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Reduced Risk of Syphilis Reinfection in Men Interviewed by Disease Intervention Specialists:A Pilot Study

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PII: S2773-0654(23)00027-5  
DOI: <https://doi.org/10.1016/j.focus.2023.100090>  
Reference: FOCUS 100090



To appear in: *AJPM Focus*

Received date: 27 August 2022  
Revised date: 6 February 2023  
Accepted date: 27 February 2023

Please cite this article as: Laura McKellar RN , Wei Hou PhD , Reduced Risk of Syphilis Reinfection in Men Interviewed by Disease Intervention Specialists:A Pilot Study, *AJPM Focus* (2023), doi: <https://doi.org/10.1016/j.focus.2023.100090>

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## REDUCED RISK OF SYPHILIS REINFECTION IN MEN

**Highlights**

- Local health departments rely on partner services to prevent the spread of syphilis.
- The association between contact tracing and syphilis reinfection risk is vastly understudied.
- Elicitation of sexual contacts appears to be associated with reduced risk of reinfection.
- Sexual partner treatment appears to be associated with reduced risk of reinfection.

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REDUCED RISK OF SYPHILIS REINFECTION IN MEN

**Reduced Risk of Syphilis Reinfection in Men Interviewed by Disease Intervention Specialists:**

**A Pilot Study**

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HPH 507: Biostatistics II

**Author Note**

Laura McKellar is a Public Health Nurse and Disease Intervention Specialist in the Sexually Transmitted Diseases Division of the Suffolk County Department of Health Services. However, she was not employed by Suffolk County in 2016, the year in which the Disease Intervention Specialist Interviews are under study. We have no other conflicts of interest to disclose.

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**Abstract**

**Background**

Syphilis is a highly transmissible Sexually Transmitted Infection (STI). Rising rates of infection and of re-infection are of great concern to Public Health officials. In local health departments across the United States Disease Intervention Specialists (DIS) attempt to interview all people diagnosed with early syphilis, to elicit sexual partner information, and to trace and treat the partners. This method of interviewing and contact tracing is evidence-based practice which reduces the spread of the disease in

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the community, but few studies address the relationship between the DIS interview and index patient reinfections. We hypothesized that patients who were interviewed, patients who provided partner information, and patients with more treated partners would have a reduced risk of reinfection.

### Methods

Our sample consisted of 82 men listed in the Suffolk County Department of Health Services syphilis log who were diagnosed with primary, secondary, or early latent syphilis. We determined if and when the patients were reinfected during a set time period, from 2016 - 2020. Kaplan-Meier analyses with log rank statistics and Cox Hazard Proportional models were used to calculate time to reinfection and hazard ratios.

### Results

Although none of the models produced p-values of  $<0.05$ , notable trends were observed. In subset analyses of interviewed patients, 23.8% of patients who named partners were reinfected during the study period, whereas 50% of those who did not name partners were reinfected in that time. Also, the HR for index patients who named partners was 0.51 (95%CI: 0.225 -1.170,  $p=0.113$ ). When some or all of the patients' partners were treated, 20% were reinfected by the end of the study, whereas 33.3% of cases with no partners treated were reinfected by the end of the study. The HR for patients with some or all partners treated was 0.48 (95% CI: 0.136 – 1.711,  $p=0.258$ ).

### Conclusion

Although none of the results was statistically significant, trends suggest that partner elicitation and partner treatment status could be associated with reduced risk of syphilis reinfection. Since this pilot study utilized a small convenience sample that was not tested for statistical power, we could not adequately address these trends. Future studies, with larger sample sizes, should address these relationships.

*Keywords:* syphilis, sexually transmitted diseases, recurrence, sexual partners, contact tracing

### **Risk of Syphilis Reinfection in Men who were Interviewed by Disease Intervention Specialists**

Syphilis is a highly transmissible Sexually Transmitted Infection (STI), and rising rates of infection are of great concern to Public Health officials.<sup>1</sup> From 2018 to 2019, cases of primary and secondary syphilis, the stages at which syphilis is most transmissible, increased 11.2%.<sup>2</sup> Reinfection is also common.<sup>1,3-6</sup> Since patients and providers often do not observe or recognize the signs and symptoms of syphilis, it is easy for patients to unknowingly pass the infection on to their sexual partners. Fortunately, syphilis is treatable with 1 to 3 doses of long-acting injectable Benzathine Penicillin G. The Center for

