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Treatment Completion With Three-Dose Series of Benzathine Penicillin Among People Diagnosed With Late Latent and Unknown Duration Syphilis, Maricopa County, Arizona

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Abstract

Background: Syphilis is a public health concern as cases are rising each year. If untreated, syphilis is associated with significant morbidity and risk of vertical transmission during pregnancy. For people with late latent and unknown duration stages, 3 injections of benzathine penicillin G (BPG) at 1-week intervals are recommended. Our study quantified treatment for people diagnosed with late latent and unknown duration syphilis in Maricopa County, Arizona with a secondary analysis of pregnant women to assess completion of 3 injections of BPG in multiple time intervals.

Methods: Maricopa County syphilis case data were extracted from the state-run database (PRISM). Records were reviewed for people with late latent and unknown duration syphilis during January 1, 2016, to December 31, 2021. Treatment types and time intervals between treatments were analyzed.

Results: Of a total of 14,924 people with syphilis reported in Maricopa County, 5372 (36.0%) were staged as late latent or unknown duration syphilis. Completion of 3 BPG injections in the time frame of 7 to 9 days was 42.9% (n = 2302). Completion among pregnant women (n = 406) with 3 injections was 68.7% (n = 279).

Conclusions: The completion rate of 3 BPG injections for people with late latent or unknown duration syphilis is low. An unmet need exists to identify barriers to treatment including access to BPG and public health follow-up after the first injection. Prioritized effort is needed to identify and classify patients as having earlier stages of syphilis that require only 1 BPG injection.

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Syphilis is on the rise. In the United States, reported syphilis rates have increased from 27.3 per 100,000 population in 2016 to 40.8 per 100,000 in 2020.[1] In Arizona, there was a 134% increase in total syphilis cases from 2016 to 2020 (1906 cases to 4460 cases).[1] Late latent and unknown duration syphilis cases in Arizona have increased by 141% from 680 cases in 2016 to 1637 cases in 2020.[2] As a consequence of the rise in adult syphilis, congenital syphilis has increased. In 2020, Arizona had the second highest rate nationally of congenital syphilis at 151.2 cases per 100,000 live births.[3] The rising incidence of syphilis is an urgent public health concern necessitating intervention by public health officials to identify persons diagnosed with syphilis, ensure treatment completion, and halt transmission.

If untreated, syphilis is a chronic infection that can progress through a series of stages.[4,5] Primary and secondary syphilis have high infectivity rates with treatment aimed at curbing both horizontal and vertical transmission (transmission from mother to child). Latent syphilis, although rarely transmitted sexually, is associated with long-term morbidity and vertical transmission.[4] Patients with syphilis of unknown duration cannot be assigned a stage due to lack of observable syphilis symptoms and unknown timing of infection. If syphilis is left inadequately treated or untreated, about a third of patients can develop clinical symptoms including neurosyphilis or cardiovascular syphilis.[5] Pregnancy poses the additional risk of transplacental transmission to the neonate, resulting in congenital syphilis.[6] Adverse outcomes of congenital syphilis include stillbirth and prematurity in addition to a variety of clinical manifestations.[6] The significant long-term morbidity associated with both adult and congenital syphilis highlights the importance of early detection and treatment.

Syphilis treatment recommendations from the Centers for Disease Control and Prevention (CDC) vary by syphilis stage, making the distinction between early and late latent syphilis important for management.[4,7] Although a single dose of benzathine penicillin G (BPG) 2.4 million units intramuscularly is indicated for early syphilis (primary, secondary, and early latent stages), the regimen for late latent and unknown duration syphilis consists of 3 doses of 2.4 million units BPG given intramuscularly at 1-week intervals.[4,7] For nonpregnant late latent patients allergic to penicillin, alternative options include doxycycline or tetracycline for 28 days.[4,8] However, for pregnant patients allergic to penicillin, BPG remains the sole treatment recommendation with guidance including desensitization to the medication.[4,7] Despite the scheduling component of the treatment guidelines for late latent cases nonallergic to penicillin, the recommendation for delayed dosing in a course of weekly therapy remains unclear. According to CDC guidelines, clinical experiences indicate an interval of 10 to 14 days between injections may be acceptable.[4] Pharmacologic considerations indicate an interval of 7 to 9 days may be preferred.[4] Furthermore, guidance for pregnant women indicates that an interval longer than 9 days between doses is not optimal and would require repeating the full course of therapy.[4] Given the recommended treatment guidelines for cases of late latent syphilis nonallergic to penicillin, defining and quantifying completion of the regimen is essential both clinically and epidemiologically.

