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Opt-out, routine emergency department syphilis screening as a novel intervention in at-risk populations

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Abstract

Background: With syphilis rates rising rapidly in the United States, novel means of reaching high-risk populations for screening and treatment are needed. Building on successful models for emergency department (ED) HIV screening, a routine opt-out syphilis screening program was implemented in a large, urban, tertiary care hospital ED in May 2019. This study aims to assess the prevalence of syphilis in this population and to evaluate the routine, opt-out syphilis screening model.

Methods: A retrospective chart review was performed of all patients screened for syphilis in the ED from June through December 2019. Demographic information, HIV status, chief complaint, and follow up visits were examined.

Results: During the study period, 9198 people ages 18 to 64 were screened for syphilis. Of these, 97 (1.1%) had presumed active syphilis infection (PAI), 354 (3.8%) were presumed not to have active syphilis, and 8747 (95.1%) were negative for infection. PAI were more likely to be male (67%, aOR 3.5, 95% CI (2.3, 5.3), p<0.001), though the percentage of women was considerably higher than the nationally-reported rate, and the majority were non-Hispanic black (93.8%). Among PAI, 23 (23.7%) were HIV positive. Only 18.6% of PAI presented with complaints related to sexually transmitted infections (STIs).

Conclusions: Syphilis rates in this community are very high, and many infections were found in populations traditionally considered lower risk by demographic or presenting complaint, indicating that universal screening is needed. Routine ED syphilis screening in high-prevalence communities will be critical to addressing the syphilis epidemic.

Short Summary:

A study of universal syphilis screening in an urban emergency department found high rates of syphilis (1.1% of population screened). Most infections were found in patients presenting for non-STI complaints.

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Keywords

syphilis; emergency department; screening; opt-out

Introduction

Syphilis infections in the United States have been steadily rising for the past two decades. The number of new cases in 2018 was the highest recorded since 1991, with rates of primary and secondary (P&S) syphilis increasing by 71% in the past five years. The number of congenital syphilis cases has surged by 185% during the same period[1]. Lack of widespread and easily available syphilis screening is a contributing factor to the current syphilis epidemic[2]. Large urban centers experience high rates of syphilis and other sexually transmitted infections (STIs). In 2018, the rate of new P&S syphilis in Chicago was 32.5 per 100,000 people, more than four times the national average[3]. The case burden disproportionately affects some of the city's most vulnerable communities, localized to geographic areas with historic economic hardship and disparate access to primary care.

While routine syphilis screening has traditionally been within the domain of outpatient clinics, many patients in these areas are more likely to rely on the emergency department (ED) for both routine and acute care[4,5]. Therefore, syphilis screening for these populations may not occur if not performed in the ED setting. However, patients evaluated in the ED are generally only tested for syphilis if they have symptoms of syphilis or other identified risk factors such as symptoms of another sexually transmitted infection, while syphilis in many cases remains asymptomatic throughout the majority of the disease course. We hypothesize that an urban ED population is likely to have a high prevalence of asymptomatic syphilis and would thus benefit from a routine, opt-out screening model, similar to the widely-accepted model for HIV screening. In May 2019, a universal, opt-out syphilis screening program was initiated in the ED of a large, urban, tertiary care hospital in Chicago that completes over 76,000 adult ED visits annually. This hospital is located on the south side of Chicago, near some of the most socioeconomically disadvantaged communities in the city, although as an academic center, it draws patients from all over the city and beyond. This pilot program was linked to an established and well-accepted universal HIV screening program in the ED, utilizing existing infrastructure to maximize patient and provider acceptance. Through partnership with infectious diseases providers, all patients screened positive for syphilis were either contacted directly or reviewed with the local public health department to determine if serofast. Follow up was arranged for those with presumed active infection (PAI). At this follow-up visit, patients received comprehensive sexual health care including further STI screening if not performed in the ED, HIV/STI prevention counseling, information about HIV pre-exposure prophylaxis (PrEP) with same-day start if desired, as well as linkage to longitudinal PrEP care, primary care, and prenatal care as needed. Seven months after the implementation of the pilot program, standardized electronic health records (EHR) were reviewed to examine rates of syphilis screening, diagnosis, and linkage to treatment and other sexual health services for patients seen in our ED.

