Treatment Units and provides health care to approximately 575 HIV-infected Department of Defense beneficiaries, approximately half of whom are currently serving on active military duty. Services offered include comprehensive primary and subspecialty health care, mental health services, prevention counseling and health promotion, and HIV and other sexually transmitted infection (STI) screening and management.[25] However, three anatomic site GC/CT screening was not routinely performed in any US Navy medical treatment facility prior to this study.

Given the lack of data on asymptomatic GC and CT infection among a US military cohort of HIV-infected men, we conducted a cross-sectional pilot study with the objectives: (1) to describe the incidence of asymptomatic urethral, pharyngeal, and rectal GC/CT infection in this population; (2) to identify specific sexual behaviors, relationship attitudes, and HIV disease attributes among this cohort; and (3) to determine specific factors associated with asymptomatic GC/CT infections.

MATERIALS AND METHODS

Participants and Procedures

All HIV-infected US Navy and Marine Corps members serving on active duty are required to participate in a biannual medical and psychosocial evaluation. Those serving at military bases in the western US and Pacific Basin report to NMCSD for these visits. Beginning in September 2010, we presented the study to each consecutive military member presenting for required HIV evaluation until we enrolled 100 participants. The study was designed as a pilot to guide design of future research. No incentive to participation was offered. Those who participated did so to optimize personal sexual health through more thorough STI screening. Inclusion criteria included: male gender, HIV-infected, receiving care at the NMCSD, and having no current symptoms referable to the pharynx, urethra, or rectum on the day of enrollment. Study participants completed a short questionnaire regarding sexual practices and relationship attitudes. In order to encourage honest responses, the written questionnaire was administered by the clinic's non-military preventive medicine counselor and all responses were confidentially maintained.

Each participant was screened for asymptomatic GC/CT infection of the urethra, pharynx, and rectum using a first-void urine sample and posterior pharyngeal and rectal swabs obtained by their primary HIV provider during their routine, biannual HIV clinic visit. All

collected specimens were collected on the day the questionnaire was completed and any infections were appropriately treated. The NMCSD laboratory previously validated the APTIMA Combo2® Assay (Gen-Probe Inc., San Diego, CA) for testing pharyngeal and rectal specimens according to Clinical Laboratory Improvement Amendments (CLIA) standard Sec 493.1253. Medical records were reviewed by an HIV clinician and data regarding demographics, prior STIs, and HIV-related data were collected. This study was previously approved with a waiver of informed consent granted by the NMCSD Institutional Review Board.

Data Analysis

The data collected (laboratory results, questionnaire responses, and medical record information) were entered into a Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA) database and analyzed with SAS® version 9.2 (SAS Institute, Cary, NC). Incidence rates were calculated for each type of infection (GC, CT, or both) at each site. The descriptive statistics included for categorical variables were counts and proportions, and means and standard deviations for continuous variables. Chi-square or Fisher's exact tests were performed, as appropriate, to analyze the bivariate relationships between the factors of interest and the outcome defined as being positive for either infection (GC and/or CT in at least one site). Odds ratios (OR), 95% confidence intervals (CI), and *P*-values were reported. *P*-values less than 0.05 were considered statistically significant.

RESULTS

One hundred six consecutive patients were offered participation in the study before one hundred were enrolled. One participant was later excluded due to recent treatment of an asymptomatic rectal CT infection prior to enrollment. Due to scheduling conflicts and technical difficulties, only 96 urine specimens and 87 rectal/pharyngeal swabs were actually tested. The cohort (n=99) included 79% who were MSM. The mean age of the cohort was 31 years, and race was reported as Black in 36%, Caucasian in 35%, Hispanic in 15%, and other in 13%. Sixty-seven percent were unmarried, and 36% had a previous history of STI. HIV-related characteristics included a mean CD4 count of 609 cells/mm^3, 43% had an HIV viral load <48 copies/µL, 51% were receiving antiretroviral therapy, and the mean time since HIV diagnosis was 63 months. (Table 1)

Twenty-four percent of the participants had either GC or CT infection in at least 1 site. The rectal swab yielded the highest incidence (18.4%), followed by the pharynx (9.2%) and the urethra (1%). Of rectal swabs, 18% were positive for CT and 3% for GC while for pharynx swabs, 8% were positive for GC and 2% for CT. Only one infection was detected in a urine specimen (GC). (Table 2) Eighty-one percent of the identified infections tested positive at only one site, 19% were positive at two anatomic sites, and none were positive at all three sites.

Using bivariate analysis, the following factors: anal sex (p=0.04), having a male partner (OR 7.02, p=0.04), and having sex at least once weekly (OR 3.28, p=0.04) were associated with infection; vaginal sex was protective (OR 0.20, p=0.03). Demographic factors associated with infection included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (Black OR 5.50, p=0.04; Hispanic OR 11.00, p=0.01; other race OR 7.33, p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001). (Table 3, 4)

Only about half of participants reported consistent use of condoms during anal sex, and less than half always required their partner to use condoms during anal sex. During oral sex, less than 15% of participants reported always using condoms and always requiring their partner to use condoms. (Table 4)

With regards to relationship attitudes, 52% of participants reported sexual relations only with a partner in a serious relationship, while 28% disagreed with this statement. Seventy-six percent of participants expected monogamy in a serious relationship, while 14% disagreed with this statement. Twenty-three percent of participants participated in most of their sexual relations with casual friends and 53% disagreed with this statement. None of these beliefs were significantly associated with infection. (Table 4)

DISCUSSION

We found an alarming incidence of GC/CT infection—nearly twice that of non-military MSM in other large California cities.[10] In fact, this may represent an underestimate, since some of our patients likely sought screening (and subsequent therapy) at the local county STD clinic prior to their military encounter, due to fear of discipline or discharge.[26 27] We believe there are two important contributors to the high incidence rates observed: DADT and the first-screen effect.

