Examining Trends in Sexually Transmitted Infections by Linkages of Secondary Data Sources

By

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Abstract

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The incidence of chlamydia, gonorrhea, and early syphilis have increased in the U.S. since 2014 after a period of relative stability. The factors associated with this increase in incidence varies by geography and are multifactorial. There are few studies that examine this time period discretely (i.e., before 2014, 2014 and onward) to identify any changes in sociodemographic trends among chlamydia, gonorrhea, and early syphilis cases. Additionally, the COVID-19 pandemic had a profound effect on sexually transmitted infections (STI) control efforts by the diversion of STI laboratory testing materials and STI control staff at health departments toward the COVID-19 response. The effects of this diversion of resources and the shelter-in-place order in San Mateo County and its surrounding counties on STI incidence and detection are still not well understood. Since the start of the COVID-19 pandemic, the incidence of congenital syphilis cases in San Mateo County, the state of California, and the U.S. have increased at an alarming rate. Congenital syphilis is considered to be fully preventable and, thus, a sentinel event to identify failures in the public health and health care delivery system. Health departments have access to a vast number of data sources that can identify and describe the sociodemographic characteristics of STI cases, including those who gave birth to infants with congenital syphilis, but there is often a lack of resources to fully investigate the association between upstream factors, such as neighborhood effects, and STIs. One such measure that is used by the California Department of Public Health (CDPH) and local health departments was the Health Places Index (HPI), a composite measure that encompasses several aspects of neighborhood quality and opportunity. Although the HPI is an ecological-level variable, it can provide information about neighborhood context in the absence of any individual-level socioeconomic status information.

This dissertation leveraged the multiple data sources available at a norther California public health department by using deterministic and probabilistic linkage to combine data from the California Reportable Disease Information Exchange (CalREDIE), the San Mateo Medical Center, the San Mateo County Public Health Laboratory, and birth records from the California Department of Public Health—Vital Records from 2010 to 2021. Although CalREDIE, a reportable disease registry, contains information about chlamydia, gonorrhea, and early syphilis cases, the demographic information captured in CalREDIE can be inconsistent in quality and

completeness. This linkage allowed us (1) to impute any missing race/ethnicity values in CalREDIE from other data sources which yielded more accurate calculations (2) join information from other secondary data sources to enrich an existing dataset (e.g., joining HPI scores to CalREDIE) or to identify unique pregnancies (e.g., joining birth records to San Mateo Medical Center records). Three studies were conducted with three datasets created from this linkage process. The first study described the trend of the incidence of chlamydia, gonorrhea, and early syphilis in San Mateo County, CA from 2010 to 2021 using a dataset created from linking CalREDIE data to hospital and laboratory records. The second study conducted a retrospective cohort analysis that examined the association between sociodemographic factors, including HPI, and chlamydia and gonorrhea reinfection from 2010 to 2021 using a dataset derived from the first study. The third study examined the change in the proportion of syphilis testing among pregnant individuals who received prenatal care at the San Mateo Medical Center before and during the COVID-19 pandemic, using San Mateo Medical Center records linked to birth records to identify unique pregnancies and to link sociodemographic information that was not available in the San Mateo Medical Center records.

The methodology and findings are intended to provide a blueprint for health departments to harness the many data sources available to them as the analyses conducted in this dissertation can be readily replicated and applied to other health outcomes.

TABLE OF CONTENTS

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CHAPTER 1

TITLE: Trends in Chlamydia, Gonorrhea, and Early Syphilis Incidence by Demographic and Neighborhood Characteristics in San Mateo County, CA 2010-2021
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ABSTRACT
Background: Sexually transmitted infections (STIs) have been on the rise in the U.S. since 2014 after a period of relative stability. The reasons for this increase in incidence vary by geography, so the demographic and neighborhood characteristics of chlamydia, gonorrhea, and early syphilis cases were examined in San Mateo County, CA. Trends in the incidence of STIs during the COVID-19 pandemic are still being studied as the impacts of the pandemic on STI control efforts are not well understood.
Methods: The California Reportable Disease Information Exchange (CalREDIE) was used to identify chlamydia, gonorrhea, and early syphilis cases. Incidence rates were calculated for these STIs by age, sex, race/ethnicity, and Healthy Places Index quartiles. Incidence rates were qualitatively compared across three distinct time periods, 2010 to 2013, 2014 to 2019, and 2020 to 2021.
Results: The incidence of chlamydia, gonorrhea, and early syphilis increased in 2014 through 2019. The incidence of these STIs were highest among Black individuals. The incidence of chlamydia was highest in women, whereas the incidence of gonorrhea and early syphilis was the highest in men. The incidence of these STIs were the lowest in those who resided in the highest HPI quartile. The trends in the incidence during the COVID-19 pandemic differed, with the incidence of chlamydia and gonorrhea having decreased in 2020, whereas the incidence of early syphilis having increased in 2020.
Conclusion: The racial disparities observed in the national trends in the incidence of chlamydia, gonorrhea, and early syphilis are also observed in San Mateo County, CA. There is no overarching trend in the change in the incidence of chlamydia, gonorrhea, and early syphilis in 2020, indicating that the COVID-19 pandemic had different effects on the incidence of these three STIs.

INTRODUCTION
The incidence of sexually transmitted infections (STIs) has been climbing in the United States since 2014, after decades of progress in reducing rates of such infections. Infections by *Chlamydia trachomatis, Neisseria gonorrhoeae,* and *Treponema pallidum* causes chlamydia, gonorrhea, and syphilis, respectively, and comprise the vast majority of infections reported to the CDC every year. Chlamydia continues to be the most frequently reported condition among the 132 health conditions reported by states to the CDC. While chlamydia, gonorrhea, and syphilis are typically cured with an appropriate antibiotic regimen, the infection itself may be difficult to identify, due to nonspecific symptoms or a lack of symptoms altogether, which is commonly observed in women, creating opportunities for continued transmission and complications resulting from untreated infection. Untreated chlamydia and gonorrhea infections can progress to pelvic inflammatory disease (PID), the infection of a woman's uterus, fallopian tubes or ovaries, which can result in ectopic pregnancy and infertility. *N. gonorrhoeae* has shown increased antibiotic resistance, making it more difficult to treat. Infection with *T. pallidum* while pregnant,

if untreated, can result in congenital syphilis, which can have devastating consequences for the infant. The reasons for the observed increases in the incidence of chlamydia, gonorrhea, and syphilis infections are still not well understood and likely result from a multiplicity of factors, which may differ according to geographic region. The Western region of the U.S. has the highest rates of early syphilis compared to other U.S. regions and increasing incidence rates of chlamydia and gonorrhea. In the 1990s, the incidence of chlamydia plateaued and the incidences of gonorrhea and early syphilis decreased due to control efforts, as outlined in *The Hidden Epidemic: Confronting Sexually Transmitted Diseases*,[1] but then the incidences of these three infections increased in the U.S. in from 2013 to 2015[2] for reasons which are multifactorial and vary by region. Demographic and social factors may account for some of these observed increases as their association with STIs have been documented.[3–9] One study found that STI risk was negatively associated with higher income and that this association was amplified for nonwhites in the U.S.[10] A systematic review of genital chlamydia infections found that young people who had lower educational attainment, lower occupational class, and resided in deprived neighborhoods had higher odds of chlamydia infection, regardless of sex.[11] A narrative review found disparities in STI rates by four categories of social determinants of health (social segregation, access to healthcare and healthcare utilization, socioeconomic status, and incarceration), a trend that is consistently observed in the literature.[12]

Despite studies having extensively documented these associations, there are few studies comparing the demographic characteristics of the cases of STIs before and after the sharp increase in the incidence rates of chlamydia, gonorrhea, and early syphilis in 2014. In studies examining the relationship between socioeconomic status (SES) and STI outcomes, SES has typically been operationalized as income or educational attainment, neither of which captures the multiple dimensions of SES.[13] It is also difficult to measure individual-level SES using secondary datasets, such as surveillance data and laboratory data, which typically prompts researchers to use more easily captured proxies for SES, such as occupation. The information available on individual-level SES may also be inaccurate or missing altogether, depending on other individual-level characteristics. For example, surveillance data are comprised of information from multiple reporting sources, ranging from laboratory results to clinical providers filling out a confidential morbidity report, whereas birth record data are directly recorded from the birthing person and medical provider. An individual may not include his occupation on a laboratory intake form, if the field is available at all, because he may not see it as relevant to the laboratory test, but the same person may state his occupation when prompted by a medical provider, as he may perceive that his occupation relevant to his medical care. As a result, the proportion of missing data by different reporting sources may not be uniform, due to the different reporting sources. Even if these demographic variables are available, secondary datasets typically contain very little individual-level information beyond basic individual identifiers, such as name, date of birth, street address, and race/ethnicity. Ecologic-level variables can help fill this gap by supplying information for geographical areas, such as census tracts, which can be derived from street addresses, as individual-level addresses are available and can be linked to these geographical areas. While ecologic-level variables are not a substitute for individual-level SES, they can still provide some information about an individual's geographical context, particularly when information about place of residence by smaller geographical unit, such as census tract, is available. One such measure is the Healthy Places Index (HPI), which was developed by the Public Health Alliance of Southern California. Although a number of

composite measures to summarize neighborhood quality have been developed, such as the CDC's Social Vulnerability Index (SVI), HPI was created to characterize neighborhoods using positive language (healthy places vs. social vulnerability) and to consider multi-faceted domains of a neighborhood's characteristics. The HPI score measures neighborhood opportunity, as opposed to neighborhood vulnerability, which "can be thought of as all of the pathways to better lives, including through health, education, and employment."[14] Neighborhood opportunity is multidimensional, as it considers how one's physical neighborhood and the social, economic, and institutional contexts of the neighborhood (e.g., gender composition, income inequality) create and guide these pathways to better lives.[14] Neighborhood environments have been linked to a variety of health outcomes, such as depression, obesity, and STIs.[15–19] Neighborhoods are associated with a wide range of health exposures and outcomes related to the availability and attainability of resources,[20] which aligns with the Fundamental Causes of Disease theory, which posits that "(1) SES influences multiple disease outcomes; (2) SES is related to multiple risk factors for disease and death; (3) the deployment of resources plays a critical role in the association between SES and health/mortality; and (4) the association between SES and health/mortality is reproduced over time via the replacement of intervening mechanisms."[21] While other measures of neighborhood opportunity exist in California (e.g., CalEnviroScreen), the HPI score incorporates a wide range of indicators that span from environmental indicators (e.g., tree canopy cover) to political engagement (e.g., percent of total voter registration) to health outcomes (e.g., percent of adults who were diagnosed with cancer).[22] It has also been compared to other indices and has shown good concordance with the Intercity Hardship Index (which measures urban hardship)[23] and with the 200% Federal Poverty Level. While other indices, such as the SVI, are available at the census tract level and are updated more regularly than the HPI, these indices were developed for specific purposes and situations, such as measuring a neighborhood's capacity to respond to hazardous events.[24] The HPI is specifically focused on the health of California neighborhoods.

The HPI score was created by drawing from a large range of data sources, such as the American Community Survey (ACS), the California Environmental Protection Agency (CalEPA), the Comprehensive Housing Assessment System (CHAS), and the National Land Cover Database (NLCD). The HPI emerged as the health equity measure of choice for California health departments during the COVID-19 pandemic, using the lowest quartile as an indicator of the most vulnerable census tracts.[25] Given California local health departments' familiarity with HPI, it was used in this study to identify the most vulnerable census tracts for easy translation to geographic areas that are already familiar to the health department (e.g., the lowest HPI quartile) of San Mateo County and other California local health departments.

STI control efforts have historically focused on individual risk factors (e.g., contraception use) as points of intervention at the individual-level. However, as the effects of structural factors (e.g., residential segregation, racism) of health outcomes are being better investigated, there is a need to examine the relationship between upstream factors, such as residential segregation and economic inequality and the incidence of STIs and related sequelae, as these composite measures summarize neighborhood and environmental quality. A recent report released by the Committee on Prevention and Control of Sexually Transmitted Infections in the United States said, "The committee adopted a Modified Social Ecological Framework of Sexual Health and STI prevention, control, and treatment that moves beyond individual-level behavioral or biomedical

constructs toward a comprehensive framework to address the interconnected and mutually reinforcing structural and social determinants of health and health inequities."[26] The HPI is one such measure that can give a wider lens for examining the structural and social determinants of STIs and their sequelae.

The observed disparities in STI rates by demographic and social factors are only as reliable as the information that is used to calculate these rates. The COVID-19 pandemic brought to light the problem of missing race/ethnicity information in public health surveillance data, including electronic laboratory reports and healthcare-submitted confidential morbidity reports (CMR). This lack of complete race/ethnicity data is a long standing limitation in public health surveillance data, making it difficult to accurately describe health disparities due to missing data, which can perpetuate these health disparities as race/ethnicity information is thought to be missing differentially due to a lack of a standardized data collection standard, language barriers, and imperfect measures of capturing this information.[27] A recent report of the results of a survey conducted by the Council for State and Territorial Epidemiologists (CSTE) that polled 45 health jurisdictions, found that 90% of these health jurisdictions responded that "reporters not providing data for various reasons" was one of the limiting factors in obtaining more complete race and ethnicity data for patients with COVID-19 for public health agencies,[28] as has been found for all other reportable conditions. One possible way to bridge this gap is for health departments to link other sources of data to public health surveillance data to impute missing values.[29]

This study's objectives were (1) to leverage reportable disease surveillance data, public health laboratory data, and San Mateo County's general hospital data to impute missing race/ethnicity data, (2) to describe the incidence rates of chlamydia, gonorrhea, and early syphilis in San Mateo from 2010-2021, (3) to calculate incidence rates of chlamydia, gonorrhea, and early syphilis, stratified by race/ethnicity, age, and HPI quartiles, (4) and to compare trends in incidence rates of chlamydia, gonorrhea, and early syphilis from 2010-2013 to 2014-2019 and 2020-2021.

MATERIALS AND METHODS

Data sources:

California Reportable Disease Information Exchange

San Mateo County residents with a diagnosis of chlamydia, gonorrhea, or early syphilis (primary, secondary, and early latent) infections were identified in the California Reportable Disease Information Exchange (CalREDIE) system, the electronic disease reporting system of the California Department of Public Health. All diseases reportable under Title 17 are mandated to be reported to local health departments, whether by a confidential morbidity report or electronic laboratory reporting, so all positive laboratory results or clinical diagnosis of these conditions are received by San Mateo County, resulting in a high level of ascertainment of diagnosed cases. San Mateo County began using CalREDIE as its primary tool for electronic disease reporting, case management, and surveillance in 2010. The CalREDIE database contains every clinician- or laboratory-reported case of chlamydia, gonorrhea, and early syphilis (defined as syphilis acquired in the last year) in San Mateo County. CalREDIE includes specific disease conditions, such as "Chlamydia with Pelvic Inflammatory Disease," "Pelvic Inflammatory Disease with Chlamydia" (two different conditions) and "Chlamydia." These specific disease conditions were all classified as chlamydia. The same approach was applied to CalREDIE conditions related to gonorrhea, so that several specific conditions were classified as gonorrhea. Early syphilis

includes three different CalREDIE conditions, "primary syphilis," "secondary syphilis," and "early non-primary, non-secondary syphilis," which were combined and classified as early syphilis. CalREDIE also specifies a resolution status, which is defined as "the current status of the disease incident."[30] Case definitions can be complicated due to the laboratory or clinical characteristics used; Tables 1 and 2 in the Appendix contain more information on the case definitions used. Chlamydial and gonococcal pelvic inflammatory disease (PID) were included in this analysis, classified as chlamydia and gonorrhea infections, respectively. It should be noted that chlamydia ceased to be a condition reportable by healthcare providers on October 1, 2019, but continued to be reportable by laboratories.[31]

There were 36,580 total observations in the dataset, comprised of 28,404 chlamydia cases, 6,781 gonorrhea cases, and 1,395 early syphilis cases in residents of San Mateo County during 2010-2021, including repeat infections in the same individual.

The CalREDIE system geocodes the address of residence of each case and automatically assigns a census tract to each record based on this address.

Automated Vital Statistics System

The Automated Vital Statistics System (AVSS) is a vital statistics database which served as a reportable disease registry for California before the creation of CalREDIE in 2010. AVSS does not have the same granularity of case descriptions by resolution status as CalREDIE, but AVSS data were included in this study because syphilis cases were not recorded in CalREDIE until 2013.

San Mateo Medical Center

San Mateo Medical Center is San Mateo County's safety net hospital clinic system, and primarily serves the county's low-income population insured through the Health Plan of San Mateo. Records from the San Mateo Medical Center were available only from 2013 onward due to a change in the records systems. Multiple race and ethnicity variables were available in the San Mateo Medical Center's records, with varying levels of completeness. A race/ethnicity variable that follows U.S. Census Bureau classifications was created from a variable that captured country of origin. These records were linked to the CalREDIE case roster through deterministic and probabilistic linkage, using patient first name, last name, and date of birth.

San Mateo County Public Health Laboratory

San Mateo County Public Health Laboratory conducts STI diagnostic testing for San Mateo Medical Center and the County Public Health clinics, including the County STI clinics. San Mateo County's Public Health Laboratory data contain separate fields for Hispanic ethnicity and for race, so a race/ethnicity variable that follows U.S. Census Bureau classifications was created from these variables. These records were linked to the CalREDIE case roster through deterministic and probabilistic linkage, using patient first name, last name, and date of birth.

Healthy Places Index

The HPI is a z-score based score that is a composite measure across eight domains, standardized for the state of California, with the bottom quartile defined as the "health equity quartile" (i.e., the quartile of least opportunity) during the COVID-19 pandemic to help identify and target

census tracts that had the least opportunity (i.e., least access to pathways for better lives) for focused COVID-19 testing and vaccination efforts. The highest quartile was used as the referent quartile, as census tracts in that quartile have greater opportunity (i.e., greater access to pathways for better lives). HPI was joined to each case according to its census tract. HPI is a one-time ecological level measurement. Two versions of HPI were used in this study: HPI version 2.0 uses data from 2011 to 2015, while HPI version 3.0 uses data from 2015 to 2019. HPI 2.0 values were assigned to cases from 2010 to 2015, while HPI version 3.0 values were assigned to cases from 2016 to 2021.

Census tract is the smallest geographical unit used by the U.S. Census Bureau. Each census tract contains between 2,500 to 8,000 residents; census tracts may not follow city boundaries, but they are always contained within county and state boundaries. Census tracts are considered to be relatively permanent, with little change over time.[32] HPI was joined to the dataset by census tract; although these characteristics (e.g., neighborhood walkability, food security) cannot be inferred down to the individual level, having this information at the census tract level provides the most granular geographical unit available.

Probabilistic linkage

Data from AVSS, CalREDIE, the San Mateo Medical Center, and the San Mateo County Public Health Laboratory were matched by deterministic and probabilistic linkage. Deterministic linkage has been used by public health agencies to identify interjurisdictional cases. However, deterministic linkage has lower sensitivity when the data vary (e.g., as a result of a name change). As a result, deterministic linkage performs best with unique identifiers, such as social security number or medical record number, that are identical across all datasets being linked. However, such information may not be routinely collected and available in surveillance data, or may not be identical. Although deterministic linkage results in high specificity of matches, it may also miss true matches if any of the matching factors are not identical.

Early syphilis cases from AVSS from 2010 to 2012 were first concatenated to the CalREDIE cases, which resulted in 36,580 total observations. Then a roster of all unique individuals who had a chlamydia, gonorrhea, or early syphilis infection was created by matching individuals from the San Mateo Medical Center records and San Mateo County Public Health Laboratory records to the CalREDIE records by deterministic linkage using first name, last name, date of birth, and year of specimen collection. Those who were not matched in the deterministic linkage were identified by probabilistic linkage, using the fastLink package in R. The fastLink package uses the Fellegi-Sunter probabilistic record linkage model and is an efficient algorithm that retains good sensitivity.[33–35] Probabilistic linkage was conducted using first name, last name, and date of birth. Date of birth may be susceptible to typographical errors from using a numeric keypad, in which transpositions of birth month and birth day may occur. To account for these potential typographical errors, a scoring system was created where at least two of the three components of the date of birth (i.e., birth month, birth day, birth year) must have matched, and then a posterior probability, which quantifies the certainty of the match, was calculated by the fastLink algorithm to create a cut off of higher than 85% for date of birth matches. The matched individuals were then joined to the original AVSS-CalREDIE data by a unique identifier used within the AVSS-CalREDIE systems with the additional information that the linkage provided from the San Mateo Medical Center records and the San Mateo County Public Health Laboratory records.

Imputing missing race and ethnicity values
The final race/ethnicity variable was created by grouping the different race and ethnicity variables across data from AVSS, CalREDIE, the San Mateo Medical Center, and the San Mateo County Public Health Laboratory. Race/ethnic groups follow U.S. Census Bureau classifications: American Indian/Alaska Native, non-Hispanic; Asian, non-Hispanic; Black or African American, non-Hispanic; Hispanic; Native Hawaiian or Other Pacific Islander, non-Hispanic; White, non-Hispanic. Hispanic ethnicity was grouped as Hispanic, regardless of race, even if race was unknown. Individuals with unknown Hispanic ethnicity were grouped as their race variable and non-Hispanic. Those missing both race and ethnicity values (n=6658) were classified as "Unknown" and were excluded from the analysis.

Analytic methods
Chlamydia, gonorrhea, and early syphilis counts and cumulative incidence rates were calculated by age category, race/ethnicity, biological sex, and HPI quartiles. Incidence calculations for the total population, age category, race/ethnicity, and biological sex used population denominators from the California Department of Finance population projections.[36] Population denominators used to calculate incidence by HPI quartile required using ACS census tract estimates.

A t-test was used to assess differences in the mean ages of chlamydia, gonorrhea, and early syphilis cases in 2010 to 2013 and 2014 to 2019 and to assess differences in the mean ages of chlamydia, gonorrhea, and early syphilis cases in 2014 to 2019 and 2020 to 2021.

All analyses were conducted using R Statistical Software (Version 4.2.1; R Core Team 2022).

RESULTS
After the data linkage, race/ethnicity information from the San Mateo Medical Center records and the San Mateo County Public Health Laboratory records was used to impute 1653 race/ethnicity values, bringing the missing race/ethnicity values from 27.8% to 23.3% in the final dataset.

Of the three STIs examined in this study, chlamydia accounted for the largest number of infections (n=28,404 cases from 2010 to 2021), followed by gonorrhea (n=6,781 cases) and early syphilis (n=1,395 cases) (Table 1). The incidence rate of chlamydia remained relatively stable from 2010 to 2013, increased every year from 2014 to 2019, and then declined by 37.2% in 2020 and 2021. The incidence rates of gonorrhea and early syphilis followed a similar trend as the incidence rate of chlamydia through the three time periods, except that the incidence rates of gonorrhea and syphilis in 2020 declined compared to 2019 (9.5% and 7.1%, respectively). The largest number of chlamydia, gonorrhea, and early syphilis cases was in 2019 combined, followed by a sharp decline in total cases in 2020 to a level last seen in 2015 (Figure 1). Despite this decline in total cases from 2019 to 2020, the overall numbers and incidence rates of chlamydia, gonorrhea, and early syphilis infections were higher in 2021 compared to 2010 (Figure 2). The incidences of chlamydia and gonorrhea decreased in 2020, whereas the incidence of early syphilis declined slightly (Table 2).

The change in the mean ages of individuals with chlamydia, gonorrhea, and early syphilis in the three time periods examined were statistically significant for chlamydia and gonorrhea, while the

change in mean age for individuals with early syphilis across the three different time periods was not statistically significant (Tables 2 and 3). The mean age for gonorrhea cases was 0.8 years higher ($p < 0.05$) in 2014 to 2019 compared to 2010 to 2013, and 0.6 years higher in 2020 to 2021 compared to 2014 to 2019, while the mean age for early syphilis cases was 1.0 years lower in 2014 to 2019 compared to 2010 to 2013 and 0.4 years lower in 2020 to 2021 compared to 2014 to 2019. The only substantial change in the mean age of individuals compared across these times periods was in the chlamydia cases, with the mean age of chlamydia cases having increased 2.4 years from the first time period (i.e., 2010 to 2013) to the third time period (i.e., 2020 to 2021).

Between 2010 and 2020, the incidence rates of chlamydia, gonorrhea, and early syphilis trended upward, with the incidence rate for chlamydia reaching a peak in 2019 (Figure 3), whereas the increases in the incidences of gonorrhea and early syphilis were more gradual (Figures 4 and 5, respectively). The incidence rate of chlamydia in 2020 then declined, but a similar decrease was not observed for gonorrhea or early syphilis (Table 4); the incidence of early syphilis increased in 2020 (Figure 5), compared to previous years.

The majority of census tracts in San Mateo were in the highest HPI quartile (65.5%), indicating that the majority of San Mateo County residents live in census tracts that have greater access to pathways of success compared to those residing in other census tracts.

Similar to U.S. national trends, women comprised the majority of chlamydia cases (60.2%) (Table 1 and Figure 7) whereas men comprised the majority of gonorrhea and early syphilis cases (74.8 % and 84.2%, respectively) (Table 1, Figure 8 and Figure 9).

Black individuals had the highest incidence rate of chlamydia and gonorrhea, compared to all other race/ethnicities (Figures 10 and 11). A decline in the incidence of chlamydia in 2020 was observed for all race/ethnic groups except non-Hispanic White individuals. Black individuals had the highest incidence rate of early syphilis compared to all other race/ethnicities from 2014 to 2016, and again in 2018 to 2020 (Figure 12). Incidence rates of gonorrhea and early syphilis increased in 2020 among all race/ethnic groups except for non-Hispanic multiracial individuals since 2014 but the greatest increases were seen in Black individuals. Black men had the highest incidence rate of chlamydia during the entire study period except in 2015, when American Indian or Alaska Native men had the highest incidence of chlamydia compared to other race/ethnicities. Black women had the highest incidence rates of chlamydia from 2010 to 2016, except in 2014 when Native Hawaiian or Pacific Islander women had the highest incidence of chlamydia and had the highest incidence of chlamydia again in 2017 to 2019. American Indian or Alaska Native women then had the highest incidence of chlamydia in 2020 and 2021 (Figure 13).

The highest incidence rates of gonorrhea throughout the study period were seen in Black men and women. Black men had the highest incidence of gonorrhea and a continued upward in incidence of gonorrhea from 2014 to 2020, after which American Indian or Alaska Native men had the highest incidence of gonorrhea in 2021. The incidence rate of gonorrhea fluctuated for Black women, particularly from 2013 through 2019, but remained higher than that among women of all other race/ethnicities (Figure 14). Black women had the highest incidence rates of early syphilis in 2011, 2015 to 2016, and 2020 to 2021, whereas Black men had incidence rates

of early syphilis that were similar to those of men of other race/ethnicities until 2018, when there was a pronounced increase in the incidence rates of early syphilis among Native Hawaiian or Pacific Islander men (Figure 15). Although Black men had the highest incidence rates of early syphilis again in 2018 to 2019, that incidence declined sharply in 2021, and Hispanic or Latino men had the highest incidence of early syphilis (Figure 15).

Incidence rates of chlamydia were highest among those 20-24 years of age. There was a particularly sharp increase in the incidence rates of chlamydia in this age group in 2014, and then a large decline in 2020, which was also observed in other age groups. As a general trend, incidence rates decreased with increasing age for those older than 25-29 years, while incidence rates among those younger than 15 years old were the lowest (Figure 16).

Incidence rates of gonorrhea were also highest in age groups 20-24 years and 25-29 years. For both of the age groups, there was a sharp increase in incidence rates of gonorrhea in 2015, a decrease for those 20-24 years of age in 2018, and then a large decline in both age groups in 2020. Those 15-34 years of age experienced a decline in the incidence rates of gonorrhea in 2020, whereas the incidence of gonorrhea in older age groups increased in 2020 (Figure 17).

The incidence rates of early syphilis increased from 2010 to 2013 in all age groups, after which those ages 20-34 years experienced the largest increases in incidence. In general, the incidence rate of early syphilis decreased with increasing age, a trend that became more apparent with widening differences in incidence rates between age groups, particularly after 2016. In 2020, the incidence rate of early syphilis decreased for those ages 20-29 years and those 60+ years of age but increased for the other age groups, most notably among those ages 40-44 years; that age group had the highest incidence rate in 2020 compared to all other age categories for the first time during the study period. In 2021, most age groups had a decrease in the incidence of early syphilis except those 45+ years of age (Figure 18).

San Mateo County did not have any census tracts in the lowest HPI quartile from 2010 to 2015, so incidence rates for chlamydia, gonorrhea, and early syphilis in the lowest HPI quartile were could be calculated only for 2016 through 2021. The highest HPI quartile consistently had the lowest incidence rate of chlamydia for the entire study period. The second lowest HPI quartile had the highest incidence rate of chlamydia until 2017, when the lowest HPI quartile had a similar but slightly higher incidence rate. In 2020, the incidence rates of chlamydia declined for the second lowest HPI quartiles and the highest HPI quartile, with a notably steep decline in incidence for the lowest HPI quartile from 810 cases per 100,000 in 2019 to 446.4 cases per 100,000 in 2020 (Figure 19), whereas the second highest HPI quartile had an increase in the incidence of chlamydia in 2020.

The incidence rate of gonorrhea increased at a similar pace as that of chlamydia across the three available HPI quartiles from 2010 to 2014, after which there was a sharp increase in the incidence rate for the third HPI quartile in 2015. The incidence rates for gonorrhea in the second and third quartiles remained similar to those from 2015 to 2019, after which in 2020, the third HPI quartile had a much higher incidence rate than the second HPI quartile (Figure 20). Although the third HPI quartile had a slight decrease in the incidence of gonorrhea in 2021 compared to 2020, the third HPI quartile continued to have the highest incidence of gonorrhea in

2021. The lowest HPI quartile followed a similar trend in the incidence of gonorrhea as the second and third HPI quartiles, also having an increase in incidence in 2020 and again in 2021. The highest HPI quartile consistently had the lowest incidence rate of gonorrhea.

The incidence rates of early syphilis in all of the HPI quartiles trended similiarly from 2010 to 2014, after which the third HPI quartile had a sharper increase in incidence rate than the second or fourth quartile in 2015. The second and third HPI quartiles had a very large increase in incidence rates of early syphilis in 2020, whereas the lowest HPI quartile had a drop in incidence rate (Figure 21). This trend did not extend into 2021, when there was a decline in the incidence rates of early syphilis for all the HPI quartiles, with the second lowest HPI quartile having the sharpest decline in incidence (Figure 21).

