Repeat Human Immunodeficiency Virus Testing by Transmission Risk Group and Rurality of Residence in North Carolina

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Background: Understanding of repeat human immunodeficiency virus (HIV) testing (RHT) is limited and the impact of rural residence as a potential barrier to RHT is unknown. Rural populations are of particular interest in the Southeastern United States because of their disproportionate HIV burden.

Methods: We used HIV surveillance data from publicly funded HIV testing sites in North Carolina to assess repeat testing by transmission risk group and residential rurality in a retrospective cohort study. Linear binomial regression models were used to estimate adjusted, 1-year cumulative incidences and cumulative incidence differences comparing RHT within transmission risk populations by level of rurality.

Results: In our total study population of 600,613 persons, 19,275 (3.2%) and 9567 (1.6%) self-identified as men who have sex with men (MSM) and persons who inject drugs (PWID), respectively. A small minority, 13,723 (2.3%) resided in rural ZIP codes. Men who have sex with men were most likely to repeat test (unadjusted, 1-year cumulative incidence after an initial negative test, 16.4%) compared with PWID (13.2%) and persons who did not identify as either MSM or PWID (13.6%). The greatest effect of rurality was within PWID; the adjusted, 1-year cumulative incidence of RHT was 6.4 (95% confidence interval, 1.4–11.4) percentage points higher among metropolitan versus rural PWID.

Conclusions: One-year cumulative incidence of RHT was low among all clients of publicly funded HIV testing sites in North Carolina, including MSM and PWID for whom annual testing is recommended. Our findings suggest a need for public health efforts to increase access to and support for RHT, particularly among rural PWID.

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An estimated 15% of persons living with human immunodeficiency virus (HIV) (PLWH) in the United States remain unaware of their infection,[1] despite national recommendations that those at high risk of infection be tested at least annually.[2,3] High-risk populations include persons who inject drugs (PWID) and their sex partners, persons who practice transactional sex, sex partners of PLWH, men who have sex with men (MSM), and persons who are infected with or are seeking testing for sexually transmitted infections.[2,3] Regular HIV testing allows for early detection of infection and serves as the gateway to care, treatment, and viral suppression.[1,4] However, current understanding of testing patterns is based on analyses restricted to cross-sectional data, self-reported testing histories, and/or individual risk groups.[5–9]

Residence in a rural area is an important barrier to HIV testing among at-risk populations due to transportation challenges, reduced numbers or availability of nearby HIV testing sites, and increased perceived stigma toward PLWH.[10,11] Although rural populations test later in the HIV disease course and have lower lifetime and past-year testing prevalences than urban populations,[10,12] little is known about repeat HIV testing behaviors by rurality. Any effects of rurality on repeat HIV testing may be especially relevant in the Southeastern United States, where the proportion of the rural population living with HIV is 3 times that of other regions.[13]

We conducted a surveillance-based analysis of HIV testing patterns and the effects of rurality on repeat testing in North Carolina (NC), where 20% of new HIV diagnoses occur in rural regions, compared with 8.9% of new diagnoses across the United States.[14] We aimed to characterize the 1-year cumulative incidence of repeat HIV testing by transmission risk group and to estimate the effect of rurality on repeat HIV testing within each population.

MATERIALS AND METHODS

Study Design, Setting, and Population

We conducted a retrospective cohort study of adults with a negative result on an initial (index) HIV test at any publicly funded testing site in NC between July 2005 and December 2012, examining surveillance records in the subsequent year to estimate the cumulative incidence of a second HIV test at a publicly funded site within 1 year of the index test.

Data were drawn from the NC Division of Public Health Counseling, Testing, and Referral Services (CTRS) database, which tracks conventional (non–point-of-care) HIV tests performed at 199 publicly funded testing sites in NC. These sites include health departments—which house HIV testing sites and

STD, family planning, and obstetrics & gynecology clinics—as well as community-based organizations, community health centers, drug treatment facilities, and county jails. The CTRS database contains data on more than 200,000 unique tests each year and is used for program planning and surveillance at the state level. The CTRS data include test setting and client-reported demographics, residential ZIP code and county, HIV testing history, risk factors for HIV infection, and reasons for testing. These data are recorded by HIV testing personnel and sent to the NC State Laboratory of Public Health for entry into the CTRS database. Testing events between July 1, 2005, and December 31, 2013, were linked by unique client in a prior study,[15] allowing reconstruction of individual testing histories.