DADT likely contributed the most to undiagnosed infection. The American Medical Association posited that this military law compromised the medical care of gay patients serving in the military.[28] Prior to repeal, military healthcare providers often believed they could not ask, document, nor counsel about sexual behaviors or orientations for fear of revealing MSM practices of their patients that could lead to adverse legal action for the service member. Therefore, all potential risks would not have been assessed such that screening all three anatomic sites did not occur. DADT likely prevented patients from providing honest answers or reports of sexual practices, for fear of adverse legal action. We started our study prior to the repeal because SECNAVINST 5300.30D (the document that governs management of HIV infection in the Navy and Marine Corps) offered protection against adverse action related to information obtained from a medical or epidemiologic interview. Unfortunately, this provision was not well known to military healthcare providers.

Second, our study facilitated the initiation of sexual risk driven screening for GC/CT infection in our healthcare facility. Hence, study data represent the first time most participants were screened for extragenital GC/CT infection. First-time screening for a condition may reveal more incident cases than subsequent screening, especially in the case of asymptomatic

infection, and may partially explain why we detected higher incidence than that found in other California cities which may represent subsequent screening data.

Our study also had several important findings regarding HIV-positive men serving in the US military. With regards to sexual practices, most respondents were MSM and engaged in oral, anal (receptive and insertive), and oral-anal sex. As expected, most respondents do not use condoms during oral sex, but surprisingly nearly half of respondents do not always use condoms or require their partners to use condoms during anal sex either. Potential contributors to the low reported rates of condom use include: safer sex fatigue, serosorting, and seropositioning.[29] Regarding relationship attitudes, about half of respondents believe sexual relations should only occur with partners in a serious relationship while approximately one-quarter engage in sex with casual friends. When in a serious relationship, the majority of respondents expect monogamy.

Our study results identified MSM, anal sex, non-Caucasian ethnicity, and younger age were more associated with GC/CT infections thus recognized as STI risk factors, in agreement with other studies.[16 30-32] Generally, those patients with a recently acquired HIV infection or prior history of STI have a higher risk for GC/CT infection. The increased risk among non-Caucasians may be related to cultural or societal stigma which may prevent an individual from seeking screening services (and need to disclose self-perceived taboo sexual behavior) in a way that DADT likely prevented military MSM from seeking or receiving appropriate screening.

We acknowledge potential limitations of our study: those inherent to an observational design, inability to achieve 100% three site screening from all participants, and small study population. Although our sample size is small, it is worth noting that trends in our data are

similar to trends noted in larger non-military studies of GC/CT infection: most infections were detected at extragenital sites, the majority of rectal infections were due to CT, and the majority of pharyngeal infections were due to GC. Finally, although there may have been some reluctance of participants to answer survey questions honestly, we believe this was minimized by our confidential survey procedures and as reflected by the candid responses we did receive.

This is the first comprehensive data set of asymptomatic GC/CT infection in a male HIV-positive US military population. Along with the CDC's recommendations, these results underscore the need for military healthcare providers to screen their MSM population for infection at all three anatomic sites. Just as noted in larger studies, we confirm that urine/urethral screening alone may fail to detect many asymptomatic infections in the MSM population. Finally, low rates of reported condom use among HIV-positive participants signals the need to enhance safer sex prevention efforts among MSM.

We hope to use the results of this study to help design and complete larger, multisite STI clinical trials for the US military. We can conclude that MSM make up a significant proportion of our HIV-infected population. Now that DADT has been repealed and the Department of Defense has mandated extension of military benefits to same sex partners,[33] we should look to modify treatment guidelines for MSM in our military to enhance overall health.

TABLES

Table 1. HIV-infected male demographic characteristics, 2011—San Diego, California (n=99)

HIV variables	
CD4 count mean (SD), cells/mm^3	609 (216)
Suppressed HIV VL (<48 copies/µL)	43%
Receiving ART	51%
Time since HIV diagnosis mean (SD), months	62.8 (59.9)
Demographic variables	
Age	
Mean (SD), years	30.9 (8.2)
<25 years	28%
25-34 years	38%
≥ 35 years	33%
Ethnicity	
Black	36%
Caucasian	35%
Hispanic	15%
Other	13%
Marital Status	
Married	33%
Single	67%
Sexual Practice	
MSM	79%
MSW	21%
Previous STI	
Yes	36%

VL = plasma viral load
ART = antiretroviral therapy
MSM = men who have sex with men
MSW = men who have sex with women
SD = standard deviation
STI = sexually transmitted infection

Table 2. Incidence of asymptomatic infection by anatomic site, HIV-infected men, 2011—San Diego, California (n=99)*

	Either Infection			CT			GC		
	Cases	N	Incidence Rate	Cases	N	Incidence Rate	Cases	N	Incidence Rate
Overall	20	83	24.1%	17	83	20.5%	8	83	9.6%
Urethra	1	96	1.0%	0	96	0.0%	1	96	1.0%
Rectum	16	87	18.4%	16	87	18.4%	3	87	3.4%
Pharynx	8	87	9.2%	2	87	2.3%	7	87	8.0%

*Some participants did not have screening at all three sites.