Materials and Methods

Study setting and population.

This study took place in the ED of a large, urban, tertiary care center in Chicago that sees only patients age 18 and older. Because the screening model utilized existing EHR infrastructure for HIV screening, patients were flagged for HIV and syphilis screening if they met the following criteria: age between 18 and 64, no documented diagnosis of HIV, and no record of HIV screening within the past 12 months (based on CDC guidelines for HIV screening[6]). People living with HIV (PLWH) were thus theoretically excluded from syphilis screening, but in actuality many were included because their HIV diagnosis was not recorded in the EHR. Eligibility for screening was independent of race, gender, sexual orientation, or presenting complaint. If eligible, a prompt appeared as a pop-up alert in the patients' charts directing the nurse or clinician to order both HIV and syphilis screening tests. The alert continued to appear until the orders were placed or someone indicated the patient was not a candidate or had declined testing. Patients were considered not to be candidates for testing if they were critically ill, psychiatrically unstable, or for any reason unable to verbally opt out of testing. While staff was directed to make testing available for all eligible patients, ordering of screening tests was ultimately dependent on human interaction with the EHR.

A retrospective chart review was performed of all patients between the ages of 18 and 64 who were screened for syphilis in the ED between June 1, 2019 and December 31, 2019. This study was approved by the University of Chicago Institutional Review Board.

Outcome measures.

The primary outcome of interest for this study was presumed active infection as defined by syphilis serology and patient history. Syphilis screening was performed using the reverse sequence algorithm. Initial testing was via qualitative multiplex flow immunoassay for syphilis IgG, which, if positive, reflexed to rapid plasma reagin (RPR) testing. If there was a discrepancy between IgG and RPR results, a second treponemal test, the T. pallidum particle agglutination assay (TP-PA) was performed. This multi-step process allows for detection of early and latent infection that may be missed by traditional RPR testing particularly in areas of high syphilis prevalence[7].

An infectious diseases physician or nurse practitioner contacted patients who required further history (i.e. not known in the EHR to be serofast), evaluation and/or treatment. Patients were contacted by phone, email, and text message; registered letters were sent for those unable to be reached through these means. For patients unable to be reached or unsure of any prior infection or treatment, collateral syphilis history was obtained from the local public health department through weekly phone calls. Syphilis test results were generally not available during the ED stay, so patients were categorized as PAI after subsequent contact.

Patients were defined as PAI in multiple ways. Any patient who met clinical criteria for P&S syphilis or neurosyphilis as defined by the 2015 CDC STD Treatment Guidelines[8] was classified as PAI. After verification with the local public health department, patients with a four-fold increase in RPR titer from prior screening were defined as PAI as well as patients

without documented history of past positive testing and/or treatment. Any patient admitted to the hospital was considered PAI if the inpatient team deemed syphilis treatment necessary. Lastly, any patient with an RPR titer greater than or equal to 1:8 who was unable to be contacted and for whom no health department records were available was also considered as PAI.

Patients with non-reactive initial syphilis IgG screens were considered true negatives. Those that had a positive RPR or TP-PA but did not meet above criteria for PAI were considered not presumed active infections (NPAI).

Covariates.

Data was extracted regarding age, sex, race/ethnicity, and ICD-10 codes associated with the ED visit for all subjects. For those with PAI, additional data points were extracted, including HIV status, pregnancy status, ED visit chief complaint, testing for other STIs during the same visit, follow-up and treatment course.

The recorded ICD-10 codes (Table 1) were used to classify each visit as STI-related or not STI-related. One STI-related code (Z11.3 Encounter for screening for infections with a predominantly sexual mode of transmission) was added to many of the charts as part of the routine screening, even though the patient did not present with STI-related complaints. In order to provide both an upper and lower limit for assessment of STI-related visits, this information is presented as a range (including Z11.3 - excluding Z11.3). For a more accurate analysis of the subset of patients with PAI, a chart review was performed to determine if the patient had a presenting STI-related complaint, defined as any complaint relating to the pelvis or genitalia or a skin finding that the provider documented as suspicious for STI.

Data Analysis.

