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Predicting Emergence of Primary and Secondary Syphilis Among Women of Reproductive Age in US Counties

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Abstract

Background: Syphilis, a sexually transmitted infection that can cause severe congenital disease when not treated during pregnancy, is on the rise in the United States. Our objective was to identify US counties with elevated risk for emergence of primary and secondary (P&S) syphilis among women of reproductive age.

Methods: Using syphilis case reports, we identified counties with no cases of P&S syphilis among women of reproductive age in 2017 and 1 case or more in 2018. Using county-level syphilis and sociodemographic data, we developed a model to predict counties with emergence of P&S syphilis among women and a risk score to identify counties at elevated risk.

Results: Of 2451 counties with no cases of P&S syphilis among women of reproductive age in 2017, 345 counties (14.1%) had documented emergence of syphilis in 2018. Emergence was predicted by the county's P&S syphilis rate among men; violent crime rate; proportions of Black, White, Asian, and Hawaiian/Pacific Islander persons; urbanicity; presence of a metropolitan area; population size; and having a neighboring county with P&S syphilis among women. A risk score of 20 or more identified 75% of counties with emergence.

Conclusions: Jurisdictions can identify counties at elevated risk for emergence of syphilis in women and tailor prevention efforts. Prevention of syphilis requires multidisciplinary collaboration to address underlying social factors.

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Syphilis, a bacterial sexually transmitted infection (STI), is particularly concerning in women of reproductive age, because syphilis can be transmitted to the fetus during pregnancy and cause congenital syphilis. Congenital syphilis is associated with miscarriage, stillbirth, preterm delivery, infant death, and physical and neurological sequelae for infants who survive.^{1,2} Since 2013, there have been substantial increases in primary and secondary (P&S) syphilis case rates among women of reproductive age (15–44 years) in the United States, with mirrored increases in congenital syphilis.

In 2019, 1870 cases of congenital syphilis were reported to the Centers for Disease Control and Prevention (CDC), with significant racial/ethnic disparities.³ Case counts continued to increase in 2020.⁴ Although once geographically concentrated, syphilis affects more US communities every year. In 2013, only 379 of the 3143 counties reported 1 or more case of P&S syphilis among women of reproductive age, whereas 899 counties reported cases in 2019 (unpublished CDC data). Prevention of congenital syphilis requires prevention of community transmission of syphilis, as well as timely diagnosis and treatment of pregnant women with syphilis.⁴

Screening for syphilis can identify infections and, when combined with prompt treatment, reduce sexual and vertical transmission. Currently, syphilis screening in women is universally recommended for women who are pregnant or living with HIV. All pregnant women should be screened for syphilis at the first prenatal visit, with repeat testing at 28 weeks' gestation and at delivery for women with individual risk factors or who live in communities with high syphilis rates.⁵

Syphilis screening based on individual risk factors has limitations. During 2012 to 2016, half of pregnant women with syphilis did not report traditional risk factors during public health case investigation, such as high-risk sexual behaviors or substance use.⁶ Individual risk factors for syphilis acquisition may also change over time, with recent increases in the reported use of methamphetamines and injection drugs among women with P&S syphilis.⁷ In addition, health care providers may not consistently or comprehensively ask patients about sexual behaviors and, therefore, fail to ascertain risk factors.^{8,9} Given the limitations of risk-based screening, understanding community prevalence and identifying communities at risk for new cases of syphilis among women of reproductive age may help guide screening and prevention efforts.

The objective of this study was to identify US counties with elevated risk for emergence of P&S syphilis among women of reproductive age. Specifically, we sought to develop a predictive model and user-friendly risk score using syphilis case report data and county-level sociodemographic data to identify counties that may have 1 or more case of P&S syphilis among women of reproductive age after reporting zero cases in the prior year. By identifying counties at elevated risk for emergence of syphilis in women of reproductive age, public health authorities can prepare for increases and implement strategies to prevent both syphilis and congenital syphilis.

METHODS

Analytic Sample and Outcome Classification

Syphilis is a reportable condition in all 50 states and the District of Columbia and is a nationally notifiable disease. Using the Council of State and Territorial Epidemiologists' stage-specific case definitions for syphilis, all US jurisdictions provide case data to CDC through the National Notifiable Diseases Surveillance System (NNDSS).¹⁰ We used the NNDSS data to create an analytic sample that included US counties and county equivalents with zero reported cases of P&S syphilis among women of reproductive age in 2017. Our outcome of interest, which we refer to as "emergence of syphilis in women," was whether a county then reported 1 or more case of P&S syphilis among women of reproductive age in 2018 (yes/no) and was chosen to identify cases of syphilis in women most likely to be incident infections. Of note, changes to Alaska county codes led to 3 inconsistent county equivalent areas between data sources, resulting in 3140 counties considered for analysis. All data management and analyses were performed using Stata (version 16, Statacorp LP).