Table 3. Survey responses – demographic & sexual practices by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Demographic variables (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Gender of sexual partner(s) (N=98)									
Women only	21	(21.4)	1	(4.8)	20	(26.0)	REF	--	--
Male (MSM)	77	(78.6)	20	(95.2)	57	(74.0)	7.02	1.88, 55.72	0.04
Race/ethnicity (N=99)									0.03
White	35	(35.4)	2	(9.5)	33	(42.3)	REF	--	--
Black	36	(36.4)	9	(42.9)	27	(34.7)	5.50	1.10, 27.64	0.04
Hispanic	15	(15.2)	6	(28.6)	9	(11.5)	11.00	1.89, 64.06	0.01
Other	13	(13.0)	4	(19.0)	9	(11.5)	7.33	1.15, 46.66	0.03
Age (N=99)									
<35 years	66	(66.7)	19	(90.5)	47	(60.3)	6.27	1.36, 28.82	0.02
≥ 35 years	33	(33.3)	2	(9.5)	31	(39.7)	REF	--	--
Previous history of STI (N=99)									
No	63	(63.6)	7	(33.3)	56	(71.8)	REF	--	--
Yes	36	(36.4)	14	(66.7)	22	(28.2)	5.10	1.81, 14.30	0.001
Number of years since HIV diagnosis (N=99)									
> 3 years	57	(57.6)	8	(38.1)	49	(62.8)	REF	--	--
≤ 3 years	42	(42.4)	13	(61.9)	29	(37.2)	2.75	1.02, 7.41	0.04
Sexual practices (N respondents)									
Vaginal sex (N=99)									
No	70	(70.7)	19	(90.5)	51	(65.4)	REF	--	--
Yes	29	(29.3)	2	(9.5)	27	(34.6)	0.20	0.04, 0.92	0.03
Oral sex[b] (N=99)									
No	3	(3.0)	0	(0)	3	(3.8)	REF	--	--
Yes	96	(97.0)	21	(100)	75	(96.2)	--	--	1.00
Anal sex[b] (N=99)									
No	15	(15.2)	0	(0)	15	(19.2)	REF	--	--
Yes	84	(84.8)	21	(100)	63	(80.8)	--	--	0.04
Insertive anal sex (N=80)									
No	15	(18.8)	5	(23.8)	10	(16.9)	1.00	--	--
Yes	65	(81.2)	16	(76.2)	49	(83.1)	0.65	0.19, 2.20	0.52
Receptive anal sex (N=80)									
No	17	(21.3)	2	(9.5)	15	(25.4)	REF	--	--
Yes	63	(78.7)	19	(90.5)	44	(74.6)	3.32	0.67, 15.57	0.21

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.
MSM = men who have sex with men (self-reported).
Oral and oral-anal sex were not significantly associated with infection with p>0.05

Table 4. Survey responses – relationship attitudes & condom use by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Relationship attitudes (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Sexual relationships with >1 partner in the past year (N=99)									
No	39	(39.4)	5	(23.8)	34	(43.6)	REF	--	--
Yes	60	(60.6)	16	(76.2)	44	(56.4)	2.47	0.82, 7.42	0.10
Frequency of sexual activity in the past year (N=99)									
< Once a week	38	(38.4)	4	(19.0)	34	(43.6)	REF	--	--
At least once a week	61	(61.6)	17	(81.0)	44	(56.4)	3.28	1.01, 10.66	0.04
Sexual relations only with partner in a serious relationship (N=99)									0.14
Strongly agree	51	(51.5)	7	(33.3)	44	(56.4)	REF	--	--
Neither agree/disagree	20	(20.2)	5	(23.8)	15	(19.2)	2.10	0.59, 7.60	0.26
Strongly disagree	28	(28.3)	9	(42.9)	19	(24.4)	2.98	0.97, 9.17	0.06
Expect monogamy in a serious relationship (N=99)									0.48
Strongly agree	75	(75.8)	14	(66.7)	61	(78.1)	REF	--	--
Neither agree/disagree	10	(10.1)	3	(14.3)	7	(9.0)	1.87	0.43, 8.14	0.41
Strongly disagree	14	(14.1)	4	(19.0)	10	(12.9)	1.74	0.48, 6.38	0.40
Sexual activities mostly with casual friends (N=99)									0.08
Strongly disagree	52	(53.0)	8	(38.0)	44	(57.2)	REF	--	--
Neither agree/disagree	24	(24.5)	9	(43.0)	15	(19.5)	3.30	1.08, 10.10	0.04
Strongly agree	22	(22.5)	4	(19.0)	18	(23.3)	1.22	0.33, 4.57	0.77
Condom use (N respondents)									
Self-condom use during oral sex (N=92)									
Always	12	(13.0)	4	(20.0)	8	(11.1)	REF	--	--
Do not always	80	(87.0)	16	(80.0)	64	(88.9)	0.50	0.13, 1.87	0.29
Partner-condom use during oral sex (N=90)									
Always	13	(14.4)	4	(19.0)	9	(13.0)	REF	--	--
Do not always	77	(85.6)	17	(81.0)	60	(87.0)	0.64	0.17, 2.34	0.49
Self-condom use during anal sex (N=82)									
Always	42	(51.2)	9	(45.0)	33	(53.2)	REF	--	--
Do not always	40	(48.8)	11	(55.0)	29	(46.8)	1.39	0.51, 3.83	0.52
Partner-condom use during anal sex (N=80)									
Always	37	(46.2)	8	(38.1)	29	(49.2)	REF	--	--
Do not always	43	(53.8)	13	(61.9)	30	(50.8)	1.57	0.57, 4.35	0.38

