Title

The Sacred Cow of Syphilis Control: Assessing the Utility and Practical Implications of Syphilis Partner Services Data in California

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The Sacred Cow of Syphilis Control:

Assessing the Utility and Practical Implications of Syphilis Partner Services Data in California

By

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Abstract

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Following the introduction of penicillin in the 1940s, the incidence of infectious syphilis in the United States dramatically declined from a high of 70.9 per 100,000 in 1946 to a historic low of 2.1 in 2000[1]. In the decade since, syphilis has shown signs of re-emergence, with the incidence rate of infectious syphilis in the U.S. increasing to 5.5 per 100,000 in 2013. Infectious syphilis trends in California have largely paralleled those of the rest of the country, but with an incidence rate consistently above the national average. After decades of substantial progress in syphilis control, the incidence of infectious syphilis in California increased from a low of 0.9 per 100,000 (284 cases) in 1999 to 9.3 in 2013 (3,554 cases)[2]. As in other major metropolitan areas in the U.S., the majority of syphilis cases in California are among men who have sex with men (MSM), with a high proportion reporting HIV co-infection. Syphilis infection can result in major health complications if untreated, and also facilitates the transmission and acquisition of HIV[3-5].

In addition to mandated reporting to health departments, syphilis partner services – in particular, partner notification - are a standard public health practice for identifying potentially infectious individuals for testing and treatment, thereby interrupting transmission of syphilis within sexual networks and reducing incidence of the illness in the general population[6]. However, the increasing incidence of syphilis in California, the frequent reporting by patients with syphilis of anonymous sex partners, and the lack of a clear measure of partner services effectiveness raise questions concerning the impact this intervention is having on spread of disease, and to what extent the data acquired through syphilis partner services provide meaningful information about how the underlying sexual networks contribute to trends in syphilis morbidity in various populations.

The objectives of this dissertation are 1) to review studies evaluating syphilis partner notification efforts and compare outcome definitions and measures of effectiveness, 2) to analyze the structure and characteristics of sexual networks detected through routine syphilis surveillance and partner notification efforts in the San Francisco Bay Area Region, and 3) to

make recommendations concerning how public health departments might use syphilis surveillance data to better understand such networks and to provide opportunities for case-finding and disease prevention.

This dissertation will directly inform a common public health intervention by assessing the utility of existing public health data for understanding and preventing transmission of syphilis within networks, and by discussing ways in which resources might be deployed to reduce the incidence of syphilis more effectively.

To Munchie, for being, without question, the hardest and most fulfilling part of this journey.
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I hope I have made you all proud.

Table of Contents

List of Tables

List of Figures

Chapter 1 - The Great Imitator

"Know syphilis in all its manifestations and relations, and all other things clinical will be added unto you." - Sir William Osler (1849-1919), Regius Professor of Medicine, Oxford University

Origins of Syphilis

Syphilis has been given many different names over the centuries – the French pox, the Neapolitan disease, the disease of the Franks, *morbus Gallicus* (the French sickness), the "bubas", the "pox", the "great pox", and the "great imitator". The name syphilis is credited to Italian physician Hieronymus Fracastorius' *Syphilis sive morbus gallIcus ("Syphilis or the French Disease"),* a long poem published in 1530 about a young shepherd named Syphilus, who angered the Sun-god Apollo and was subsequently stricken with a terrible illness that followed the clinical and pathological course of syphilis. The origin of syphilis in Europe have long been the topic of debate, with scholars ascribing it to either an Old World or New World source.[7] Proponents of the New World or Columbian theory hold that syphilis was endemic in the region of the world now called Haiti, and acquired and carried back to Europe by Columbus in the late 1400s. Proponents of the Old World or pre-Columbian theory hold that syphilis can be traced back to Central Africa and was introduced into Europe prior to the arrival of Columbus. Regardless of its origins, historians agree the first definitive mention of venereal syphilis coincides with the invasion of Naples by France, including 50,000 mercenaries from various regions at the onset of the Italian Wars in 1495[8]. Upon returning home to their respective countries after the war, this army also carried this new disease; within a decade, syphilis had spread throughout Europe.

Etiology and transmission of syphilis

Syphilis is caused by infection with the bacterium *Treponema pallidum,* subspecies *pallidum,* a delicate spiral organism known as a spirochete. *T. pallidum* has a total length of 6-20 micrometers and a spiral shape with 10-14 coils, moving in a corkscrew motion. The primary mode of transmission of syphilis is sexual contact, followed by mother-to-child transmission in utero. Humans are the only known reservoir of *T. pallidum;* the mucosal membranes of the human body offer the best environment for the organism to grow and thrive. Infection with *T. pallidum* is spread through direct contact between open sores and mucosal membranes or abrasions of the skin. Once the organism enters the body, it immediately begins multiplying, entering the lymph capillaries and incubating in regional lymph nodes. Within a short timeframe, the organisms enter the bloodstream, resulting in both local and systemic manifestations of infection[9,10].

Clinical manifestations of syphilis

Syphilis is often referred to as the "great imitator", due to the similarity of the signs and symptoms it produces with those of other diseases[9,11]. There are four distinct stages of syphilis infection - primary, secondary, latent and tertiary (late) syphilis[12]:

Primary syphilis. Primary syphilis is characterized by at least one firm, indurated and painless ulcerative lesion known as a chancre that appears at the site of infection, after an incubation period of 3-90 days. Multiple lesions are present in a small proportion of cases. Chancres are highly infectious, but spontaneously resolve without treatment within three to six weeks. Without treatment, however, infection progresses to the secondary stage of syphilis.

Secondary syphilis. Secondary syphilis is characterized by a non-pruritic rash and/or mucous membrane lesions in the mouth, vagina, or anus. Symptoms can develop six weeks to six months after infection, or one to five weeks after the primary chancre resolves. Although the rash can be widely distributed on the body, it frequently produces rough, red or reddish brown spots on the palms of the hands and the soles of the feet (also referred to as a "palmar plantar" rash). Lesions known as mucous patches also form in warm, moist areas of the body, particularly the mouth or genital region. As with the chancre of primary syphilis, these mucous membrane patches are generally painless. Other manifestations of secondary syphilis include condolymata lata (i.e., wart-like genital lesions), fever, swollen lymph glands, sore throat, alopecia (i.e., hair loss), headaches, weight loss, body aches, and fatigue. Without treatment, the signs and symptoms of secondary syphilis spontaneously resolve within three to six weeks.

Latent (asymptomatic) syphilis. Once the manifestations of primary and secondary (P&S) syphilis resolve, the latent or hidden stage of syphilis infection begins. Without treatment, *T. pallidum* infection remains dormant in the body and asymptomatic for as long as 10-30 years. Early latent syphilis refers to infection that occurred within 12 months prior to diagnosis; late latent syphilis refers to infection that occurred more than 12 months prior to diagnosis.

Tertiary (late) syphilis. Approximately 33% of individuals with untreated syphilis progress to late stage syphilis[13]. By this time, the spirochetes may have damaged blood vessels, nerves, and multiple organs, including the brain, heart, liver, and bones. This systemic infection can manifest itself through gradual development of blindness, hearing loss, paralysis, numbness, difficulty with movement, dementia, and in severe cases, death.

In addition, neurosyphilis and congenital syphilis are considered conditions of public health priority that require distinct clinical and case management:

Neurosyphilis. Neurosyphilis is the invasion of the central nervous system by *T. pallidum.* Infection can be asymptomatic or result in a wide range of symptoms, including headaches, altered behavior, and speech/motor problems that can resemble Parkinson's disease. Neurological involvement can occur during any stage of syphilis.

Congenital syphilis. Untreated or inadequately treated maternal syphilis infection during pregnancy can result in infection with *T. pallidum* in utero, leading to stillbirth, neonatal death, or a variety of physical and developmental disorders. Signs and severity of congenital syphilis vary, with the most severe cases having clinical manifestations at birth. Infants and toddlers (age < 2 years) may have rash, condylomata lata, rhinorrhea, jaundice, anemia, or edema.

Older children may have interstitial keratitis, nerve deafness, anterior bowing of shins, frontal bossing, mulberry molars, Hutchinsonian teeth, saddle nose deformities, or Clutton joints.

Diagnosis and staging of syphilis

The diagnosis and staging of syphilis are dependent on laboratory test results, physical examination, and a patient's serologic history.

Standard laboratory tests for syphilis. Detailed laboratory standards and methods for the diagnosis of syphilis have been published elsewhere[13,14]. Briefly, laboratory diagnostic methods for syphilis encompass two broad approaches – direct detection of *T. pallidum* and serologic tests for syphilis antibodies[7,15]. *T. pallidum* cannot be readily cultivated in vitro or stained with laboratory stains.

Darkfield microscopy is the most sensitive and specific method available for direct identification of *T. pallidum* in fluid taken from the surface of a primary syphilis lesion or from condylomata lata. Darkfield examination is most likely to be positive during the stages of syphilis when moist lesions containing large numbers of treponemes are present: primary, secondary, relapsing infectious conditions, or early congenital syphilis. Treponemes can also be detected in secondary syphilis lesions, although it is much more difficult to prepare a sample properly for testing. Advantages of using the darkfield exam are that it provides rapid results with a definitive, immediate diagnosis of syphilis. In addition, primary syphilis can be identified several days to weeks prior to serologic tests become reactive[13] . However, darkfield exam is rarely used to diagnose syphilis, given the technological difficulty of preparing the sample, and the need for both specialized equipment and a highly trained, experienced microscopist to perform the test and interpret the results. Negative darkfield exams also do not rule out syphilis, as topical treatments such as soap or antibiotics can alter the spirochete, or there may be too few organisms present to detect.

The direct fluorescent-antibody tissue test for *T. pallidum* (DFAT-TP), combined with histologic stains, is another direct detection method that can be used to diagnose late or congenital syphilis, and distinguish skin lesions during secondary and late syphilis from those that occur with Lyme disease[13] . Tissue for DFAT-TP testing is most frequently collected from the brain, gastrointestinal tract, placenta, umbilical cord, or skin.

In the absence of direct identification methods, serologic tests that detect syphilis antibodies are relatively low cost, easy to run, and logistically simple to carry out. These tests can be grouped into two categories – nontreponemal and treponemal tests. The most commonly used nontreponemal tests are the Rapid Plasma Reagin (RPR) and Venereal Disease Research Laboratory (VDRL) tests; the RPR 18-mm circle card and the toluidine red unheated serum test (TRUST) are also recognized as standard tests for syphilis[13,14]. These tests detect immunoglobulins IgG and IgM antibodies formed in response to lipoidal material released from damaged host cells during initial infection. Nontreponemal tests can be used as quantitative tests for establishing baseline reactivity and for monitoring treatment response, or as qualitative tests for initial screening. Qualitative tests examine undiluted sera for the presence or absence of antibodies, and are reported as being reactive, weakly reactive, or nonreactive.

Quantitative tests measure titers, or serial two-fold dilutions of serum samples, until an endpoint of reactivity is reached. The highest dilution in which the specimen is reactive establishes the baseline from which staging and treatment response can be assessed. Following syphilis infection, nontreponemal tests can remain minimally reactive for life or revert to non-reactivity after two to three years. As suggested by the name, nontreponemal tests are non-specific for syphilis – several factors, such as autoimmune conditions, older age, pregnancy, injection drug use, and viral infections, can produce antibodies that generate a false positive result on nontreponemal tests. Lack of sensitivity in early darkfield-positive primary cases and late cases of syphilis is another limitation of the nontreponemal tests, making them insufficient as diagnostic tests.

Standard treponemal tests include the *T. pallidum* particle agglutination (TP-PA) and fluorescent treponemal antibody absorbed (FTA-ABS) tests. Unlike the RPR or VDRL, these tests measure antibodies directed specifically against *T. pallidum* antigens. Treponemal tests are reported qualitatively, with 85% of adequately treated persons remaining reactive for life. These tests are primarily used as confirmatory tests to verify reactive nontreponemal test results or to identify individuals with late syphilis infection and clinical manifestations, but nonreactive titers. More recently, enzyme immunoassays (EIAs) and the recently CLIA-waived[i] rapid Syphilis Health Check test have been developed as screening tests, resulting in two algorithms for laboratory identification of syphilis infection: the traditional and the reverse sequence testing algorithms[16,17].

The sensitivity of these serologic tests varies by stage of syphilis, whereas their specificity is similar across the stages (Table 1). Antibodies detectable by serological nontreponemal or treponemal tests appear one to four weeks after the primary chancre forms. Approximately 30% of early primary syphilis infections will have nonreactive nontreponemal test results. Serologic tests are all reactive by the time syphilis progresses to the secondary stage, with treponemes being detectable in lesions using direct microscopic exam.

Table 1. Sensitivity and specificity of serological tests for untreated syphilis

	Sensitivity Range (by stage of syphilis)				
Test	Primary	Secondary	Latent	Tertiary	Specificity (%)
VDRL	78 (74-87)	100	96 (88-100)	71 (34-94)	98 (96-99)
RPR	86 (77-99)	100	98 (95-100)	73	98 (93-99)
FTA-ABS	84 (70-100)	100	100	96	97 (84-100)
TP-PA	88 (86-100)	100	97 (97-100)	94	96 (95-100)
EIA	93	100	100	---	

Source: Ratnam S (2005); Self-Study STD Modules for Clinicians. Centers for Disease Control and Prevention. Available online: http://www2a.cdc.gov/stdtraining/self-study/syphilis/syphilis_slide_diagnostic_1.html

[i] Clinical Laboratory Improvement Act

Physical examination. A thorough examination of the lymph nodes, skin, torso, palms of the hands, soles of the feet, genitalia and oral cavities is necessary to identify signs of early syphilis. In addition, the abdomen should be checked for liver tenderness, and women and girls should undergo a pelvic exam. A neurologic exam should be conducted to assess visual, facial, and auditory nerve function[18].

Patient's serologic history. Unlike chlamydia and gonorrhea infections, in which a positive laboratory test signifies new infection, the serologic tests used to identify syphilis infection can remain positive throughout life, even after successful treatment[6]. As a result, the likelihood of a current positive syphilis test result being indicative of a new syphilis infection must be assessed before clinical case management and public health action can be taken. For example, a younger individual with high nontreponemal test titers (≥ 1:32) is likely to have a new syphilis infection, whereas an older individual with low nontreponemal test titer is more likely to be exhibiting a serofast reaction, or the persistence of nontreponemal antibodies despite adequate treatment[16]. Obtaining a detailed serological history on a patient is critical for determining the duration of infection and for staging the disease. In particular, healthcare providers should assess the patient's history of syphilis infection, history of syphilis serologic test results, exposure to someone diagnosed with primary or secondary syphilis, and the presence of signs or symptoms of syphilis infection in the past 12 months[18].

Treatment of syphilis

Syphilis is readily treatable in any stage, using the appropriate penicillin preparation[16] (Table 2). For persons diagnosed with primary, secondary, and early latent syphilis, a single intramuscular injection of benzathine penicillin G is curative. For persons diagnosed with late syphilis, three doses of benzathine penicillin G at weekly intervals are recommended. Data to support the use of alternative treatment regimens are limited, although men and non-pregnant women with a penicillin allergy have the option of taking doxycycline or tetracycline. For pregnant women, penicillin is the only acceptable course of treatment; in instances of allergy, pregnant women must be desensitized and then given the appropriate penicillin-based treatment.

Following treatment, persons must refrain from sexual contact until the syphilis lesions are completely healed to prevent further transmission of infection[19]. While treatment kills the bacteria, it cannot restore damage already done to the host. For both the recommended and alternative treatments, follow-up serologic treponemal tests should be done to ensure a drop in antibody titer indicative of cure. Patients with early syphilis who receive adequate treatment should have at least a four-fold decline in titer three to four months post-treatment, compared to the titer at the time of treatment; most patients should have minimal or no nontreponemal reactivity by one year post-treatment[16]. Late syphilis patients receiving adequate treatment may see a more gradual decline in antibody titer, with 50% of patients remaining minimally reactive two years post-treatment[13].

Case-based syphilis surveillance

Case-based syphilis surveillance depends on ongoing identification and reporting of persons with infection at any stage. In California, Title 17 of the California Code of Regulations mandates that healthcare providers and laboratories are to report all probable or confirmed syphilis cases to local public health departments within seven days of identification[20,21]. Health departments triage incoming laboratory and provider reports by the patient's gender, age and serological titer, so as to identify individuals who are most likely to have a new infection in need of treatment. Some health departments may also factor in local syphilis epidemiology and program priorities when deciding how to prioritize follow-up of individuals with a positive serologic syphilis test[6]. Laboratory test and physical examination results, and the patient's serologic history are all factored into the classification of infected persons, based on the Centers for Disease Control and Prevention's (CDC) Sexually Transmitted Disease (STD) Surveillance Case Definitions[22].

Patients with a diagnosis of probable or confirmed early syphilis are contacted by disease investigation specialists (DIS)[ii] to ensure appropriate clinical management and conduct a detailed interview to record demographic, clinical, serological, and risk profile information. Case interview information is systematically collected using the California Syphilis Interview Record. This interview process is referred to as "enhanced syphilis surveillance". All interview /information is subsequently sent to the California Department of Public Health, Sexually Transmitted Diseases Control Branch for compilation and analysis of early syphilis morbidity trends statewide.

In addition to conducting enhanced syphilis surveillance, DIS dedicate significant time to eliciting information about partners and notification efforts. Partners who are located, tested and diagnosed with primary, secondary or early latent syphilis infection are then themselves interviewed and undergo partner elicitation, for the purposes of notifying them of possible syphilis exposure. This process is repeated until no further partners are named, no further partners can be located, and/or no new early syphilis infections are diagnosed. Partner investigation information and outcomes are captured on a form called the STD Field Record. This component of syphilis control is meant to identify sources of infection and at-risk individuals, and help interrupt transmission of infection in the sexual networks of patients, thereby reducing the overall incidence and prevalence of infectious syphilis in the population. Elicitation of information on an infected person's non-sexual contacts, a process known as clustering, is another intervention used to identify persons who may be at risk and likely benefit from syphilis testing[23].

[ii] Disease Investigation Specialists (DIS): A health department staff member who is specially trained to interview persons infected with HIV or another STD; elicit information about their partners and associates; notify the partners of their possible exposure; ensure that the partners are offered appropriate services, including examination, treatment, and referrals; and provide prevention counseling to index patients, partners, social contacts, and associates. *Centers for Disease Control and Prevention. MMWR 2008:57(RR09);74-77*.

Table 2. CDC Treatment Guidelines 2010 for Syphilis in Adults and Children

	Disease	Recommended Rx	Dose/Route	Alternative Rx
Adults	Primary, secondary, early latent (< 1 year)	Benzathine penicillin G	2.4 million units IM in a single dose	Doxycycline 100mg 2x/day for 14 days, OR Tetracycline 500 mg orally 4x/day for 14 days
	Latent (> 1 year) or latent of unknown duration	Benzathine penicillin G	2.4 million units IM in 3 doses every week (7.2 million units total)	Doxycycline 100mg 2x/day for 28 days, OR Tetracycline 500 mg orally 4x/day for 28 days
	Neurosyphilis	Aqueous crystalline penicillin G	3-4 million units IV every 4 hours for 10-14 days (18-24 million units/day)	
Children	Congenital	Aqueous crystalline penicillin G, OR Procaine penicillin G	100,000-150,000 units/kg/day (50,000 units/kg/dose IV every 12 hours) during the first 7 days of life and every 8 hours thereafter for 10 days 50,000 units/kg/day IM in a single dose for 10 days	
	Children: primary, secondary, or early latent (< 1 year)	Benzathine penicillin G	50,000 units/kg/day IM in a single dose (max: 2.4 million units)	
	Children: latent (> 1 year), or latent of unknown duration	Benzathine penicillin G	50,000 units/kg/day IM for 3 doses at 1 week intervals (max: 7.2 million units)	

Source: CDC STD Treatment Guidelines 2010. Centers for Disease Control and Prevention. Available online: http://www.cdc.gov/std/treatment/2010/toc.

Chapter 2 – Recent Epidemiology of Early Syphilis

National Profile

United States

In the 1980s, the syphilis epidemic in the U.S. was primarily among men who have sex with women (MSW), women and racial/ethnic minority populations[24,25]. The rate of primary and secondary (P&S) syphilis reported in the U.S. subsequently decreased 89.7% between 1990 and 2000, reaching the lowest rate (2.1 cases per 100,000) since 1941[1]. Subsequently, the incidence increased annually between 2001 and 2009, before decreasing in 2010 and remaining unchanged in 2011. The incidence then increased 22% from 2011 to 2013 (4.5 to 5.5 cases per 100,000, respectively), more than double the nadir rate in 2000.

Region & State[3]

Historically, the South has consistently had the highest regional rate of P&S syphilis in the U.S. In 2013, the South accounted for 40% of P&S syphilis cases nationwide; however, for the first time in 50 years, the rate in the West (6.8 cases per 100,000) exceeded that in the South (6.0)[1]. From 2011 to 2013, the P&S syphilis rate increased 38.8% in the West (4.9 to 6.8 cases per 100,000), compared to 28.1% in the Midwest (3.2 to 4.1), 26.3% in the Northeast (3.8 to 4.8), and 13.2% in the South (5.3 to 6.0). Since 2010, the 15 states with the highest rates of P&S syphilis nationally have accounted for 70% of all P&S syphilis cases reported in the U.S.

Gender

The incidence of P&S syphilis among men increased 27.2% between 2011 and 2013, from 8.1 to 10.3 cases per 100,000. In contrast, the incidence among women remained unchanged at 0.9 cases per 100,000 over this same time period. The male-to-female rate ratio increased sharply from 2000 to 2003 (1.5 to 5.3), remained stable from 2003 to 2007, and then sharply increased again from 2008 to 2013 (5.0 to 11.3), reflecting the higher burden of P&S syphilis among men. In 2013, men accounted for 91% of P&S syphilis cases in the U.S.

Gender of sex partners

Starting in 2005, CDC began to collect information about the gender of sex partners of persons with early syphilis. In 2013, the majority of cases were among MSM[1]. Among 33 areas reporting data concerning the gender of sex partner for at least 70% of P&S syphilis cases from 2007 to 2013, increases in the number of cases were observed for MSW, MSM, and women during 2007 to 2008. Among MSM, the number of cases increased annually from 2007 to 2013 (75%); among MSW and women, the number of cases decreased from 2008 to 2011 (25.9% among MSW and 18.4% among women), then increased again from 2011 to 2013 (14.4% and 2.9%, respectively).

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[3] CDC STD Surveillance report based on U.S. Census regions. See Appendix A.

Age

In 2013, the highest age-specific incidences of P&S syphilis were among persons ages 20-24 years and 25-29 years (16.1 and 15.6 cases per 100,000, respectively), for a sixth consecutive year[1,12]. Between 2011 and 2013, the rate increased 21.5% for men ages 20-24 years (22.8 to 27.7 cases, respectively) and 15.6% for men ages 25-29 years (21.2 to 24.5 cases, respectively). Rates among women ages 20-24 years increased slightly from 2011 to 2013 (3.7 to 3.9 cases, respectively).

Race/ethnicity

In 2013, among the 48 jurisdictions that submitted data according to current Office of Management and Budget (OMB) standards for reporting race/ethnicity data[26], the highest rates of P&S syphilis were among African Americans (16.8 cases per 100,000 per population). This rate was 5.6 times higher than the rate among whites (3.0 cases per 100,000). The rate among American Indian/Alaskan Native (4.6) was 1.5 times that of whites; the rate among Native Hawaiians/Other Pacific Islanders (8.6) was 2.9 times that of whites; the rate among Hispanics (6.3) was 2.1 times than that of non-Hispanic whites; and the rate among Asians (2.5) was 0.8 times that of whites[1] Non-Hispanic African Americans, Non-Hispanic whites, and Hispanics accounted for 92.3% of reported P&S syphilis cases in 2013.

Between 2009 and 2013, among the 40 jurisdictions that submitted data according to the current OMB standards for reporting race/ethnicity for the entire time period, the rates of P&S syphilis increased 65.3% among Hispanics (from 3.9 to 6.5 cases per 100,00 population), 42.5% among non-Hispanic whites (from 2.2 to 3.1 cases), 77.2% among American Indian/Alaskan Natives (from 2.8 to 5.0 cases), 55.6% among Asians (from 1.4 to 2.7 cases), 57.4% among Native Hawaiian/Other Pacific Islanders (from 5.4 to 8.5), and 188.9% among multi-race persons (from 0.7 to 1.9)[1]. In contrast, the rate among non-Hispanic African Americans decreased 7.4% (from 18.7 to 17.3 cases).

Race/ethnicity and gender

In 2013, among the 48 jurisdictions that submitted data according to current OMB standards, the highest rate of P&S syphilis among men was in non-Hispanic African Americans (30.2 cases per 100,000), followed by Native Hawaiian/Other Pacific Islanders (15.8), Hispanics (11.6), American Indian/Alaskan Natives (7.1), non-Hispanic whites (5.7), Asians (4.9) and multi-race (3.4) men[1]. Among women, the highest rate of P&S syphilis was among non-Hispanic African Americans (4.5 cases per 100,000 population), followed by American Indian/Alaska Natives (2.1), Native Hawaiian/Other Pacific Islanders (1.2), Hispanics (0.8), non-Hispanic whites (0.3), multi-race (0.3) and Asian (0.2) women.

Race/ethnicity, gender, and age

In 2013, among the 48 jurisdictions that submitted data according to current OMB standards, the highest rates of P&S syphilis among African Americans were among men ages 20-24 years and 25-29 years (96.4 and 97.2 cases per 100,000 population, respectively), and women ages 20-24 years (17.0 cases). Among Hispanics, the highest rates were among men ages 20-24 years and 25-29 years (27.2 and 28.4 cases, respectively), and women ages 20-24 years and 25-29 years (2.5 and 2.1 cases, respectively). By comparison, the highest rates of P&S

syphilis among non-Hispanic whites were among slightly older men ages 25-29 years and 30-34 years (12.6 and 11.8 cases per 10,000, respectively), and women ages 20-24 years (1.2 cases). Among Asians, the highest rates were among men ages 25-29 years (10.3 cases per 100,000) and women ages 15-19 years and 20-24 years (1.0 cases per 100,000). Among American Indian/Alaskan Natives, the highest rates were among men ages 20-24 years (17.9 cases per 100,000) and women ages 20-24 years (3.5 cases per 100,000). Among Native Hawaiian/Other Pacific Islanders, the highest rates were among men ages 25-29 years (34.8 cases per 100,000) and women ages 20-24 years (9.0 cases per 100,000). For multi-race persons, the highest rates were among men ages 30-34 years (11.7 cases per 100,000) and women ages 35-39 years (1.5 cases per 100,000).

Race/ethnicity, gender, and gender of sex partners

In 2013, the majority of women and MSW with P&S syphilis were African American (57.9% and 52.6%, respectively), followed by non-Hispanic whites (20.2% and 20.9%, respectively), Hispanics (14.0% and 20.2%, respectively) and other race/ethnicities (4.1% and 3.2% respectively)[1]. In contrast, there was greater racial/ethnic diversity among MSM with P&S syphilis: 38.2% white, 32.8% African American, 21.2% Hispanic, and 4.9% other race/ethnicities.

Co-infection of P&S syphilis and HIV

Among MSM presenting at STD Surveillance Network (SSuN) STD clinics around the country with P&S syphilis infection in 2013, the proportion co-infected with HIV ranged from 15.8% in Los Angeles to 47.4% in Philadelphia[1]. HIV status information obtained from SSuN sites is based on laboratory report, provider diagnosis, or patient self-report. HIV and syphilis co-infection is a significant public health concern, because HIV-infected individuals with infectious syphilis, particularly primary syphilis, are more likely to transmit HIV to sex partners than HIV-infected individuals without syphilis infection.

