Asymptomatic Sexually Transmitted Infections in HIV-Infected Men Who Have Sex with Men: Prevalence, Incidence, Predictors, and Screening Strategies

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Abstract

Sexually transmitted infections (STIs) have increased among men who have sex with men (MSM) and are associated with unsafe sex practices, intrinsic morbidity, and enhanced genital shedding and transmission of HIV. Screening for asymptomatic STIs is recommended as part of the HIV prevention efforts, however, optimal screening strategies among HIV-infected MSM have not been well defined. In this study, conducted from April 2004 to September 2006, 212 HIV-infected MSM from two urban HIV clinics were screened for asymptomatic STIs. Testing for *Neisseria gonorrhea* and *Chlamydia trachomatis* from pharynx, rectum, and urine, as well as serologic testing for syphilis were performed initially, and then after 6 and 12 months. A self-administered questionnaire was used to assess possible predictors of incident asymptomatic STIs. A cost analysis was performed to assess different screening strategies for detecting incident STIs. The baseline prevalence of STIs was 14% ($n = 29$; 95% confidence interval [CI] 9%–19%) and the incidence of new infections was 20.8 cases per 100 person years (95% CI 14.8–28.4 cases per 100 person years). Younger age, higher CD4 cell count, and marijuana use were associated with increased risk of acquiring an asymptomatic STI. The laboratory cost to detect one positive STI did not significantly differ between once- and twice-yearly screening. However, almost half of all incident STIs were detected at the 6-month screening visit, potentially resulting in an increased duration of infectivity if these cases remained undiagnosed. In conclusion, prevalent and incident asymptomatic STIs are common among HIV-infected MSM. Our data support current Center for Disease Control and Prevention STI guidelines that recommend routine screening at increased frequency for HIV-infected MSM.

Introduction

IN RECENT YEARS, HIV prevention efforts have increasingly shifted their focus from targeting the uninfected to those known to be HIV infected. This strategy is supported by data demonstrating increasing evidence of unsafe sexual practices among HIV-infected persons, especially men who have sex with men (MSM), an increased rate of symptomatic sexually transmitted infections (STIs), and the persistent rate of newly diagnosed HIV infection in the United States.^{1–3}

In addition to behavioral interventions, early diagnosis and treatment of STIs have been suggested as ways to prevent transmission by HIV-infected patients, because there is good

evidence that symptomatic STIs are associated with enhanced efficiency of HIV transmission.^{1,4} STIs can present in patients without causing symptoms, so-called asymptomatic infections, and still potentially be transmitted to others. Asymptomatic STIs may function as a hidden reservoir contributing to the ongoing epidemic of symptomatic STIs. Furthermore, STIs are a marker for unsafe sex practices and are associated with intrinsic morbidity. Consequently, recent STI guidelines from the Centers for Disease Control and Prevention (CDC)³ emphasize the need for routine screening of high-risk individuals for asymptomatic STIs.

Current guidelines recommend that annual screening be performed in sexually active MSM, and perhaps as often as

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every 3–6 months in those at highest risk, e.g., individuals with multiple sex partners, those using drugs and alcohol in conjunction with sex, or having partner(s) who participate in these activities.^{2,3} Although these guidelines are supported by the high prevalence of asymptomatic STIs observed in MSMs,^{5,6} there are limited longitudinal data demonstrating the incidence of asymptomatic STI in HIV-infected MSM or the utility of current screening recommendations in clinical practice. This study was conducted to evaluate a comprehensive screening strategy for asymptomatic bacterial STIs among HIV-infected MSM, examining the prevalence and incidence of these infections at different body sites, predictors of incident STIs, and the costs of STI screening in this population.

Methods

Study population

We enrolled HIV-infected men receiving medical care at one of two urban HIV clinics, who were at least 18 years of age, who admitted to ever having sex with men, and who had no symptoms of an active STI. Patients were asked to participate regardless of whether or not they reported being sexually active in the months prior to entry into the study. The study was approved by the Institutional Review Board (IRB) of the Los Angeles Biomedical Research Institute. Informed written consent was obtained from all participants, in compliance with the human-experimentation guidelines of the US Department of Health and Human Services.