We excluded testing clients who reported being pregnant at the index test because NC prenatal care guidelines require opt-out HIV testing at the first visit and during the third trimester of pregnancy,[16] and our interest was in repeat testing behaviors outside of this context. We also excluded clients who did not report a ZIP code and county of residence in NC at the index test, clients with a positive result on the index test, pediatric clients (age, < 18 years) and those missing age, and clients with an index test after December 31, 2012.

Outcome, Exposure, and Covariate Definitions

Our outcome of interest was repeat testing, which we defined as any HIV test captured by CTRS within 1 year after the index test to correspond with annual testing recommendations.[2,3] Outcome assessment was based only on the first repeat test, because the intent of the current analysis was only to determine whether testing occurred again within a year; description of longitudinal testing patterns will be the focus of future work. We relaxed the assessment period to 15 months in a sensitivity analysis to allow flexibility in assessing testing guideline adherence. In the main analysis, we included repeat tests performed in the context of pregnancy to avoid censoring by the competing risk of pregnancy. We performed an additional sensitivity analysis to assess the impact of this decision, excluding all repeat tests conducted during a reported pregnancy or at a pregnancy/obstetrics testing site.

We based the main exposure, rurality of residence, on client-reported residential ZIP code at the index test, collapsing the US Department of Agriculture's 2010 Rural-urban Commuting Areas (RUCA) classifications[17] into metropolitan (RUCA score, 1–3), micropolitan (RUCA score, 4–9), and rural (RUCA score, 10). The RUCA scheme classifies census tracts into 10 levels of rurality/urbanicity based on measures of population density, urbanization, and daily commuting, and then further assigns rurality at the ZIP code level according to census tract classifications within each ZIP code. In a sensitivity analysis, we assigned rurality of residence based on residential county under the 2013 NCHS Urban-rural Classification Scheme.[18] This framework classifies counties according to the Office of Management and Budget's 2013 delineation of metropolitan and micropolitan statistical areas within each county. We collapsed the Urban-rural Classification Scheme scores in an analogous manner to the RUCA classifications defined above as metropolitan, micropolitan, and rural.

All stratification and confounder variables were generated from client-reported values at the index test. We created 4 risk group categories according to MSM and PWID status: clients identifying as MSM but not PWID (MSM-only), clients identifying as PWID but not MSM (PWID-only), clients identifying as both MSM and PWID (MSM + PWID), and clients not identifying as either MSM or PWID (neither MSM nor PWID). In multivariable models (see below), we dichotomized gender as female and male because there were no rural testers who identified as transgender. We coded race/ethnicity with disjoint indicators as white/non-Hispanic, black/non-Hispanic, Hispanic, Asian or Pacific Islander/non-Hispanic, Native American/non-Hispanic, and other/multiracial, with white/non-Hispanic serving as the referent group. Age was represented with linear and quadratic terms in multivariable models.

Statistical Analyses

We first examined covariate distributions overall and by the full set of 4 transmission risk groups (MSM-only, PWID-only, MSM + PWID, neither MSM nor PWID). Due to small numbers of MSM + PWID, we conducted all subsequent analyses with a reduced set of 3 transmission risk group categories: MSM, PWID, and neither MSM nor PWID. Clients who reported being both MSM and PWID (MSM + PWID) were included both as MSM in analyses restricted to MSM and as PWID in analyses restricted to PWID.

We calculated unadjusted 1-year cumulative incidences of repeat testing in each of the transmission risk groups in our reduced set (MSM, PWID, and neither MSM nor PWID) by rurality of residence and several relevant covariates. To assess the effect of rurality on repeat testing within each group, we then constructed distinct linear binomial regression models tailored to each population. We selected minimum sufficient adjustment sets using directed acyclic graphs[19] after a comprehensive literature review, adjusting for age and race/ethnicity in the model restricted to MSM; for age, race/ethnicity, gender, and MSM status in the model restricted to PWID; and for age, race/ethnicity, and gender