County-Level Predictive Factors

Candidate factors considered for inclusion were factors with available county-level data from 2017 that we theorized to be associated with syphilis or were previously identified as being associated with syphilis or congenital syphilis.^{6,7,11,12} All candidate factors considered for inclusion had less than 10% missing data. Candidate factors were county-level measures of social and economic status, population size and urbanicity, health care access, and sexual and reproductive health. Data on candidate variables were drawn from multiple sources, including the County Health Rankings Roadmaps 2019 and 2020 analytic files, which compile data from the US Census, Federal Bureau of Investigation's Uniform Crime Reporting program, US Department of Agriculture, American Community Survey, National Center for Health Statistics, Small Area Health Estimates, and Area Health Resource files.¹³ We also used data from the 2018 CDC Social Vulnerability Index and NNDSS. When available, we used data from 2017, although some data were based on a range of years, such as 2014 to 2018.

County demographics (proportions of persons identifying with racial and Hispanic ethnicity groups, proportions of persons living in urban areas, and population size), socioeconomic status (income inequality measured by the ratio of household income at the 80th percentile relative to household income at the 20th percentile) and health status (ratio of primary care physicians to population, number of births per 1000 female population aged 15 to 19 years, proportion of the population uninsured) were obtained from the County Health Rankings and Roadmaps 2019 and 2020 analytic files. We also considered the county violent crime rate (crimes per 100,000 persons) as a proxy for complex relationships between socioeconomic status and substance use.¹² In addition, we considered proportions of the population identifying as White, Black, Hispanic, American Indian/Alaskan Native, Asian, and Hawaiian/Pacific Islander from the County Health Rankings and Roadmaps 2019 file, based on census population estimates for 2017, to investigate the underlying social, environmental, and structural factors for which race and ethnicity may serve as a proxy.¹⁴

We used county-level data from the 2018 CDC Social Vulnerability Index for estimates on the proportion of the population living below the poverty line, unemployment rate, and household crowding (measured as the proportion of occupied housing units with more people than rooms), which is based on the American Community Survey from 2014 to 2018.¹⁵ The presence of a metropolitan area was obtained from the 2010 US Department of Agriculture Rural Urban Commuting Area Codes, and we defined counties with metropolitan areas as those with metropolitan rural-urban commuting area codes.¹⁶

We hypothesized that syphilis rates in men may predict increases in syphilis among women. County-level case rates of P&S syphilis among men were calculated as the number of cases reported to NNDSS in 2017 per 100,000 male population. In addition, we hypothesized that “spillover” from neighboring counties might contribute to syphilis emergence. We used 2017 NNDSS data and the Polygon Neighbors tool in ArcGIS Pro to create a binary (yes/no) variable for whether a county had a neighboring county with P&S syphilis among women of reproductive age.¹⁷

Predictive Factor Selection and Model Building

The first step in building our predictive model was to explore descriptive statistics of all candidate predictive factors. All factors that were continuous variables were transformed into binary (dichotomized at the median) and tertile forms, and the functional form with better model fit for each factor was selected for model building. We assessed the crude association between the binary and tertile forms of the factors and our outcome of interest (emergence of syphilis) and used Akaike Information Criterion to determine which form had better fit. We used adaptive least absolute shrinkage and selection operator (lasso) regression with 10-fold cross validation to select factors for retention in a final multivariable model.¹⁸ Through penalizing the absolute size of coefficients in the regression model, lasso excludes the weaker factors from the model and includes only the strongest predictors. An adaptive lasso was chosen as the method for factor selection to create a more parsimonious model. Nineteen predictive factors were included in the lasso regression. The factors identified through lasso regression for optimal predictive performance were included in the final logistic regression model to generate adjusted odds ratios.

Risk Score Creation and Cutoff Selection

Using the final predictive model, we created risk scores and determined an optimal risk score cutoff to define counties at elevated risk of syphilis emergence. We assigned each factor in the final model a predictor score, calculated by multiplying the adjusted odds ratio by 2 and rounding to the nearest integer. We summed predictor scores to obtain an overall risk score for each county. To identify the optimal risk score cutoff, we calculated the sensitivity and specificity of each potential risk score cutoff by comparing the counties predicted to have elevated risk for emergence at each risk score with the counties that truly reported 1 or more case of P&S syphilis in 2018.¹² We determined a priori that we wanted a risk score cutoff with a sensitivity and specificity closest to 80%, prioritizing a higher sensitivity, and that identifies a lower number of counties.

