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Notifying partners of patients with early syphilis in Madagascar: case-finding effectiveness and public health implications

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Summary

OBJECTIVE—To evaluate the case-finding effectiveness of a clinic-based partner notification effort for early syphilis in Madagascar.

METHODS—We asked index cases who had proven early syphilis to identify and provide contact information of recent sex partners (in the past 3, 6, and 12 months for primary, secondary, and early latent syphilis, respectively). Named sex partners were contacted by index cases (patient notification) or, if approved by the index case, clinic staff members (provider notification); notified of their potential exposure to syphilis; and asked to come to the clinic for evaluation. We assessed case-finding effectiveness and calculated the ‘brought-to-treatment’ index (number of newly-diagnosed syphilis cases per number of index cases interviewed).

RESULTS—Of 565 index cases, 534 reported recent sex with at least one sex partner. A total of 3167 sex partners were reported, of whom 276 were contactable (9% of 3167). Providers notified 76% and cases notified 24% of these partners. 270 partners were contacted (98% of 276), and of these, 199 presented to the clinic for evaluation (74% of 270). A total of 99 partners tested positive for syphilis and received treatment (50% of 199). The ‘brought-to-treatment’ index was 0.18 (99 diagnoses per 565 index cases).

CONCLUSION—Partner notification was possible in this setting, resulting in treatment of syphilis-infected individuals who otherwise would likely have remained untreated. However, given <10% of the partners reported by index cases were contactable; the results highlight the limitations of partner notification and the need for additional sexually transmitted infection control strategies.

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Keywords

partner notification; provider notification; syphilis; sexually transmitted infections; Madagascar; resource-poor

Introduction

Sexually transmitted infections (STIs) constitute a significant public health concern globally, and resource-poor settings experience a disproportionate burden of infection (WHO 2001; Low *et al.* 2006). Partner notification is an important component of STI control, which involves questioning STI patients to elicit names and details of recent sex partners; identifying and notifying partners of potential exposure to infection; and providing diagnosis and, as needed, treatment of infected partners (Mathews *et al.* 2007). Partner notification has contributed meaningfully to case finding (Brewer 2005) and has the potential to reduce STI-related morbidity among partners, risk of reinfection among index patients, and community-level STI prevalence by identifying asymptomatic disease and interrupting transmission within sexual networks (Rothenberg 2002).

Evidence suggests that partner notification is most effective when clinicians perform the contact tracing or aid the index patient in the process (provider notification) (Mathews *et al.* 2007). In resource-poor settings, while clinicians may encourage index patients to notify sex partners (patient notification), they generally remain uninvolved in the contact tracing effort because of inadequate resources. There has been limited documentation of the effectiveness of partner notification in resource-poor settings, including efforts that involve both patient and provider notification. Research is needed to evaluate the case-finding effectiveness of patient and provider notification in resource-poor settings and to identify which partner notification stage—elicitation of partners' names and contact information, location and notification of partners, or presentation of partners to the clinic for medical evaluation—is in greatest need of improvement.

We assessed a clinic-based partner notification effort for early syphilis in Madagascar, where very high syphilis levels have been measured in a number of populations including among women attending STI clinics, sex workers (range: 13–31%) (Behets *et al.* 1996, 1999, 2001, 2003), and pregnant women (12%) (Behets *et al.* 1996) in urban areas and among men in rural areas (10% and 16%) (Leutscher *et al.* 2003). Currently in Madagascar, there is no law mandating the report of infectious syphilis cases to the Ministry of Health or notification of partners of patients with infectious syphilis. However, according to National STI Treatment Guidelines, health care providers are encouraged to counsel their STI patients so that patients know that partners should be notified, medically evaluated, and treated if indicated, both for the sake of the partner and in the interest of avoiding re-infection among patients. Because resources for STI control are limited in Madagascar, partner notification efforts generally involve patient notification while notification by providers is not routinely offered. Using partner notification and treatment data collected as part of a randomized control trial (RCT) on early syphilis treatment, we measured the case-finding effectiveness of a partner

notification strategy that involved partner and provider notification, and we evaluated the relative effectiveness of provider *vs.* patient notification.

Methods

Participants

The main trial methods have been described in detail (Hook *et al.* 2010). Briefly, the trial was carried out at public health clinics located in the capital city Antananarivo and the coastal port cities Mahajanga and Toamasina. We recruited participants through advertisements on the radio and through community outreach. Advertisements encouraged persons with symptoms of genital ulcer disease to come to the study clinics for care. Health care providers in the study area also referred potential participants to study clinics. At the study clinics, potential participants were invited to be screened for potential participation in a research study.

