

Optimizing Screening for HIV

Antoine Chaillon,^{1,a} Martin Hoenigl,^{1,a} Lorri Freitas,² Haruna Feldman,² Winston Tilghman,² Lawrence Wang,² Davey Smith,^{1,3} Susan Little,¹ and Sanjay R. Mehta^{1,3,4,●}

¹Department of Medicine, University of California San Diego, San Diego, California, USA, ²County of San Diego Health and Human Services Agency, Division of Public Health Services, San Diego, California, USA, ³Department of Medicine, San Diego Veterans Affairs Medical Center, San Diego, California, USA, and ⁴Department of Pathology, University of California San Diego, San Diego, California, USA

Background. The HIV epidemic is unevenly distributed throughout the United States, even within neighborhoods. This study evaluated how effectively current testing approaches reached persons at risk for HIV infection across San Diego (SD) County, California.

Methods. HIV case and testing data, sexually transmitted infection (STI) data, and sociodemographic data for SD County were collected from the SD Health and Human Services Agency and the “Early Test” community-based HIV screening program between 1998 and 2016. Relationships between HIV diagnoses, HIV prevalence, and STI diagnoses with screening at the ZIP code level were evaluated.

Results. Overall, 379 074 HIV tests were performed. The numbers of HIV tests performed on persons residing in a ZIP code or region overall strongly correlated with prevalent HIV cases ($R^2 = .714$), new HIV diagnoses ($R^2 = .798$), and STI diagnoses ($R^2 = .768$ [chlamydia], .836 [gonorrhea], .655 [syphilis]) in those regions. ZIP codes with the highest HIV prevalence had the highest number of tests per resident and fewest number of tests per diagnosis. Even though most screening tests occurred at fixed venues located in high-prevalence areas, screening of residents from lower-prevalence areas was mostly proportional to the prevalence of HIV and rates of new HIV and STI diagnoses in those locales.

Conclusions. This study supported the ability of a small number of standalone testing centers to reach at-risk populations dispersed across SD County. These methods can also be used to highlight geographic areas or demographic segments that may benefit from more intensive screening.

Keywords. HIV; prevalence; screening; sexually transmitted infections.

HIV infects 38 000 persons in the United States each year [1]. The HIV epidemic is not uniformly distributed geographically or across demographics [1, 2]. HIV prevalence and incidence rates can also vary even within neighborhoods. HIV infection is also associated with sexually transmitted infections (STIs) [3], which may predispose to viral shedding and acquisition of HIV [4], but this association may have weakened due to demographic shifts and the availability of HIV pre-exposure prophylaxis [5, 6]. Understanding the relationships between screening efforts, STI rates, HIV prevalence, and HIV incidence in different communities could provide new insight on how to optimize targeting of screening for HIV and STIs.

HIV has been present in San Diego (SD) County since at least 1981, and nearly 16 000 residents have been diagnosed with AIDS since then [7]. In 2010, there were an estimated 11 252 residents living with HIV in SD County, resulting in a prevalence of 0.36% [8]. The geospatial dispersal of the local HIV epidemic in SD is also unique, with 2 central ZIP codes having prevalence rates >4% [2]. The epidemic is predominantly among men who have sex with men (MSM; >80%) and has been more concentrated in the non-Hispanic white population than in other racial or ethnic groups. Recently, there has been a shift in demographics such that Hispanics account for a markedly higher percentage of new HIV diagnoses than non-Hispanic whites (46% vs 33%, respectively, in 2016; total new diagnoses = 443) [7], while in this same year, 34% of SD County residents were Hispanic and 45% were non-Hispanic whites [9]. However, the HIV prevalence rate remains highest in the African American population (40.1 per 100 000 in 2016 vs 22.1 per 100 000 in Hispanics and 10.9 per 100 000 in non-Hispanic whites), and African Americans account for 13.1% of prevalent cases. An estimated 10% of people living with HIV in San Diego County are unaware of their diagnosis [7]. Currently, most positive HIV test results occur at standalone centers where clients self-select for testing. Overall, the location of these testing centers seems to largely match the location where large proportions

Received 3 December 2019; editorial decision 3 January 2020; accepted 14 January 2020.

^aEqual contribution

Correspondence: S. Mehta, MD, DTM&H, D(ABMM), Division of Infectious Diseases and Global Public Health, University of California San Diego, 200 West Arbor Drive #8208, San Diego, CA 92103 (smehta@ucsd.edu).

Open Forum Infectious Diseases®

© The Author(s) 2020. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
DOI: 10.1093/ofid/ofaa024

of MSM in SD reside and where HIV prevalence has historically been the highest [10, 11]. However, given demographic shifts in SD driven notably by gentrification, which has reshaped the urban landscape [12], it is unclear if current HIV testing programs are still adequately covering at-risk populations in various parts of the county.

In this study, we overlaid epidemiologic information on geographically coded testing information to evaluate the correlation between epidemiologic markers of HIV transmission risk (HIV prevalence, HIV incidence, and diagnosis of other STIs) and HIV screening data. We then used these results to identify geographic regions and demographic groups that might benefit from additional HIV screening programs.