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.

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CONTRIBUTORSHIP STATEMENT

Robert J. Carpenter contributed to conception and design, acquisition of data, and analysis and interpretation of data, participated in drafting the article or revising it critically for important intellectual content, and was involved in final approval of the version to be published.

All other authors listed contributed to acquisition of data, participated in drafting the article or revising it critically for important intellectual content, and were involved in final approval of the version to be published.

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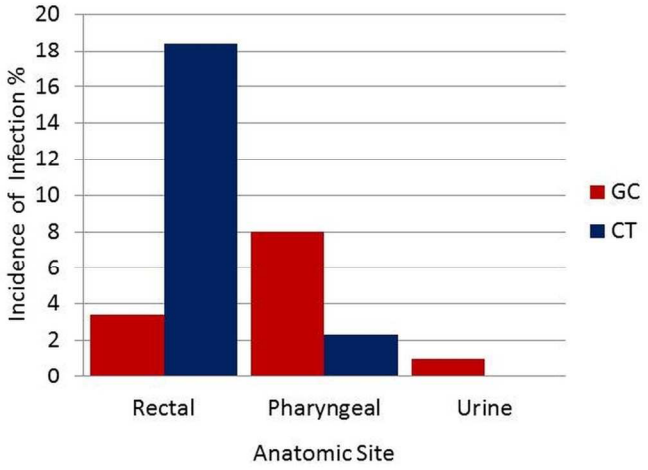

Distribution of asymptomatic gonococcal (GC) and chlamydial (CT) infection among HIV-infected men, San Diego, California, 2011
119x90mm (300 x 300 DPI)

Title: Incidence and Factors Associated with Asymptomatic Gonococcal and Chlamydial Infection among US Navy and Marine Corps Men Infected With the Human Immunodeficiency Virus

Running Title: HIV and gonococcal/chlamydial infection in US Navy and Marine Corps men

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ARTICLE SUMMARY

FOCUS

- Is asymptomatic gonorrhea and chlamydia infection prevalent among US military men with HIV?
- If so, are those infections associated with any specific sexual practice or relationship beliefs?

KEY MESSAGES

- Men who have sex with men (MSM) in the US military are at risk for asymptomatic gonorrhea and chlamydia infection, predominantly at extragenital sites.
- Sex with men, anal sex, non-Caucasian ethnicity, age <35 years, and HIV infection for <3 years were all associated with asymptomatic infection.
- Repeal of DADT fostered a change in US military medical culture, allowing clinicians to counsel and screen MSM according to established guidelines.

STRENGTHS

- First comprehensive data set of asymptomatic gonorrhea/chlamydia infection in a male US military population previously infected with HIV
- First study to describe health needs of men who have sex with men in a US military population

WEAKNESSES

- Observational study
- Small n (pilot study)
- Inability to obtain 3 site anatomic screening from all participants

ABSTRACT:

Objectives: *Neisseria gonorrheae* (GC) and *Chlamydia trachomatis* (CT) can facilitate transmission of HIV.; M and men who have sex with men (MSM) may harbor infections at genital and extragenital sites. Data regarding extragenital GC and CT infections in military populations are lacking. We examined the incidence and factors associated with asymptomatic GC and CT infection among this category of HIV-infected military personnel.

Methods: Cross-sectional pilot study of asymptomatic men who underwent nucleic acid amplification screening for GC and CT of the pharynx, rectum, and urine at a single military treatment facility in San Diego, CA. Inclusion criteria: male, HIV-infected, Department of Defense beneficiary. Exclusion criteria: any symptom related to urethra, pharynx, or rectum. One participant was also excluded for recent CT treatment. Data on demographics, sexual practices, and HIV variables were collected. Factors associated with infection were analyzed using chi-square tests.

Results: Ninety-nine HIV-positive men were evaluated - 79% MSM, mean age 31 years, 36% Black, and 33% married. Twenty-four percent were infected with either GC or CT. Rectal swabs were positive in 18% for CT and 3% for GC; pharynx swabs were positive in 8% for GC and 2% for CT. Only 1 infection was detected in urine (GC). Anal sex (p=0.04), male partner (OR 7.02, p=0.04), and sex at least once weekly (OR 3.28, p=0.04) were associated with infection. Associated demographic included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001).