Sensitivity Analysis

Previous studies used the rate of P&S syphilis among men who have sex with men (MSM) to predict county-level increases in congenital syphilis.¹² We conducted a sensitivity analysis to assess whether including the rate of P&S syphilis among MSM as a factor in the model improved model fit, in addition to or instead of the rate of P&S syphilis among all men. The rate of P&S syphilis among MSM was derived similarly to the rate of P&S syphilis among all men, using NNDSS syphilis data from 2017, identified by gender and gender of sex partners and estimated MSM population.¹⁹ The P&S syphilis rate among all men and among MSM were included in the lasso regression, together and separately, and model fit diagnostics were used to identify which predictor to use in the final model.

RESULTS

Among 3140 US counties, 2451 (78.1%) counties had no reported cases of P&S syphilis among women of reproductive age in 2017 and were included in the analysis. Of the 2451 counties with no cases in 2017, 2254 (92.0%) had no cases in 2016 and 1993 (81.3%) had no cases in 2013 to 2016. In 2018, 345 counties (14.1%) had emergence of syphilis among women of reproductive age. Most of the 345 counties ($n = 195$; 56.5%) were in the south, followed by the midwest ($n = 80$; 23.2%), west ($n = 44$; 12.8%), and northeast ($n = 26$; 7.5%). For the 345 counties with documented emergence in 2018, the range of cases was 1 to 6.

Nineteen predictive factors were considered for inclusion in the final multivariable model (Table 1). For most factors, there were differences between counties with and without emergence of syphilis in women in 2018. For example, the median population size and the proportion of the population living in an urban area were higher for counties with emergence of syphilis. Based on the lasso regression, 10 factors were selected for inclusion in the final predictive model: neighboring county with 1 or more case of P&S syphilis among women of reproductive age, P&S syphilis rate among men, violent crime rate, proportions of the population identifying as Black, White, Asian, and Hawaiian/Pacific Islander, proportion of the population living in an urban area, presence of a metropolitan area, and population size (Table 2).

In the final multivariable logistic regression model, large population size, high P&S syphilis rate in men, and high proportion of the population identifying as Black were the strongest predictors of emergence of syphilis in women with the largest adjusted odds ratios. The area under the receiver operating characteristic curve for the predictive model was 80.6% (Fig. 1).

Based on the adjusted odds ratios from the final model, the predictor scores for each factor ranged from 0 to 7, and the overall county-level risk scores (summation of the predictor scores) ranged from 0 to 32. We identified the optimal risk score cutoff of 20 or higher, which corresponded to a sensitivity of 75.4%, a specificity of 65.6%, and identification of 984 counties with elevated risk for emergence of P&S syphilis among women of reproductive age (Table 3).

In a sensitivity analysis to determine whether including the rate of P&S syphilis among all men and the rate of P&S syphilis among MSM improved model fit, lasso regression selected only the rate among all men for inclusion in the final model. The model using only P&S syphilis among all men had slightly better model fit compared with the model using only P&S syphilis among MSM, based on Akaike Information Criterion and area under the receiver operating characteristic curve.

Of the 984 counties that were identified with elevated risk for emergence through the predictive model and risk score, 260 had documented emergence of syphilis in 2018. Eighty-five counties were not identified as being at elevated risk but did have documented emergence in 2018. Of these 85 counties, 71 counties had only 1 case reported in 2018.

DISCUSSION

Using available county-level sociodemographic and health factors, we built a predictive model to identify counties with elevated risk for emergence of P&S syphilis among women of reproductive age. Public health authorities can use available data (Supplemental Table, <http://links.lww.com/OLQ/A767>) and these risk scores to identify counties with elevated risk for emergence of syphilis in women and can allocate resources and tailor interventions to prevent syphilis among women. Through preventing syphilis in women and through identifying and treating women and their partners who have syphilis, the worsening congenital syphilis epidemic in the United States could be stopped.⁴

For counties identified with elevated risk for emergence (Supplemental File, <http://links.lww.com/OLQ/A768>), focused prevention efforts for syphilis might include the following: prioritization of health department investigations for reactive syphilis tests among women of reproductive age and their partners, health care provider education on syphilis, partnership building to facilitate partner services and ensure access to timely treatment, innovative approaches for screening and community engagement, and culturally competent sexual health education and promotion for persons of reproductive age in the community. These efforts should be coupled with strategies to prevent congenital syphilis, which might include improving access to prenatal care, ensuring syphilis screening at the first prenatal care visit with repeat screening at 28 weeks' gestation and delivery when indicated, and ensuring adequate treatment for pregnant women with syphilis.^{4,5} Public health authorities could consider regional approaches to syphilis and congenital syphilis prevention, as well as strategies for specific counties and for specific communities, which may not be identified through county designations.