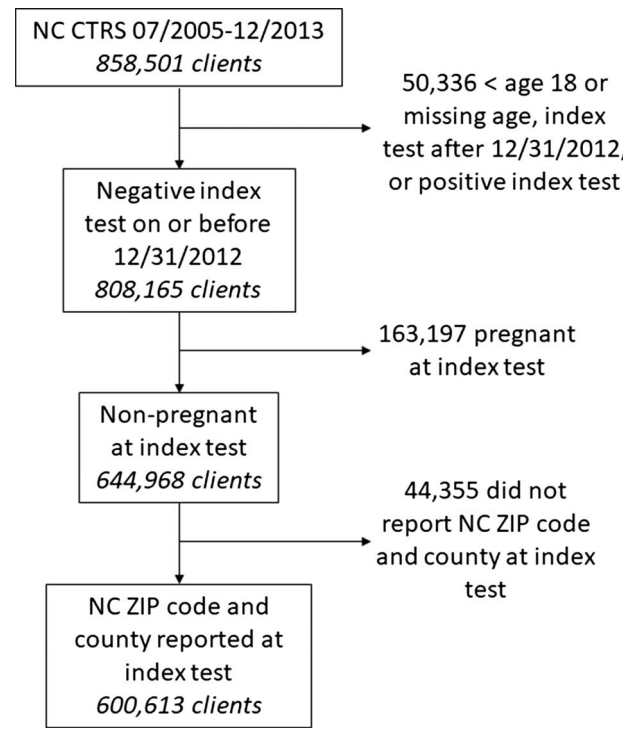

Figure 1. Application of inclusion and exclusion criteria to form study population. Of 858,501 testing clients, we excluded pediatric clients and those missing age, clients with an index test after December 31, 2012, clients with a positive result on the index test, clients who reported being pregnant at the index test, and clients who did not report a NC ZIP code and county of residence at the index test, for a total of 600,613 included clients.

in the model restricted to neither MSM nor PWID. These models were used to estimate the adjusted, 1-year cumulative incidences and 95% confidence intervals (95% CIs) of repeat HIV testing by level of rurality within each population, along with the corresponding cumulative incidence differences (CIDs) and 95% CIs comparing micropolitan and rural residents (separately) to metropolitan residents within each population.

The institutional review board at the University of North Carolina at Chapel Hill approved this secondary analysis of public health surveillance data. All statistical analyses were conducted in SAS 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Of 858,501 persons testing during the study period, 600,613 were eligible for analysis (Fig. 1). The majority were female (57%) (Table 1). Clients in the "neither MSM nor PWID" group were most likely to be black/non-Hispanic (46%), whereas MSM-only, PWID-only, and MSM + PWID clients were most likely to be white/non-Hispanic. The PWID-only clients tended to be older compared with other testing populations, and the percentage of white/non-Hispanic clients was particularly high (70%) in this population. Testing site type varied widely across risk groups, although STD testing and treatment sites accounted for the largest number of index tests in each group. Most repeat tests across all risk groups occurred at the same testing site type as a client's initial test. A large majority of all clients resided in metropolitan ZIP codes at index testing, with slightly larger proportions of MSM-only, PWID-only, and MSM + PWID clients residing in metropolitan areas compared with neither MSM nor PWID clients.

Men who have sex with men and PWID made up 3.2% and 1.6% of testing clients, with MSM + PWID clients contributing to both populations. Transmission risk group, including MSM and PWID status, was missing for 8.3% of male clients and 10.0% of all clients, respectively, suggesting underreporting of these identifiers. No other substantial missingness was present.

In univariate analyses, 16.4% of MSM clients returned for repeat testing within 1 year of index testing compared with

TABLE 1. Characteristics by Transmission Risk Group of Persons Undergoing an HIV Test at Publicly Funded Testing Sites in North Carolina at First (index) Visit, 2005–2012