METHODS

Health Data

HIV-related and sociodemographic data for SD County were collected from several sources for the time period between 1998 and 2016. HIV prevalence, incident diagnoses, and STI diagnosis data were obtained from the SD County Health and Human Services Agency (HHSA). “HIV incident diagnoses” refers to new HIV diagnoses made during the year. Sociodemographic data from the 2010 census for SD County were downloaded from the American Factfinder Website [13]. HIV testing data were obtained from the HHSA and from the SD Primary Infection Resource Consortium (SDPIRC) and its “Early Test” program [8, 11]. The “Early Test” program operates an independent testing center located in central SD, where most of its tests are administered. The “Early Test” research program offers free HIV screening to persons who provide informed consent to participate. Data from the “Early Test” were used to gain a more complete understanding of testing in SD County and to use the sociodemographic data available for these persons to gauge how access to testing may impact timeliness of diagnosis. Data were geographically organized by either ZIP code (HIV prevalence, STI diagnosis, and HIV testing) or HHSA region (new HIV diagnoses). All data were imported into ArcGIS 10.0 (ESRI, Redlands, CA, USA) and the R Statistical Packages rgeos [14], raster [15], and maptools [16] for visualization and analysis.

Geographic Analyses

To evaluate how effectively current testing reaches persons at risk for HIV infection across SD County, we evaluated the relationships between new HIV diagnoses, HIV prevalence, and STI rates with HIV screening at a ZIP code level. A stepwise approach was used for analyses. First, sociodemographic data from the US 2010 census [13] and HIV screening, prevalence, and new diagnosis data from the HHSA and SDPIRC program were imported into ArcGIS 10.0 (ESRI, Redlands, CA, USA) and R [14, 15, 17]. Second, the relationship between

the numbers of HIV screening tests administered by HHSA in each ZIP code of residence within SD County and HIV prevalence in those ZIP codes based on HHSA estimates for 2010 and 2016 were evaluated. Third, the correlation between HIV screening and new HIV diagnoses within the 6 HHSA regions of SD County were examined. The data were amalgamated from individual ZIP code-level data to the HHSA regions to reduce the risk of privacy breach from ZIP codes with low numbers of new diagnoses. Fourth, the association between STI diagnosis rates and HIV testing by ZIP code of residence was analyzed. Finally, to better understand how a standalone testing site can test individuals living across the County, the geographic and sociodemographic characteristics of individuals presenting to the “Early Test” HIV testing program were evaluated. Unlike data from the HHSA, detailed sociodemographic and geographic data were available for each individual consenting for testing and enrollment into the SDPIRC research program.

Statistical Analyses

SPSS, version 24.0 (Armonk, NY, USA), and R Statistical Package [17] were used to perform statistical analyses and graphing. The relationship between geographic descriptors, geospatial location, and sociodemographic variables was evaluated using parametric testing and nonparametric testing. Correlations were assessed using Spearman’s *R*.

RESULTS

HIV Testing in San Diego (1998–2016)

The SD County HHSA performed 341 259 HIV tests between 1998 and 2016 [8]. These tests were predominantly performed at 5 testing centers in SD County (Figure 1), located in the Central HHSA Region ($n = 2$), and 1 each was performed in the North Coastal, South, and North Central HHSA Regions. The HHSA also operated a mobile testing van that screened individuals at various events throughout the county. Before 2012, the rates of testing per year ranged from a low of 9236 tests in 2006 to 16 797 tests in 1999. Beginning in mid-2011, the state of California implemented the Expanded Testing Program, leading to increased testing, with an average of >30 000 tests annually from 2012 to 2016. (Figure 1C).

The SDPIRC began its “Early Test” in February of 2007, and by the end of 2016 it had administered 37 815 HIV tests. Approximately 13.5% of these tests were reported to the county and included in the HHSA data above. Of the remaining tests, >92% were administered within the Central HHSA region either at testing centers, special events, or door-to-door. The remaining 8.2% were administered by the “Early Test” mobile van at events throughout central SD.

Epidemiology of the San Diego County HIV Epidemic (1997–2016)

The geographical distribution of HIV in SD County has remained steady since 1997, with the Central HHSA Region