Despite having an effective therapy for syphilis, obstacles exist that result in inadequate treatment. Because of high cost and particular storage requirements as a sterile injectable medication, few private practice and community health providers stock BPG.[9,10] Patients

are then advised to receive treatment at STD or other publicly-funded clinics that qualify for BPG at reduced cost.[9] Patients might be reluctant to obtain treatment at an alternative clinic.[11] Maricopa County has only 1 government run STD health facility, potentially posing an added obstacle for patients with transportation needs.[12] In addition, if a dose is missed, restarting a series of 3 injections could discourage patients from completing the whole course. As syphilis rates continue to increase, treatment barriers can inform public health interventions.

Given the rise of syphilis cases in Arizona and the long-term morbidity associated with both adult and congenital infection, quantifying treatment rates can inform intervention strategies. To date, limited data exist that quantify treatment completion rates among individuals with late latent or unknown duration syphilis.[13] Maricopa County, the fourth largest county and health jurisdiction in the United States, is an ideal site to conduct this study with Arizona's high national syphilis rank.[1] The goal of this study was to quantify treatment completion with 3 injections of BPG in the 7- to 9-day interval. We conducted a retrospective investigation of all persons diagnosed with late latent and unknown duration syphilis in Maricopa County, AZ during 2016 to 2021 to track treatment completion and timing between doses.

MATERIALS AND METHODS

Data Collection

For persons diagnosed with syphilis in Maricopa County, demographic characteristics and treatment data were extracted from the Patient Reporting Investigation Surveillance Manager (PRISM). The PRISM database is hosted and supported by the Arizona Department of Health Services. Data were imported into SAS Enterprise Guide 8.2 for analysis.

Study Population

Maricopa County syphilis records were reviewed for persons diagnosed with late latent and unknown duration syphilis during January 1, 2016, to December 31, 2021.

Treatment data were provided through epidemiological surveillance conducted by Maricopa County STD clinic trained communicable disease investigators (CDIs). A CDI follow-up is essential in acquiring the treatment information for each patient as providers report the disease before treatment completion. The CDIs capture treatment doses through calling providers directly, obtaining medical records, and reviewing patient charts to most accurately disposition patients. For this analysis, all positive syphilis cases were included, regardless of the level of CDI investigation.

Given the high positivity rate, CDIs are unable to obtain treatment information for all patients. Each person diagnosed with syphilis in Maricopa County is assigned a priority category based on an internal Reactor Grid classification system that factors in personal characteristics and risk factors (eg, pregnancy status, titer level, and HIV coinfection). Persons classified as "higher priority" (pregnancy, women, high nontreponemal titer, younger age, early stage of infection) are assigned to CDIs to conduct patient interviews and follow-up on treatment status. Therefore, it was assumed that patients who were interviewed

had the most complete treatment records in PRISM, including details of treatment type and date. Lower priority is given to patients with low titers, males, and those older than 60 years. However, CDIs also worked to obtain treatment information for patients classified as "low priority."

For each patient, the following demographic variables were collected: sex, age, sexual orientation, race/ethnicity, distance to Maricopa County STD clinic (miles), pregnancy status, coinfection with HIV, history of a prior sexually transmitted disease, history of substance use, and history of incarceration within the last 12 months. Distance to the Maricopa County STD clinic was calculated as the mileage difference between the center of the patient's reported zip code and the Maricopa County STD clinic zip code.

Definitions

For our primary analysis, treatment completion was defined as 3 injections of BPG spaced at 7- to 9-day intervals consistent with the interval recommended by the CDC's STI treatment guidelines.[4,7]

Given the 6-year study timeline, we accounted for changes in CDI treatment documentation practices. Before 2020, options for logging treatment in PRISM included selecting BPG by individual dose (eg, "Benzathine Penicillin G 2.4 MU IM (Dose 1)") or selecting an entry that included all 3 injections, "Benzathine Penicillin G 2.4 MU IM for 3 doses at 1 week intervals." The latter did not document dates of individual doses and relied on CDI endorsement that all 3 injections were appropriately spaced. As a result, we classified cases with at least 1 treatment entry logged as "3 doses at 1 week intervals" to be included as "nonvalidated" treatment. Validated treatment indicates the CDI logged doses with the appropriate individual treatment description and dates. The "3 doses at 1 week intervals" entry option was removed in 2020, therefore all cases in 2020 and 2021 were considered validated.