Characteristics	MSM-only, n (%)*	PWID-only, n (%)*	MSM + PWID, n (%)*	Neither MSM nor PWID, n (%)*	Total, N (%)*
Gender					
Male	18,252 (100)	4642 (55)	1023 (100)	234,214 (41)	258,131 (43)
Female	0 (0)	3755 (45)	0 (0)	334,469 (59)	338,224 (57)
Transgender†	0 (0)	1 (0)	0 (0)	131 (0)	132 (0)
Race/ethnicity					
White, non-Hispanic	8598 (49)	5790 (70)	474 (48)	189,012 (35)	203,874 (36)
Black, non-Hispanic	6423 (37)	1841 (22)	376 (38)	251,104 (46)	259,744 (45)
Hispanic	2012 (12)	510 (6)	124 (13)	89,298 (16)	91,944 (16)
Asian/Pacific Islander	230 (1)	43 (1)	5 (1)	7924 (2)	8202 (1)
American Indian/Alaska Native	156 (1)	112 (1)	6 (1)	7284 (1)	7558 (1)
Other/multiracial	17 (0)	7 (0)	0 (0)	644 (0)	668 (0)
Age, y					
18–24	7843 (43)	2310 (27)	344 (34)	232,117 (41)	242,614 (40)
25–34	5129 (28)	2728 (32)	301 (29)	174,227 (30)	182,385 (30)
35–44	2868 (16)	1803 (21)	176 (17)	92,327 (16)	97,174 (16)
≥ 45	2412 (13)	1703(20)	202 (20)	74,123 (13)	78,440 (13)
Initial testing site					
LHD/CBO	2516 (15)	644 (8)	70 (7)	30759 (6)	33989 (6)
STD testing and treatment	8878 (51)	2310 (28)	517 (53)	25,4954 (47)	266,659 (47)
Drug treatment	206 (1)	1471 (18)	54 (6)	7710 (1)	9441 (2)
Family planning/sexual health	158 (1)	660 (8)	2 (0)	119,769 (22)	120,589 (21)
CHC/PHC	638 (4)	220 (3)	30 (3)	16,166 (3)	17,054 (3)
Jail	362 (2)	1341 (16)	63 (7)	34,200 (6)	35,966 (6)
Other	4631 (27)	1572 (19)	232 (24)	80,690 (15)	87,125 (15)
Repeat test at same site type‡					
Yes	6572 (97)	2901 (98)	356 (98)	207,637 (99)	595,786 (99)
No	204 (3)	62 (2)	8 (2)	1104 (1)	4827 (1)
Rurality of residence					
Metropolitan	15,194 (83)	6833 (80)	813 (80)	435,531 (76)	458,371 (76)
Micropolitan	2827 (16)	1491 (18)	186 (18)	124,015 (22)	128,519 (21)
Rural	231 (1)	220 (3)	24 (2)	13,248 (2)	13,723 (2)
Repeat HIV testing					
No repeat test	11,476 (63)	5581 (65)	659 (64)	364,053 (64)	381,769 (64)
Repeat test ≤ 1 y	3361 (18)	1247 (15)	142 (14)	88,106 (15)	92,856 (16)
Repeat test > 1 y	3415 (19)	1716 (20)	222 (22)	120,635 (21)	125,988 (21)
Total	18,252	8544	1023	572,794	600,613

*Missing values are not included in calculation of percentage.

†Includes male-to-female and female-to-male transgender clients.

‡Includes first repeat test following the index test, regardless of time elapsed between tests. Percentage is out of only those with at least 1 repeat test.

LHD/CBO, local health department/community-based organization; CHC/PHC, community health center/primary health care.

TABLE 2. Adjusted 1-y Cumulative Incidence of Repeat HIV Testing within Transmission Risk Group of Persons Undergoing an HIV Test at Publicly Funded Testing Sites in North Carolina by Rurality of Zip Code of Residence at First (Index) Visit, 2005–2012

	MSM*		PWID†		Neither MSM nor PWID‡	
Rurality of residence	Cumulative Incidence (95% CI)	CID (95% CI)§	Cumulative Incidence (95% CI)	CID (95% CI)§	Cumulative Incidence (95% CI)	CID (95% CI)§
Metropolitan	0.17 (0.16–0.18)	—	0.17 (0.16–0.18)	—	0.16 (0.15–0.16)	—
Micropolitan	0.14 (0.13–0.15)	−0.03 (−0.05 to −0.02)	0.13 (0.11–0.15)	−0.03 (−0.05, −0.01)	0.14 (0.13–0.14)	−0.02 (−0.02 to −0.02)
Rural	0.15 (0.10–0.19)	−0.02 (−0.07 to 0.02)	0.10 (0.05–0.15)	−0.06 (−0.11, −0.01)	0.11 (0.11–0.12)	−0.04 (−0.04 to −0.04)
Unadjusted total	0.164		0.132		0.136	

*Model conducted only among MSM (including MSM + PWID) clients and adjusts for age and race/ethnicity.
†Model conducted only among PWID (including MSM + PWID) clients and adjusts for age, race/ethnicity, gender, and MSM status.
‡Model conducted only among neither MSM nor PWID clients and adjusts for age, race/ethnicity, and gender.
§Referent group is metropolitan clients within transmission risk group (MSM, PWID, or neither MSM nor PWID).