Study design

The study was conducted from April 2004 to September 2006. All study visits occurred during regular clinical care with the baseline visit occurring at the time of enrollment, and visits 2 and 3 occurring after approximately 6 and 12 months. At each study visit, participants were asked to complete a questionnaire that included demographics, any history of STIs in the last 6 months and during their lifetime, detailed sexual practices, drug and alcohol use, use of sildenafil and depression. The questionnaire was self-administered during each study visit and available in both English and Spanish.

STI testing at each visit included serum for rapid plasma reagin/fluorescent treponemal antibody (RPR/FTA), *Neisseria gonorrhea* (NG) culture (using standardized bedside methods for culture on Thayer-Martin medium) from rectum and pharynx, nucleic acid amplification testing (NAAT) (Aptima®, Gen-Probe, San Diego, CA) for *Chlamydia trachomatis* (CT), and NG from rectum, pharynx, and urine. NAAT for rectal and pharyngeal sampling was validated internally by the local Clinical Laboratory Improvement Amendments (CLIA)-approved laboratory.

If an STI was detected in the pharynx or rectum, the participant was asked to return to clinic for repeat NAAT to confirm the findings. All participants testing positive for an STI were treated according to the California STI treatment recommendations and were asked to inform their partner(s) to seek testing and treatment. Expedited partner treatment was not offered. At all visits, participants were advised of safe sex practices and to disclose their HIV status and any STIs identified by screening to their sex partner(s). After treatment for any STI, all subjects were asked to return for follow-up test of cure.

Incident STIs were defined as those positive at study visits 2 and 3, since everyone was either negative at the prior visit or, if found to be previously infected was treated and proven to be cured at the time of posttreatment testing.

Statistical analysis

All data were collected on structured data collection forms, entered in a Microsoft Access 2003 database (Microsoft Corporation, Redmond, WA) and translated into native SAS format using DBMS/Copy version 8 (DataFlux Corporation, Cary, NC). Data analysis was conducted using SAS version 9.1.3 (SAS Institute, Cary, NC) and Stata version 9.2 (Stata Corporation, College Station, TX). Numerical variables are summarized as medians with interquartile ranges (IQRs) and compared using the non-parametric Wilcoxon rank sum test. Proportions were compared using Fisher's exact test or the χ^2 test, as appropriate. Exact binomial or Poisson confidence intervals (CIs) were calculated for proportions and incidence rates, respectively, using the "cii" command in Stata. Incidence rates are defined on a "per subject" basis, rather than "per STI." A maximum p value of 0.05 was considered statistically significant and no correction was made for multiple comparisons.

Generalized estimating equations (GEE), implemented using Proc GENMOD in SAS, were used to determine predictors of new incident STIs, which accounting for within-subject correlations and the repeated measure study design. The outcome on dependent variable was dichotomous, representing any new incident STI at a follow up visit, a logit link function was used, and an exchangeable correlation structure was assumed. Predictor variable were considered individually, rather than in multivariable models, to avoid over-fitting the data given the relatively small number of incident STIs observed.

To evaluate the cost associated with different screening strategies, we considered only the laboratory testing costs based on Medicare reimbursements (www.medicarenhic.com, accessed February 7, 2008). The cost per incident STI detected using the every 6 months strategy was determined as a simple ratio of the total laboratory costs to the number of incident STIs. We assumed all incident STIs occurring during the 12 months period would continue to be present at the time of screening (i.e., we assumed a spontaneous cure rate of zero and no "accidental" cures from incidental antibiotic exposures).

