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GONORRHEA AND CHLAMYDIA TESTING INCREASING BUT STILL LAGGING IN HIV CLINICS IN THE UNITED STATES

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Abstract

Screening persons living with HIV for gonorrhea and chlamydia has been recommended since 2003. We compared annual gonorrhea/chlamydia testing to syphilis and lipid testing among 19,368 adults (41% men who have sex with men, 30% heterosexual men, 29% women) engaged in HIV care. In 2004, 22%, 62%, and 70% of all patients were tested for gonorrhea/chlamydia, syphilis, and lipid levels, respectively. Despite increasing steadily (OR per year 1.14 [1.13, 1.15]), gonorrhea/chlamydia testing in 2010 remained lower than syphilis and lipid testing (39%, 77%, 76%, respectively). Interventions to improve gonorrhea/chlamydia screening are needed. A more-targeted screening approach may be warranted.

Keywords

Gonorrhea; Chlamydia; Screening; Guidelines; HIV secondary prevention

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Conflicts of Interest

S.A.B. has been a consultant for Bristol-Myers Squibb. K.A.G. has been a consultant for Bristol-Myers Squibb and Tibotec and has been an expert witness for the US government. C.U.L. is a board member of the International Medical Informatics Association and an editor of Applied Clinical Informatics, has received support from the World Congress on Information Technology, and receives textbook royalties from Springer Verlag. B.R.Y. has been a consultant and received research support from Gilead. A.L.A. has provided expert testimony unrelated to this work for various attorneys. There were no potential conflicts for the remaining authors.

INTRODUCTION

Among patients attending HIV clinics, the prevalence of *Neisseria gonorrhoeae* (NG) and/or *Chlamydia trachomatis* (CT) is approximately 10%, and the majority of cases are asymptomatic.¹⁻⁵ Detecting and treating NG and CT among persons living with HIV (PLWH) may decrease HIV transmission by prompting counseling to modify sexual behaviors and by reducing genital fluid inflammation and HIV RNA levels.^{6,7} In 2003, the Centers for Disease Control and Prevention (CDC) began recommending at-least-annual NG/CT screening for most PLWH.⁸

In a large Baltimore HIV clinic, we previously observed an increase in the proportion of patients receiving annual NG/CT testing from 12% before the guidelines in 1999 to 33% in 2007.⁹ Overall, women and men who have sex with men (MSM) were more likely to be tested than heterosexual men, but increases were seen for all three groups. Data on NG/CT screening rates from other locations are lacking, and how compliance for NG/CT compares to compliance for other HIV-related health maintenance guidelines within the same clinical population is not well described.

This study describes NG/CT testing stratified by groups of MSM, heterosexual men, and women during 2004-2010 in a geographically-diverse multisite HIV cohort. We hypothesized that NG/CT rates would increase over time in response to the 2003 guidelines. This study also compares NG/CT testing to syphilis and lipid testing. Lipid testing is recommended annually for persons using ART,^{10,11} which was the case for at least 70% of our cohort each year. Like NG/CT and syphilis, lipid testing is a Department of Health and Human Services HIV care quality indicator,¹² and is thus a useful non-sexually transmitted infection comparator.

METHODS

The HIV Research Network is a United States (U.S.) HIV clinical cohort with 12 adult care sites.¹³ Each site prospectively collects demographic, laboratory, and utilization data from electronic databases and structured chart reviews. Our study population included all patients at least 18 years-old who had at least one calendar year of active care (at least one kept HIV outpatient visit and one CD4 count result in the year) among the seven care sites (located in CA, OR, PA, MD, NY) with complete NG/CT, syphilis, and lipid testing data available. Institutional review boards at the coordinating center at Johns Hopkins University and at each participating site approved the study.

The primary outcome was whether at least one test for NG, CT, or both occurred within each calendar year of active care. Annual syphilis and lipid testing were respectively defined as the presence of at least one rapid plasma reagin (RPR) or *T. pallidum* specific test; and one test for total cholesterol, low- or high-density lipoprotein, and/or triglyceride level within a calendar year. Having multiple tests (for example, repeated RPRs) within one year was considered the same as having a single test. We did not have data on test results so could not include these as outcomes.

MSM were men (including bisexual men) who reported same-sex contact as an HIV risk factor.