Of the 10 factors that were predictive of county-level emergence of syphilis in women of reproductive age, 2 were measures of local syphilis epidemiology: the rate of P&S syphilis among men and the presence of a neighboring county with 1 or more case of P&S syphilis in women of reproductive age. Eight factors were general social, structural, and economic factors, indicating the importance of the social determinants of health in the ongoing heterosexual syphilis epidemic in the United States. Similar factors were found in previous analyses to predict the emergence of congenital syphilis¹²; this was expected given that congenital syphilis is a downstream effect of untreated syphilis during pregnancy.

This analysis emphasizes the need for multilevel, multifactorial approaches for syphilis prevention.

Our analysis highlights complex relationships between social, environmental, and structural factors and sexual health within communities. The inclusion of the proportions of the population identifying as Black, White, Asian, and Hawaiian/Pacific Islander as predictors in the model demonstrate the complexity of the underlying social factors, the impact of structural racism on sexual health, and the need for tailored, culturally sensitive, prevention efforts to address inequities.¹⁴ Each of these racial groups may represent geographically diverse communities with diverse experiences.²⁰ Understanding the epidemiology of syphilis at the county level, as well as social factors of the communities who might be disproportionately affected, will be important for the development and implementation of public health interventions for communities at elevated risk. These interventions should be developed and implemented with a health equity focus.

Prior studies and frameworks have demonstrated the interaction of individual behaviors, social and sexual networks, sociocultural contexts, and community prevalence in the prevention of STIs.^{21,22} Sexual network characteristics, not individual behaviors, account for the higher prevalence of HIV among Black MSM.^{23,24} Studies of sexual partnership mixing in both heterosexual and MSM networks have demonstrated that people in racial or ethnic minority groups often have sex partners of the same race/ethnicity, contributing to worsening disparities in STIs.^{25,26} As sexual networks and social factors such as poverty and discrimination drive disparities in STI rates in the United States,²⁷ effective prevention of syphilis will require multidisciplinary collaborations. Public health research and programs can improve health equity by recognizing racism as a root cause.^{14,28}

This analysis is limited by the availability, accuracy, and timeliness of county-level data. Data on some factors that we hypothesized to be important predictors, such as substance use or homelessness, were either not available or not useable due to high levels of missing data. In addition, most of the factors that were included in our final model were general social factors and were indirect and imperfect measures of other constructs. Specifically, violent crime is likely a proxy for substance use and other factors related to socioeconomic status and structural inequities,^{29,30} and race is likely a proxy for complex social, environmental, and structural factors.¹⁴ Future analyses can improve understanding of the relationship between the social determinants of health and syphilis in women by incorporating direct measures of additional predictors, such as substance use, as they become available. Further, county-level estimates for a given year may reflect data from 1 to 10 years before our outcome of interest, depending on the data source. Thus, recent changes in predictive factors may not be captured in our analysis.

This analysis should be interpreted within the ecological framework and may be subject to biases. Because this is an ecological model, the identified county-level factors should not be interpreted as modifiable risk factors for acquisition of syphilis. Most counties with zero syphilis cases in 2017 had zero cases in the preceding years, suggesting that counties included in our analytic sample represent areas without syphilis. Still, underreporting or overreporting of a single case could result in miscategorization of our outcome of interest.

Underreporting is possible if a person with syphilis does not present for clinical evaluation because of the limited access to care or other barriers or if clinicians or health department staff do not appropriately diagnose or report cases of syphilis. Continued education for providers and public health personnel and reduction of barriers to quality sexual health care can improve clinical care and minimize misclassification bias in future case reporting and analyses. Finally, as most counties with emergence of P&S syphilis in women of reproductive age in 2018 were in the south, this model may be more predictive for the south compared with other US regions. We did not build regional predictive models due to sample size limitations. Given regional differences in syphilis incidence and prevalence, future analyses are needed to understand regional predictive factors.³