Outcomes

The primary outcome was completion of 3 injections of BPG with each injection spaced 7- to 9-days apart. We quantified the number of BPG doses per individual in addition to calculating the time interval between each treatment. Analyses were performed for all persons diagnosed with syphilis including pregnant women in the study timeframe. Patients were organized into treatment groups based on their treatment type and the 7- to 9-day (correct) interval (Box 1, http://links.lww.com/OLQ/A905).

In addition to the 7- to 9-day interval, a sensitivity analysis was conducted to quantify treatment completion using alternative intervals between doses. The CDC standard treatment recommendation of 7 days was included.[4,7] In addition, to account for the CDC recommended pharmacologic consideration (7–9 days) and clinical experience consideration (10–14 days), a time interval of 7 to 14 days was calculated.

Statistical Analyses

We computed descriptive statistics for demographic variables by treatment group for the time interval of 7 to 9 days. Frequencies were calculated for treatment group categories by year for all persons diagnosed with syphilis and for pregnant women diagnosed with syphilis. All statistical analyses were conducted using SAS Enterprise Guide 8.2. Disease surveillance, data collection, evaluation, and analysis are ongoing public health surveillance activities, and thus are considered nonresearch according to Title 45 Code of Federal Regulations 46.102(*l*).

RESULTS

Demographic and Other Characteristics

From January 1, 2016, to December 31, 2021, a total of 14,924 syphilis cases were reported in Maricopa County, AZ. Of these, 5372 (36.0%) were staged as late latent or unknown duration syphilis (Fig. 1). The mean age at syphilis diagnosis was 36 years (Table 1). There were 1950 female, of whom, 406 were pregnant at diagnosis (20.8%). By race/ethnicity, Hispanic persons represented 43.4% of syphilis infections (n = 2329). By sexual orientation, 46.8% of the sample identified as heterosexual (n = 2513).

The average distance to the Maricopa County STD clinic was 10 miles with 68.2% of persons diagnosed with syphilis living greater than 5 miles away (n = 3665). Persons living greater than 5 miles from the clinic received 3 injections at a rate of 43.1% (n = 1581) compared with persons living within 5 miles who had a completion rate of 42.2% (n = 721).

For patients with a history of an STD, 49.6% (n = 877) completed 3 injections compared to 59.0% (n = 836) for patients with no history of an STD. A total of 1211 (22.5%) persons reported substance use, of which, 53.2% (n = 644) completed treatment. The completion rate for persons incarcerated in the last 12 months was 53.8% (n = 465), whereas persons not incarcerated during the prior year had a completion rate of 59.8% (n = 1250).

Treatment Completion

For all persons diagnosed with late latent and syphilis of unknown duration during 2016–2021, 2302 (42.9%) completed 3 injections of BPG in the defined time interval of 7–9 days (Table 2). The 2020 and 2021 rates represent validated results with 45.5% completion (n = 439) in 2020 and 40.9% (n = 660) in 2021. There was an increase in total cases of late latent and syphilis of unknown duration each year.

The rate of non-benzathine penicillin regimen use varied yearly with a peak in 2019 at 17.7% (n = 152). Alternative regimens included: doxycycline, aqueous crystalline penicillin G, ceftriaxone, or procaine penicillin plus (Supplemental Table 1, http://links.lww.com/OLQ/A905). For patients who received doxycycline, we were unable to confirm if they had a penicillin allergy.

Sensitivity Analysis

The sensitivity analysis compared treatment completion rates for alternative time intervals during the 6-year study period (Table 3). A 7- to 14-day interval between the first and second dose and the second and third dose had the highest rate of completion (n = 2402, 44.7%). Expansion of the interval between doses from 7–9 days to 7–14 represented a 1.8% (n = 100) increase in completion of 3 injections of BPG. The lowest rate of completion was using a strict 7-day interval (n = 2003, 37.3%).

Pregnant Cases

For pregnant women, completion of 3 injections spaced 7–9 days apart was 68.7% (n = 279) (Table 4). From 2020 to 2021, there was a decrease in completion from 77.2% (n = 71) to 61.0% (n = 72). Across the 6-year period, 5.2% (n = 21) of pregnant women were not treated for syphilis.