13.2% of PWID clients and 13.6% of neither MSM nor PWID clients. We refer the reader to Supplemental Table 1 (http://links.lww.com/OLQ/A270) for a summary of these cumulative incidences by selected covariates.

Across all subpopulations of interest, metropolitan MSM and PWID clients were most likely to return for repeat testing (adjusted, 1-year cumulative incidence, 0.170; 95% CI, 0.16–0.18 in both populations) and rural PWID clients were the least likely (adjusted, 1-year cumulative incidence, 0.102; 95% CI, 0.05–0.15) (Table 2). Among MSM, rural and micropolitan clients showed adjusted, 1-year cumulative incidences of repeat testing that were 2.4 (95% CI, −2.0 to 6.8) and 3.2 (95% CI, 1.9–4.6) percentage points lower than those of their metropolitan peers, respectively. Similar trends were observed among PWID and neither MSM nor PWID. The greatest effect of rurality on repeat testing was within PWID; the 1-year cumulative incidence of repeat testing was 6.4 (95% CI, 1.4–11.4) percentage points lower among rural versus metropolitan PWID.

Sensitivity analyses allowing 15 months of observation showed slightly larger adjusted cumulative incidences of repeat testing across all populations and levels of rurality (Supplemental Table 2, http://links.lww.com/OLQ/A270), reflecting an uptick in repeat testing between 12 and 15 months (Supplemental Figure 1, http://links.lww.com/OLQ/A270). The increased cumulative incidences were smaller among PWID than the other testing populations. Cumulative incidence differences in the 15-month analyses were very similar to those in the main analyses. Sensitivity analyses with rurality assigned by county of residence at the index test shifted approximately 4% of clients from the micropolitan classification to both the metropolitan and rural classifications and yielded effect estimates within approximately 1 percentage point of the absolute effect estimates identified in the primary analyses (Supplemental Table 3, http://links.lww.com/OLQ/A270). A final sensitivity analysis excluding all repeat tests that occurred during pregnancy or were conducted at pregnancy/obstetrics testing sites showed slightly lower cumulative incidences among PWID and neither MSM nor PWID clients, but CIDs were again similar to the main results (Supplemental Table 4, http://links.lww.com/OLQ/A270).

DISCUSSION

Although regular HIV testing among at-risk groups is essential to maximize clinical and public health benefits, little is known about repeat HIV testing based on objective measures across multiple risk groups, and the effect of rurality as a potential barrier to HIV testing is unknown. In this study, we examined these measures and effects using surveillance data from publicly funded testing sites in a large, diverse population. Despite recommended annual testing for all high-risk individuals, including MSM and PWID,[2,3] the 1-year cumulative incidence of repeat testing in our setting was only 16% among MSM and 13% among PWID. After inclusion of repeat tests that occurred within 15 months of the index test, cumulative incidence remained suboptimal (21% among MSM and 18% among PWID). These results indicate a clear need for public health efforts to increase access to and support for regular HIV testing in NC.

The rural/urban disparities that we observed in repeat HIV testing mirror disparities that have been identified previously with other HIV testing metrics.[11–14,20–24] Lifetime testing prevalence estimates range from 43.6% among residents of the most urban areas of the United States to 32.2% among residents of the most rural areas, whereas past-year testing prevalence ranges from 13.5% to 7.3% in those areas, respectively.[14] Of note, our estimated 1-year cumulative incidences of testing among persons who had already had a negative HIV test are slightly higher at all rurality levels than corresponding past-year estimates calculated irrespective of prior testing status,[14] suggesting that previously reported rural-urban disparities in testing prevalences and disease stage at diagnosis[14,23] may be largely due to differences in first-time testing behaviors rather than repeating testing behaviors. Although repeat HIV testing should be encouraged among all at-risk clients, our results indicate that interventions aiming to reduce rural-urban disparities within the full population may be best targeted toward introduction of new rural testing clients to the existing HIV testing infrastructure in NC.

Although metropolitan MSM clients were more likely to repeat-test within 1 year than any other testing population, the 1-year cumulative incidence of repeat HIV testing among MSM clients in NC across all levels of rurality was lower than might be expected from previous estimates. In 1 study among HIV-uninfected Black MSM ages 18 to 30 years in NC, 83% reported ever receiving an HIV test. Among those subjects who had previously tested, 71% of this particularly at-risk population reported testing at least once every 6 months and 40% reported testing at least quarterly.[8] Further, 21% of a sample of MSM with HIV-negative primary partners in the United States reported testing at least once every 6 months and 29% reported testing at least once per year.[11] The apparent discrepancies between our results and those of prior studies may be due to differences in study populations and measures, our capture of only those tests performed at publicly-funded testing sites, and/or earlier studies' reliance on self-reported HIV testing.