In conclusion, public health authorities can use available county-level data and this risk score to identify US counties with elevated risk for emergence of P&S syphilis among women of reproductive age and can implement tailored prevention and control efforts for syphilis and congenital syphilis. Effective prevention of syphilis and congenital syphilis will require multidisciplinary collaborations to address the underlying social and structural predictors of sexual health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Cooper JM, Sánchez PJ. Congenital syphilis. *Semin Perinatol* 2018; 42:176–184. [PubMed: 29627075]
2. Schlueter A, Doshi U, Garg B, et al. Adverse pregnancy outcomes associated with maternal syphilis infection. *J Matern Fetal Neonatal Med* 2021; 1–6. doi: 10.1080/14767058.2021.1895740.
3. 2019 Surveillance Report: Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2019. Atlanta, GA: Department of Health and Human Services, 2021. Available at: <https://www.cdc.gov/std/statistics/2019/default.htm>. Accessed April 19, 2021.
4. Bowen VB, McDonald R, Grey JA, et al. High congenital syphilis case counts among U.S. infants born in 2020. *N Engl J Med* 2021; 385:1144–1145. [PubMed: 34525291]
5. Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *MMWR Recomm Rep* 2021; 70:1–187.
6. Trivedi S, Williams C, Torrone E, et al. National trends and reported risk factors among pregnant women with syphilis in the United States, 2012–2016. *Obstet Gynecol* 2019; 133:27–32. [PubMed: 30531570]
7. Kidd SE, Grey JA, Torrone EA, et al. Increased methamphetamine, injection drug, and heroin use among women and heterosexual men with primary and secondary syphilis—United States, 2013–2017. *MMWR Morb Mortal Wkly Rep* 2019; 68:144–148. [PubMed: 30763294]
8. Brookmeyer KA, Coor A, Kachur RE, et al. Sexual history taking in clinical settings: A narrative review. *Sex Transm Dis* 2021; 48:393–402. [PubMed: 33093285]
9. Wimberly YH, Hogben M, Moore-Ruffin J, et al. Sexual history-taking among primary care physicians. *J Natl Med Assoc* 2006; 98:1924–1929. [PubMed: 17225835]

10. Council of State and Territorial Epidemiologists. Syphilis 2018 Case Definition. Atlanta, GA: U.S. Department of Health & Human Services, 2018. Available at: <https://www.cdc.gov/nndss/conditions/syphilis/case-definition/2018/>. Accessed February 10, 2021.
11. Gregory ECW, Ely DM. Trends and characteristics of sexually transmitted infections during pregnancy: United States, 2016–2018. *Natl Vital Stat Rep* 2020; 69:1–11.
12. Cuffe KM, Kang JDY, Dorji T, et al. Identification of US counties at elevated risk for congenital syphilis using predictive modeling and a risk scoring system. *Sex Transm Dis* 2020; 47:290–295. [PubMed: 32044864]
13. Robert Wood Johnson Foundation. 2019, 2020 County Health Rankings & Roadmaps. Available at: <https://www.countyhealthrankings.org/explore-health-rankings/rankings-data-documentation>. Accessed November 2, 2020.
14. Boyd RW, Lindo EG, Weeks LD, McLemore MR. On racism: A new standard for publishing on racial health inequities. 2020. Available at: <https://www.healthaffairs.org/doi/10.1377/hblog20200630.939347/full/>. Accessed July 2, 2020.
15. Centers for Disease Control and Prevention/ Agency for Toxic Substances and Disease Registry/ Geospatial Research, Analysis, and Services Program. CDC/ATSDR Social Vulnerability Index 2018 Database US. Available at: https://www.atsdr.cdc.gov/placeandhealth/svi/data_documentation_download.html. Accessed November 10, 2020.
16. United States Departments of Agriculture. Rural-urban commuting area codes. Available at: <https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes/>. Accessed November 11, 2020.
17. Esri Inc, 2020. ArcGIS Pro 2.6.4.
18. Stata. Introduction to Lasso. Available at: <https://www.stata.com/manuals/lassolassointro.pdf>. Accessed November 12, 2020.
19. Grey JA, Bernstein KT, Sullivan PS, et al. Estimating the population sizes of men who have sex with men in US states and counties using data from the American Community Survey. *JMIR Public Health Surveill* 2016; 2:e14. [PubMed: 27227149]
20. U.S. Department of Health and Human Services, Office of Minority Health. Profile: Native Hawaiians/Pacific Islanders. Available at: <https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=3&lvlid=65>. Accessed February 11, 2021.
21. Hogben M, Dittus PJ, Leichter JS, et al. Social and behavioural research prospects for sexually transmissible infection prevention in the era of advances in biomedical approaches. *Sex Health* 2020; 17:103–113. [PubMed: 32119815]
22. Baral S, Logie CH, Grosso A, et al. Modified social ecological model: A tool to guide the assessment of the risks and risk contexts of HIV epidemics. *BMC Public Health* 2013; 13:482. [PubMed: 23679953]
23. Zarwell M, Robinson WT. Network properties among gay, bisexual and other men who have sex with men vary by race. *AIDS Behav* 2019; 23:1315–1325. [PubMed: 30725398]
24. Bohl DD, Raymond HF, Arnold M, et al. Concurrent sexual partnerships and racial disparities in HIV infection among men who have sex with men. *Sex Transm Infect* 2009; 85:367–369. [PubMed: 19773457]
25. Doherty IA, Adimora AA, Muth SQ, et al. Comparison of sexual mixing patterns for syphilis in endemic and outbreak settings. *Sex Transm Dis* 2011; 38:378–384. [PubMed: 21217418]
26. Birkett M, Neray B, Janulis P, et al. Intersectional identities and HIV: Race and ethnicity drive patterns of sexual mixing. *AIDS Behav* 2019; 23:1452–1459. [PubMed: 30242531]
27. Adimora AA, Schoenbach VJ. Social context, sexual networks, and racial disparities in rates of sexually transmitted infections. *J Infect Dis* 2005; 191(Suppl 1):S115–S122. [PubMed: 15627221]
28. Ford CL, Airhihenbuwa CO. Critical race theory, race equity, and public health: Toward antiracism praxis. *Am J Public Health* 2010; 100(S1):S30–S35. [PubMed: 20147679]
29. White HR, Jackson KM, Loeber R. Developmental sequences and co-morbidity of substance use and violence. In: Krohn MD, Lizotte AJ, Hall GP, eds. *Handbook on Crime and Deviance*. New York, NY:Springer, 2009:433–468.