Results

Study subjects

Between April 2004 and March 2005, 281 eligible patients were approached with 212 consenting to enroll and 69 declining or deferring participation. None of those enrolling had symptoms suggestive of an active STI at the time of entry into the study. Patient demographics are summarized in Table 1 and are similar to those of the clinic populations from which the study subjects were recruited. Fifty-five percent of subjects were Hispanic, 21% African American, and 20% Caucasian with most having an annual income of less than \$40,000. The CD4⁺ T-cell count at enrollment was greater than 200 cells/mm³ in 81% and the plasma HIV-1 RNA was less than 400 copies per milliliter in 67% of participants. Follow-up study visits at approximately 6 and 12 months occurred in 90% ($n = 191$) and 79% ($n = 168$) of the enrolled subjects, respectively. The median interval between

TABLE 1. BASELINE CHARACTERISTICS

Patient characteristics	No. (%) of study participants (n=212)
Age, years	
18–29	13 (6)
30–44	139 (66)
≥45	60 (28)
Ethnicity	
Hispanic	116 (55)
African American	44 (21)
Caucasian	42 (20)
Asian/Pacific Islander	9 (4)
Other	1 (0)
Highest level of education	
Graduate school	10 (5)
College	98 (46)
High school	81 (38)
Less than high school	23 (11)
Annual Income (\$)	
>100,000	1 (0)
40,000–100,000	7 (3)
10,000–39,999	88 (42)
<10,000	116 (55)
CD4 cell count (cells/mm ³) ^a	
<200	35 (19)
>200	150 (81)
HIV-1 RNA (copies/mL) ^b	
<50	89 (49)
50–399	31 (17)
400–999	6 (3)
1000–10,000	10 (6)
>10,000	46 (25)

^an = 185.^bn = 182.

the first and second visit was 190 days (IQR 175 to 231), and 192 days (IQR 161 to 231) between the second and third visit. A total of 571 of the predicted 636 visits (90%) occurred with 4870 of the potential 5724 tests (85%) for STIs being available for analysis. The most common reason for tests not being available was refusal of rectal swab, not being able to produce urine during the visit, or technical problems such as bacterial overgrowth or handling error of the specimen.

STI testing

Of the 212 participants, 59 (28%; 95% CI 22%–34%) tested positive for an STI at least once during the course of the study with seven testing positive at more than one visit. At entry, 38 prevalent infections were identified in 29 of the 212 (14%; 95% CI 9%–19%) participants (Table 2). NG was most common, occurring in 20 sites in 13 participants, followed by CT, which occurred in 12 sites in 11 subjects. Newly positive serologic evidence of syphilis occurred in six subjects. Sixty-eight percent of infections were identified at pharyngeal and/or rectal sites with all but one STI detected by NAAT.

Overall there were 187.8 person-years of observation, yielding 20.8 incident cases per 100 person-years (95% CI 14.8–28.4 cases per 100 person-years). During the two follow up visits, 45 STIs were detected in 39 participants, 18 subjects (9.4%; 95% CI 5.7%–14.5%) having evidence of an incident STI at visit 2 and 21 (12.5%; 95% CI 7.9%–18.5%) at visit 3 (Table 2). Every effort was made to acquire assays for confirmation and test of cure for those found to have a positive pharyngeal or rectal STI by NAAT. Thirty-six individuals with positive NAAT from rectal or pharyngeal sites were retested prior to treatment with more than 70% being repeatedly positive and all 19 participants available for test of cure were found to be negative after treatment.

TABLE 2. NUMBER OF BASELINE AND INCIDENT SEXUALLY TRANSMITTED INFECTIONS (STIs) AT EACH SITE FOR EACH INFECTION AT EACH VISIT^a

STI/screened, n/N (%)	Visit 1 (%) (baseline)	Visit 2 (%)	Visit 3 (%)
Total	29/212 (13.7)	18/191 (9.4)	21/168 (12.5)
Newly reactive RPR	6/206 (2.9)	5/155 (3.2)	5/156 (3.2)
Gonorrhea			
Pharynx			
Culture	0/207 (0)	0/172 (0)	0/141 (0)
NAAT	7/212 (3.3)	5/191 (2.6)	3/164 (1.8)
Rectal			
Culture	1/202 (0.5)	0/170 (0)	0/140 (0)
NAAT	9/209 (4.3)	1/188 (0.5)	1/162 (0.6)
Urine			
NAAT	3/204 (1.5)	1/175 (0.6)	2/155 (1.3)
Chlamydia (NAAT)			
Pharyngeal	3/212 (1.4)	0/191 (0)	0/164 (0)
Rectal	6/209 (2.9)	6/188 (3.2)	11/163 (6.8)
Urine	3/204 (1.5)	3/175 (1.7)	2/155 (1.3)

^aResults not available on all subjects screened for various reasons such as refused rectal study, unable to provide urine during visit, or for technical problems. STI organisms detected in more than one site: NG from pharynx and rectum (n = 2); NG from pharynx, rectum and urine (n = 1); CT from pharynx and rectum (n = 1); NG from pharynx and CT from rectum (n = 2); NG from rectum and CT from urine (n = 1); NG from urine and CT from rectum (n = 1) and CT from rectum and newly positive serum RPR/FTA (n = 1). NG and CT simultaneously detected on one site: rectum (n = 4).