Data were analyzed using descriptive statistics (percentages, means, standard deviations) to describe the distribution of patient characteristics in the study sample. Chi-squared tests were used to detect differences in populations, and logistic regression was used to generate odds ratios, adjusted odds ratios, and corresponding confidence intervals to examine factors associated with PAI. All data analyses were performed using R 3.4.

Results

During the study period, the EHR flagged 25,167 unique patients as eligible for screening. In total, 9198 patients (approximately 36.0%) of eligible patients ages 18 through 64 were screened for syphilis during this time. The EHR does not provide sufficient data to determine the reasons a potentially-eligible patient was not screened, however the sex, age, and race distributions of patients screened were very similar to those of patients not screened (Table 2). Of those screened, 97 (1.1%) had PAI, 354 (3.8%) were NPAI, and 8747 (95.1%) screened negative.

The screened population was 38% male; 87% were non-Hispanic black (NHB) and 6% non-Hispanic white (NHW). The mean age was 38, with a relatively even distribution among all age groups. As determined by ICD-10 code, 775–2049 (8.4–22.3%) of screened patients

presented for an STI-related reason. The upper end of the range represents all STI-related ICD codes, while the lower end excludes code Z11.3.

Of 97 patients with PAI (Tables 3 and 4), 65 (67%) were male (aOR 3.5, 95% CI (2.3, 5.3), p<0.001)), 91 (93.8%) were NHB (aOR 14.2, 95% CI (0.9, 222.2), p=0.06).), 3 (3.1%) were Latinx, and 3 (3.1%) reported unknown or multiple races. The mean age was 38.6 years, with a range of 19 to 64. Infections were distributed evenly among age groups from 25 to 49 (20% in each age group 25–29, 30–39, and 40–49), with somewhat fewer in the lowest age group (13% in ages 18–24) and more in the highest age group (26% in ages 50–64). There were 2 pregnant women (9.1% of women under age 50) and 3 (13.6%) for whom no pregnancy test was ordered. All these women were HIV negative.

Of those with PAI, 18 (18.6%) presented with an STI-related chief complaint. Prevalence of PAI was similar regardless of symptoms, with an asymptomatic prevalence of 1.0% and a symptomatic prevalence of 1.4%. Only 39 (40.2%) patients with PAI were tested for other STIs during the original ED encounter, ensuing inpatient stay or at a follow-up clinic or ED visit for positive syphilis testing. Of these, 13 (33.3%) tested positive for at least one other STI. Over half (7) of these did not present with an STI-related complaint. Infections diagnosed included gonorrhea (2), chlamydia (7), both gonorrhea and chlamydia (1), trichomonas (2) and both chlamydia and trichomonas (1). In total, 23 (23.7%) patients with PAI had HIV, 3 of whom (13%, or 3% of the entire PAI group) were newly diagnosed with HIV at the time of their syphilis diagnosis.

In terms of treatment, 35 (36.1%) of those with PAI were admitted to the hospital and treated. Among those patients admitted to the hospital, 3 (8.6% of patients admitted) were believed to have neurosyphilis, and their syphilis diagnosis was directly related to the reason for admission (altered mental status). All these patients were HIV-negative. It is unclear from chart review if syphilis testing would have been performed for admitted patients, had the routine screening not been in place. One patient was believed to have ocular syphilis, though vision complaints were not the main reason for admission. The others were admitted for unrelated reasons and treated when screening tests returned positive. Of those not admitted to the hospital, 29 (29.9%) made appointments to follow up at an STI clinic, 11 (11.3%) had treatment initiated in the ED, although it is unclear how many followed up for an appropriate course of treatment, 10 (10.3%) stated they would follow up elsewhere or with their primary care provider, and 12 (12.4%) were unable to be contacted.

For the subgroup of HIV-negative PAI, 44 (59.5%) were male, and 69 (93.2%) were NHB. The average age was 40.1 years, with a range of 19–64, and 16 (21.6%) presented with STI-related complaints. Of HIV-negative patients or those who had no pre-existing diagnosis of HIV, 32 (41.5%) were tested for other STIs, of which 11 (34.3% of those tested) were positive. In comparison, 7 (35.0%) known PLWH were tested for other STIs, of which 2 (28.6% of those tested) were positive. Of HIV-negative patients with PAI, 25 (33.7%) were admitted to the hospital, including the 3 with neurosyphilis referenced above, 22 (29.7%) made appointments to follow up in an affiliated STI clinic, 10 (13.5%) were treated in the ED, 7 (9.5%) stated they would follow up elsewhere, and 10 (13.5%) were unable to be contacted.