At the screening visit, study staff evaluated eligibility for participation in the trial; conducted a physical exam; collected blood specimens for rapid plasma reagin (RPR) testing; collected samples from genital ulcers or condylomata lata, as clinically indicated, for darkfield microscopy; tested for pregnancy; and collected information on sociodemographic characteristics and recent sex partners.

Individuals diagnosed with early syphilis who had laboratory evidence of syphilis were recruited for the partner notification effort. Specifically, individuals diagnosed with primary syphilis had darkfield-positive genital ulcers; those diagnosed with secondary syphilis had condylomata lata or skin rash or darkfield-positive lesions; and individuals were diagnosed with early latent syphilis if they had a current RPR-positive test result and had received an RPR-negative test in the past 12 months or had sex with a partner who was infected in the past 12 months with early syphilis. Patients with syphilis were treated following national treatment guidelines with benzathine penicillin, unless they were eligible for recruitment in the trial in which case they were randomized to either benzathine penicillin or azithromycin (one 2 g oral dose). Syphilis screening and care were provided at no cost to all study participants, as a benefit of study participation.

Planning and assessment of partner notification

All patients who were diagnosed with early syphilis received counselling from a trained social worker or a clinician who emphasized the importance of notifying recent sex partners and referring them to the clinic for medical evaluation. To improve the likelihood that partner notification efforts reached all partners who were potentially exposed to syphilis infection, staff members asked primary syphilis cases to report on all sex partners in the past 3 months, secondary syphilis cases to report on all sex partners in the past 6 months, and early latent syphilis cases to report on all sex partners in the past 12 months. Detailed contact information was obtained for all contactable partners. Clinic staff inquired whether patients wished to inform partners of potential syphilis exposure on their own (patient notification), or whether they wanted clinic staff to contact their sex partners (provider notification). Among patients reporting the desire to notify their partners, clinic staff asked

for permission to notify the partner if the partner did not present to the clinic (conditional provider notification). If provider or conditional provider notification was requested, clinic staff obtained partners' names and home addresses and made home visits to perform the partner notification as needed (in the case of conditional provider notification, staff conducted home visits if named partners did not present to the clinic within 1 week of the date when the index patient was interviewed). During the visit, clinic staff informed the partners that they had potentially been exposed to syphilis and asked the partners to come to the clinic for evaluation. If on the first attempt the partner was not available, clinic staff returned and re-attempted the partner notification visit, at least three times, unless information was obtained to indicate that contacting the partner was not possible.

We assessed the numbers of contactable partners who were subsequently contacted using patient, provider, or conditional provider notification. In cases of provider notification, providers recorded whether a contactable partner was contacted in the clinic records. In cases of patient notification, study staff questioned patients about whether a contactable partner was contacted; this was carried out by questioning patients during a follow-up visit, among those who were RCT participants, or by locating and questioning patients in the community, among those who were not RCT participants.

Measures

The primary outcomes included the total number of recent sex partners reported by index syphilis cases and, among these, the number of partners who were contactable, who were contacted by the patient or the provider, who presented to the clinic and received medical evaluation, who were found to be infected with syphilis determined by a reactive RPR during the medical evaluation, and who received treatment. We calculated the 'brought-to-treatment index,' defined as the number of newly diagnosed and treated patients with syphilis per number of index cases interviewed during the partner notification effort (Iskrant & Kahn 1948; Brewer 2005).

Data analysis

All analyses were conducted in Stata Version 9.1 (Stata Corp., College Station, TX, USA). We described background characteristics of index syphilis cases at the time of screening. We described results of the partner notification process, including the number of partners reported by index syphilis cases; the number and percentage of partners who were contactable, among all reported partners; the number and percentage of partners contacted by the patient or the provider, among all contactable partners; the number and percentage of partners who presented to the clinic and received medical evaluation, among all contacted partners; and the number and percentage of partners who were infected with syphilis and received treatment, among all partners who presented to the clinic for medical evaluation. We also examined whether the partner notification process differed depending on whether the index case was male *vs.* female and reported gender differences when observed.