NAAT, Nucleic Acid Amplification Test; RPR, rapid plasma regain; NG, *Neisseria gonorrhoea*; CT, *Chlamydia trachomatis*.

TABLE 3. PREDICTORS OF INCIDENT ASYMPTOMATIC SEXUALLY TRANSMITTED INFECTIONS

	Visit 2 n = 191 Results of STI testing		Visit 3 n = 168 Results of STI testing		Odds ratio	95% CI	p-value
	Negative (%) n = 173	Positive (%) n = 18	Negative (%) n = 147	Positive (%) n = 21			
Age (median)	41	37.5	41	37	0.55 (per 10 yrs)	0.37–0.83	0.0038
CD4 cell count (cells/mm ³) (median)	408	500	436	458	1.15 (per 100 cells/mm ³)	1.01–1.30	0.036
HIV-1 RNA (copies/mL)	<50	<50	<50	<50	1.22 (per log ₁₀)	0.89–1.67	0.22
Any history of STI	102/167 (61)	13/18 (72)	79/138 (57)	17/21 (81)	2.28	0.98–5.33	0.057
STI in last 12 months	23/166 (14)	3/17 (18)	22/142 (15)	5/20 (25)	1.16	0.37–3.65	0.8
Sexually active last 6 months	109/170 (64)	11/18 (61)	94/143 (66)	16/21 (76)	1.11	0.55–2.23	0.78
Number of partner(s) in last 6 months:					1.28 (per category)	0.90–1.81	0.16
0	61/163 (37)	7/18 (39)	49/133 (37)	5/21 (24)			
1	52/163 (32)	5/18 (28)	47/133 (35)	5/21 (24)			
2–5	40/163 (25)	4/18 (22)	27/133 (20)	8/21 (38)			
>5	10/163 (6)	2/18 (11)	10/133 (8)	3/21 (14)			
Sex practices							
No condoms							
Anal receptive	12/173 (7)	4/18 (22)	8/147 (5)	0/21 (0)	2.11	0.66–6.73	0.21
Anal insertive	7/173 (4)	3/18 (17)	9/147 (6)	1/21 (5)	2.07	0.65–6.55	0.22
Oral receptive	29/173 (17)	6/18 (33)	26/147 (18)	4/21 (19)	1.64	0.68–3.95	0.27
Oral insertive	31/173 (18)	4/18 (22)	32/147 (22)	5/21 (24)	1.06	0.47–2.38	0.88
Anonymous sex	33/169 (20)	4/18 (22)	31/144 (22)	4/21 (19)	0.91	0.41–2.03	0.82
Sex while using drugs or alcohol	22/169 (13)	4/18 (22)	14/143 (10)	3/21 (14)	1.56	0.63–3.89	0.34
Partners who practice high risk sex ^a	21/165 (13)	1/18 (6)	29/140 (21)	4/21 (19)	0.62	0.22–1.78	0.38
Drug use in last 6 months							
Crystal meth- amphetamine	32/168 (19)	6/18 (33)	33/143 (23)	6/21 (29)	1.51	0.70–3.22	0.29
Cocaine	10/146 (7)	3/15 (20)	10/120 (8)	0/15 (0)	1.20	0.31–4.67	0.79
Cocaine	6/142 (4)	1/13 (8)	3/113 (3)	0/15 (0)	0.97	0.008–11.8	0.98
Heroin	1/136 (1)	0/12 (0)	0/110 (0)	0/15 (0)	—	—	— ^b
Marijuana	13/149 (9)	2/14 (14)	15/125 (12)	6/21 (29)	2.33	1.08–5.05	0.031
Sildenafil use	16/167 (10)	3/18 (17)	21/145 (14)	2/21 (10)	1.10	0.38–3.20	0.86
Depression	55/165 (33)	4/17 (24)	49/142 (35)	6/21 (29)	0.71	0.32–1.60	0.41

^aPartners who use drugs or ethyl alcohol while having sex or having other anonymous partners.^bInsufficient data for analysis.