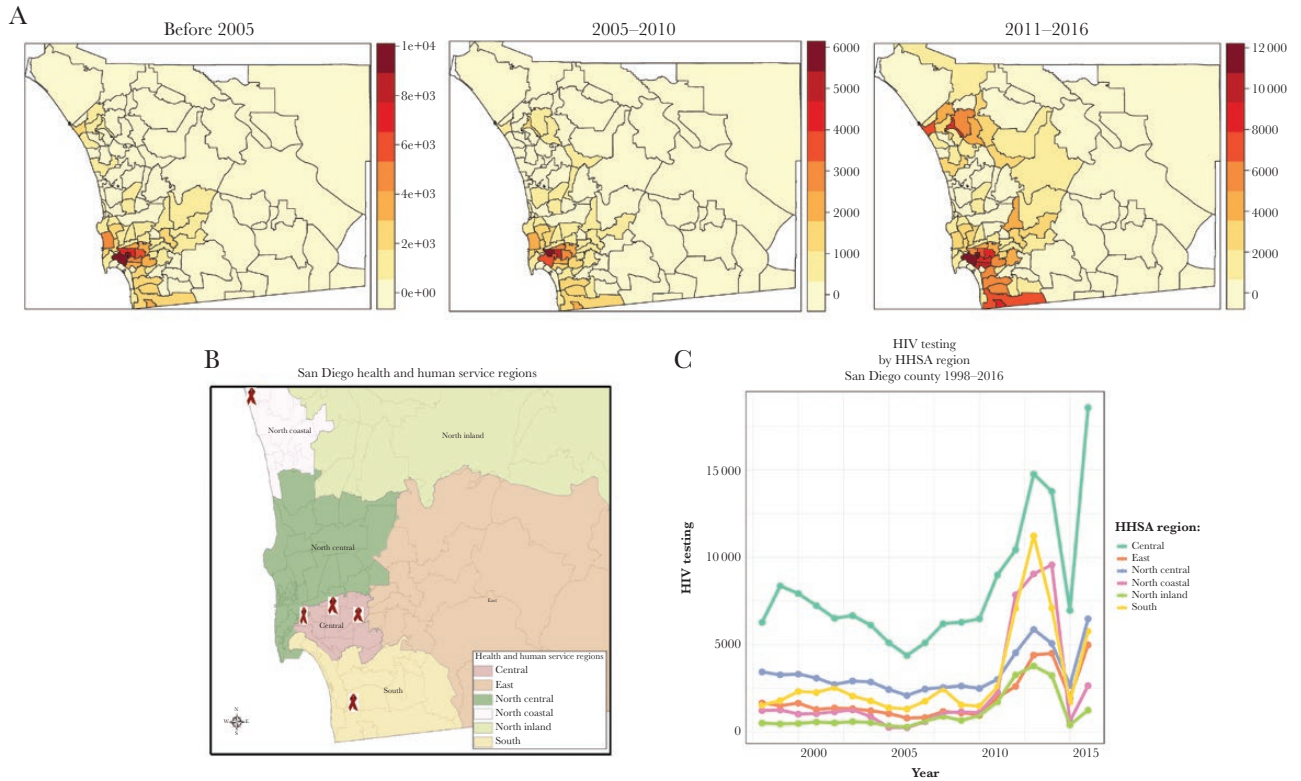


Figure 1. HIV testing in San Diego County (by Health and Human Services Agency [HHSA] and SD Primary Infection Resource Consortium [SDPIRC]), 1998–2016. A, Maps of San Diego County depicting the number of HIV tests administered in each ZIP code over 3 time periods. B, Map of the HHSA Regions of San Diego County with the 5 testing venues marked by a red ribbon. C, Annual number of HIV tests administered by HHSA and SDPIRC by HHSA region from 1998 to 2016. A notable drop in the number of tests performed occurred in 2014 due to programmatic changes.

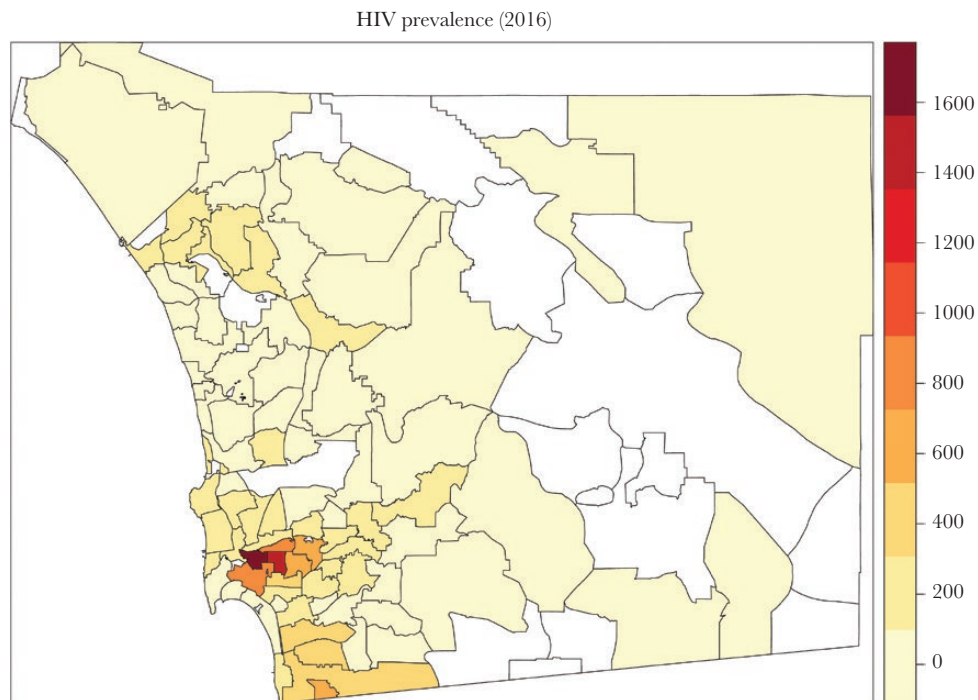


Figure 2. 2016 map of HIV prevalence in San Diego County by ZIP code. Heat map is color-coded according the number of prevalent cases residing in that ZIP code (data from the Health and Human Services Agency).

persistently having the highest estimated prevalence [8]. This region also contains the 2 highest-prevalence ZIP codes, with 2016 estimated prevalence rates of 5.2% and 3.5%. These 2 ZIP codes accounted for 3090/13 643 (22.7%) of the prevalent HIV cases in SD in 2016 (Figure 2; Supplementary Figure 1). A third ZIP code in this region had an additional 794 prevalent cases. Of the remaining 5 HHSA regions, the South Region had the ZIP code with the next highest number of cases, at 625 [8]. The HIV prevalence in the other ZIP codes in SD County with reported HIV infections (range) remained below 2% (0.0%–2.0%).