DISCUSSION

The trends in the incidence of chlamydia, gonorrhea, and early syphilis in San Mateo County during the time period 2010 to 2021 were similar to trends reported for the Western region of the U.S. and the U.S. overall,[37] with chlamydia, gonorrhea, and early syphilis case counts and incidence rates increasing overall from 2010 to 2021. Though there was a steep decline in the numbers of cases of chlamydia, gonorrhea, and early syphilis in 2020, the total number of cases of those STIs in 2021 was still higher than that in 2010, even as San Mateo County's population stayed relatively steady from 2010 to 2021 (estimated population 721,169 to 756,655 people, respectively[38]). The increase in the incidence rate of chlamydia and gonorrhea in 2014 to 2019, compared to the 2010 to 2013 period, may have been due to increased testing, as the CDC 2015 STD Treatment Guidelines recommended annual screening for all sexually active females under the age of 25 years and screening for pregnant individuals under the age of 25 years during the first prenatal visit.[39] The increase in the incidence rate of chlamydia in the 2014 to 2019 time period among those 20-24 years of age in particular may have resulted, in part, from these screening guidelines (Figure 16). Increased detection may also have contributed to the observed increase in the incidence of gonorrhea in the 2014 to 2019 time period, but the age groups with the highest incidence rates of gonorrhea during that time period were those ages 20-24 years, which would be consistent with the CDC 2015 STD screening guidelines, and those 25-29 years of age, who fall out of the age range of the CDC 2015 STD screening guidelines (Figure 17). The screening recommendations for syphilis in the CDC 2015 STD Treatment Guidelines targeted special populations, such as men-who-have-sex-with-men (MSM), individuals in correctional facilities, and pregnant individuals. The incidence of early syphilis in San Mateo County was largely driven by men (Figure 9), with a particularly sharp increase observed from 2011 to 2013, and again from 2015 to 2019. The pattern of increases in the incidence of early syphilis was different in women; the rise in incidence occurred in 2019 through 2021, indicating that the factors driving syphilis infection in men and women may have been different. The CDC 2015 STD Treatment Guidelines recommends annual screening for syphilis for sexually active MSM, with no similar recommendation made for non-pregnant women. However, there are recommendations for pregnant individuals to be screened for syphilis in the first trimester of their pregnancy.[39] MSM comprise the majority of syphilis infections compared to women, men with unknown sex of sex partners, and men who have sex with women only, which may account for the majority of primary and secondary syphilis cases being in men.[40,41] An increase in the incidence of early syphilis in women in the mid-2010s, particularly in heterosexual women, has been reported in the U.S.[37] and in other countries,[42–45] as observed in San Mateo County. In

addition, the rise in the incidence of congenital syphilis mirrored the increase in the incidence of early syphilis in women.[46] Primary and secondary (P&S) syphilis, along with congenital syphilis, are considered sentinel events that indicate missed opportunities in prevention.[47–49] The increases in the incidence of chlamydia, gonorrhea, and early syphilis may also have been due to increased detection, due to increased access to health care. In 2010, the Affordable Care Act (ACA) was signed into law, and many consumer-facing changes were enacted in 2013 and 2014, such as open enrollment in a marketplace for health insurance and a requirement for individuals to have health insurance.[50] In San Mateo County, the American Community Survey (ACS) estimated that in 2012, 11.0% of the population was uninsured, after which that percentage fell to 10.7% and 10.2%, in 2013 and 2014, respectively. The percentage of uninsured San Mateo County residents continued to decrease until 2021, when 3.8% were uninsured. With more of the San Mateo County population insured, the observed increase in the incidence rates for chlamydia, gonorrhea, and early syphilis could be due to better detection as more people had access to affordable health care.

The trends in chlamydia, gonorrhea, and early syphilis by race/ethnicity in San Mateo County also broadly followed the U.S. trends. Black individuals experienced the highest incidence rates of chlamydia and gonorrhea compared to other race/ethnicities (Figures 10 and 11), and had the highest incidence rates of early syphilis for all but two years during the study period (Figure 12). This trend was observed in Black men and in Black women for the majority of the study period (Figures 13, 14, and 15). Additionally, the gap in the incidence rates for gonorrhea and early syphilis for Black individuals compared to other race/ethnic groups widened from 2014 to 2019. An increase in incidence rates of chlamydia, gonorrhea, and early syphilis in 2014 was not observed in all race/ethnic and age groups. These racial disparities have been previously noted in the Western region of the U.S..[51] Racial/ethnic disparities in STI incidence and outcomes are well established;[7,9,52–54] with one study finding that there was an income gradient that was associated with risk of infection and that this gradient was more pronounced among Black individuals and Hispanics by sex, with poor Black women having the highest risk of an STI diganosis.[10]

Younger San Mateo County residents, particularly those ages 20-25 years of age, had the highest incidence rates of chlamydia, gonorrhea, and early syphilis, consistent with what has been observed in the U.S. overall. Though there is variation in the mean age of sexual debut for adolescents in the U.S.,[55] one study that examined data from the latest wave of the National Longitudinal Study of Adolescent Health estimated that four out of five adolescents participated in at least one of the sexual behaviors asked about in the survey (oral-genital, vaginal, or anal intercourse) by age 18 years,[56] whereas another study that examined data from the Youth Risk Behavior Surveillance System estimated that the majority (58% for Caucasian females, 53% for Caucasian males; 59% for Hispanic females, 69% for Hispanic males; and 74% for African-American females and 82% for African-American males) of adolescents had a sexual experience by age 17, except in Asian males and females.[57]

Chlamydia was the most commonly reported condition in San Mateo County throughout the time period, except in 2020 and 2021, when COVID-19 was the most common reportable condition. Chlamydia was the only STI for which a large change in incidence rates for all sexes, race/ethnicities, and age groups was observed in 2020 (Figures 7, 10, 16). Though there were

changes in the incidence rates for gonorrhea and early syphilis by race/ethnicity and age groups, the change in chlamydia incidence rates in 2020 compared to 2019, across race/ethnicity and age groups, suggests that an ecologic-level factor, such as reduced access to chlamydia testing or to STI clinic,[58] impacted chlamydia detection. There may also have been a change in sexual behaviors and sexual networks due to the COVID-19 pandemic.[59–61] Given these changes in behavior and sexual networks, it is difficult to know whether the observed decreases in incidence rates were due to decreases in infection, decreases in detection of infection, or both. Recent studies suggest that the observed decreases in the rates of chlamydia may due to both.[62,63] Sexual behaviors changed during the pandemic period as social distancing measures and fear of SARS-CoV-2 infection led people to reduce their casual sexual encounters,[64–67] particularly after a national emergency was declared in the U.S. on March 13, 2022.[68] Natural disasters and hazards, such as the COVID-19 pandemic, are known to reduce sexual activity, in part due to the resulting chronic stress.[69] A meta-analysis examining the effects of the COVID-19 pandemic on sexual activity and functioning found that across the 21 studies examined, the leading factors contributing to reduced sexual activity and functioning were fear of infecting their partner with the SARS-CoV-2 virus (80%), anxiety (75%) and depression (70%).[70] There was also a national shortage of STI testing materials in the early months of the COVID-19 pandemic, particularly for chlamydia and gonorrhea nucleic acid amplification tests (NAAT).[71] Clinical providers were given guidance to prioritize for testing those who may be at higher risk of chlamydia or gonorrhea infection, such as pregnant women, MSM, or those with PID, so these individuals may have had a higher probability of chlamydia or gonorrhea testing. Nevertheless, the rate of chlamydia infection in San Mateo County and in the U.S. did not rebound in the same way that gonorrhea and early syphilis did.[72,73] This suggests that the decline in the incidence rate of chlamydia in 2020 across both sexes and all race/ethnicities and age groups was, in part, due to reduced sexual activity and reduced chlamydia testing.

The highest HPI quartile in San Mateo County had the lowest incidence rates of chlamydia, gonorrhea, and early syphilis, which was an expected outcome. However, higher incidence rates did not always correspond with the lowest HPI quartiles throughout the study period, especially after 2020. The incidences of chlamydia, gonorrhea, and early syphilis were highest in the second highest HPI quartile in 2020, which was a change from 2019, when the incidence of chlamydia was the highest in the second lowest HPI quartile and the incidences of gonorrhea and early syphilis were the highest in the lowest HPI quartile. These higher incidence rates of STIs in lower HPI quartiles compared to the highest HPI quartile are consistent with prior reports of the link between place-based measures (e.g., neighborhood, environment, social factors), such as HPI, and a higher incidence of STIs and related sequelae.[18,74–76] However, the similarity of the incidence rates of STIs of the three lowest HPI quartiles, compared to the highest HPI quartile, may also indicate that HPI quartiles 1, 2, and 3 may be very similar, given that San Mateo County is a wealthy county. Neighborhoods are known to be indicators of access to material and social resources which are associated with many health outcomes, often with poorer neighborhood quality and access having associations with adverse health outcomes.[20]

In this study, we recovered missing race/ethnicity values in the CalREDIE roster from other data sources. In total, 1653 missing values of race/ethnicity were recovered through linkage to San Mateo Medical Center records and San Mateo Public Health Laboratory records. This brought the missingness from 27.8% to 23.3%. Although decreasing the percentage of missing

race/ethnicity values by 4.5% seems to be a modest amount, this linkage process recovered values for small populations in San Mateo County, such as American Indian or Alaska Natives (n=9), Black individuals (n=83), and Native Hawaiian or Pacific Islanders (n=30). Due to the small counts in these populations, missing race/ethnicity information can result in large changes in the calculated incidence rates, so recovering this race/ethnic information allowed for a more accurate calculation of incidence, which in the absence of this race/ethnic information may have led to underestimation of the true incidence. The linkage method used in this analysis can be used for any health department that has access to multiple sources of data, such as general hospital records or the public health laboratory, to recover missing values. The same can be done with surveillance datasets in which an individual may be present for multiple conditions, as in CalREDIE.

Strengths and Limitations

This study has several strengths. The first is that this study covered a twelve-year time span so that trends over time could be observed. Second, this study used multiple data sources to supplement a reportable disease surveillance dataset with imputed missing values, such as race/ethnicity information. This approach can be particularly useful when analyzing datasets such as reportable disease registries, in which race/ethnicity information may not have been captured. Third, this study utilized existing datasets to which a health department would typically have access, which can then be joined to data from other sources, such as the ACS and the HPI. The use of probabilistic linkage also allows for the possibility of creating such a dataset, depending on the availability of data in that health department. This is a highly reproducible analysis and can be helpful for other health departments to use as a blueprint to characterize their own STI patient characteristics.

This study also has several limitations. Though some missing race/ethnicity values could be recovered, the probability of recovering that value was not equal for all cases with missing race/ethnicity values. In other words, the recovery of missing values was likely differential by health insurance status, as San Mateo Medical Center patients and individuals whose specimens were tested at the San Mateo County Public Health Laboratory are not representative of the general San Mateo County population. The San Mateo Medical Center serves primarily those covered by the Health Plan of San Mateo or other low-income patients, and the San Mateo County Public Health Laboratory tests specimen collected from the San Mateo Medical Center or from health clinics or programs operated by San Mateo County, which also primarily serve low-income populations. Though the method used for creating the final race/ethnicity variable[77] allows for using existing information (e.g., an individual who has race value available but for whom the ethnicity value is missing is classified as the race value and assumed to be non-Hispanic) to make an informed guess at the missing value, the probability of having partial race/ethnicity values may be differential by how the infection was reported (e.g., electronic laboratory report, confidential morbidity report) and potentially biased. The second limitation is not knowing the case's sexual orientation, the biological sex, or gender, or number of sexual partners. Sexual orientation data are not routinely collected as a part of STI case investigations, particularly for chlamydia, which is typically reported through electronic laboratory reports. The epidemiologic features of chlamydia, gonorrhea, and early syphilis can be very different in depending on the subpopulation, such as comprising the overall proportion of gonorrhea cases compared to women and men who have sex with women only.[78] Due to the lack of this

information, we were unable to describe the trends in the incidence of chlamydia, gonorrhea, and early syphilis by these very important factors of sexual behavior and gender identity. The third limitation is that HPI was created using 2010 census tracts; the census tract boundaries for later years may have changed and any data associated with the 2010 census tracts may have been out of date, particularly for areas that experienced the greatest change in population size. This may be reflected in the chlamydia, gonorrhea, and early syphilis cases that could not be matched to an HPI quartile based on the census tract information in CalREDIE.

CONCLUSION

Trends in chlamydia, gonorrhea, and early syphilis cases in San Mateo County during the 2010-2021 time period were similar to those observed at the national and regional levels. Overall, the incidence rates for chlamydia, gonorrhea, and early syphilis remained fairly stable from 2010 to 2013, after which the incidence rates for these infections increased. These observed increases may be due to a true increase in chlamydia, gonorrhea, and syphilis infections, increased detection due to the CDC 2015 STD screening guidelines that were published during the study period, better access to healthcare, or a combination of the factors. Notably, there was a decline in the incidence rate of chlamydia in 2020 across all demographic groups, likely due to factors associated with the COVID-19 pandemic. Chlamydia, gonorrhea, and early syphilis disproportionately affected Black individuals, who had the highest incidence rates for all three STIs in San Mateo County. Chlamydia disproportionately affected women, whereas gonorrhea and early syphilis disproportionately affected men, mirroring the epidemiologic feature of these STIs at the national and regional levels. The use of additional data sources allowed for imputation of missing race/ethnicity information to calculate more accurate incidence rates for chlamydia, gonorrhea, and early syphilis, which is particularly important for race/ethnic groups with small population counts.

Incidence rates of STIs have increased in San Mateo County, California, and the U.S. after a period of relative stability and likely changed during to the COVID-19 pandemic in 2020 in ways that researchers are still seeking to understand. The effect of the COVID-19 pandemic on access to care, sexual behaviors and networks, and general health may continue to impact STI transmission, screening, and detection.

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APPENDIX

Table 1. Case Definitions for Chlamydia, Gonorrhea, and Early Syphilis

Disease	CalREDIE Disease Condition	Resolution Status
Chlamydia	Chlamydia	Suspect, Probable, Confirmed
Gonorrhea	Gonorrhea	Suspect, Probable, Confirmed
Early Syphilis	Syphilis (Primary) Syphilis (Secondary) Syphilis (Early non-primary non-secondary)	Suspect, Probable, Confirmed

Table 2. Resolution Status Definitions for Chlamydia, Gonorrhea, and Early Syphilis[79]

Disease	CalREDIE Disease Condition	Resolution Status	Description
Chlamydia	Chlamydia	Confirmed	A case that is laboratory confirmed (See appendix for laboratory criteria for diagnosis.)
Chlamydia	Chlamydia with Pelvic Inflammatory Disease or Pelvic Inflammatory Disease with Chlamydia	Confirmed	A clinical syndrome resulting from the ascending spread of the microorganisms from the vagina and endocervix to the endometrium, fallopian tubes, and/or contiguous structures; among sexually active women, characterized by pelvic or lower abdominal pain, with no cause for the illness other than PID identified. Must also meet the surveillance case definition of *C. trachomatis* infection.[80]
		Probable	A sexually active woman with pelvic or lower abdominal pain, with no cause for the illness other than PID identified with one or more of the following minimum criteria present on pelvic examination: cervical motion tenderness OR uterine tenderness OR adnexal tenderness; AND treated for PID by a medical provider. Must also meet the surveillance case definition of *C. trachomatis* infection.[80]
Gonorrhea	Gonorrhea	Confirmed	A person with laboratory isolation of typical gram-negative, oxidase-positive diplococci by culture (presumptive *Neisseria gonorrhoeae*) from a clinical specimen, or demonstration of *N. gonorrhoeae* in a clinical specimen by detection of antigen or detection of nucleic acid via nucleic acid amplification

			(e.g., PCR) or hybridization with nucleic acid probe. (See appendix for laboratory criteria for diagnosis.)
		Probable	Demonstration of gram-negative intracellular diplococci in a urethral smear obtained from a male or an endocervical smear obtained from a female.
Gonorrhea	Gonorrhea with Pelvic Inflammatory Disease or Pelvic Inflammatory Disease with Gonorrhea	Confirmed	A clinical syndrome resulting from the ascending spread of the microorganisms from the vagina and endocervix to the endometrium, fallopian tubes, and/or contiguous structures; among sexually active women, characterized by pelvic or lower abdominal pain, with no cause for the illness other than PID identified. Must also meet the surveillance case definition of gonorrhea infection.[80]
		Probable	A sexually active woman with pelvic or lower abdominal pain, with no cause for the illness other than PID identified with one or more of the following minimum criteria present on pelvic examination: cervical motion tenderness OR uterine tenderness OR adnexal tenderness; AND treated for PID by a medical provider. Must also meet the surveillance case definition of gonorrhea infection.[80]
Syphilis	Syphilis (Primary)	Confirmed	A case that meets the clinical description of primary syphilis and the confirmatory laboratory criteria. (See appendix for clinical description and confirmatory laboratory criteria.)
		Probable	A case that meets the clinical description of primary syphilis and the supportive laboratory criteria. (See appendix for clinical description and supportive criteria.)
Syphilis	Syphilis (Secondary)	Confirmed	A case that meets the clinical description of secondary syphilis and the confirmatory laboratory criteria. (See appendix for clinical description and confirmatory laboratory criteria.)

		Probable	A case that meets the clinical description of secondary syphilis and the supportive laboratory criteria. (See appendix for clinical description and supportive criteria.)
Syphilis	Syphilis (Early non-primary, non-secondary)	Confirmed	A case that meets the clinical description of early non-primary, non-secondary syphilis and the confirmatory laboratory criteria. (See appendix for clinical description and confirmatory laboratory criteria.)
		Probable	A person with no clinical signs or symptoms of primary or secondary syphilis who has one of the following: No prior history of syphilis, AND a current reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods), AND a reactive treponemal test (e.g., TP-PA, EIA, CIA, or equivalent serologic methods), OR A prior history of syphilis and meets the supportive laboratory criteria. (See appendix for supportive laboratory criteria.) AND evidence of having acquired the infection within the previous 12 months based on epidemiological or laboratory criteria. (See appendix for epidemiological and laboratory criteria).

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FIGURES AND TABLES

Table 1. Demographic characteristics of chlamydia, gonorrhea, and early syphilis cases in 2010 to 2021 compared to the demographic characteristics of San Mateo County, CA in 2021.

	Chlamydia (2010-2021)		Gonorrhea (2010-2021)		Early Syphilis (2010-2021)		San Mateo County (2021)	
	Count	%	Count	%	Count	%	Count	%
Total	28,404	--	6,781	--	1,395	--	774,990	--
Sex								
Women	17,110	60.2%	1,666	24.6%	98	7.0%	392,065	50.6%
Men	11,208	39.5%	5,073	74.8%	1,175	84.2%	382,925	49.4%
Race/Ethnicity								
American Indian or Alaska Native	59	0.2%	14	0.2%	<10	0.1%	1,319	0.2%
Asian	3,871	13.6%	953	14.1%	211	15.1%	195,921	25.3%
Black	1,831	6.4%	721	10.6%	78	5.6%	19,791	2.6%
Hispanic or Latino	8,665	30.5%	2,037	30.0%	479	34.3%	203,839	26.3%
Multiracial	128	0.5%	52	0.8%	11	0.8%	28,152	3.6%
Native American or Pacific Islander	704	2.5%	127	1.9%	15	1.1%	11,144	1.4%
White, non-Hispanic	5,671	20.0%	1,954	28.8%	493	35.3%	314,824	40.6%
Age Category (years)								
< 15	87	0.3%	<10	0.1%	-	0.0%	139,790	18.0%
15-19	4,601	16.2%	455	6.7%	28	2.0%	33,195	4.3%
20-24	9,356	32.9%	1,362	20.1%	166	11.9%	37,072	4.8%
25-29	5,900	20.8%	1,513	22.3%	271	19.4%	44,175	5.7%
30-34	3,265	11.5%	1,171	17.3%	229	16.4%	46,965	6.1%
35-39	1,978	7.0%	766	11.3%	184	13.2%	53,469	6.9%
40-44	1,207	4.2%	547	8.1%	147	10.5%	54,579	7.0%
45-49	816	2.9%	372	5.5%	134	9.6%	56,257	7.3%
50-54	547	1.9%	280	4.1%	113	8.1%	57,904	7.5%
55-59	329	1.2%	192	2.8%	76	5.4%	53,914	7.0%
≥ 60	255	0.9%	109	1.6%	46	3.3%	197,670	25.5%
Healthy Places Index								
Quartile 1	226	0.8%	45	0.7%	8	0.6%	6,272	0.8%
Quartile 2	4,867	17.1%	953	14.1%	171	12.3%	42,432	5.5%
Quartile 3	6,750	23.8%	1,705	25.1%	336	24.1%	81,600	10.5%
Quartile 4	14,809	52.1%	3,656	53.9%	766	54.9%	507,347	65.5%

Figure 1. Chlamydia, gonorrhea, and early syphilis case counts, San Mateo County, CA, 2010-2021

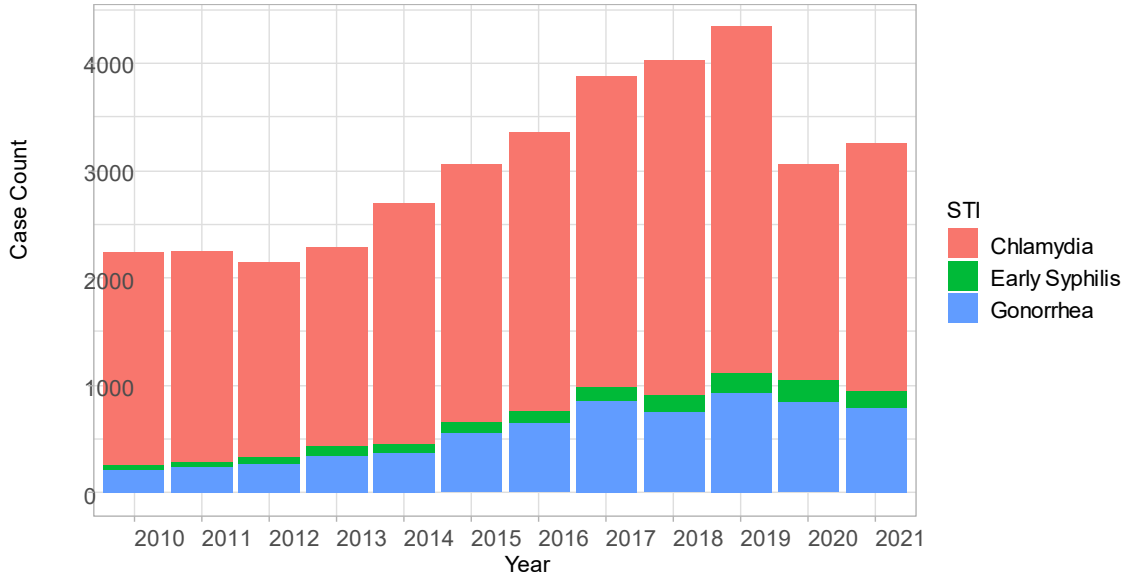


Table 2. Incidence of chlamydia, gonorrhea, and early syphilis per 100,000, San Mateo County, CA, 2010-2021

Year	Chlamydia	Gonorrhea	Early Syphilis
2010	274.5	30.2	4.9
2011	269.3	32.2	6.4
2012	243.7	35.8	8.6
2013	246.7	45.3	12.5
2014	295.4	48.4	11.1
2015	313.0	72.9	13.6
2016	337.7	83.3	15.7
2017	375.5	110.0	17.3
2018	402.3	96.8	20.6
2019	414.2	119.5	24.7
2020	260.1	108.2	26.6
2021	298.5	101.9	19.9

Table 3. Mean ages of chlamydia, gonorrhea, and early syphilis cases by time period

	Mean Age in Years in 2010 to 2013	Mean Age in Years in 2014 to 2019	Mean Age in Years in 2020 to 2021
Chlamydia	25.9	27.8*	28.3*
Gonorrhea	31.3	32.1*	32.7
Early Syphilis	37.7	36.7	36.3

*$p<0.05$, indicating that this change is statistically significant from the mean age from the previous time period

Figure 2. Incidence of chlamydia, gonorrhea, and early syphilis, San Mateo County, CA, 2010-2021

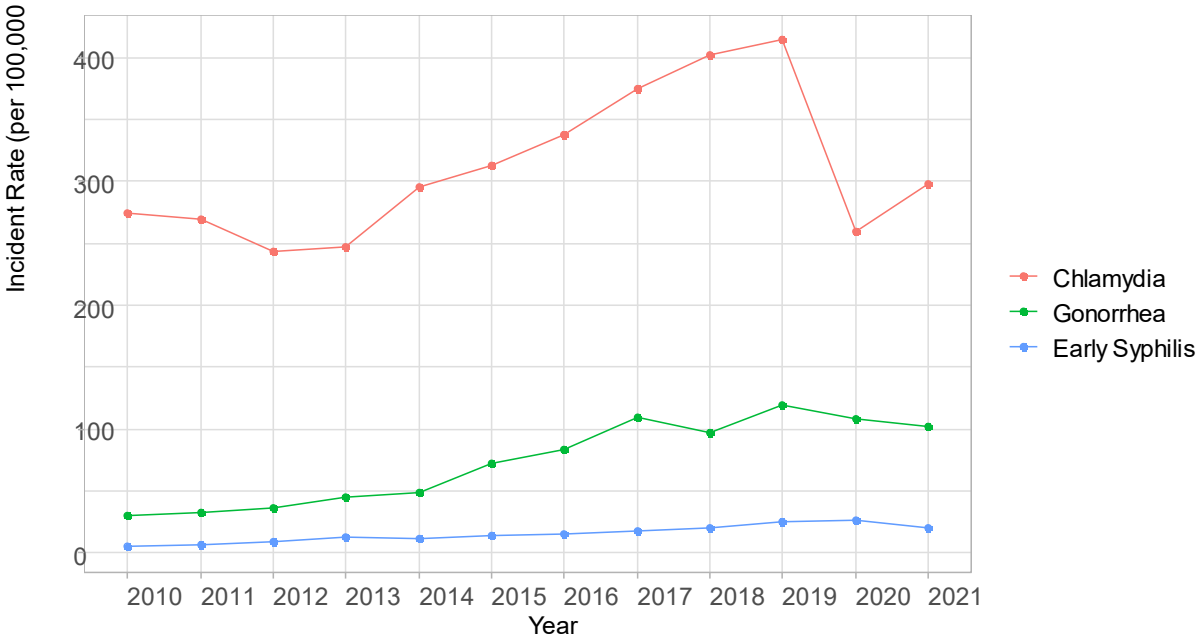


Figure 3. Incidence of chlamydia, San Mateo County, CA, 2010-2021

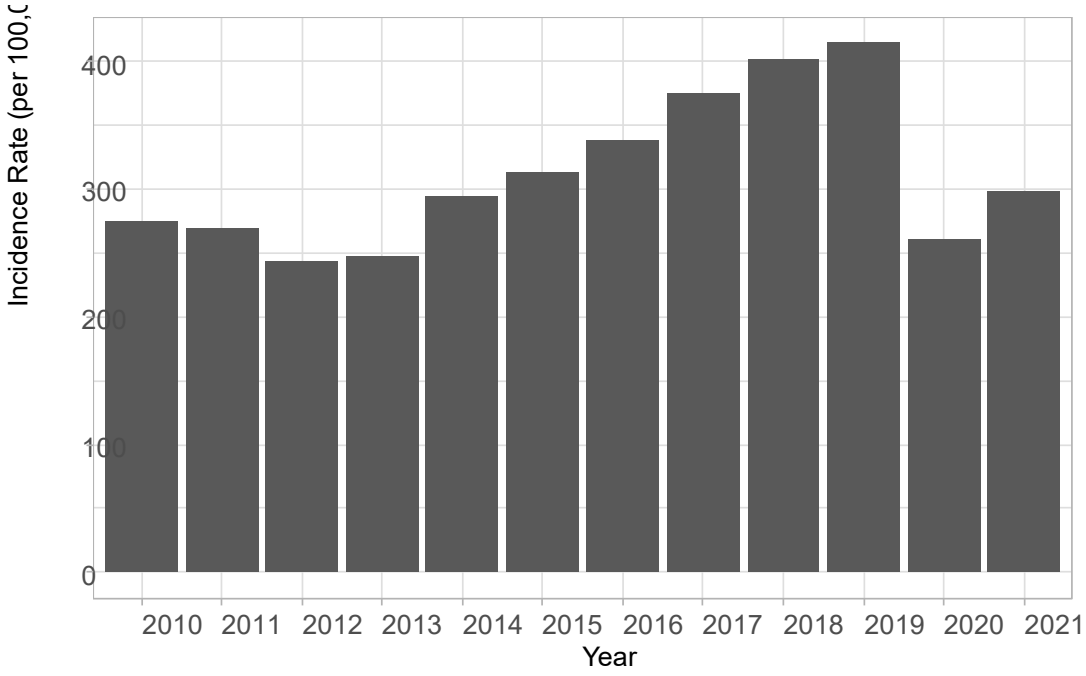


Figure 4. Incidence of gonorrhea, San Mateo County, CA, 2010-2021

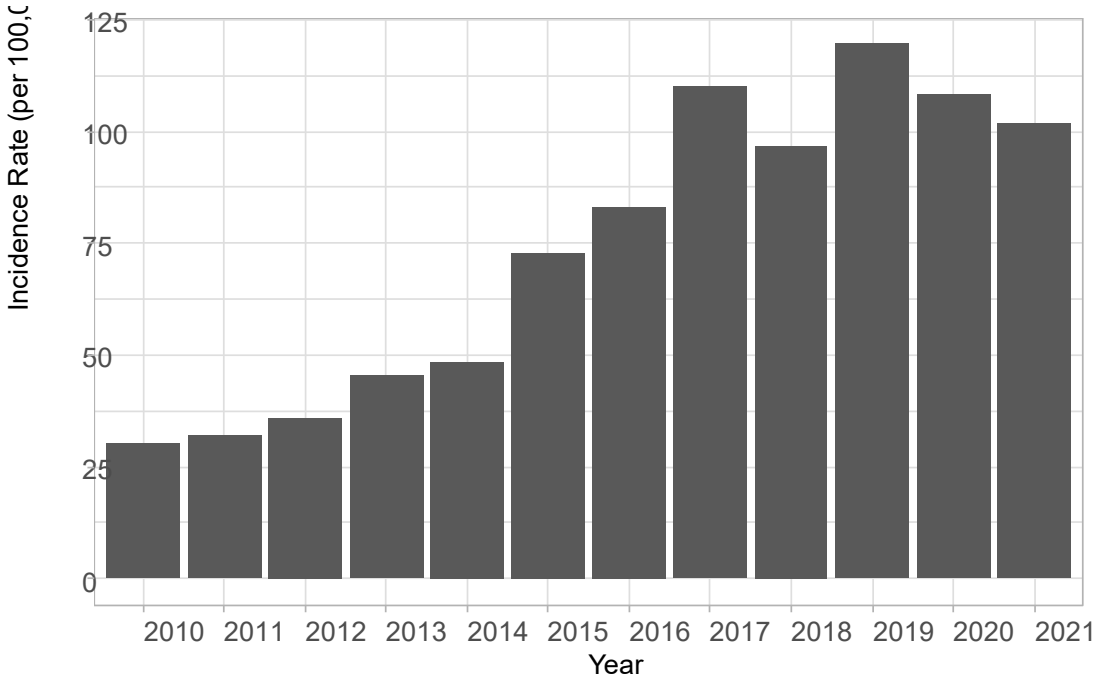


Figure 5. Incidence of early syphilis, San Mateo County, CA, 2010-2021

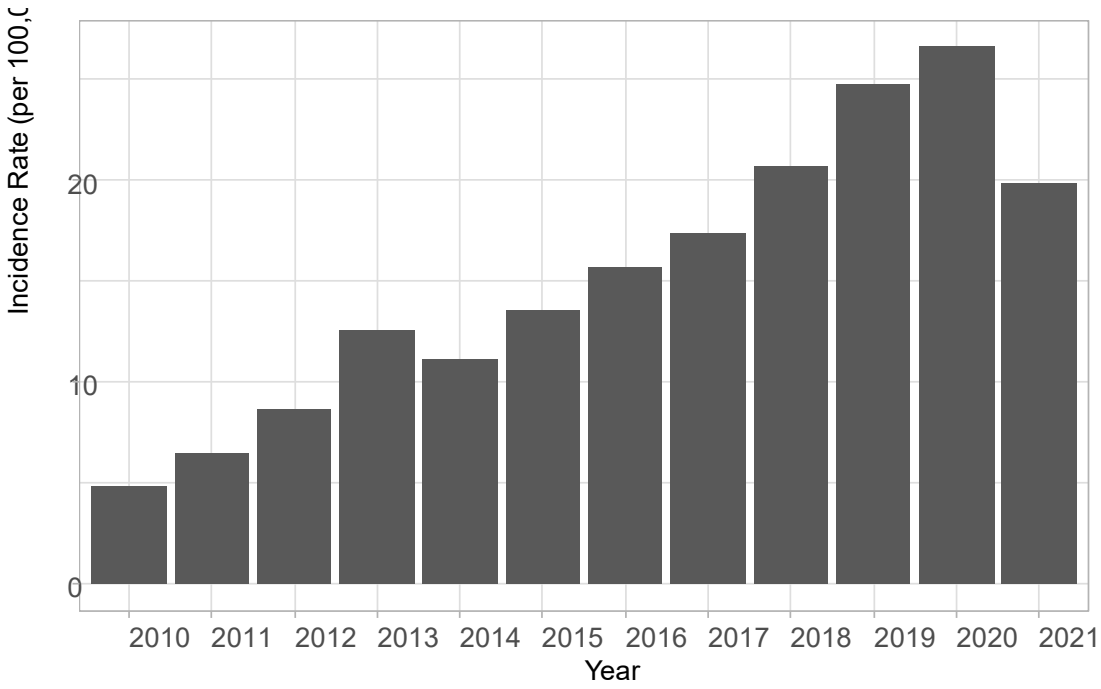


Figure 6. Distribution of Healthy Places Index quartiles, San Mateo County, CA, 2010-2021