Discussion

High rates of undiagnosed syphilis were observed in this sample of patients participating in universal, opt-out syphilis testing. The identified prevalence of 1.1% is an order of magnitude higher than the CDC recommended routine opt-out screening threshold for HIV, another high-morbidity disease, which is at least 0.1% prevalence of undiagnosed infection[6]. The current reported rate of P&S syphilis in the local area is 0.02–0.13%[3]. While some of the PAI cases may be latent rather than P&S syphilis, the difference in these numbers implies there are high rates of undiagnosed syphilis in our population, partly due to lack of widespread screening. While this study examines only one geographic area, results would likely be generalizable to other urban communities, though more study is needed.

There are currently no CDC guidelines for syphilis screening outside of the pregnant, HIV positive and men who have sex with men (MSM) populations[8]. This study found high infection rates outside of these populations and across the age span. Women are a population of special concern, especially given the recent increase in congenital syphilis cases. Our study found 33% of cases in women, more than double the national rate of 14% of cases[1]. High syphilis rates in women when screening is performed regardless of risk factors suggest that targeted screening may miss cases in women, possibly because they are not traditionally considered a high-risk group.

Importantly, a large percentage of those testing positive did not present with complaints that would have triggered testing based on traditional risk-based screening recommendations, and prevalence rates were similar between symptomatic and asymptomatic populations. Although this study was not specifically designed to evaluate differences in testing approach, the findings imply that in populations that are at increased risk, universal screening should be considered, as many PAI would have been missed with targeted screening algorithms. Additionally, opt-out testing has been shown to result in much higher rates of testing than opt-in approaches[9], so a universal, opt-out approach is likely to reach the widest population.

While EDs have been proposed as a key location for STI control interventions[10] due to a presumed high rate of asymptomatic STIs, to our knowledge this is the first study to examine universal syphilis screening in the emergency department setting. Several earlier studies have examined a universal screening strategy for gonorrhea and chlamydia, finding rates of asymptomatic STIs as high as 10%[11,12] in adolescents and 15%[13,14] in adults. Furthermore, in the adolescent population universal screening for STIs has been shown to be highly acceptable[15,16]. One previous study during a local outbreak of syphilis found rates of 2–4% in patients without STI-related complaints[17], and similar rates were found during a small study that actively enrolled ED patients after determining behavioral risk factors[18].

In-depth risk stratification through assessment of sexual history is rarely possible within the time constraints of the ED setting. Screening asymptomatic patients allows for identification of patients at high risk for HIV and other bacterial STIs who would otherwise not have been identified as at-risk. Through partnerships with STI providers, these ED screenings present an opportunity for further STI and HIV education, prevention and care. In the program described here, attempts were made to contact all discharged patients and, when possible,

they were treated in one of several partnering sexual health/STI clinics. Through this visit, linkage to primary and obstetric care was provided. While relatively few patients diagnosed with syphilis were pregnant women, performing universal syphilis screening, particularly in a population with low utilization of outpatient prenatal care, could be instrumental in averting cases of congenital syphilis and linking these pregnant women with appropriate prenatal care.

Interestingly, a third of the patients with PAI who were tested for other bacterial STIs were found to be infected with at least one other STI, and three had previously-undiagnosed HIV. Given that half of these patients had non-STI related complaints, this suggests that a syphilis diagnosis can also lead to diagnoses of other asymptomatic STIs. Furthermore, 60% of patients with PAI were not tested for other STIs. This lack of testing resulted partly from difficulties contacting patients for follow up and because some followed up outside of our system. Nevertheless, this likely represents a major missed opportunity for intervention on other bacterial STIs, given the high positivity rate among those who were tested, and suggests a need for more provider education.