Analyses were performed on the person-year (PY) level. Associations with annual NG/CT testing were estimated using repeated measures logistic models using generalized estimating equations to account for within-person correlation. We had no prior hypothesis that calendar trends in NG/CT testing would be non-linear, and after visually confirming (Figure 1) the general fit, we modeled year linearly. Analyses were performed with Stata 12.1 (StataCorp LP, College Station, TX, USA).¹⁴

RESULTS

A total of 19,368 patients contributed 68,458 PY during 2004-2010. The median number of years in care was 3 (interquartile range [IQR], 1-6). While significant differences over time existed for all demographic and clinical covariates (Table, Supplemental Digital Content 1), the percentages of MSM, heterosexual men, and women remained generally stable at approximately 41%, 30%, and 29%, respectively, as did racial/ethnic percentages (47% Non-Hispanic Black, 27% Non-Hispanic White, and 24% Hispanic). Greater variation was evident in other covariates with increases in median age (43 years [IQR 37-49] in 2004 and 47 [40-53] in 2010), median CD4 (376 cells / μ L [209-568] and 445 [268-644]), and percentage with HIV RNA < 400 copies/mL (47% and 68%) and a decrease in median annual visits (5 [3-9] and 4 [3-7]).

During 2004-2010, NG/CT testing occurred in 21,561 (31%) of the 68,458 total PY. In 79% of the 21,561 PY with NG/CT testing, the testing occurred on only one occasion, in 16% on two occasions, and in 5%, three or more occasions. Simultaneous testing of NG and CT occurred 97% of the time. Overall, 52% of patients were tested at least once during the study period. This varied among MSM (54%), heterosexual men (34%), and women (69%), $p < 0.001$.

The proportion of all patients tested for NG/CT increased steadily from 22% in 2004 to 39% in 2010 (Figure 1A), with the unadjusted odds of being tested increasing by 14% per year (odds ratio [OR] per year 1.14 [95% confidence interval, 1.13, 1.15]). Across all study years, the proportions of patients tested annually were 32%, 18%, and 45% for MSM, heterosexual men, and women, respectively. There were increasing linear time trends in the odds of being tested among all subgroups, but the increases were greater for MSM (OR per year 1.23 [1.22, 1.25]) and heterosexual men (1.23 [1.20, 1.25]) than for women (1.02 [1.01, 1.04]) (Figure 1B-D).

Within the full cohort across all study years, the proportion of patients tested annually for syphilis was 66% (increasing from 62% in 2004 to 77% in 2010, OR per year 1.11 [1.10, 1.12]) and the proportion for lipid levels was 74% (increasing from 70% in 2004 to 76% in 2010, OR per year 1.06 [1.05, 1.07]). Significant increases in annual syphilis and lipid testing were noted for MSM, heterosexual men, and women (Figure 1B-D).

After adjustment for age, race/ethnicity, reported history of injection drug use, number of annual visits, CD4 count, HIV RNA, and clinical site (Table 1), annual NG/CT testing

increased within the full group, adjusted OR per year 1.21 (1.20, 1.22), and within each subgroup, with the slopes again steeper for MSM (1.41 [1.39, 1.44]) and heterosexual men (1.33 [1.30, 1.36]) than for women (1.06 [1.05, 1.08]). Within the full sample and within each subgroup, significant multivariate associations were evident with most variables. In addition to calendar time, the strongest associations were seen with lower age and with more annual visits.

Because we suspected syphilis and lipid testing may be associated with NG/CT testing and because annual syphilis and lipid testing increased over calendar time, we fit multivariate models which iteratively added syphilis and lipid testing to the set of previous covariates (Table, Supplemental Digital Content 2). Within the full group, syphilis testing (AOR 2.44 [2.33, 2.56] in the model including both syphilis and lipid testing) and lipid testing (1.27 [1.21, 1.32]) were both associated with NG/CT testing. Similar associations were seen within each subgroup. However, the addition of syphilis and lipid testing did not meaningfully change the calendar time trends for NG/CT testing within the full group (AOR per year for NG/CT testing 1.18 [1.17, 1.20]) nor within any subgroup.

We previously observed an increase in NG/CT testing at one study site 1999-2007. A sensitivity analysis excluding this site had an unchanged pattern of results.

DISCUSSION

In our analysis of seven geographically-diverse U.S. HIV clinics, NG/CT testing increased steadily from 22% in 2004, shortly after guidelines publication, to 39% in 2010. Increases were seen within each subgroup of MSM, heterosexual men, and women. In addition to calendar time, factors most strongly correlated with NG/CT testing included female gender, age <40, and 4 annual clinic visits. Despite increasing, NG/CT testing coverage continued to lag far behind syphilis and lipid coverage.