Among sex partners who were successfully contacted and notified of their potential syphilis exposure, we assessed whether the likelihood of coming to the clinic for medical evaluation differed by background factors including characteristics of the referring index syphilis case

(gender, age, number of recent partners reported at screening, and whether infected with primary, secondary, or early latent syphilis) or whether the partner was contacted via provider or partner notification. Specifically, we estimated unadjusted and adjusted prevalence ratios (PR) and 95% confidence intervals (CIs) for the associations between background factors and presentation of contacted partners to the clinic using generalized estimating equations (GEE) to account for repeated measurements. Because each index syphilis case could name more than one sex partner, each syphilis case served as his or her own cluster (Zeger & Liang 1986). We specified a log link, a Poisson distribution, an exchangeable correlation matrix structure, and a robust variance estimator to correct for overestimation of the error term resulting from use of Poisson regression with binomial data (Zocchetti *et al.* 1995; McNutt *et al.* 2003; Zou 2004). Adjusted models examined the association between each background factor and presentation to the clinic, adjusting for all factors of interest.

Ethical approval

The ethical review boards of the Ministry of Public Health, Antananarivo, Madagascar; the University of North Carolina at Chapel Hill; the University of Washington; and the University of Alabama at Birmingham approved the research. The trial is registered at Clinical-Trials.gov (Identifier #: NCT00031499).

Results

Participant characteristics

Of 565 index cases at the three sites, 52% were men (Table 1). Men were on average slightly older (25 years) than women (23 years). Thirty-six per cent of index cases were diagnosed with primary syphilis, 52% with secondary syphilis, and 12% with early latent syphilis.

Evaluation of partner notification

Most index cases reported having had sex during the time they were infected with syphilis: 534 of 565 index cases reported having at least one recent sex partner (95% of all index cases) (Figure 1, Table 1). A total of 3167 sex partners were reported by the 534 index cases; among them, 41% reported having had one recent partner, 20% reported two partners, 19% reported between three and nine partners, and 14% reported 10 or more partners. Index cases reported a mean of 5.6 partners. Women, on average, reported higher numbers of recent partners (eight partners) than men (three partners).

Of the 534 index cases who reported at least one sex partner, 284 were unable to provide contact information for any recent sex partners (53% of 534 index cases) (Figure 1). Just over half of both male and female index patients reported that no partner was contactable. Index cases who reported having the highest recent partnership levels (three or more recent partners) were more likely to report that no recent partner was contactable (60%) than those with two recent partners (42%) or one recent partner (53%). A total of 250 cases reported having at least one contactable partner, 90% of whom reported one contactable partner and 10% of whom reported two or more contactable partners. Of the 3167 partners reported by index cases, a total of 276 were contactable (9% of 3167 partners), and 6% of partners

named by women were contactable *vs.* 15% of partners named by men. The vast majority of reported sex partners could not be contacted because index cases were unable to provide the names and/or addresses of these partners.

Provider notification was used to contact approximately 76% of the 276 contactable partners, and patient notification was used to contact 24% (Table 2). Conditional provider notification composed approximately half of all provider notification efforts. Two partners who were contactable were not contacted, because index cases reported that they had already received medical care.

Of the 250 index cases with at least one contactable partner, 245 had at least one partner who was contacted (98% of 250 cases) (Figure 1). Of the 276 contactable partners, 270 were contacted (98% of 276 partners). Of 245 index cases with at least one contacted partner, 184 had at least one partner who presented to the clinic for medical evaluation (75% of 245 cases) (Figure 1). Of 270 contacted partners, 199 presented to the clinic for medical evaluation (74% of 270 partners). For male and female index cases, we observed comparable levels of notification and medical evaluation of partners.

Syphilis was diagnosed and treated among 99 partners who received medical evaluation. Hence syphilis prevalence was 50% among 199 partners who presented for medical evaluation. Fifty-seven per cent of the partners named by women who were notified and seen at the clinic were infected with syphilis *vs.* 43% of the partners named by men who were notified and seen at the clinic. The mean ‘brought-to-treatment’ index was 0.18 (99 syphilis diagnoses per 565 index cases interviewed). The inverse of the index indicates that in this clinic setting, approximately 6 index cases need to be interviewed to yield one newly diagnosed syphilis case.

Factors associated with presentation to the clinic, among contacted sex partners

Most characteristics of the referring index cases—gender, age, or syphilis infection stage—were not correlated with partners’ presentation to the clinic for medical evaluation (Table 3). Among partners who were successfully contacted and notified about their potential exposure to syphilis infection, those who recently had sex with an index case who reported 3–9 recent partners were less likely to present to the clinic for medical evaluation than those who were referred by an index case who reported having one recent partner (adjusted PR: 0.76, 95% CI: 0.60–0.96). Presentation to the clinic was comparable between those reporting two and one recent partners. Levels of presentation to the clinic were slightly lower among partners contacted by providers than by patients (adjusted PR: 0.84, 95% CI: 0.71–0.99).