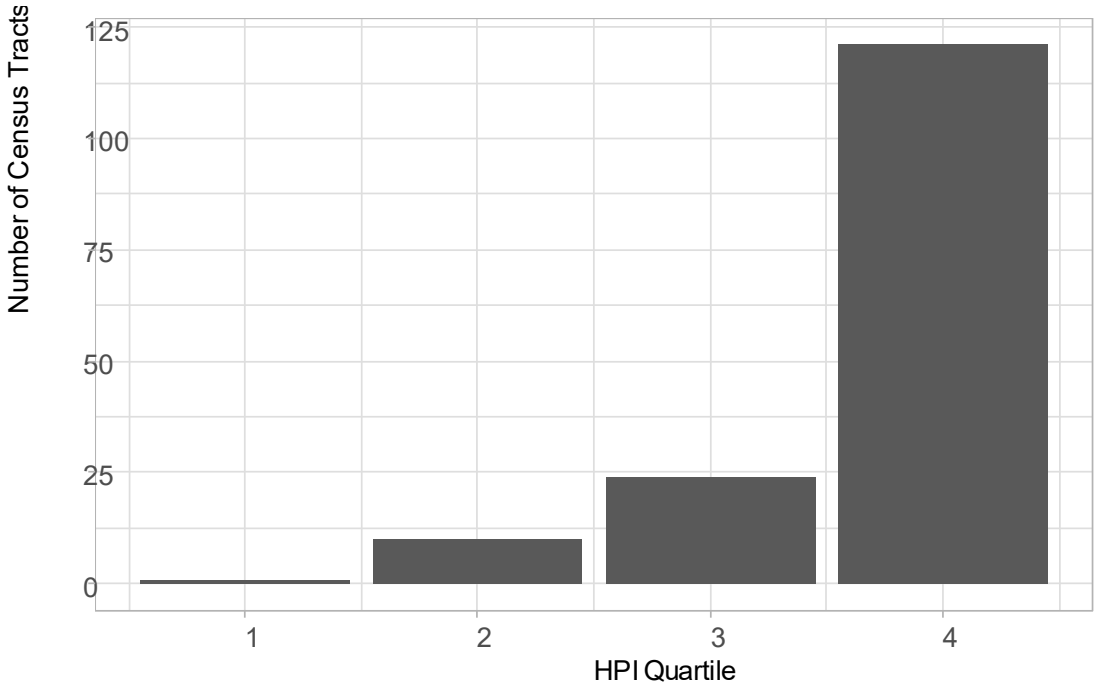


Figure 7. Incidence of chlamydia by sex, San Mateo County, CA, 2010-2021

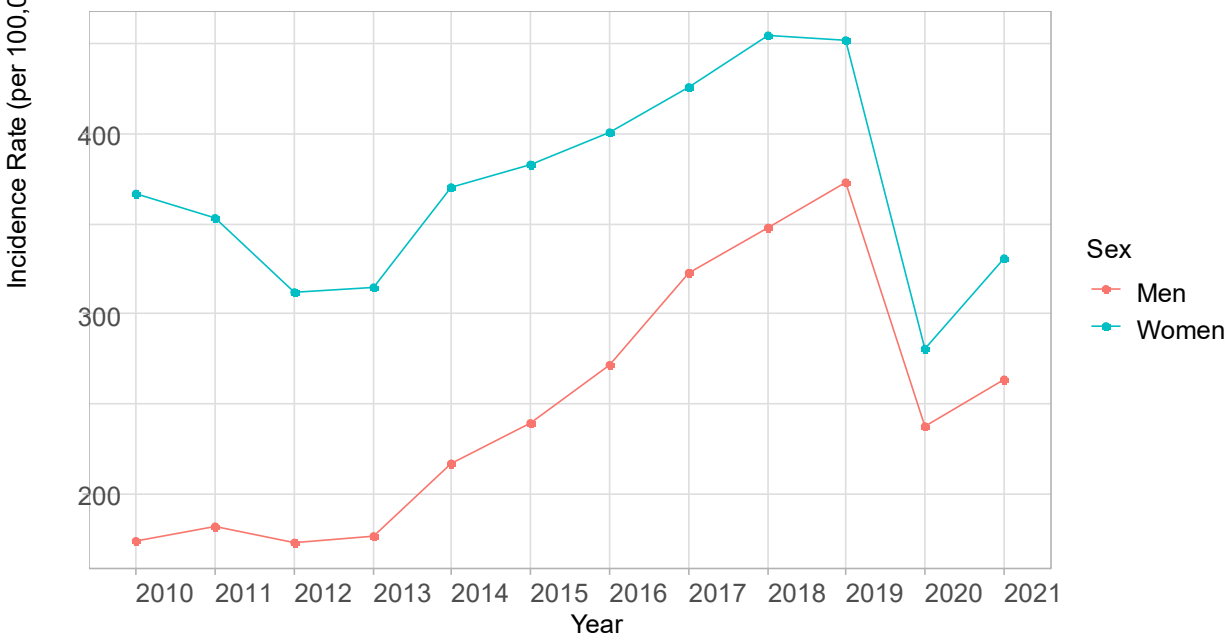


Figure 8. Incidence of gonorrhea by sex, San Mateo County, CA, 2010-2021

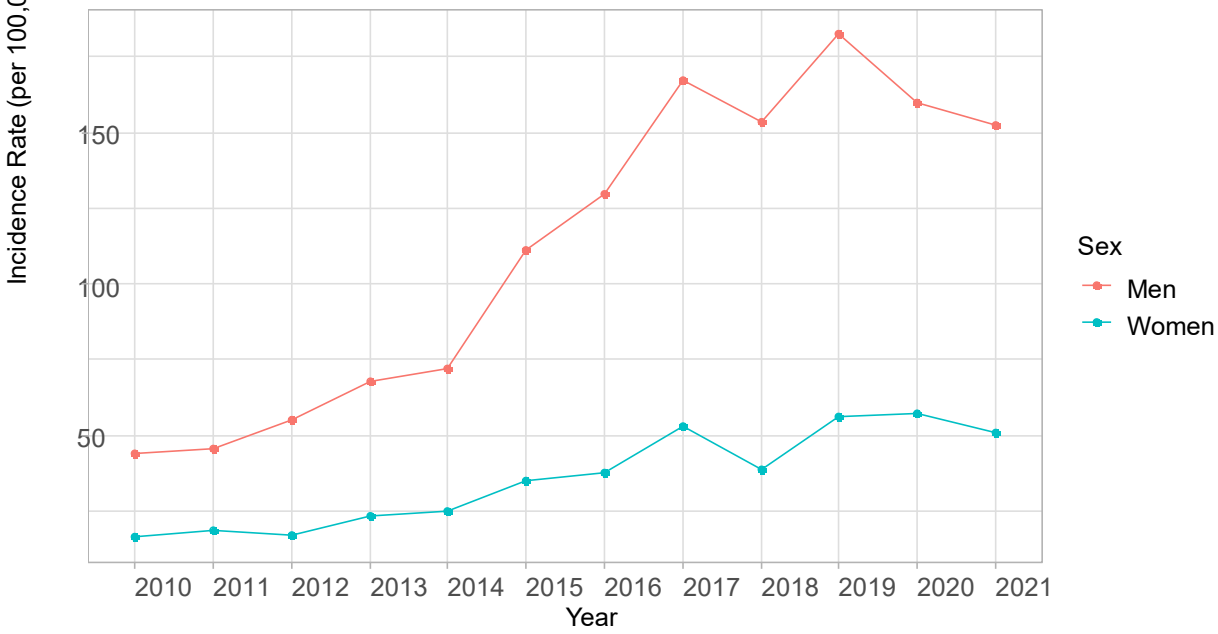


Figure 9. Incidence of early syphilis by sex, San Mateo County, CA, 2010-2021

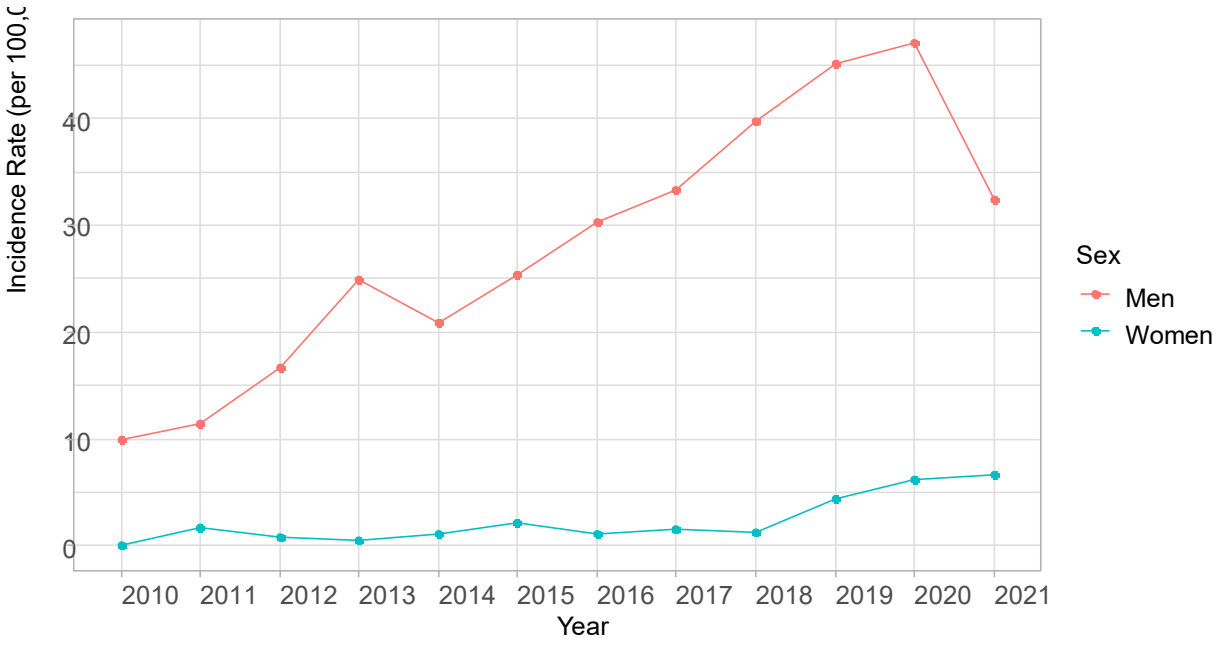


Figure 10. Incidence of chlamydia by race/ethnicity, San Mateo County, CA, 2010-2021

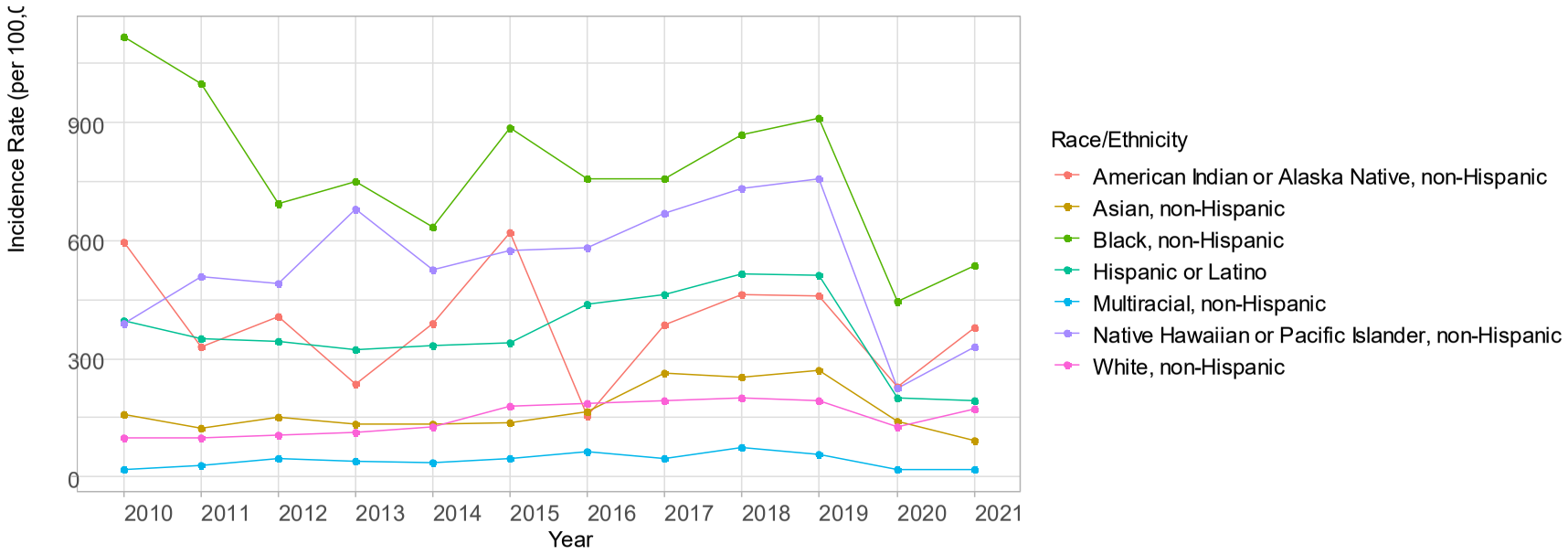


Figure 11. Incidence of gonorrhea by race/ethnicity, San Mateo County, CA, 2010-2021

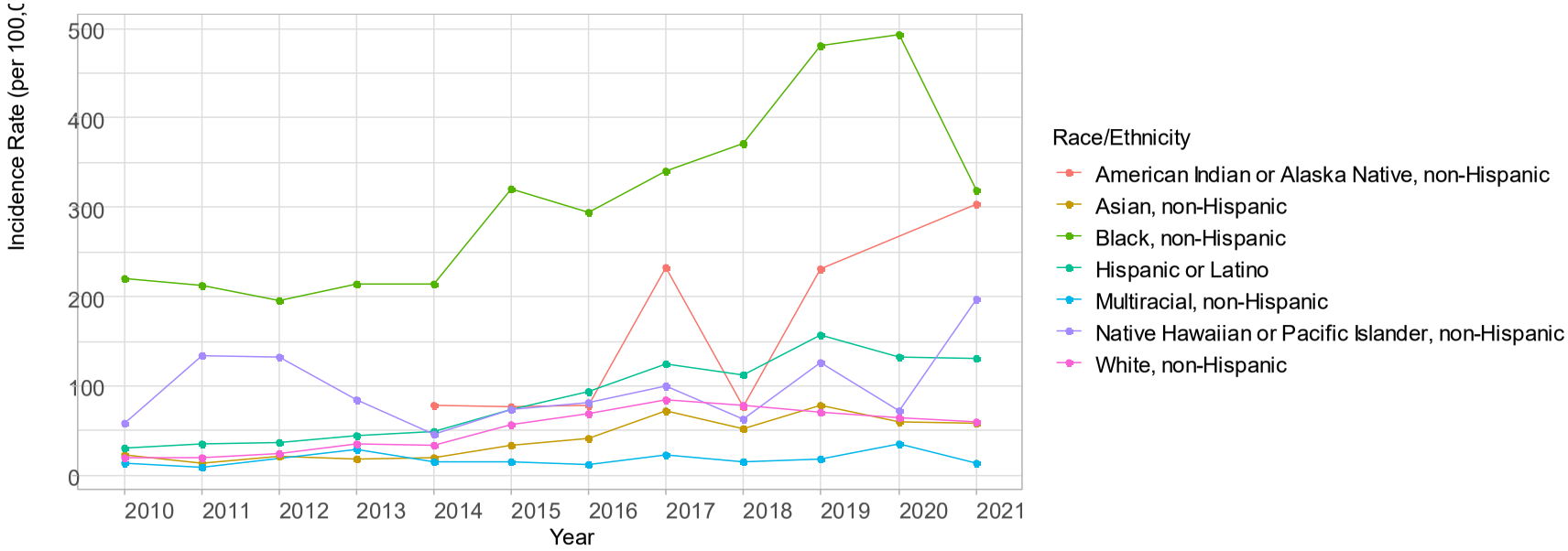


Figure 12. Incidence of early syphilis by race/ethnicity, San Mateo County, CA, 2010-2021

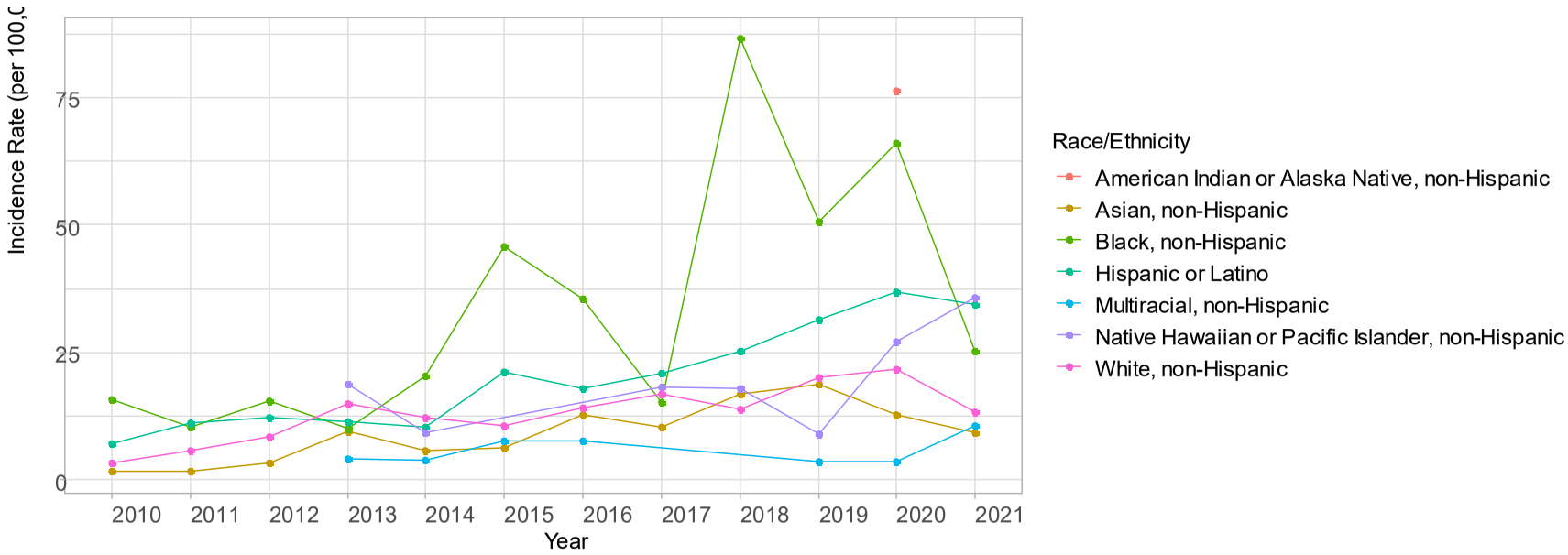


Figure 13. Incidence of chlamydia by race/ethnicity, stratified by sex, San Mateo County, CA, 2010-2021

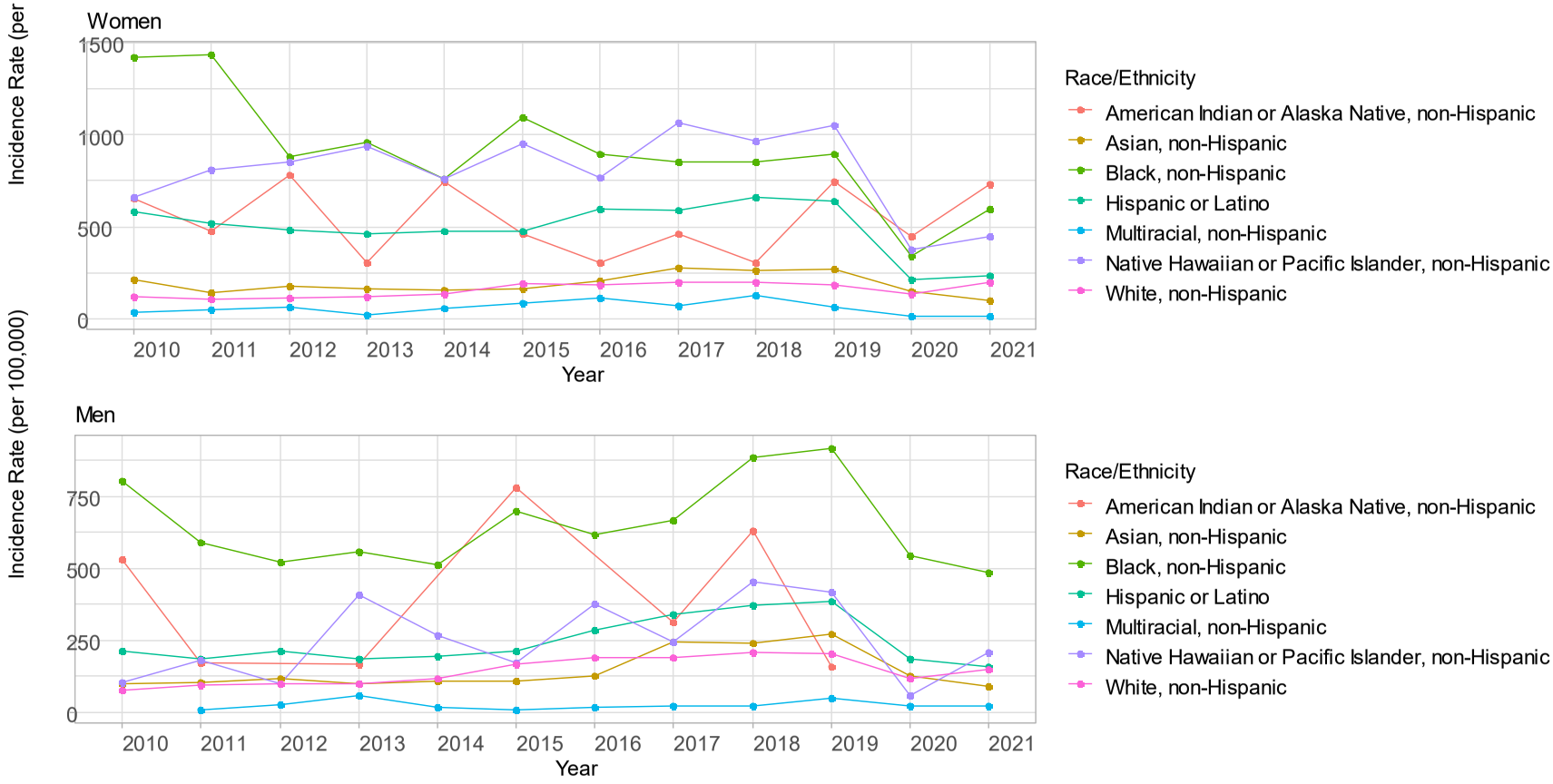


Figure 14. Incidence of gonorrhea by race/ethnicity, stratified by sex, San Mateo County, CA, 2010-2021

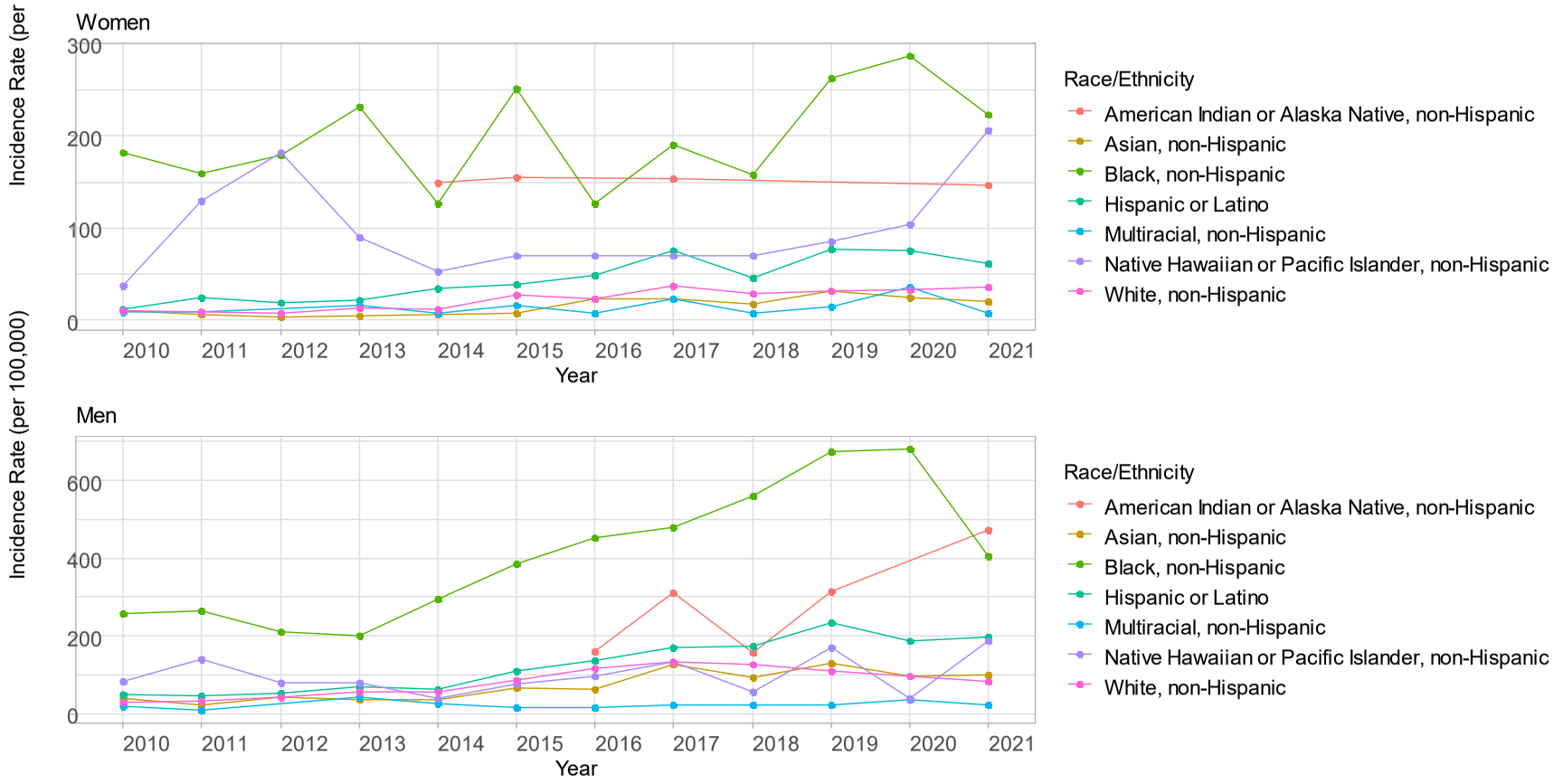
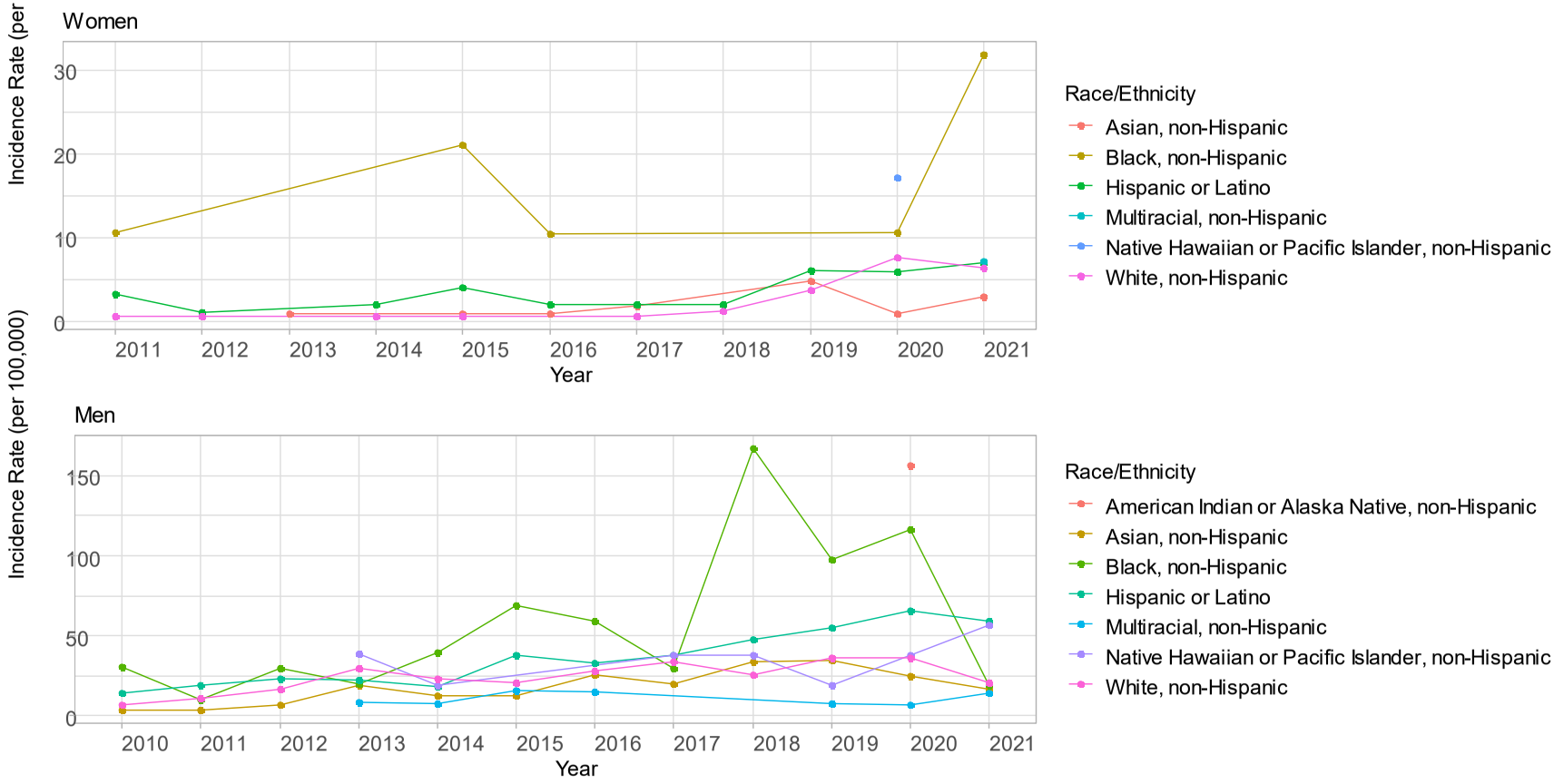


Figure 15. Incidence of early syphilis by race/ethnicity, stratified by sex, San Mateo County, CA, 2010-2021



Note: There were no cases of early syphilis reported for women in 2010.