Congenital syphilis

After 14 years of consecutive decreases, the rate of congenital syphilis increased 28% between 2005 and 2008 (from 8.2 to 10.7 cases per 100,000 live births), followed by a 20% decrease through 2012 (8.4 cases)[1]. This decrease in congenital syphilis was preceded by the decreasing rates of P&S syphilis among women of reproductive age (15-44 years) since 2008. In 2013, however, 348 cases of congenital syphilis were reported in the U.S., resulting in a 3.6% rate increase to 8.7 cases per 100,000 live births.

By region, the South consistently has the highest rates of both P&S syphilis in women and congenital syphilis; the three states with the highest rates of congenital syphilis in 2013 were Louisiana (51.3 cases per 100,000 live births), Arkansas (31.1 cases per 100,000 live births) and Texas (19.4 cases per 100,000 live births)[1]. However, the West was the only region to experience an increase in the rate of P&S syphilis in 2013, primarily due to a 69% increase observed in California (from 6.5 to 11.0 cases per 100,000 live births)[1,22].

By maternal race/ethnicity, the 2013 rate of congenital syphilis was highest among non-Hispanic African Americans (29.0 cases per 100,000 live births), followed by American Indians/Alaska Natives (14.8), Hispanics (9.7), Asian/Pacific Islanders (3.4), and non-Hispanic whites (2.8)[1]. Only non-Hispanic African Americans experienced a decrease in the rate of congenital syphilis from 2012 to 2013 (8.5%); all other race/ethnicities experienced increases in the rate of P&S syphilis during that time period.

California Profile

California

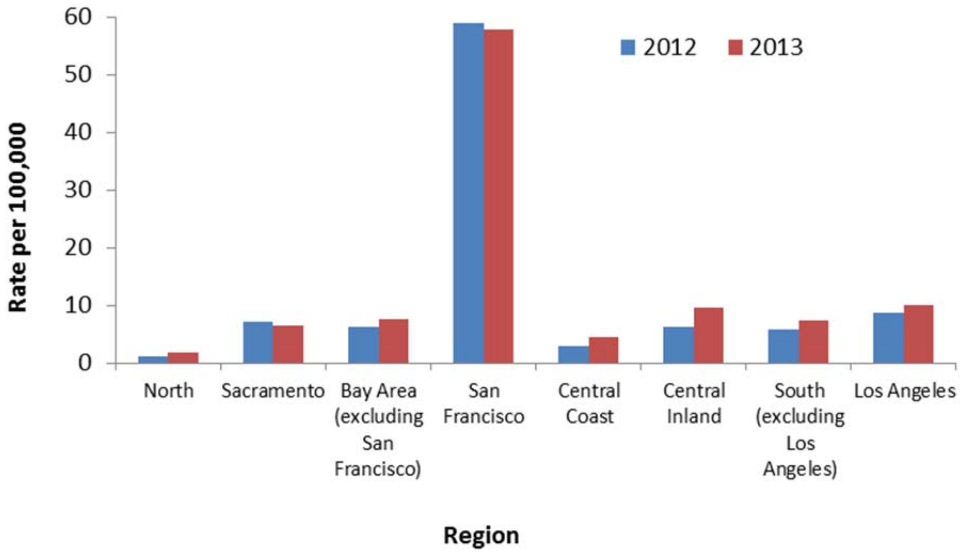
Recent trends in P&S syphilis in California largely parallel those seen elsewhere in the U.S., with increases in the 1980s associated with crack cocaine use among heterosexual men and women[25]. The rate of P&S syphilis subsequently decreased 94.0% between 1990 and 1999, reaching the lowest rate (0.9 cases per 100,000) since 1946[27]. The rate of P&S syphilis then increased annually between 2000 and 2008 before decreasing in 2009 to 5.5 cases per 100,000. The rate began increasing again the following year, reaching 9.3 cases per 100,000 by 2013, well above the national rate of 4.5 cases per 100,000.

Region & Local Health Jurisdiction

California STD Control Branch divides the state into eight regions: North, Sacramento, Bay Area (excludes San Francisco), San Francisco, Central Coast, Central Inland, South (excludes Los Angeles), and Los Angeles (See Appendix B for specific counties within each region). San Francisco and Los Angeles STD Control programs are considered separate regions from the Bay Area and the South, respectively, as both counties receive independent funding from CDC for STD control. Of the 3,540 cases of P&S syphilis in California reported in 2013, Los Angeles accounted for the highest proportion of cases (28.8%), followed by the South (23.8%), the Bay Area (14.4%), San Francisco (13.7%), Central Inland (11.8%), Sacramento (4.0%), Central Coast (2.8%) and the North (0.7%). San Francisco had the highest incidence of P&S syphilis (57.9 per 100,000). For the first time since the current outbreak of syphilis among MSM began in 2000, however, the Bay Area accounted for a higher proportion of P&S syphilis cases statewide than San Francisco.

San Francisco has consistently had the highest incidence of P&S syphilis in California (Figure 1). From 2012 to 2013, the rate of P&S syphilis increased 63% in the North (from 1.15 to 1.88 cases per 100,000), 52% in the Central Inland (6.35 to 9.66 cases per 100,000), 45% in the Central Coast (from 3.06 to 4.43), 25% in the South (from 5.89 to 7.38), 20% in the Bay Area (from 6.36 to 7.62 cases per 100,000), and 16% in Los Angeles (from 8.78 to 10.18). In contrast, the rate of P&S syphilis decreased 10% in Sacramento (from 7.19 to 6.5) and 2% in San Francisco (from 58.9 to 57.9). In 2013, nine local health jurisdictions (LHJs) accounted for 75% of the cases statewide: Los Angeles (n=1,021), San Francisco (n=484), San Diego (n=351), Orange (n=199), Santa Clara (n=146), Alameda (n=145), Riverside (n=130), Kern (n=119) and Sacramento (n=115).

Figure 1. Primary and secondary syphilis rates (per 100,000 population) by California region, 2012-2013

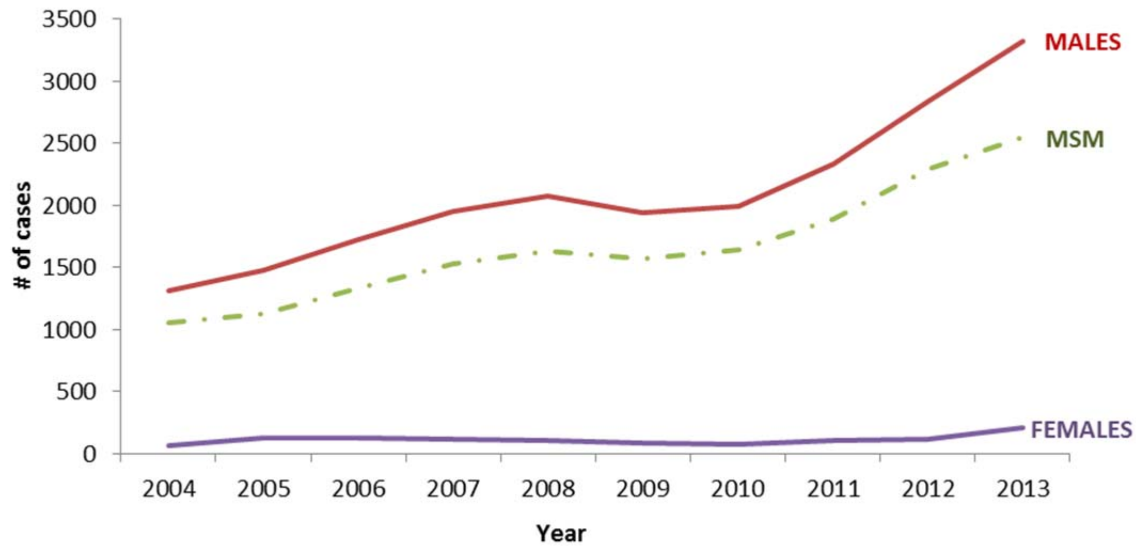


Gender & Sexual Orientation

The rate of P&S syphilis among men in California reached a low in 1998 (1.2 cases per 100,000), and then increased to 10.9 in 2008[27]. This rate then decreased to 10.0 in 2009 before increasing again in 2010. In 2013, the rate of P&S syphilis among men reached 17.6 cases per 100,000, a 41.9% increase from 2011 (12.4 cases per 100,000). The rate of P&S syphilis among women reached a low in 2002 (0.2 cases per 100,000), increased to 0.7 cases per 100,000 in 2007, decreased to 0.4 cases per 100,000 in 2010 and then increased annually to reach a rate of 1.1 cases per 100,000 in 2013.

Since 2000, the majority of P&S syphilis cases in California have been among MSM (Figure 2). In 2013, 87.4% of male P&S syphilis cases with available data on gender of sex partners were among MSM. Of these, 5.8% reported having both male and female partners, compared to 2.9% in 2008.

Figure 2. Primary and secondary syphilis case counts by gender, 2004-2013



Age

Similar to the national trends, California has seen a shift in the age group most affected by infectious syphilis. In 2013, the highest rates of P&S syphilis for men were among those ages 25-29 years (41.1 cases per 100,000), compared to in the early 2000s, when the highest rates for men were among those ages 30-39 years. The highest rate of P&S syphilis for women in 2013 was among those ages 20-24 years (3.7 cases per 100,000), consistent with prior years.

Race/ethnicity

In 2013, the highest rate of P&S syphilis among men in California was in non-Hispanic African Americans (39.3 cases per 100,000), followed by Native American/Alaskan Natives (17.0), Hispanics (16.2), non-Hispanic whites (16.0), and Asians/Other Pacific Islanders (8.6). Among women, the highest rate of P&S syphilis was among non-Hispanic African Americans (5.5 cases per 100,000), a 39.5% increase from the rate of 4.3 in 2006. Rates among non-Hispanic white and Asian/Other Pacific Islander women have remained low and stable, while rates have increased slightly among Hispanic women.

Age, race/ethnicity and sexual orientation

Among MSM, the largest proportion of P&S syphilis cases in California in 2013 were ages 20-29 years (30.9%), reflecting the ongoing shift towards younger cases observed at the statewide level. In addition, the proportion of MSM P&S syphilis cases less than 20 years of age increased to 6.7% in 2013 (Figure 3). All California regions have observed this shift, with the exception of San Francisco, where the largest proportion of MSM P&S syphilis cases in 2013 was among cases ages 40-49 years (37.9%). However, San Francisco also observed an increasing proportion of MSM P&S syphilis cases among those ages 20-29 years, from 14.1% in 2008 to 19.2% in 2013 (Figure 4).

Figure 3. Age distribution of MSM primary and secondary syphilis cases, California 2008-2013

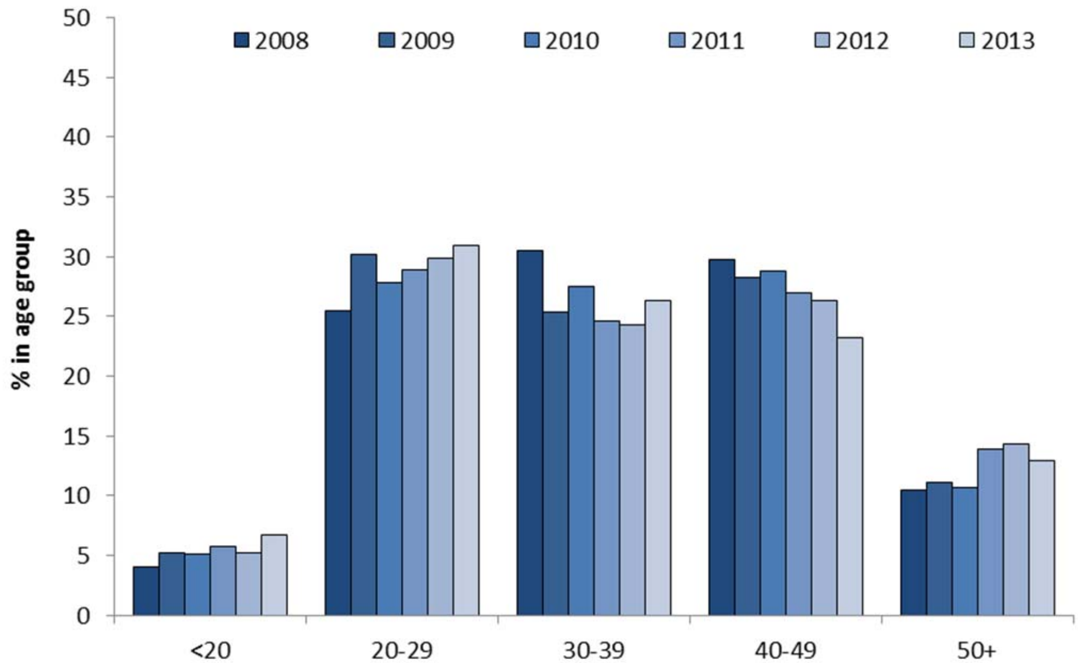
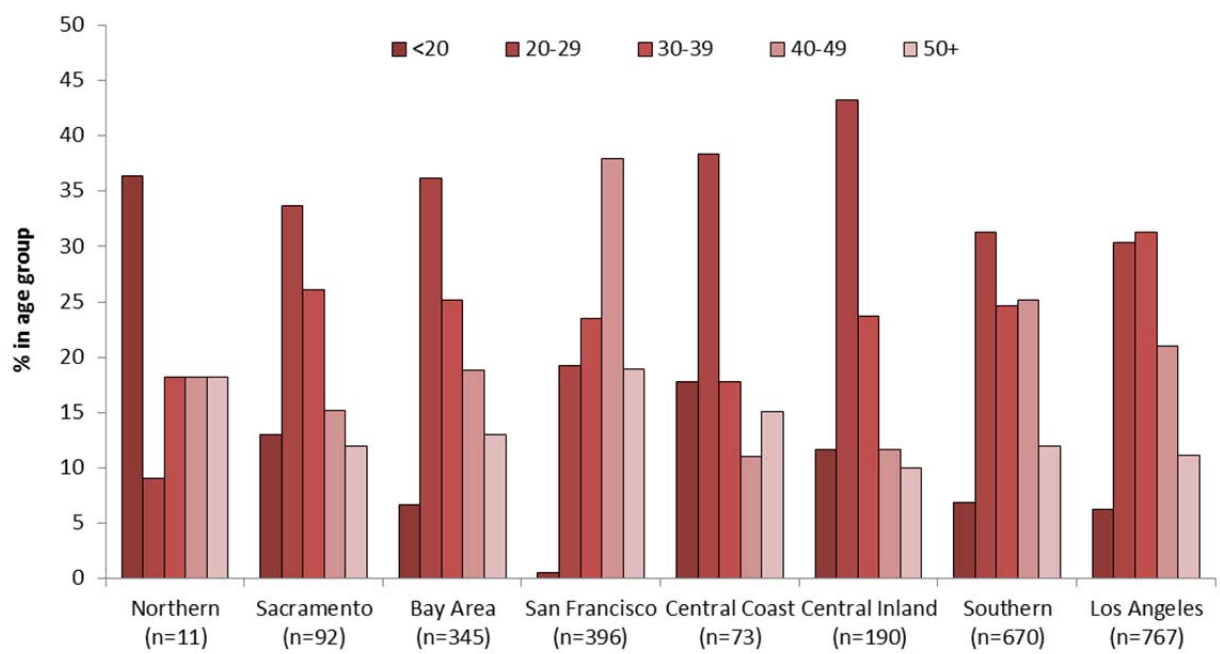
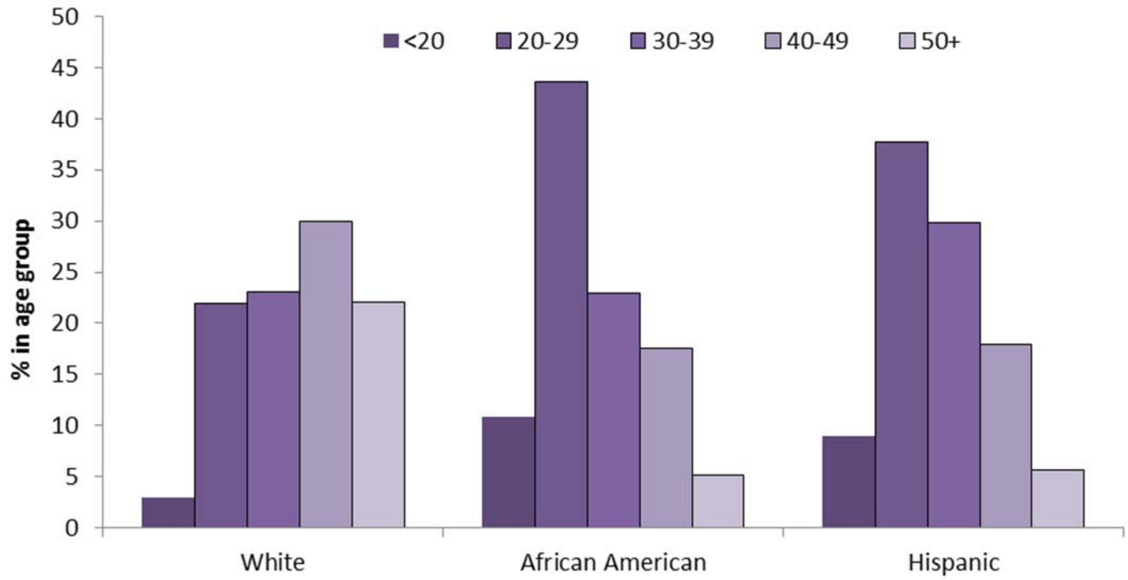


Figure 4. Age distribution of MSM primary and secondary syphilis cases, by region, California 2013



The shift to younger MSM is observed among African American and Hispanic MSM, whereas the largest proportion of white MSM cases are among those ages 40-49 years (Figure 5).

Figure 5. Age distribution of MSM primary and secondary syphilis cases, by race/ethnicity, California 2013



Co-infection with HIV

In 2013, 44.9% of cases of P&S syphilis among MSM for whom data were available reported being HIV-infected, compared to 52.3% in 2012. By comparison, reported HIV co-infection was lower among MSW and female P&S syphilis cases (8.9% and 3.2%, respectively).

Congenital syphilis

Congenital syphilis trends in California generally follow those of P&S syphilis among women of reproductive age (15-44 years), with a one to two year lag. This pattern can be observed in California during the 1990s, when declining P&S syphilis rates were followed by declines in congenital syphilis. The rate of congenital syphilis reached a historic low (6.0 cases per 100,000 live births) in 2012. However, with the 2013 increase in the rate of P&S syphilis among women came a parallel increase in the rate of congenital syphilis (11.1 cases per 100,000).

Chapter 3 – National Efforts to Eliminate Syphilis

In his landmark 1937 book *Shadow on the Land: Syphilis,* then U.S. Surgeon General Thomas Parran declared syphilis to be "the most urgent public health problem in this country today", and proposed a control program that involved five components: 1) case finding through serologic screening, 2) timely, effectively treatment of cases, 3) identification of persons exposed to infectious cases, 4) mandatory screening of persons with opportunity to transmit infection, and 5) public education concerning symptoms and consequences[8]. These strategies, coupled with the discovery of penicillin in the 1940s as an effective treatment and increased condom use in response to HIV/AIDS, are credited with bringing the incidence of syphilis to historic lows by 2000 (2.0 per 100,000), making public health officials optimistic about the feasibility of eliminating syphilis in the U.S.[28]. This optimism was further fueled by the geographic concentration of infectious syphilis cases and the increasingly inexpensive, accessible and effective tools for diagnosis and treatment.

In 1999, Surgeon General David Satcher announced the release of the *National Plan to Eliminate Syphilis in the United States*[29]*.* This plan was largely designed to address heterosexual populations in 28 U.S. counties (<1% of counties nationwide) located primarily in the South, which accounted for nearly 50% of infectious cases of syphilis in the U.S at that time. At the national level, elimination was defined as "controlling the manifestations of a disease so that it is no longer considered a public health problem" or as "a reduction to zero of a specified disease in a defined geographic area as a result of deliberate efforts", with the goal of fewer than 1000 P&S syphilis cases annually by 2005. Projections estimated that a fully funded elimination program could reduce morbidity nearly 80% by 2003, compared to a likely 40% increase that would otherwise occur. Just two years after the plan was announced, however, the incidence of syphilis began to slowly increase, reaching 2.9 per 100,000 by 2005[25,30]. During this time, the epidemiologic features of syphilis shifted from a problem primarily found in heterosexual men and women, to one among MSM, resulting in a need for CDC to reframe its elimination efforts[31]. In 2006, CDC released revised goals of the plan: 1) reducing the annual incidence of P&S syphilis to less than 2.2 per 100,000 population; 2) reducing the incidence of congenital syphilis to less than 3.9 per 100,000 live births; and 3) reducing the African American:White racial disparity in the incidence of syphilis to less than 3:1[32]. As of 2013, none of these goals had been met, with CDC's STD Surveillance 2013 Report showing the incidence of P&S syphilis being 5.5 per 100,000 population, congenital syphilis being 8.7 per 100,000 live births, and an African American:White P&S syphilis incidence rate ratio of 6.7:1[12].

Syphilis elimination strategies

The 1999 Syphilis Elimination Effort (SEE) goals expanded on Parran's original syphilis control campaign by promoting enhanced surveillance and strong community partnerships. In the 2006 SEE update, CDC proposed a "3-by-3 approach", highlighting the public health infrastructure and proposed levels of investment in program planning, evaluation, and research to meet the elimination goals (Table 3).

The first SEE goal is that "public health services will achieve excellence in the diagnosis and management of syphilis, partner services, and reporting of syphilis and its adverse outcomes, especially for those at greatest risk of health disparities"[32]. This objective focuses on enhancement of surveillance and outbreak response, and improving quality assurance related to clinical, laboratory, and partner services.

Table 3. The 3-by-3 approach, the National Plan to Eliminate Syphilis in the United States, 2006[32]

Syphilis Elimination Goal	Syphilis Elimination Strategies
1. Investment in, and enhancement of, public health services and interventions	1. Improve and enhance syphilis surveillance and outbreak response 2. Improve and assure the quality of clinical and partner services 3. Improve and assure the quality of laboratory services
2. Prioritization of evidence-based, culturally competent interventions.	1. Mobilization of affected communities 2. Tailoring intervention strategies for affected populations 3. Mobilization and creation of alliances with health care providers
3. Accountable services and interventions	1. Training and staff development 2. Evidence-based action planning, monitoring, and evaluation 3. Research and development

The second SEE goal is to "improve public health services through advocacy, acceptability, and appropriateness of the public health response to syphilis epidemics by prioritizing and delivering evidence-based and culturally competent interventions in partnership with external stakeholders in partnership with external stakeholders and affected communities". This objective largely focuses on increasing local capacity to respond to syphilis outbreaks by establishing collaboration between public health entities and key members of the community, strategic organizational partnerships, and tailored interventions to meet the needs of populations disproportionately affected by syphilis.

The third SEE goal is to "improve the public health services' response to syphilis epidemics by improving the effectiveness of interventions through enhanced accountability in the planning, implementation, and evaluation of interventions." To ensure the quality and relevancy of public health interventions, this objective focuses on evidence-based evaluation plans, program monitoring, and routine evaluation. In addition, CDC emphasizes the need for public health programs to maintain competent and trained staff dedicated to syphilis elimination activities, as well as research into the social determinants that, in part, drive syphilis epidemics in various populations.

Comprehensive STD Prevention Systems Program

To assist public health departments in implementing the Syphilis Elimination plan within a robust STD prevention and control program, CDC's Division of STD Prevention (DSTDP) developed the Comprehensive STD Prevention Systems (CSPS) Program Announcement and

Program Operation Guidelines[33]. The accompanying Performance Measures Companion Guidance provided further rationale for recommended measures, operational definitions for analysis, and potential for insight into the real-world program application and improvement[34]. The guidance outlined five categories for which programs were to report on a set of performance measures reflecting specific STD prevention and control activities:

- CSPS Medical and Laboratory Services
- CSPS Partner Services
- CSPS Surveillance and Data Management
- Infertility Prevention Project Clinical Services
- Syphilis Elimination Enhanced Surveillance

The performance measures outlined in the CSPS Partner Services category constituted the first time CDC had attempted to measure the impact of this intervention in a systematic way across the country. Project areas were asked to submit data on the timeliness of interviews and the treatment of P&S syphilis cases, the timeliness of treating sexual partners of P&S syphilis cases, and the number of non-sexual contacts of P&S syphilis cases that were tested and treated[34]. These measures were discontinued in January 2012, due to limited evidence that program improvement was being achieved, as well as feedback from STD programs that the measures were uninformative and ineffective for responding to ongoing increases in the incidence of P&S syphilis[35].

STD AAPPS 2015-2018

In January 2014, two years after the discontinuation of CSPS Performance Measures, CDC DSTDP launched a new initiative, Improving Sexually Transmitted Disease Programs through Assessment, Assurance, Policy Development and Prevention Strategies (STD AAPPS)[36]. This approach is reminiscent of the 1988 recommendations from the Institute of Medicine, which identified assessment, policy development and assurance as the core functions of all government public health agencies[37]. The STD AAPPS five-year Funding Opportunity Announcement (FOA) provides support through December 2018 to 50 states, seven cities and two territories for the specific task of decreasing the burden of and morbidity associated with STDs. The FOA highlighted four national STD program priorities: 1) STD prevention among adolescents and young adults; 2) STD prevention among MSM; 3) monitoring the emergence of antibiotic-resistant *Neisseria gonorrhoeae*; and 4) eliminating congenital syphilis.

While the CSPS Program created distinct components dealing with the Infertility Prevention Project and Syphilis Elimination Effort, STD AAPPS eliminated this program separation, enabling public health agencies to direct resources towards local priorities. As outlined in the IOM 1988 *Future of Public Health* report[37], STD AAPPS defines three core public health functions, each with its own priority STD prevention activities[36]:

- Assessment: Assessment involves determining current strengths and threats to a community's health through regular surveillance and review of health indicators, in conjunction with public health and healthcare partners. Priority activities include: a) conducting systematic surveillance; b) monitoring screening rates; c) assessing gaps in service; and d) monitoring emerging STD threats, including antibiotic resistant infection and congenital syphilis.

- Assurance: Assurance addresses current and emerging community health needs and threats through leadership, collaboration, and communication with partners. Priority activities include: a) promoting healthy behaviors and preventing STI acquisition; b) preventing transmission through rapid identification and treatment of infection; c) identification and treatment of sexual partners at risk for infection; and d) providing or improving structural conditions that facilitate healthy behavior and prompt treatment.

- Policy Development: Policy Development involves working with partners to promote and protect the health of the community through formal and informal policies, program guidelines, and environmental change. Priority activities include: a) monitoring the impact of policies; b) educating the public, providers, and stakeholders regarding effective policy approaches or anticipated impact on STD control efforts; and c) collaborating with external partners in primary care to improve access to and quality of STD prevention services.