Discussion

Partner notification involving co-operation of index patients and providers in Madagascar was possible and resulted in treatment of many syphilis-infected individuals who otherwise likely would have remained untreated. Approximately half of tested partners were found to be infected with syphilis upon presentation to the clinic and received treatment. The brought-to-treatment index (the number of syphilis patients treated per number of index cases interviewed) was 0.18. We observed high levels of partner notification, medical

evaluation, and identification of syphilis infections among contactable partners named by male- and female-referring index cases, although a somewhat greater proportion of the partners named by women who were notified and evaluated were found to be syphilis-infected than the partners named by men.

Overall, interviewing about six syphilis patients at the clinics and implementing a partner notification strategy yielded one newly diagnosed case. This case-finding effectiveness level was comparable to that measured in US-based syphilis partner notification efforts (median brought-to-treatment index: 0.22, range: 0.05–0.46) (Brewer 2005). The individual-level effects of partner notification on improved health are clear; the effort leads to treatment of newly diagnosed cases, thereby stopping disease progression. It also is likely that partner notification had beneficial effects at the partnership level, by reducing re-infection of referring index cases and/or new transmission within other primary and casual partnerships of treated patients.

It was encouraging that the majority of all partners who were contacted and informed of their syphilis infection risk presented to the clinic for medical evaluation (approximately three-quarters). The vast majority of partners were contacted through provider or conditional provider notification with the patient's approval, highlighting the importance of involving providers in the partner notification process. These results are congruent with findings from studies conducted in developed country settings that indicated the involvement of providers increases the effectiveness of partner notification efforts (Mathews *et al.* 2007). Because provider notification requires considerable resources and hence has not been implemented in many resource-poor settings, research evaluating the effectiveness of provider notification in these settings has been limited. One randomized trial was conducted in Zambia and indicated that offering provider notification, partner notification counselling, and contact cards lead to a greater number of notified partners than giving the full responsibility of partner notification to the patient (Faxelid *et al.* 1996). The results, which pointed to the potential importance of offering provider notification in developing country settings, are further supported by the current findings from Madagascar. However, because provider notification as part of routine STI services in Madagascar would require considerable additional resources in terms of staffing and transportation costs, it is imperative to weigh these additional costs against using these resources to implement alternative STI control measures. Further, the costs of routine primary care including syphilis treatment are generally paid by patients. The inability for patients to pay these costs or for the clinic to cover the costs for those who cannot pay because of scarce clinic resources represents an important barrier to effective implementation of an expanded partner notification effort.

Partners informed of infection risk through patient notification were slightly more likely to come into the clinic than those informed by provider notification. It is possible that partners who were informed by patient notification were more likely to present to the clinic because patients chose to notify the 'easiest' partners who willingly presented to the clinic. Patients may have relied on the help of providers to notify more difficult partners because of fear of violence as a result of the notification, as has been documented previously (Mathews *et al.* 2007; Hawkes *et al.* 2003). Hence, while scarce resources constitute one barrier to expanded partner notification, an important social barrier to partner notification is fear of disclosing

syphilis infection status to partners. Hence, when devising a partner notification strategy with syphilis patients, providers must remain cognizant of the potential adverse social and psychological effects of partner notification. For example, for patients whose syphilis infection is identified based on signs and symptoms, providers can tell patients to emphasize to their partner that there is suspicion of syphilis and hence a need for the partner to receive care, but that diagnosis is not a certainty. Doing so helps minimize social harm and fear associated with disclosure.

While partner notification in Madagascar likely had important benefits at the individual and partnership levels, the population-level influence of partner notification as a syphilis control strategy in this setting can be expected to be very limited. The number of partners who were contacted and seen at the clinics represented <10% of all reported partners. Levels of sex partner exchange were high in this population, and index patients were unable to provide contact information for the majority of their sex partners. These results suggest that partner notification is limited, in particular, in subpopulations with high levels of partner exchange because the likelihood that contacts are anonymous or that no contact information is available is high. It is possible that many non-contactable partners also were infected with syphilis yet remained undetected and untreated. Untested, and untreated sex partners with syphilis may constitute a sizeable reservoir of syphilis infection in Madagascar, highlighting the limitations of partner notification alone as a means of disrupting population-level transmission. This important limitation of partner notification has been observed in other partner notification efforts for STIs in the United States, during which substantial proportions of reported partners (approximately 75–80%) were not located, brought to medical evaluation, and/or treated (Gunn *et al.* 1995; Peterman *et al.* 1997). Our findings corroborate these prior studies and suggest that partner notification should be used in tandem with alternative STI control measures. For example, targeted mass screening and treatment among members of core groups may yield higher treatment rates of syphilis-infected patients (Cates *et al.* 1996).