Figure 16. Incidence of chlamydia by age category, San Mateo County, CA, 2010-2021

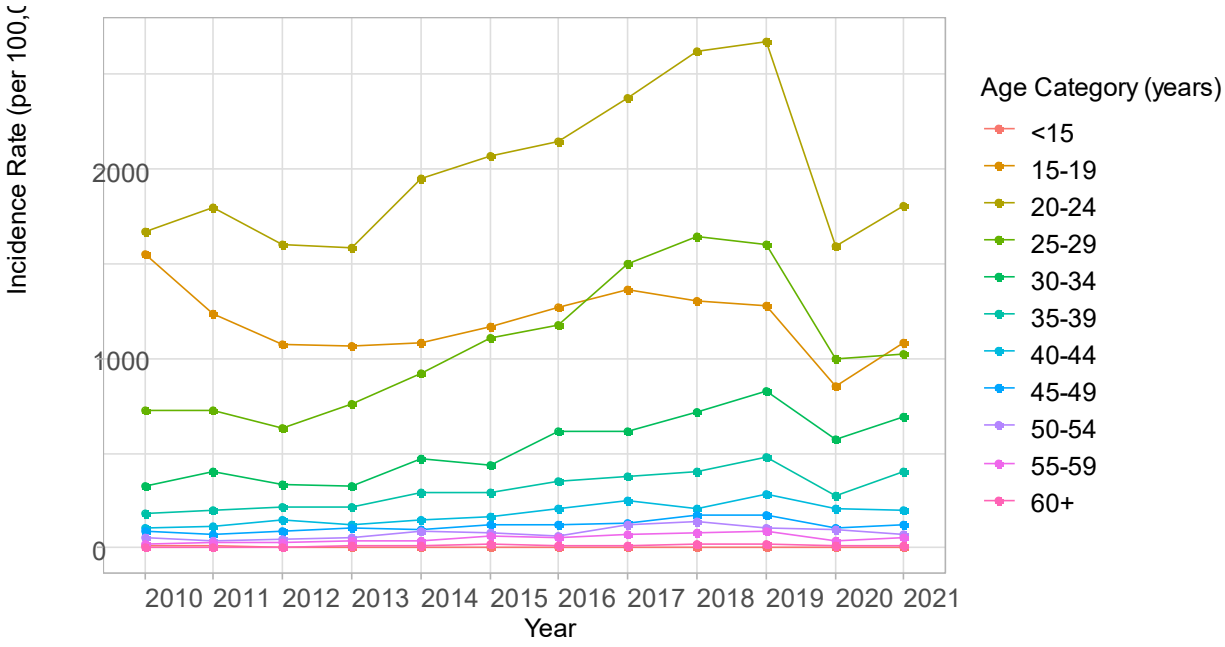


Figure 17. Incidence of gonorrhea by age category, San Mateo County, CA, 2010-2021

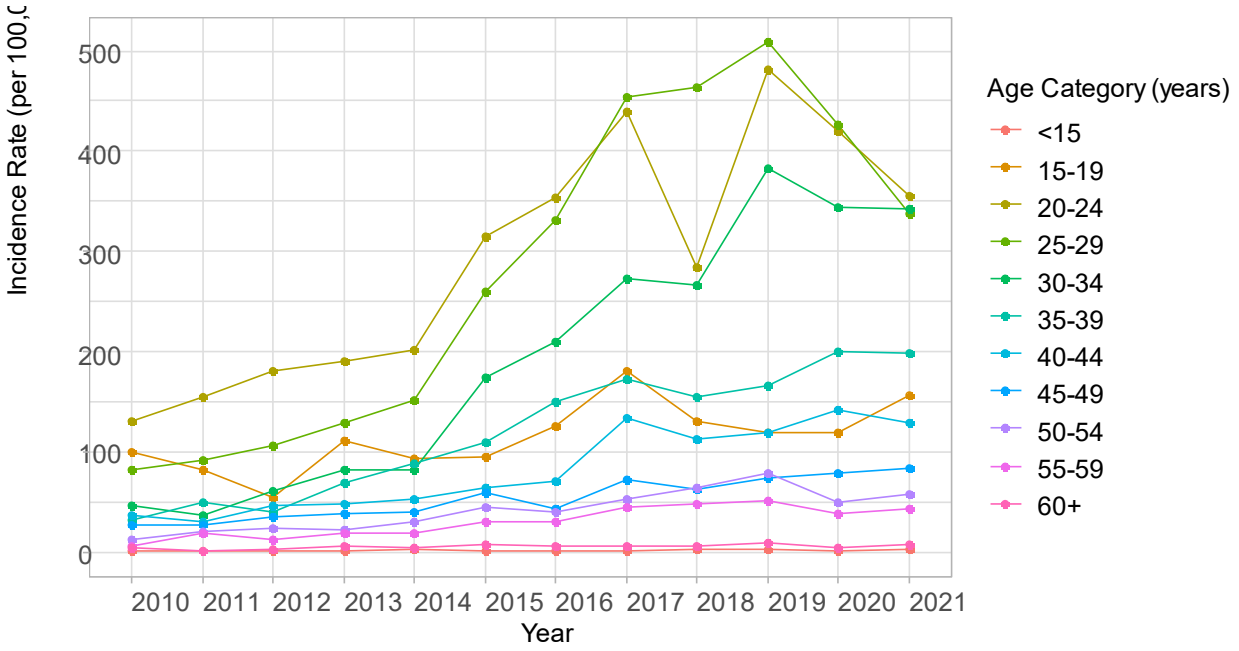


Figure 18. Incidence of early syphilis by age category, San Mateo County, CA, 2010-2021

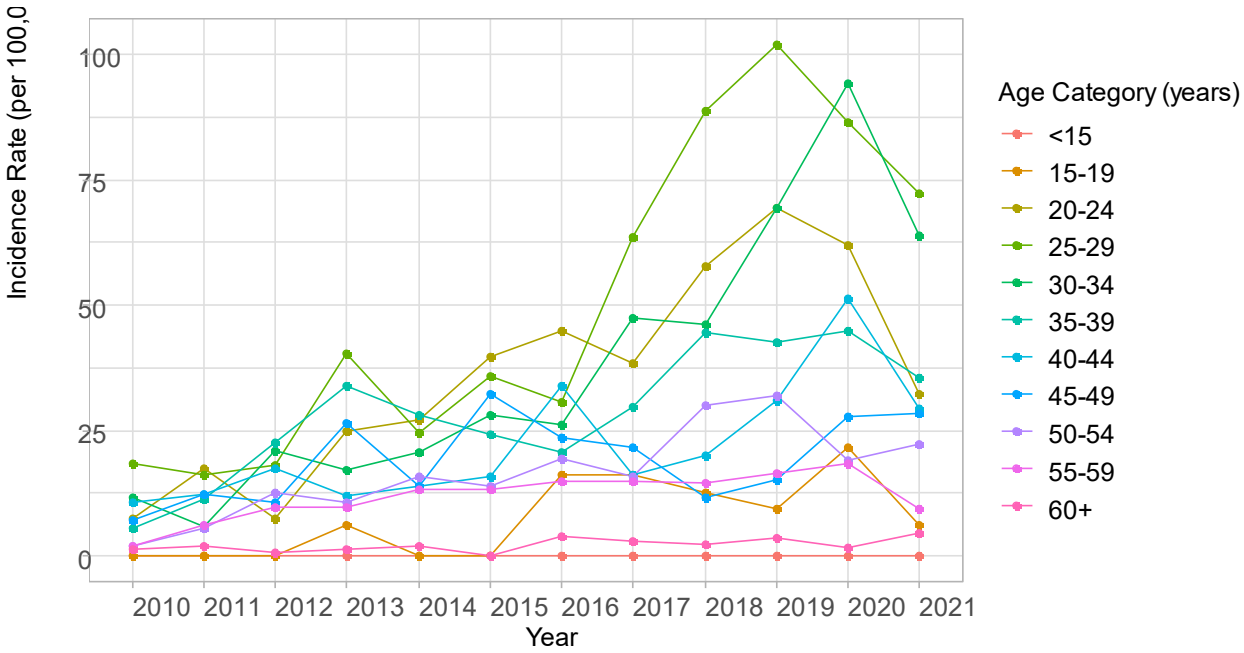


Figure 19. Incidence of chlamydia by Healthy Places Index score quartile, San Mateo County, CA, 2010-2021

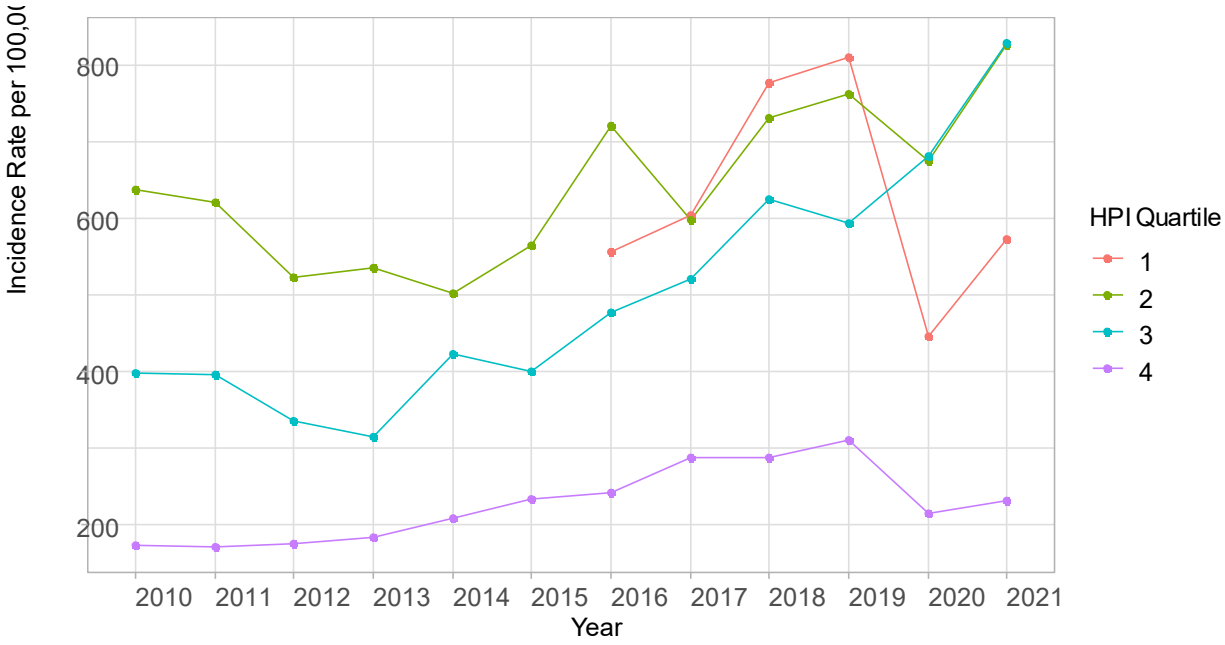


Figure 20. Incidence of gonorrhea by Healthy Places Index score, San Mateo County, CA, 2010-2021

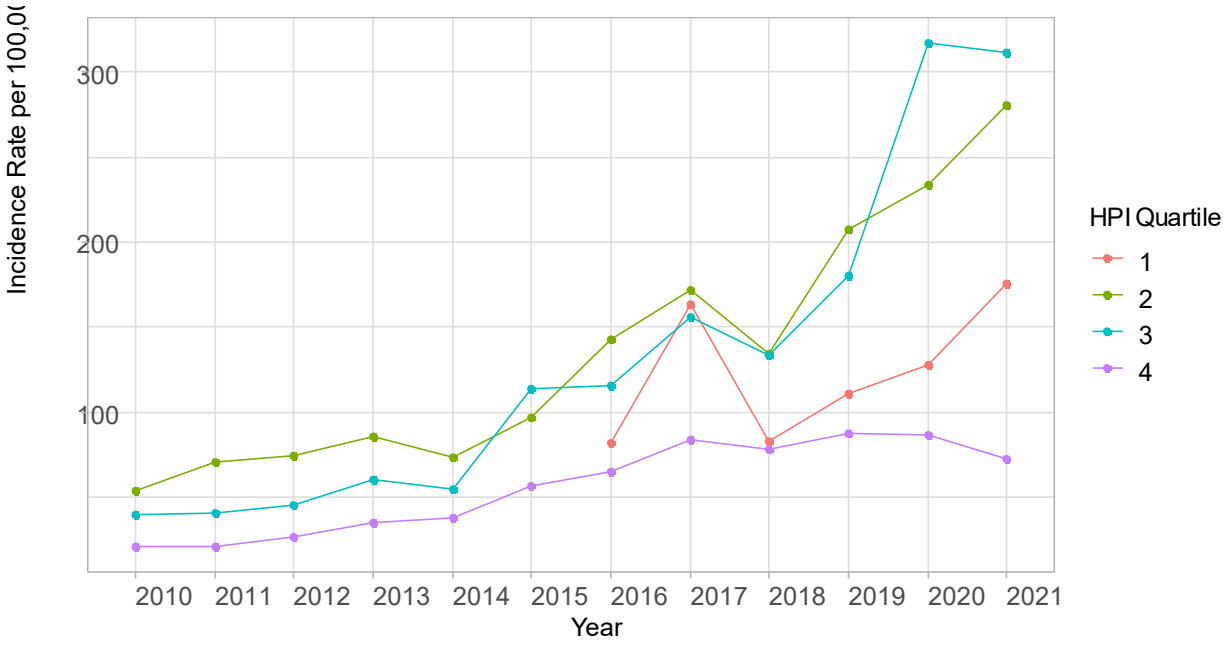
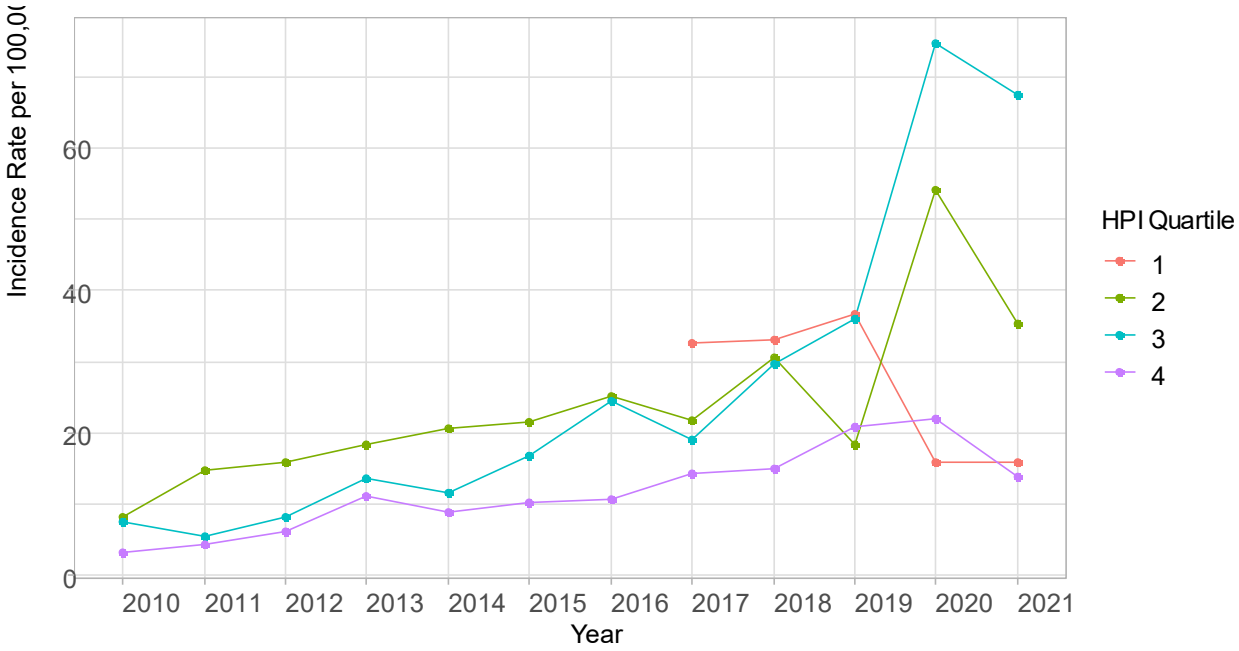


Figure 21. Incidence of early syphilis by Healthy Places Index score, San Mateo County, CA, 2010-2021



CHAPTER 2

TITLE: Demographic and Neighborhood Factors Associated with Chlamydial and Gonorrheal Reinfection
AUTHORS: Moon Choi-McInturff, Asa Ohsaki, Aracely Tamayo, Elizabeth Jump, Stefano Bertozzi, Vivian Levy, Arthur Reingold

ABSTRACT
Background: Patterns in chlamydia and gonorrhea reinfections are not well understood. Repeat chlamydia or gonorrhea infections can lead to sequelae, such as pelvic inflammatory disease (PID) in women, as chlamydia and gonorrhea reinfections are known to occur in a small, core group of individuals. There is little known about how neighborhood factors and social contexts are associated with chlamydia and gonorrhea reinfection.
Methods: The California Reportable Disease Information Exchange (CalREDIE) was used to identify chlamydia and gonorrhea reinfections from 2010 to 2021 were linked to public health laboratory data and to general hospital records. A retrospective cohort analysis was conducted using generalized estimating equations to calculate rate ratios of chlamydia and gonorrhea reinfection, with age, sex, race/ethnicity, and Health Places Index quartiles (as a measure of neighborhood opportunity) as independent predictors.
Results: The majority of individuals with a chlamydia or gonorrhea reinfection only had one reinfection (69.4% for chlamydia, 60.7% for gonorrhea). The rate ratio of chlamydia and reinfection was highest in Black individuals (IRR: 1.15, 95% CI: 1.00, 1.33) compared to White individuals, whereas the rate ratio of gonorrhea reinfection was highest in Multiracial individuals (IRR: 1.33, 95% CI: 0.62, 2.86), though this result was not statistically significant. There was no discernable association between HPI quartile and chlamydia and gonorrhea reinfection.
Conclusion: The epidemiological characteristics of those with chlamydia and gonorrhea reinfections correlate with the epidemiology of chlamydia and gonorrhea cases. Future studies should focus on those with high counts of chlamydial and gonorrheal reinfection, as they may differ epidemiologically from those who have only had one or two reinfections of chlamydia and gonorrhea.

INTRODUCTION
The incidence of sexually transmitted infections (STIs) has been rising in the USA since 2014, after decades of progress toward reducing rates of these infections. Infection by *Chlamydia trachomatis* and *Neisseria gonorrhoeae* cause chlamydia and gonorrhea, respectively, and comprise the vast majority of STIs reported to the U.S. Centers for Disease Control and Prevention (CDC) every year. Chlamydia was the most frequently reported condition among the 132 health conditions reported to the CDC before the COVID-19 pandemic, with 1,808,703 cases of chlamydia; 616,392 cases of gonorrhea were also reported in 2019.[1,2] While chlamydia and gonorrhea infections are typically cleared by treatment with an appropriate antibiotic regimen, the infection may be difficult to identify, due to nonspecific symptoms or a lack of symptoms altogether, particularly in women, creating opportunities for continued transmission and complications resulting from untreated infection. Untreated chlamydia and gonorrhea infections can progress to pelvic inflammatory disease (PID), caused by the infection of a woman's uterus, fallopian tubes or ovaries, which can result in ectopic pregnancy and infertility. *N. gonorrhoeae* is showing increased antibiotic resistance, making it more difficult to treat.

Infection with chlamydia or gonorrhea is also associated with an elevated risk of HIV infection.[3] With the increasing incidence rates of chlamydia and gonorrhea, there are more opportunities for individuals with a previous infection to be reinfected. Despite the increase in chlamydia and gonorrhea rates and the elevated risk of infection and of related sequelae, chlamydia and gonorrhea reinfection patterns are still poorly understood. Prior epidemiological studies of chlamydia and gonorrhea reinfections have focused on individual-level risk factors, such as age and sexual behaviors, often excluding ecologic-level variables that are typically upstream structural factors, such as neighborhood quality,[4] incarceration rates,[5] male to female ratios,[6] and residential segregation by census tract.[7] While chlamydia infections disproportionately affect women and gonorrhea infections disproportionately affect men, particularly men who have sex with men (MSM),[1] the rates of reinfections with chlamydia and gonorrhea also vary by age and race/ethnicity. Adolescents and young adults have the highest rates of chlamydia and gonorrhea,[1] but they have had fewer opportunities for reinfection compared to those older in age, as those older in age have had more time to have sexual encounters and potential exposure to chlamydia or gonorrhea infection and reinfection. Studies of chlamydia and gonorrhea reinfection have examined on adolescent and young adult populations (i.e., ages 14 to 25 years), but they typically have been conducted in urban STD clinics, and populations have rarely been in the context of a county, or some other large administrative geographical unit, over a long period of time.

STI transmission can be mathematically summarized as the product of an individual's sexual network (c: the mean rate of sexual partner change within the population); the probability of transmission (β: mean probability of transmission per exposure); and the duration of infectiousness (D: mean duration of infectiousness of newly infected persons).[8] The transmission model that best describes infection with *C. trachomatis* and *N. gonorrhoeae* is the S-I-S model, where an individual is susceptible to infection, is infected, then either naturally clears the infection or is treated for it, which then allows for the individual to become susceptible to infection again.[9] As a result, once an individual is cured of an infection, each subsequent infection is considered to be a new infection. The demographic profile of those who have subsequent infections (i.e., reinfections) is not well characterized, beyond the fact that chlamydia reinfections occur primarily in young women[10] and gonorrhea reinfections occur primarily in young men.[11] To date, there have been no studies examining the association of neighborhood quality, such as that measured by CDC's Social Vulnerability Index (SVI) or the California Healthy Places Index (HPI), and reinfections with chlamydia or gonorrhea. Neighborhood characteristics, such as poverty and racial segregation, are known to be associated with differences in chlamydia and gonorrhea incidence.[12] Recurrent chlamydia infections are associated with higher risk of ectopic pregnancy and intrauterine pregnancy.[13] Reducing transmission, then, requires a reduction in one or more of the three components previously mentioned—the rate of sexual partner change within the population, the probability of transmission, or the duration of infectiousness. These are proximal risk factors for STI transmission and infection. There are distal factors that can influence these three factors, such as social networks, access to screening and health care, and socioeconomic resources. The link between socioeconomic status (SES) and STI incidence has been established in prior studies,[14–16] but SES is typically operationalized as individual-level income or educational attainment, which does not always capture the multiple dimensions of SES.[17] Additionally, it is often difficult or impossible to measure individual-level SES in secondary datasets, such as public health

surveillance data and laboratory data, which typically prompts researchers to use proxies for SES such as race/ethnicity or occupation, variables that are more typically available in such datasets. The accuracy of these data concerning demographic and SES variables varies, depending on the dataset. For example, surveillance datasets are comprised of information from multiple reporting sources, ranging from laboratory results to providers completing a confidential morbidity report, whereas birth record data are collected from the birthing person and medical provider. Laboratory results may not have race/ethnicity information available at all, whereas self-reported records, such as birth records, are more accurate and standardized. In addition to the potential for misclassification of demographic and SES information, secondary datasets often contain very little or no individual-level SES data. Ecological-level variables, such as median household income for a census tract, can help fill this gap by including information for geographical areas where people live, such as census tract, given that cases' addresses are typically available and can be placed in these geographical areas. While these ecological-level SES variables are not substitutes for individual-level SES, they can still provide some of an individual's geographical context, especially with smaller geographical units, such as census tract. One such ecological-level measure of SES is the Healthy Places Index (HPI), which was developed by the Public Health Alliance of Southern California. Although there are other composite measures to summarize neighborhood quality, such as the CDC Social Vulnerability Index, HPI was created to characterize neighborhoods with positive language (healthy places vs. social vulnerability) and to consider different domains of a neighborhood's characteristics. HPI emerged in California as the health equity measure of choice during the COVID-19 pandemic, using the lowest quartile as an indicator of the most vulnerable census tracts.[18] Given California local health departments' familiarity with HPI, it was used in this analysis to identify the most vulnerable census tracts.

HPI also considers multi-faceted domains of a neighborhood's characteristics. The HPI score is a measure of neighborhood opportunity which "can be thought of as all of the pathways to better lives, including through health, education, and employment."[19] Neighborhood opportunity has many facets, as it considers how an individual's physical neighborhood and the social, economic, and institutional contexts of the neighborhood (e.g., gender composition, income inequality) create and guide these pathways to better lives.[19] It is well established that neighborhood environments are linked to many health outcomes, such as obesity, depression, asthma, and STIs.[4,20–23] Neighborhoods are associated with a variety of health exposures and outcomes, in part because of the availability and of access to resources.[24] This association can be explained by the Fundamental Causes of Disease theory, which posits that "(1) SES influences multiple disease outcomes; (2) SES is related to multiple risk factors for disease and death; (3) the deployment of resources plays a critical role in the association between SES and health/mortality; and (4) the association between SES and health/mortality is reproduced over time via the replacement of intervening mechanisms."[25] While California has other measures of neighborhood opportunity, such as CalEnviroScreen, the HPI contains a wide range of thematic areas called "domains," from health outcomes (e.g., percent of adults who were diagnosed with cancer) to political engagement (e.g., percent of total voter registration) to environmental indicators (e.g., tree canopy cover).[26] The HPI has shown good concordance with the Intercity Hardship Index (which measures urban hardship)[27] and with the 200% Federal Poverty Level, and has been compared to other indices that measure social determinants of health. While the HPI is not updated as regularly as other indices, such as the SVI, it is available at the census tract level, as these other indices are. Other composite measures or indices, created for other purposes,

such as the CalEnviroScreen, are often used as a proxy for neighborhood health, such as a neighborhood's capacity to respond to hazardous events,[28] whereas the HPI is specifically focused on the healthiness of California neighborhoods. San Mateo County has been ranked as one of the healthiest counties in California.[29] Although San Mateo County has better health outcomes compared to California and the U.S. as a whole, a county-wide average masks the underlying disparities in household income, access to health care, and neighborhood quality.

Prior research on STIs has focused on individual-level risk factors to help target interventions at the individual-level. As the body of literature on the effects of structural factors and their relationship with health outcomes grows,[30–33] it is important to examine distal factors (e.g., residential segregation and neighborhood quality) and their relationship to the incidence of STIs and related sequelae. A recent report released by the Committee on Prevention and Control of Sexually Transmitted Infections in the United States stated, "The committee adopted a Modified Social Ecological Framework of Sexual Health and STI prevention, Control, and Treatment that moves beyond individual-level behavioral or biomedical constructs toward a comprehensive framework to address the interconnected and mutually reinforcing structural and social determinants of health and health inequities."[34] The HPI is one such measure of social determinants of health that can provide a wider lens to the structural and social determinants of STI outcomes. HPI has been used by local and county health departments in California and is widely available. Studies that describe and examine associations between structural factors and STI outcomes should be conducted by health departments to better understand which subgroups within their populations are disproportionately burdened by STIs and related sequelae. The objectives of this study were (1) to use and link data sources concerning *C. trachomatis* and *N. gonorrhoeae* reports and laboratory data typically available at health departments to build datasets with more information than any of the original datasets alone (e.g., CalREDIE) and to impute missing values and (2) to characterize the age, sex, and racial/ethnic composition of individuals in San Mateo County with chlamydia and gonorrhea reinfections and to explore the association between these demographic factors, along with HPI, with chlamydia and gonorrhea reinfection.

MATERIALS AND METHODS

Study sample

California Reportable Disease Information Exchange

San Mateo County residents who are at least 14 years of age with a diagnosis of chlamydia or gonorrhea infection were identified in the California Reportable Disease Information Exchange (CalREDIE) system, the electronic disease reporting system of the California Department of Public Health. All diseases reportable under Title 17 are mandated to be reported to local health departments, whether by a confidential morbidity report or electronic laboratory reporting. All positive laboratory results or a clinical diagnosis of these conditions are received by San Mateo County, resulting in the most complete ascertainment of diagnosed cases possible. San Mateo County began using CalREDIE as its primary tool for electronic reporting, case management, and surveillance in 2010, and CalREDIE contains every clinician- or laboratory-reported case of chlamydia and gonorrhea in San Mateo County. CalREDIE has specific disease conditions, such as chlamydia with pelvic inflammatory disease (PID), which were included as a case of chlamydia. CalREDIE also specifies a resolution status, which is defined as "the current status of the disease incident."[35] Case definitions can be nuanced; Tables 1 and 2 in the Appendix contain

more information on the definitions used for cases of chlamydia and gonorrhea infection. It should be noted that chlamydia ceased to be a condition required to be reported by healthcare providers on October 1, 2019 but continued to be required by laboratories.[36]

There were 28,404 chlamydia cases and 6,781 gonorrhea cases in San Mateo County, CA in CalREDIE from 2010 to 2021. It was possible for the same individual to be in CalREDIE for both chlamydia and gonorrhea or for repeat infections by the same organism.

The CalREDIE system automatically assigns a census tract to each record according to the registered address. The CalREDIE system contains data on the biological sex of the case, which were used in this analysis in the absence of information on gender. The CalREDIE dataset was used as the dataset to which the other data were matched, so that the final dataset had the most complete roster of individuals with chlamydia or gonorrhea infection.

San Mateo Medical Center

San Mateo Medical Center is San Mateo County's safety net hospital and clinic system, and primarily serves the county's low-income population, who are insured through the Health Plan of San Mateo. Records were available only from 2013 onward due to a change in records systems. There were several race and ethnicity variables available in this dataset with varying levels of completeness. A race/ethnicity variable that followed U.S. Census Bureau classifications was created from a variable for ethnic nationalities with unknown values imputed from another race/ethnicity variable, if available. These records were linked to the CalREDIE case roster through deterministic and probabilistic linkage, using patient first name, last name, and date of birth.

San Mateo County Public Health Laboratory

San Mateo County Public Health Laboratory conducts *C. trachomatis* and *N. gonorrhoeae* diagnostic testing for San Mateo Medical Center and the County Public Health clinic, including the County STI clinics. San Mateo County's Public Health Laboratory data contain separate fields for Hispanic ethnicity and race, so a race/ethnicity variable that follows U.S. Census Bureau classifications was created from these variables. These records were linked to the CalREDIE case roster through deterministic and probabilistic linkage, using patient first name, last name, and date of birth.

Probabilistic linkage

Deterministic linkage has been used by public health agencies to identify interjurisdictional cases. However, deterministic linkage has lower sensitivity when the data vary (e.g., name change). As a result, deterministic linkage performs best with unique identifiers, such as social security number or medical record number, that are identical across all datasets to be linked. However, this information may not be routinely collected and available in surveillance data, or may not be identical. Although deterministic linkage results in high specificity of matches, it may also miss true matches if any of the matching factors are not identical. In these instances, probabilistic linkage can be used to use close or partial matches based on a set parameter of matching criteria. This was applied in this analysis by creating a roster of all unique individuals who have had a chlamydia or gonorrhea infection by matching individuals from the San Mateo Medical Center records and San Mateo County Public Health Laboratory records to the CalREDIE records by

deterministic linkage using first name, last name, date of birth, and year of specimen collection. Those who were not matched in the deterministic linkage were identified by probabilistic linkage, using the fastLink package in R. The fastLink package uses the Fellegi-Sunter probabilistic record linkage model and is an efficient algorithm that retains good sensitivity.[37–39] Probabilistic linkage was conducted using first name, last name, and date of birth, then a posterior probability, which quantifies the certainty of the match, was calculated by the fastLink algorithm to create a cut off of higher than 85% for date of birth matches. The matched individuals were then joined back to the original CalREDIE data by a unique identifier used within the CalREDIE systems with the additional information that the linkage provided from the San Mateo Medical Center records and the and San Mateo County Public Health Laboratory records.

Imputing missing race and ethnicity values

The final race/ethnicity variable was created by grouping the different race and ethnicity variables across data for CalREDIE, San Mateo Medical Center, and San Mateo County Public Health Laboratory. Race/ethnic groups followed U.S. Census Bureau classifications: American Indian/Alaska Native, non-Hispanic; Asian, non-Hispanic; Black or African American, non-Hispanic; Hispanic; Native Hawaiian or Other Pacific Islander, non-Hispanic; White, non-Hispanic; and multiracial. Hispanic ethnicity was classified as Hispanic, regardless of race, even if race was unknown. Individuals with unknown Hispanic ethnicity were grouped as their race variable and non-Hispanic. Those with missing race and ethnicity values were grouped as "Unknown" and were excluded from the analysis. This classification approach was described in Yoon et al. 2021, where they used race or ethnicity information to make a "best guess" at imputing the missing values.