Predictors of STIs

Combining data from visits 2 and 3, at 65% (230/352) of visits the participants stated that they had been sexually active in the last 6 months, at 45% (104/230) of the visits those who were sexually active admitted to having more than one sex partner during the interval, and at 20% (72/352) of the visits participants acknowledged having anonymous sex. Condom use was reported at 80% (179/223) of the visits by sexually active participants with insertive or receptive anal sex and 43% (104/241) with insertive and receptive oral sex. Illegal drug use was reported at 22% (77/352) of the visits, with crystal methamphetamine use being reported at 30% (23/77) of those visits. Drug use in conjunction with sex was reported at 12% (43/352) of visits. Self-reported depression was reported at 33% (114/345) of the visits by subjects and sildenafil use by 12% (42/351). A history of an STI was reported by 61% (211/344) of participants, and at 15% (53/345) of the visits subjects admitted to having an STI in the previous 12 months.

Using repeated measure modeling, only younger age, higher CD4 cell count and marijuana use were significant predictors of having an incident STI. Any history of a STI in the past was associated with a trend toward being predictive of having an incident STI ($p = 0.057$). In contrast, self reported behavioral information such as unsafe sex practices, having partners with unsafe sex practices, drug use overall, alcohol use, depression, or use of sildenafil were not predictive of incident STIs (Table 3).

Cost analysis of screening MSM for asymptomatic STIs

Using the data from the current study, we calculated the estimated laboratory costs per year for detecting a positive STI using the Medicare reimbursement cost for each test (Table 4). The annual costs of screening every 6 versus 12 months did not differ substantially with regard to the cost to detect an asymptomatic STI. Performance of testing every 12 months cost \$10,681 per STI detected if all MSM were tested, and \$7304 per STI detected if screening was limited to MSM who reported being sexually active in the preceding 6

months. Performing screening tests every 6 months on all MSM had a similar annual cost, per STI detected, of \$10,640 and \$7972 per STI detected if screening was limited to those reporting being sexually active in the preceding 6 months. However, compared to testing every 6 months, annual screening would have delayed diagnosing an STI in up to 46% of cases. Specifically, the 18 individuals who had incident infections at visit 2 would have potentially remained infectious for an additional 6 months if screening were not performed at a semiannual interval. Assuming that these STIs would persist for 6 months and therefore remain neither identified nor treated until the time of annual screening, an annual screening strategy would have led to 9 additional patient-years with potentially transmissible STIs, or approximately 5% of the total observed follow-up. Limiting screening to only those MSM who reported being sexually active in the preceding 6 months would have missed up to 24% of asymptomatic STIs, compared to screening all subjects, as was done in this study.

Discussion

There is increasing appreciation that STIs are important cofactors for HIV transmission and markers of unprotected sexual activity. This, along with the observation that many people are asymptomatic carriers of STIs, has led to guidelines endorsing the screening of all at-risk individuals for such infections.³ Despite these guidelines, there are limited data defining the incidence and predictors of having acquired an asymptomatic STI. Moreover, data are limited as to the costs and benefits of comprehensively testing at-risk individuals for asymptomatic STIs. To our knowledge, the current study is the first to longitudinally test HIV-infected MSM for asymptomatic STIs, and revealed a prevalence of asymptomatic STIs of approximately 1 in 7 with over 20 incident cases per 100 person-years of follow-up. Over 60% of the infections were identified from extragenital mucosal sites such as pharynx and rectum that are often not tested in clinical practice, but are high risk sites for transmission by sexual exposure.