There was a mean of 426 annual new diagnoses between 1997 and 2016, with new HIV diagnoses mirroring the HIV prevalence in the HHSA regions (Figure 3). Since 2013, ~10% of new diagnoses annually have been made in SD County clinics, and 10% by the SDPIRC. As expected, the highest-prevalence Central HHSA Region had the highest proportion of annual new diagnoses. Over 50% of newly diagnosed cases from 2007 to 2012 resided in the Central HHSA Region, dropping to 42.9% in 2016. In contrast, the proportion of new diagnoses in the rest of SD County increased in the South (18.2% to 20.4%) and the North Inland Regions (4.0% to 7.2%). These are the regions with the highest (60.1%) and third highest (29.1%) proportions of Hispanic individuals, respectively.

HIV Prevalence in Racial/Ethnic Groups Does not Correlate With HIV Testing

The relationship between HIV testing and HIV prevalence among racial/ethnic groups in SD County was evaluated to determine if the rates of HIV testing performed on individuals in

a racial/ethnic group were proportional to prevalence in that group. This was examined for race and ethnicity using data from 2016. Interestingly, when comparing testing in relation to HIV prevalence or new diagnoses, white San Diegans were tested less frequently than Hispanics and African Americans (Supplementary Table 1).

HIV Prevalence in ZIP Codes Correlates With HIV Testing

We evaluated the relationship between HIV testing and HIV prevalence in SD County to determine if the rates of HIV testing performed on individuals from each ZIP code were proportional to prevalence. For the initial comparison, HIV prevalence data from 2010 were chosen for the analysis, as corresponding sociodemographic data were available for that year through the US Census. The total number of HIV tests administered by the HHSA and SDPIRC between 1998 and 2016 for individuals from each ZIP code had a strong correlation with HIV prevalence, ranging from an R^2 of .641 to .932 when using 2010 prevalence estimates (in relation to testing data from 1998, 2002, 2007, 2012) and for the 2016 prevalence estimate (in relation to 2016 testing data) (Figure 4; Supplementary Figure 2). The 3 ZIP codes with the highest HIV prevalence in 2010 were outliers demonstrating fewer tests per prevalent case compared with the expected number by the regression line when using testing data from 1998, 2002, 2007, and 2012. In 2016, 2 additional ZIP codes became outliers, with fewer tests than expected by the regression. Overall, HIV testing was proportionally distributed throughout SD County, with more tests being administered to residents living in areas with higher prevalence. This was despite administration of most of the tests occurring predominantly at 6 testing centers (HHSA: 5; SDPIRC “Early Test”: 1) with fixed locations within the high-prevalence ZIP codes. Specifically focusing on the high-prevalence Hillcrest neighborhood, from 2011 to 2016, the HHSA and SDPIRC administered 0.26 tests per person in the Hillcrest neighborhood alone (ZIP codes 92103 and 92104) compared with 0.06 tests per person in SD County.

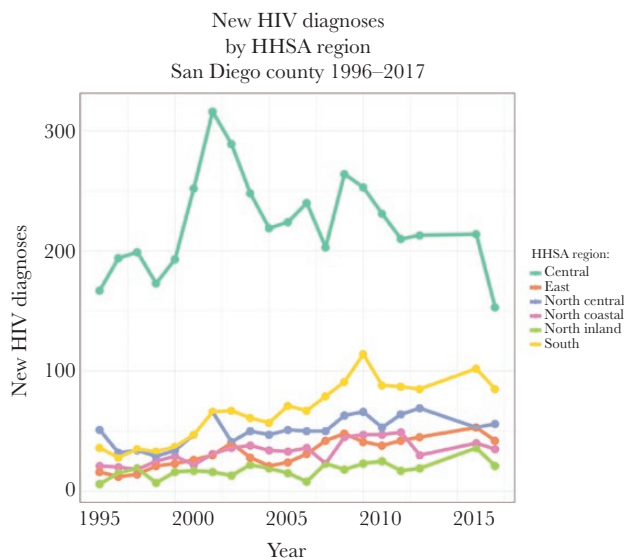


Figure 3. New HIV diagnoses in San Diego County. This figure presents the annual number of new HIV diagnoses in each Health and Human Services Agency (HHSA) region reported to the HHSA from 1996 to 2017. When examining the years 2009–2017, we found a significant decrease in new diagnoses in the Central region ($P = .008$) but no change in the other regions.

New HIV Diagnoses Correlate With HIV Testing by HHSA Regions

Figure 3 illustrates the numbers of new diagnoses each year in each region of the county, and Figure 1 demonstrates the annual number of HIV tests performed in each region. HIV testing in each HHSA region was strongly correlated with the number of new diagnoses the following year in that region ($R^2 = .8$) (Figure 4C).