Measures

Dependent variables

Chlamydia reinfections were defined as any individual who appeared in CalREDIE with a disease condition of chlamydia or related to chlamydia (refer to Table 2 in the Appendix) at least 30 days after the last date they were entered into the CalREDIE system for any chlamydia-related condition. This one-month interval was chosen because it is unlikely that detection of the organism after a one-month period is due to treatment failure and is assumed to be due to reinfection.[40,41] Gonorrhea reinfections were defined as any individual who appeared in CalREDIE with a disease condition of gonorrhea or related to gonorrhea (refer to Table 2 in the Appendix) at least 14 days after the last date they were entered into the CalREDIE system for any gonorrhea-related condition. This fourteen-day interval was chosen because it is beyond the seven-day period in which one has a higher likelihood of testing as a false positive.[41] Reinfections with chlamydia or gonorrhea were identified by searching in CalREDIE for duplicates of a Person ID number, a unique identification number assigned to an individual, with a different Incident ID number, a unique identification number assigned to each separate incident infection. Duplicates were then identified by those that had specimen collection dates at least 30 days apart for chlamydia and 14 days apart for gonorrhea. A systematic review of the literature on recurrent chlamydia and gonorrhea infections defined a repeat infection for chlamydia as occurring ≥30 days after an initial positive result and for gonorrhea as occurring ≥14 days after an initial positive result. This same review found that reinfection rates with chlamydia and gonorrhea did not vary with the proportion re-tested, meaning that the reinfection rates measured

are likely to represent a true reinfection rate.[42] It is also thought that the majority of what are perceived to be treatment failures are actually reinfections.[42,43]

Covariates

The HPI is a z-score based score that is a composite measure across eight domains, standardized for the State of California. The bottom quartile was defined as the "health equity quartile" (i.e., the quartile of least opportunity) during the COVID-19 pandemic and was used to target COVID-19 testing and vaccination efforts on census tracts that had the least opportunity (i.e., least access to pathways for better lives). The highest quartile was used as the referent quartile, as those census tracts have greater opportunity, which is generally defined as having greater access to pathways for better lives. HPI was joined to each case using the census tract assigned in CalREDIE that corresponded to the case's street address. HPI is a one-time ecological level measurement. Two versions of HPI were used in this study: HPI version 2.0 uses data from 2011 to 2015, whereas HPI version 3.0 uses data from 2015 to 2019. HPI 2.0 values were assigned to cases from 2010 to 2015, while HPI version 3.0 values were assigned to cases from 2016 to 2021. HPI is California-specific measure, similar to the CDC's SVI. The California Department of Public Health (CDPH) uses the HPI as a key indicator for health equity by stratifying statewide incidence rates of STIs by HPI quartiles, as done in this analysis.

Census tracts are the smallest geographical unit reported by the U.S. Census Bureau. Each census tract contains 2,500 to 8,000 residents; census tracts may not follow city boundaries, but are always contained within county and state boundaries. Census tracts are considered to be relatively permanent, with little change over time.[44] HPI was joined to the dataset by census tract. Although these neighborhood characteristics (e.g., neighborhood walkability, food security) cannot be inferred down to the individual level, having this information at the census tract level provides the most granular geographical unit available.

Analytic methods

Chlamydia and gonorrhea reinfection counts and incidence rates were calculated by age category, race/ethnicity, biological sex, and HPI quartiles. Incidence rate calculations for the total population, age category, race/ethnicity, and biological sex used population denominators from the California Department of Finance population projections.[45] Incidence rates for chlamydia and gonorrhea reinfections were calculated by using denominators derived from the total San Mateo County population, such as the total population or the total number of women. For example, the incidence rate of chlamydia reinfection for women in 2020 was calculated by dividing the incident cases of chlamydia reinfection in women age 15 to 45 in 2020 by the total population of women age 15 to 45 in San Mateo County in 2020. Population denominators for calculating rates by HPI quartile required using ACS census tract estimates, as the California Department of Finance population projections do not have census tract estimates.

A retrospective cohort analysis was conducted, with the outcome defined as any reinfection of chlamydia or gonorrhea, as defined in the dependent variables section above. Each reinfection was considered a new outcome. A rate ratio was calculated with a Poisson regression, using generalized estimating equations (GEE) to account for the longitudinal nature of the cohort, which took the general form:

$$Y_{ij} = \beta_0 + \beta_1 X_{1ij} + \beta_2 X_{2ij} + \beta_3 X_{3ij} + \beta_j W_j + e_{ij}$$

where,
Y_{ij}: Binary indicator of whether an individual has had a chlamydia or gonorrhea reinfection
β_0: Intercept term (grand mean intercept)
X_{1ij}: Race/ethnicity (ref. White)
X_{2ij}: Age (ref. age 20-24 years)
X_{3ij}: Sex (ref. male)
W_j: HPI quartile (ref. highest quartile)

A second model included an interaction term between age group and HPI, as those who are older may have had more time residing in a census tract with greater opportunity, and therefore for exposure to contextual neighborhood effects, such as neighborhood opportunity, than those who are younger in age. An independence correlation structure was used, as this assumes every observation was independent but gives robust standard errors, even if this assumption is incorrect.[46] As GEE is a quasi-likelihood-based method, it is inappropriate to use typical model selection tools such as the likelihood ratio test or Akaike's Information Criterion (AIC). Instead, the Quasi-likelihood Information Criterion (QIC) was used to select the most appropriate model.[47]

All analyses were conducted using R Statistical Software (Version 4.2.1; R Core Team 2022).

RESULTS

There were 5,797 chlamydia reinfections and 1,531 gonorrhea reinfections during the 2010 to 2021 study period (Tables 1 and 2, respectively). Most individuals with a chlamydia or gonorrhea reinfection had only one reinfection (69.4% for chlamydia, 60.7% for gonorrhea); the maximum number of reinfections with chlamydia was nine reinfections (Figure 1) and the maximum number of reinfections with gonorrhea was thirteen reinfections (Figure 2). The mean interval between chlamydia reinfections was 69.2 weeks, whereas the mean interval between gonorrhea reinfections was 70.1 weeks. The median number of weeks between reinfections trended downward with increasing number of reinfections for both chlamydia and gonorrhea (Figures 3 and 4).

The observed incidence rates for chlamydia and gonorrhea reinfections increased steadily from 2010 to 2013, then increased sharply from 2014 to 2019 (Figure 5). In 2020, the incidence rate of chlamydia reinfections decreased to 83.8 cases per 100,000, a 35% decrease from the incidence rate of chlamydia reinfections in 2019, which was 129.1 cases per 100,000. The rates of chlamydia reinfections then increased again in 2021 to 97.9 cases per 100,000 (Figure 5). While the incidence rate of chlamydia reinfections decreased in 2020, the rates of gonorrhea reinfection increased in 2020, reaching the highest rate at 38.3 cases per 100,000 and then decreased in 2021 to 34.6 cases per 100,000 (Figure 6).

To differentiate the effect of changes in rates of real rates of reinfection from the effects of increasing period of observation with time, we plotted a two-year lag for reinfections was introduced where only reinfections of chlamydia or gonorrhea within two years of the previous infection with the same organism. Most reinfections occurred within this two-year period, as seen in Figure 3 for chlamydia reinfections and Figure 4 for gonorrhea reinfections, with the

third quartile of reinfections falling at around 100 weeks for both chlamydia and gonorrhea reinfections. The trend for the incidence rates of chlamydia and gonorrhea reinfections within two years of the previous infection reveals that steep increases in both that are unrelated to the truncated period of observation.

The incidence rates of chlamydia reinfections in men were lower than the incidence rates of chlamydia reinfections in women during the study period, except for in 2019 when the incidence rate of chlamydia reinfection in men was marginally higher than that of the incidence rate of chlamydia reinfection in women for the only time in the study period. However, the patterns over time were broadly similar (Figure 9). For gonorrhea, the incidence of gonorrhea reinfections in men was much higher than the incidence rate of reinfection of gonorrhea in women for the entire study period and the incidence curves diverged rapidly (Figure 10). While the incidence of gonorrhea reinfection in men increased through nearly the entire study period, particularly from 2014 to 2017, the incidence of gonorrhea reinfection in women continued at a low rate through the study period (Figure 10).

Racial/ethnic trends for the incidence rates of chlamydia reinfection and gonorrhea reinfection reflected the overall incidence rates of chlamydia and gonorrhea—Black individuals experienced the highest incidence rates of reinfection for both chlamydia and gonorrhea. The gap in the incidence rates of chlamydia reinfection widened for Black individuals and Native Hawaiians/Pacific Islanders compared to other race/ethnic groups throughout the study period, though all race/ethnic groups experienced a drop in incidence rates of chlamydia reinfection in 2020 (Figure 11). A similar widening gap in the incidence rates of gonorrhea reinfection was observed for Black individuals. In 2013, the incidence rate of gonorrhea reinfection for Black individuals increased rapidly, whereas the rate of gonorrhea reinfection for other race/ethnicities remained stable and similar to those of other race/ethnicities. It is notable that the rate of gonorrhea reinfection for Black individuals increased dramatically in 2020 compared to 2019, from 143.1 cases per 100,000 in 2019 to 207.2 cases per 100,000 in 2020. This was then followed by a sharp decrease in the rate of gonorrhea reinfection in Black people in 2021, to 108.8 cases per 100,000 (Figure 12).

The incidence rate of chlamydia reinfection was highest among those ages 20-24 years, followed by those ages 15-19 years and 25-29 years. While the incidence rate of chlamydia reinfection remained relatively stable throughout the study period for those ages 15-19 years, the incidence rate of chlamydia reinfection increased every year during the study period for those ages 20-29 years, except for a decrease in 2020 (Figure 13). Generally, the incidence rates for chlamydia reinfection decreased as age increased (Figure 13). The same general trend was not observed in the incidence of gonorrhea reinfections. In 2016, those ages 30-34 years overtook those ages 20-24 years in having the highest rate of gonorrhea reinfection, which continued through 2020 (Figure 14). The incidence rate of gonorrhea reinfection continued to increase in 2020 for all age groups except those ages 25-29 years and 50 years and older (Figure 14).

Those who resided in census tracts in the second highest HPI quartile had the highest rates chlamydia reinfection, though those who resided in census tracts in the lowest HPI quartile had the highest reinfection rates of chlamydia in 2017, 2019, and 2021 (Figure 15). The incidence rates of chlamydia reinfection remained similar between those who resided in census tracts in the

second and third HPI quartiles (Figure 15). There was a less pronounced difference in the incidence rates of gonorrhea reinfection between the different HPI quartiles from 2010 to 2014, though from 2015 to 2019, the incidence rate of gonorrhea reinfection in all the HPI quartiles except the highest quartile remained similar (Figure 16). In 2020, the incidence rate of gonorrhea reinfection in the second highest HPI quartile increased dramatically to 128.9 cases per 100,000, an over 100% increase from the incidence in 2019, which was 59.5 cases per 100,000 (Figure 16). This gap in the incidence of gonorrhea reinfection between the HPI quartiles continued in 2021.

The multivariable regression results showed that Black individuals had 1.15 times the rate of chlamydia reinfections compared to White people (Table 3). Those ages 15-19 years had 0.8 times the rate of chlamydia reinfection compared to those 20-24 years old. Compared to those ages 20-24 years, those ages 25-44 years had lower rates of chlamydia reinfection, although these rate ratios were also not statistically significant. Those 45 years and older had higher rates of chlamydia reinfection compared to those 20-24 years old, though these rate ratios were not statistically significant. Women had 0.89 times the rate of chlamydia reinfection compared to men. Those who resided in census tracts in the lowest HPI quartile had 1.79 times the rate of chlamydia reinfection compared to those who resided in the highest HPI, quartile whereas those residing in the second highest HPI quartile had 0.81 times the rate of chlamydia reinfection compared to those residing in the highest quartile. Those who resided in the second lowest HPI quartile had 1.15 times the rate of chlamydia reinfection compared to those who resided in the highest HPI quartile (Table 3).

Hispanics had 1.05 times the rate of gonorrhea reinfection compared to non-Hispanic White individuals, though this was not statistically significant. American Indians/Alaska Natives, Asians, Black individuals, and Native Hawaiians/Pacific Islanders had lower rates of gonorrhea reinfection compared to White individuals (Table 4), although these differences were not statistically significant. Compared to those 20-24 years old, those 25-29 years old had 1.59 times the rate of gonorrhea reinfection; those 30-34 years old had 1.85 times the rate of gonorrhea reinfection; and those 35-39 years old had 1.63 times the rate of gonorrhea reinfection. These results were statistically significant. Those ages 40 years and older also had higher rates of gonorrhea reinfection compared to those 20-24 years old, but the rate ratios were not statistically significant. Women had 0.32 times the rate of gonorrhea reinfection compared to men. Compared to those who resided in census tracts in the highest HPI quartile, those who resided in census tracts in the lowest HPI had 1.38 times the rate of gonorrhea reinfection; and those who resided in census tracts in the second lowest HPI quartile had 0.8 times the rate of gonorrhea reinfection; those who resided in census tracts in the second highest HPI quartile had 1.21 times the rate of gonorrhea reinfection (Table 4). None of these rate ratios for HPI quartiles were statistically significant.

A second model included an interaction term between age groups and HPI quartiles for chlamydia reinfections and gonorrhea reinfections. It showed a general trend that the second lowest HPI quartile had the lowest rate of chlamydia and gonorrhea reinfection compared to the highest HPI quartile. However, this trend varied by age group. The rate of chlamydia reinfection by age group decreased in a linear fashion from lowest to highest HPI quartile, until ages 40 years and older, at which the second lowest HPI quartile had the lowest rate of reinfection. None

of these results were statistically significant, except for those ages 25-29 years residing in a census track in the lowest HPI quartile, who had over two times the incidence rate of chlamydia reinfection compared to those ages 20-24 years (IRR: 2.24; 95% CI: 1.00, 5.03) and those ages 45 years and older who resided in census tracts in the lowest HPI quartile (IRR: 4.36; 95% CI: 1.20, 15.85) (Table 3). The rates of gonorrhea reinfections showed a similar pattern. The second highest and second lowest HPI quartiles generally had lower rates of gonorrhea reinfection compared to the highest HPI quartile, except for those 30-34 years old who resided in census tracts in the second highest HPI quartile (IRR: 1.43; 95% CI: 0.71, 2.86) and those 45 years and older who resided in census tracts in the second highest HPI quartile (IRR: 1.35; 95% CI: 0.54, 3.38) and the second lowest HPI quartile (IRR: 1.19; 95% CI: 0.63, 2.25) (Table 4). None of the interaction results for gonorrhea reinfections were statistically significant. Individuals who were American Indian or Alaska Native, or lived in a census tract in the lowest HPI quartile were excluded from the interaction model for gonorrhea reinfection as cell counts were too sparse for the regression to converge successfully.

DISCUSSION

This study examined the trends in chlamydia and gonorrhea reinfections by sex, age, and race/ethnicity. In San Mateo County, we found that (1) the majority of chlamydia and gonorrhea reinfections have only one repeat infection during the period of observation (69.4% and 56.9%, respectively); (2) women had the highest unadjusted incidence rate of chlamydia reinfection, whereas men had the highest incidence rate of gonorrhea reinfection, although the multivariable regression calculated a rate ratio higher in which women had a lower rate of chlamydia reinfection compared to men; (3) Black individuals had the highest incidence rates of chlamydia; and (4) there was no discernable relationship between the incidence rates of chlamydia or gonorrhea reinfection and HPI quartiles.

Although the maximum number of chlamydia and gonorrhea reinfections were high (nine and 13, respectively), there were progressively fewer individuals who had repeat infections after one repeat infection (Figures 1 and 2). This is consistent with prior studies that found that most of chlamydia and gonorrhea reinfections occur in a small, core group of individuals.[48,49] Women are known to have a higher incidence of chlamydia infection than men and men are known to have a higher incidence of gonorrhea compared to women.[1] However, we observed that women had a rate ratio of 0.89 (95% CI: 0.82, 0.96) for chlamydia reinfection compared to men. This may be due to more frequent screening in sexually active women under the age of 25 years, as is the CDC screening guideline. Screening for chlamydia and gonorrhea are considered to be effective in specific geographies and populations (e.g., women[50] and MSM,[41] respectively). According to CDPH guidelines for retesting individuals with chlamydial and gonorrheal infections, the best practice for preventing repeat chlamydial and gonorrheal infections is to screen for these infections in health care settings, to treat the infected individual and their recent partners, and to retest in three months in non-pregnant persons.[51] These guidelines are similar to general STI treatment guidelines, although retesting in three months is not part of the guidelines for uncomplicated primary chlamydia and gonorrhea infections.[52,53] Although these screening guidelines for those diagnosed with chlamydia or gonorrhea infection and their partners are similar to the guidelines for those with chlamydia or gonorrhea reinfections, there has been higher vigilance and attention called to these guidelines,[51] as chlamydia and gonorrhea rates have increased in California since 2013.

Our findings are also consistent with the those of prior studies that have documented racial disparities in STI incidence and subsequent sequelae, such as PID.[1,32,54,55] Those who have repeat infections of chlamydia or gonorrhea are at increased risk of PID, as previously mentioned, most repeat infections of STIs occur in a small, core group of individuals.[48,49] A prior study found that sexual networks for Black individuals were more intraracial than other race/ethnicities, meaning that Black individuals are more likely to have sexual experiences with those who are of the same race/ethnicity, and that STI rates remained higher in Black populations because individual partner choices were more segregated compared to other race/ethnic groups.[54] Another factor that potentially contributes to observed racial and ethnic disparities in STI incidence and STI-related sequelae is racial and ethnic disparities in access to care, particularly for Black individuals and Hispanics. Such disparities would impact the ability to access testing, treatment, and follow up for chlamydia and gonorrhea infection, which could potentially create more opportunities for continued infection and reinfection.[51] Black and Hispanic individuals had less access to care compared to White individuals before the Affordable Care Act.[56–59] Although the Affordable Care Act helped to reduce these disparities in access to care, disparities in access to care have persisted.[60,61] Although prior studies have shown that adolescents (i.e., ages 15-19 years) and young adults (i.e., ages 20-29 years) comprise the majority of new chlamydia infections, and that young adults comprise the majority of new gonorrhea infections, this association was not present in this study. The unadjusted incidence rates (Figures 13 and 14) reflect this trend but the rate ratios from the multivariable regressions indicate that those ages 15-19 years had a lower rate of chlamydia gonorrhea reinfections (IRR: 0.80; 95% CI: 0.72, 0.89 and IRR: 0.72; 95% CI: 0.45, 1.13, respectively) compared to those ages 20-24 years old. This suggests that the other factors included in the regression are also associated with chlamydia and gonorrhea reinfection.

The lack of any clear association between chlamydia and gonorrhea reinfections and HPI quartile was unexpected, as it is known that poorer neighborhood quality and less neighborhood opportunity (e.g., neighborhood, environment, social factors, HPI) are correlated with a higher incidence of STIs and related sequelae,[4,12,24,62,63] so the expectation was for the lowest HPI quartile to have the highest rate ratio of chlamydia and gonorrhea reinfection compared to the highest HPI quartile. However, we observed that the second to the lowest HPI quartile had the lowest rate of chlamydia and gonorrhea reinfection, although the rate ratio for gonorrhea reinfection was not statistically significant.

While we expected to find that the highest HPI quartile had the lowest unadjusted incidence rates for chlamydia and gonorrhea reinfection, as these cases resided in census tracts with greater opportunity, the incidence rate ratios derived from the multivariable regression showed that the second lowest quartile had the lowest rate ratio for chlamydia and gonorrhea reinfection compared to the highest HPI quartile, indicating that there was no discernable trend in the relationship between HPI quartile and the rate ratio of chlamydia and gonorrhea reinfection. The absence of any trend between the association of HPI quartiles and the rate ratios of chlamydia and gonorrhea reinfection may indicate that the three lowest HPI quartiles of San Mateo County are more similar to each other than they are to the highest HPI quartile. This may be due to HPI quartile inadequately capturing SES, whether for the census tract (i.e., variation in the indicators

that construct the HPI within a census tract) or that the quartiles not meaningfully capturing the difference in SES. The lack of statistically significant findings, particularly in the models that contain the interaction term between age group and HPI quartile may be due to the models being underpowered due to insufficient variation in certain age groups residing in different census tracts (e.g., a single census tract may not have many young people living in it).

Strengths and Limitations

This study has several strengths. First, a retrospective cohort was constructed from twelve years of notifiable disease registry data for all of San Mateo County, which was supplemented by two additional datasets to impute missing race/ethnicity information. Constructing a cohort in which all reported chlamydia and gonorrhea cases were detected allowed calculating incidence rate ratios while adjusting for confounding through multivariable regression. Second, this study used datasets that are typically available at health departments, making this a highly reproducible analysis that can be used by health departments to characterize their own chlamydia and gonorrhea reinfections cases. Third, census tract data were available for all cases that had a valid street address in CalREDIE. This allowed enhancing the CalREDIE data with census tract level variables, such as HPI or ACS variables. Disease registry data typically do not include socioeconomic data. Although census tract level variables should not be inferred down to the individual level, having some information about the geographical context in which an individual lives can contribute some information in the absence of any information about an individual's SES level.

There were also several limitations in this study. First, some key variables were unavailable, namely sexual preferences and data concerning sexual partners. MSM communities experience high rates of chlamydia and gonorrhea infection,[1,64] making sexual preference and partner data important explanatory variables that should be considered in any analyses pertaining to chlamydia and gonorrhea. Second, the dates when an individual's treatment began and ended were also unavailable. These dates are used in identifying treatment failure and treatment windows in which a reinfection would be considered a true reinfection.[41] The date that these chlamydia and gonorrhea cases were reported to the CalREDIE system were used as an approximation of these dates, which may not accurately reflect the true sequence of events pertaining to diagnosis, treatment initiation, and treatment completion. Third, there was left censoring in this study. The number of reinfections will accumulate over time as those who were previously infected with chlamydia and gonorrhea have the opportunity to become infected again. An individual was classified as a first infection the first time they had a reported infection in the study period, regardless of whether they had been reported as having an infection prior to 2010 as this information was unavailable. This results in the potential misclassification of reinfections as first infections. In this analysis, the median number of weeks between chlamydia and gonorrhea infections among those with chlamydia and gonorrhea reinfections were 35.1 weeks and 41.1 weeks, respectively, so it is likely that some chlamydia and gonorrhea infections classified as first infections were actually reinfections. Fourth, this analysis did not take gender identity and sexual preference into consideration, as this information was not available. Surveillance systems typically do not have fields that distinguish biological sex and gender, but given that STIs rely on sexual activity for transmission, important information such as gender and sexual preference are important for contextualizing these results with sexual network preferences and behaviors. It is likely that gonorrhea reinfections disproportionately affect MSM,

as MSM comprise the majority of gonorrhea case counts.[65] It is also important to have information concerning the anatomical site at which the infection occurred for chlamydia and gonorrhea, as there are different rates of transmissibility and length of infection, depending on the anatomical site of infection.[64,66] Fifth, regression modeling alone cannot capture the complexity of STIs because individual sexual networks are heterogenous. Network analysis would elucidate the effect that these sexual network patterns have in different demographic populations.[5,67,68] And last, these results are not generalizable outside of the San Mateo County population.

CONCLUSION

The racial and ethnic disparities previously observed in chlamydia and gonorrhea infections were also observed in chlamydia and gonorrhea reinfections. These findings provide evidence that race/ethnicity is strongly associated with chlamydia reinfection, with Black individuals bearing the highest burden of both chlamydia and gonorrhea reinfection. Men had higher rates of chlamydia and gonorrhea reinfection; women had higher rates of chlamydia reinfections. However, the expected association of those residing in lower HPI quartiles having higher rates of chlamydia or gonorrhea reinfection was not observed, likely due to HPI quartiles insufficiently capturing the effects of SES. Future studies should examine the number of chlamydia and gonorrhea reinfections as the outcome, as this study examined chlamydia and gonorrhea reinfection as a binary outcome rather than as an ordinal or categorial outcome. The majority of reinfections in this study were in those who only had one reinfection, suggesting that those who have more than one reinfection may have a different epidemiologic profile than those who had only one chlamydia or gonorrhea reinfection.

This analysis is highly reproducible in health department settings. Even in the absence of individual-level sociodemographic data, a common limitation in surveillance datasets, area-level variables can be used to at least provide some information where there typically is none.

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APPENDIX

Table 1. Case Definitions for Chlamydia and Gonorrhea

Disease	CalREDIE Disease Condition	Resolution Status
Chlamydia	Chlamydia	Suspect, Probable, Confirmed
Gonorrhea	Gonorrhea	Suspect, Probable, Confirmed

Table 2. Resolution Status Definitions for Chlamydia and Gonorrhea[69]

Disease	CalREDIE Disease Condition	Resolution Status	Description
Chlamydia	Chlamydia	Confirmed	A case that is laboratory confirmed (See appendix for laboratory criteria for diagnosis.)
Chlamydia	Chlamydia with Pelvic Inflammatory Disease or Pelvic Inflammatory Disease with Chlamydia	Confirmed	A clinical syndrome resulting from the ascending spread of the microorganisms from the vagina and endocervix to the endometrium, fallopian tubes, and/or contiguous structures; among sexually active women, characterized by pelvic or lower abdominal pain, with no cause for the illness other than PID identified. Must also meet the surveillance case definition of *C. trachomatis* infection.[70]
		Probable	A sexually active woman with pelvic or lower abdominal pain, with no cause for the illness other than PID identified with one or more of the following minimum criteria present on pelvic examination: cervical motion tenderness OR uterine tenderness OR adnexal tenderness; AND treated for PID by a medical provider. Must also meet the surveillance case definition of *C. trachomatis* infection.[70]
Gonorrhea	Gonorrhea	Confirmed	A person with laboratory isolation of typical gram-negative, oxidase-positive diplococci by culture (presumptive *Neisseria gonorrhoeae*) from a clinical specimen, or demonstration of *N. gonorrhoeae* in a clinical specimen by detection of antigen or detection of nucleic acid via nucleic acid amplification (e.g., PCR) or hybridization with nucleic acid probe. (See appendix for laboratory criteria for diagnosis.)
		Probable	Demonstration of gram-negative

			intracellular diplococci in a urethral smear obtained from a male or an endocervical smear obtained from a female.
Gonorrhea	Gonorrhea with Pelvic Inflammatory Disease or Pelvic Inflammatory Disease with Gonorrhea	Confirmed	A clinical syndrome resulting from the ascending spread of the microorganisms from the vagina and endocervix to the endometrium, fallopian tubes, and/or contiguous structures; among sexually active women, characterized by pelvic or lower abdominal pain, with no cause for the illness other than PID identified. Must also meet the surveillance case definition of gonorrhea infection.[70]
		Probable	A sexually active woman with pelvic or lower abdominal pain, with no cause for the illness other than PID identified with one or more of the following minimum criteria present on pelvic examination: cervical motion tenderness OR uterine tenderness OR adnexal tenderness; AND treated for PID by a medical provider. Must also meet the surveillance case definition of gonorrhea infection.[70]

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FIGURES AND TABLES

Table 4. Distribution of chlamydia single infections and reinfections, San Mateo County, CA, 2010-2021

Year	Single Infection		Reinfection	
	Count	Percentage	Count	Percentage
2010	1826	92.6%	146	7.4%
2011	1712	87.5%	245	12.5%
2012	1513	83.9%	290	16.1%
2013	1515	82.4%	323	17.6%
2014	1834	82.4%	392	17.6%
2015	1909	80.3%	468	19.7%
2016	2048	79.4%	530	20.6%
2017	2243	78.3%	623	21.7%
2018	2316	74.7%	784	25.3%
2019	2363	74.1%	827	25.9%
2020	1461	73.1%	538	26.9%
2021	1674	72.6%	631	27.4%
TOTAL	22,414	--	5797	--

Table 5. Distribution of gonorrhea single infections and reinfections, San Mateo County, CA, 2010-2021

Year	Single Infection		Reinfection	
	Count	Percentage	Count	Percentage
2010	203	94.9%	11	5.1%
2011	213	92.2%	18	7.8%
2012	240	90.6%	25	9.4%
2013	293	87.2%	43	12.8%
2014	294	82.8%	61	17.2%
2015	431	80.0%	108	20.0%
2016	471	76.1%	148	23.9%
2017	606	74.6%	206	25.4%
2018	517	70.8%	213	29.2%
2019	666	74.4%	229	25.6%
2020	575	70.0%	246	30.0%
2021	550	71.2%	223	28.8%
TOTAL	5059	--	1531	--

Figure 22. Distribution of the number of chlamydia reinfections, San Mateo County, CA 2010-2021

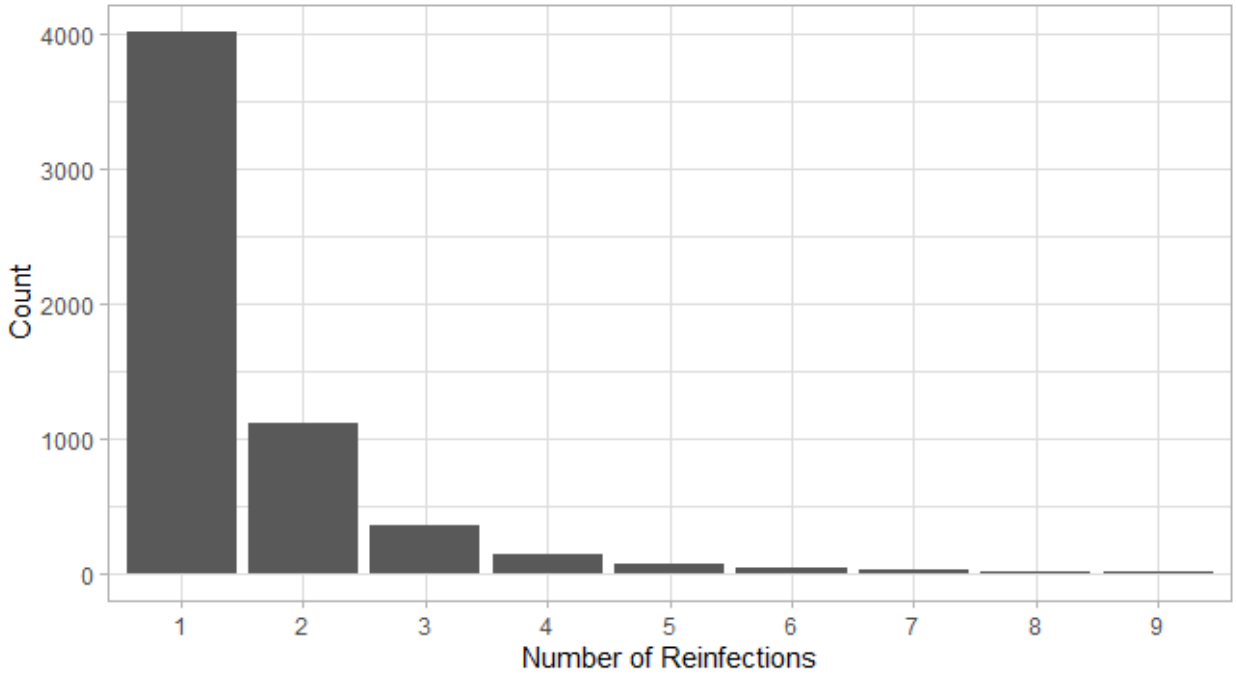


Figure 23. Distribution of the number of gonorrhea reinfections, San Mateo County, CA 2010-2021