Although rural and micropolitan populations represent a minority of the total, at-risk, and testing populations in NC, the substantial burden placed on rural areas by the recent opioid

epidemic heightens the need for improved understanding of rural HIV testing behaviors, especially among PWID. Only 10% of PWID in rural areas in our setting returned for repeat testing within a year of their index test, a substantially smaller percentage compared with their metropolitan peers. This difference may be due to greater accessibility of resources for PWID in metropolitan compared with micropolitan, and particularly, rural areas. A lack of harm reduction resources for PWID, including HIV testing, has previously been linked to anomalous HIV outbreaks in rural areas,[25] highlighting the potential hazard of infrequent HIV testing among rural PWID.

More generally, the low 1-year cumulative incidence of repeat testing observed among PWID overall underscores a need for increased repeat HIV testing among PWID in NC, regardless of region of residence. To this end, the 2016 legalization of syringe service programs in NC offers improved opportunities to reach PWID with harm reduction services, including HIV testing.[26] Although we did not examine hepatitis C virus (HCV) testing, our results may have similar implications for the provision of HCV testing, which has substantial overlap with HIV testing in NC. Integration of point-of-care HIV and HCV testing into syringe service programs, just as these tests have already been introduced into many other nontraditional HIV testing sites, could improve early detection and treatment of both diseases among the high-risk PWID populations served by these programs. Integration of services may be particularly beneficial in rural regions where transportation is an obstacle to accessing testing and other harm reduction resources.[24]

Our reliance on CTRS data results in underestimation of the true 1-year cumulative incidence of repeat testing because secondary tests performed outside of publicly funded testing sites in NC and point-of-care secondary tests are not captured. There is a clear need for increased collaboration, including data sharing, between public and private organizations offering testing services to fully characterize HIV testing patterns in NC. The reliance on CTRS data may also bias rurality effect estimates if the likelihood of receiving a secondary test at a publicly versus privately funded testing site is related to rurality. In 1 prior study, residents of rural areas were more likely to report testing in a hospital, whereas residents of urban areas were more likely to report testing at publicly funded testing centers.[12] Exclusion of persons with missing age or county/ZIP of residence may have resulted in some selection bias, but it is difficult to speculate on the magnitude or direction of any such bias.

Substantial missing data for both MSM and PWID risk behaviors indicate that both factors were likely underreported, potentially in part due to stigma, which limits inference from our findings in these groups to those who disclose MSM and PWID status to testing personnel. One recent study of acute HIV cases diagnosed in NC showed substantially increased reporting of MSM behaviors after diagnosis compared with reporting at the time of testing,[27] supporting the likelihood that some MSM and PWID were misclassified in our analysis as not belonging to either group. Additionally, the small number of rural MSM and PWID clients resulted in comparatively imprecise estimates among these subpopulations, and we were unable to separately examine repeat testing in the population of MSM + PWID clients. Further, this analysis is unable to distinguish between true first-time testing and those who had received HIV tests at publicly funded testing sites prior to initiation of data collection, as well as confirmatory repeat testing. Only 1.5% of repeat tests occurred within 1 month of the index test, suggesting that testers seeking confirmation of prior negative results had a minimal effect on our estimates. Finally, CTRS data are limited in scope and were collected for surveillance rather than research. Thus, there may be uncontrolled confounding by variables not available in the database, including socioeconomic status. The restricted nature of CTRS data also limited us to evaluating populations of testing clients in broad strokes instead of by more nuanced individual risk factors for infection.

One-year cumulative incidence of repeat HIV testing was low among all clients of publicly funded testing centers in NC, including populations of MSM and PWID in whom annual testing is recommended. This study also suggests that the effect of rurality on 1-year cumulative incidence of repeat HIV testing is substantively small overall and among MSM in North Carolina. However, this effect is slightly more pronounced within PWID. There is a need for increased repeat HIV testing, as well as general STD screening, across all at-risk testing populations in NC, with perhaps the greatest need among rural populations of PWID.

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