In addition to the core functions of public health, the STD AAPPS framework also reflects an overall need for public health departments to respond to and leverage the evolving technological and collaborative landscape of healthcare in the U.S.:

- Improvement of STD surveillance, electronic laboratory reporting, electronic disease surveillance and integrated data systems, and meaningful use of data for public health
- Expansion of surveillance information to increase understanding of disease transmission, sexual and social networks, and access to care
- Foster collaboration between public health and primary care to identify new ways of expanding and maintaining quality STD prevention services
- Foster collaborations and integrated systems between STD and HIV programs to improve linkages to care and other healthcare services

As with the earlier CSPS program, programs receiving funding through STD AAPPS are required to report on nationally defined Program Outcome Measures (POM) within each domain and priority activity[38]. Those measures specific to syphilis control are focused on preventing onward transmission of infection via the timely identification and treatment of partners of HIV co-infected early syphilis cases and prevention of congenital syphilis through timely identification and treatment of partners of women with P&S syphilis infection.

The core functions of public health as outlined by CDC with respect to syphilis control in the U.S. have not changed significantly since the 1930s, although interest and priority populations have shifted over time in response to changing epidemiologic features of syphilis. In the 1990s, CDC's syphilis elimination efforts were focused on heterosexual populations and congenital syphilis prevention; strategies were adapted in the mid-2000s, following the emergence of syphilis among the MSM population. The World Health Organization also implemented a congenital syphilis global elimination plan in 2007, through political advocacy, improved access to and quality of maternal and child healthcare, screening and adequate treatment of pregnant women and their partners, and establishment of surveillance, monitoring and evaluation systems[39]. With the steady increases in the national incidence rate of P&S syphilis, and the more recent increase in the rate of congenital syphilis, the STD AAPPS framework comes at an opportune time to have a meaningful influence on syphilis control efforts around the country.

Chapter 4 – Syphilis Partner Notification: Literature Review

Since Parran outlined his comprehensive syphilis control strategy in 1937, syphilis partner notification has been considered an essential public health approach for identifying potentially infected individuals for testing and treatment. However, the increasing incidence of syphilis in California and the U.S. as a whole raises questions as to how much impact this intervention has on spread of the disease. In some sense, partner notification is a sacred cow among public health interventions, given the long history of its use in the U.S., the ongoing high level of resources involved in sustaining it, and the uncertainty regarding its effectiveness in reducing the incidence and prevalence of syphilis infection in the context of the current MSM syphilis epidemic.

Several reviews of partner notification as an STD control measure have been published, with the most recent review on its effectiveness being published in 2005. The objective of this chapter is to complement existing literature by providing an updated summary of recent studies through 2014, examining the effectiveness of syphilis partner services, with a particular focus on outcome measures and the benchmarks of success used.

Method

Search Strategy

A systematic search was performed in PubMed/MedLine, Scopus and Web of Science, based on relevant Medical Subject Headings (MeSH) terms and keywords, used in various combinations: syphilis; syphilis, congenital; contact tracing; partner notification; partner services. Specific search queries are included in Appendix A. Relevant citations in the articles identified were also manually reviewed for possible inclusion. The searches were conducted on October 16, 2014.

Eligibility Criteria

Studies eligible for inclusion met the following criteria: 1) the study's primary objective(s) included evaluation or discussion of the effectiveness of partner services for syphilis control, 2) the study was conducted in the U.S., 3) the study was published in English, and 4) the primary study population consisted of individuals diagnosed with primary, secondary, or early latent syphilis. Studies were limited to the U.S. and a primary language of English, as this context and population is the most relevant for interpretation and application in California. While there were no inclusion criteria specified for publication timeframe during the search, articles published from 2005 to 2014 were of primary interest, so as to complement review articles that searched similar literature from the early 1970s to 2005[31,40], and to increase relevancy to the current epidemiology of syphilis.

Study Selection

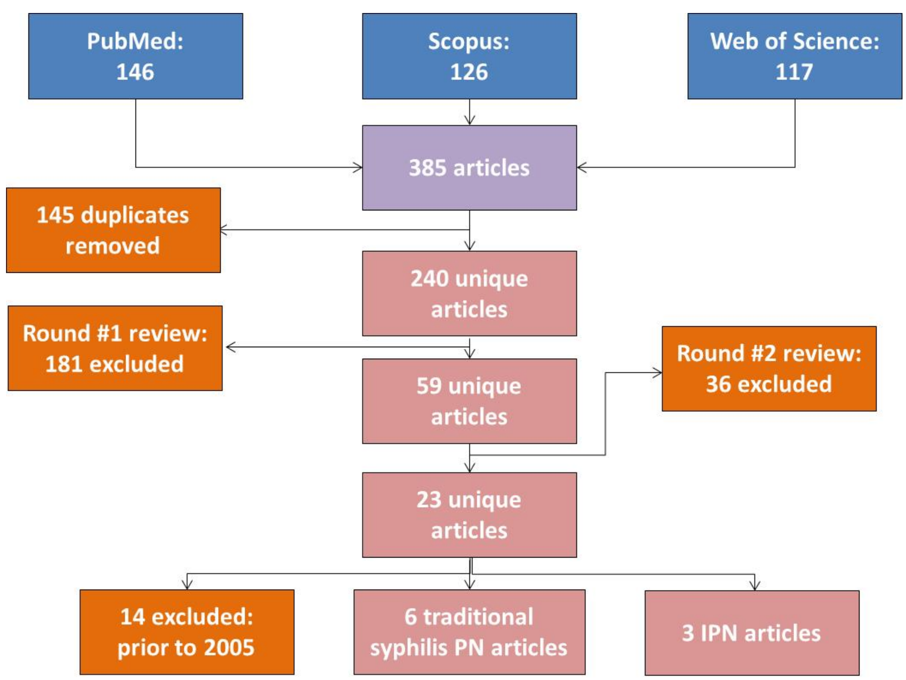
The first round of review looked broadly at the titles and abstracts of identified articles; those whose primary focus was evaluating outcomes of early syphilis partner notification were retained. The second round of review looked at the introduction and method sections of the remaining articles to further determine relevancy according to the above eligibility criteria. Close review of the full text was then conducted on the remaining articles, with a focus on definitions and indicators of partner notification outcomes, and explicit benchmarks used to evaluate effectiveness.

Results

Three hundred eighty-five articles were initially identified; of these, 145 articles were immediately removed as duplicates across electronic databases (Figure 6). Of the remaining 240 articles, 181 were excluded in the first round of review for being conducted outside the U.S., for not being syphilis-specific, or for not having a primary objective of measuring outcomes of early syphilis partner notification efforts. In the second round review of the remaining 59 articles, nine were excluded as editorials or commentaries and 27 were excluded for not having a primary objective of measuring early syphilis partner notification outcomes or for not reporting outcomes specific to early syphilis cases (e.g., one study reported only combined outcomes for HIV-infected individuals, HIV co-infected syphilis individuals, and HIV co-infection with multiple STIs). The remaining 23 articles were subjected to a full text review to make a final determination about inclusion.

Of these 23, 14 were published prior to 2005 and thereby excluded from data extraction. Of the nine articles remaining, six focused specifically on the effectiveness of traditional syphilis partner notification for early syphilis cases and three focused on outcomes from Internet Partner Notification (IPN) efforts. No additional unique references were found during the citation review, resulting in nine articles for data extraction.

Figure 6. Flowchart of article inclusion and exclusion



Traditional Partner Notification. Table 4 details several measures of yield consistently reported across studies: contact index (number of partners elicited for investigation per interviewed case); preventive index (number of partners presumptively treated for syphilis per interviewed case); and brought-to-treatment index (number of partners newly diagnosed and treated per interviewed case). Some studies also focused on the proportion of cases interviewed, the proportion of contacts located, and the proportion of early syphilis cases detected as a result of partner notification.

Table 4. Measures of yield found in studies identified for review

Measures of Yield	Numerator	Denominator
Contact index	# of partners initiated for notification	# of interviewed early syphilis cases
Brought-to-treatment index	# partners newly diagnosed with syphilis and treated	# of interviewed early syphilis cases
Preventive treatment index	# of partners receiving preventive treatment	# of interviewed early syphilis cases
Cluster index	# of suspects or associates initiated for notification[4]	# of interviewed early syphilis cases

Analysis of 2010 data from STD control programs in New York City, Philadelphia, Texas, and Virginia found that the proportion of interviewed cases who named partners varied from 32% to 74%, but that only 4-13% of interviewed syphilis cases had at least one partner brought to treatment[41]. Samoff et al. found similar brought-to-treatment indices among MSM and male heterosexual syphilis cases in Georgia (0.10 and 0.14, respectively); however, MSM had a higher overall proportion of contacts that were not notified[42]. A Los Angeles study that examined the impact of a community-embedded DIS on partner notification found a contact index range of 0.7 to 2.2, with 15% of partners elicited being brought-to-treatment[43]. An assessment of syphilis control efforts in King County, Washington reported low contact and brought-to-treat indices (1.73 and 0.14, respectively)[44]. A study of partner notification outcomes among heterosexual syphilis cases in Louisiana found a moderate contact index (1.9); however, 25% of early syphilis cases reported over the four-year study period were detected through partner notification[45].

Two systematic reviews looking at the effectiveness of traditional syphilis partner notification efforts have been published since 2005[31,40]. Brewer et al. found 18 reports from 1975-2003 that demonstrated a mean brought-to-treatment index of 0.22 (0.05-0.46) new

[4] "Suspects" refers to social contacts named an infected person (e.g., the index case, or infected partner or cluster). "Associates" refers to social contacts named by an uninfected partner or cluster.

infections per interview[40]. Hogben et al. focused specifically on partner notification among MSM in eight U.S. cities, and found a lower median brought-to-treatment index (0.09) and only slightly lower median contact index (0.94) compared to historical estimates among heterosexuals; however, the proportion contacted among all partners claimed was only 14%, indicating an even lower impact of syphilis partner notification on the syphilis epidemic among MSM.

Internet Partner Notification. Internet Partner Notification, or IPN, is the utilization of Internet-based locating information to contact sex partners and notify them of their potential exposure to an STD. Hunter et al. explored the use of Facebook as a complement to traditional syphilis partner notification among young African American MSM in Wisconsin, resulting in a contact index of 2.2, a cluster index of 0.6 (i.e., the number of suspects and associates initiated for investigation per interviewed case), and a treatment index of 1.6[46]. Evaluation of traditional partner notification efforts in Washington, DC's STD program in 2007-2008 found a contact index of 1.40 and a treatment index of 0.57; when partners contacted through IPN were included, the contact and treatment indices increased 75% (to 2.46) and 26% (to 0.71), respectively[46,47].

Discussion

Partner notification has been a mainstay of syphilis control efforts since Parran's national campaign to eliminate the disease in the 1930s. To date, no randomized controlled trials definitively demonstrating the impact of syphilis partner notification on either the incidence or prevalence of syphilis in the population have been conducted. Conducting such a trial today would be difficult, if not impossible, given that partner notification is currently considered a standard of STD care in the United States. Numerous studies of syphilis partner notification efforts have, instead, focused on measures of yield and contact-related indices, including numbers of partners elicited, partners presumptively treated, and partners brought to treatment[40]; in more recent years, publications have begun focusing on the use of Internet-based prevention activities and social networking media to conduct investigations and find new cases.

The current review found a contact index range of 0.29 to 1.73, a preventive treatment index range of 0.0 to 0.64, and a newly diagnosed/treated index range of 0.0 to 0.14. These same indices varied slightly, but not significantly, between MSM and male heterosexual populations. The difficulty of interpreting these measures is demonstrated by the larger numbers of contacts reported by MSM compared to heterosexuals, which equates to much lower proportions of sexual contacts being notified of exposure and brought-to-treat overall, despite the similar indices. These findings compare with those of other studies describing high proportions of anonymous online partners who cannot be contacted by health departments for exposure notification and testing[48-50]. As was demonstrated by CDC's CSPS Performance Measures, indices can also be difficult to compare across programs or to define as successful, given there are no standard or nationally recognized benchmarks by which programs can gauge effectiveness. Only one study in this review explicitly stated a locally defined benchmark for success[46]. While such measures are certainly helpful for understanding how well a program is implementing partner notification from a process perspective, they offer an incomplete picture of that program's impact with respect to prevention on a larger scale, particularly because morbidity continues to increase[35].

Over ten years have passed since use of an Internet chatroom to meet sex partners was first associated with an outbreak of syphilis among MSM in San Francisco[51,52]. Since that time, CDC has released recommendations on conducting partner notification via the Internet and the National Coalition of STD Directors has released guidance for STD programs on how to conduct Internet Partner Services[23]. As this review found, there are very few recent studies that measure the impact of IPN or Internet-based prevention activity on syphilis partner notification outcomes related to disease prevention. However, the two articles highlighted in this review contribute knowledge on innovative Internet-based prevention activities and use of social networking media to augment traditional partner notification efforts, as well as the overall acceptability and public uptake of methods such as e-cards for notifying partners of exposure[52-54]. Results from Washington, DC are also consistent with a prior analysis in San Francisco that found added value in contacts elicited, notified, tested and brought-to-treat for syphilis infection as a result of IPN activity[55]. At the time of this review, Hunter et al.'s study was the only one to look at Facebook as an additional tool for health departments to use in syphilis notification and case-finding. An evaluation in North Carolina also found that centralized IPN activity and notification of syphilis and/or HIV exposure via text messaging potentially enhanced both case-finding and re-engagement in HIV care[56]. Understanding how the Internet and newly emerging mobile networks have changed the ways in which partnerships form and dissolve is important for designing relevant intervention activities that protect privacy and confidentiality.

Since the time this analysis was done, a 2015 review of syphilis control efforts was published by Peterman and Furness, in which the authors note the number of newly identified infections resulting from syphilis partner notification efforts has been declining substantially in recent years[57]. These results are consistent with our findings of lower contact and brought-to-treatment indices compared to those previously reported. One 2006 study highlighted in Peterman's review looked at the value of several syphilis control strategies in preventing transmission and determined that partner notification identified relatively few individuals of "high prevention value", compared to the contribution of private physicians, jails and STD clinics[58]. Attempts to identify criteria for prioritizing syphilis case interviews that are available in initial case reports have shown potential for modest gains in efficiency in individual local programs, but too much outcome variability overall to easily predict on a generalizable scale when follow-up would maximize return on partner notification efforts[41,59,60].

From a cost-effectiveness perspective, Reynolds et al. found case-finding via partner notification to cost more per new case identified than selective screening, and only marginally more cost-effective when the likely impact of preventive treatment was taken into account[61]. A randomized controlled trial in 1997 looking at the relative effectiveness of different partner notification strategies reported greater success with partner elicitation for contract referrals compared to provider coaching; however, the partner indices and associated costs for preventive treatment and brought-to-treatment across strategies were not significantly different[60,62]. It is important to note that these studies were performed in the context of 1990s syphilis morbidity, and therefore are of questionable relevance to the current MSM syphilis epidemic. There is a need for STD programs to reconsider the cost-effectiveness of syphilis partner notification efforts in a modern context of DIS resources, local epidemiology, and national prevention priorities. Still, the argument that the value of partner notification goes beyond what cost-effectiveness studies or aggregate yield indicators can measure begs the question as to what added value can be immediately gleaned from data currently being collected during partner notification efforts to inform STD programs about opportunities to reprioritize control efforts appropriate to the local epidemiologic features of syphilis[63].

Determining the utility of syphilis surveillance and partner notification data for identifying at-risk individuals, treating infected partners, and reducing the incidence of syphilis is challenging, due to a number of factors:

- *Lack of clarity in defining and measuring effectiveness* – Despite being a standard of care in public health[23], there have been few studies attempting to measure effectiveness of this intervention, and a lack of consensus on the best measurements to use in the absence of such studies.
- *Fewer specialized staff to conduct disease intervention activity* – Syphilis control previously meant a county or area had multiple DIS assigned to follow-up with reported cases of syphilis within that county. This arrangement fostered DIS familiarity with the social environment and networks present in a community, and enabled them to leverage information gleaned from interviews for the purposes of investigation. As the number and mobility of DIS have decreased due to budget constraints, DIS have become less connected to the communities for which they are responsible. At the same time, individuals are more willing and better able to travel across county lines to engage in risky behaviors or meet partners. As a result, DIS must interview patients about environments and neighborhoods with which they are unfamiliar, thereby missing potential clues or insights into community nuances possibly affecting transmission of syphilis[64,65].
- *The impact of evolving technology on sexual networks & partner follow-up* – The recent emergence of social networking websites and mobile device applications using geospatial positioning systems to facilitate connections has created challenges for DIS concerning identification and notification of partners, by expanding the way in which people can choose partners, negotiate risk-taking behaviors such as HIV sero-sorting, and find/provide locating information on partners for the purposes of health department notification[31]. Such technological advancement has made it necessary for public health programs to innovate ways of recreating virtual relationships and notifying partners for whom they have only web-based locating information (e.g., email addresses; chatroom IDs; or website usernames/handles).
- *Anonymity of partners limits the impact of the intervention* – An increasingly high proportion of patients with syphilis report having had sex with anonymous partners, or partners for whom they don't have any identifying or locating information[2,31,49,50]. This behavior presents a barrier to contacting, testing, and treating members of a patient's sexual network, which in turn directly impacts disease prevention – if infected persons within a network remain undetected, disease can spread both within and between groups of people. In addition, patients can name all partners, name only some partners, report only anonymous partners, or refuse to provide any information on partners. This range of potential responses influences which sexual networks are detected through syphilis surveillance and partner notification activities.

Syphilis partner notification is considered a traditional, standard public health approach for identifying potentially infected individuals for testing and treatment. However, the increasing incidence of syphilis in California and the U.S. as a whole raises questions as to how much impact this intervention has on preventing the spread of syphilis, and in particular, to what degree the data currently acquired through syphilis partner services efforts reveal relevant and meaningful information about the underlying sexual networks that help drive syphilis morbidity trends.

Chapter 5 – Role of Sexual Networks in Syphilis Transmission

The concept of sexual networks is, at least in part, based on Parran's syphilis control approach, which promoted partner notification as a method of treatment and prevention[8]. Networks are interconnected structures of individual units ("nodes") linked by defined relationships ("ties"). The distinctive feature of network analysis is the explicit emphasis on those relationships and the resulting network structure, as well as individual node attributes. Network epidemiology, or the study of patterns and structures resulting from person-to-person relationships, has influenced communicable disease control efforts since long before a direct connection was made between public health and formal social network study[66]. In the early days of tuberculosis surveillance, efforts were made to ensure the medical management and if necessary, isolation of infected persons reported by the provider, as well as the infected person's family and close contacts[67]. One of the earliest explicit links between social network methods and sexual network epidemiology was made in Klovdahl's 1985 sociogram, which demonstrated the connectivity of the first known AIDS cases to a "patient 0"[68]. This analysis offered a relational framework more befitting the natural dynamics of HIV transmission than the traditional approach of linking only individual behavior to an individual health outcome. Since 1985, theoretical and empirical STI/HIV research has attempted to understand how social processes influence individual partnership choices, and how these partnership dynamics aggregate to form a population-level network structure with implications for the spread of infection and resulting disease[69,70].

Partnership dynamics

"Partnership dynamics" refers to the nature of the relationships that form between individuals within a network. For example, the criteria people use to choose partners (e.g., gender, preferences for sexual behavior, proximity, HIV status), the locations where people meet partners and/or have sex, the rate of partner change, the duration of partnerships, and the frequency of exposure within relationships are all examples of partnership dynamics[71]. Klovdahl (1985) demonstrated that, not surprisingly, partner selection is not random, contrary to early mathematical assumptions of choice[68]. External factors, such as social mores, cultural norms, political climate, employment opportunities and incarceration rates influence partner availability and selection in a given community. These partnerships come together in network configurations that can then be analyzed for patterns or structure related to endemic or epidemic disease transmission. Selective mixing and partnership timing are two specific behaviors often identified as affecting the speed and likelihood of STI/HIV propagation[69].

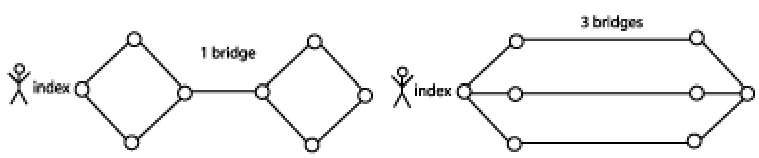
Selective mixing describes partnerships within and between population subgroups, based on attributes such as age, sex, race/ethnicity, sexual orientation, and sexual activity[72,73]. Assortative mixing (homophily, or "like-with-like") lends itself to multiple disconnected epidemics, while disassortative mixing results in slower, but more widespread epidemics. Partnership timing describes the duration and sequence of relationship formation, particularly the degree of overlap between any two partnerships. Duration of infectivity affects the likelihood of transmission, while sequencing or overlap of partnerships, as well as frequency of sexual intercourse, affects network transmission structure. Serial monogamy refers to when each partnership ends before the next one begins; in concurrent relationships, two or more partnerships are active at the same time. This type of partnering not only increases network connectivity, but also removes the protective nature of sequence that serial monogamy provides. For example, if persons A and B form a partnership, and shortly thereafter persons A and C form a partnership that overlaps with the former, then person B is no longer protected from any infections introduced into the network by person C[73].

Structural characteristics

Influenced by underlying partnership dynamics, network structure has been found to both facilitate and hinder STI transmission, depending on a variety of factors, including the etiological agent, the host-pathogen interaction[68,74], individual behaviors, and social norms.

While individual-level data may show low risk of transmission between infected and susceptible individuals, the structures resulting from partnership choices have implications for transmission. Figure 7 depicts two networks of the same size, but with differing structures that result from partnership selection patterns. These structural differences in turn have a meaningful impact on risk of infection for the network overall and the interventions that would halt spread of infection.

Figure 7. Role of sexual network structure in risk configuration



Source: Center for AIDS Prevention Studies at the University of California, San Francisco (2003)

For example, a Colorado Springs study of sex workers, injection drug users, and their close personal contacts showed a low risk of HIV transmission based on individual-level risk behavior data; however, a network analysis of this same population found a high degree of connectivity that placed everyone within a few steps of HIV infection[75]. Thus, a small change in individual behavior could have greater impact on spread of infection through the network structure than an analysis of just individual-level data might reveal.

Network structures can also be indicative of different phases of an epidemic, with a lack of connectivity between infected and susceptible persons resulting in stable or declining prevalence of infection[76], versus the more rapid STI/HIV transmission or intense outbreaks observed in short-term or concurrent partnerships that form cyclical or closed loops[77-81].

Bridging is another structural feature of sexual networks that affects transmission and encourages consideration of heterogeneous groupings of people as they interact in the real-world, not just in the pre-defined silos of public health priority (e.g., adolescents; MSM; incarcerated; drug-users; HIV infected)[74]. Spatial bridging can occur when infected persons have partners in different neighborhoods, cities, or states, resulting in geographical spread[78]. The importance of geographic space when thinking about STI transmission and formation of sexual networks has been recognized by CDC, which recommends that DIS ask about where people meet sex partners and where the exposure took place as part of routine case investigation and partner follow-up[82]. Temporal bridging occurs in concurrent partnerships, when exposure periods of a given partnership overlap with another[83,84]. Related to partnership dynamics, bridging also occurs when there is cross-over between groups based on behavioral or risk characteristics – examples include bi-sexual men and their female partners[68], commercial sex workers and patrons, and HIV discordant couples. Recent literature has explored the utility of conceptualizing “place” in network formation, and how nodes can represent physical locations that facilitate the connection of otherwise heterogeneous risk groups.

While DIS routinely, albeit informally, employ the concepts of networks in their interviews and the groundwork linkage of individuals across case investigations, this relational approach to describing syphilis epidemiologically is rarely utilized in a formal way at the state level, outside of investigations of recognized STI outbreaks within a specific geographic area. Routine surveillance approaches use absolute numbers of cases, prevalences and incidence rates to describe morbidity and mortality. While moderately high incidence rates in densely populated urban areas likely correlate with large numbers of cases, surveillance data may not accurately differentiate between emerging outbreaks and random fluctuations in cases in smaller, less populous communities[79,85].

Syphilis is a clinically complex disease with a long and fascinating history in the United States. While the burden of syphilis in the general population is not as significant as that caused by other STDs with respect to either prevalence or incidence, the devastating nature of the illness and the readily available and inexpensive treatment for infected persons have made it a priority disease for public health intervention and prevention. Partner notification has been a standard public health approach to syphilis control around the country. However, partner notification has never been demonstrated to be as effective for reducing the incidence of syphilis at a population-level. In California, an epidemiological shift in syphilis from heterosexuals to MSM, diminishing resources to conduct investigations effectively, evolving networking technologies, and difficulty in defining meaningful measures of effectiveness are all challenges to the implementation and evaluation of syphilis partner notification. There has been little work done to assess what types of networks are detected through California’s routine syphilis surveillance and partner notification efforts. However, this type of analysis could reveal patterns of mixing or bridging between geographic regions or associations that may exist between patient characteristics and network detection. This information could then be used to target limited resources toward subpopulations or areas with a higher likelihood of preventing disease transmission. In addition, while local health departments are typically limited to accessing data that originate from their own counties or investigations, the California Department of Public Health is in a unique position to construct and view syphilis network connections across county borders. With the recent implementation of California Reportable Disease Information Exchange (CalREDIE), a web-based electronic disease reporting system that uses a patient-based, integrated surveillance approach to monitor communicable diseases statewide, understanding the strengths, and limitations of using these data to understand networks for disease prevention purposes is increasingly relevant[86].

Chapter 6 – Conceptual Framework

In response to the current epidemiologic features of infectious syphilis in California, the limited ability of current aggregate yield measures to help prioritize traditional partner notification, and the immediate relevancy of sexual networks to syphilis control, this dissertation will examine the degree to which network data collected through routine syphilis surveillance and partner notification efforts can be used to better understand patterns of transmission and influence partner notification strategies. This approach builds on an understanding of STI transmission between individuals and within networks, the goals of public health surveillance in STI control, and the ethical responsibilities and boundaries of public health intervention.

Transmission dynamics of STI pathogens

The basic reproductive rate, R_0, is the number of secondary cases generated from a single infected case, when introduced into a fully susceptible population[87]. In the context of STI transmission, this rate – also known as the Anderson-May equation - is calculated as follows:

$$R_0 = \beta * C * D$$

where β is the probability of transmission per partner, C is the turnover of sex partners (number of different sex partners per unit time), and D is the duration of infectiousness. The probability of transmission between a susceptible and infected person is affected by a number of factors, including underlying community-level prevalence of infection, infectivity or probability of transmission per sex act, biology of the pathogen, duration of infectiousness, number and frequency of exposures, treatment, preventive practices (i.e., condom use), symptoms, and presence of co-morbidity.

This reproductive rate is critical to understanding emerging epidemics, as it measures the transmission potential of a disease. If R_0 is greater than 1, the number of infections will increase within a susceptible population; if R_0 is less than 1, the number of secondary infections is not enough to sustain ongoing transmission in the population. The value of all components combined at which R_0 exceeds 1 is referred to as the "epidemic threshold". The ability of any syphilis control strategy to reduce incidence rates within a population is dependent on bringing R_0 down below 1.0.

STI transmission within sexual networks

The Anderson-May equation highlights that STI transmission occurs as a result of sexual contact between infected and susceptible persons. Evidence suggests that these partnerships do not form randomly, as previously assumed. In addition, the risk of transmission or acquisition within these partnerships is not solely based on an individual's risk-taking behaviors, but also – and perhaps more so - on the behaviors of the partner.

Aral, Padian, and Holmes (2005)[71] proposed a multi-level framework - individual, partnership, network, and population – to help describe STI transmission dynamics beyond individual-level behaviors. The authors conceptually broke down these four levels to examine their interactions with each other and their influence on transmission dynamics and the observed spread of infection.