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Disease Control (CDC) includes syphilis in its list of mandatory reportable infections, and local departments across the United States attempt to interview all people who test positive and are diagnosed with early syphilis: primary, secondary or early latent syphilis.<sup>1,7</sup> The interview serves 3 purposes: linkage to affordable treatment, education, and sexual partner elicitation. A health department disease intervention specialist (DIS) conducts the interview with the positive person, i.e. the index patient. The DIS attempts to elicit the names and contact information for all sexual partners during the infectious period and the period in which the index patient became infected, in order to link the partners to testing and prophylactic treatment.<sup>6-9</sup>

This method of interviewing patients and tracing their sexual contacts is evidence-based practice which reduces the spread of the disease in the community,<sup>7,10</sup> but do these tactics also reduce the index patient's likelihood of becoming reinfected? CDC publications and DIS training materials, along with previous studies and meta-analyses, have focused on the "value" of partner services in terms of treatment of partners and infection rates in the community.<sup>7,8,10-13</sup> Few studies have analyzed reinfection rates<sup>3-6,14</sup> and fewer still have addressed a possible relationship between the disease intervention interview and syphilis reinfection. Analysis of this relationship will provide information that can enable health departments to better assess and to improve the interview process as a method of disease intervention and prevention.

Since syphilis rates are higher in men than in women,<sup>1,4,13</sup> it is important to address reinfection interventions in the male population. Infection rates are especially high in men who have sex with men (MSM).<sup>1,4,13</sup> However, since not all MSM agree to participate in the interview or are willing to provide honest information about male partners, the sex and gender of the partners may remain unknown. Therefore, studies about the effectiveness of DIS interviews should include all men.

We hypothesized that patients who were interviewed and patients who provided information about their sexual partners would have a lower risk of reinfection and longer time until reinfection than

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those who do not participate in the interview or provide information about their partners. We hypothesized that a greater number of elicited partners would be associated with an increase in time to reinfection and a decrease in risk of reinfection. Finally, we hypothesized that patients who have a greater percentage of treated partners would also have increased in time to reinfection and a reduced risk of reinfection.

### Methods

This study was an observational retrospective record review study. We reviewed the Suffolk County Department of Health Services (SCDHS) syphilis log and serology records. We first selected patients who were diagnosed with primary, secondary, or early latent syphilis in 2016. We then examined the historical serology records of each patient in order to determine if and when the patient was reinfected, from initial infection in 2016 through December 31, 2020. Reinfection date was determined by selecting the mid-point between the reinfection positive test and the most recent negative test. For patients who were not reinfected, we gathered the last negative test date. Last, we used interview records to determine whether or not the index patient was interviewed, whether or not the patient provided the DIS worker with partner information, the number of partners elicited from the index patient, and whether or not those partners were prophylactically treated for syphilis. Treatment outcomes for partners were verified by DIS with health care providers. We also gathered data on two potentially confounding variables from the interview record: having anonymous partners and the use of hook-up smartphone apps to meet partners.

The sample consisted of all Suffolk County men diagnosed with early syphilis (primary, secondary, or early latent syphilis) in 2016 who had 2 or more subsequent syphilis tests after the 2016 diagnosis listed in Suffolk County's syphilis serology records. Inclusion criteria also included: male gender;  $\geq 18$  years of age; and a Suffolk County address. Participants were excluded from the study if their gender identity was female or non-binary, if they were under 18 at the time of the initial syphilis

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diagnosis, or if they had no subsequent syphilis testing or only one subsequent syphilis test on record at the SCDHS. Participants were also excluded if there was no record indicating whether or not they were interviewed by a SCDHS DIS worker. We included all races and ethnicities. Non-English speakers were also included, as DIS workers are required to use interpreters to communicate with patients in their own languages. Anyone identified as incarcerated was excluded.

Since this was an observational study, the sample size was based on the available data in SCDHS's syphilis logs, serology records, and interview records for syphilis testing between January 1, 2016 to December 31, 2020. This was a small pilot study, and the sample size was not tested for statistical power.

This study used Kaplan-Meier analyses with log rank test to estimate and compare the survival curves and the mean time to event in number of months from initial positive test in 2016 to reinfection or censure. Index patients were categorized as interviewed/not-interviewed and categorized as partners elicited/not elicited. The number of partners elicited was categorized as none, low (1-2), medium (3-4), and high ( $\geq 5$ ). Time zero was the date of the first positive syphilis test in 2016, for each individual subject. A positive test was defined according to CDC protocols, by either a change in syphilis antibody test, from negative to positive, or by a four-fold increase in RPR titer. Reinfection was defined as a 4-fold increase in RPR titer from the most recent RPR test.<sup>15</sup> The date of reinfection was estimated to be the midpoint between the last "negative" test and the reinfection "positive" test. Subjects who remained negative were censored at the date of the last negative test in the 2016 – 2020 time-period.