Conclusions: We found a high incidence of extragenital GC/CT infection among HIV-infected military men. Only one infection was detected in the urine, signaling the need for aggressive three site screening of MSM. Clinicians should be aware of high incidence in order to enhance health through comprehensive STI screening practices.

INTRODUCTION

Neisseria gonorrheae (GC) and *Chlamydia trachomatis* (CT) may cause infection in the male urethral, pharyngeal, and rectal mucosa, facilitating transmission of the human immunodeficiency virus (HIV).[1-3] Men who have sex with men (MSM) are at particular risk for harboring these infections at extragenital sites.[4-10] The institution of the United States (US) law, 'don't ask, don't tell' (DADT), allowed gay persons to serve in the military but made it unlawful for a service member to reveal his/her sexual orientation. ~~and was the cause of separation of~~Until its repeal in 2011, nearly 14,000 qualified service members were separated from the military.[11] Although there are several published reports regarding GC/CT infections in MSM, limited data existed among US military members.[7 9 10 12-15] Since 1986, the US military maintains a natural history study of HIV-infected persons receiving military healthcare and reports of GC/CT infection status in this cohort have been published.[16] ~~Additionally, others have reported on~~Several other reports document GC/CT infections in US military men.[17-24] However, because of the DADT policy these reports ~~fail to~~could not represent the full spectrum of GC/CT infection in a military MSM population because they only included data from urine/urethra specimens. ~~Extragenital~~ Presently, extragenital anatomic site data ~~has never been previously captured nor reported by US military studies and, again largely because of DADT~~and, comprehensive sexual practices and behaviors ~~have also never been previously captured nor~~may now be reported. ~~This dearth of data is largely a byproduct of DADT which prohibited the recognition and study of MSM health needs; the law was repealed in 2011.~~

The Naval Medical Center San Diego (NMCSD) is one of three US Navy HIV Evaluation and Treatment Units and provides health care to approximately 575 HIV-infected Department of Defense beneficiaries, approximately half of whom are currently serving on active military

duty. Services offered include comprehensive primary and subspecialty health care, mental health services, prevention counseling and health promotion, and HIV and other sexually transmitted infection (STI) screening and management.[25] However, three anatomic site GC/CT screening was not routinely performed in any US Navy medical treatment facility prior to this study. ~~As US Department of Defense beneficiaries, these patients receive open, unrestricted access to care without copayments.~~

Given the lack of data on asymptomatic GC and CT infection among a US military cohort of HIV-infected men, we conducted a cross-sectional pilot study with the objectives: (1) to describe the incidence of asymptomatic urethral, pharyngeal, and rectal GC/CT infection in this population; (2) to ~~describe~~ identify specific sexual behaviors, relationship attitudes, and HIV disease attributes among this cohort; and (3) to ~~identify~~ determine specific factors associated with asymptomatic GC/CT infections.

MATERIALS AND METHODS

Participants and Procedures

All HIV-infected US Navy and Marine Corps members serving on active duty are required to participate in a biannual medical and psychosocial evaluation. Those serving at military bases in the western US and Pacific Basin report to NMCSD for these visits. ~~In order to minimize selection bias, b~~Beginning in September 2010, we presented the study to each consecutive military member presenting for required HIV evaluation until we enrolled 100 participants. The study was designed as a pilot to guide design of future research. No incentive to participation was offered. Those who participated did so to optimize personal sexual health through more thorough STI screening. Inclusion criteria included: male gender, HIV-infected, receiving care at the NMCSD, and having no current symptoms referable to the pharynx, urethra, or rectum on the day of enrollment. ~~Those who voluntarily agreed to participate~~Study participants completed a short questionnaire regarding sexual practices and

relationship attitudes. In order to encourage honest responses, the written questionnaire was administered by the clinic's non-military preventive medicine counselor and all responses were confidentially maintained.

Each participant was screened for asymptomatic GC/CT infection of the urethra, pharynx, and rectum using a first-void urine sample and posterior pharyngeal and rectal swabs obtained by their primary HIV provider during their routine, biannual HIV clinic visit. All collected specimens were collected on the day the questionnaire was completed and ~~all~~ any infections were appropriately treated. The NMCSD laboratory previously ~~verified~~ validated the APTIMA Combo2® Assay (Gen-Probe Inc., San Diego, CA) for ~~use in the~~testing pharyngeal~~x~~ and rectal specimens~~um~~ according to Clinical Laboratory Improvement Amendments (CLIA) standard Sec 493.1253~~s~~. Medical records were reviewed by an HIV clinician and data regarding demographics, prior STIs, and HIV-related data were collected. ~~The~~ This study was previously approved ~~and~~ with a waiver of informed consent ~~was~~ granted by the NMCSD Institutional Review Board.

Data Analysis

The data collected (laboratory results, questionnaire responses, and medical record information) were entered into a Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA) database and analyzed with SAS® version 9.2 (SAS Institute, Cary, NC). Incidence rates were calculated for each type of infection (GC, CT, or both) at each site. The descriptive statistics included for categorical variables were counts and proportions, and means and standard deviations for continuous variables. Chi-square or Fisher's exact tests were performed, as appropriate, to analyze the bivariate relationships between the factors of interest and the outcome defined as being positive for either infection (GC and/or CT in at

least one site). Odds ratios (OR), 95% confidence intervals (CI), and *P*-values were reported. *P*-values less than 0.05 were considered statistically significant.