At the individual level, demographic and behavioral characteristics are associated with varying levels of risk for infection or membership in higher or lower risk networks. Aggregation of these individual attributes and their associations with individual outcomes are commonly the focus of epidemiological analyses[69]. Individual decision-making then influences the formation and dynamics of partnerships, which in turn have an impact on the structure and evolution of overall networks. There is an independent effect of network structure on STI transmission; for example, individuals classified as "low-risk" based on individual behavior may be "high-risk" when accounting for partner behavior or position within a larger network. Multiple networks are then possible, depending on how one defines the population or subgroup of interest – for example, by behavior, geography, demographic characteristics, behavioral characteristics (e.g., condom use, drug use), HIV co-infection, or a combination of factors.

Contextual factors influence the prevalence and incidence of infection, as well as the effectiveness of intervention efforts. Social structure plays a role in the spread of communicable disease, as risk behaviors or conditions associated with infection tend to cluster at lower levels of the social ladder. Unstable political environments, such as those precipitated by war and civilian unrest, as well as restrictive or discriminatory legislation can limit the choices people make and the opportunity for individuals to protect their sexual health. Similarly, poor or failing economies can increase unemployment, resulting in reliance on sex work to earn a living. Urbanization and growing economies can also encourage migration from rural to urban areas, changing the demographic landscape in both locations. Being aware of how the individual, partnership, network and population levels influence each other is not only important for understanding the epidemiologic features of STI transmission potential, but also the likely impact of partner notification efforts on the incidence of syphilis.

Goals of Public Health Surveillance in STI Control

Referred to as the "cornerstone of public health practice"[88], surveillance is defined by the Centers for Disease Control and Prevention as the "ongoing systematic collection, analysis, and interpretation of health-related data essential to the planning, implementation, and evaluation of public health practice."[89] Surveillance lays the groundwork for timely prevention and control of communicable disease through rapid case reporting and characterizing disease trends, outbreaks, and affected populations. Surveillance also informs the design and implementation of public health prevention efforts and resource allocation. Surveillance data also provide the ability to monitor and evaluate the effectiveness of interventions in reducing disease transmission, as well as the utility of case definitions and screening criteria. Last, high quality surveillance data allow for the formulation of research hypotheses regarding the spread of infection, the risk factors associated with an increased likelihood of disease, and the effectiveness of various intervention approaches.

Figure 8. Public health surveillance cycle, Centers for Disease Control and Prevention

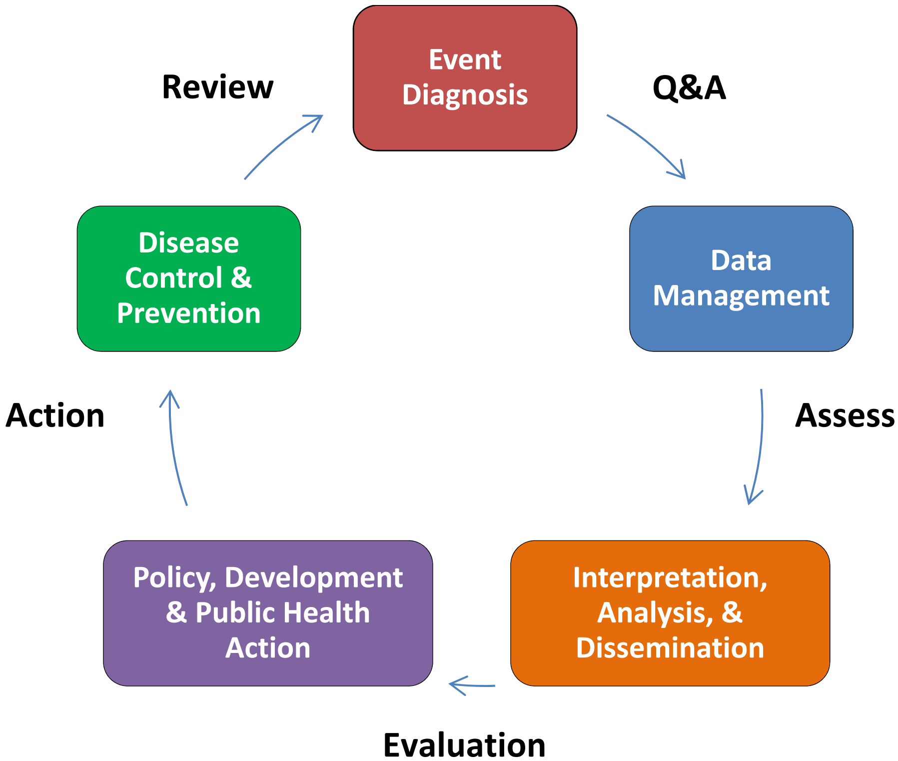


Figure 8 presents the public health surveillance cycle used by CDC to inform STI programs on the core functions, goals, and context for surveillance activities (CDC STI Program Management Training Course, 2012). Cases or "events" are diagnosed and subsequently reported to local health departments, which then gather, manage, and interpret data that can then be used or disseminated for the purposes of public health action. As new disease control or prevention efforts are rolled out, evaluation of both the activity's process and outcomes is needed to ensure that the system is achieving its goals. CDC defines the goals of STI surveillance as follows:

- To understand the distribution and spread of sexually transmitted infections
- To identify outbreaks and clusters of cases to prioritize field investigations
- To inform health care policy and public health response, in support of intervention and disease control planning efforts
- To evaluate disease control efforts and direct resources to the most cost effective interventions
- To identify emergent issues affecting STI diagnosis and treatment

Key considerations for surveillance of any disease include the public health importance of the condition; the human and financial resources necessary to carry out the activity; the local context (i.e., who will be affected by the activity); the specific rationale for collecting the information; and the specific public health actions that the activity will inform.

Public health ethics and syphilis control

"It is when our assumptions seem most intuitively obvious that we are at greatest risk of neglecting to determine to what extent they are supported by real evidence." – N.E. Kass (2001)

While medical ethics has traditionally been focused on the individual patient-physician relationship, the focus of public health efforts is to achieve and maintain overall population health, sometimes to the detriment of the individual.[90-93] STD surveillance is often justified as a means of accomplishing this goal through the monitoring of morbidity and mortality trends related to specified priority illnesses. Furthermore, partner notification is thought to help preserve both individual and population health. By identifying potentially exposed persons, there is the opportunity to notify them of their exposure, to test them for infection, to ensure appropriate treatment, and to pass on knowledge related to reducing the risk of infection, thereby preventing the ongoing spread of infection within a community. To this end, partner notification has been utilized by public health professionals as a standard approach to syphilis control in the United States. While not challenged as a control measure for syphilis or other communicable diseases like tuberculosis or measles, the ethics of partner notification in the case of HIV/AIDS been highly scrutinized with respect to protection of the general population's health vs. individual autonomy, respect for individual privacy rights, and the need for well-defined goals and measures to demonstrate effectiveness.

Balance of protecting the health of general population vs. individual autonomy

Partner notification is triggered by case reporting that is part of surveillance: providers are mandated by law to report the names of infected individuals to the public health department, with detailed locating, demographic, and clinical information. The compulsory nature of surveillance makes it so that infected persons have no say as to whether they will be reported or not, which can be regarded as an infringement on privacy. Once identified by the health department, infected individuals are contacted and interviewed by disease intervention specialists, who are trained to elicit the names of sexual and needle-sharing partners, along with other sensitive information (e.g., sexual practices, recreational drug use, HIV infection status). Persons always have the right to refuse an interview or to withhold information, which helps to mitigate the ethical concerns of collecting these data. However, the partners who are identified in these interviews and subsequently contacted by the health department have no say as to whether their names are disclosed to a government agency.

Respect for individual privacy rights and confidentiality

An additional challenge of partner notification is that partner names and available identifying information are maintained by the public health department, regardless of whether individuals are ultimately located or deemed infectious. This fact is particularly relevant to sexual network analysis, as understanding the overall dynamics of infection transmission in a population requires characterizing all potentially exposed individuals and even social contacts of infected persons, regardless of whether they themselves acquire infection. Public health departments have rigorous data security and confidentiality regulations and procedures in place to protect against breaches of confidentiality. Even if these processes are secure, however, there remains a need to provide a clear justification for why public health departments should collect and store personal, identifying information on non-infected persons (i.e., individuals with no legally reportable condition).

Well-defined goals and measures to demonstrate effectiveness

A component of any ethical framework related to the implementation of an intervention is to provide well-defined goals and measures to assess the effectiveness or progress towards reaching those goals. In the 2008 Recommendations for Partner Services, CDC suggested partner notification played a role in the reduction in the prevalence of syphilis in the 1990s and spurred the national efforts in support of syphilis elimination[23]. CDC also cited a 1997 randomized controlled trial comparing the costs of three different approaches to partner notification, and stated that the findings on cost per partner treated were on a par with the costs of more recent, alternative syphilis elimination strategies[60]. However, in the 2010 STD Treatment Guidelines, CDC stated that there were limited data to indicate whether partner notification effectively decreases exposure to STDs or reduces incidence of infection in a community[16].

Given the limitations of current partner indices and the relevance of network structure and dynamics in transmission, this dissertation examines the degree to which visualization and analysis of sexual networks detected through STD surveillance and partner notification efforts can be incorporated into routine evaluation and prioritization of syphilis control efforts.

Chapter 7 – Sexual Network Analysis of San Francisco Bay Area Syphilis Cases, 2008-2014

This chapter describes the use of a probabilistic matching algorithm and network software to visualize sexual networks detected through routine syphilis surveillance and partner notification processes in the San Francisco Bay Area between 2008 and 2014. Knowing whether these data reveal meaningful information about the structure and characteristics of those underlying sexual networks that contribute to syphilis morbidity trends over time in varying populations could be helpful for refining California's surveillance system and prioritizing STD control efforts.

Methods

Data Sources

California is divided into 51 independent local health jurisdictions, each of which has autonomy over its STD control programs. San Francisco County and Los Angeles County (excluding Long Beach and Pasadena) maintain their own STD surveillance systems, distinct from each other and from that used by the California Department of Public Health. The remaining local health jurisdictions, including Long Beach and Pasadena, are collectively referred to as the California Project Area (CPA). For this analysis, data came from the CPA and San Francisco STD surveillance systems, but not Los Angeles County.

California Project Area. Prior to late 2012, a network of state-based computers strategically located in designated regional offices across California was used to process syphilis reactors and report new syphilis cases from local health departments to state headquarters. State staff stationed in each region – the Northern Region, Bay Area Region, Central Region, and Southern Region - were responsible for handling incoming syphilis reports from a handful of surrounding local health jurisdictions. A standard DOS-based program was loaded onto the computers, which was used for case-based syphilis surveillance through entry of incoming laboratory reports of positive syphilis serologic test results (i.e., "reactors"), new syphilis case information, early syphilis case interview data from the California Syphilis Interview Record, and partner investigation outcomes from the STD Field Record.

Starting in late November 2012, CPA local health jurisdictions transitioned syphilis reporting via the regional office structure to reporting all syphilis morbidity via CalREDIE, or the California Reportable Disease Information Exchange, a web-based disease reporting and surveillance system utilized by six branches within the Division of Communicable Disease Control at the California Department of Public Health[94]. In contrast to the prior case-based regional surveillance system, CalREDIE is a person-based disease registry, which assigns multiple instances of disease, lab or provider reports, and investigations to a single, uniquely identifiable individual over time. Both the California Syphilis Interview Record and STD Field Record were built into CalREDIE, for ongoing entry of enhanced case interviews and tracking of partner investigation outcomes.

In April 2013, the final data transmission from the regional computer system was sent to state headquarters to close out 2012, and the system was considered officially retired. These static data, along with the computers, are now referred to collectively as the "legacy" data and system, respectively.

San Francisco. San Francisco Department of Public Health STD Control Branch uses a custom patient-based registry, ISCHTR, which contains surveillance, screening, partner notification, and STD clinic medical record data. Once a week, San Francisco transmits STD surveillance data to the California Department of Public Health, STD Control Branch for inclusion in statewide reporting of STD morbidity to CDC via National Electronic Telecommunications System for Surveillance (NETSS). San Francisco also sends select case management and risk data obtained through enhanced syphilis case interviews. San Francisco does not routinely send identifying information from partner investigations; however, for the purposes of this analysis, San Francisco agreed to send a one-time file with names and demographic variables of partners initiated for notification of potential syphilis exposure during the study timeframe.

Study Population

Index cases

Index cases were defined as primary, secondary or early latent syphilis cases with a diagnosis date from January 1, 2008 to December 31, 2014, and residing in the San Francisco Bay Area Region, which consisted of nine CPA counties (Alameda, Berkeley, Contra Costa, Marin, Napa, San Mateo, Santa Clara, Solano, Sonoma) and San Francisco (Appendix B).

Contacts

Contacts were defined as partners or clusters initiated for notification of potential syphilis exposure to the index cases identified using the criteria above.

Matching

A probabilistic matching algorithm developed by the California Department of Public Health, STD Control Branch was used to turn the CPA legacy case-based surveillance dataset into a person-based dataset, which could then be used to generate the network[95]. Probabilistic matching uses similarity scores to assign points to each record based on selected matching criteria (e.g., first name, last name, date of birth), sums the similarity scores for each potential match and then determines whether a match has occurred based on a threshold defined by the user.

Data cleaning and preparation for matching. To prepare the data for matching, case and partner records with missing first name or last name were excluded. Punctuation (e.g., apostrophes, dashes, extra spaces) and suffixes (e.g., Sr., Jr., III) were removed from names, and all character data were formatted in uppercase to improve matching. Case and partner datasets were each then subset to a few select variables: ID, first name, last name, date of birth, gender, race/ethnicity, county of residence, diagnosis, address and year of diagnosis. Variable names and formats in each dataset were reviewed and modified where necessary to ensure consistency between files. The cleaned and formatted case and partner datasets were then stacked, resulting in a single surveillance dataset of names and selected variables to be used for matching.

Matching process. Once cleaned and standardized, the surveillance dataset was matched to itself, in order to identify persons who had re-infection or multiple investigations during the analysis timeframe. The matching algorithm, which utilizes Proc SQL in Statistical Analysis Software (SAS), works by creating one block of paired records based on an exact first name match, a second block based on an exact last name match, and a third block based on an exact date of birth match. Within each block of paired records, first name, last name, date of birth, sex, and race/ethnicity were compared, with each comparison being assigned a similarity score based on a scoring rubric that defined the points awarded for similarities between specific criteria, and the points penalized for differences (Table 5). The scoring rubric was modified from a report by Olson et. al. (2011), which used an early adaptation of this matching algorithm to match California STD and HIV/AIDS population-based case registry data, and describe demographic and risk profiles of co-infected persons[95].

The three blocks were combined and de-duplicated, so even if a pair of records matched exactly on first name (block 1), last name (block 2) and date of birth (block 3), it would only appear once in the dataset. Visual review of the similarity score distribution, as well as a cursory manual review of the matched records, was done as a first step to setting a cut-off point above which each record would be considered a “true” match (Figure 9). Based on this initial review, records with scores below ten were determined to not be true matches and records above 20 were determined to be true matches. Potential matches with scores of 10-20 were then closely reviewed, and a “true match” threshold of 14.3 or higher was set to maximize the sensitivity and specificity of matches. True matches were then grouped together and assigned a unique “person” ID, so that a single individual with multiple infections or investigations over time would have a single identifier across each event[96]. Each record with its newly assigned person ID was then matched back to the initial surveillance dataset, and all remaining individuals without a person ID (i.e., those that were not matched) were assigned one via sequential numbering that started well above the highest person ID generated by the matching algorithm, so as to avoid duplicates.

Figure 9. Distributions of matching scores used to determine cutoff threshold. A) Full distribution of scores. B) Scores above 0. C) Scores above 10. D) Scored 10-20.

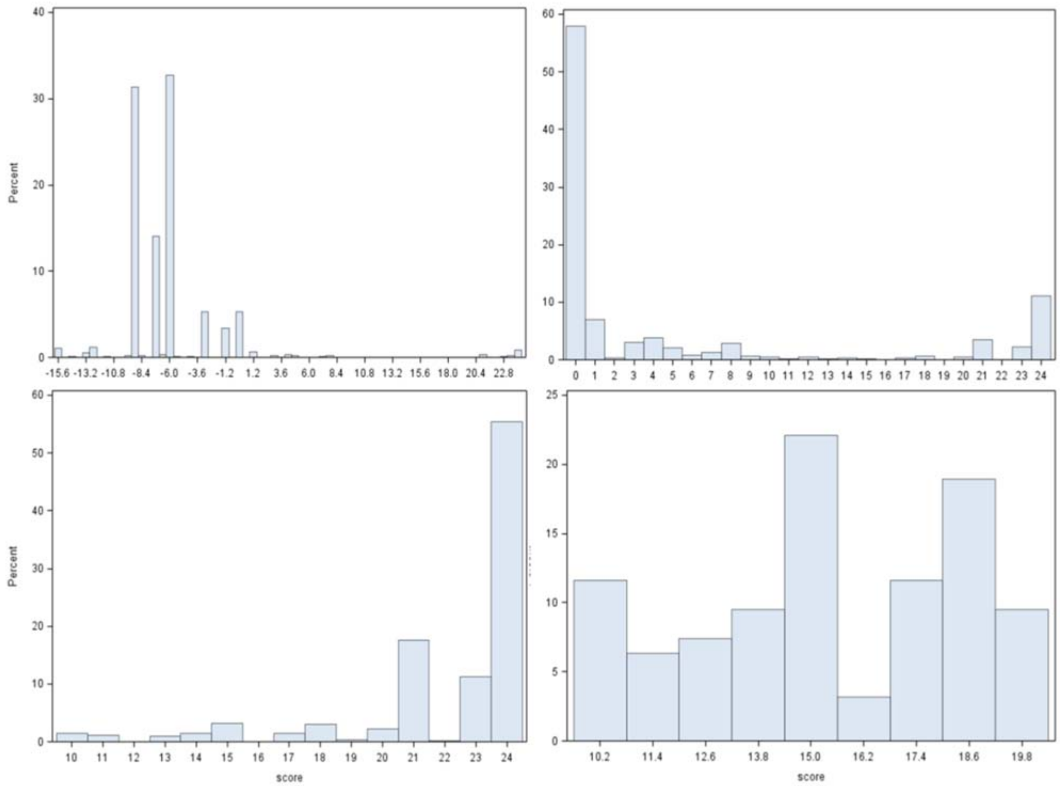


Table 5. Scoring rubric for matching algorithm

Data Element	Max pts award	Max pts penalty
Exact match on first name	4	-6
Exact match on last name	4	-6
Exact match on sex	1	-5.5
Exact match on birth date	14	-6
Exact match on race	1	-2
Exact match on LHD, *conditional* on exact matches for first name, last name, sex, and missing birth date on Field Record	5	0
Total Score (Max)	29	-25.5
Cut-off for True Match	14.3	

Preparing data for network visualization

Once unique person IDs were incorporated into the primary case-based surveillance dataset, two additional files were generated: nodes (persons) and edges (partnerships).

Nodes, or persons, contained a single record for each unique person in the dataset, along with select demographic (gender, age, race/ethnicity, syphilis diagnosis, year of diagnosis, county of residence) and behavioral/risk characteristics (HIV status, repeat syphilis infections) of interest. For infection status, persons were classified as infected if they were diagnosed with syphilis at least once during the study period; as uninfected if they were not diagnosed with syphilis but received preventive treatment; and as unknown infection status, if they were named as contacts, but were never located or tested during the study period. For HIV status, persons were classified as HIV positive if they self-reported as such anytime during the study period; as HIV negative, if no HIV infection was reported and there was a documented negative test result anytime during the study period; and as unknown HIV status, if they had no documented HIV status. Discrepancies in a person's gender or race/ethnicity over time were manually reviewed and coded, based on the most reliable source of information available. For example, data from a case interview trumped data from partner follow-up document, due to the likelihood of more complete and accurate information on case investigations.

For partners who were named outside the San Francisco Bay Area Region, the county variable was set to reflect the appropriate region instead of the individual county. For example, partners who were named in San Diego or Riverside were both given the new county name of "Region: South". Additional categories were also created to reflect persons who resided in multiple counties during the study period. Persons who resided in multiple San Francisco Bay Area counties were assigned the new county category of 'Inter-Bay Area'. Persons who resided in other California counties outside the San Francisco Bay Area were assigned the new county category of "Bay-CA". Persons who resided in other U.S. states were assigned the new county category of "Bay-US". Persons who resided in a combination of these categories were assigned the new county category of "Bay-CA-US". No partners were named outside the U.S.

Edges, or partnerships, contained every pairing of case and named partner or cluster. Edge characteristics were coded to identify partnerships between persons who resided in different counties, and partnerships between persons with differing infection status.

Analysis

Epidemiologic measures. Descriptive analysis looked at absolute numbers of cases and frequencies of demographic and behavioral factors obtained during case interview. The CPA Bay Area (i.e., 9 California Project Area counties) and San Francisco were analyzed and reported separately, to take into account the latter's disproportionate contribution to overall morbidity in the region.

Partner notification outcomes. Table 6 outlines the various partner notification outcome measures included in this analysis. Frequently used partner notification outcome measures were calculated for the CPA Bay Area overall, and for Alameda, Contra Costa, San Mateo and Santa Clara counties individually, as these four counties account for 84% of early syphilis morbidity in the CPA Bay Area. For index cases, the measures included the proportion of interviewed cases with at least one partner initiated for follow-up. For partners, measures included the number of partners initiated for notification and the distribution of standard codes, or dispositions, used by DIS statewide to reflect various outcomes of partner investigation. Partner indices included contact index, brought-to-treatment index, and preventive treatment index, as well as the number of cases needed to interview (NNTI) in order to locate and treat one partner with new infection. Contact index was calculated by dividing the number of partners with investigations initiated by the number of interviewed cases. Brought-to-treatment index was calculated by dividing the number of partners who were newly diagnosed with syphilis and treated (disposition C) by the number of interviewed cases. Preventive treatment index was calculated by dividing the number of partners who received preventive treatment (disposition A) by the number of interviewed cases. NNTI was calculated by dividing the number of cases interviewed by the number of partners that were either newly diagnosed and treated, or received preventive treatment. Data were stratified by year, to adjust for the potential impact on data quality of switching syphilis surveillance systems from legacy to CalREDIE in 2013. Partner notification outcomes data from San Francisco were not available for analysis.

Table 6. Definitions of partner notification outcome measures

Index Cases	Numerator	Denominator
Proportion of interviewed cases with at least one partner initiated for notification	# of cases with at least one partner initiated for notification	# of interviewed early syphilis cases
Partner indices		
Contact index	# of partners initiated for notification	# of interviewed early syphilis cases
Brought-to-treatment index	# partners newly diagnosed with syphilis and treated	# of interviewed early syphilis cases
Preventive treatment index	# of partners receiving preventive treatment	# of interviewed early syphilis cases
Number needed to interview (NNTI)	# of interviewed early syphilis cases	# partners newly diagnosed with syphilis and treated

Node characteristics. Nodes were stratified by infection status and then characterized by gender, county, age, and race/ethnicity.

Network structure. Analysis of network structure included node degree distribution, distribution of component sizes, and the proportion of total nodes represented by each component grouping. Node degree distribution was defined as the number of connections a node has to others in the network. Components are defined as a group of nodes that are all connected to each other – examining the distribution of component sizes and the proportion of total nodes represented within each size group provides insight into overall connectivity of the network. Visual inspection of components within select counties and the overall San Francisco Bay Area Region was done to assess whether networks involved partnerships between persons from different counties (“bridging”), to help interpret partner services outcome measures, and to assess connectivity of HIV-positive persons within the network.

Visualization was aided by formatting colors, lines and node size according to different characteristics of interest. Colors were used to depict either county of residence or HIV status; line types (solid vs. dashed) were used to highlight partnerships between infected persons, and node size was used to emphasize persons with repeat infections during the study time frame.

Demographic, behavioral/risk, and partner notification outcomes analysis was conducted in SAS 9.3. Network statistics and visualization were conducted in Cytoscape 3.2.1. This study was approved by the Committee for the Protection of Human Subjects at the California Department of Public Health and the Committee for the Protection of Human Subjects at University of California, Berkeley.

Results

Demographic and Behavioral/Risk Characteristics

8,924 early syphilis cases were identified in the San Francisco Bay Area from 2008 to 2014, with San Francisco accounting for 59.8% of cases. The rate of early syphilis among men in the region more than doubled between 2008 and 2014, increasing from 22.1 cases per 100,000 to 47.3 cases per 100,000. Similarly, the rate of early syphilis among women more than doubled from 0.8 cases per 100,000 to 1.82 cases per 100,000.

Among CPA counties, Alameda (n=1,202), Santa Clara (n=894), Contra Costa (n=527) and San Mateo (n=361) accounted for 84% of cases (Table 7). Primary and secondary syphilis cases accounted for 68% of cases, with the overwhelming majority being among men, particularly MSM. While the proportion of men has remained consistent, fewer have had available gender of sex partner information in recent years. Cases ages 20 to 29 years accounted for the highest proportion of cases (30%); however, there has been a striking increase in the proportion of cases that are ages 45 years and older. By race/ethnicity, the highest proportion of cases was among Whites (34.1%), followed by Hispanics (28.8%), African Americans (19.5%), and Asians (7.2%).

Since 2008, the proportion of cases that receive an interview has decreased in the CPA counties, from 84.5% in 2008 to 65.1% in 2014 (Table 8). Among those interviewed, a consistently high proportion of cases reported having had anonymous sex partners, and an increasing proportion reported methamphetamine use of the Internet meet sex partners. Among those with available data on HIV status, the proportion of cases co-infected with HIV decreased from 51.2% in 2008 to 35.7% in 2014.

In San Francisco, the majority of cases in 2013 and 2014 were diagnosed with early latent syphilis, in contrast to prior years when P&S syphilis consistently accounted for 56-60% of cases in the county (Table 9). Nearly all reported cases were among men, particularly MSM. From 2008 to 2010, the highest proportion was among cases ages 35 to 44 years; more recently, there has been a shift to cases ages 45 years and older. There has also been an overall increase in the proportion of cases ages 20 to 29 years, from 13.5% (n=72) in 2008 to 17.4% (n=193) in 2014. The majority of cases has consistently been among Whites, although the proportion of Hispanic cases has increased, from 19.5% (n=104) in 2008 to 22% (n=246) in 2014.

A notably low proportion of early syphilis cases in San Francisco were interviewed in 2014 (38.9%) compared to the high in 2011 (84.4%) (Table 10). Among those interviewed, one-quarter reported methamphetamine use and nearly half reported using the Internet to meet sex partners. Among those with available data on HIV status, the proportion of cases co-infected with HIV remained high, despite a decrease from 81.4% in 2008 to 72.2% in 2014.