TABLE 4. LABORATORY COST ANALYSIS OF DETECTING INCIDENT SEXUALLY TRANSMITTED INFECTION

Test	Laboratory cost of test	Screening every 6 months				Screening every 12 months			
		Screening all MSM		Screening sexually active MSM		Screening all MSM		Screening sexually active MSM	
		Positive tests	Cost per year/positive test	Positive test	Cost per year/positive test	Positive test	Cost per year/positive test	Positive test	Cost per year/positive test
RPR	\$5.96	10/311	\$185	6/204	\$203	5/156	\$186	3/104	\$207
NG/CT in urine	\$98.08	8/350	\$4,291	7/214	\$2,998	4/155	\$3,801	4/103	\$2526
NG/CT(NAAT)	\$98.08	8/355	\$4,352	7/229	\$3,209	3/164	\$5,362	3/108	\$3531
pharynx rectum		19/351	\$1,812	14/223	\$1,562	12/163	\$1,332	10/106	\$1040
Total cost/year to detect one positive STI			\$10,640		\$7,972		\$10,681		\$7304

RPR, rapid plasma regain; NG, *Neisseria gonorrhea*; CT, *Chlamydia trachomatis*.

Younger age, higher CD4 cell count, and marijuana use were each associated with a significantly greater risk of having an incident asymptomatic STI while any history of an STI was associated with a trend toward being at increased risk for an asymptomatic STI. In contrast to other studies,⁷⁻⁹ crystal methamphetamine use was less frequently reported in this cohort and additionally was not found to be a predictor of incident STIs. The lower frequency of crystal methamphetamine use in this cohort compared to others could be explained by differences in demographics and may in part explain why this factor was not associated with increased risk of STIs. In addition, crystal methamphetamine is often associated with the use of other recreational drugs⁹ and patients may be more likely to self-report marijuana use than crystal methamphetamine if they are using both. This may also explain why marijuana use was found to be predictive of incident STIs in this cohort.

In contrast, other factors including unsafe sex practices, overall drug and alcohol use other than marijuana were not found to be predictive of having an asymptomatic STI. In fact, even those who denied sexual activity were at risk for both prevalent and incident infections, suggesting the sexual history obtained in the clinic setting is unreliable. While the cost of identifying an STI was minimally influenced by increased frequency of screening, the number of potentially infectious patient-years was substantially reduced.

This study is one of the first to address the prevalence and incidence of asymptomatic STIs in HIV-infected MSM; however, others have shown results that are largely consistent with our findings. Phipps and colleagues¹⁰ showed a prevalence of CT and NG among patients in primary HIV care in San Francisco of 12%, similar to the 14% seen in the current study. These findings are further supported by cross-sectional studies targeting HIV-infected and uninfected MSM reporting prevalence rates of asymptomatic STIs of 5% to 6.9% for rectal NG,^{5,11,12} 5% to 9.2% for pharyngeal NG,^{5,11,12} and 7.9% to 8% for rectal CT.^{5,11} These and other studies further emphasize the importance of screening extragenital mucosal sites for asymptomatic STIs.^{5,10-12} In fact, Morris and colleagues¹² found that NG was almost 10 times more frequently present in pharyngeal and rectal sites than the urethral site. The relative scarcity of asymptomatic urethral STIs in MSM was also recently shown in a study from the greater Boston area reporting a prevalence rate of asymptomatic urethral STIs of less than 1% among MSM.¹³

Longitudinal studies of incident asymptomatic STIs are relevant since cross-sectional studies do not identify newly acquired infections and it has been shown that NG and CT can persist in asymptomatic individuals for many months, with such individuals being persistent reservoirs of infection.¹⁴ In the current study, incident infections were diagnosed in more than 1 in 10 patients. A recent study of HIV-uninfected MSM from San Francisco tested for pharyngeal NG at 6 month intervals revealed an incidence of NG at the pharyngeal site of 11.2 to 11.7 cases per 100 person-years follow-up.¹² Subsequent screening for rectal and urethral NG in the same cohort showed an incidence of 3.5 cases and 1.5 cases per 100 person-years, respectively. These results are consistent with our observation that incident cases are not uncommon and frequently involve nongenital sites. Together, these results may justify the need for more frequent screening of multiple mucosal sites in clinical practice.