RESULTS

One hundred six consecutive patients were offered participation in the study~~, six declined, and~~ before one hundred were enrolled. One participant was later excluded due to recent treatment of an asymptomatic rectal CT infection prior to enrollment. Due to scheduling conflicts and ~~inability of participant to return to the clinic~~technical difficulties, only 96 urine specimens and 87 rectal/pharyngeal swabs were actually tested.~~, and despite several attempts to do so, a urine specimen was not collected from 3 participants and rectal/pharyngeal swabs from 12.~~ The cohort (n=99) included 79% who were MSM. The mean age of the cohort was 31 years, and race was reported as Black in 36%, Caucasian in 35%, Hispanic in 15%, and other in 13%. Sixty-seven percent were unmarried, and 36% had a previous history of STI. HIV-related characteristics included a mean CD4 count of 609 cells/mm^3, 43% had an HIV viral load <48 copies/μL, 51% were receiving antiretroviral therapy, and the mean time since HIV diagnosis was 63 months. (Table 1)

Twenty-four percent of the participants had either GC or CT infection in at least 1 site. The ~~site with the~~rectal swab yielded the highest incidence ~~was the rectum~~ (18.4%), followed by the pharynx (9.2%) and the urethra (1%). Of rectal swabs, 18% were positive for CT and 3% for GC while for~~. Of~~ pharynx swabs, 8% were positive for GC and 2% for CT. Only one infection was detected in a urine specimen(GC). (Table 2) Eighty-one percent of ~~those with GC/CT~~the identified infections ~~had a positive screening test~~tested positive at only one site, 19% were positive at two anatomic sites, and none were positive at all three sites.

~~In~~ Using bivariate analysis, the following factors: anal sex (p=0.04), having a male partner (OR 7.02, p=0.04), and having sex at least once weekly (OR 3.28, p=0.04) were associated with infection; vaginal sex was protective (OR 0.20, p=0.03). Demographic factors associated with infection included age <35 years (OR 6.27, p=0.02), non-Caucasian ethnicity (Black OR

5.50, p=0.04; Hispanic OR 11.00, p=0.01; other race OR 7.33, p=0.03), <3 years since HIV diagnosis (OR 2.75, p=0.04), and previous STI (OR 5.10, p=0.001). (Table 3, 4)

Only about half of participants reported ~~always using~~consistent use of condoms during anal sex, and less than half always required their partner to use condoms during anal sex. During oral sex, less than 15% of participants reported always using condoms and always requiring their partner to use condoms. (Table 4)

With regards to relationship attitudes, 52% of participants reported sexual relations only with a partner in a serious relationship, while 28% disagreed with this statement. Seventy-six percent of participants expected monogamy in a serious relationship, while 14% disagreed with this statement. Twenty-three percent of participants participated in most of their sexual relations with casual friends and 53% disagreed with this statement. None of these beliefs were significantly associated with infection. (Table 4)

DISCUSSION

We found an alarming incidence of GC/CT infection—nearly twice that of non-military MSM in other large California cities.[10] In fact, ~~our incidence~~this may represent an underestimate, since some of our patients ~~may seek~~likely sought screening (and subsequent therapy) at the local county STD clinic prior to their military encounter, due to fear of discipline or discharge.[26 27] We believe there are two important contributors to the high incidence rates observed: DADT and the first-screen effect.

DADT likely contributed the most to undiagnosed infection. The American Medical Association posited that this military law compromised the medical care of gay patients serving in the military.[28] Prior to repeal, military healthcare providers often believed they could not ask, document, nor counsel about sexual behaviors or orientations for fear of revealing MSM practices of their patients that ~~they believed would~~could lead to adverse legal action for the service member. Therefore, all potential risks would not have been assessed ~~and the need for~~such that screening ~~was unknown and~~all three anatomic sites did not occur. DADT ~~also~~ likely prevented patients from providing honest answers or reports of sexual practices, ~~again~~ for fear of adverse legal action. We started our study prior to the repeal because SECNAVINST 5300.30D (the document that governs management of HIV infection in the Navy and Marine Corps) offered protection against adverse action related to information obtained from a medical or epidemiologic interview. Unfortunately, this provision was not well known to military healthcare providers.

Second, our study facilitated the initiation of sexual risk driven screening for GC/CT infection in our healthcare facility. Hence, study data represent the first time most participants were screened for extragenital GC/CT infection. First-time screening for a condition may reveal

more incident cases than subsequent screening, especially in the case of asymptomatic infection, and may partially explain why we detected higher incidence than that found in other California cities which may represent subsequent screening data.

Our study also had several important findings regarding HIV-positive men serving in the US military. With regards to sexual practices, most respondents were MSM and engaged in oral, anal (receptive and insertive), and oral-anal sex. As expected, most respondents do not use condoms during oral sex, but sx. Surprisingly though was that nearly half of respondents do not always use condoms or require their partners to use condoms during anal sex either. Safer sex fatigue, serosorting, and seropositioning Potential may be contributors to the low reported rates of condom use include: safer sex fatigue, serosorting, and seropositioning.[29] Regarding relationship attitudes, about half of respondents believe sexual relations should only occur with partners in a serious relationship while approximately one-quarter engage in sex with casual friends. When in a serious relationship, the majority of respondents expect monogamy.