Table 7. Demographic characteristics of early syphilis cases, CPA Bay Area counties (excluding San Francisco), 2008-14

	Total		2008		2009		2010		2011		2012		2013		2014	
	n=3,586	%	n=296	%	n=315	%	n=402	%	n=505	%	n=615	%	n=726	%	n=727	%
CPA Bay Area (excludes San Francisco)	3586	100.0	296	100.0	315	100.0	402	100.0	505	100.0	615	100.0	726	100.0	727	100.0
ALAMEDA	1202	33.5	108	36.5	100	31.7	155	38.6	184	36.4	199	32.4	225	31.0	231	31.8
BERKELEY	102	2.8	16	5.4	11	3.5	17	4.2	20	4.0	13	2.1	17	2.3	8	1.1
CONTRA COSTA	527	14.7	42	14.2	48	15.2	46	11.4	85	16.8	89	14.5	105	14.5	112	15.4
MARIN	85	2.4	7	2.4	4	1.3	8	2.0	10	2.0	16	2.6	20	2.8	20	2.8
NAPA	40	1.1	3	1.0	6	1.9	3	0.7	5	1.0	6	1.0	8	1.1	9	1.2
SAN MATEO	361	10.1	34	11.5	26	8.3	34	8.5	45	8.9	65	10.6	80	11.0	77	10.6
SANTA CLARA	894	24.9	66	22.3	87	27.6	112	27.9	101	20.0	146	23.7	207	28.5	175	24.1
SOLANO	181	5.0	11	3.7	25	7.9	13	3.2	26	5.1	31	5.0	29	4.0	46	6.3
SONOMA	194	5.4	9	3.0	8	2.5	14	3.5	29	5.7	50	8.1	35	4.8	49	6.7
Syphilis stage																
Primary	880	24.5	68	23.0	80	25.4	94	23.4	125	24.8	165	26.8	182	25.1	166	22.8
Secondary	1560	43.5	117	39.5	146	46.3	183	45.5	232	45.9	254	41.3	327	45.0	301	41.4
Early latent	1146	32.0	111	37.5	89	28.3	125	31.1	148	29.3	196	31.9	217	29.9	260	35.8
Gender																
Female	280	7.8	26	8.8	25	7.9	31	7.7	42	8.3	34	5.5	58	8.0	64	8.8
Male	3302	92.1	270	91.2	290	92.1	371	92.3	463	91.7	578	94.0	668	92.0	662	91.1
Unknown	4	0.1	0	0.0	0	0.0	0	0.0	0	0.0	3	0.5	0	0.0	1	0.1
Age (years)																
< 15	3	0.1	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	1	0.1	1	0.1
15-19	141	3.9	11	3.7	22	7.0	23	5.7	20	4.0	14	2.3	33	4.5	18	2.5
20-24	515	14.4	36	12.2	47	14.9	52	12.9	73	14.5	78	12.7	130	17.9	99	13.6
25-29	578	16.1	42	14.2	43	13.7	70	17.4	73	14.5	86	14.0	136	18.7	128	17.6
30-34	499	13.9	46	15.5	46	14.6	60	14.9	72	14.3	97	15.8	78	10.7	100	13.8
35-39	412	11.5	30	10.1	37	11.7	38	9.5	61	12.1	75	12.2	75	10.3	96	13.2
40-44	438	12.2	45	15.2	46	14.6	64	15.9	61	12.1	70	11.4	73	10.1	79	10.9
45+	1000	27.9	86	29.1	74	23.5	95	23.6	144	28.5	195	31.7	200	27.5	206	28.3
Race/ethnicity																
White	1222	34.1	95	32.1	92	29.2	135	33.6	186	36.8	234	38.0	249	34.3	231	31.8
African American	701	19.5	73	24.7	80	25.4	103	25.6	128	25.3	97	15.8	118	16.3	102	14.0
Asian	258	7.2	23	7.8	25	7.9	23	5.7	28	5.5	36	5.9	65	9.0	58	8.0
Hispanic	1032	28.8	84	28.4	91	28.9	119	29.6	121	24.0	197	32.0	213	29.3	207	28.5
Other	126	3.5	9	3.0	14	4.4	8	2.0	22	4.4	26	4.2	22	3.0	25	3.4
Unknown	247	6.9	12	4.1	13	4.1	14	3.5	20	4.0	25	4.1	59	8.1	104	14.3
Sexual orientation																
MSM only	2242	62.5	185	62.5	176	55.9	261	64.9	314	62.2	410	67.0	449	61.8	447	61.6
Male bi-sexual	254	7.1	14	4.7	21	6.7	27	6.7	39	7.7	51	8.3	58	8.0	44	6.1
Male heterosexual	374	10.4	33	11.1	37	11.7	40	10.0	50	9.9	68	11.1	75	10.3	71	9.8
Females	280	7.8	26	8.8	25	7.9	31	7.7	42	8.3	34	5.6	58	8.0	64	8.8
Male unknown	432	12.0	38	12.8	56	17.8	43	10.7	60	11.9	49	8.0	86	11.8	100	13.8
Unknown	4	--	0	--	0	--	0	--	0	--	3	--	0	--	1	--

Table 8. Behavioral/risk characteristics of interviewed early syphilis cases, CPA Bay Area counties (excludes San Francisco), 2008-14

	Total		2008		2009		2010		2011		2012		2013		2014	
	n=3,586	%	n=296	%	n=315	%	n=402	%	n=505	%	n=615	%	n=726	%	n=727	%
CPA Bay Area (excludes San Francisco)	3586	100.0	296	100.0	315	100.0	402	100.0	505	100.0	615	100.0	726	100.0	727	100.0
Interviewed	2585	72.1	250	84.5	246	78.1	299	74.4	359	71.1	452	73.5	506	69.7	473	65.1
Anonymous partners in past 12 mo.	1228	47.5	123	49.2	110	44.7	136	45.5	168	46.8	234	51.8	248	49.0	209	44.2
HIV status																
Positive	938	44.2	103	51.2	100	51.5	121	50.0	136	44.9	180	45.9	170	39.5	128	35.7
Negative	1183	55.8	98	48.8	94	48.5	121	50.0	167	55.1	212	54.1	260	60.5	231	64.3
Unknown/refused	464	--	49	--	52	--	57	--	56	--	60	--	76	--	114	--
Methamphetamine use in 12 mo.	365	14.1	32	12.8	34	13.8	45	15.1	47	13.1	71	15.7	77	15.2	59	12.5
Internet use to meet sex partners	940	36.4	95	38.0	83	33.7	114	38.1	134	37.3	165	36.5	206	40.7	143	30.2

Table 9. Demographic characteristics of early syphilis cases, San Francisco, 2008-14

	Total		2008		2009		2010		2011		2012		2013		2014	
	n=5,338	%	n=532	%	n=518	%	n=643	%	n=668	%	n=861	%	n=1,006	%	n=1,110	%
San Francisco	5338	100.0	532	100.0	518	100.0	643	100.0	668	100.0	861	100.0	1006	100.0	1110	100.0
Syphilis stage																
Primary	1095	20.5	120	22.6	112	21.6	150	23.3	146	21.9	186	21.6	203	20.2	178	16.0
Secondary	1706	32.0	211	39.7	199	38.4	212	33.0	232	34.7	301	35.0	281	27.9	270	24.3
Early latent	2537	47.5	201	37.8	207	40.0	281	43.7	290	43.4	374	43.4	522	51.9	662	59.6
Gender																
Female	112	2.1	13	2.4	7	1.4	15	2.3	18	2.7	21	2.4	23	2.3	15	1.4
Male	5203	97.5	518	97.4	510	98.5	626	97.4	645	96.6	836	97.1	976	97.0	1092	98.4
Unknown	23	0.4	1	0.2	1	0.2	2	0.3	5	0.7	4	0.5	7	0.7	3	0.3
Age (years)																
< 15	1	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
15-19	24	0.4	3	0.6	0	0.0	4	0.6	2	0.3	5	0.6	5	0.5	5	0.5
20-24	296	5.5	23	4.3	37	7.1	32	5.0	31	4.6	58	6.7	53	5.3	62	5.6
25-29	581	10.9	49	9.2	49	9.5	63	9.8	71	10.6	91	10.6	127	12.6	131	11.8
30-34	689	12.9	66	12.4	66	12.7	72	11.2	79	11.8	115	13.4	136	13.5	155	14.0
35-39	750	14.1	101	19.0	94	18.1	100	15.6	82	12.3	106	12.3	117	11.6	150	13.5
40-44	1031	19.3	112	21.1	104	20.1	151	23.5	130	19.5	168	19.5	178	17.7	188	16.9
45+	1966	36.8	178	33.5	168	32.4	221	34.4	273	40.9	318	36.9	389	38.7	419	37.7
Race/ethnicity																
White	2965	55.5	317	59.6	291	56.2	381	59.3	375	56.1	482	56.0	547	54.4	572	51.5
African American	469	8.8	57	10.7	46	8.9	58	9.0	54	8.1	81	9.4	83	8.3	90	8.1
Asian	365	6.8	38	7.1	50	9.7	32	5.0	48	7.2	48	5.6	68	6.8	81	7.3
Hispanic	1156	21.7	104	19.5	104	20.1	140	21.8	153	22.9	189	22.0	220	21.9	246	22.2
Other	196	3.7	11	2.1	24	4.6	23	3.6	21	3.1	40	4.6	41	4.1	36	3.2
Unknown	187	3.5	5	0.9	3	0.6	9	1.4	17	2.5	21	2.4	47	4.7	85	7.7
Sexual orientation																
MSM only	3054	57.5	310	58.3	295	56.9	343	53.3	499	75.3	592	68.8	486	48.3	529	47.7
Male bi-sexual	94	1.8	10	1.9	7	1.4	8	1.2	18	2.7	24	2.8	16	1.6	11	1.0
Male heterosexual	99	1.9	10	1.9	7	1.4	3	0.5	18	2.7	24	2.8	25	2.5	12	1.1
Females	112	2.1	13	2.4	7	1.4	15	2.3	18	2.7	21	2.4	23	2.3	15	1.4
Male unknown	1956	36.8	188	35.3	201	38.8	272	42.3	110	16.6	196	22.8	449	44.6	540	48.6
Unknown	23		1		1		2		5		4		7		3	

Table 10. Behavioral/risk characteristics of interviewed early syphilis cases, San Francisco, 2008-14

	Total		2008		2009		2010		2011		2012		2013		2014	
	n=5,338	**%**	**n=532**	**%**	**n=518**	**%**	**n=643**	**%**	**n=668**	**%**	**n=861**	**%**	**n=1,006**	**%**	**n=1,110**	**%**
San Francisco	5338	100.0	532	100.0	518	100.0	643	100.0	668	100.0	861	100.0	1006	100.0	1110	100.0
Interviewed	3199	59.9	331	62.2	325	62.7	377	58.6	564	84.4	651	75.6	519	51.6	432	38.9
Anonymous partners in past 12 mo.[1]	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
HIV status																
Positive	1664	76.4	171	81.4	157	81.3	212	81.9	325	83.1	355	73.7	228	66.1	216	72.2
Negative	515	23.6	39	18.6	36	18.7	47	18.1	66	16.9	127	26.3	117	33.9	83	27.8
Unknown/refused	1020		121		132		118		173		169		174		133	
Methamphetamine use in 12 mo.	850	26.6	105	31.7	78	24.0	94	24.9	125	22.2	180	27.6	151	29.1	117	27.1
Internet use to meet sex partners	1516	47.4	163	49.2	150	46.2	194	51.5	283	50.2	308	47.3	219	42.2	199	46.1

[1]Anonymous sex partners data is not available for San Francisco.

Partner Services Outcomes

Among the 2,585 CPA Bay Area interviews conducted from 2008-2014, 39% (n=1,001) resulted in at least one partner being initiated for follow-up (Figure 10). By year, the proportion that named at least one partner for notification of potential syphilis exposure decreased from 60.4% in 2008 to 38.5% in 2012, and further declined to 20.1% in 2014 after the transition to CalREDIE (Table 12) in 2013. Of the partners initiated for follow-up, the proportion that was newly infected and brought to treatment overall was 7%, ranging from 3.5% to 9.0% by year. The proportion that received preventive treatment was 22% overall, ranging from 18.0% to 27.1%. In comparison, the proportion of partners who could not be located (dispositions G, H, S), who were located but not notified of exposure (disposition Q), who were located and notified, but refused medical exam (disposition J), and who were notified and have unconfirmed results and/or treatment (dispositions M, N) ranged annually from 39% to 47%.

The contact index decreased from 1.42 contacts in 2008 to 0.42 in 2014, resulting in 0.78 contacts initiated per interview overall (Table 12). The brought-to-treatment index and preventive treatment index had similar decreases from 2008 to 2014, resulting in 0.07 and 0.18 contacts being newly diagnosed and treated or receiving preventive treatment overall, respectively. Overall, the NNTI measure found 4.1 interviews were necessary to identify one previously undiagnosed case of syphilis or an opportunity to administer preventive treatment; however, the NNTI more than tripled from 2008 to 2014.

Figure 10. Partner notification outcomes, CPA Bay Area counties, 2008-2014

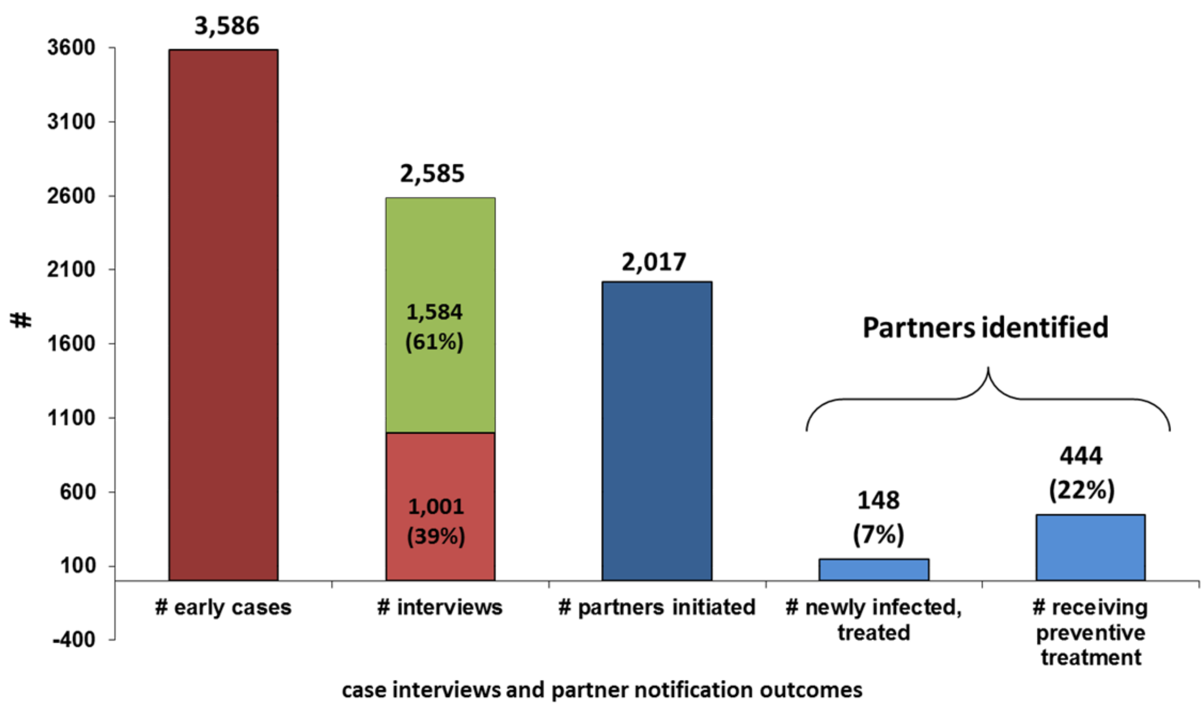


Table 11. Partner notification outcomes, early syphilis cases, CPA Bay Area counties, 2008-14

	2008-14		2008		2009		2010		2011		2012		2013		2014	
# early syphilis cases - CPA BAY AREA COUNTIES	3586		296		315		402		505		615		726		727	
# interviewed	2585	72.1	250	84.5	246	78.1	299	74.4	359	71.1	452	73.5	506	69.7	473	65.1
# cases with at least one partner initiated	1001	38.7	151	60.4	140	56.9	156	52.2	153	42.6	174	38.5	132	26.1	95	20.1
# contacts initiated	2017		355		316		245		348		322		232		199	
Investigation outcomes ("dispositions")																
A-preventively treated	457	22.7	64	18.0	64	20.3	65	26.5	83	23.9	59	18.3	63	27.2	46	23.1
B-not preventively treated	6	0.3	3	0.8	1	0.3	1	0.4	1	0.3	--	--		--	1	0.5
C-newly infected, brought to treat	180	8.9	28	7.9	19	6.0	22	9.0	18	5.2	39	12.1	15	6.5	7	3.5
D-infected, not treated	3	0.1	--	--	2	0.6	--	--	1	0.3	--	--		--	2	1.0
E-previously treated	360	17.8	58	16.3	52	16.5	59	24.1	56	16.1	54	16.8	27	11.6	13	6.5
F-not infected	217	10.8	44	12.4	33	10.4	18	7.3	45	12.9	28	8.7	21	9.1	11	5.5
G-insufficient information to investigate	68	3.4	8	2.3	10	3.2	10	4.1	19	5.5	8	2.5	5	2.2	2	1.0
H-unable to locate	411	20.4	77	21.7	76	24.1	34	13.9	54	15.5	68	21.1	34	14.7	49	24.6
K-Out of jurisdiction	14	0.7	1	0.3	1	0.3	1	0.4	3	0.9	1	0.3	6	2.6	9	4.5
L-Other	24	1.2	9	2.5	3	0.9	--	--	6	1.7	1	0.3	4	1.7	2	1.0
M-Notified of exposure, agrees to testing, results self-reported	155	7.7	--	--	21	6.6	18	7.3	24	6.9	33	10.2	26	11.2	31	15.6
N-Notified of exposure, agrees to testing, results unknown	18	0.9	--	--	7	2.2	3	1.2	2	0.6	2	0.6	2	0.9	7	3.5
Q-Initial contact made, no health information shared	22	1.1	--	--	--	--	3	1.2	--	--	7	2.2	5	2.2	1	0.5
S-Email bounce-back (for Internet partner notification)	24	1.2	--	--	2	0.6	1	0.4	1	0.3	10	3.1	--	--	1	0.5
Missing	23	1.1	--	--	--	--	--	--	3	0.9	--	--	20	8.6	11	5.5
Partner indices																
Contact index (# partners initiated per interviewed case)	0.78		1.42		1.28		0.82		0.97		0.71		0.46		0.42	
Brought-to-treat index (# partners newly infected, treated per interviewed case)	0.07		0.11		0.08		0.07		0.05		0.09		0.03		0.01	
Preventive treatment index (# partners preventively treated per interviewed case)	0.18		0.26		0.26		0.22		0.23		0.13		0.12		0.10	
NNTI (# interviews necessary to identify identify one new infection or preventive treatment opportunity)	4.1		2.7		3.0		3.4		3.6		4.6		6.5		8.9	

Alameda experienced a large decline in the proportion of early syphilis cases that received an interview, from 78.7% (n=85) in 2008 to 49.8% (n=231) in 2014 (Table 13). The proportion that named at least one partner for notification decreased from 46.3% in 2008 to 11.8% in 2012, and then an additional slight decrease to 11.3% in 2014. Alameda's contact index decreased from 1.48 contacts in 2008 to 0.60 in 2014, resulting in 0.78 contacts initiated per interview overall. Of the partners initiated for follow-up, the proportion newly infected and brought to treatment overall was 6.7%, ranging from 4.2% to 11.1% by year. The proportion that received preventive treatment was 19% overall, ranging from 4.3% to 25.9%. Alameda's brought-to-treatment index and preventive treatment index had similar decreases, resulting in 0.05 and 0.10 contacts being newly diagnosed and treated, or receiving preventive treatment overall, respectively. Overall, the NNTI measure found five interviews were necessary to identify one previously undiagnosed case of syphilis or an opportunity to administer preventive treatment; however, nearly seven times more interviews were necessary in 2014 than in 2014 (2.4 and 16.4, respectively).

Contra Costa experienced yearly fluctuations in the proportion of early syphilis cases interviewed, but overall the proportion stayed relatively similar with a range of 77.1% to 89.9% (Table 14). The proportion that named at least one partner for notification, however, decreased substantially from 47.6% in 2008 to 20.2% in 2012, and further still to 4.5% in 2014. The contact index also decreased from 1.31 in 2008 to 0.05 in 2014, resulting in 0.42 contacts initiated per interview overall. Of the partners initiated for follow-up, the proportion of newly infected and brought to treatment was 10.9% overall, but had a wide range from 5.0% (n=1) to 33.3% (n=7). The proportion that received preventive treatment was 16.3% overall, ranging from 12.9% to 33.0%. Contra Costa's brought-to-treatment index and preventive treatment index both declined from 2008 to 2012, with no new infections being found in either 2013 or 2014. Overall, the NNTI measure found 8.8 interviews were necessary to identify one previously undiagnosed case of syphilis or an opportunity to administer preventive treatment.

Similar to Contra Costa, Santa Clara experienced modest yearly variation in the proportion of early syphilis cases interviewed, but overall maintained a high interview proportion ranging from 74.9% to 89.3% (Table 15). The proportion of cases that named at least one partner was 62.1% (n=41) in 2008, declined slightly to 56.2% (n=57) in 2012, and then sharply declined to 29.1% (n=51) in 2014. Santa Clara's contact index decreased from 1.17 contacts in 2008 to 0.75 in 2014, resulting in 1.12 contacts initiated per interview overall. Santa Clara reported the highest contact index of the four CPA Bay Area counties assessed. Of the partners initiated for follow-up, the proportion newly infected and brought to treatment overall was 6.1%, ranging from 1.8% to 14.7%. The proportion that received preventive treatment increased from 10.3% in 2008 to 32.1% in 2014, resulting in one-quarter of overall partners initiated having received preventive treatment. Santa Clara's brought-to-treatment index decreased over time, resulting in 0.07 contacts being newly diagnosed and treated per interview. In contrast, the preventive treatment index increased from 0.12 contacts in 2008 to a high of 0.46 in 2011, before decreasing to 0.24 in 2014. Overall, the NNTI measure found only 2.8 interviews were necessary to identify one previously undiagnosed case of syphilis or an opportunity to administer preventive treatment, with some variation by year.

San Mateo also experienced yearly variation in the proportion of early syphilis cases interviewed, but overall maintained a high interview proportion of 74% to 92.3% (Table 7.16).

The proportion of cases that named at least one partner was 23.5%, due to increasing numbers of cases and decreasing numbers of interviews in recent years. San Mateo's contact index decreased from 1.79 contacts in 2008 to 0.14 in 2014, resulting in 0.60 contacts initiated per interview overall. Of the partners initiated for follow-up, the proportion newly infected and brought to treatment overall was 4.5%, and the proportion that received preventive treatment varied from 11.5% to 62.5%, resulting in nearly one-quarter of overall partners initiated having received preventive treatment. San Mateo had a low brought-to-treatment index, at 0.03 contacts being newly diagnosed and treated per interview. The preventive treatment index was 0.14 contacts overall, with a notable decrease from 0.46 to 0.09 between 2008 and 2014. Overall, the NNTI measure found 5.9 interviews were necessary to identify one previously undiagnosed case of syphilis or an opportunity to administer preventive treatment.

Node Characteristics

Of the 12,227 unique nodes that were identified in the syphilis surveillance dataset, 8,339 (68.2%) had at least one detected partnership (Table 17). Of these nodes, 39.2% (n=3,291) were classified as infected, 6.3% (n=529) were classified as receiving prophylactic treatment, and 55% (n=4,579) as unknown infection status. The percent infected was higher among women (41.2%) than men (39.2%); however, the men had a higher proportion of unknown infection status (55.1%) than women (44%). The percent infected was higher among Hispanics (58.4%) compared to Whites (37.1%), African Americans (38.2%) or Asians (39.2%); as with gender, however, the latter three groups had high proportions of unknown infection status (56.1%, 53.3%, and 54.4%, respectively).

County distribution overall shows San Francisco accounted for nearly half of the network (47.2%), followed distantly by "SF-Unknown" (15.1%), which reflects additional persons named by San Francisco cases for whom no further information on county was available. Of the CPA Bay Area counties, Santa Clara accounted for the most nodes in the network (11.3%). Just under 25% of contacts in Napa and Sonoma were not traced or tested compared to a range of 33.5 to 61.7% in the other Bay Area counties. Within the 2008-14 time frame, 1.5% (n=122) of nodes appeared to reside in multiple Bay Area counties. In addition, 3.1% (n=254) of nodes were California residents outside the San Francisco Bay Area and 1.7% (n=144) of nodes were not California residents. By age, the percent infected was highest among persons ages 40 to 49 years (50.1%); however, the proportion of persons with unknown status was high among all age groups. Proportionately more contacts were traced among persons ages 15 to 19 years.