DISCUSSION

This retrospective review of syphilis surveillance data quantifies treatment completion among patients with late latent and syphilis of unknown duration in Maricopa County, Arizona during 2016 to 2021. Using the CDC recommended treatment interval of 7 to 9 days, the overall completion rate for all persons was 42.9%. Although no literature exists that establishes a reference benchmark, we believe there is room for improvement. To our knowledge, this study is the first to quantify and compare treatment rates among patients with late latent and unknown duration syphilis in Arizona and in the United States. Our study demonstrates the need to further investigate factors contributing to the low syphilis treatment completion rate.

The sensitivity analysis examined completion rates for alternative treatment intervals and provided support for expanding the time interval between doses to improve treatment completion. The CDC's syphilis guidelines recommend doses at 1-week intervals but includes both clinical (10–14 days) and pharmacologic (7–9 days) considerations for expanded dosing intervals.[4] Our study found treatment completion to be highest within the expanded interval of 7 to 14 days (44.7%). There was a 1.8% increase in completion using a 7- to 14-day interval compared with the CDC STI guidelines preferred interval of 7 to 9 days, a difference of 100 patients. Although the pharmacodynamics of BPG between expanded intervals has not been studied, allowing patients more flexibility in obtaining doses could increase treatment completion. There is potential for treatment dosing flexibility; however, guidelines for pregnant women are more conservative.

There is an increasing public health focus on maternal syphilis to prevent vertical transmission. In our study, we found a higher rate of completion among pregnant women with 3 injections of BPG compared with all persons diagnosed with syphilis. There are several factors contributing to the higher rate including frequent prenatal visits, testing, and public health interventions to identify and bring women to treatment. For women located in high syphilis rate areas, the CDC recommends 3 screenings during pregnancy: a first trimester screen, a retest at 28 weeks gestation, and a test at delivery.[4] Arizona ranks sixth

nationally for total rate of syphilis cases.[1] A study surveying providers in Maricopa County found that all providers in the study performed at least 1 syphilis test during a patient's pregnancy in the first trimester and 89% tested again in the third trimester.[14] Awareness of the importance of screening and treatment in pregnancy can further increase the treatment rates.

Although the completion rate is higher among pregnant women, there is opportunity for improvement as the congenital syphilis rates continue to increase each year.[3] Gaps in prenatal care potentially contribute to the rate of congenital syphilis cases. A national study found the most commonly missed prevention opportunity was lack of maternal treatment despite timely diagnosis of syphilis during pregnancy.[15] Because of BPG access limitations, women diagnosed at their obstetrician's office have to seek treatment elsewhere.[10] The second most common missed opportunity was lack of timely prenatal care.[15] The CDC guidelines recommend maternal syphilis treatment initiation greater than 30 days from delivery as this is associated with the most clinical benefit.[4] A study conducted by Arizona Department of Health Services identified missed opportunities for prevention in the Arizona Medicaid system and found time to treatment as a barrier to preventing congenital syphilis.[16] Early prenatal care and treatment is vital to prevent congenital syphilis.[17]

The completion rates for all persons diagnosed with syphilis and pregnant women documented in this study are likely a result of several factors. Specific barriers patients face that influence treatment include BPG access, obtaining time off from work, having reliable transportation, and securing childcare.[10] Despite being the gold standard therapy for syphilis, BPG is not universally available at all healthcare facilities.[10] Patients are often required to leave their primary care provider and utilize publicly funded STD clinics or other healthcare facilities for treatment. Health clinics that supply BPG are often only open Monday through Friday, 8:00 AM to 5:00 PM, disadvantaging individuals who cannot leave work during the day. As a result, patients who miss a dose can feel an added burden of having to restart the series while navigating barriers to be able to travel to the appropriate healthcare facility. Maricopa County CDIs report decreased follow-up because of active substance use, limited access to transportation, and Maricopa County STD clinic wait times. At the clinic, wait times and a 20-dollar payment for each treatment appointment likely further hindered patients from complying with treatment. To combat transportation issues, the Maricopa County STD clinic has provided ride share app vouchers to patients. These services can be expanded in addition to improving clinic wait times and lengthening the treatment time interval. Patient and institutional barriers exist that decrease patients' ability to receive their BPG injections.