Our findings should be interpreted in the context of the study limitations. First, the partner notification effort took place in the context of recruitment for a trial. The numbers and the types of individuals who presented to the clinic for treatment of symptoms during trial recruitment may differ from those who present for care under typical circumstances, when advertisements to encourage care-seeking are uncommon. A second limitation is that we cannot establish why partners were not contactable. It is possible that index cases reported that partners were not contactable, not because the partner's location was unknown, but because they feared disclosing their syphilis infection status. If the latter was common, then partner notification efforts should include in-depth counselling and skills-building to improve confidence in disclosing STI infection status, as was carried out in Zimbabwe (Moyo *et al.* 2002).

Partner notification, a major component of STI control in developed country settings, should be expanded in Madagascar and other resource-poor settings for ethical and public health reasons to reduce syphilis-related mortality and morbidity among infected patients and to prevent transmission to their partners and other members of their sexual networks. However as noted, barriers to partner notification include feasibility concerns because of the need for

considerable resources for staffing, transportation, and increased syphilis testing and treatment as well as patient concerns about disclosing syphilis infection status to partners; these must be addressed to improve effectiveness of expanding partner notification. Further, given the inability for patients to provide contact information for the vast majority of partners, our findings make clear that partner notification must be used in conjunction with community-based interventions to reduce and eventually eradicate the current unacceptably high levels of syphilis in Madagascar.

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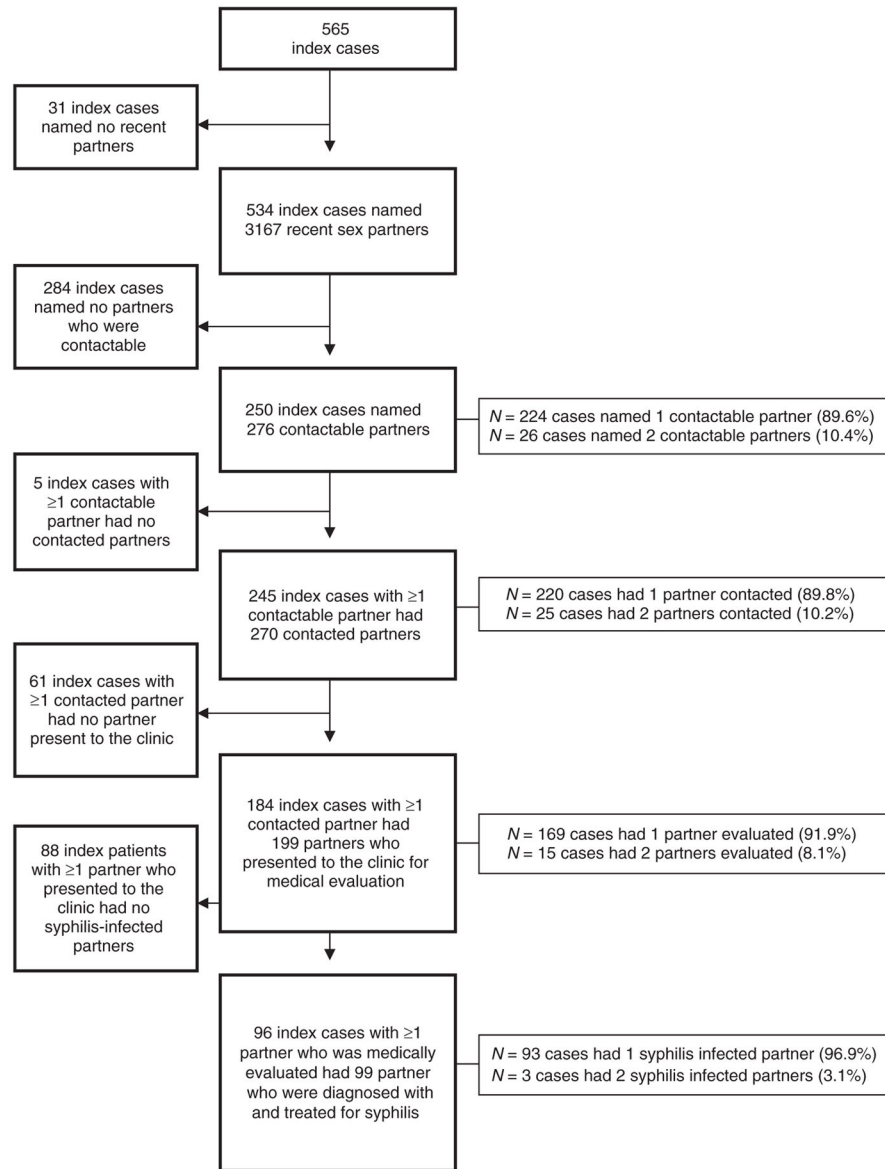