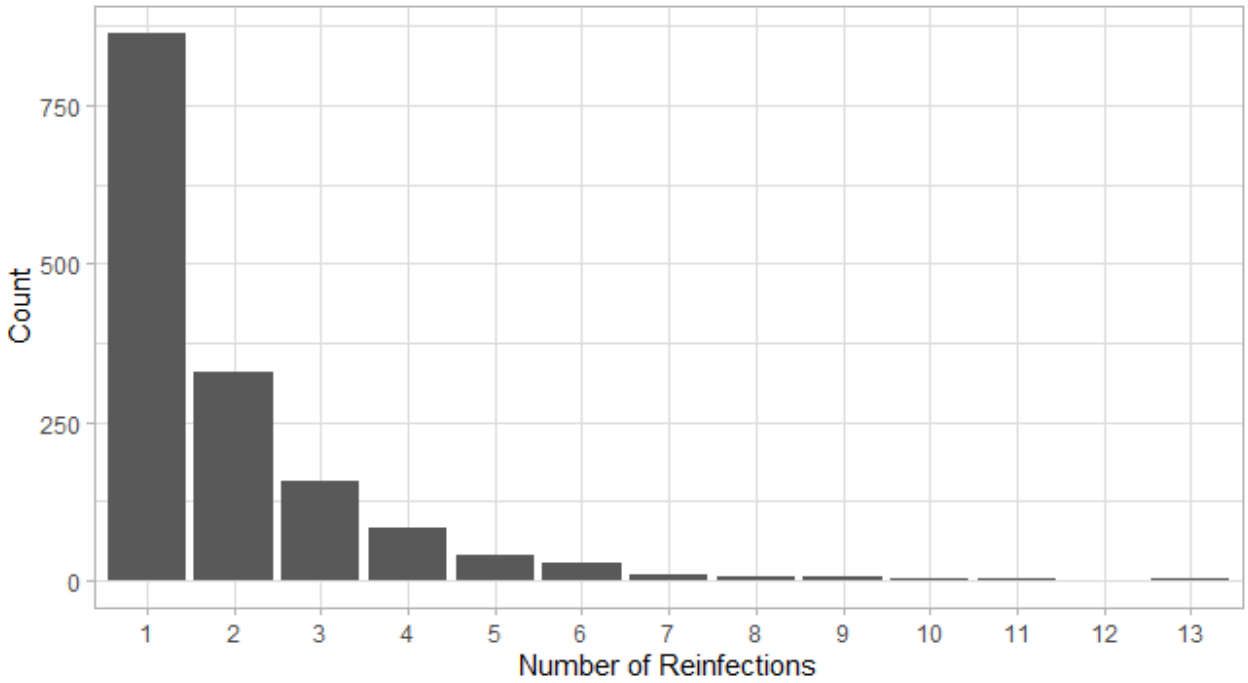


Figure 24. Box and whisker plot of the weeks between chlamydia reinfections by number of reinfections, San Mateo County, CA, 2010-2021

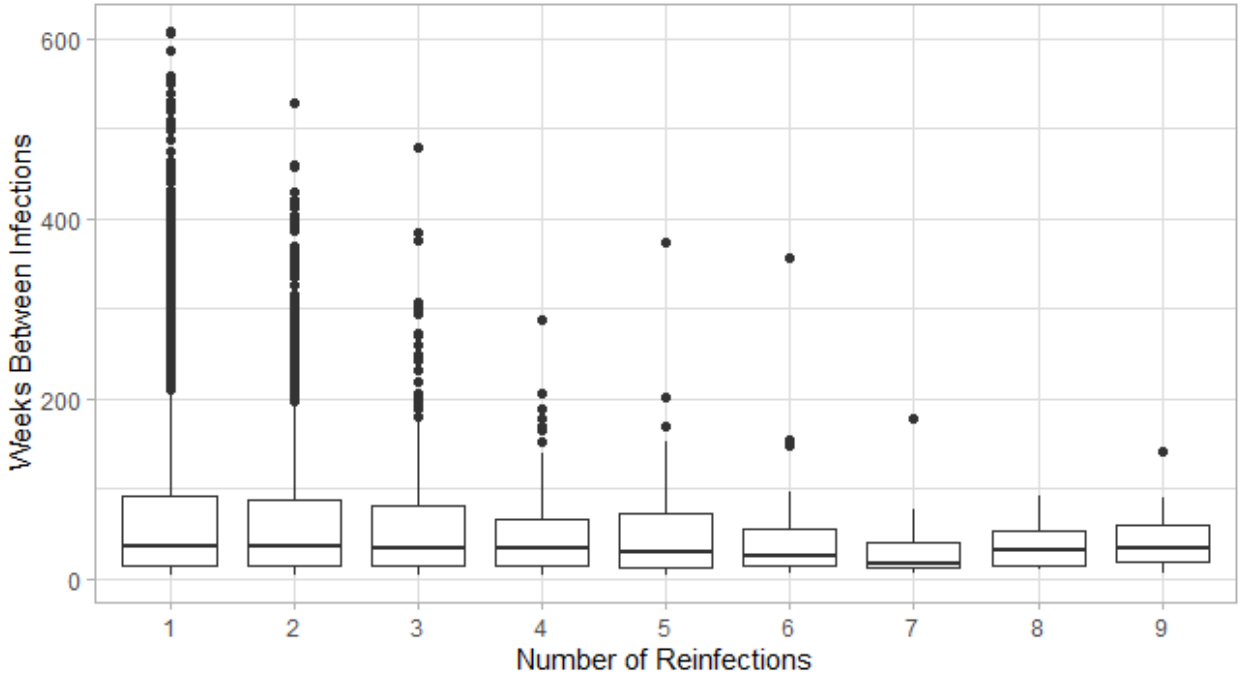


Figure 25. Box and whisker plot of the weeks between chlamydia reinfections by number of reinfections, San Mateo County, CA, 2010-2021

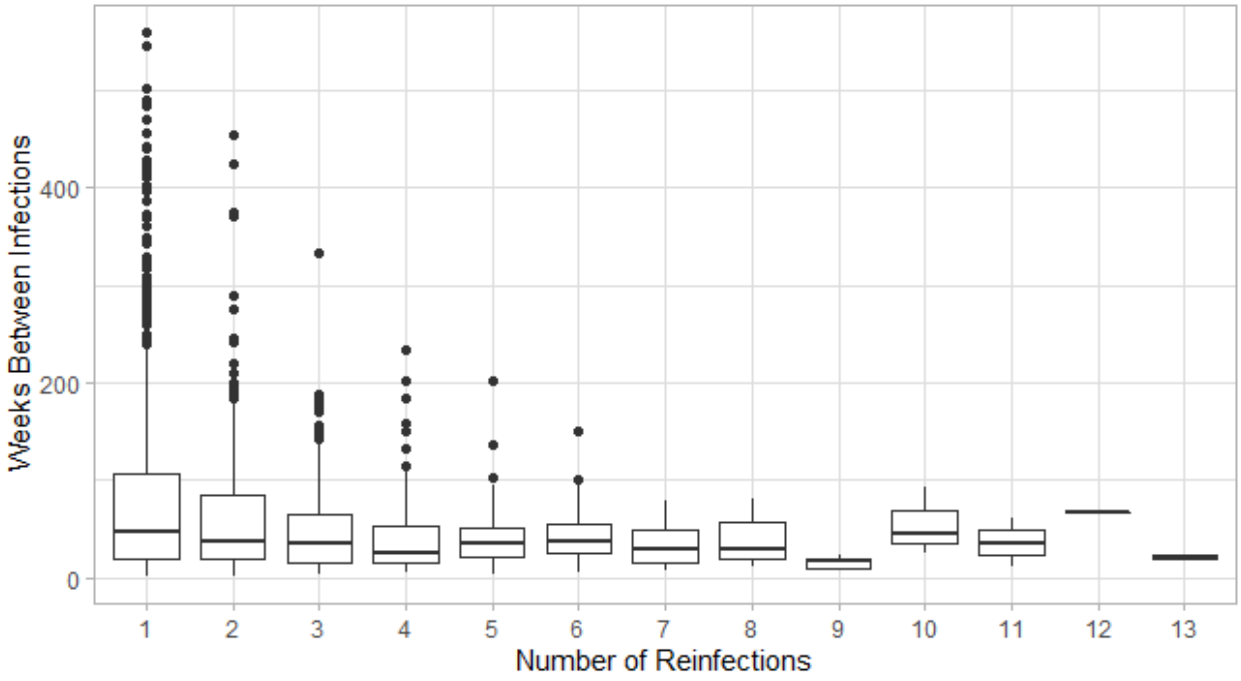


Figure 26. Incidence of chlamydia reinfections, San Mateo County, CA, 2010-2021

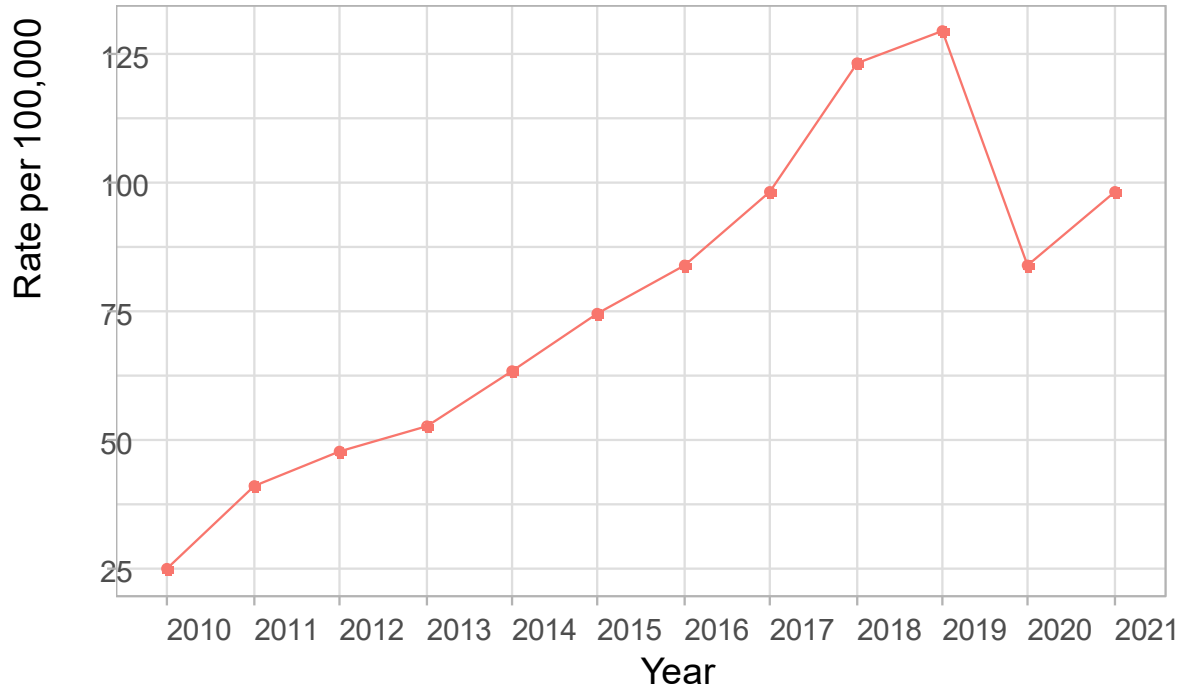


Figure 27. Incidence of gonorrhea reinfections, San Mateo County, CA, 2010-2021

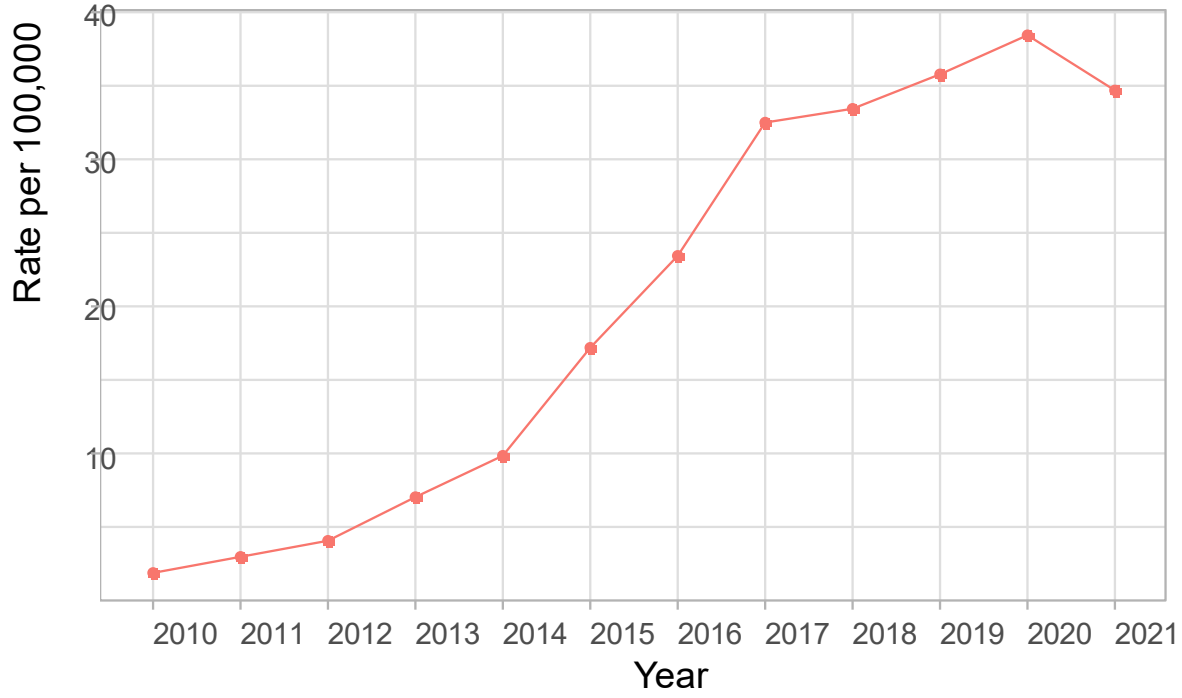


Figure 28. Incidence of chlamydia reinfections within two years of the previous infection, San Mateo County, CA 2010-2021

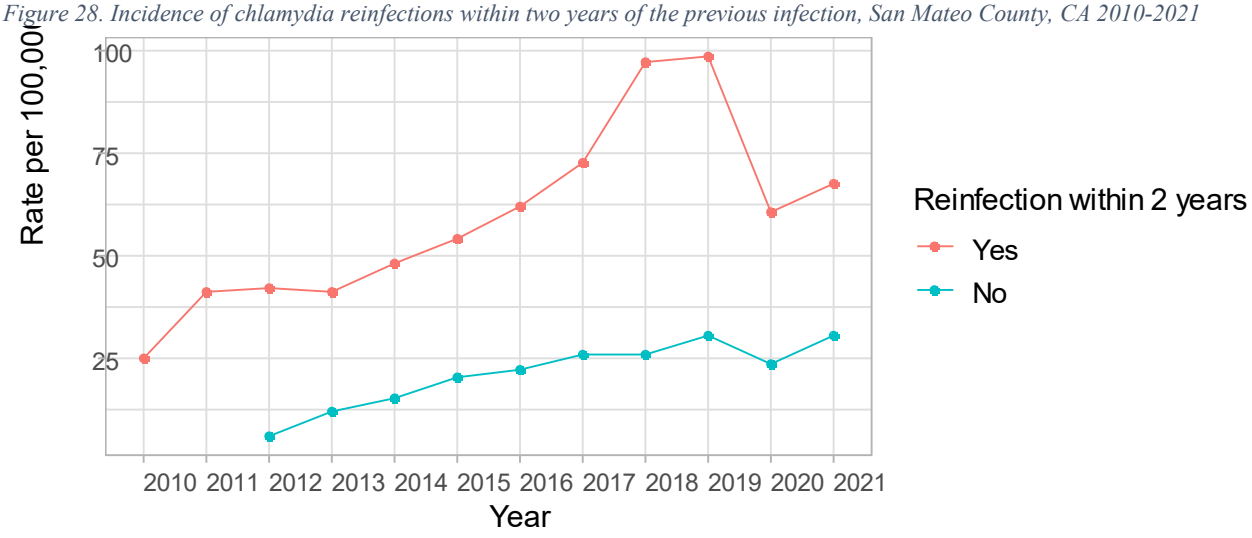


Figure 29. Incidence of gonorrhea reinfections within two years of the previous infection, San Mateo County, CA 2010-2021

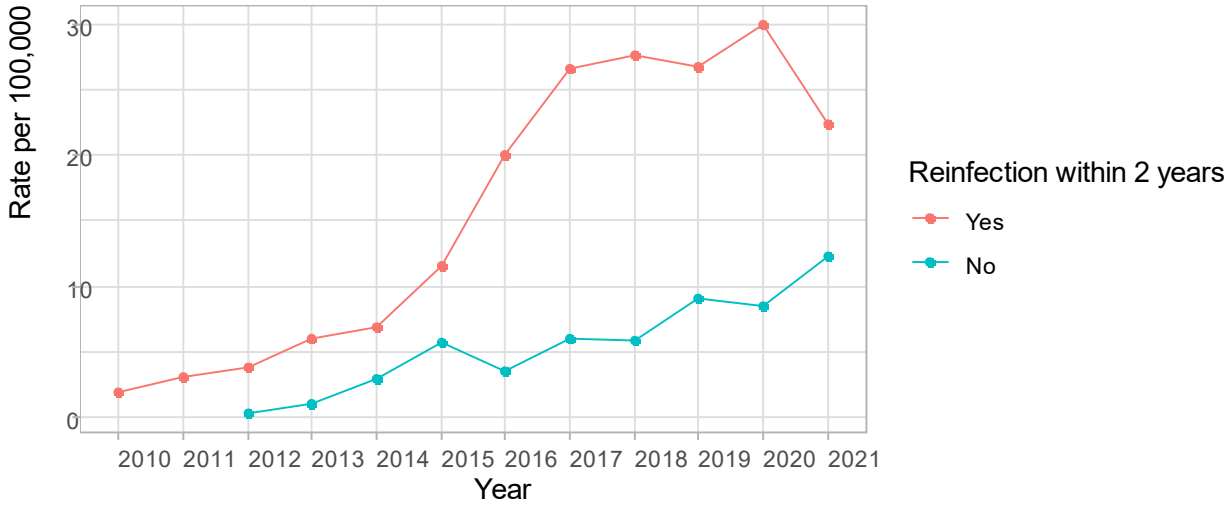


Figure 30. Incidence of chlamydia reinfections by sex, San Mateo County, CA, 2010-2021

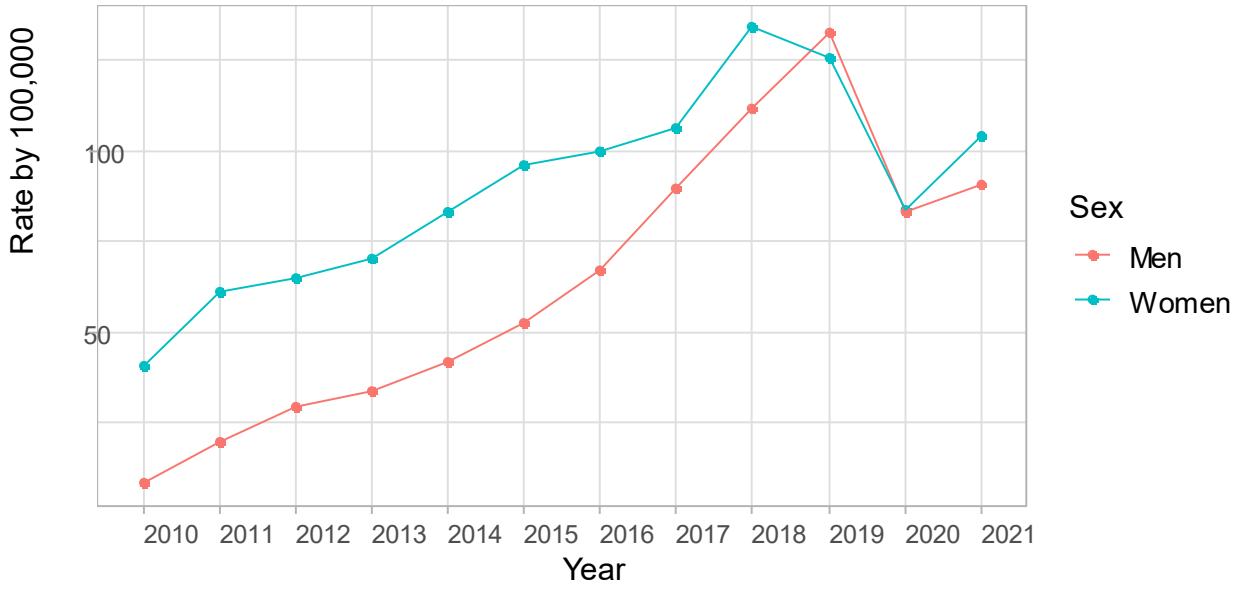


Figure 31. Incidence of gonorrhea reinfections by sex, San Mateo County, CA, 2010-2021

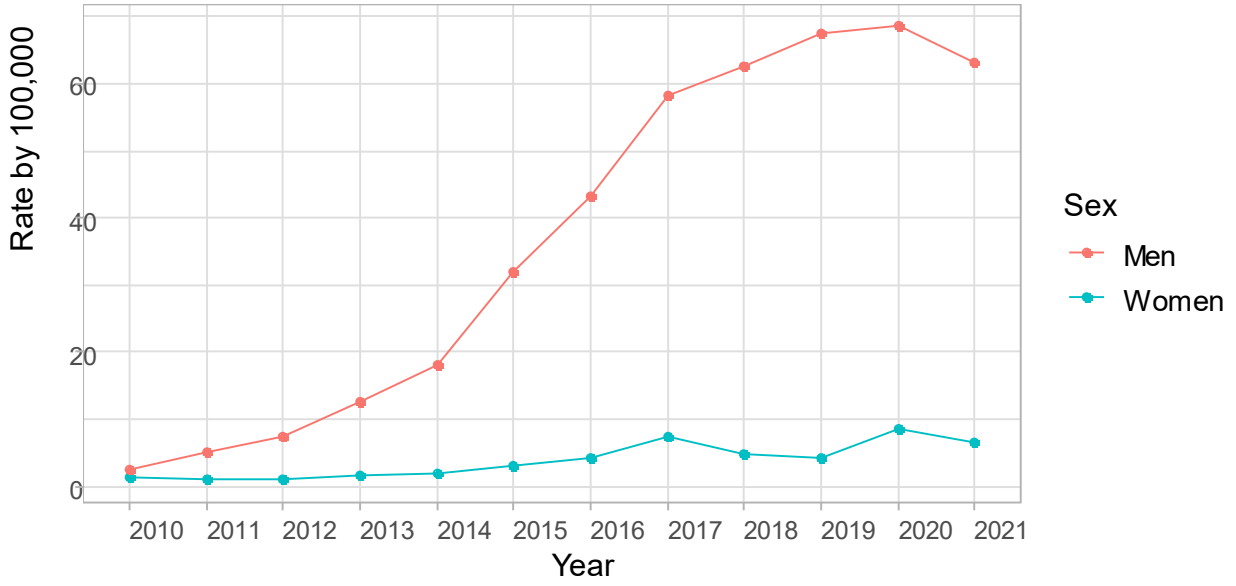


Figure 32. Incidence of chlamydia reinfections by race/ethnicity, San Mateo County, CA, 2010-2021

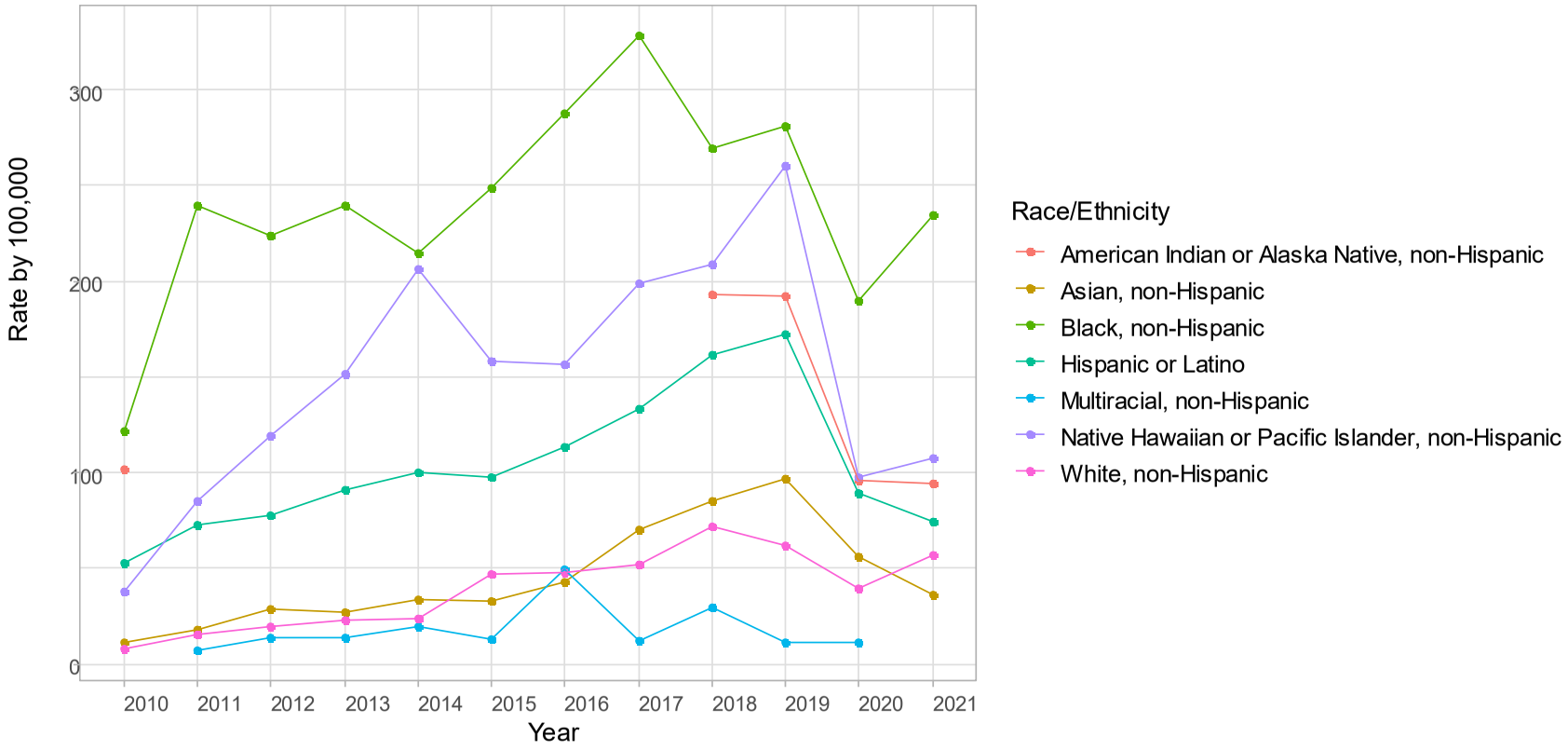
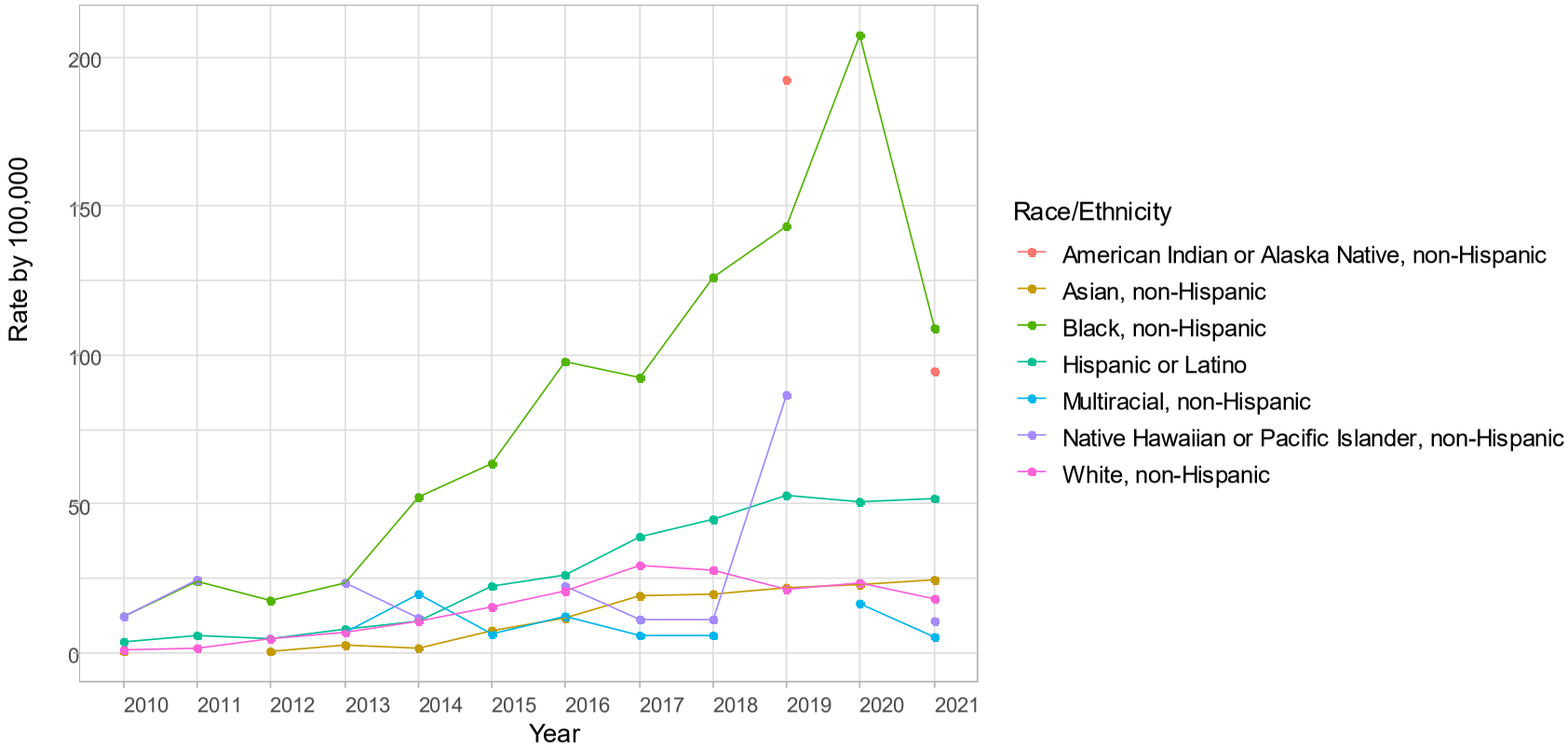


Figure 33. Incidence of gonorrhea reinfections by race/ethnicity, San Mateo County, CA, 2010-2021



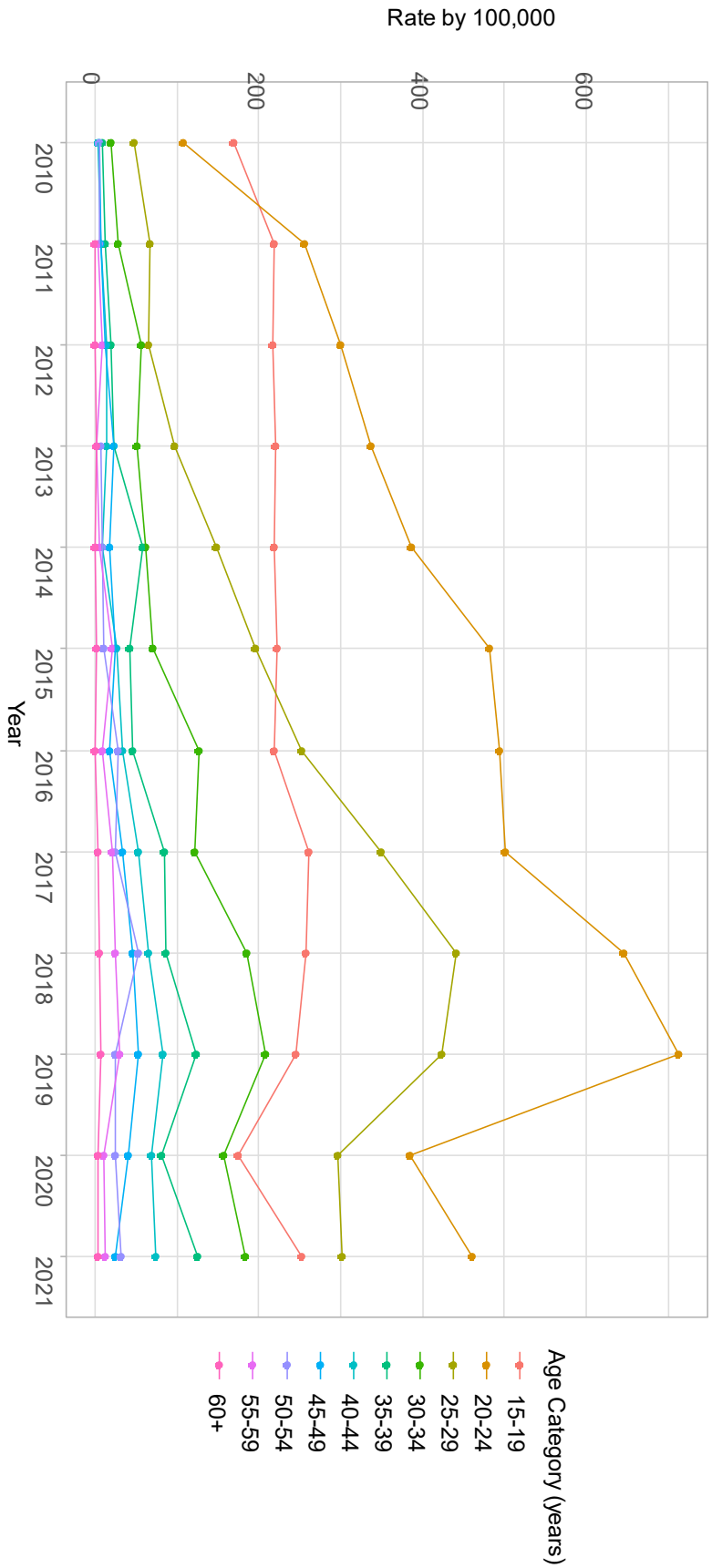


Figure 34. Incidence of chlamydia reinfections by age category, San Mateo County, CA, 2010-2021