We propose several changes to improve treatment of persons with syphilis (Box 2, http://links.lww.com/OLQ/A905). The first is prioritization of correct staging to classify patients into earlier syphilis stages that only require 1 BPG injection. An effort should be made to improve provider education and bolster efforts by CDIs.[18] Providers should conduct a comprehensive physical exam to identify lesions that would place patients in an earlier stage. CDIs are imperative to conducting partner tracking and identifying syphilis acquisition within a 1-year timeframe (early syphilis). Because of surges in syphilis cases, early syphilis staging may be improved by additional CDI staffing to reduce the number of

cases each CDI is responsible for interviewing allowing for better staging of cases. Recent investments in CDIs and other Disease Intervention Specialists can be leveraged to better track syphilis treatment.[18] We also propose making BPG more affordable by expanding 340B pricing to private practices and using mobile health clinics to delivery BPG to patients' homes.[19] In the interim, although BPG access is still limited, healthcare provider education is needed to know where patients can receive BPG. Finally, consideration should be given to expanding the time interval between therapies. As previously discussed, our sensitivity analysis demonstrated a completion rate of 44.7% with a widened interval of 7 to 14 days. Each of these strategies can help ensure syphilis case identification and treatment completion.

Our study was not without limitations. First, the Maricopa County STD clinic prioritizes patients to be investigated and tracked by CDIs. Patients classified as low priority are less likely to have treatment information recorded by CDIs. As a result, the calculated treatment completion rates are likely underestimates, and this limits the generalizability of our study to accurately capture treatment completion for all persons diagnosed with late latent and unknown duration syphilis. However, the prioritization does focus on patient characteristics and risk factors, such as untreated syphilis among pregnant women and women of child-bearing age. Due to the inclusion of all investigated positive cases, there are instances in which treatment was received, but not documented in the system. Although we recognize that this occurs, it is a low like-lihood as CDIs work diligently to obtain treatment records before dispositioning a patient as "not treated." Second, variations in documentation practice from 2016 to 2019 resulted in variable representations of accurately tracked injections. From 2016 to 2019, inclusion of the data entry option "3 injections at 1-week intervals," did not equate to all 3 injections being tracked or completed in the appropriate time frame. For our analysis, we considered this entry as acceptable, albeit the entry was categorized as nonvalidated. Results from 2016 to 2019 may, therefore, be skewed due to inclusion of this nonvalidated measure and demonstrated the importance of removing such data entry options to improve disease treatment tracking. Third, for pregnant women, we analyzed treatment independent of expected delivery date and intent to cure before delivery. We did not track if the patient initiated treatment 30 days before delivery or if the baby was born with congenital syphilis. Finally, our study period included the start of the COVID-19 pandemic. We did not account for potential changes in public health tracking and treatment follow-up that could have been affected by lock downs and pandemic behaviors.

Despite these limitations, our study lays the foundation for additional studies. The first is to quantify time to treatment and identify differences based on where a patient is diagnosed (eg, STD clinic compared with private clinic). Studies should also be initiated to analyze the rate of congenital syphilis in pregnant women based on the timing of treatment relative to delivery (eg, starting 30 days prior), the number of injections received, and time interval between doses.

This is a quantitative assessment of the treatment completion rates among late latent and unknown duration syphilis cases in Maricopa County, Arizona. The findings from this study provide an important baseline of an indicator not previously studied. With the yearly increases in all stages of syphilis observed both locally and nationally, understanding access