Figure 1. Identification, notification, testing and treatment of recent sex partners for early syphilis in Madagascar.

Table 1

Characteristics of syphilis index cases invited to participate in the partner notification effort ($N= 565$ index cases)

Index syphilis cases ($N = 565$)		
	N	%
Sex		
Female	270	47.8
Male	295	52.2
Age (years)		
14–19	167	29.7
20–24	193	34.3
25–29	104	18.5
30+	98	17.4
Number of recent sex partners*		
0 partners	31	5.5
1 partners	231	40.9
2 partners	113	20.0
3–9 partners	109	19.3
10–19 partners	49	8.7
20+ partners	32	5.7
Syphilis stage		
Primary	206	36.5
Secondary	292	51.7
Latent	67	11.9

* Number of sex partners in the past 3 months among patients with primary syphilis, the past 6 months among patients with secondary syphilis, and in the past 12 months among patients with early latent syphilis.

Table 2

Partner notification methods used to inform contactable sex partners of potential syphilis exposure ($N = 250$ index cases reported 276 contactable partners)

	Number of contactable partners ($N = 276$)	
	<i>N</i>	%
Percentage of sex partners contacted by...		
Provider (including conditional) notification *	209	75.7
Patient notification	65	23.6
Neither – index case reported that partner already received care	2	0.7
Total	276	100.0

* Among patients reporting the desire to notify their partners, clinic staff asked for permission to notify the partner if the partner did not present to the clinic. This type of provider notification was referred to as conditional provider notification.

Table 3

Presentation of contacted sex partners to the clinic for medical evaluation: unadjusted and adjusted prevalence ratios (PR) and 95% confidence intervals (CI) for the associations with index case characteristics and partner notification method (N = 270 contacted partners)

Presentation to the clinic for medical evaluation among contacted partners, by index case characteristics and partner notification method				
Background factors	No partners presented/No contacted partners	% of contacted partners who presented	Unadjusted PR (95% CI)	Adjusted PR* (95% CI)
Index case characteristics				
Sex of referring index case				
Female	93/128	72.7	Referent	Referent
Male	99/142	69.7	0.93 (0.79–1.11)	0.96 (0.80–1.15)
Age of referring index case (years)				
14–19	47/69	68.1	Referent	Referent
20–24	72/98	73.5	1.01 (0.49–2.07)	1.04 (0.85–1.27)
25–29	38/52	73.1	1.22 (0.47–3.11)	1.07 (0.84–1.37)
30 +	35/51	68.6	0.90 (0.41–1.98)	1.01 (0.80–1.28)
Number of recent sex partners [†]				
1 partners	84/109	77.1	Referent	Referent
2 partners	57/79	72.2	0.94 (0.78–1.13)	0.92 (0.75–1.13)
3–9 partners	51/82	62.2	0.78 (0.62–0.98)	0.76 (0.60–0.96)
Syphilis stage				
Primary	63/94	67.0	Referent	Referent
Secondary	97/136	71.3	1.03 (0.84–1.26)	0.99 (0.81–1.21)
Latent	32/40	80.0	1.16 (0.91–1.49)	1.14 (0.91–1.43)
Partner notification method				
Partner was contacted by the				
Patient	48/62	77.4	Referent	Referent
Provider	144/208	69.2	0.85 (0.73–1.01)	0.84 (0.71–0.99)

* The association between each background factor and the outcome, presentation to the clinic for medical evaluation, was adjusted for all other background factors in the table.

[†] Number of sex partners in the past 3 months among patients with primary syphilis, the past 6 months among patients with secondary syphilis, and in the past 12 months among patients with early latent syphilis.