30. Carter PM, Cranford JA, Buu A, et al. Daily patterns of substance use and violence among a high-risk urban emerging adult sample: Results from the Flint Youth Injury Study. *Addict Behav* 2020; 101:106127. [PubMed: 31645000]

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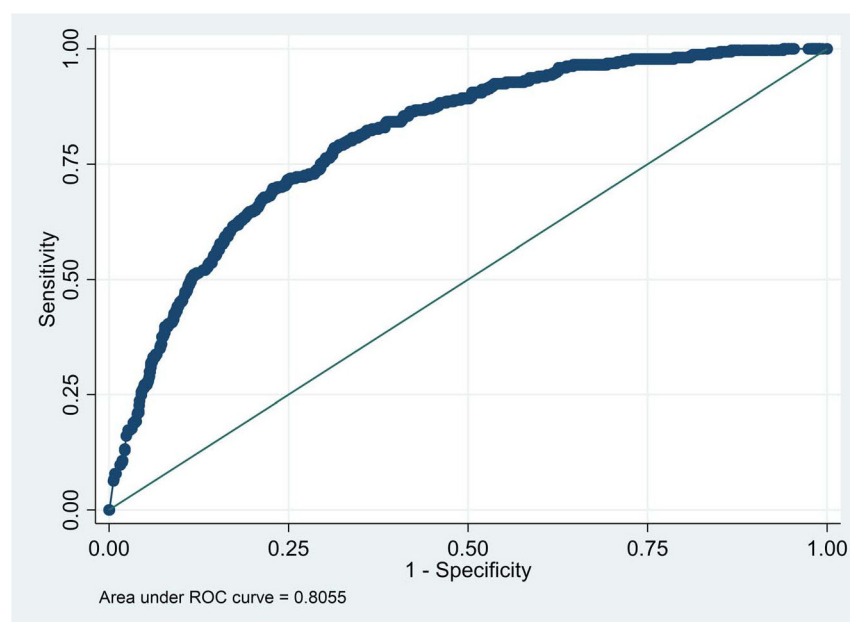


Figure 1.
Receiver operating characteristic curve for final predictive model.

TABLE 1.

Demographic, Socioeconomic, and Health Factors in US Counties With No Reported Cases of Primary and Secondary Syphilis Among Women of Reproductive Age in 2017 (N = 2451 Counties)