and barriers to treatment is imperative in helping develop public health strategies to decrease the incidence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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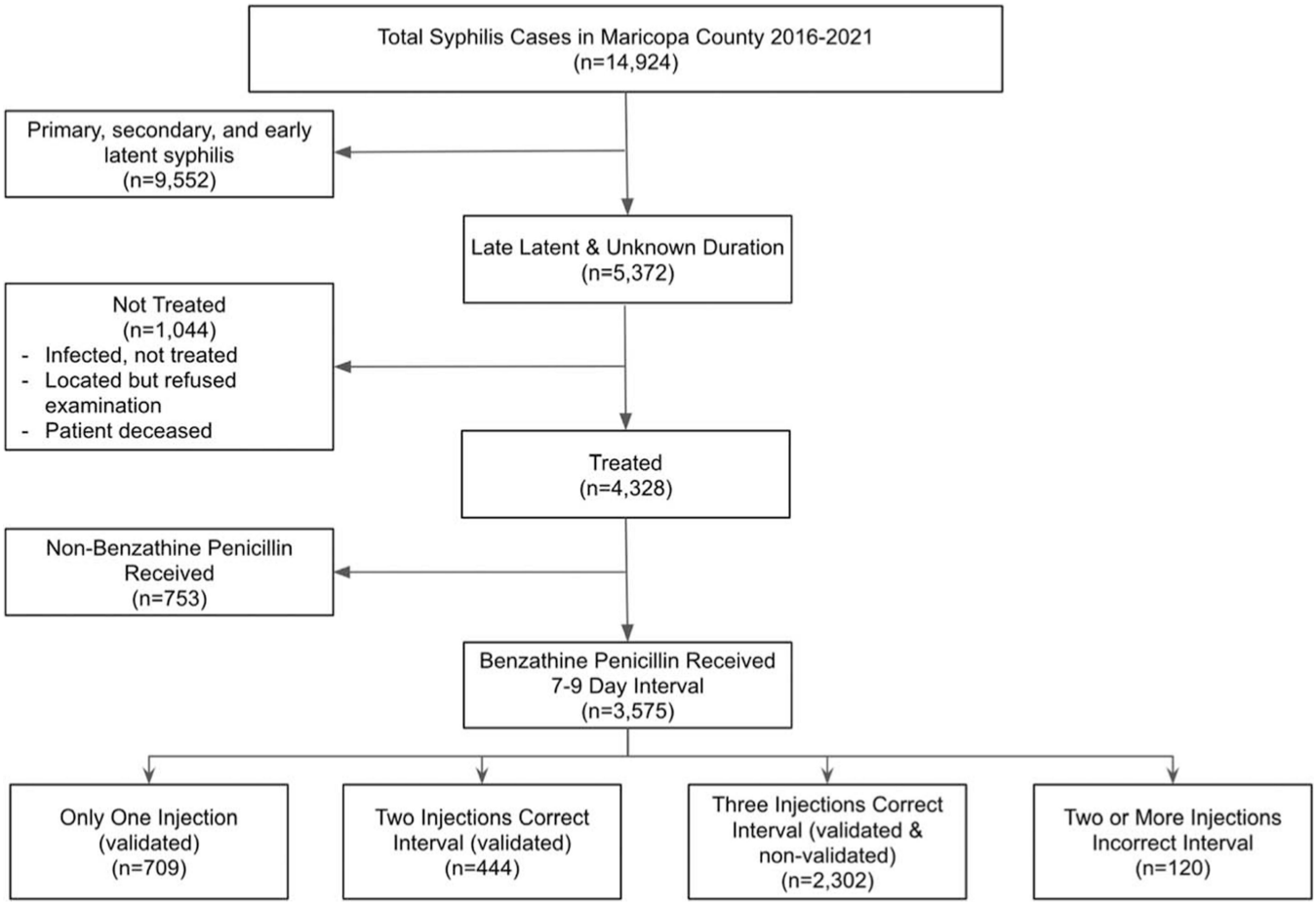

Figure 1.
Syphilis Cases in Maricopa County 2016–2021 Flow Chart.

TABLE 1.

Demographic Features of Patients With Late Latent or Syphilis of Unknown Duration in Maricopa County (7- to 9-Day Interval, 2016–2021)