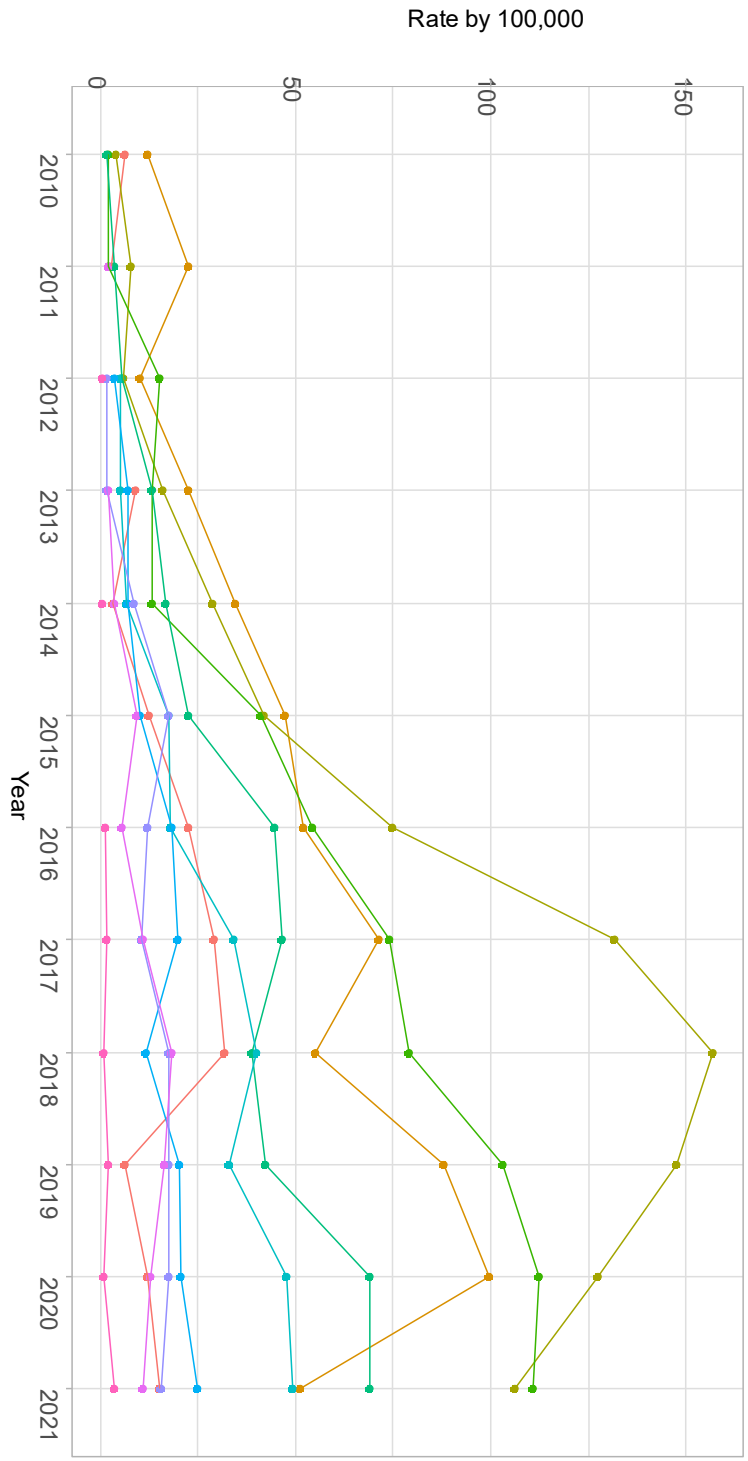


Figure 35. Incidence of gonorrhea reinfections by age category, San Mateo County, CA, 2010-2021

Figure 36. Incidence of chlamydia reinfections by Healthy Places Index score quartile, San Mateo County, CA, 2010-2021

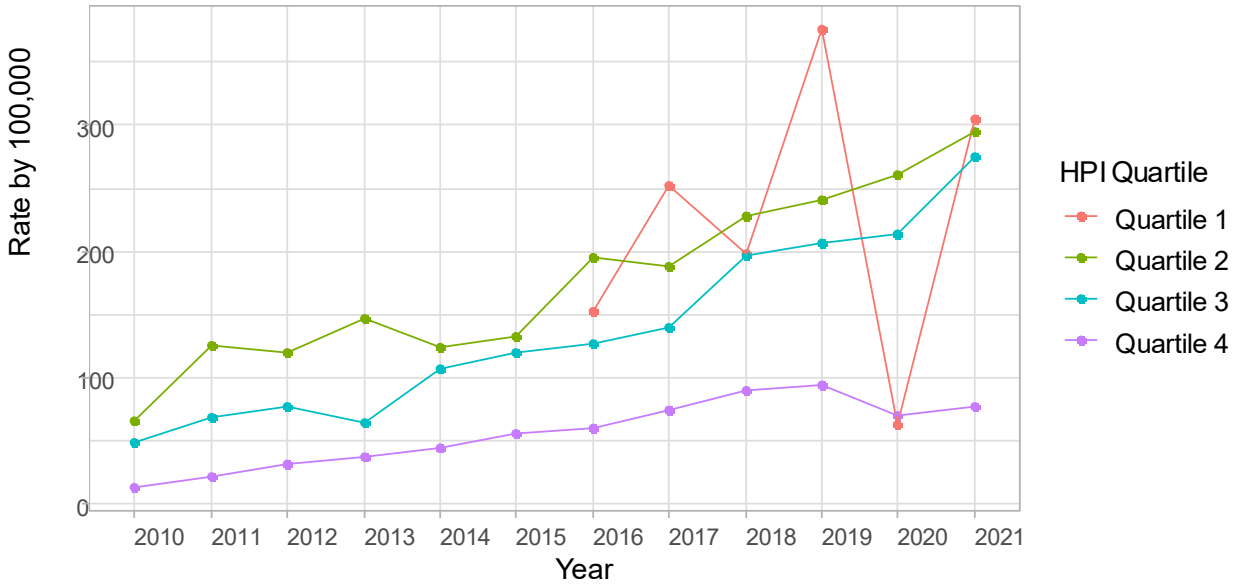


Figure 37. Incidence of gonorrhea reinfections by Healthy Places Index score quartile, San Mateo County, CA, 2010-2021

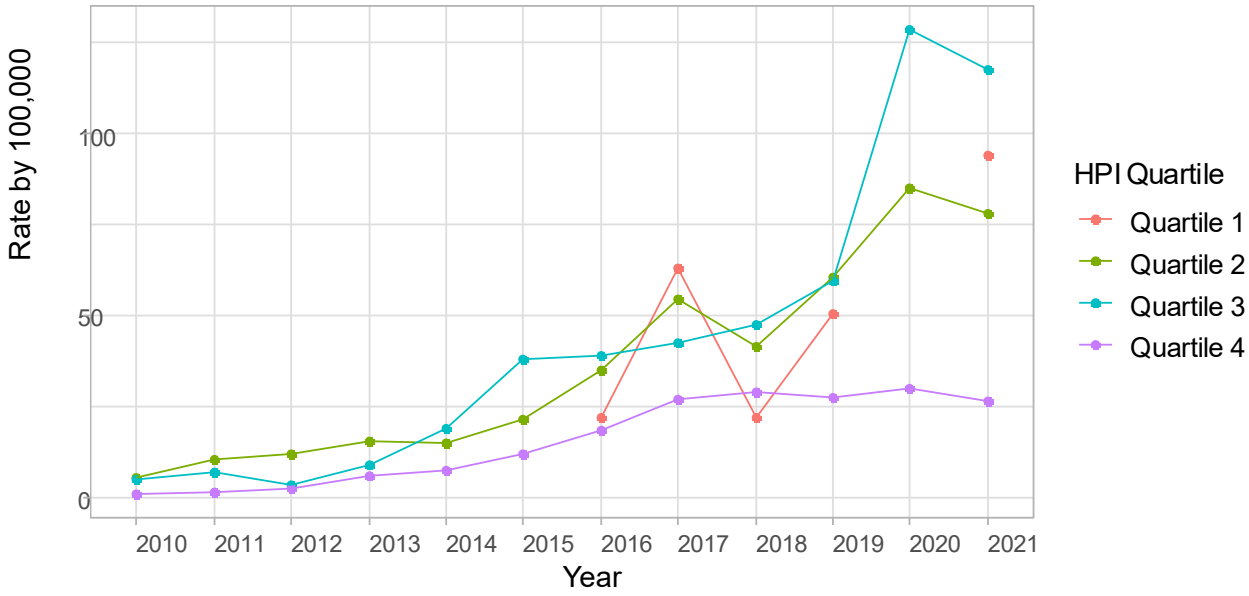


Table 6. Incidence rate ratios for race/ethnicity, age category, sex, and HPI quartile as independent predictors of chlamydia reinfection

	Model 1		Model 2	
	IRR	**95% CI**	**IRR**	**95% CI**
Race/Ethnicity				
American Indian or Alaska Native	0.30	(0.09, 1.01)	0.32	(0.10, 1.05)
Asian	1.02	(0.90, 1.15)	1.09	(0.96, 1.24)
Black	1.15	(1.00, 1.33)	1.2	(1.03, 1.39)
Hispanic or Latino	0.96	(0.86, 1.06)	0.99	(0.89, 1.10)
Multiracial	1.05	(0.70, 1.60)	1.11	(0.73, 1.68)
Native Hawaiian or Pacific Islander	1.01	(0.81, 1.25)	1.05	(0.85, 1.31)
White, non-Hispanic (ref)	1	--	1	--
Age Category				
15-19 years old	0.80	(0.72, 0.89)	0.79	(0.68, 0.93)
20-24 years old (ref)	1	--	1	--
25-29 years old	0.97	(0.87, 1.07)	1.02	(0.88, 1.18)
30-34 years old	0.96	(0.84, 1.11)	1.04	(0.86, 1.26)
35-39 years old	0.87	(0.74, 1.04)	0.94	(0.74, 1.18)
40-44 years old	0.94	(0.77, 1.16)	1.12	(0.85, 1.46)
45+ years old	1.14	(0.98, 1.36)	1.16	(0.94, 1.42)
Sex				
Women	0.89	(0.82, 0.96)	0.89	(0.83, 0.97)
Men (ref)	1	--	1	--
HPI Quartile				
1st Quartile	1.79	(1.45, 2.82)	1.18	(0.64, 2.18)
2nd Quartile	0.81	(0.78, 0.97)	0.83	(0.71, 0.97)
3rd Quartile	1.15	(1.03, 1.24)	1.27	(1.10, 1.47)
4th Quartile (ref)	1	--	1	--
HPI Quartile for ages 15–19				
1st Quartile			1.05	(0.36, 3.04)
2nd Quartile			1.20	(0.92, 1.58)
3rd Quartile			0.88	(0.68, 1.14)
4th Quartile (ref)			1	--
HPI Quartile for ages 25–29				
1st Quartile			2.24	(1.00, 5.03)
2nd Quartile			1.01	(0.77, 1.32)
3rd Quartile			0.80	(0.63, 1.03)
4th Quartile (ref)			1	--
HPI Quartile for ages 30–34				
1st Quartile			1.60	(0.44, 5.87)
2nd Quartile			0.83	(0.58, 1.18)
3rd Quartile			0.83	(0.60, 1.15)
4th Quartile (ref)			1	--
HPI Quartile for ages 35–39				
1st Quartile			2.09	(0.65, 6.74)

2nd Quartile	0.88	(0.56, 1.38)
3rd Quartile	0.83	(0.57, 1.2)
4th Quartile (ref)	1	--
HPI Quartile for ages 40–44		
1st Quartile	0.99	(0.22, 4.45)
2nd Quartile	0.37	(0.18, 0.73)
3rd Quartile	0.80	(0.51, 1.25)
4th Quartile (ref)	1	--
HPI Quartile for ages 45+		
1st Quartile	4.36	(1.20, 15.85)
2nd Quartile	0.66	(0.37, 1.20)
3rd Quartile	1.12	(0.75, 1.66)
4th Quartile (ref)	1	--

Table 7. Incidence rate ratios for race/ethnicity, age category, sex, and HPI quartile as independent predictors of gonorrhea reinfection

	Model 1		Model 2*	
	IRR	**95% CI**	**IRR**	**95% CI**
Race/Ethnicity				
American Indian or Alaska Native	0.66	(0.10, 4.36)	--	--
Asian	0.80	(0.62, 1.04)	1.09	(0.96, 1.24)
Black	0.97	(0.72, 1.32)	1.2	(1.03, 1.39)
Hispanic or Latino	1.05	(0.84, 1.29)	0.99	(0.89, 1.10)
Multiracial	1.33	(0.62, 2.86)	1.11	(0.73, 1.68)
Native Hawaiian or Pacific Islander	0.96	(0.55, 1.68)	1.05	(0.85, 1.31)
White, non-Hispanic (ref)	1	--	1	--
Age Category				
15-19 years old	0.72	(0.45, 1.13)	0.79	(0.68, 0.93)
20-24 years old (ref)	1	--	1	--
25-29 years old	1.59	(1.25, 2.03)	1.02	(0.88, 1.18)
30-34 years old	1.85	(1.42, 2.42)	1.04	(0.86, 1.26)
35-39 years old	1.63	(1.22, 2.18)	0.94	(0.74, 1.18)
40-44 years old	1.41	(0.99, 2.02)	1.12	(0.85, 1.46)
45+ years old	1.25	(0.94, 1.68)	1.16	(0.94, 1.42)
Sex				
Women	0.32	(0.25, 0.41)	0.89	(0.83, 0.97)
Men (ref)	1	--	1	--
HPI Quartile				
1st Quartile	1.38	(0.59, 3.22)	--	--
2nd Quartile	0.80	(0.61, 1.05)	0.83	(0.71, 0.97)
3rd Quartile	1.21	(1.00, 1.47)	1.27	(1.10, 1.47)
4th Quartile (ref)	1	--	1	--
HPI Quartile for ages 15–19				
2nd Quartile			0.63	(0.21, 1.92)
3rd Quartile			0.61	(0.21, 1.77)

4th Quartile (ref)	1	--
HPI Quartile for ages 25–29		
2nd Quartile	0.80	(0.40, 1.62)
3rd Quartile	0.94	(0.55, 1.58)
4th Quartile (ref)	1	--
HPI Quartile for ages 30–34		
2nd Quartile	1.43	(0.71, 2.86)
3rd Quartile	0.87	(0.48, 1.58)
4th Quartile (ref)	1	--
HPI Quartile for ages 35–39		
2nd Quartile	0.60	(0.27, 1.31)
3rd Quartile	0.70	(0.37, 1.34)
4th Quartile (ref)	1	--
HPI Quartile for ages 40–44		
2nd Quartile	0.45	(0.12, 1.68)
3rd Quartile	0.86	(0.40, 1.83)
4th Quartile (ref)	1	--
HPI Quartile for ages 45+		
2nd Quartile	1.35	(0.54, 3.38)
3rd Quartile	1.19	(0.63, 2.25)
4th Quartile (ref)	1	--

*American Indian or Alaska Native and the 1st HPI Quartile were excluded from Model 2 as there were too few observations to conduct a valid statistical analysis.

CHAPTER 3

TITLE: Changes in Syphilis Testing in Pregnant Individuals During the COVID-19 Pandemic
AUTHORS: Moon Choi-McInturff, Asa Ohsaki, Aracely Tamayo, Elizabeth A. Jump, Vivian Levy, Stefano M. Bertozzi, Arthur L. Reingold

ABSTRACT

Background: The impact of the COVID-19 pandemic on access to testing for and detection of syphilis infection in pregnant individuals remains unknown. Syphilis and congenital syphilis incidence rates have increased in the past decade in California. We examined the change in the proportion of pregnant individuals who are clients at the San Mateo Medical Center who were tested for syphilis.

Methods: Individuals who had a pregnancy-related visit to San Mateo Medical Center who were 14-45 years old were included in this study. The outcome of interest was at least one syphilis test during the pregnancy. We compared the odds of syphilis testing during the COVID-19 pandemic to the odds of syphilis testing before the COVID-19 pandemic, controlling for age, educational attainment, and insurance type.

Results: The odds of syphilis testing during the COVID-19 pandemic were lower than the odds of syphilis testing before the COVID-19 pandemic (OR: 0.74, 95% CI: 0.58, 0.94). Notably, White individuals had a much lower odds of syphilis testing during the COVID-19 pandemic (OR: 0.55, 95% CI: 0.34, 0.89) compared to Hispanic individuals. [In this predominantly Hispanic pop (X%), the odds of testing for syphilis post-pandemic were OR=Y.] [Don't need to mention anything about racial differences. Might want to say "despite lower numbers of births…" This is a conservative estimate bc decline in perinatal services, still saw decline in syphilis testing, so it's likely that the cause is covid.]

Conclusion:

Syphilis testing in pregnant individuals decreased during the COVID-19 pandemic at the San Mateo Medical Center, likely due to reduced access to health care and the diversion of health care resources, both personnel and laboratory.

INTRODUCTION

The COVID-19 pandemic resulted in diversion of hospital, clinic, and public health resources to mount a response to this once-in-a-lifetime health event. Staff and resources at public health departments and hospitals were reallocated toward COVID-19 control and care efforts.[1–3] The San Mateo County STD/HIV Program saw the effects of missed or delayed screening for sexually transmitted infections (STI) in increases in the number of congenital syphilis cases and in first detections of syphilis in later stages, compared to the prepandemic period.[4,5] Congenital syphilis is considered a sentinel health event, as each case indicates a failure of the healthcare system and STD control program to detect syphilis infection in a pregnant individual and prevent infection in the newborn baby.[6] A recent study from the U.S. Centers for Disease Control and Prevention (CDC) indicated that among the surveyed 59 sexually transmitted diseases (STD) programs, comprised of states, cities, and US territories, 91% experienced a moderate to a substantial/large impact of the COVID-19 pandemic on personnel and resource diversion.[7] The diversion of personnel and resources during COVID-19 happened at a time of increasing incidences of chlamydia, gonorrhea, and early syphilis in the U.S.[8] The Western region of the U.S. has the highest rates of reported chlamydia and gonorrhea cases compared to other U.S.

regions, and the incidence of syphilis has been increasing in the country, including in San Mateo County, since the mid-2010s after a period of relatively steady incidence. Infection with *Treponema pallidum* causes syphilis and, if left untreated, can progress to neurological involvement and be fatal.[9] Syphilis is primarily transmitted through sexual intercourse, but it can also be transmitted from a pregnant individual to the fetus *in utero* and to the infant during delivery. Infants born to someone who has untreated or previously undiagnosed syphilis infection are assessed clinically and serologically for syphilis infection, with comparison of infant to maternal syphilis serology used for congenital syphilis diagnosis and treatment. Pregnant individuals with syphilis who are not treated during pregnancy are able to pass the infection to the fetus or to the infant during delivery, which may result in the infant having congenital syphilis.[10] Untreated syphilis infection in a pregnant individual can lead to a host of adverse pregnancy and birth outcomes, such as spontaneous abortion, stillbirth, or perinatal death.[10] Congenital syphilis can lead to developmental delays, seizures, or death.[9] Cases of congenital syphilis in California, which have been steadily increasing in California since 2012,[11] have typically been a result of delayed or no prenatal care during pregnancy,[12] similar to the situation in the entire Western region of the U.S.[13]

Laboratory syphilis screening is one of the most effective forms of STI control.[14,15] The CDC recommends laboratory screening for all pregnant individuals for syphilis at the first prenatal visit[16] and most states, including California, mandate syphilis testing of all pregnant persons during the first trimester.[17,18] The CDC's syphilis screening guidelines in the third trimester of pregnancy rely on the provider's discretion (see appendix). However, California had the sixth highest congenital syphilis rate in the nation in 2020,[19] which prompted the California Department of Public Health to recommend in December 2020 that syphilis testing also occur in pregnant persons during 28-32 weeks gestation in addition to testing at time of pregnancy diagnosis and for testing pregnant persons seen in emergency departments or in correctional facilities in areas with high numbers of cases of congenital syphilis.[12]

Given the severity of the complications of congenital syphilis infection, it is important to understand how the COVID-19 pandemic affected syphilis testing and detection in pregnant individuals. The COVID-19 pandemic resulted in a sudden shift in the allocation of resources, both personnel and laboratory within healthcare settings.[20,21] The effect of this shift on syphilis testing in pregnant individuals is still not well understood. The goal of this study was to (1) describe the demographic characteristics and syphilis screening histories of those who received prenatal care at the San Mateo Medical Center before and during the COVID-19 pandemic and (2) to measure the association between syphilis screening and whether the pregnancy occurred in the prepandemic or pandemic period.

MATERIALS AND METHODS

Data sources

Two data sources were used in this study. The first source was birth records from the California Department of Public Health – Vital Records (CDPH-VR), which were accessed from the Vital Records Business Intelligence System (VRBIS). VRBIS contains all live birth records for California, with each jurisdiction (e.g., San Mateo County) having access only to records for their jurisdiction. The second data source was records from the San Mateo Medical Center, for pregnant individuals ages 14 to 45 years who received prenatal care during the study period. This

study was restricted to those ages 14 to 45 years as this analysis pertains to those of reproductive age. This age cut off was determined by examining the ages of birthing mothers in San Mateo County, which ranged from ages 14 to 45 years.

There were 3,645 unique pregnancies in individuals who received prenatal care at San Mateo Medical Center and who gave birth from January 1, 2018 to December 31, 2021. Prenatal care was defined as one or more visits to the San Mateo Medical Center with a pregnancy-related ICD-9 or ICD-10 code. Prenatal care was identified by identifying ICD-9 and ICD-10 codes associated with pregnancy (e.g., ICD-10 group Z34 defined as "encounter for supervision of normal pregnancy"). ICD-9 and ICD-10 codes associated with labor, delivery, or the postpartum period were excluded, as this analysis aimed to capture the impact of the COVID-19 pandemic on syphilis screening as a part of prenatal care (i.e., before labor and delivery). Although the San Mateo Medical Center is not a birthing hospital, it provides prenatal care to birthing persons, most of who have Medi-Cal coverages, and serves as the public hospital and clinic system for San Mateo County.

Dependent Variable

The outcome of interest was at least one syphilis screening during a unique pregnancy. To identify whether a pregnancy had at least one syphilis screening, the San Mateo Medical Center data were converted from a long format, meaning that multiple rows could pertain to the same individual and the same pregnancy (e.g., five rows for five prenatal visits for one pregnancy or ten rows for five prenatal visits for one pregnancy and five prenatal visits for another pregnancy), to a wide format so that each row was a summary of each unique pregnancy, including an indicator variable for at least one syphilis screening during the pregnancy. For example, an individual could have had multiple visits during one pregnancy and could have also had multiple visits for multiple pregnancies. In order to transform these records from a long format to a wide format so that each row represented a unique pregnancy, unique pregnancies were identified first in the birth records by calculating an estimated date of conception by subtracting the gestational age at birth, information that was available in the birth records, from the child's birth date. Then this date range, beginning with the calculated date of conception and ending with the child's birth date, was linked to a unique birth ID assigned to each live birth in the birth records. For example, a child's unique birth ID of 12345 was assigned to his date range beginning with the calculated date of conception and ending with his birth date, January 1, 2018 to September 30, 2018. Due to a lack of a unique identifier between the San Mateo Medical Center records and the birth records, deterministic linkage and then probabilistic linkage using the fastLink package[22] were used to identify the birthing parent so that the child's unique birth ID (e.g., 12345) can be assigned to each unique pregnancy. The fastLink package uses the Fellegi-Sunter probabilistic record linkage model and is an efficient algorithm that retains high sensitivity for determining matches.[22–24] The variables used to identify matches were mother's first name, mother's last name, mother's date of birth, the infant's birth year, and visit date to the San Mateo Medical Center.

The maximum number of gestational weeks was defined to be 46 weeks. The trimester of the birthing parent's visit was determined by the infant's recorded weeks of gestation at the time of birth in the birth records.

Indicator Variable

An indicator variable was created using the March 17, 2020 shelter-in-place date, so that all births from January 1, 2018 to March 16, 2020 were considered to be in the prepandemic period and March 17, 2020 to December 31, 2021 were considered to be in the pandemic period. As there is no one date that demarcates the start of the COVID-19 pandemic, March 17, 2020 was chosen as the start to the COVID-19 pandemic because that is when the shelter-in-place order began in San Mateo County, along with five other counties in the San Francisco Bay Area. This shelter-in-place order was the most restrictive in the U.S. at the time, as it required that people stay in their residence, except for essential activities.[25] Due to the major disruption to daily life and health service access and availability, this was identified as an appropriate date for the start of the pandemic period. The study population was then further restricted to those who were not pregnant at the time of March 17, 2020 when the shelter-in-place order began. Those who were pregnant during the shelter-in-place order may have been in differing trimesters of their pregnancy. Those who were in their second or third trimester of pregnancy at the start of the shelter-in-place order may have received syphilis testing in the first trimester, whereas those who were in the first trimester of pregnancy at the start of the shelter-in-place order may have experienced a disruption or delay of care, so may not have been tested for syphilis during the first trimester or may have missed syphilis testing altogether. Excluding pregnancies that overlapped with the shelter-in-place date resolved this issue. After excluding the pregnancies that overlapped with the start of the shelter-in-place date (n=557) and those who had missing or unknown values for race/ethnicity and educational attainment (n=1,045), there were 1,953 pregnant individuals who met all inclusion criteria and were in the final study population.

Analysis

Chi-square tests of independence were used to compare the proportions of pregnant individuals who receive syphilis testing in the prepandemic period and the pandemic period by birthing parent's age, level of educational attainment, and race/ethnicity. Multivariable logistic regression was then used to calculate the odds of syphilis screening at least once in the pandemic period compared to the odds of syphilis screening at least once in the prepandemic period, adjusting for birthing parent's age, level of educational attainment, and insurance type. Due to the San Mateo Medical Center not being a birthing hospital, the pregnancy-related care that clients received may have not been routine or may have been different from typical prenatal care. To account for this, the same model was applied to a dataset that was further restricted to Medi-Cal only clients who had at least two visits to the San Mateo Medical Center.

All analyses were conducted using R Statistical Software (Version 4.2.1; R Core Team 2023).

The multivariable logistic regression took the form of:

$$\text{logit}(Y) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5$$

where,

Y: Odds of being tested for syphilis

X_1: Visit date occurring before or during the COVID-19 pandemic (i.e., January 1, 2018 to March 16, 2020 vs. March 17, 2020 to December 30, 2021) (ref. January 1, 2018 to March 16, 2020)

X_2: Birthing parent's age (categorical) (ref. 18-24 years old)

X_3: Birthing parent's race/ethnicity (ref. Hispanic)

X_4: Birthing parent's educational attainment (categorical) (ref. Bachelor/Advanced Degree)
X_5: Birthing parent's insurance type (ref. private insurer)

RESULTS

San Mateo County birth rate decreased in the pandemic period compared to the prepandemic period (Table 1). The biggest decrease occurred in 2020, when there were 488 fewer births than in 2019, a 6.0% decrease. A similar decrease was observed among the number of unique pregnant clients at the San Mateo Medical Center. In 2020, there were 163 fewer pregnant clients than in 2019, a 15.8% decrease; the decrease continued in 2021, when there were 392 fewer pregnant clients than in 2020, a 45.3% decrease (Table 2). The race/ethnic composition of the San Mateo Medical Center was not reflective of the race/ethnic composition of those who gave birth in San Mateo County, with the majority (80.9%) of the San Mateo Medical Center client population being Hispanic (Figure 1).

During the prepandemic period, 18.4% of pregnant individuals were not screened for syphilis whereas during the pandemic period had 24.2% of pregnant individuals were not screened for syphilis (Figure 2). This change in the proportion of pregnant individuals not screened for syphilis was statistically significant (p=0.03). The proportion of individuals not screened for syphilis in the first trimester increased from 9.3% to 14.6% (p=0.02). The proportion of those unscreened for syphilis in the second trimester remained similar (16.6% and 16.3% during the prepandemic and pandemic period, respectively) but the proportion of those unscreened for syphilis in the third trimester increased from 63.7% to 76.6% (Figure 3), though this difference was not statistically significant (p=0.4). Asian, Black, Hispanics or Latino, and Native Hawaiian or Pacific Islander individuals were less likely to have been tested for syphilis after the shelter-in-place order, although this decline was statistically significant only for Hispanics or Latinos (Table 3 and Figure 4).

The proportion of pregnant individuals tested for syphilis decreased during the pandemic period across all levels of educational attainment, with the biggest decrease (18.9%) seen in those with an associate's degree (Table 3 and Figure 5), although none of these decreases were statistically significant. There were decreases in testing among both those under 25 years of age and those 25 years and older (Table 3 and Figure 6). This binary age classification was examined as the CDC has different screening guidelines for those under 25 years old and those 25 years and older.[12] Figure 7 contains the results by more granular age categories, showing that there was a decrease in screening for syphilis testing during the pandemic period in all age groups except those ages 14-17 years and 35-39 years of age, although none of these differences were statistically significant (Table 3).

The unadjusted odds ratio for syphilis screening in the pandemic period compared to the prepandemic period was 0.71 (95% CI: 0.55, 0.89). The adjusted odds ratio was 0.74 (OR: 0.74; 95% CI: 0.58, 0.94), adjusting for age, race/ethnicity, educational attainment, and insurance type (Table 4). The model yielded similar results for the dataset that had the restricted dataset of Medi-Cal only clients who had two or more visits (OR: 0.53; 95% CI: 0.34, 0.81).

Table 5 shows the results of a second model that included an interaction term between the prepandemic/pandemic indicator and race/ethnicity. The ORs from this model suggest that the

reduction in syphilis testing probability is not statistically significantly different from the Hispanic or Latino comparator group for any racial/ethnic group.

DISCUSSION

The main finding of this study was that the odds of syphilis testing among pregnant individuals at the San Mateo Medical Center decreased after the March 17, 2020 shelter-in-place order. This decreased occurred even as the total number of pregnancies also declined.

Before the COVID-19 pandemic, racial disparities in syphilis screening of pregnant individuals were evident at the San Mateo Medical Center (Figure 3); after the shelter-in-place order and the related changes to healthcare access and resource allocation, all racial/ethnic groups saw a decrease in syphilis testing. The reasons for a decrease in syphilis testing among pregnant individuals, for whom there are clear screening guidelines, are likely multifactorial. One study that examined a national laboratory database found that while the volume of testing for chlamydia and gonorrhea declined sharply after the COVID-19 national emergency was declared on March 13, 2020, test positivity increased after that date,[26] suggesting that the observed decrease in the number of chlamydia and gonorrhea cases was due to a decline in testing individuals with chlamydia and gonorrhea infection. Another retrospective chart review in an urban emergency department, where universal syphilis screening was implemented, found that there was an increase in the rate of presumed active syphilis infection (i.e., positive syphilis serology and patient history) during the first months of the pandemic.[27] These increases in rates were found to be highest in women and adolescents. In this study, only 19.2% of the patients who were presumed to have active, or early, syphilis infection actually presented to the emergency department with an STI-related complaint, indicating that the majority of the presumed active syphilis infections had little to no symptoms. While it is possible that this increase was due to an increase in incidence of new infections, this is unlikely as others have reported a decrease in risky sexual behavior associated with the shelter-in-place order. A more likely explanation is that testing during routine visits, especially prenatal testing, had declined.