Table 12. Partner notification outcomes for early syphilis cases, Alameda 2008-2014

	2008-14		2008		2009		2010		2011		2012		2013		2014	
# early syphilis cases - ALAMEDA	1202		108		100		155		184		199		225		231	
# interviewed	730	60.7	85	78.7	71	71.0	101	65.2	113	61.4	114	57.3	131	58.2	115	49.8
# cases with at least one partner initiated	271	37.1	50	46.3	32	32.0	50	32.3	45	24.5	24	12.1	44	19.6	26	11.3
# contacts initiated	567		126		72		72		96		51		81		69	
A-preventively treated	108	19.0	27	21.4	17	23.6	12	16.7	22	22.9	6	11.8	21	25.9	3	4.3
B-not preventively treated	2	--	--	--	--	--	--	--	1	1.0	--	--	--	--	1	1.4
C-newly infected, brought to treat	38	6.7	8	6.3	5	6.9	8	11.1	4	4.2	4	7.8	5	6.2	4	5.8
D-infected, not treated	1	--	--	--	--	--	--	--	--	--	--	--	--	--	1	1.4
E-previously treated	107	18.9	19	15.1	10	13.9	28	38.9	21	21.9	16	31.4	9	11.1	4	5.8
F-not infected	38	6.7	16	12.7	6	8.3	2	2.8	4	4.2	2	3.9	4	4.9	4	5.8
G-insufficient information to investigate	12	2.1	1	0.8	1	1.4	3	4.2	5	5.2	--	--	1	1.2	1	1.4
H-unable to locate	146	25.7	35	27.8	19	26.4	13	18.1	21	21.9	15	29.4	17	21.0	26	37.7
J-Located, refused examination	45	7.9	20	15.9	7	9.7	1	1.4	10	10.4	3	5.9	2	2.5	2	2.9
K-Out of jurisdiction	1	0.2	--	--	1	1.4	--	--	--	--	--	--	--	--	--	--
L-Other	8	1.4	--	--	1	1.4	--	--	3	3.1	3	5.9	--	--	1	1.4
M-Notified of exposure, agrees to testing, results self-reported	48	8.5	--	--	4	5.6	3	4.2	4	4.2	4	7.8	16	19.8	17	24.6
N-Notified of exposure, agrees to testing, results unknown	7	1.2	--	--	1	1.4	1	1.4	1	1.0	--	--	1	1.2	3	4.3
Q-Initial contact made, no health information shared	6	1.1	--	--	--	--	1	1.4	--	--	1	2.0	4	4.9	--	--
S-Email bounce-back (for Internet partner notification)	0	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Missing	3	0.5	--	--	--	--	--	--	--	--	--	--	1	1.2	2	2.9
Partner indices																
Contact index (# partners initiated per interviewed case)	0.78		1.48		1.01		0.71		0.85		0.45		0.62		0.60	
nt-to-treat index (# partners newly infected, treated per interviewed case)	0.05		0.09		0.07		0.08		0.04		0.04		0.04		0.03	
ve treatment index (# partners preventively treated per interviewed case)	0.1		0.32		0.24		0.12		0.19		0.05		0.16		0.03	
NNTI (# interviews necessary to identify identify one new infection or preventive treatment opportunity)	5.0		2.4		3.2		5.1		4.3		11.4		5.0		16.4	

Table 13. Partner notification outcomes for early syphilis cases, Contra Costa 2008-2014

	2008-14		2008		2009		2010		2011		2012		2013		2014	
# early syphilis cases - CONTRA COSTA	**527**		42		48		46		85		89		105		112	
# interviewed	441	83.7	35	83.3	37	77.1	35	76.1	68	80.0	80	89.9	93	88.6	93	83.0
# cases with at least one partner initiated	107	20.3	20	47.6	22	45.8	17	37.0	15	17.6	18	20.2	10	9.5	5	4.5
# contacts initiated	184		46		31		20		46		21		15		5	
A-preventively treated	30	16.3	6	13.0	4	12.9	3	15.0	9	19.6	7	33.3	--	--	1	20.0
B-not preventively treated	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
C-newly infected, brought to treat	20	10.9	4	8.7	4	12.9	1	5.0	4	8.7	7	33.3	--	--	--	--
D-infected, not treated	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
E-previously treated	24	13.0	9	19.6	8	25.8	3	15.0	2	4.3	1	4.8	--	--	1	20.0
F-not infected	38	20.7	3	6.5	3	9.7	5	25.0	20	43.5	1	4.8	6	40.0	--	--
G-insufficient information to investigate	18	9.8	6	13.0	4	12.9	4	20.0	3	6.5	1	4.8	--	--	--	--
H-unable to locate	26	14.1	13	28.3	6	19.4	1	5.0	5	10.9	--	--	--	--	1	20.0
J-Located, refused examination	5	2.7	1	2.2	1	3.2	1	5.0	2	4.3	--	--	--	--	--	--
K-Out of jurisdiction	6	3.3	--	--	--	--	1	5.0	--	--	--	--	4	26.7	1	--
L-Other	4	2.2	4	8.7	--	--	--	--	--	--	--	--	--	--	--	--
M-Notified of exposure, agrees to testing, results self-reported	6	3.3	--	--	1	3.2	1	5.0	--	--	3	14.3	--	--	1	20.0
N-Notified of exposure, agrees to testing, results unknown	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Q-Initial contact made, no health information shared	1	0.5	--	--	--	--	--	--	--	--	1	4.8	--	--	--	--
S-Email bounce-back (for Internet partner notification)	1	0.5	--	--	--	--	--	--	1	2.2	--	--	--	--	--	--
Missing	5	2.7	--	--	--	--	--	--	--	--	--	--	5	33.3	--	--
Partner indices																
Contact index (# partners initiated per interviewed case)	0.42		1.31		0.84		0.57		0.68		0.26		0.16		0.05	
nt-to-treat index (# partners newly infected, treated per interviewed case)	0.05		0.11		0.11		0.03		0.06		0.09		--		--	
ve treatment index (# partners preventively treated per interviewed case)	0.07		0.17		0.11		0.09		0.13		0.09		--		0.01	
NNTI (# interviews necessary to identify identify one new infection or preventive treatment opportunity)	8.8		3.5		4.6		8.8		5.2		5.7		--		93.0	

Table 14. Partner notification outcomes for early syphilis cases, Santa Clara 2008-2014

	2008-14		2008		2009		2010		2011		2012		2013		2014	
# early syphilis cases - SANTA CLARA	894		66		87		112		101		146		207		175	
# interviewed	746	83.4	58	87.9	75	86.2	100	89.3	89	88.1	123	84.2	155	74.9	146	83.4
# cases with at least one partner initiated	409	45.7	41	62.1	56	64.4	65	58.0	57	56.4	82	56.2	57	27.5	51	29.1
# contacts initiated	834		68		164		123		133		138		99		109	
A-preventively treated	212	25.4	7	10.3	26	15.9	43	35.0	41	30.8	30	21.7	30	30.3	35	32.1
B-not preventively treated	--	--	1	1.5	--	--	1	0.8	--	--	--	--	--	--	--	--
C-newly infected, brought to treat	51	6.1	10	14.7	3	1.8	10	8.1	6	4.5	11	8.0	8	8.1	3	2.8
D-infected, not treated	--	--	--	--	1	0.6	--	--	1	0.8	--	--	--	--	--	--
E-previously treated	124	14.9	19	27.9	29	17.7	21	17.1	15	11.3	23	16.7	13	13.1	4	3.7
F-not infected	84	10.1	13	19.1	18	11.0	10	8.1	14	10.5	14	10.1	8	8.1	7	6.4
G-insufficient information to investigate	28	3.4	1	1.5	3	1.8	3	2.4	10	7.5	7	5.1	3	3.0	1	0.9
H-unable to locate	143	17.1	9	13.2	45	27.4	14	11.4	14	10.5	26	18.8	13	13.1	22	20.2
J-Located, refused examination	43	5.2	8	11.8	13	7.9	5	4.1	5	3.8	6	4.3	2	2.0	4	3.7
K-Out of jurisdiction	12	1.4	--	--	--	--	--	--	1	0.8	1	0.7	2	2.0	8	7.3
L-Other	8	1.0	--	--	2	1.2	--	--	1	0.8	--	--	4	4.0	1	0.9
M-Notified of exposure, agrees to testing, results self-reported	79	9.5	--	--	16	9.8	11	8.9	15	11.3	18	13.0	6	6.1	13	11.9
N-Notified of exposure, agrees to testing, results unknown	--	--	--	--	6	3.7	2	1.6	--	--	2	1.4	1	1.0	3	2.8
Q-Initial contact made, no health information shared	3	0.4	--	--	--	--	2	1.6	--	--	--	--	--	--	1	0.9
S-Email bounce-back (for Internet partner notification)	3	0.4	--	--	2	1.2	1	0.8	--	--	--	--	--	--	--	--
Missing	26	3.1	--	--	--	--	--	--	10	7.5	--	--	9	9.1	7	6.4
Partner indices																
Contact index (# partners initiated per interviewed case)	1.12		1.17		2.19		1.23		1.49		1.12		0.64		0.75	
nt-to-treat index (# partners newly infected, treated per interviewed case)	0.07		0.17		0.04		0.10		0.07		0.09		0.05		0.02	
ve treatment index (# partners preventively treated per interviewed case)	0.28		0.12		0.35		0.43		0.46		0.24		0.19		0.24	
NNTI (# interviews necessary to identify identify one new infection or preventive treatment opportunity)	2.8		3.4		2.6		1.9		1.9		3.0		4.1		3.8	

Table 15. Partner notification outcomes for early syphilis cases, San Mateo 2008-2014

	2008-14		2008		2009		2010		2011		2012		2013		2014	
# early syphilis cases - SAN MATEO	361		34		26		34		45		65		80		77	
# interviewed	299	82.8	28	82.4	24	92.3	27	79.4	39	86.7	55	84.6	69	86.3	57	74.0
# cases with at least one partner initiated	85	23.5	19	55.9	12	46.2	8	23.5	16	35.6	15	23.1	10	12.5	5	6.5
# contacts initiated	179		50		23		8		43		26		21		8	
A-preventively treated	43	24.0	13	26.0	9	39.1	1	12.5	5	11.6	3	11.5	7	33.3	5	62.5
B-not preventively treated	--	--	2	4.0	1	4.3	--	--	--	--	--	--	--	--	--	--
C-newly infected, brought to treat	8	4.5	2	4.0	1	4.3	--	--	1	2.3	3	11.5	1	4.8	--	--
D-infected, not treated	--	--	--	--	1	4.3	--	--	--	--	--	--	--	--	1	12.5
E-previously treated	34	19.0	6	12.0	3	13.0	5	62.5	12	27.9	6	23.1	2	9.5	--	--
F-not infected	13	7.3	5	10.0	1	4.3	--	--	--	--	5	19.2	2	9.5	--	--
G-insufficient information to investigate	2	1.1	--	--	1	4.3	--	--	1	2.3	--	--	--	--	--	--
H-unable to locate	34	19.0	11	22.0	4	17.4	1	12.5	10	23.3	4	15.4	4	19.0	--	--
J-Located, refused examination	21	11.7	10	20.0	2	8.7	--	--	8	18.6	1	3.8	--	--	--	--
K-Out of jurisdiction	0	0.0	--	--	--	--	--	--	--	--	--	--	--	--	--	--
L-Other	4	2.2	1	2.0	--	--	--	--	2	4.7	1	3.8	--	--	--	--
M-Notified of exposure, agrees to testing, results self-reported	9	5.0	--	--	--	--	1	12.5	3	7.0	2	7.7	3	14.3	--	--
N-Notified of exposure, agrees to testing, results unknown	--	--	--	--	--	--	--	--	1	2.3	--	--	--	--	1	12.5
Q-Initial contact made, no health information shared	2	1.1	--	--	--	--	--	--	--	--	1	3.8	1	4.8	--	--
S-Email bounce-back (for Internet partner notification)	1	0.6	--	--	--	--	--	--	--	--	--	--	--	--	1	12.5
Missing	0	0.0	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Partner indices																
Contact index (# partners initiated per interviewed case)	0.60		1.79		0.96		0.30		1.10		0.47		0.30		0.14	
nt-to-treat index (# partners newly infected, treated per interviewed case)	0.03		0.07		0.04		--		0.03		0.05		0.01		--	
ve treatment index (# partners preventively treated per interviewed case)	0.14		0.46		0.38		0.04		0.13		0.05		0.10		0.09	
NNTI (# interviews necessary to identify identify one new infection or preventive treatment opportunity)	5.9		1.9		2.4		--		6.5		9.2		8.6		--	

Table 16. Node characteristics for San Francisco Bay Area syphilis network, 2008-2014

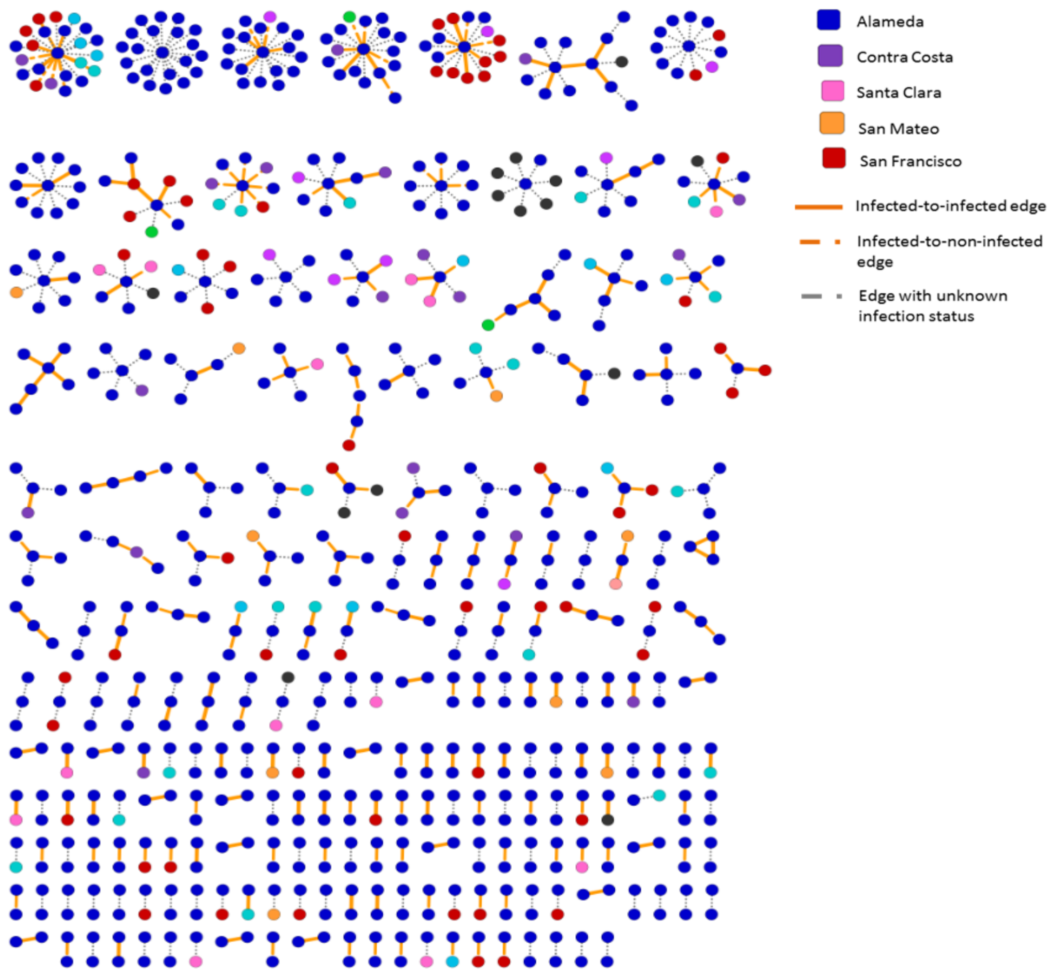
	All nodes (n=8,399)		Infection status					
			Not Infected		Infected		Unknown	
	n	%	n	%	n	%	n	%
Total nodes	8399		529		3291		4579	
Gender								
Female	514	6.1	76	14.4	212	6.4	226	4.9
Male	7849	93.5	453	85.6	3075	93.4	4321	94.4
Transgender	4	0.0	0	0.0	3	0.1	1	0.0
Unknown	32	0.4	0	0.0	1	0.0	31	0.7
Race/ethnicity								
White	3757	44.7	257	48.6	1392	42.3	2108	46.0
African American	904	10.8	77	14.6	345	10.5	482	10.5
Hispanic	1343	16.0	43	8.1	784	23.8	516	11.3
Asian	467	5.6	30	5.7	183	5.6	254	5.5
Other	680	8.1	76	14.4	533	16.2	71	1.6
Unknown	1248	14.9	46	8.7	54	1.6	1148	25.1
Had a repeat infection	180	2.1	--	--	--'	--	--	--
County								
ALAMEDA	787	9.4	91	17.2	310	9.4	386	8.4
BAY-CA	10	0.1	1	0.2	9	0.3	0	0.0
BAY-US	3	0.0	1	0.2	2	0.1	0	0.0
BERKELEY	62	0.7	9	1.7	19	0.6	34	0.7
CONTRA COSTA	295	3.5	49	9.3	138	4.2	108	2.4
MARIN	60	0.7	7	1.3	16	0.5	37	0.8
NAPA	23	0.3	6	1.1	12	0.4	5	0.1
SAN FRANCISCO	3963	47.2	51	9.6	2025	61.5	1887	41.2
SAN MATEO	269	3.2	32	6.0	105	3.2	132	2.9
SANTA CLARA	948	11.3	210	39.7	420	12.8	318	6.9
SOLANO	74	0.9	11	2.1	34	1.0	29	0.6
SONOMA	117	1.4	25	4.7	65	2.0	27	0.6
SF-UNKNOWN	1268	15.1	0	0.0	0	0.0	1268	27.7
INTER-BAY	122	1.5	9	1.7	109	3.3	4	0.1
R-COAST	28	0.3	2	0.4	4	0.1	22	0.5
R-INLAND	56	0.7	5	0.9	6	0.2	45	1.0
R-LA	52	0.6	1	0.2	1	0.0	50	1.1
R-NORTH	13	0.2	0	0.0	3	0.1	10	0.2
R-SAC	63	0.8	10	1.9	8	0.2	45	1.0
R-SOUTH	42	0.5	2	0.4	1	0.0	39	0.9
OUTSIDE CA	144	1.7	7	1.3	4	0.1	133	2.9
Age								
<15	20	0.3	8	1.5	8	0.2	4	0.1
15-19	305	4.3	45	8.7	114	3.5	146	4.5
20-29	1849	26.3	163	31.5	867	26.4	819	25.5
30-39	1858	26.5	113	21.8	881	26.8	864	26.9
40-49	1984	28.3	108	20.8	993	30.2	883	27.5
50+	1002	14.3	81	15.6	427	13.0	494	15.4
Unknown	1381		11		1		1369	

County-level networks, 2008-14

For each of the county-level networks, colored nodes are used to indicate variation in the county of residence and line type is used to indicate whether partnerships are between infected persons (bold solid line), between infected and non-infected persons (orange dotted line), and either of those with an unknown status case (gray dotted line). Components refer to groups of nodes that are all connected to each other – examining the distribution of component sizes and the proportion of total nodes represented within each size group provides insight into overall connectivity of the network.

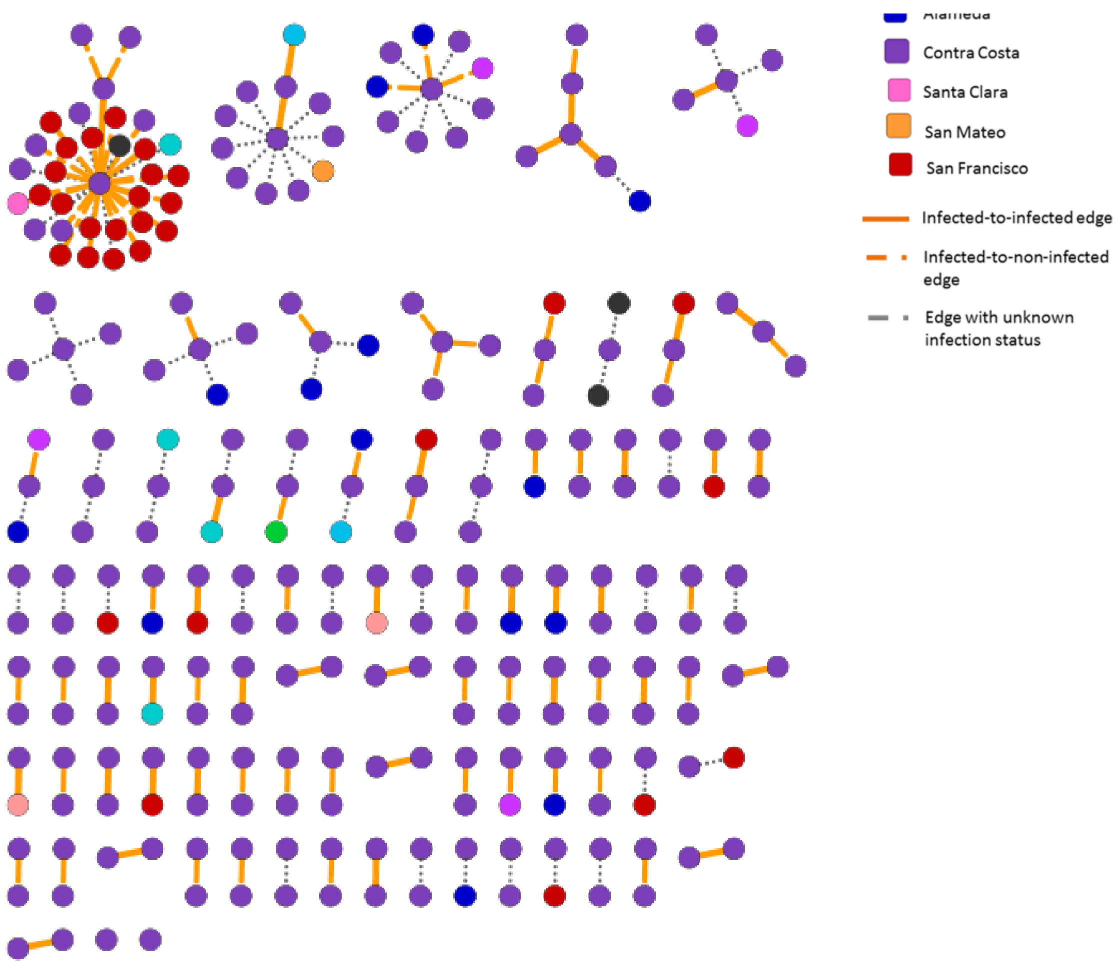
Alameda. Alameda's network was comprised of 514 partnerships with at least one infected person, distributed across 213 components (Figure 11). The majority of persons had only one partner (86%). Dyads comprised 64% of all components. The largest component was made up of 23 nodes, of which two were infected, nine were non-infected, and 12 were of unknown status. Bridging between Alameda, two Bay Area counties, and another California region was observed in 55% (n=12) of the large component partnerships. Overall, at least one inter-jurisdictional partnership was observed in 40% (n=87) of total components and 34% (n=173) of total partnerships.

Figure 11. Alameda early syphilis network, 2008-14. *Note: Only select counties are delineated in the legend.*



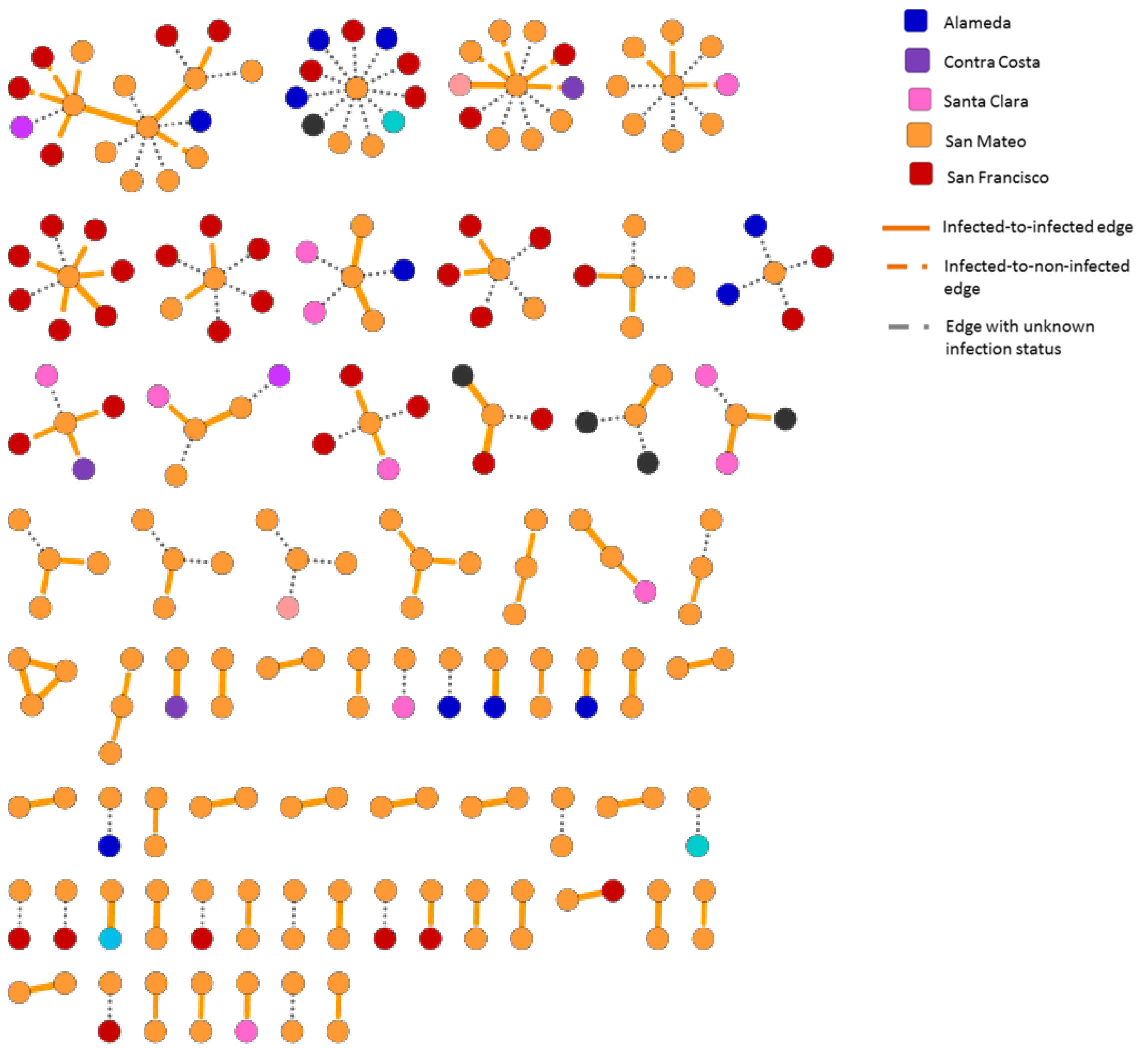
Contra Costa. Contra Costa's network was comprised of 168 partnerships with at least one infected person distributed across 90 components (Figure 12). Nearly all persons had 1-2 partners (96%), with dyads and triads accounting for 90% of all components. The largest component was made up of 33 nodes, with three infected persons, 21 non-infected, and nine of unknown status. Bridging between persons in Contra Costa and other Bay Area counties, another California region, or another U.S. state was observed in 72% (n=23) of partnerships in the largest component. Overall, at least one inter-jurisdictional partnership was observed in 37% (n=33) of components and 14% (n=23) of partnerships.

Figure 12. Contra Costa early syphilis network, 2008-14. *Note: Only select counties are delineated in the legend.*



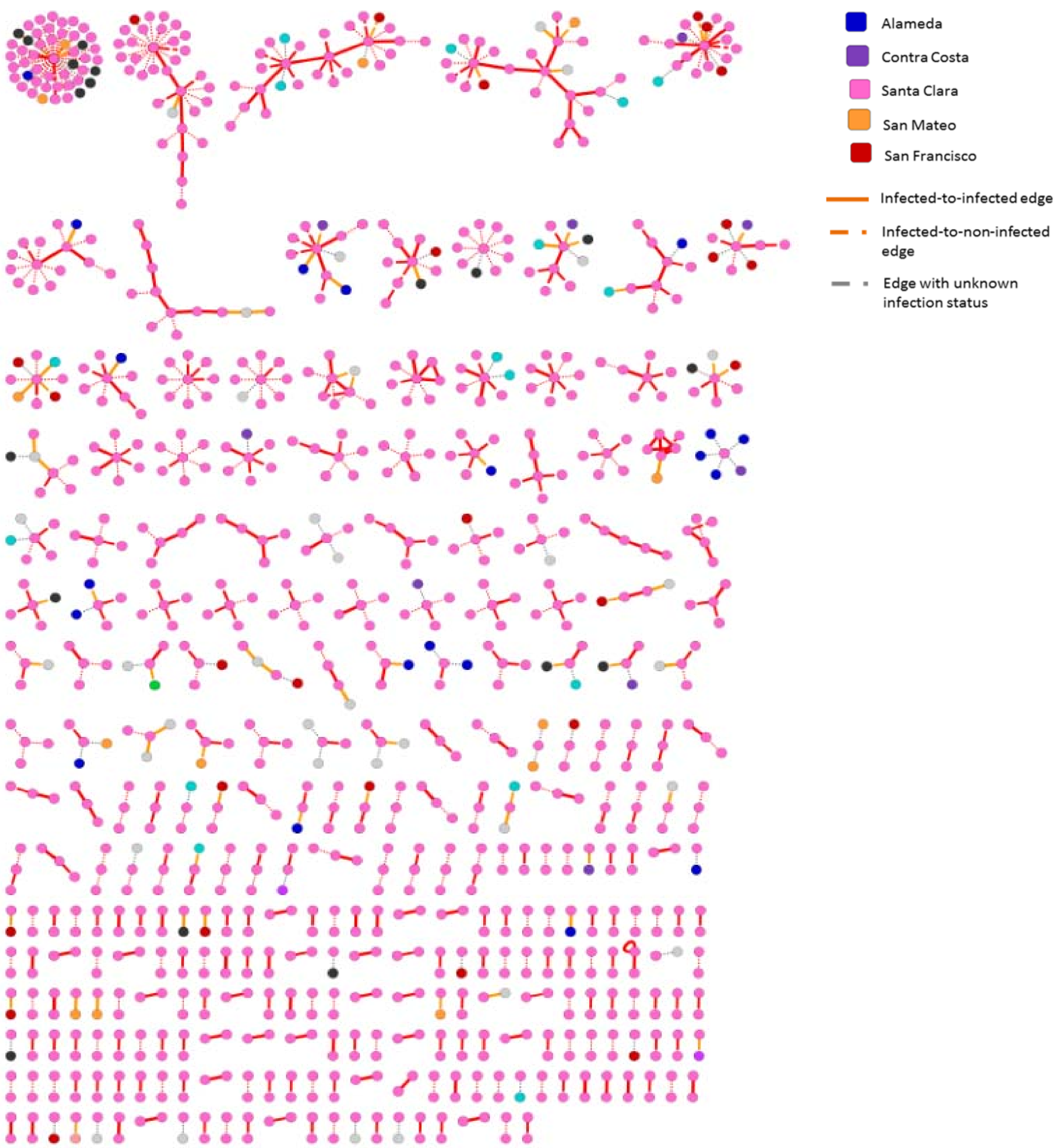
San Mateo. San Mateo's network was comprised of 163 partnerships with at least one infected person distributed across 68 components (Figure 13). The majority of persons had 1-3 partners (94%), with dyads consisting of 70% of all components. The largest component was made up of 17 nodes, with three infected persons, six non-infected, and eight of unknown status. Bridging between San Mateo, San Francisco and two Bay Area was observed in 44% (n=7) of partnerships in the largest component. Overall, at least one inter-jurisdictional partnership was observed in 47% (n=32) of components and 50% (n=82) of partnerships.