STI Diagnoses Correlate With New HIV Diagnoses and Testing

Next, STI diagnosis data were analyzed in relation to new HIV diagnoses and HIV testing. Supplementary Figure 3 demonstrates the geographic distribution of new STI diagnoses over time in each HHSA region of the county. From 2013 to 2016, SD County clinics diagnosed 5.5% of reported

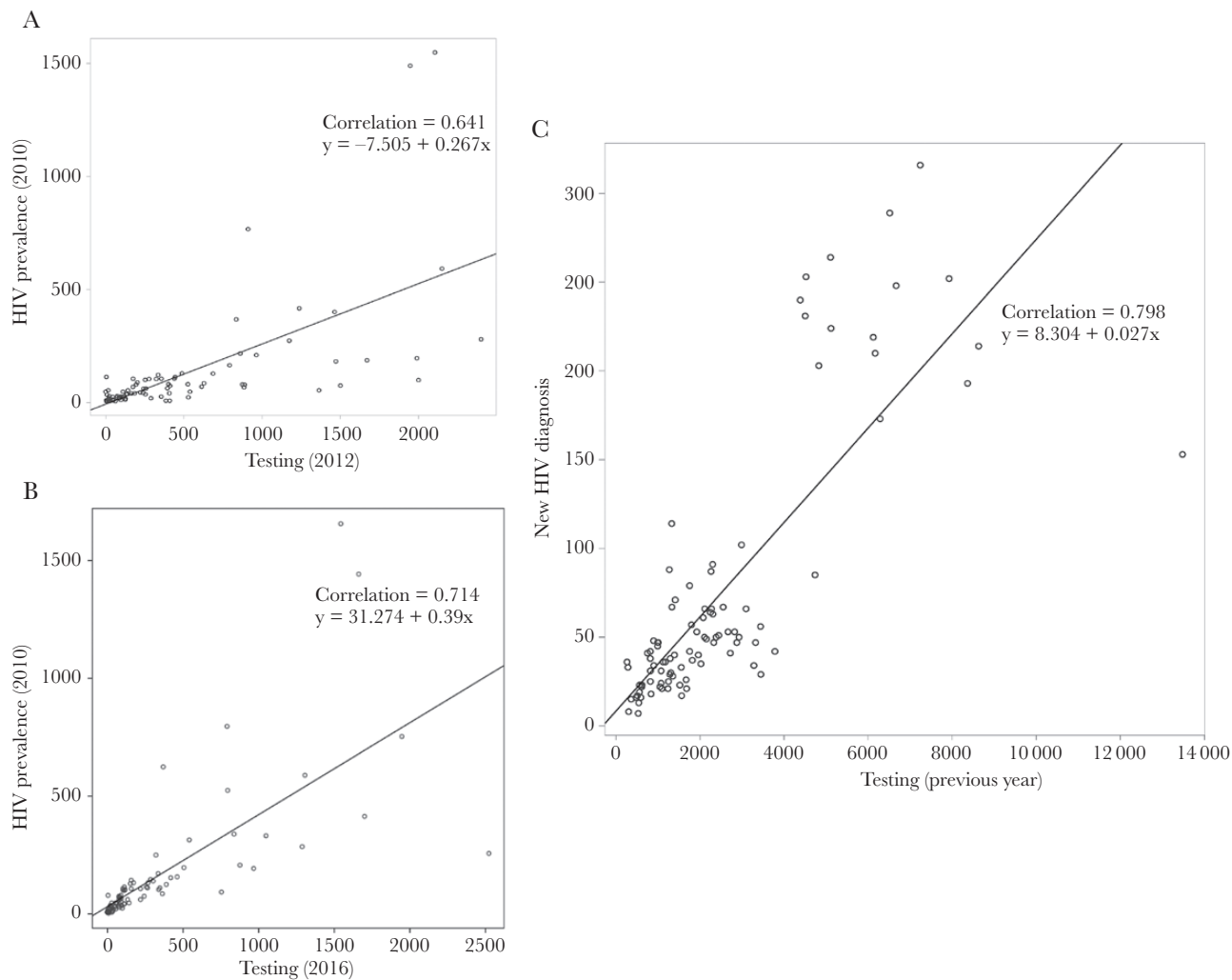


Figure 4. HIV testing by prevalence and new diagnoses in San Diego County. This figure presents the HIV tests administered by San Diego County Public Health and SD Primary Infection Resource Consortium (SDPIRC) in 2012 (A) and 2016 (B) for each ZIP code vs the estimated HIV prevalence of those ZIP codes. The estimated prevalence from 2010 was used for comparisons with 2012 testing data, and the estimated prevalence from 2016 was used for comparisons with 2016 testing data. Tight correlations were observed, with R^2 values of .64 for 2012 and .71 for 2016. C, The relationship between HIV testing and future incident diagnosis HIV tests administered by the Health and Human Services Agency (HHSA) and SDPIRC by HHSA region vs HIV incident diagnoses for those regions demonstrates a strong association ($R^2 = .80$).