n (Row %)	Not Treated	Only One Injection*	2 Injections Correct Interval*	3 Injections Correct Interval†	2 or More Injections Incorrect Interval	Non-Benzathine Penicillin Received	Total Cases
Characteristics	1044 (19.4)	709 (13.2)	444 (8.3)	2302 (42.9)	120 (2.2)	753 (14.0)	5372
Sex							
Male	724 (21.2)	471 (13.8)	272 (8.0)	1371 (40.0)	71 (2.1)	513 (15.0)	3422
Female	320 (16.4)	238 (12.2)	172 (8.8)	931 (47.7)	49 (2.5)	240 (12.3)	1950
Pregnant	21 (5.2)	43 (10.6)	42 (10.3)	279 (68.7)	13 (3.2)	8 (2.0)	406
Age, mean (SD)	37 (12.5)	35 (11.9)	34 (10.8)	35 (12.1)	34 (10.7)	38 (12.7)	36 (12.2)
Race/ethnicity							
American Indian/Alaskan Native, non-Hispanic	66 (15.7)	68 (16.2)	41 (9.7)	192 (45.6)	16 (3.8)	38 (9.0)	421
Asian, non-Hispanic	9 (16.7)	8 (14.8)	2 (3.7)	22 (40.7)	2 (3.7)	11 (20.4)	54
Black, non-Hispanic	162 (21.1)	110 (14.3)	59 (7.7)	317 (41.2)	21 (2.7)	100 (13.0)	769
Hispanic	364 (15.6)	285 (12.2)	220 (9.5)	1128 (48.4)	45 (1.9)	287 (12.3)	2329
Multiracial, non-Hispanic	38 (25.2)	12 (8.0)	13 (8.6)	71 (47.0)	8 (5.3)	9 (6.0)	151
Native Hawaiian/Pacific Islander, non-Hispanic	1 (5.9)	4 (23.5)	1 (5.9)	11 (64.7)	0 (0)	0 (0)	17
Other, non-Hispanic	7 (38.9)	2 (11.1)	1 (5.6)	5 (27.8)	0 (0)	3 (16.7)	18
Unknown	160 (59.5)	24 (8.9)	9 (3.4)	38 (14.1)	2 (0.7)	36 (13.4)	269
White, non-Hispanic	237 (17.6)	196 (14.6)	98 (7.3)	518 (38.5)	26 (1.9)	269 (20.0)	1344
Sexual orientation							
Heterosexual	362 (14.4)	300 (11.9)	232 (9.2)	1230 (49.0)	62 (2.5)	327 (13.0)	2513
Bisexual	26 (8.0)	41 (12.6)	25 (7.7)	171 (52.6)	3 (0.9)	59 (18.2)	325
Gay/lesbian	154 (11.9)	224 (17.3)	106 (8.2)	550 (42.4)	30 (2.3)	234 (18.0)	1298
Other	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2
Unknown	500 (40.5)	144 (11.7)	81 (6.6)	351 (28.4)	25 (2.0)	133 (10.8)	1234
Distance to STD Clinic							
<5 miles	377 (22.1)	231 (13.5)	151 (8.9)	721 (42.2)	31 (1.8)	196 (11.5)	1707
≥5 miles	667 (18.2)	478 (13.0)	293 (8.0)	1581 (43.1)	89 (2.4)	557 (15.2)	3665

n (Row %)	Not Treated	Only One Injection*	2 Injections Correct Interval*	3 Injections Correct Interval†	2 or More Injections Incorrect Interval	Non-Benzathine Penicillin Received	Total Cases
HIV coinfection							
HIV+ before/within 30 d of STD	145 (16.6)	155 (17.7)	96 (11.0)	317 (36.2)	23 (2.6)	139 (15.9)	875
HIV+ infection after 30 d of STD	11 (12.4)	19 (21.4)	5 (5.6)	37 (41.6)	4 (4.5)	13 (14.6)	89
Unknown	888 (20.2)	535 (12.1)	343 (7.8)	1948 (44.2)	93 (2.1)	601 (13.6)	4408
History of prior STD							
Yes	178 (10.1)	258 (14.6)	156 (8.8)	877 (49.6)	42 (2.4)	256 (14.5)	1767
No	45 (3.2)	121 (8.6)	125 (8.8)	836 (59.0)	33 (2.3)	256 (18.1)	1416
Did not ask	701 (40.8)	259 (15.1)	117 (6.8)	423 (24.6)	34 (2.0)	185 (10.8)	1719
Refused to answer	21 (22.8)	11 (12.0)	12 (13.0)	24 (26.1)	3 (3.3)	21 (22.8)	92
Unknown	99 (26.2)	60 (15.9)	34 (9.0)	142 (37.6)	8 (2.1)	35 (9.3)	378
Substance use							
Yes	96 (7.9)	149 (12.3)	96 (7.9)	644 (53.2)	35 (2.9)	191 (15.8)	1211
No	38 (2.3)	182 (11.0)	154 (9.3)	951 (57.4)	32 (1.9)	300 (18.1)	1657
Did not ask	883 (37.3)	364 (15.4)	179 (7.6)	664 (28.0)	46 (1.9)	232 (9.8)	2368
Refused to answer	27 (19.9)	14 (10.3)	15 (11.0)	43 (31.6)	7 (5.2)	30 (22.1)	136
Incarcerated in last 12 mo							
Yes	104 (12.0)	94 (10.9)	93 (10.8)	465 (53.8)	26 (3.0)	81 (9.4)	864
No	36 (1.7)	215 (10.3)	179 (8.6)	1250 (59.8)	42 (2.0)	367 (17.6)	2089
Did not ask	877 (38.6)	380 (16.7)	157 (6.9)	544 (23.9)	46 (2.0)	270 (11.9)	2274
Refused to answer	27 (18.6)	20 (13.8)	15 (10.3)	42 (29.0)	6 (4.1)	35 (24.1)	145

*Validated: captures communicable disease investigator documentation of each individual injection.