Figure 13. San Mateo early syphilis network, 2008-14. *Note: Only select counties are delineated in the legend.*



Santa Clara. Santa Clara's network was comprised of 763 partnerships with at least one infected person distributed across 288 components (Figure 14). The overwhelming majority of persons had 1-3 partners (94%), with dyads consisting of 70% of all components. The largest component was made up of 48 nodes, with two infected persons, four non-infected, and the remaining of unknown status. Bridging between San Mateo, Alameda, and areas outside California was observed in 21% (n=10) of partnerships in the largest component. At least one interjurisdictional partnership was observed in 28% (n=81) of components and 19% (n=145) of partnerships overall.

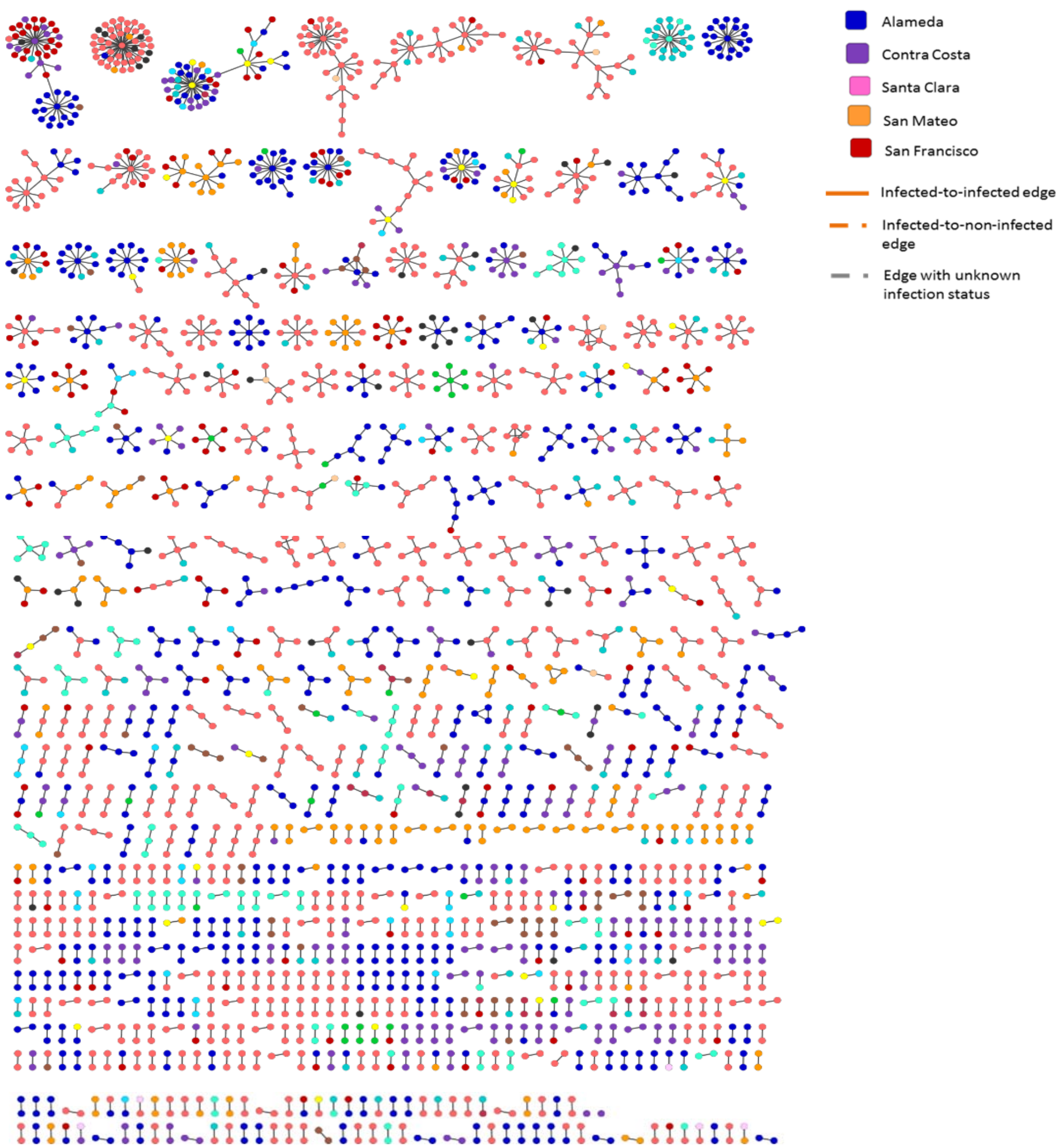
Figure 14. Santa Clara early syphilis network, 2008-2014. *Note: Only select counties are delineated in the legend.*



CPA Bay Area Regional network

The CPA Bay Area Regional network was comprised of 1,796 partnerships with at least one infected person distributed across 729 components (Figure 15). As expected, given the LHJ-specific results, the overwhelming majority of persons had 1-3 partners (95%), with dyads and triads comprising 77% of all components. The largest component was made up of 50 nodes, not much larger than that identified in the four county-level assessments. At least one inter-jurisdictional partnership was observed in 37% (n=267) of components and 33% (n=600) of partnerships overall. Among dyads alone, 27% involved partners residing in different counties.

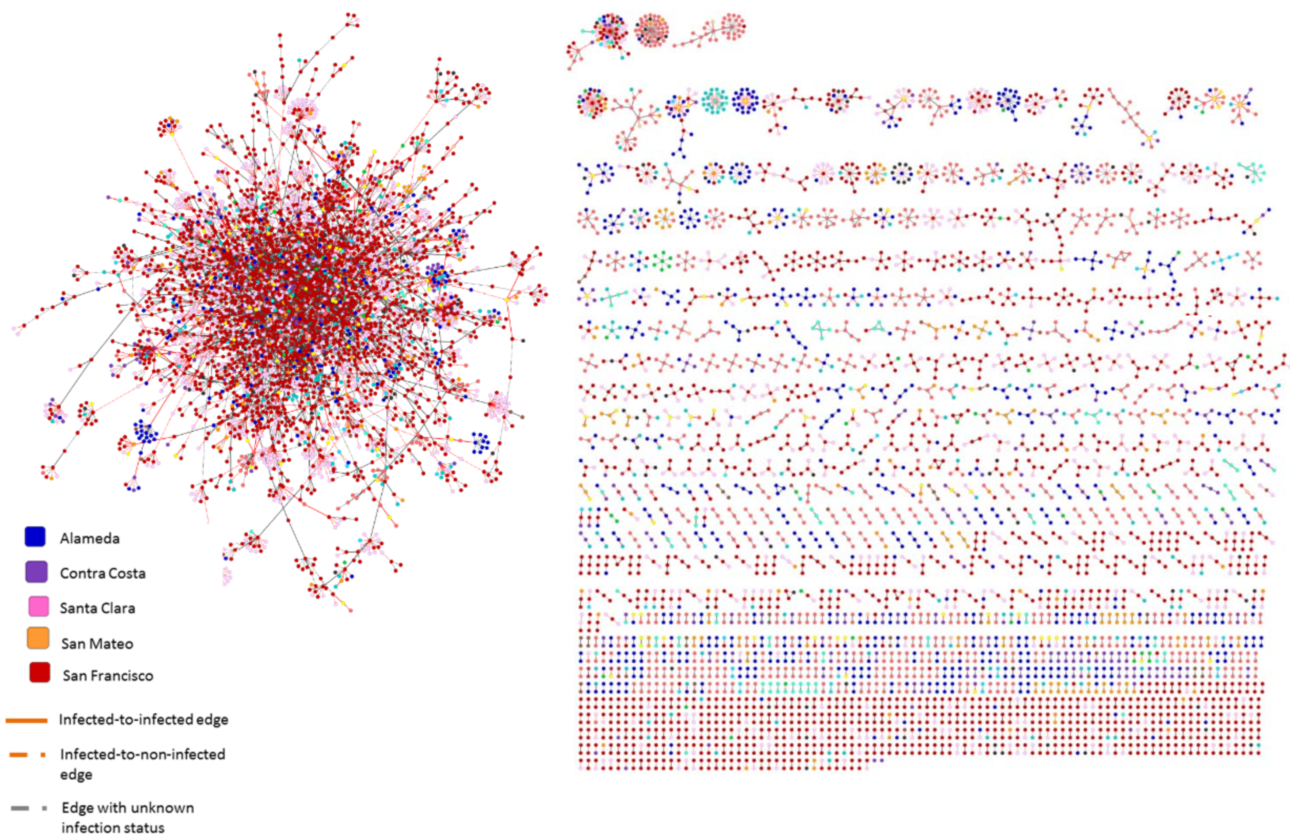
Figure 15. California Project Area-Bay Area early syphilis network, 2008-2014. *Note: Only select counties are delineated in the legend.*



San Francisco Bay Area Region

While there is limited connectivity observed within and between the CPA Bay Area counties, incorporating San Francisco's network data into the CPA regional data reveals a large component (i.e., a "mega-network", based on earlier work done by Kohn et al.) comprised of 3,879 persons and 4,550 partnerships (Figure 16). San Francisco makes up the majority of this mega-network, accounting for 59% (n=2,288) of nodes. An additional 14.6% of nodes are residents of CPA Bay Area counties, while the remaining nodes live in another California region, outside California, or have unknown county information. Overall, 41% (n=1,869) of the partnerships within this mega-network are inter-jurisdictional.

Figure 16. San Francisco Bay Area early syphilis networks, 2008-2014. *Note: Only select counties are delineated in the legend.*



To better see the inter-jurisdictional partnerships within the large component, Alameda residents and persons within one degree (i.e., immediate partner to the Alameda resident) were identified and graphed separately, resulting in the components in Figure 17. In contrast to the largest component of 28 nodes found just using Alameda's LHJ-centric partner notification data, the largest component in this grouping consisted of 147 nodes and demonstrates a chain of partnerships that move in and out of multiple jurisdictions.

Figure 17. Alameda nodes plus 1-degree connections within the San Francisco Bay Area early syphilis mega-network, 2008-2014. *Note: Only select counties are delineated in the legend.*

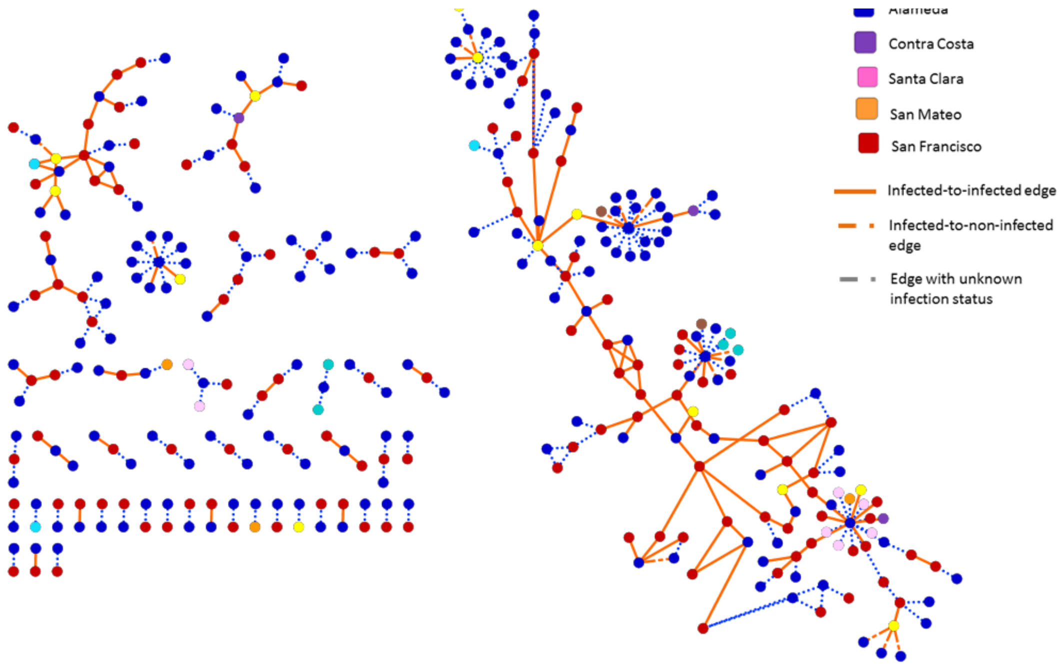
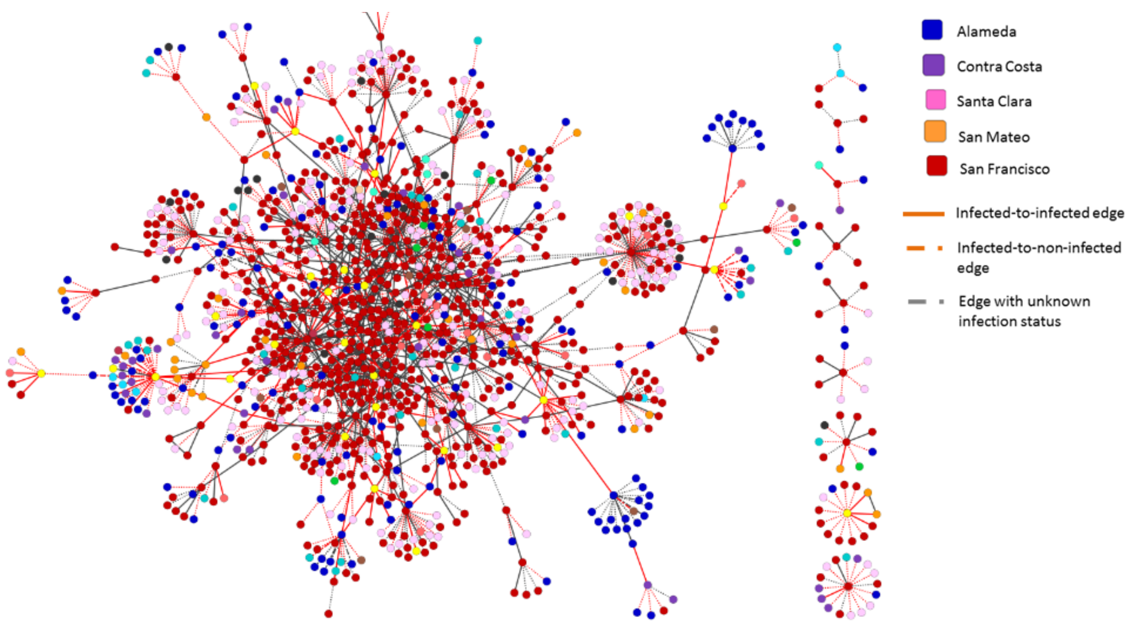


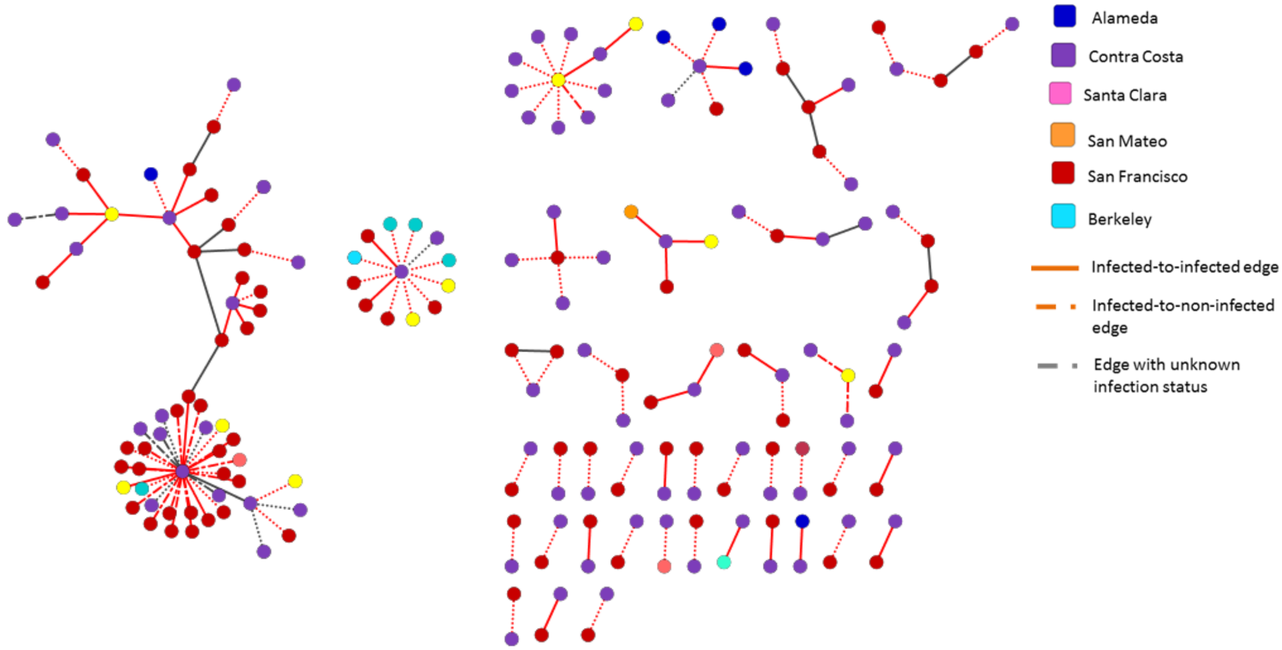
Figure 18. Alameda nodes, plus 2-degree connections – by county of residence and infected year - within the San Francisco Bay Area early syphilis mega-network, 2008-2014.



Allowing the above node selection to move out just one more degree conveys the impact of San Francisco's connectivity on network density (Figure 18), as the number of nodes and partnerships quadruple (nodes: 328 to 1,300 / partnerships: 295 to 1,553).

Similarly, if the same 1-degree selection from the mega-network is applied to Contra Costa, we see similar chains of cases and partnerships in the resulting components that bridge Contra Costa, San Francisco, and introduce Berkeley into the network as well (Figure 7.19).

Figure 19. Contra Costa nodes, plus 1-degree connection – by county of residence and partnership type - within the San Francisco Bay Area early syphilis mega-network, 2008-14



By combining the largest of Alameda and Contra Costa's 1-degree components, some of the structure hidden in the density of the mega-network begins to emerge (Figure 20). While this is only a small part of the larger mega-network, we can see these initial connections of 1-3 degrees result in a more dendritic, or branching, network structure, as opposed to dense clusters. In addition, the use of pink colored lines to indicate where inter-jurisdictional partnerships occur, and the use of node size to emphasize repeat infections highlights where individuals who have been infected multiple times create a bridge for potential infection between counties.

Examining the same Alameda and Contra Costa network under different filters also allows for an assessment of connectivity, as it relates to syphilis cases co-infected with HIV (Figure 21). Of the 249 partnerships in this subset, 72 (28.9%) are among persons of the same HIV status. This leaves a potential 71% for HIV discordant partnerships. Within this small subset of nodes, 33% (n=80) were HIV-infected; of those, 15% (n=12) were persons who acquired syphilis more than once in the six-year timeframe.

Figure 20. Alameda and Contra Costa nodes, plus 1-degree connections – by county, inter-jurisdictional partnership, and repeat infection - San Francisco Bay Area early syphilis mega-network, 2008-2014.

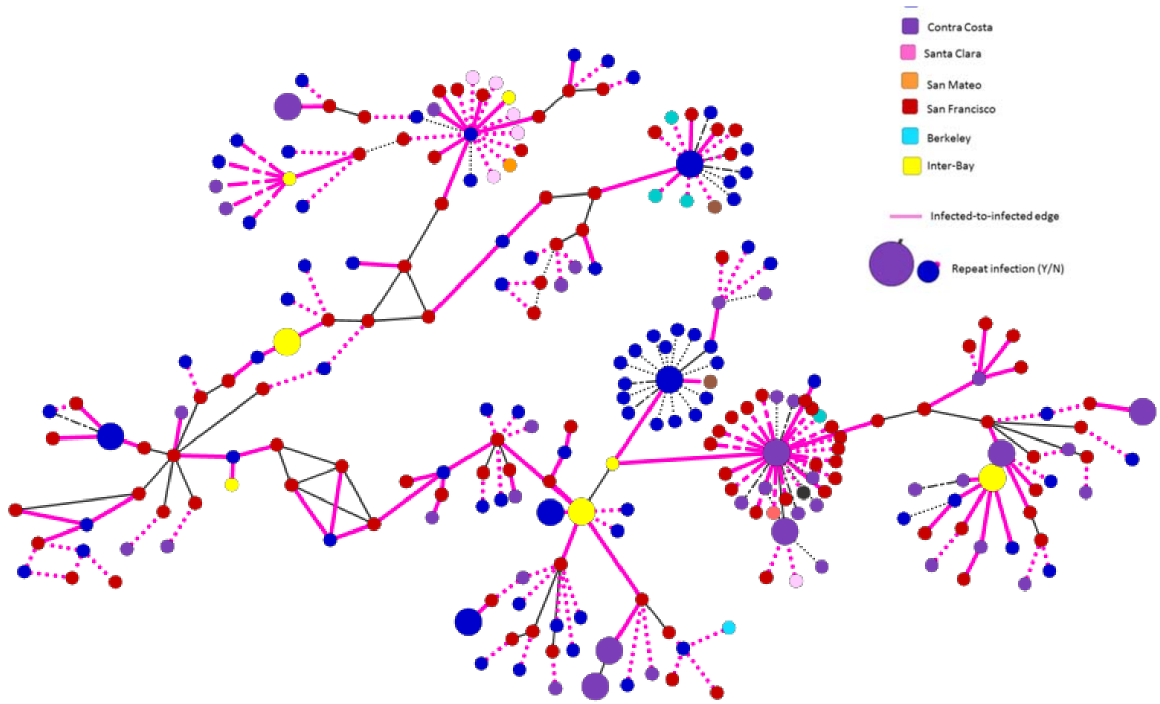
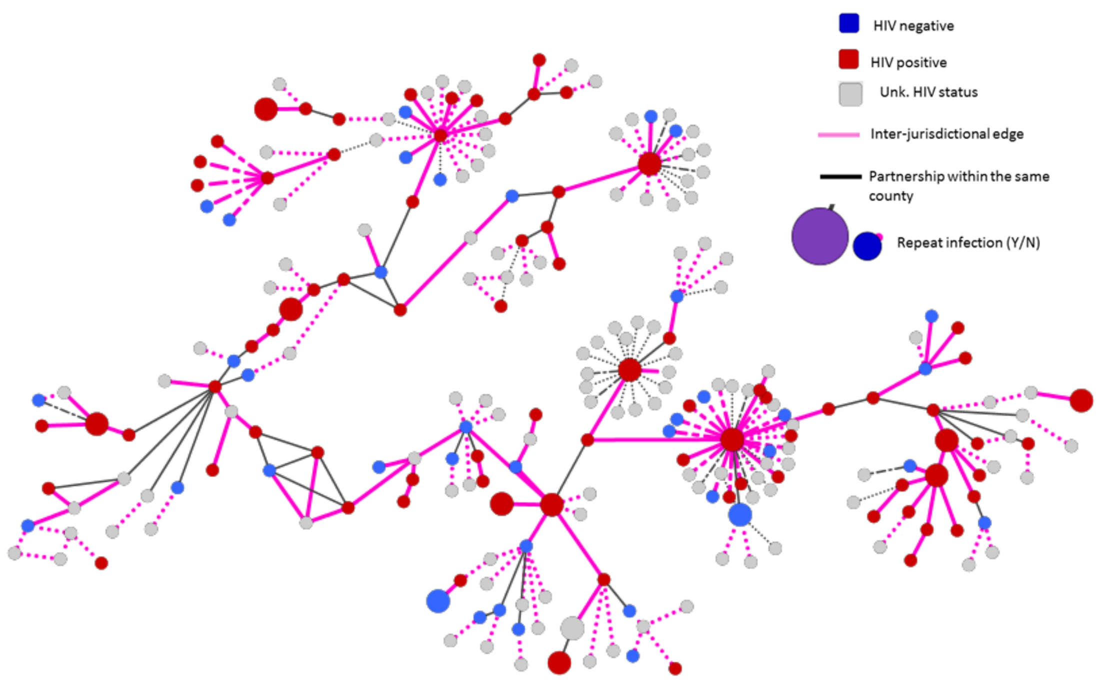


Figure 21. Alameda and Contra Costa nodes, plus 1-degree connections – by HIV status, partnership type, and repeat infection - San Francisco Bay Area early syphilis mega-network, 2008-2014



Limitations

As is common with network studies, one primary limitation of this analysis is incomplete network ascertainment, due to 1) high proportions of cases not reporting partners, 2) anonymous sex partners for whom limited identifying information was available, 3) insufficient or inaccurate information for locating partners, and 4) missed opportunities to match names within the network, thereby hiding relationships between person and networks. The matching algorithm used to transform the case-based surveillance data into a person-based dataset for network visualization may have missed a few true matches or matched some records that are, in reality, not the same people. Both a cursory and manual review of the matches was performed in an effort to minimize this problem.

The transition from the legacy system to CalREDIE for syphilis surveillance involved a steep learning curve for DIS, and no doubt had an impact on the documentation of partner notification efforts in 2013 and 2014 in such a way that results likely underestimate success of partner investigation outcomes and true connectivity of syphilis cases within and between counties.

Data analysis was done retrospectively and in aggregate, resulting in what appears to be cross-sectional networks; in reality, the network structures and relationships observed represent cumulative growth across the six year study period. This cumulative approach over such a wide timeframe makes it harder to interpret real-time network dynamics related to time-dependent factors, such as age, HIV infection, drug use, or venue use for meeting sex partners, which are immediately relevant for disease intervention and STD prevention policy.

San Francisco's separate surveillance system posed a unique challenge, in that its weekly transmission of surveillance data to the state includes only the names of individuals for whom an interview was attempted. However, early latent syphilis cases in San Francisco were not consistently interviewed, due to resource limitations. As a result, 859 early latent syphilis cases reported by San Francisco to the state did not have interview-based data; in addition, none of these individuals had been named as a partner of a known infectious case in San Francisco. In addition, San Francisco does not routinely send identifying information on partners to the state. As described earlier in this chapter, San Francisco agreed to send a one-time file with names and demographic data of partners initiated for notification of potential syphilis exposure during the study timeframe, for the purposes of this analysis. However, sharing of identifying information for persons for whom no interview attempt was made and who were not named as a partner of a known case, was deemed more than the minimum necessary, due to their minimal influence on overall network connectivity. This approach may have resulted in an underestimation of persons with repeat infections; for example, an individual reported by San Francisco as an early latent case that was subsequently reported by Alameda for another syphilis infection would not appear as a repeat infection in the network. Unavailability of data from San Francisco also likely resulted in an overestimation of truly discordant HIV partnerships, as HIV status for all partners in San Francisco was not readily available at the state.