Many questions remain to be answered. The optimal frequency of screening for syphilis is unknown, particularly in an ED environment. Because this program was tied to HIV screening, both syphilis and HIV screening are prompted annually. Commonly used guidelines recommend determining screening frequency based on risk factors[19], but identification of risk factors can be challenging in the ED. Our study excluded patients aged 65 and above, and it is possible that this population also has high rates of syphilis. It could also be argued that patients who report attending HIV or prenatal care do not need ED screening, as they should be tested for syphilis in the outpatient context, however, many HIV practitioners do not provide adequate sexual health services[20,21], requiring several STI interventions to be deployed. Studies have also shown that many women who attend prenatal care are not adequately screened for syphilis[22]. Our study found many examples of PLWH with untreated syphilis infection. Some of these patients had lapsed in their outpatient care, but others were on anti-retroviral treatment and attending appointments. The fact that 20% of our PAI population, who were screened due to lack of previous HIV diagnosis data in the EHR, had known HIV suggests that ED screening for syphilis is worthwhile even in PLWH.

There are several barriers to implementing syphilis screening in the ED. Concerns likely parallel those cited in HIV screening programs, such as insufficient time, inadequate knowledge/training, lack of patient acceptance, and concerns about follow-up care[23,24]. In this program, we utilized automated ordering reminders for eligible patients to minimize provider time and effort, and we built upon existing HIV screening infrastructure to maximize acceptance of the program. All members of the care team shared responsibility for ordering screening tests, and ongoing education about the screening program was provided. Although the number of patients screened was lower than the number of eligible patients who visited the ED, likely due in large part to alert fatigue and lack of staff engagement with the screening program, our screening rates are similar to and even exceed reported numbers for other ED HIV screening programs[25,26]. Because of limitations of the EHR, however, we are not able to report exactly how many patients opted out as opposed to being excluded due to acuity or mental status or were simply not offered testing. Through a partnership with the

STI care team, there was timely follow up for all patients screening positive, which relieved the burden on the ED team and ensured comprehensive STI care at time of follow up. While some patients were unable to be contacted, our team utilized multiple modes of communication to maximize the chance of contacting patients, a model that is widely accepted in ED HIV screening programs[27]. Point of care testing could potentially represent another solution to the difficulty of contacting patients after ED discharge, and is already in use in some low-resource settings[28]. Multiple testing modalities represent an additional concern for syphilis screening programs. In this case, a reverse sequence testing algorithm was used, which may be the optimal solution for testing on a large scale, such as through a universal screening program, as it minimizes cost and lab resource utilization.

In summary, ED screening reaches populations who traditionally underutilize the health care system, and these are some of the communities most at risk for syphilis and other STIs. This study found a 1.1% prevalence of untreated active syphilis, including a much larger percentage of cases among women than expected based on national reports, a majority of whom presented with non-STI related complaints, suggesting that targeting screening to only those deemed “high-risk” by behavior or symptoms will miss a large portion of cases. ED screening has the potential to identify many asymptomatic patients who otherwise might never have received a diagnosis, interrupting the cycle of transmission, and preventing long-term complications. Through partnerships with outpatient providers, syphilis diagnosis in the ED can also lead to HIV prevention, improved sexual health, and linkage to primary and prenatal care. Routine, universal, opt-out screening for syphilis in the ED should be considered for all adult age groups in high-prevalence populations.

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Table 1.

STI-related ICD-10 codes

Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission
A63	Other predominantly sexually transmitted diseases, not elsewhere classified
A64	Unspecified sexually transmitted disease
N34	Urethritis and urethral syndrome
N89.8	Other specified noninflammatory disorders of vagina
R10.2	Pelvic and perineal pain
A60	Anogenital herpesviral [herpes simplex] infections
N76	Other inflammation of vagina and vulva
N73	Other female pelvic inflammatory diseases
N72	Inflammatory disease of cervix uteri
N48	Other disorders of penis
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission

Table 2.