The significant findings noted in our study were not unexpected. Our study results identified MSM, anal sex, non-Caucasian ethnicity, and younger age were more associated with GC/CT and have been identified asinfections thus recognized as STI risk factors, in agreement with other studies.[16 30-32] Also, it follows that a person whoGenerally, those patients with a recently acquired HIV infection or has aprior history of STI would be athave a higher risk for GC/CT infection. The increased risk among non-Caucasians may be related to cultural or societal stigma which may prevent an individual from seeking screening services (and need to disclose self-perceived taboo sexual behavior) in a way that DADT likely prevented military MSM from seeking or receiving appropriate screening.

We acknowledge potential limitations of our study: those inherent to an observational design, inability to achieve 100% three site screening from all participants, and small study population. Although our sample size is small, it is worth noting that trends in our data are similar to trends noted in larger non-military studies of GC/CT infection: most infections were detected at extragenital sites, the majority of rectal infections were due to CT, and the majority of pharyngeal infections were due to GC. Finally, although there may have been some reluctance of participants to answer survey questions honestly, ~~although~~ we believe this was minimized by our confidential survey procedures and as reflected by the candid responses we did receive.

~~We have generated~~This is the first comprehensive data set of asymptomatic GC/CT infection in a male HIV-positive US military population. ~~Although much of what we have learned was assumed to be true, this is the first systematic description~~Along with the CDC's recommendations, these results ~~and~~ underscore~~s~~ the need for military healthcare providers to screen their MSM population for infection at all three anatomic sites. ~~Also,~~Just as noted in larger studies, we ~~found~~ confirm that ~~reliance on~~ urine/urethral screening alone ~~will~~ may fail to detect ~~the vast majority of~~many asymptomatic infections in the~~an~~ MSM population. Finally, low rates of reported condom use among HIV-positive participants signals the need to enhance safer sex prevention efforts among MSM.

We hope to use the results of this~~our pilot~~ study ~~will inform and motivate those who~~to help design and complete larger, multisite STI clinical trials for the US military. ~~Although our study was small, w~~We can conclude that MSM make up a significant proportion of our HIV-infected population. Now that DADT has been repealed and ~~US Defense Secretary Panetta~~the Department of Defense has mandated extension of military benefits to same sex

partners,. [33] ~~Therefore, we believe it's also time to include~~we should look to modify treatment guidelines for MSM in our military ~~research~~ to enhance overall health.

TABLES

Table 1. HIV-infected male demographic characteristics, 2011—San Diego, California (n=99)

HIV variables	
CD4 count mean (SD), cells/mm^3	609 (216)
Suppressed HIV VL (<48 copies/μL)	43%
Receiving ART	51%
Time since HIV diagnosis mean (SD), months	62.8 (59.9)
Demographic variables	
Age	
Mean (SD), years	30.9 (8.2)
<25 years	28%
25-34 years	38%
≥ 35 years	33%
Ethnicity	
Black	36%
Caucasian	35%
Hispanic	15%
Other	13%
Marital Status	
Married	33%
Single	67%
Sexual Practice	
MSM	79%
MSW	21%
Previous STI	
Yes	36%

VL = plasma viral load
ART = antiretroviral therapy
MSM = men who have sex with men
MSW = men who have sex with women
SD = standard deviation
STI = sexually transmitted infection

Table 2. Prevalence of asymptomatic infection by anatomic site, HIV-infected men, 2011—San Diego, California (n=99)*

	Either Infection			CT			GC		
	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate	Cases	N	Prevalence Rate
Overall	20	83	24.1%	17	83	20.5%	8	83	9.6%
Urethra	1	96	1.0%	0	96	0.0%	1	96	1.0%
Rectum	16	87	18.4%	16	87	18.4%	3	87	3.4%
Pharynx	8	87	9.2%	2	87	2.3%	7	87	8.0%

*Some participants did not have screening at all three sites.