| Demographic factors | All Eligible Counties* (N = 2451) | | | Counties With Emergence of Syphilis in Women in 2018 [†] (n = 345) | | | Counties With No Emergence of Syphilis in Women in 2018 [‡] (n = 2106) | | |
|---|-----------------------------------|-----------------|--|---|--------------------|--|---|-----------------|--|
| | Median | IQR | | Median | IQR | | Median | IQR | |
| American Indian/Alaskan Native population (%) | 0.6 | 0.4–1.4 | | 0.6 | 0.4–1.4 | | 0.6 | 0.4–1.4 | |
| Asian population (%) | 0.6 | 0.4–1.0 | | 0.9 | 0.5–1.7 | | 0.6 | 0.4–0.9 | |
| Black population (%) | 1.4 | 0.6–6.0 | | 5.3 | 1.5–19.3 | | 1.2 | 0.6–4.7 | |
| Hawaiian/Pacific Islander population (%) | 0.05 | 0.03–0.1 | | 0.07 | 0.04–0.1 | | 0.05 | 0.02–0.09 | |
| Hispanic population (%) | 3.7 | 2.1–8.0 | | 4.8 | 2.7–9.0 | | 3.5 | 2.0–7.8 | |
| White population (%) | 86.9 | 70.9–93.5 | | 76.3 | 61.2–87.3 | | 88.4 | 73.0–93.9 | |
| Population size (count) | 19,076.5 | 8809.0–40,801.0 | | 45,032.0 | 21,718.0–102,429.0 | | 16,886 | 7969.0–35,110.0 | |
| Population living in urban area (%) | 33.1 | 0.0–55.3 | | 50.3 | 28.8–71.4 | | 30.7 | 0.0–52.1 | |
| Socioeconomic factors | | | | | | | | | |
| | Median | IQR | | Median | IQR | | Median | IQR | |
| Household crowding (% of occupied housing units with more people than rooms) | 1.8 | 1.1–2.8 | | 2.1 | 1.4–2.9 | | 1.7 | 1.1–2.7 | |
| Income inequality (80:20 ratio) | 4.3 | 4.0–4.8 | | 4.5 | 4.1–5.1 | | 4.3 | 3.9–4.8 | |
| Population living below poverty line (%) | 14.5 | 10.8–19.0 | | 16.0 | 11.6–20.6 | | 14.4 | 10.6–18.6 | |
| Unemployment (proportion of civilian adults in labor force who are unemployed) | 5.2 | 3.7–6.9 | | 5.9 | 4.3–7.4 | | 5.1 | 3.5–6.8 | |
| Violent crime (cases per 100,000) [§] | 178.4 | 105.5–288.2 | | 248.0 | 161.9–373.0 | | 169.2 | 98.9–273.8 | |
| Health factors | | | | | | | | | |
| | Median | IQR | | Median | IQR | | Median | IQR | |
| Primary care physician ratio (population served by 1 physician) [§] | 2190.3 | 1490.2–3267.0 | | 2141.6 | 1440.9–3167.7 | | 2203.6 | 1497.5–3282.0 | |
| P&S syphilis rate in men (cases per 100,000) | 0.0 | 0.0–5.7 | | 5.3 | 0.0–11.1 | | 0.0 | 0.0–4.4 | |
| Teen births (number of births per 1000 female population aged 15–19 y) [§] | 28.8 | 19.5–39.8 | | 30.4 | 21.6–40.4 | | 28.6 | 19.2–39.8 | |
| Uninsured (%) | 10.7 | 7.4–14.8 | | 11.2 | 7.0–14.6 | | 10.6 | 7.5–14.8 | |
| Categorical health and demographic factors | n | % | | n | % | | n | % | |
| Neighboring county with cases of P&S syphilis in women of reproductive age in 2017, n (%) | 1359 | 55.5% | | 267 | 77.6% | | 1092 | 51.9% | |
| Presence of metropolitan area, n (%) | 1150 | 47.0% | | 233 | 67.5% | | 917 | 43.6% | |

* All eligible counties included US counties with no reported cases of primary and secondary syphilis among women of reproductive age in 2017.

† Counties with emergence of syphilis in women included US counties with no cases of primary and secondary syphilis among women of reproductive age in 2017 and 1 case in 2018.

‡ Counties with no emergence of syphilis in women included US counties with no cases of primary and secondary syphilis among women of reproductive age in 2017 and no cases in 2018.

§ Missing data were 7.1% for violent crime, 5.8% for primary care physician ratio, 6.3% for teen births. All other factors had no missing data or <1% missing.

IQR, interquartile range.

Adjusted Odds Ratios and Predictor Scores for US Counties With Emergence of Primary and Secondary Syphilis Among Women of Reproductive Age, 2017–2018 (N = 2451 Counties)

TABLE 2.

| Predictive Factor | Adjusted B | 95% CI | Adjusted OR | 95% CI | Predictor Score (2 × aOR) |
|--|------------|-------------|-------------|---------|---------------------------|
| Neighboring county with cases of P&S syphilis in women of reproductive age in 2017 | | | | | |
| No | Reference | | Reference | | 0 |
| Yes | 0.5 | 0.1–0.8 | 1.6 | 1.1–2.2 | 3 |
| P&S syphilis in men (cases per 100,000) | | | | | |
| At or below median | Reference | | Reference | | 0 |
| Above median | 0.8 | 0.5–1.1 | 2.2 | 1.6–3.0 | 4 |
| Violent crime (cases per 100,000) | | | | | |
| 128.0 | Reference | | Reference | | 0 |
| 128.1–243.3 | 0.2 | –0.2 to 0.6 | 1.3 | 0.9–1.9 | 3 |
| 243.4 | 0.5 | 0.1–0.9 | 1.6 | 1.1–2.4 | 3 |
| Black population (%) | | | | | |
| 0.76% | Reference | | Reference | | 0 |
| 0.77%–3.69% | 0.3 | –0.2 to 0.7 | 1.3 | 0.8–1.0 | 3 |
| 3.7% | 0.6 | 0.2–1.1 | 1.9 | 1.2–3.0 | 4 |
| White population (%) | | | | | |
| 77.8% | Reference | | Reference | | 0 |
| 77.9%–91.9% | –0.3 | –0.6 to 0.0 | 0.7 | 0.5–1.0 | 1 |
| >92.0% | –0.5 | –1.0 to 0.0 | 0.6 | 0.4–1.0 | 1 |
| Asian population (%) | | | | | |
| 0.47% | Reference | | Reference | | 0 |
| 0.48%–0.84% | –0.4 | –0.8 to 0.0 | 0.7 | 0.4–1.0 | 1 |
| 0.85% | –0.3 | –0.7 to 0.2 | 0.8 | 0.5–1.2 | 2 |
| Hawaiian/Pacific Islander population (%) | | | | | |
| 0.03% | Reference | | Reference | | 0 |
| 0.04%–0.08% | 0.1 | –0.3 to 0.5 | 1.1 | 0.8–1.7 | 2 |
| 0.09% | 0.5 | 0.1–0.9 | 1.6 | 1.1–2.4 | 3 |
| Population living in urban area (%) | | | | | |