Patients age 18–64 eligible for syphilis screening in the emergency department from June through December 2019

	Patients screened for syphilis	Eligible patients not screened
	Number (%)	Number (%)
	9198 (100)	15969 (100)
Sex		
Male	3514 (38.2)	6666 (41.7)
Female	5684 (61.8)	9303 (58.3)
Race/ethnicity		
Non-Hispanic Black	8005 (87.0)	12810 (80.2)
Non-Hispanic White	537 (5.8)	1416 (8.9)
Latinx	371 (4.0)	726 (4.5)
Other or Unknown	285 (3.1)	1017 (6.4)
Age		
18–24	1776 (19.3)	3023 (18.9)
25–29	1444 (15.7)	2324 (14.6)
30–39	1960 (21.3)	3429 (21.5)
40–49	1619 (17.6)	2792 (17.5)
50–64	2399 (26.1)	4401 (27.6)
ICD-10 Codes *		
All STI-related	2049 (22.3)	108 (6.8)
STI-related except Z11.3	775 (8.4)	106 (6.6)
Not STI-related	7149 (77.7)	15861 (99.3)

*All STI-related includes any chart associated with at least one of the codes in Table 1. STI-related except Z11.3 excludes those charts that had only code Z11.3 associated with them. This was done because some charts had this code associated as part of routine screening without an actual STI-related complaint.

Table 3.

Demographic information by group: presumed active infection, not presumed active infection, and true negative, among patients ages 18–64 screened for syphilis in the emergency department

	PAI Number (%) 97 (100)	NPAI Number (%) 354 (100)	True Negative Number (%) 8747 (100)	Chi Squared P value
Sex				
Male	65 (67.0)	154 (43.5)	3295 (37.7)	<0.0001
Female	32 (33.0)	200 (56.5)	5452 (62.3)	
Race/ethnicity				
Non-Hispanic Black	91 (93.8)	342 (96.3)	7573 (86.6)	<0.0001
Non-Hispanic White	0 (0.0)	1 (0.3)	536 (6.1)	
Latinx	3 (3.1)	2 (0.5)	366 (4.2)	
Other or Unknown	3 (3.1)	10 (2.8)	272 (3.1)	
Age				
17–24	13 (13.4)	17 (4.8)	1746 (20.0)	<0.0001
25–29	19 (19.6)	31 (8.8)	1394 (15.9)	
30–39	20 (20.6)	45 (12.7)	1895 (21.7)	
40–49	20 (20.6)	82 (23.2)	1517 (17.3)	
50–64	25 (25.8)	179 (50.6)	2195 (25.1)	
ICD-10 Codes				
All STI-related	27 (27.8)	69 (19.5)	1953 (22.3)	N/A
STI-related except Z11.3	11 (11.3)	23 (6.5)	741 (8.5)	
Not STI-related	70 (72.2)	285 (80.5)	6794 (77.7)	

Table 4.

Odds ratios and adjusted odds ratios for demographic characteristics of patients with presumed active syphilis infection compared to true negatives

	Odds Ratios (95% CI)	P-values	Adjusted odds ratios (95% CI)	P-values
Sex				
Male	3.3 (2.2, 5.1)	<0.001	3.5 (2.3, 5.3)	<0.001
Female	1.0 (ref)		1.0 (ref)	
Race/ethnicity *				
Non-Hispanic Black	1.0 (ref)		1.0 (ref)	
Latinx	0.8 (0.3, 2.3)	0.67	0.7 (0.3, 2.2)	0.06
Other or Unknown	1.1 (0.4, 3.1)	0.91	1.0 (0.3, 2.8)	0.59
Non-Hispanic White	0.1 (0.0, 1.3)	0.07	0.1 (0.00, 1.1)	0.94
Age				
17–24	0.7 (0.4, 1.4)	0.30	0.7 (0.4, 1.5)	0.39
25–29	1.3 (0.7, 2.3)	0.44	1.3 (0.7, 2.4)	0.42
30–39	1.0 (0.5, 1.8)	0.94	1.0 (0.6, 1.9)	0.93
40–49	1.2 (0.7, 2.2)	0.57	1.2 (0.7, 2.2)	0.52
50–64	1.0 (ref)		1.0 (ref)	
ICD-10 codes				
All STI-related	1.3 (0.7, 2.2)	0.37	1.5 (0.9, 2.3)	0.09
Not STI-related	1.0 (ref)		1.0 (ref)	

* Firth logistic regression used