chlamydia, 21.5% of gonorrhea, and 30.4% of early syphilis cases. Of note, before 2016, HIV screening in the SD County STI clinics was risk-based, but since 2016 opt-out testing has been in place. The numbers of diagnoses of gonorrhea, chlamydia, and syphilis correlated strongly with new HIV diagnoses in the 5 HHSA regions ($R^2 = .7$ for chlamydia, $R^2 = .7$ for gonorrhea, and $R^2 = .67$ for syphilis) (Supplementary Figure 4). HIV testing was also proportionally distributed throughout the county, with more tests being administered to residents of ZIP codes with higher numbers of syphilis and gonorrhea cases (Figure 5). However, there were again outlier ZIP codes that demonstrated fewer HIV tests per STI case compared with the expected number by the regression line. The correlation was less robust, and a larger number of outliers was noted for the relationship between chlamydia rates and HIV testing.

DISCUSSION

Using a combination of demographic data from the 2010 US census, regional public health data, and research cohort data, the spatio-temporal relationships between HIV testing and the epidemiology of HIV and STIs in SD County were evaluated. Given the geographic heterogeneity of regional HIV epidemics, where particular neighborhoods can have HIV prevalence rates >10 times higher than others, it is important that prevention resources are targeted judiciously. One of the cornerstones of HIV prevention is the early identification of persons with HIV. We assessed the distribution of HIV screening in SD County and found that the numbers of HIV tests performed on individuals residing in particular ZIP codes or HHSA regions were strongly correlated with both prevalent HIV cases, new HIV diagnoses, and STI diagnoses, with only a few outliers. Even though the vast majority of screening

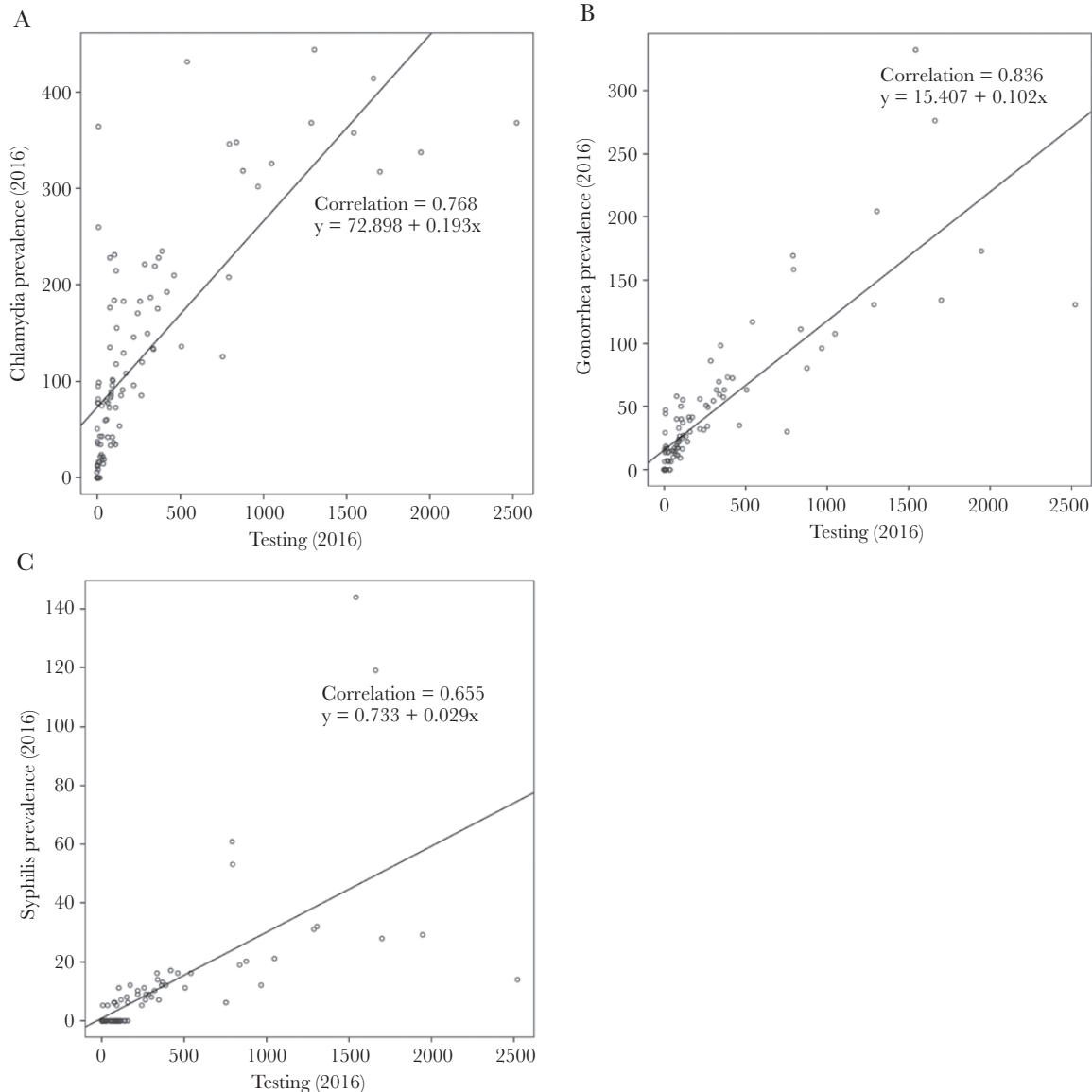


Figure 5. HIV testing by sexually transmitted infection (STI) incident diagnoses in San Diego County. The 2016 STI diagnoses in each ZIP are plotted against the number of HIV tests performed by the Health and Human Services Agency and SD Primary Infection Resource Consortium. A tight correlation was observed, with an R^2 of .77 for chlamydia (A), .84 for gonorrhea (B), and .66 for syphilis (C). However, a number of high-STI incidence ZIP codes are noted (particularly for chlamydia) that have fewer tests than expected based on regression lines utilizing data from all ZIP codes in the county.