While the identification of frequent incident STIs at multiple sites in at-risk individuals is supportive of current CDC guidelines for screening, there are no prior data demonstrating the cost and benefits of such strategies or defining specific populations to target based on risk factors or reported behavior. Younger age, higher CD4 cell count, and marijuana use were found to predict incident asymptomatic STIs but neither high-risk sexual behavior, nor overall drug including crystal methamphetamine use and alcohol use were predictors of incident STI.

In fact, the current study highlights the limitations of patient-provided information, since many prevalent and incident infections were identified in subjects who denied recent sexual activity. Consequently, the decision regarding who should be screened and how often cannot be guided by sociodemographic or self-reported behavioral factors alone.

The lack of strong predictors defining who, how, and when to screen for asymptomatic STIs suggests that further analyses should focus on the actual cost and benefit of testing at-risk populations at various frequencies. The marginal cost of testing patients in ongoing care, primarily relates to that of collecting the clinical material and the performance of the assays. The potential benefits of increased screening include the fact that detection of STIs is a marker for unprotected sexual practices, is potentially associated with increased shedding of HIV in genital secretion and the possibility that early treatment could reduce the risk of developing symptomatic STIs or the transmission to others.^{4,15,16}

In a mathematical model, Chesson and Pinkerton¹⁷ estimated the annual number and the cost of new HIV infections attributable to symptomatic STIs (syphilis, NG, CT, and HSV) for the year 1996. They concluded that 5052 new HIV cases (6%–13% of all new HIV infections) were attributable to STIs resulting in a direct lifetime HIV treatment cost of \$985 million in 1996—a cost estimated to be 4 to 6 times higher in 2006.¹⁸ Additionally, the rate of new HIV infections attributable to STIs may currently be even higher due to the increase in the rate of STIs in recent years among MSM.¹⁹

The benefits of early treatment of STIs and early detection of asymptomatic STIs need to be balanced by the cost of routine screening strategies. Using the data derived from our study, we were able to show that the actual laboratory cost per year to detect one STI in an HIV-infected MSM was minimally influenced changing the frequency of testing from 6 to 12 months. However, to limit screening to every 12 months would likely have left some patients infectious to others for a substantially longer period of time. Attempting to target screening, such as to those who admitted to being sexually active, reduced the overall cost to diagnose an STI, but would have missed up to 24% of the STIs diagnosed.

The current study is limited by a relatively modest sample size and thus limited power to address all of the relevant questions. Nevertheless, it is the largest study of its kind to assess the utility of screening practices currently recommended by CDC guideline.³ Another potential limitation of the current study is the use of NAAT for diagnosing NG and CT at pharyngeal and rectal sites. While NAAT is not FDA-approved for testing at these sites, culture techniques are cumbersome, not universally available, and insensitive, particularly when attempts are made to implement them in the clinic setting. For these reasons, CDC guidelines have not been explicit with re-

gards to which tests to use for screening these mucosal sites and most research in this area has utilized and validated NAAT as a sensitive assay at these sites.^{20–23} Further support for the validity of these methods is provided by the fact that 70% of the patients in our study with positive NAATs, who were retested prior to treatment, were repeatedly positive and 100% of those treated were subsequently documented to be negative. There are also limitations of the self-administered behavioral surveys, due to the dependency on reliable patient responses. Nevertheless, similar limitations exist in the clinic setting where providers must rely on patient history. Finally, these results can not necessarily be extrapolated to groups not included in the current study, such as HIV-uninfected individuals, non-MSM, and women.

In conclusion, prevalent and incident asymptomatic STIs are common among HIV-infected MSM. Our study results suggest that routine screening is appropriate and should not be limited to those who report to being sexually active, or to those with other behavioral factors associated with risk for transmission. Our findings are also consistent with current guidelines recommending that comprehensive screening include multiple mucosal sites. While the optimal frequency of testing can not be definitively determined from the current study, these results do suggest that there is little additional cost per diagnosed STI with semiannual versus annual screening. However, at little additional cost, there are potentially substantial benefits associated with screening at increased frequency, including reducing the period in which STI-infected individuals might remain infectious to others.

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Author Disclosure Statement

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