| Predictive Factor | Adjusted B | 95% CI | Adjusted OR | 95% CI | Predictor Score (2 × aOR) |
|-------------------------------|------------|-------------|-------------|---------|---------------------------|
| <16.5% | Reference | | Reference | | 0 |
| 16.6%–47.6% | 0.2 | −0.3 to 0.7 | 1.2 | 0.8–1.9 | 2 |
| 47.7% | 0.4 | −0.1 to 0.9 | 1.5 | 0.9–2.6 | 3 |
| Presence of metropolitan area | | | | | |
| No | Reference | | Reference | | 0 |
| Yes | 0.2 | −0.1 to 0.5 | 1.2 | 0.9–1.6 | 2 |
| Population size (count) | | | | | |
| 11,764 | Reference | | Reference | | 0 |
| 11,765–31,234 | 0.7 | 0.1–1.2 | 1.9 | 1.1–3.2 | 4 |
| 31,235 | 1.2 | 0.6–1.8 | 3.4 | 1.9–6.0 | 7 |

B, beta coefficient; OR, odds ratio; CI, confidence interval; aOR, adjusted OR.

TABLE 3.

Risk Score Cutoffs, Sensitivity, and Specificity for US Counties With Emergence of Primary and Secondary Syphilis Among Women of Reproductive Age, 2017–2018 (Maximum Risk Score = 32)

| Risk Score Cutoff* | Sensitivity [†] | Specificity [†] | No. Counties Identified as Being at Elevated Risk |
|--------------------|--------------------------|--------------------------|---|
| 0 | 100% | 0% | 2451 |
| 1 | 100% | 0.3% | 2445 |
| 2 | 100% | 3.3% | 2382 |
| 3 | 99.7% | 4.3% | 2360 |
| 4 | 99.1% | 6.0% | 2321 |
| 5 | 99.1% | 9.6% | 2245 |
| 6 | 98.3% | 12.3% | 2185 |
| 7 | 97.4% | 15.1% | 2123 |
| 8 | 97.1% | 18.5% | 2051 |
| 9 | 95.9% | 21.8% | 1978 |
| 10 | 94.8% | 24.9% | 1908 |
| 11 | 94.2% | 28.7% | 1827 |
| 12 | 93.3% | 32.5% | 1743 |
| 13 | 92.2% | 36.7% | 1651 |
| 14 | 90.4% | 41.7% | 1539 |
| 15 | 89.9% | 45.6% | 1456 |
| 16 | 87.0% | 49.5% | 1363 |
| 17 | 84.9% | 53.5% | 1273 |
| 18 | 82.0% | 57.6% | 1175 |
| 19 | 78.6% | 62.3% | 1066 |
| 20 | 75.4% | 65.6% | 984 |
| 21 | 70.1% | 68.7% | 902 |
| 22 | 66.4% | 73.2% | 794 |
| 23 | 62.0% | 76.7% | 705 |
| 24 | 57.4% | 79.6% | 628 |
| 25 | 53.3% | 82.6% | 551 |
| 26 | 49.6% | 85.3% | 481 |
| 27 | 44.9% | 88.4% | 399 |
| 28 | 38.3% | 90.6% | 329 |
| 29 | 30.1% | 93.8% | 235 |
| 30 | 22.0% | 95.3% | 175 |
| 31 | 13.6% | 97.6% | 97 |
| =32 | 2.0% | 99.6% | 15 |

The data in boldface show the risk score cutoff that was chosen, with the corresponding sensitivity, specificity, and number of counties, which align with the risk score cutoff described in the text.

* Overall risk scores for each county were calculated by summing the predictor scores for all factors. A priori determinations for the ideal risk score cutoff were a sensitivity and specificity closest to 80%, prioritizing a higher sensitivity and lower number of counties identified as at elevated risk. The ideal risk score cutoff was 20.

[†]The criterion standard for the sensitivity and specificity calculations was the true emergence of syphilis in women with report of 1 case of P&S syphilis in 2018.

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