tests occurred at fixed venues located in high-prevalence areas (Figure 1), screening of residents of lower-prevalence areas was usually proportional to the prevalence of HIV and rates of new HIV and STI diagnoses in those locales. In other words, at-risk persons from low-prevalence areas of the county were able to travel to these testing venues for HIV screening. This suggested that although the SD epidemic is heterogeneously distributed throughout the county, efforts to screen individuals for HIV that are targeted to the highest-prevalence areas will, at least to some extent, reach at-risk individuals throughout the county.

We also noted that the highest-HIV prevalence ZIP codes in SD County had both the highest number of tests per resident

and the lowest number of tests per diagnosis, suggesting that in these ZIP codes increased and optimized/targeted testing may still be warranted. Phylogenetic and epidemiologic studies have demonstrated a gravity model of transmission in HIV epidemics, where the highest-prevalence zones are drivers of regional epidemics [18, 19]. In terms of demographics, when comparing testing in relation to population HIV prevalence or new diagnoses, white San Diegans were getting tested less frequently than Hispanics and African Americans. Although these results could inform future testing initiatives targeted toward the white population of SD, it has to be emphasized that young Hispanic MSM have been shown to be disproportionately

affected by HIV in SD County [20], and African American MSM have been shown to be significantly more frequently diagnosed in later stages of HIV infection compared with other races [11]. Thus, we still need to optimize screening within these general ethnic and racial breakdowns within SD County.

The HHS regions and ZIP codes with the highest numbers of new STI diagnoses often had fewer HIV tests administered than would be expected if HIV testing was perfectly proportional to STI incidence. STI diagnosis, and in particular rectal gonorrhoea, has been associated with HIV acquisition before, and more HIV testing may be beneficial in those ZIP codes [21, 22]. We also found a strong correlation between new diagnoses of gonorrhoea, chlamydia, and syphilis and new diagnoses of HIV infection. However, in the correlation analyses between HIV testing and STI diagnoses, there were a number of ZIP codes that were outliers, with fewer HIV screening tests than expected based on STI cases, particularly for chlamydia. Although this suggests that rates of STI diagnoses could be used to improve the delivery of HIV screening programs to these ZIP codes or neighborhoods, the expanding implementation of pre-exposure prophylaxis could lead to a disassociation of STI diagnoses with HIV incidence [23].

There are several caveats to these conclusions. Most importantly, it is possible that our observations were impacted by sampling bias. In other words, the more frequent testing in particular ZIP codes may lead to increased diagnosis of HIV infection, thus directly affecting the observed new diagnosis rates and prevalence in that region. This bias seems unlikely to be contributing significantly to our observations, as these analyses included data over a 20-year period, limiting the effect of year-to-year changes in new diagnoses and prevalence. In addition, we did not observe any increases in new diagnoses during the expanded testing performed over the 2011–2012 time period. Second, these data include repeat testers, and it is unclear in the HHS data how many individuals obtained multiple tests over the course of these analyses. In the SDPRIC data, although a similar proportion of Hispanic and white individuals obtaining screening at the Early Test were repeat testers, African Americans were less likely to get tested repeatedly for HIV [24]. This also should not significantly affect the conclusions, as those individuals testing frequently were also likely to have the highest risk of HIV acquisition [24]. Additionally, HIV tests administered as part of routine medical care were not included in these testing data. Given that these voluntary screening tests are usually obtained because of subjective risk for HIV acquisition, they may better reflect perceptions of risk in these geographically defined populations than routine medical tests. However, this may also explain the decreased testing rates observed in the white population, as these individuals may have better access to health care and obtain more HIV testing directly from health care providers. Finally, it remains unclear what the optimal ratio of tests to number of HIV prevalent or

incident cases is. This number will likely depend on the predominant risk factors in the population, and the self-selection of vulnerable individuals for testing.

Mathematical models have suggested that aggressive regular testing for HIV and earlier treatment based on earlier diagnosis have the ability to reduce HIV incidence and drive an epidemic toward extinction [25, 26]. This retrospective study of SD County supported the ability of a small number of standalone testing centers to reach at-risk populations dispersed across the county. More importantly, these methods can highlight geographic areas or demographic segments that may benefit from more intensive screening. The changing demographics of the HIV epidemic in SD need to be considered to continue optimizing screening strategies to reach individuals whom the current testing centers are not reaching.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

All authors have no potential conflicts of interest. We would like to thank the UCSD GIS Library and Kimberly Brouwer for her assistance with the GIS work.