Due to the large decrease in the number of births in San Mateo County (n=488) and the number of pregnant clients at the San Mateo Medical Center (n=163) in 2020, it is unlikely that there was an increase in demand for prenatal care and any related syphilis screening associated with prenatal care as there were fewer births and pregnant clients seeking these services.

Syphilis screening may have decreased during the pandemic period because the effects of the shelter-in-place order may have impacted a clinician's perception of patient risk, such as having sex with multiple sex partners during pregnancy, late entry to prenatal care, and unstable housing.[28] Another possible explanation for the observed decrease in syphilis screening may be that pregnant individuals who were already having difficulty gaining access to appropriate prenatal care were encountering even more barriers to accessing that care, such as loss of health insurance or an unstable housing situation resulting in homelessness. It is likely that there was some delay in or absence of prenatal care during the pandemic period, as evidenced by the three-fold increase in congenital syphilis cases in San Mateo County compared to the total number of congenital syphilis cases in the prior nine-year period. As congenital syphilis is considered a sentinel health event, this increase in cases of congenital syphilis, not only in San Mateo County, but also in California and in the U.S., points to increasing failure of the healthcare system to

identify, screen, and treat pregnant individuals with a syphilis infection during the pandemic period. Finally, it is possible that for any prenatal visit, the probability that the client was offered screening may have declined, reflecting a difference in provider performance (i.e., due to staffing shortages) rather than differences in access to care. This could be further explored by analyzing the number and timing of antenatal visits pre- and during the pandemic.

One thing is certain: the number of diagnosed cases of congenital syphilis is at historically high levels in San Mateo County, California, and in the U.S.[5,29] Although the absolute numbers of cases in San Mateo County are too small to draw robust conclusions about the trend, the observed increase in the incidence of congenital syphilis in San Mateo County after the COVID-19 pandemic is consistent with national trends. San Mateo County had a total of three cases of congenital syphilis during the nine years from 2010 to 2018, two cases in 2011, and only one case in 2015. In 2019 and 2020, there was one case of congenital syphilis reported in San Mateo County. However, in 2021, there were three cases of congenital syphilis reported.[30] In other words, San Mateo County had doubled the case count of congenital syphilis during the COVID-19 pandemic period (2020 to 2022) compared to the total number of cases of congenital syphilis in the nine-year period preceding it (2010 to 2019).

Congenital syphilis is considered to be a barometer for how well the healthcare system is performing, as congenital syphilis is fully preventable if CDC prenatal syphilis testing guidelines are followed.[12] With this increase in congenital syphilis seen in San Mateo County, California, and in the U.S., it is important to understand how the COVID-19 pandemic affected syphilis control efforts in pregnant individuals so as to identify vulnerable populations and to better allocate resources for STI prevention and treatment.

Strengths and Limitations

This study has several strengths. First, deterministic and probabilistic linkage were used to identify unique pregnancies of San Mateo Medical Center clients, which would not have been possible using the hospital records alone. This linkage created a dataset that contained important individual-level socioeconomic information, such as the birthing parent's educational attainment, that would not have been available in the San Mateo Medical Center records. Second, this analysis used birth records, which are complete for all live births that occurred within that health department's jurisdiction (e.g., county). These birth records also contain information regarding prenatal care and birth-related metrics, such as number of prenatal visits, Apgar scores, and the infant's gestational age at birth. This information was used to further supplement the hospital records, primarily by providing information that allowed calculating date ranges for each unique pregnancy. And third, this analysis can be reproduced in any health department that has access to hospital records and birth records, data typically available at health departments.

This study also had several limitations. Since the San Mateo Medical Center is not a birthing hospital, the pregnancy-related care that clients received may have not been routine or may have been different from typical prenatal care. However, the more restrictive dataset, which included only those who had Medi-Cal and had two or more visits to the San Mateo Medical Center, had an OR that was further from the null compared to the full dataset, suggesting that the results of this study are consistent with those using a dataset restricted to those who meet more strict definitions of being an established client who received regular prenatal care from the San Mateo

Medical Center. Although the aim of this analysis was to establish a baseline of syphilis testing among pregnant individuals, there needs to be the additional assumption that these testing patterns for pregnant individuals remained consistent through the prepandemic period. In the same vein, it was also difficult to identify visits that were only pregnancy-related and not related to delivery or postpartum care by ICD codes alone. The ICD code is primarily an administrative code used for medical billing and may not be an accurate description of the reason for the visit. Also, the study population was largely homogenous as 80.9% of the clients were Hispanic or Latino. This may have resulted in the largely not statistically significant findings of this analysis with respect to racial/ethnic differences. Although this analysis can, and should, be reproduced, the race/ethnic composition of the study population may pose a challenge with respect to statistical power and interpretability of results if one race/ethnic group constitutes the large majority of the study population. Lastly, the outcome variable of this study did not encode whether or not the syphilis testing occurred at recommended points in the pregnancy (i.e., first prenatal appointment in the first trimester and, for those considered to be at high risk of syphilis infection, in the third trimester). Future analyses should examine the expanded recommendation of timely syphilis screening as the outcome as defined by the CDPH. This expanded recommendation was not used as the outcome in this study due to small numbers.

CONCLUSION

The San Mateo Medical Center saw a decline in syphilis testing of pregnant individuals during the COVID-19 pandemic compared to the prepandemic period. This decline was statistically significant as a whole and for the Hispanic and Latino subgroup; the sample size of all the other racial/ethnic groups were much smaller and none of their changes in probability of screening were statistically significant. Ultimately, more data on the availability and utilization of prenatal care after the start of the COVID-19 pandemic are necessary to contextualize these findings. Although we were able to observe this decline in syphilis screening, the underlying drivers of this decline, which are multifactorial, are still being researched. Future research should examine data specifically from prenatal care settings, such as birthing hospitals that provide obstetrician and maternity care, to quantify the number of prenatal care visits, which points to individuals accessing care, and to identify if these visits included syphilis screening through ICD codes or other diagnostic coding, which points to the quality of care provided by the medical facility and its clinical providers. Additionally, this analysis should be replicated by health departments, particularly at a time of rising incidence of congenital syphilis, to identify populations in which syphilis screening during pregnancy has declined.

ACKNOWLEDGEMENTS

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APPENDIX

Sexually Transmitted Infections (STI) Screening Guideline for Syphilis[16]

Disease	CDC Recommendation
Syphilis	***First prenatal visit:*** Screen all pregnant women. ***Third trimester (28 weeks and at delivery):*** Rescreen women who: • Are at risk for syphilis during pregnancy (e.g., misuses drugs; has had another STI during pregnancy; or has had multiple sex partners, a new partner, or a partner with an STI); • Live in areas with high numbers of syphilis cases, and/or; • Were not previously tests, or had a positive test in the first trimester.

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FIGURES AND TABLES

Table 8. San Mateo County births, 2013-2021

	2013	2014	2015	2016	2017	2018	2019	2020	2021
No. births	8633	8883	8827	8785	8432	8203	8124	7636	7373
% change	--	2.90%	-0.63%	-0.48%	-4.02%	-2.72%	-0.96%	-6.01%	-3.44%

Singletons only (i.e., number of unique pregnancies that resulted in live birth)

Table 9. San Mateo Medical Center pregnant clients, 2013-2021

	2013	2014	2015	2016	2017	2018	2019	2020	2021
No. unique clients	1414	974	1043	1088	1076	989	1029	866	474
% change	--	-31.12%	7.08%	4.31%	-1.10%	-8.09%	4.04%	-15.84%	-45.27%

This includes all individuals who received pregnancy-related care at the San Mateo Medical Center, regardless of whether the shelter-in-place order occurred during their pregnancy.

Figure 38. Race/ethnic composition of birthing parents in San Mateo County and the San Mateo Medical Center, San Mateo County, CA, 2018-2021

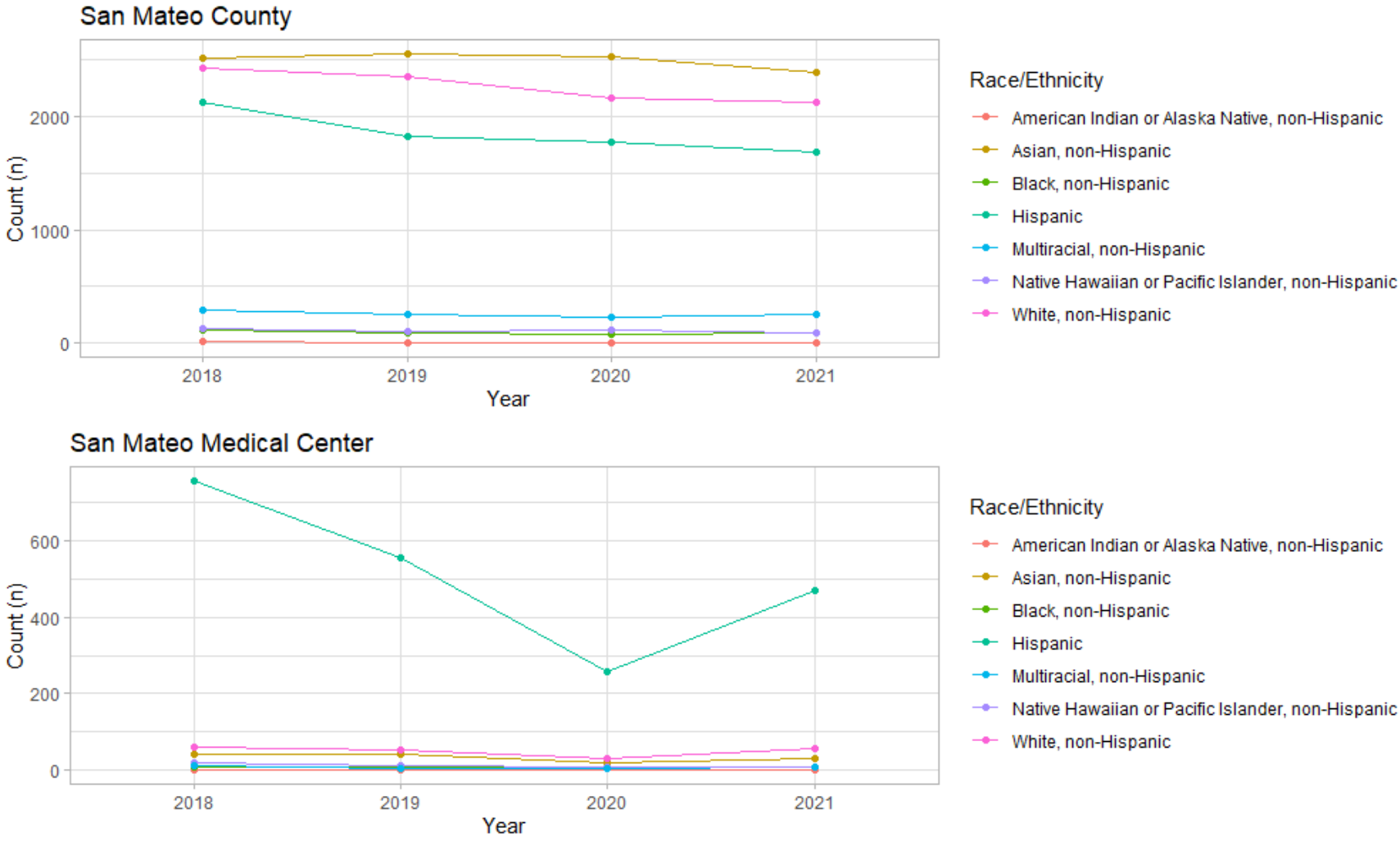

Figure 39. Syphilis screening among pregnant individuals who received prenatal care at the San Mateo Medical Center before and after COVID-19 shelter-in-place order, 2018-2021

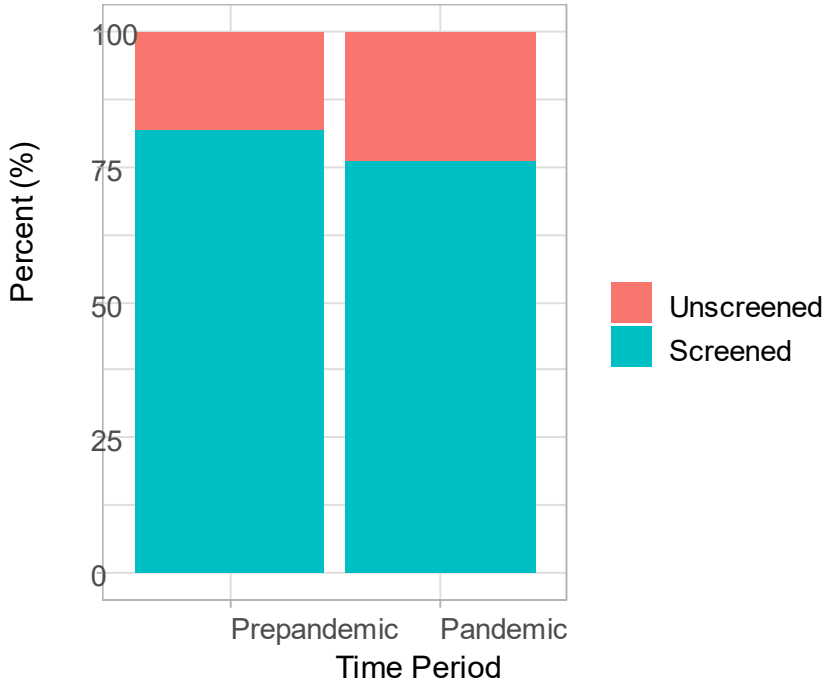

Figure 40. Syphilis screening per unique pregnancy in the prepandemic period and in the pandemic period by visit trimester, 2018-2021

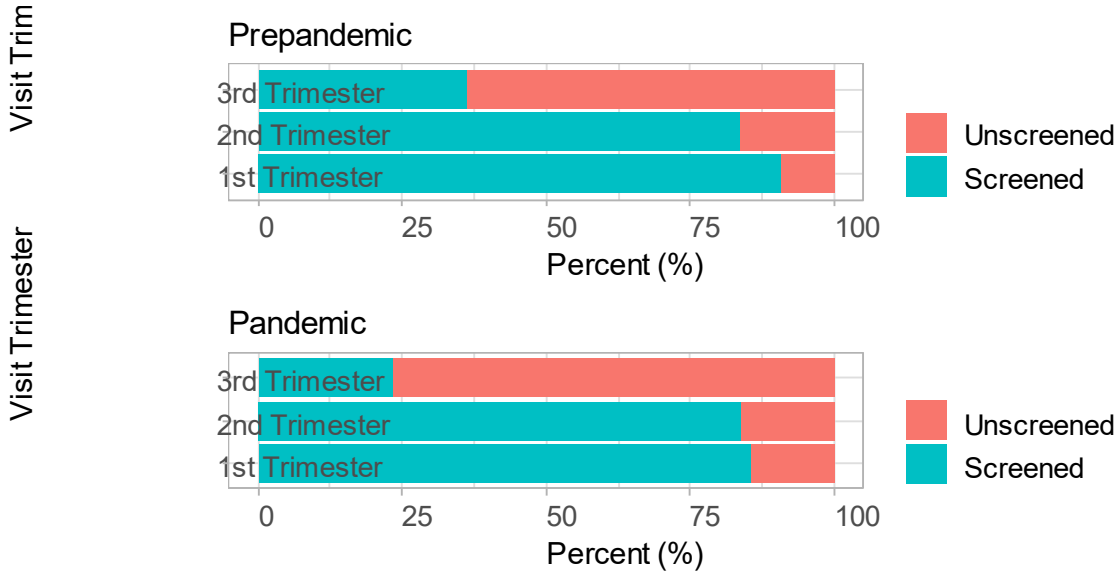

Table 10. Demographic characteristics of pregnant individuals unscreened for syphilis during prenatal care visits in the prepandemic and pandemic period, 2018-2021

	Prepandemic Period		Pandemic Period		Percent Change
	Total	Unscreened (%)	Total	Unscreened (%)	
Age Category (years)					
< 25 years old	439	18.7%	157	25.5%	6.8%
≥ 25 years	1002	18.3%	355	23.7%	5.4%
Age Category (years)					
<18	26	34.6%	11	27.3%	-7.3%
18-24	413	17.7%	146	25.3%	7.7%
25-29	479	19.6%	163	28.8%	9.2%
30-34	256	15.2%	93	20.4%	5.2%
35-39	214	19.6%	78	17.9%	-1.7%
40-45	53	15.1%	21	19.0%	4.0%
Race/Ethnicity					
American Indian or Alaska Native	3	33.3%	3	0.0%	-33.3%
Asian	77	23.4%	37	32.4%	9.1%
Black	14	35.7%	8	50.0%	14.3%
Hispanic or Latino	1195	16.2%	385	23.9%	7.7%*
Multiracial	29	48.3%	8	25.0%	-23.3%
Native Hawaiian or Pacific Islander	19	21.1%	6	50.0%	28.9%
White, non-Hispanic	104	28.8%	65	16.9%	-11.9%
Educational Attainment					
Less than high school	538	13.8%	141	17.0%	3.3%
High school graduate	527	19.4%	213	23.5%	4.1%
Some college	189	23.3%	84	32.1%	8.9%
Associate's degree	59	18.6%	24	37.5%	18.9%
Bachelor's degree and higher	128	26.6%	50	28.0%	1.4%

* $p < 0.05$

Figure 41. Proportion of pregnant clients who received prenatal care at the San Mateo Medical Center tested for syphilis by race/ethnicity, prepandemic and pandemic period, 2018-2021

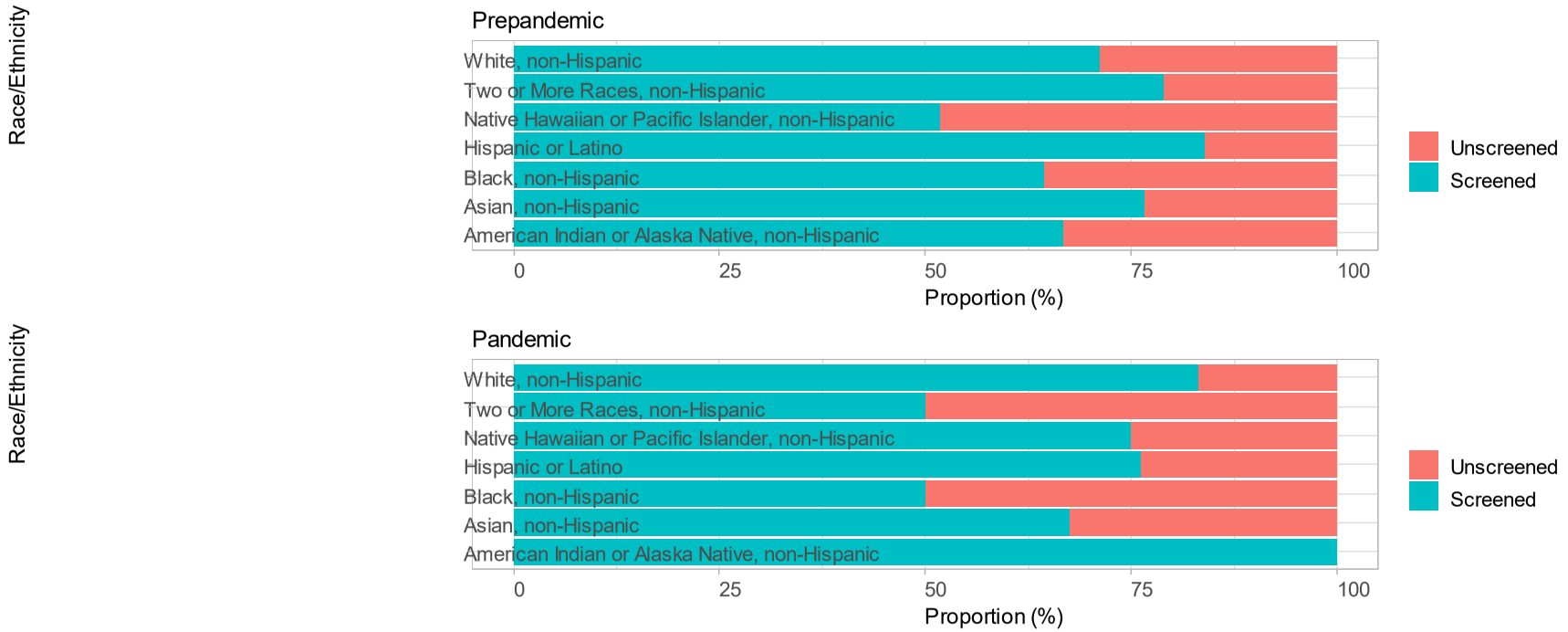

Figure 42. Proportion of pregnant clients who received prenatal care at the San Mateo Medical Center tested for syphilis by educational attainment, prepandemic and pandemic period, 2018-2021

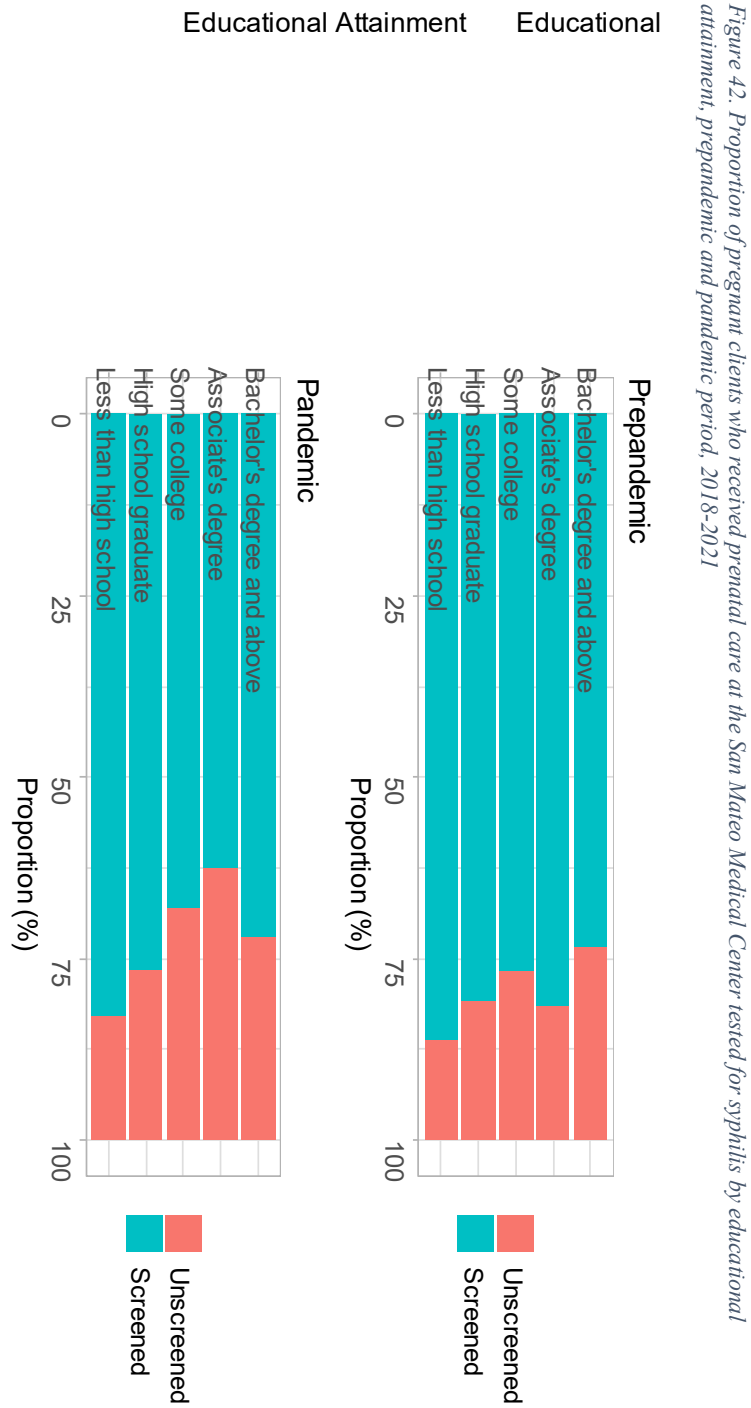

Figure 43. Proportion of pregnant clients who received prenatal care at the San Mateo Medical Center tested for syphilis by a binary age group, prepandemic and pandemic period, 2018-2021

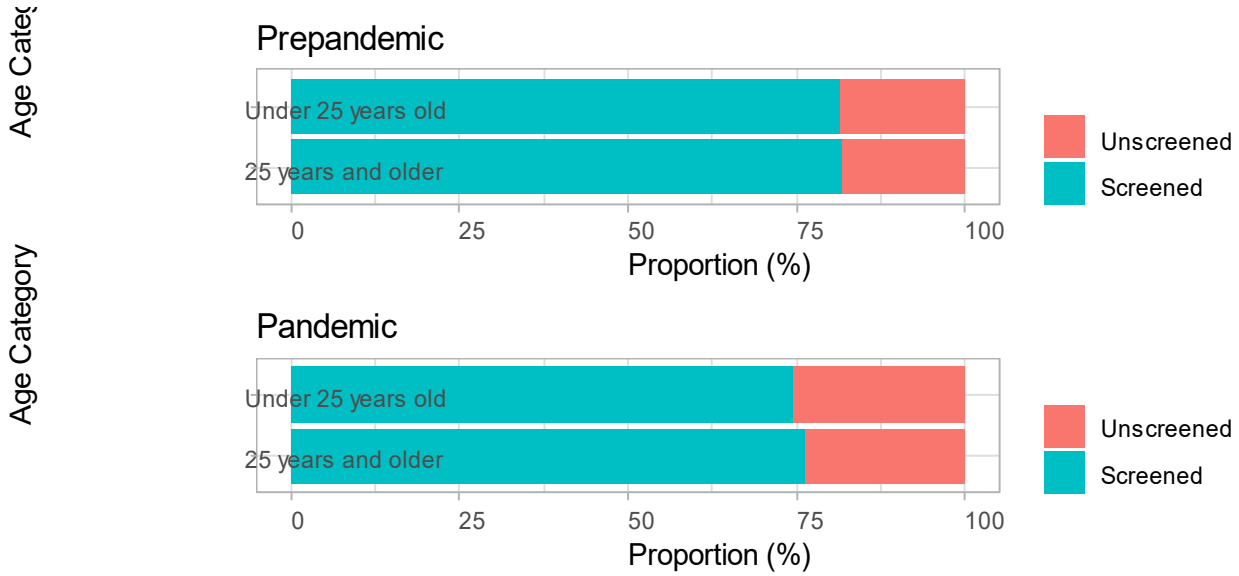

Figure 44. Proportion of pregnant clients who received prenatal care at the San Mateo Medical Center tested for syphilis by age group, prepandemic and pandemic period, 2018-2021

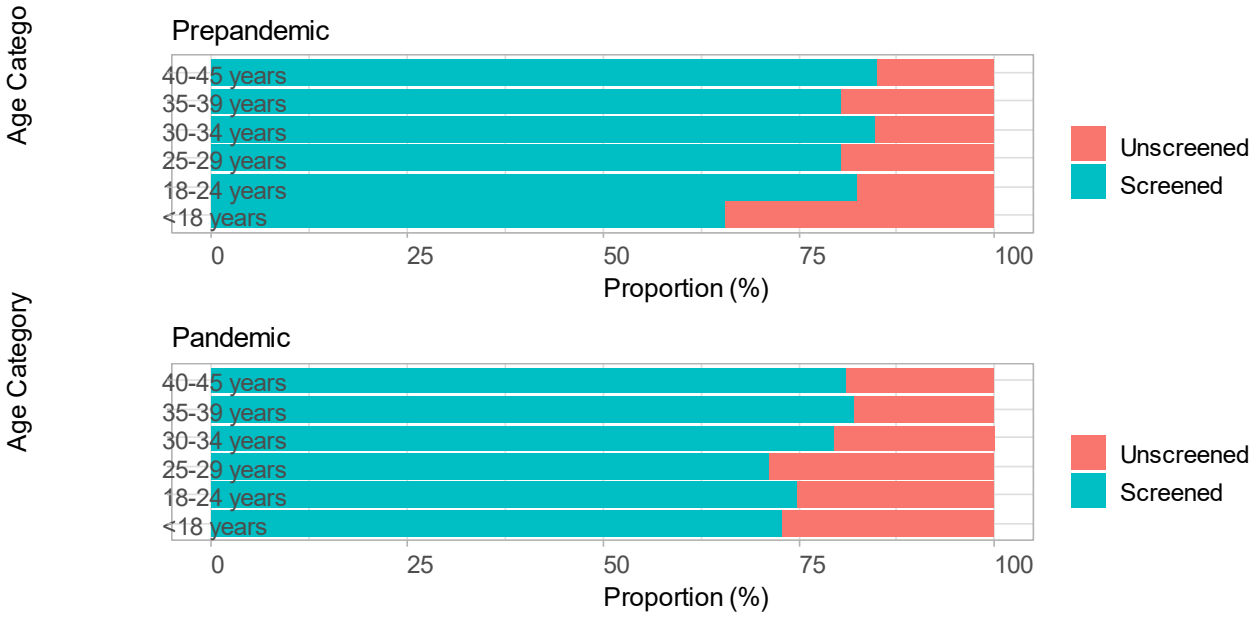

Table 11. Multivariable logistic regression results for the association between the COVID-19 shelter-in-place order and syphilis screening in pregnant individuals, controlling for age, educational attainment, and insurance type

	OR	95% CI
COVID-19 Indicator		
Prepandemic	1	--
Pandemic	0.74	(0.58, 0.94)

Table 12. Odds Ratios of Syphilis Testing During the Pandemic Period Compared to the Prepandemic Period, by Race/Ethnicity

	OR	95% CI
Pandemic period		
American Indian or Alaska Native*	N/A	N/A
Asian	0.77	(0.43, 1.38)
Black	0.35	(0.12, 1.08)
Hispanic or Latino	1	--
Multiracial	0.89	(0.29, 2.75)
Native Hawaiian or Pacific Islander	0.22	(0.10, 0.47)
White	0.55	(0.34, 0.89)

*Excluded from this model due to small numbers

Note: Adjusted for age, educational attainment, and type of insurance

CONCLUSION AND FURTHER RESEARCH

The effects of the COVID-19 pandemic on STI control efforts are still being studied and understood. However, the incidence of chlamydia, gonorrhea, and early syphilis remain high even after a once-in-a-generation pandemic. The analyses conducted in this dissertation have shown different ways that data sources available at health departments can be harnessed to examine these STI trends by supplementing a reportable disease registry and hospital records. Through these analyses, we have learned that racial disparities in the incidence of chlamydia, gonorrhea, and early syphilis persisted in San Mateo County, a norther California county, even during the COVID-19 pandemic. We also learned that the HPI may have limitations in its application in a medium-size county, such as San Mateo County, outside of identifying census tracts that have the least and the greatest opportunity. This was evident in the results of the second chapter, as HPI quartiles likely did not adequately capture any expected differences in the rate of chlamydia and gonorrhea reinfections by SES. And lastly, we found that the proportion of pregnant individuals tested for syphilis decreased after the start of the COVID-19 pandemic, suggesting that the effects of the pandemic have downstream effects that we are now only able to observed and report, such as increases in congenital syphilis.
Although the HPI as a composite measure of neighborhood opportunity likely did not capture SES adequately in the analyses in this dissertation, composite measures, such as the HPI, can be used when there is no information on individual-level SES to at least provide some information on an ecological level about the context in which an individual lives.

There are still many unknown effects of the COVID-19 pandemic on STIs, particularly with respect to how these effects may have interacted with demographic factors such as gender and race/ethnicity. It is our hope that health departments will see through this dissertation the possibility in the wide range of data sources available to them to find novel ways to answer questions of how upstream factors are associated with various health outcomes and how these associations were affected by the COVID-19 pandemic.