NG/CT testing coverage of 10-40%, representing poor adherence to local guidelines, has been noted in multiple studies from the early 2000's in the U.S., United Kingdom, and Australia and more recently in Ontario, Canada.^{3,9,15-20} Our results extend US findings through 2010 and illustrate direct contrasts with syphilis and lipid coverage. NG/CT testing coverage of 100% of the population was not expected. The CDC guidelines published in 2003 and reiterated in 2004 and 2009 recommended annual NG/CT screening only for 'sexually active' PLWH.^{8,11,21} However, this proviso applied equally to syphilis screening, making the contrast between NG/CT and syphilis particularly relevant. Other groups have had relatively more success with NG/CT screening. Clinics participating in the HIVQUAL-US quality improvement network achieved 50-60% genital NG/CT screening coverage in 2011.²²

The increase in NG/CT testing (and potentially also syphilis) may have been at least partly due to the published guidelines and to medical literature during the study period demonstrating high NG/CT prevalence among HIV clinic patients.^{2,4,8,11,21} Another factor may have been urine specimens and vaginal swabs, which are less-invasive than traditional urethral and cervical swabs. Urine and vaginal assays became available at all sites prior to

2004, but providers may have adopted them gradually. A steady increase in the proportion of patients using ART (from 70% in 2004 to 87% in 2010) may have contributed to the trend in lipid testing.

Much of the contrast between syphilis and NG/CT testing coverage may stem from barriers to engaging in sexual histories and to obtaining urine, rectal, and oral specimens. Required time and provider discomfort with the topic may be the most important barriers.²³

The relative strength of recommendations may also contribute to the contrast. Syphilis screening for all sexually-active patients and rectal (NG/CT) and oral (NG) screening for all patients with a history of receptive rectal or oral sex are firmly recommended.^{8,11,21} However, genital (urine, urethral, cervical, or vaginal) NG/CT screening is to be “considered” based on a provider’s assessment of factors identified during sexual history and on local NG/CT prevalence. Thus the lower rate of NG/CT screening could be partly due to providers obtaining histories and only screening the fraction of patients who report receptive rectal or oral sex. Our data are limited by not including specimen source, and we are unable to assess the proportion of testing episodes that included oral and/or rectal (extragenital) samples. We suspect extragenital testing was infrequent. Even if providers take regular sexual histories, patients are likely to underreport receptive rectal and oral sex.²⁴ Data available through 2007 from one of our study clinics showed extragenital testing among MSM occurred much less frequently than genital testing and in <5% of MSM annually.⁹ This low rate resembles rates reported from other centers^{19,22} despite evidence that, among MSM, extragenital sites are more likely to screen positive.^{1,2,4}

The strong association of NG/CT testing with younger age may be appropriate given that NG/CT incidence typically correlates with younger age.^{3,9} More frequent testing among women than men has been previously observed and may reflect the combination of NG/CT screening with cervical cancer screening.^{3,9} The slower increase in NG/CT testing over time among women may indicate a relative ceiling on how many women readily accept screening and/or which patients providers believe need screening.

Our findings have several implications. Implementation of NG/CT screening in HIV clinics should be improved. Interventions promoting routine screening of all appropriate body sites are needed. Task shifting to nurses, self-administered swabs, and electronic reminders have shown efficacy and deserve further study and implementation.^{1,2,25,26} The suboptimal response to the current guidelines also suggests that a more targeted approach to screening may be preferable. Having clear groups (e.g. all heterosexual men under 35, all MSM under 45) could facilitate task shifting and electronic reminders. Considering genital site screening on a case by case basis may be prohibitively time consuming. A future direction for research is to help define target groups by using NG/CT result data to determine NG/CT incidence stratified by body site, sexual risk group, age, and other predictors.

The strengths of this study include the seven-year period, the large sample, and the geographic diversity. An acknowledged limitation is the lack of data on body site. Another limitation is that we did not have available data to include a urine-based screening test (such as proteinuria) as a comparator for NG/CT. We also acknowledge that some outcome data

may have been missed due to patients receiving care outside the local institution health system from which each site obtains laboratory data. If this were to introduce any bias, it would most likely be to bias lipid testing closer to NG/CT testing (i.e. closer to the null hypothesis) because non-HIV providers, especially primary care providers and cardiologists, would probably be more focused on cardiovascular preventive health than on HIV-specific guidelines.

A final limitation is that we cannot distinguish screening assays from symptomatic or exposure-based testing. Some of the increase in NG/CT testing probably occurred as a response to symptomatic infections or reported exposures. National surveillance data indicate combined NG and CT reported incidence increased by 22% from 2004 to 2010.²⁷ Similar increases were seen in each of the metropolitan areas included in this study.²⁸⁻³² However, we doubt such relatively modest increases would explain the majority of the 77% increase in testing we observed.