†Validated and nonvalidated: captures communicable disease investigator documentation of patient reported “3 injections with benzathine penicillin at 1-week intervals” from 2016 to 2019.

TABLE 2.

Treatment Completion for All Cases of Late Latent or Syphilis of Unknown Duration by Year (2016–2021)

Year	Not Treated	Only One Injection*	2 Injections Correct Interval*	3 Injections Correct Interval†	2 or More Injections Incorrect Interval	Non-Benzathine Penicillin Received	Total Cases
2016	72 (14.6)	60 (12.2)	11 (2.2)	265 (53.6)	9 (1.8)	77 (15.6)	494
2017	115 (19.7)	73 (12.5)	34 (5.8)	266 (45.6)	14 (2.4)	82 (14.0)	584
2018	169 (19.7)	126 (14.7)	91 (10.6)	341 (39.8)	28 (3.3)	102 (11.9)	857
2019	138 (16.1)	143 (16.7)	82 (9.6)	331 (38.6)	11 (1.3)	152 (17.7)	857
2020	157 (16.3)	103 (10.7)	95 (9.8)	439 (45.5)	26 (2.7)	145 (15.0)	965
2021	393 (24.3)	204 (12.6)	131 (8.1)	660 (40.9)	32 (2.0)	195 (12.1)	1615
Total	1044 (19.4)	709 (13.2)	444 (8.3)	2302 (42.9)	120 (2.2)	753 (14.0)	5372

*Validated: captures communicable disease investigator documentation of each individual injection.

†Validated and nonvalidated: captures communicable disease investigator documentation of patient reported “3 injections with benzathine penicillin at 1-week intervals” from 2016 to 2019.

TABLE 3.

Treatment Completion Among All Late Latent or Syphilis of Unknown Duration Cases by Injection Interval (2016–2021)

Injection Interval	Not Treated	Only One Injection*	2 Injections Correct Interval*	3 Injections Correct Interval†	2 or More Injections Incorrect Interval	Non-Benzathine Penicillin Received	Total Cases
7 d	1044 (19.4)	709 (13.2)	594 (11.06)	2003 (37.3)	269 (5.0)	753 (14.0)	5372
7–9 d	1044 (19.4)	709 (13.2)	444 (8.3)	2302 (42.9)	120 (2.2)	753 (14.0)	5372
7–14 d	1044 (19.4)	709 (13.2)	388 (7.2)	2402 (44.7)	76 (1.4)	753 (14.0)	5372

*Validated: captures communicable disease investigator documentation of each individual injection.

†Validated and nonvalidated: captures communicable disease investigator documentation of patient reported “3 injections with benzathine penicillin at 1-week intervals” from 2016 to 2019.

TABLE 4.

Treatment Completion for Pregnant Cases of Late Latent or Syphilis of Unknown Duration by Year (2016–2021)

Year	Not Treated	Only One Injection*	2 Injections Correct Interval*	3 Injections Correct Interval†	2 or More Injections Incorrect Interval	Non-Benzathine Penicillin Received	Total Cases
2016	0 (0)	4 (15.4)	0 (0)	21 (80.8)	1 (3.9)	0 (0)	26
2017	1 (2.6)	2 (5.3)	6 (15.8)	29 (76.3)	0 (0)	0 (0)	38
2018	1 (1.4)	8 (11.4)	13 (18.6)	45 (64.3)	1 (1.4)	2 (2.9)	70
2019	1 (1.6)	8 (12.9)	9 (14.5)	41 (66.1)	1 (1.6)	2 (3.2)	62
2020	10 (10.9)	2 (2.2)	4 (4.4)	71 (77.2)	2 (2.2)	3 (3.3)	92
2021	8 (6.8)	19 (16.1)	10 (8.5)	72 (61.0)	8 (6.8)	1 (0.9)	118
Total	21 (5.2)	43 (10.6)	42 (10.3)	279 (68.7)	13 (3.2)	8 (2.0)	406

*Validated: captures communicable disease investigator documentation of each individual injection.

†Validated and nonvalidated: captures communicable disease investigator documentation of patient reported “3 injections with benzathine penicillin at 1-week intervals” from 2016 to 2019.