Table 3. Survey responses – demographic & sexual practices by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Demographic variables (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Gender of sexual partner(s) (N=98)									
Women only	21	(21.4)	1	(4.8)	20	(26.0)	REF	--	--
Male (MSM)	77	(78.6)	20	(95.2)	57	(74.0)	7.02	1.88, 55.72	0.04
Race/ethnicity (N=99)									0.03
White	35	(35.4)	2	(9.5)	33	(42.3)	REF	--	--
Black	36	(36.4)	9	(42.9)	27	(34.7)	5.50	1.10, 27.64	0.04
Hispanic	15	(15.2)	6	(28.6)	9	(11.5)	11.00	1.89, 64.06	0.01
Other	13	(13.0)	4	(19.0)	9	(11.5)	7.33	1.15, 46.66	0.03
Age (N=99)									
<35 years	66	(66.7)	19	(90.5)	47	(60.3)	6.27	1.36, 28.82	0.02
≥ 35 years	33	(33.3)	2	(9.5)	31	(39.7)	REF	--	--
Previous history of STI (N=99)									
No	63	(63.6)	7	(33.3)	56	(71.8)	REF	--	--
Yes	36	(36.4)	14	(66.7)	22	(28.2)	5.10	1.81, 14.30	0.001
Number of years since HIV diagnosis (N=99)									
> 3 years	57	(57.6)	8	(38.1)	49	(62.8)	REF	--	--
≤ 3 years	42	(42.4)	13	(61.9)	29	(37.2)	2.75	1.02, 7.41	0.04
Sexual practices (N respondents)									
Vaginal sex (N=99)									
No	70	(70.7)	19	(90.5)	51	(65.4)	REF	--	--
Yes	29	(29.3)	2	(9.5)	27	(34.6)	0.20	0.04, 0.92	0.03
Oral sex[b] (N=99)									
No	3	(3.0)	0	(0)	3	(3.8)	REF	--	--
Yes	96	(97.0)	21	(100)	75	(96.2)	--	--	1.00
Anal sex[b] (N=99)									
No	15	(15.2)	0	(0)	15	(19.2)	REF	--	--
Yes	84	(84.8)	21	(100)	63	(80.8)	--	--	0.04
Insertive anal sex (N=80)									
No	15	(18.8)	5	(23.8)	10	(16.9)	1.00	--	--
Yes	65	(81.2)	16	(76.2)	49	(83.1)	0.65	0.19, 2.20	0.52
Receptive anal sex (N=80)									
No	17	(21.3)	2	(9.5)	15	(25.4)	REF	--	--
Yes	63	(78.7)	19	(90.5)	44	(74.6)	3.32	0.67, 15.57	0.21

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.
MSM = men who have sex with men (self-reported).
Oral and oral-anal sex were not significantly associated with infection with p>0.05

Table 4. Survey responses – relationship attitudes & condom use by infection status, HIV-infected men, 2011—San Diego, California

	Total		CT and/or GC Infection		Neither infection				
Relationship attitudes (N respondents)	n	(%)	n	(%)	n	(%)	OR	95% CI	p value[a]
Sexual relationships with >1 partner in the past year (N=99)									
No	39	(39.4)	5	(23.8)	34	(43.6)	REF	--	--
Yes	60	(60.6)	16	(76.2)	44	(56.4)	2.47	0.82, 7.42	0.10
Frequency of sexual activity in the past year (N=99)									
< Once a week	38	(38.4)	4	(19.0)	34	(43.6)	REF	--	--
At least once a week	61	(61.6)	17	(81.0)	44	(56.4)	3.28	1.01, 10.66	0.04
Sexual relations only with partner in a serious relationship (N=99)									0.14
Strongly agree	51	(51.5)	7	(33.3)	44	(56.4)	REF	--	--
Neither agree/disagree	20	(20.2)	5	(23.8)	15	(19.2)	2.10	0.59, 7.60	0.26
Strongly disagree	28	(28.3)	9	(42.9)	19	(24.4)	2.98	0.97, 9.17	0.06
Expect monogamy in a serious relationship (N=99)									0.48
Strongly agree	75	(75.8)	14	(66.7)	61	(78.1)	REF	--	--
Neither agree/disagree	10	(10.1)	3	(14.3)	7	(9.0)	1.87	0.43, 8.14	0.41
Strongly disagree	14	(14.1)	4	(19.0)	10	(12.9)	1.74	0.48, 6.38	0.40
Sexual activities mostly with casual friends (N=99)									0.08
Strongly disagree	52	(53.0)	8	(38.0)	44	(57.2)	REF	--	--
Neither agree/disagree	24	(24.5)	9	(43.0)	15	(19.5)	3.30	1.08, 10.10	0.04
Strongly agree	22	(22.5)	4	(19.0)	18	(23.3)	1.22	0.33, 4.57	0.77
Condom use (N respondents)									
Self-condom use during oral sex (N=92)									
Always	12	(13.0)	4	(20.0)	8	(11.1)	REF	--	--
Do not always	80	(87.0)	16	(80.0)	64	(88.9)	0.50	0.13, 1.87	0.29
Partner-condom use during oral sex (N=90)									
Always	13	(14.4)	4	(19.0)	9	(13.0)	REF	--	--
Do not always	77	(85.6)	17	(81.0)	60	(87.0)	0.64	0.17, 2.34	0.49
Self-condom use during anal sex (N=82)									
Always	42	(51.2)	9	(45.0)	33	(53.2)	REF	--	--
Do not always	40	(48.8)	11	(55.0)	29	(46.8)	1.39	0.51, 3.83	0.52
Partner-condom use during anal sex (N=80)									
Always	37	(46.2)	8	(38.1)	29	(49.2)	REF	--	--
Do not always	43	(53.8)	13	(61.9)	30	(50.8)	1.57	0.57, 4.35	0.38

[a]Fisher's exact test was performed for variables with expected cell frequencies <5, otherwise a Chi-square test was performed.
[b]Odds ratios and 95% confidence intervals not available due to one or more zero cells.

LICENSE FOR PUBLICATION STATEMENT

CONTRIBUTORSHIP STATEMENT

Robert J. Carpenter contributed to conception and design, acquisition of data, and analysis and interpretation of data, participated in drafting the article or revising it critically for important intellectual content, and was involved in final approval of the version to be published.

All other authors listed contributed to acquisition of data, participated in drafting the article or revising it critically for important intellectual content, and were involved in final approval of the version to be published.

DATA SHARING STATEMENT

No additional data available.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.