In summary, despite increasing since guidelines were published in 2003, annual NG/CT testing remains infrequent, occurring in only half as many PLWH as annual syphilis and lipid testing. Interventions to improve screening are needed, and a more targeted approach to screening may be considered when data are available to define the target groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX: HIV RESEARCH NETWORK DETAILS

Participating Sites

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Montefiore Medical Center, Bronx, New York (Lawrence Hanau, M.D., Uriel Felsen, M.D.)

Oregon Health and Science University, Portland, Oregon (P. Todd Korthuis, M.D.)

Parkland Health and Hospital System, Dallas, Texas (Ank Nijhawan, M.D., Muhammad Akbar, M.D.)

St. Jude's Children's Research Hospital and University of Tennessee, Memphis, Tennessee (Aditya Gaur, M.D.)

St. Luke's Roosevelt Hospital Center, New York, New York (Victoria Sharp, M.D., Stephen Arpadi, M.D., Antonio Urbina, M.D.)

Tampa General Health Care, Tampa, Florida (Charurut Somboonwit, M.D.)

Trillium Health, Rochester, New York (Roberto Corales, D.O.)

University of California, San Diego, California (W. Christopher Mathews, M.D.)

Sponsoring Agencies

Agency for Healthcare Research and Quality, Rockville, Maryland (Fred Hellinger, Ph.D., John Fleishman, Ph.D., Irene Fraser, Ph.D.)

Health Resources and Services Administration, Rockville, Maryland (Robert Mills, Ph.D., Faye Malitz, M.S.)

Data Coordinating Center

Johns Hopkins University (Richard Moore, M.D., Jeanne Keruly, C.R.N.P., Kelly Gebo, M.D., Cindy Voss, M.A., Nikki Balding, M.S.)

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Figure 1.

Trends in the percentages of patients tested annually for Gonorrhea (NG) / Chlamydia (CT), Syphilis, and Lipid levels. (A) All patients, (B) Men who have sex with men, (C) Heterosexual men, (D) Women.

Table 1

Multivariate analysis of factors associated with NG/CT testing

Variable (N, patients)	All Patients (19,368)	MSM (7,898)	Heterosexual Men (6,036)	Women (5,434)
Calendar Time				
Linear parameter 2004-2010, per year	1.21 (1.20, 1.22)	1.41 (1.39, 1.44)	1.33 (1.30, 1.36)	1.06 (1.05, 1.08)
Age (years)				
18 – 29	2.49 (2.28, 2.71)	3.02 (2.65, 3.45)	2.56 (2.00, 3.27)	2.25 (1.95, 2.59)
30 – 39	1.95 (1.83, 2.08)	2.10 (1.89, 2.33)	1.77 (1.54, 2.05)	2.00 (1.81, 2.20)
40 – 49	1.45 (1.38, 1.53)	1.42 (1.30, 1.56)	1.40 (1.26, 1.56)	1.56 (1.43, 1.70)
50	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Race / Ethnicity				
Non-Hispanic Black	1.44 (1.35, 1.53)	1.18 (1.06, 1.31)	1.32 (1.15, 1.51)	1.37 (1.22, 1.54)
Non-Hispanic White *	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Hispanic	1.14 (1.07, 1.22)	1.09 (0.99, 1.21)	1.08 (0.92, 1.27)	1.29 (1.13, 1.46)
History of IDU				
No	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Yes	0.93 (0.88, 0.99)	0.93 (0.82, 1.05)	1.07 (0.97, 1.18)	1.05 (0.97, 1.14)
Annual HIV Care Visits				
1 – 3	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
4 – 6	1.56 (1.49, 1.63)	1.57 (1.46, 1.69)	1.53 (1.38, 1.68)	1.76 (1.63, 1.90)
7	2.10 (2.00, 2.21)	2.14 (1.97, 2.32)	1.94 (1.73, 2.17)	2.67 (2.46, 2.89)
CD4 count[†] (cells/μl)				
200	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
201 – 350	1.13 (1.07, 1.19)	1.16 (1.05, 1.28)	1.07 (0.95, 1.21)	1.16 (1.05, 1.27)
351	1.32 (1.25, 1.39)	1.25 (1.14, 1.37)	1.25 (1.12, 1.41)	1.34 (1.22, 1.46)
HIV RNA value[†] (cells/μl)				
400	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
> 401 or Missing	1.16 (1.11, 1.21)	1.28 (1.19, 1.37)	1.20 (1.09, 1.31)	1.09 (1.02, 1.16)

All models included an indicator variable to adjust for HIVRN site

* For analytic purposes, other/unknown race (2%) of sample was combined with non-Hispanic White

[†] First yearly value