Financial support. This work was supported by grants from the National Institutes of Health (grant numbers AI036214, AI106039, AI93163, MH113477, DA034978, AI100665, AI131385) and the California HIV-1 Research Program (grant number RN07-SD-702).

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. CDC. HIV in the United States and dependent areas. Available at: <https://www.cdc.gov/hiv/statistics/overview/atagance.html>. Accessed 25 January 2019.
2. AIDSvu. AIDSvu. Available at: <http://aidsvu.org/map/?city=SanDiego>. Accessed 25 January 2019.
3. Chen SY, Gibson S, Katz MH, et al. Continuing increases in sexual risk behavior and sexually transmitted diseases among men who have sex with men: San Francisco, Calif, 1999–2001, USA. *Am J Public Health* 2002; 92:1387–8.
4. Johnson LF, Lewis DA. The effect of genital tract infections on HIV-1 shedding in the genital tract: a systematic review and meta-analysis. *Sex Transm Dis* 2008; 35:946–59.
5. Truong HM, Truong HH, Kellogg T, et al. Increases in sexually transmitted infections and sexual risk behaviour without a concurrent increase in HIV incidence among men who have sex with men in San Francisco: a suggestion of HIV serosorting? *Sex Transm Infect* 2006; 82:461–6.
6. Chow EPF, Grulich AE, Fairley CK. Epidemiology and prevention of sexually transmitted infections in men who have sex with men at risk of HIV. *Lancet HIV* 2019; 6:e396–405.
7. County SD. HIV/AIDS Epidemiology Report 2016. San Diego, CA: County of San Diego; 2018.
8. Freitas L. HIV epidemiologic data from San Diego County Department of Public Health. In: Mehta SR, ed. *HIV Testing and Screening Data*. 2019.
9. US Census Bureau. Quick Facts: San Diego County 2019. Washington DC: US Department of Commerce; 2019.
10. Morris SR, Little SJ, Cunningham T, et al. Evaluation of an HIV nucleic acid testing program with automated Internet and voicemail systems to deliver results. *Ann Intern Med* 2010; 152:778–85.
11. Hoenigl M, Green N, Mehta SR, Little SJ. Risk factors for acute and early HIV infection among men who have sex with men (MSM) in San Diego, 2008 to 2014: a cohort study. *Medicine (Baltimore)* 2015; 94:e1242.

12. Governing.com. Gentrification. Available at: <https://www.governing.com/gov-data/san-diego-gentrification-maps-demographic-data.html>. Accessed June 2019.
13. US Census Bureau. American Factfinder. Washington DC: US Department of Commerce; **2019**.
14. Bivand R, Rundel C. rgeos: Interface to Geometry Enging - Open Source ["GEOS"]. *R Package, Version 04-3*. Vienna: R Foundation for Statistical Computing; **2019**.
15. Hijmans R. raster: Geographic Data Analysis and Modeling. *R Package, Version 29-5*. Vienna: R Foundation for Statistical Computing; **2019**.
16. Bivand R, Lewin-Koh N. maptools: Tools for Handling Spatial Objects. *R Package, Version 09-5*. Vienna: R Foundation for Statistical Computing; **2019**.
17. R Core Team. R: A Language and Environment for Statistical Computing. Vienna: R Foundation for Statistical Computing; **2013**.
18. Chaillon A, Avila-Rios S, Dennis A, et al. Phylogeographic analysis suggests gravity model of HIV transmission in Mexico. Boston: CROI; **2018**.
19. Faria NR, Rambaut A, Suchard MA, et al. HIV epidemiology. The early spread and epidemic ignition of HIV-1 in human populations. *Science* **2014**; 346:56–61.
20. Hoenigl M, Chaillon A, Morris SR, Little SJ. HIV infection rates and risk behavior among young men undergoing community-based testing in San Diego. *Sci Rep* **2016**; 6:25927.
21. White E, Dunn DT, Desai M, et al. Predictive factors for HIV infection among men who have sex with men and who are seeking PrEP: a secondary analysis of the PROUD trial. *Sex Transm Infect* **2019**; 95:449–454.
22. Mullick C, Murray J. Correlations between HIV infection and rectal gonorrhoea incidence in men who have sex with men: implications for future HIV pre-exposure prophylaxis trials. *J Infect Dis* **2020**; 221:214–217.
23. Serpa JA, Huynh GN, Nickell JB, Miao H. HIV pre-exposure prophylaxis and increased incidence of sexually transmitted infections in the United States. *Clin Infect Dis* **2019**. [Epub ahead of print]
24. Hoenigl M, Anderson CM, Green N, et al. Repeat HIV-testing is associated with an increase in behavioral risk among men who have sex with men: a cohort study. *BMC Med* **2015**; 13:218.
25. Cohen MS, Smith MK, Muessig KE, et al. Antiretroviral treatment of HIV-1 prevents transmission of HIV-1: where do we go from here? *Lancet* **2013**; 382:1515–24.
26. Granich R, Kahn JG, Bennett R, et al. Expanding ART for treatment and prevention of HIV in South Africa: estimated cost and cost-effectiveness 2011–2050. *PLoS One* **2012**; 7:e30216.