Summary

Syphilis partner notification indices have been decreasing since 2008, due to increasing proportions of cases not being interviewed or cases not providing sufficient locating due information to conduct notification. Of those cases with data available, network analysis of syphilis partner services data in the CPA Bay Area demonstrated very little connectivity among cases within and between counties. Analysis also showed notable proportions of the network that involve inter-jurisdictional partnerships. Inclusion of San Francisco's partnership data in the network further revealed a large multi-jurisdictional component in which many bridges between counties help to sustain the network. In addition, assessment of network connectivity by HIV status showed that while HIV sero-sorting does occur, there remains the potential for testing of persons with previous negative or unknown HIV status as part of notification efforts for individuals co-infected with syphilis and HIV. The final chapter of this dissertation will discuss potential recommendations based on this analysis.

Chapter 8 – Recommendations

This chapter outlines potential opportunities for programmatic action based on the surveillance trends, partner notification outcomes, and structure and characteristics of sexual networks detected through routine syphilis surveillance and partner notification efforts in the San Francisco Bay Area Region.

Syphilis partner services cascades are a useful tool for feedback.

Partner notification as a means of syphilis control was historically designed for case-finding and prevention in heterosexual populations that had more non-anonymous partners based on drug use or sex work, resulting in more identified sexual networks[8,25]. In the current syphilis epidemic, health departments are engaging with a primarily MSM population who more frequently report anonymous sex partners for whom there is no identifying information provided, thereby rendering partner notification impossible[1,25,32]. One of the challenges then for health departments is to identify where the intervention is succeeding or falling short, and determine how disease intervention expertise and resources might be utilized to address gaps. Findings from this analysis highlighted a type of syphilis partner services cascade that could be used to outline the sequential stages of intervention, to quantify the number of early syphilis cases engaged at each stage, and to assist programs with identifying gaps in service provision or intervention uptake. Figures 22 and 23 provide examples of syphilis partner services cascades for two fictitious counties. The left-hand portion of the cascade models activity related to the case interviews; the right-hand portion of the cascade models activity related to the partner investigations

Figure 22. Example of a syphilis partner services cascade – County A.

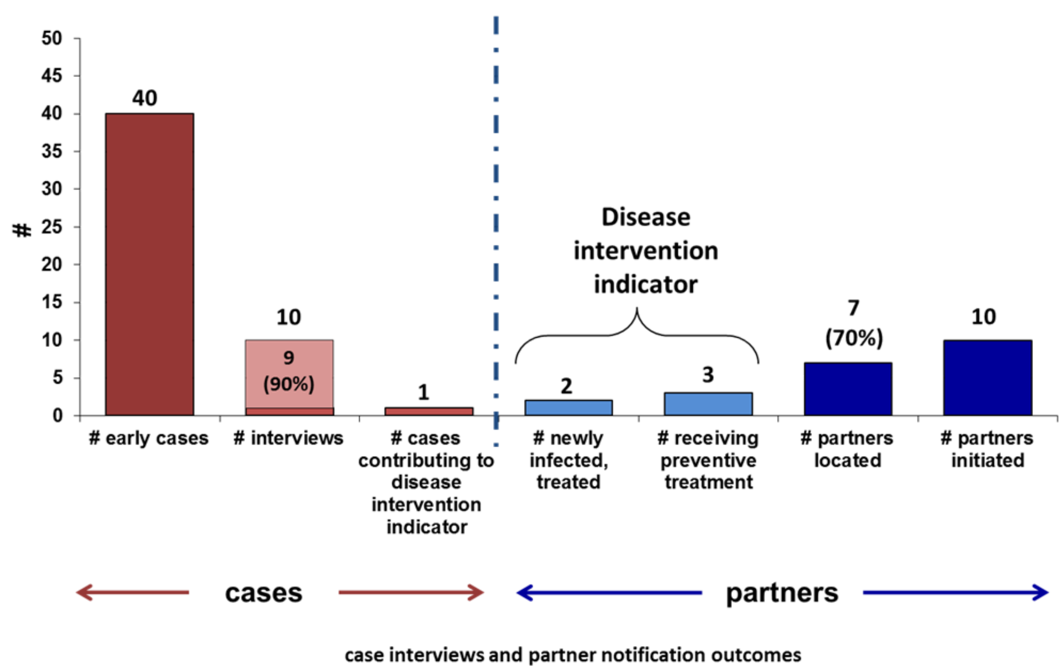
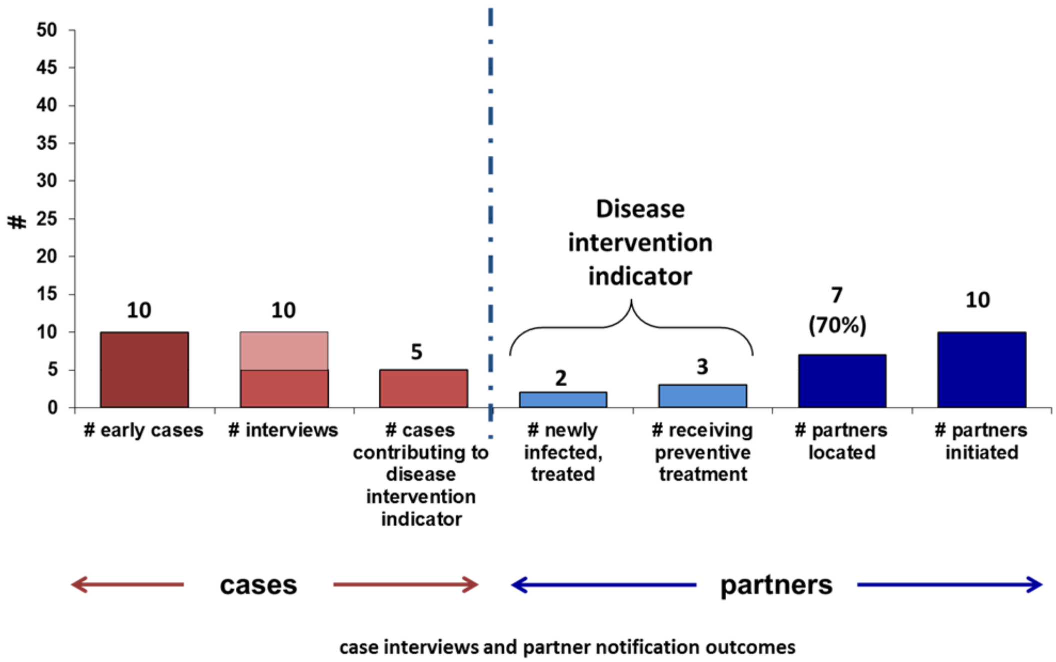


Figure 23. Example of a syphilis partner services cascade – County B.



Cases interviewed. The findings show during the study interval, the proportion of early syphilis cases interviewed decreased in the region overall, with some variation by county. This decrease reflects a reduction in the number of persons to whom the health department had the opportunity to offer partner services. Typically, patients have declined the health department's request to meet, they have not responded to the health department's contact attempt, or the partner's locating information was not correct. Staff shortages also affect a county's ability to interview and conduct partner notification for early cases, particularly when a steady handful of staff is responsible for interviewing an increasing number of cases. For example, San Francisco consistently attempts to interview primary and secondary syphilis cases; however, they have cut back on interviewing early latent syphilis cases due to limited staff capacity.

Cases with at least one partner initiated by the health department. Suppose County A has 40 cases of early syphilis, and interviews ten (Figure 8.1). Of those ten, one person names ten partners to be notified by the health department. Now suppose County B has ten early syphilis cases and manages to interview all of them (Figure 8.2). Of those ten cases, five name two partners each for a total of ten partners to be notified by the health department. In these examples, County A and County B have the same contact index value – 1.0 contact initiated per interviewed case – even though the uptake of interviews and partner services was notably better in County B than in County A. One is hard-pressed to conclude that a contact index of 1.0 appropriately reflects what actually happened by way of network detection in either county.

Even in counties where the interview rate stayed relatively stable, the number of partners that health departments were able to initiate per interview (i.e., contact index) declined. One reason often cited is the increase in cases who report at least one, if not all, anonymous sex partners[31]. Anonymous sex partners may be persons for whom there is really no identifying information available (e.g., one-time hook-ups at bathhouses or sex clubs), or they may be persons for whom locating information is available, but very limited. For the latter group, some investigators may be more adept at utilizing that limited information to successfully locate and notify partners. There has also been speculation as to whether something akin to risk messaging fatigue among MSM is occurring, particularly among those with repeat early syphilis infections, such that reporting "anonymous partners" provides a way to avoid further interactions with the health department[97].

Another reason for decreasing contact indices may be differences stemming from telephonic vs. in-person interviews. Syphilis interviews have traditionally been conducted in-person at the convenience of the patient, using a conversational approach to gathering information, rather than regimented survey or question-and-answer formats. With increasingly limited staff and travel restrictions due to budget cuts, however, the use of in-person interviews is decreasing in favor of interviews done over the phone. The relative success of one method compared to the other in California has not been assessed.

Cases contributing to overall disease intervention indicator. Building on the above examples of County A and County B, suppose that of the ten partners initiated in each county, three were treated prophylactically and two were newly identified infections. Again, these counties would have the same preventive treatment index (0.3 contacts per interviewed case) and brought-to-treatment index (0.2 contacts per interviewed case), despite overall differences in uptake by county.

Partners initiated, partners located, and *newly identified infections or preventively treated* (i.e., partners contributing to the disease prevention indicator). As demonstrated above, elicitation and initiation of partners is not a simple one-for-one ratio of number of partners initiated to number of interviews or even to number of cases who name partners for notification. Displaying case and partner data together in this simple visualization can be a concise way for programs to portray the nuances behind partner services indices and outcome measures.

Local capacity building is necessary to sustain this intervention

All counties examined in this analysis were having challenges with contact tracing during the study interval, although two counties – Napa and Sonoma – appear to have had moderately more success. It could be that the relatively lower morbidity in those counties translates into a more manageable workload, whereas counties with higher rates of syphilis find their investigators to be overburdened and unable to keep up with the number of cases assigned. It could also be that counties with fewer specialized DIS or STD staff are struggling to keep up with syphilis investigations, in addition to managing other communicable diseases. Comparison of workforce size, dedicated STD staff, and syphilis intervention outcomes across counties could help local health departments with growing numbers of syphilis cases make a case to their city councils for increased support.

In the early days of syphilis elimination, California was equipped to send staff into struggling counties to temporarily assist with case investigations and partner follow-up. Given budget cuts and depleted workforces in the years since, that level of state support is no longer available. In its place, the STD Control Branch recently created the Local Capacity Building Unit within the Disease Intervention Section. This Unit is responsible for providing support to counties in the development, implementation, and evaluation of STD/HIV disease interventions, partner services and prevention initiatives. Collaboration between this specialized team and staff trained in program evaluation would help ensure a comprehensive, data-driven response to local needs, as well as a feedback chain to epidemiology and surveillance staff regarding challenges in the field.

Use of network data to start inter-jurisdictional dialogue around syphilis control.

Within the CPA Bay Area, 37% of components and 33% of partnerships involved persons from different counties. This relationship is hard to see on a case-by-case basis, particularly as the majority of cases reported relatively few partners. Where contact tracing for cases of tuberculosis and measles focuses on high priority groups of close contacts, such as individuals in the household, workspace, classroom or healthcare setting. It may be that sexual networks don't abide by those same rules of proximity[98,99]. If networks are increasingly crossing county lines, and there is differential success by county with respect to interviews and identifying partners, routine communication between counties about conducting investigations could help shift perceptions of disease control from being a local responsibility to a collective responsibility among counties. Regularly scheduled chalk talks between counties previously provided a forum for collective investigative brainstorming; however, this approach has fallen out of practice in recent years due to large workloads and a perceived lack of need. It may be time to re-prioritize these conversations as part of good disease intervention practice and local capacity building.

In the CPA Bay Area, the majority of syphilis cases who named partners provided information on 1-3 partners. In kind, dyads and triads made up the majority of components in each of the counties assessed, revealing a lack of connectivity among cases overall. Undoubtedly, some of the lacking connectivity was due to the 60% of cases for whom there was no information. In contrast, the largest component in San Francisco was 3,629 nodes, revealing a high degree of internal connectivity. This finding was not surprising, given Kohn et al.'s finding of a "mega-network" in San Francisco in 2013[100]. When the CPA Bay Area and San Francisco data were combined, the largest component size grew by 7.4%, suggesting that San Francisco adds connectivity to CPA Bay Area cases that is not obvious when looking at cases individually. Also, 53% of San Francisco's early syphilis cases were made up of early latent syphilis cases, who do not undergo routine interview. If their partners reside in CPA Bay Area counties where data indicate that interviews and partner yield are low, it will be very difficult to detect and stop spread of infection. Addressing this situation requires an ongoing collaborative effort between counties because ultimately, sexual networks and transmission of syphilis does not pay heed to county lines, so neither can disease control programs.

Visualization of select CPA Bay Area counties within the largest network component also allowed for assessment of HIV sero-discordant partnerships. Even with the limitation due to the lack of data on the HIV status of partners in San Francisco, using this type of network diagram in risk reduction counseling may be more compelling than numbers in communicating the benefits of pre-exposure prophylaxis (PrEP). Among HIV positive persons, 15% were identified as having had multiple syphilis infections within the study period, with several having served as bridges between counties, further emphasizing the benefits of inter-jurisdictional collaboration in disease investigation and ensuring appropriate linkage to HIV care or re-engagement in HIV care, as needed.

Asking questions that can drive program action

Results showed a high proportion of early syphilis cases in San Francisco, and lower but increasing proportions of cases in the CPA Bay Area that reported using methamphetamines in the year prior to diagnosis. While these data may be useful as a proxy measure of risk in a population, asking about risk within a shorter timeframe help produce meaningful and immediate programmatic action related to real-time localized or inter-jurisdictional syphilis networks. This touches on a broader ongoing discussion about the purpose of enhanced interviews of syphilis cases, in particular how to balance the interests of case management versus epidemiology. For example, in the early days of syphilis elimination, interview forms in California were one page in length, with only 20 questions that focused primarily on information needed to determine staging of cases; today, this same interview form has grown to nine pages with more than 100 questions that span case management, epidemiology and partner elicitation. While this structure was intended to systematize the collection of interview data and thereby inform program action, an unintended effect may be that the immediate intervention of partner elicitation and notification has been diluted by lengthy lists of questions that are not immediately relevant to case management. In the present day of increasing incidence rates of syphilis and a diminishing public health workforce, it may be time to scale back and rethink what data are needed for intervention.

Nearly half of the syphilis cases in San Francisco and just over one-third of the cases in the CPA Bay Area reported using the Internet to meet sex partners in the year prior to syphilis diagnosis. Anecdotally, the increasing proportion of anonymous sex partners is often attributed to this increase in meeting sex partners online. If more partnerships are indeed forming through online networking sites, and such partners are being classified as anonymous, there may be a compelling case for ensuring investigators are well-equipped to elicit contact information on “online partners”. In California, prior attempts to evaluate outcomes from notification of partners via online networking sites (also known as Internet Partner Notification, or IPN) was challenging due to a lack of consensus on key definitions, inconsistent protocols, poor data quality, and structural barriers that prevented counties from being able to conduct online notification themselves. Recent 2014 modifications to CalREDIE now allow for streamlined capture and evaluation of IPN activity and outcomes. To date, however, there has also been no assessment of the degree to which partnerships formed online are, in fact, facilitating transmission of syphilis across a wider geographic area. Knowing how meeting partners online contributes to sexual network connectivity across counties could inform the dialogue between health departments and websites around promotion of STD and HIV testing.

The incidence of early syphilis among younger men has been increasing in California and in major metropolitan areas in the U.S. since 2008. The findings from this analysis show such increases in the Bay Area through 2014; in addition, the increasing proportion of cases greater than 40 years may warrant a closer look at existing health department protocols for triaging incoming lab and provider reports. The standard process of prioritizing those most likely to be newly infected with syphilis is based on an initial assessment of a patient’s gender, age, and serologic titer[23]. These criteria are flexible, based on emerging trends and local epidemiology. For example, in response to increases in congenital syphilis in 2013-14, the California STD

Control Branch proposed modifications to its syphilis investigation protocol, making follow-up of all pregnant women and women of reproductive age (15-44 years), along with adolescent males, the highest priority for health department action[101]. Further analysis should be done to assess how the observed increase in syphilis among both older and younger men might reflect age mixing or relate to HIV prevention messaging, given the high frequency of HIV co-infection among syphilis cases and the possibility of HIV discordant partnerships between older and younger men.

Maintain ethical standards of collection and storage of partnership data

In the background of syphilis partner services and sexual network analysis is a primary ethical dilemma related to the lack of informed consent. The primary goal of a public health surveillance system is to prevent and control disease or injury in the population. In the case of STD Control in California, this goal is operationalized by mandating laboratories and healthcare providers to report identifying information on persons with positive test results to the health department without that person's knowledge or explicit consent[20]. This information is then stored in the surveillance database. This process violates the principle of patient autonomy, which traditional biomedical ethics considers central to a person's decision-making power in the context of the individual patient-provider relationship[102]. In the case of syphilis partner services, there is an added layer about collection and storage of information on sex partners, also without their knowledge or consent. In contrast to mandated laboratory and provider reporting, the provision of partner identifying information by infected persons to the health department has been and should continue to be voluntary. Those who are notified are never informed of the person who named them, thereby preserving confidentiality. However, the names and identifying information on partners is retained in the surveillance system, regardless of their infection status. To date, however, there has been little explicit discussion about the ethical justification for maintaining information on non-infected persons.

In 2009, Lee and Gostin proposed ten ethical guidelines for national public health data privacy standards, which are immediately relevant to the collection and storage of data related to partner services[103]. Most of these standards do not pose unique challenges to the partner services process that are not already addressed by ensuring security of public health surveillance data: implementing policy to secure the privacy of personally identifiable data; ensuring security of physical and electronic data; respecting the rights of individuals and communities, with minimal undue burden; disseminating of data to relevant stakeholders; developing data sharing agreements with other relevant public health professionals to achieve legitimate public health intent; and fostering data stewardship and public trust. However, there are a few standards that warrant a closer look in the context of sexual network detection via syphilis partner services.

Data are collected and used for a legitimate public health purpose. The initial collection of names and locating information on partners is generally considered relevant and legitimate for the prevention of transmission of infection, the question is whether it is necessary to retain that information in the surveillance database if the individual is found to be non-infected or investigators are unable to locate that individual (i.e., are unable to determine his/her final infection status). One argument might be that as a part of a sexual network at risk for acquisition and transmission of infection, the person has made his/her information relevant for detecting partnership formation on a population level, particularly if that individual ends up being named as a partner by multiple persons. Being able to discern that an individual named by, for example, three different people is, in fact, the same person can help guide risk reduction counseling for that individual, who may or may not realize he/she is positioned within a larger sexual network. Matching methods like those used in this analysis can help identify multiple records for a single individual that might not otherwise have been associated with a single person, thereby detecting more of the underlying network. However, explicit language should be developed around the public health purposes of maintaining non-infected persons' names in public health surveillance databases, if this is to be considered standard practice.

Minimum personal identifiable information necessary to conduct the activity. Similar to the above standard, DIS are trained to gather as much information as possible to help them identify and locate partners. Some of these descriptive data only relevant to partner investigation (e.g., hair color; height; distinguishing tattoos or scars) are not entered into the surveillance database; however, without explicit language detailing the public health purpose of maintaining non-infected persons' names, it is hard to know what the minimum information necessary is, once the partner investigation has been closed.

Reduce the number of persons with access to identifiable data to a minimum. This principle parallels that of minimum data necessary to conduct a public health activity, in that the minimum is not necessarily standard across all health departments. In California, each local health department is allowed access to information only on persons who are residents of their respective county. The California STD Control Branch has access to identifiable data for all persons diagnosed or investigated as residents of California, with the exception of partners residing in San Francisco and Los Angeles, due to their separate surveillance systems. Currently, California's Division of Communicable Disease Control has formed a Data Sharing Workgroup to come to consensus on the minimum information necessary for counties to be able to conduct timely follow-up and case investigation. The challenge to health departments is to assure that each person is trained to the highest level regarding data security and privacy, and to thoughtfully design electronic surveillance systems with permission structures that allow users with varying types of access to maintain the principle of minimum data necessary, while not creating barriers that actually impede timely public health intervention and cause more harm than good.

Ensure quality and accurate data that promotes objective and evidence-based policies. The results of this analysis show that when investigators are able to elicit partners for notification, 7% of partners are newly identified infections. However, the results also show large gaps in the ability of partner services to reach and benefit the broader population. In addition to local capacity building for carrying out the intervention, California must ensure that the system is flexible enough to respond quickly to emerging trends, and that it allows for the efficient capture of quality data necessary to evaluate the activity and drive health department policy.

Summary conclusions

- Fewer cases of syphilis are being interviewed, and among those interviewed, fewer cases are resulting in partner notification.

- When partners are initiated for follow-up, 7% are newly identified cases and 27% are treated prophylactically for syphilis.

- STD control programs are set up to function within artificial county boundaries; however, partnerships contributing to syphilis transmission in the Bay Area frequently cross these boundaries.

- Sexual network diagrams are routinely utilized by DIS to map connections between cases and partners locally. However, this fundamental component of syphilis control is not routinely used in traditional epidemiological reports. Reliance on absolute numbers and traditional syphilis surveillance measures provides a necessary, but incomplete picture of prevention opportunities. Similarly, partner services indices are good indicators of intervention uptake and DIS effort, but mask nuances about how many persons are naming partners and contributing to the "successful" outcomes of newly identified infections and prophylactic treatment. In addition, counties are unable to "see" networks beyond their borders; working with counties on a case-by-case investigation makes it harder to see the larger picture of connectivity. Simple visualization of networks, particularly in real-time and given advanced person-based surveillance systems with network functionality, can more readily identify networks as they emerge and mobilize investigation staff to prevent further transmission within a community.

Summary recommendations

- A syphilis partner services cascade may be a good visual tool for providing feedback on partner services delivery in counties, identifying gaps in service provision or intervention uptake, and fostering collective problem-solving.

- Comprehensive assessment of local syphilis trends should routinely include review of syphilis incidence rates, case counts, enhanced epidemiological data obtained through focused interviews, review of partner notification outcomes, and assessment of sexual networks.

- STD control programs require a shift in thinking about disease control from one of localized silos to one of collective responsibility across counties or regions.

- California should provide feedback to local health jurisdictions on both a county and regional level, foster collaboration between counties with respect to disease intervention activity, and support and/or conduct routine assessments of network connectivity across counties.

- Data that focus on characteristics of an individual's current partnerships and position within real-time networks might better serve case management and disease prevention priorities.

Conclusion

After decades of declining rates and reaching a historical low, syphilis has re-emerged in the United States, most recently driven by increasing rates in a handful of states, including California. A the hallmark of the public health approach to syphilis control in the U.S. since the 1940s has been partner notification, in which sexual partners of persons diagnosed with syphilis are identified, notified of their potential exposure, tested, and treated, as necessary. Analysis of data obtained from interviews of these early syphilis cases shows that a high proportion report having had at least one anonymous sex partner in the infectious period, calling into question whether this sacred cow of partner notification is yielding meaningful information on the underlying networks that may contribute to syphilis trends over time.

This analysis demonstrated that visualization of networks detected through syphilis partner notification efforts yields important information about underlying network connectivity that would not otherwise be obvious using traditional epidemiologic measures. In particular, results suggest that if this intervention is going to be effectively implemented, there must be a shift in thinking from localized to collective and collaborative responsibility for successful partner investigation outcomes and identification of transmission networks. This shift requires a serious reconsideration of the purpose of enhanced syphilis case interviews, the practical and ethical implications of collaborative sharing of health information among public health agencies, and the ongoing concurrent evaluation of surveillance data, partner notification outcomes, and emerging networks.

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Appendix A – Search queries by Database

Date of Search	Database	Search terms or Strategies Used (LIMITS: Humans; English)	# records found	Search Query
11/16/14	PubMed/MedLine	MeSH #1: Syphilis; Contact Tracing; Syphilis, Congenital OR MeSH #2: Syphilis, Congenital Keywords #2: partner notification; partner referral; partner services; partner disclosure *(will include those w/o MeSH: Contact Tracing)*	142	("syphilis"[MeSH Terms] AND "humans"[MeSH Terms] AND English[lang]) AND ((("contact tracing"[MeSH] AND "humans"[MeSH Terms] AND English[lang]) OR (("partner notification"[All Fields] OR "partner disclosure"[All Fields] OR "partner referral"[All Fields] OR "partner services"[All Fields]) AND "humans"[MeSH Terms] AND English[lang])) AND "humans"[MeSH Terms] AND English[lang]) AND ("humans"[MeSH Terms] AND English[lang]) OR ("syphilis, congenital"[MeSH] AND "humans"[MeSH Terms] AND English[lang]) AND ((("contact tracing"[MeSH] AND "humans"[MeSH Terms] AND English[lang]) OR (("partner notification"[All Fields] OR "partner disclosure"[All Fields] OR "partner referral"[All Fields] OR "partner services"[All Fields]) AND "humans"[MeSH Terms] AND English[lang])) AND "humans"[MeSH Terms] AND English[lang]) AND ("humans"[MeSH Terms] AND English[lang])
11/16/14	Scopus	Article Title, Abstract, Keywords: Syphilis; Contact Tracing; partner notification; partner referral; partner services; partner disclosure	126	((TITLE-ABS-KEY("contact tracing")) OR (TITLE-ABS-KEY("partner notification" OR "partner referral" OR "partner disclosure" OR "partner services"))) AND (TITLE-ABS-KEY(syphilis)) AND (LIMIT-TO (AFFILCOUNTRY, "United States")) AND (LIMIT-TO(LANGUAGE, "English")) AND (LIMIT-TO(SRCTYPE, "j"))
11/16/14	Web of Science	Keywords: Syphilis; Congenital syphilis; Contact	117	((TS=("congenital syphilis") AND TS=(("contact

	tracing; partner services; partner disclosure; partner notification; partner referral	tracing" OR "partner notification" OR "partner services" OR "partner referral" OR "partner disclosure")))*AND* LANGUAGE: (English)) OR (TOPIC: (syphilis) AND TOPIC: (("contact tracing" OR "partner notification" OR "partner services" OR "partner referral" OR "partner disclosure")) Refined by: COUNTRIES/TERRITORIES: (USA) AND LANGUAGES: (ENGLISH))

Appendix B – Map of California Regions

Northern	**Sacramento**	**Bay Area**	**Central Coast**	**Central Inland**	**Southern**
Butte	El Dorado	Alameda	Monterey	Alpine	Imperial
Colusa	Placer	Berkeley	San Luis Obispo	Amador	Long Beach
Del Norte	Sacramento	Contra Costa	Santa Barbara	Calaveras	Orange
Glenn	Yolo	Marin	Santa Cruz	Fresno	Pasadena
Humboldt		Napa	Ventura	Inyo	Riverside
Lake		San Mateo		Kern	San Bernardino
Lassen		Santa Clara		Kings	San Diego
Mendocino		Solano		Madera	
Modoc		Sonoma		Mariposa	
Nevada				Merced	
Plumas				Mono	
Shasta				San Benito	
Sierra				San Joaquin	
Siskiyou				Stanislaus	
Sutter				Tulare	
Tehama				Tuolumne	
Trinity					
Yuba					

Note: Long Beach and Pasadena are located in Los Angeles County; however, for the purposes of STD Control, these two jurisdictions are considered part of the Southern Region in the California Project Area.