The Cox Proportional Hazard model was used to assess the risk for reinfection over 60 months from January 1, 2016 – December 31, 2020. Unadjusted and adjusted hazard ratios (HR) of syphilis reinfection with 95% confidence intervals were calculated based on the Cox models. Independent variables and co-variables included in the models were: Interviewed (Y/N), Named Partner (Y/N), and Number of Partners Named (none, low, med, high).



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Further, Kaplan-Meier and Cox Proportional Hazard analyses were conducted, with the sample limited to interviewed patients. We assessed the relationship between the following characteristics of the interviews and the number of months until reinfection: whether or not partners were elicited; number of partners elicited; whether or not any partners were prophylactically treated; and if some, none, or all partners were treated. We also assessed additional characteristics of the interviewed subjects, i.e. engaging in anonymous sex and the use of “hook-up apps,” in order to determine if these characteristics were related to the outcome and were possible confounding variables.

Researchers used IBM SPSS Statistical software, version 28.0.1, for all analyses.

Since this study was a record review observational study, subjects were at minimal risk of harm. Patient identifying information was removed from all data and patients were protected from breaches of confidentiality. The Stony Brook University IRB board and the SCDHS Research and Publications Review Committee reviewed and approved the study.

### Results

#### Descriptive Statistics

The Suffolk County syphilis log listed 162 men as diagnosed with early syphilis in 2016, 82 of whom met the inclusion criteria for this study. Of the 82, 28 (34.1%) were reinfected at some point by December 31, 2020, and 54 (65.9%) did not have any test results indicating reinfection as of December 31, 2020. DIS interviewed 68 (82.9%) of the men in the sample. Of those who were interviewed, 23 patients (33.8%) were reinfected by December 31, 2020. In the not-interviewed group, 5 patients (35.7%) were reinfected by the end of the study period. (Table 1)

The interview group was analyzed separately as a subset of the sample. Of those interviewed, 42 (61.6%) provided partner information, and 26 (38.2%) did not. Of those who provided partner information, 10 (23.8%) were reinfected by the end of the study. Of those who did not provide partner information, 13 (50%) were reinfected by the end of the study. Of those interviewed, 30 (45.6%) of

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index patients had some or all of their elicited partners treated for syphilis. Seventeen (25%) of the interviewed patients had all of their named partners treated, 13 (19.1%) had some but not all partners treated, and 12 (17.6%) had no partners treated. 33.3% of those with no treated partners were reinfected by the end of the study period, whereas only 20% of those with some or all partners treated became reinfected. The same trend is seen in the categorical variable, breaking the groups down into no partners treated, some but not all treated, and all named partners treated. 23.1% of those with some partners treated were reinfected, and 17.6% of cases with all partners treated were reinfected by the end of the study period. Of those interviewed, 67.6% of interviewed cases claimed to have anonymous partners, and 32.4% stated that they met partners through hook-up apps such as Grindr and Tinder. (Table 2)

### **Kaplan-Meier Analyses**

The mean time to reinfection for the entire sample was 44.73 (95% CI: 40.64 – 48.83) months. Mean time until reinfection for interviewed patients was 44.01 months (95% CI: 39.74 – 48.41) as compared to 44.31 months (95% CI: 34.18 - 54.44) for patients who were not interviewed. There was not a statistically significant difference in time to reinfection (log rank  $p=0.899$ ). (Table 1, Figure 1)

When the sample was limited to interviewed patients, the mean number of months until reinfection in those who provided partner information was 47.07 (95% CI: 41.72 – 52.42), as compared to 39.09 months (95% CI: 32.67 – 45.50) in those who did not provide partner information. Although the log rank value was 0.106, the difference in months until reinfection does suggest a possible trend. (Table 2, Figure 2) In looking at partner treatment variables, neither the binary measure nor the categorical measure of partner treatment status was statistically significant, with log rank values of  $p=0.248$  and  $p=0.469$  respectively. However, the mean number of months until reinfection for those who had some or all partners treated was 49.19 (95% CI: 42.67 – 45.50), as compared to 40.64 months (95% CI: 28.23 – 53.06) for those who provided partner information but had no partners treated. This

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difference also suggests a possible trend. Having anonymous partners was not significantly associated mean time to reinfection ( $p=0.781$ ), nor was using hook-up apps to meet sexual partners ( $p=0.071$ ).

### Cox Hazard Regression analyses

When looking at the entire sample of men who were diagnosed with early syphilis in 2016, none of the models was statistically significant, and no models were statistically significant when the sample was limited to interviewed patients. Of the models, the best fit was the model from the interviewed patient sub-set that included only the “named partners yes/no” variable, with a p-value of 0.111. The hazard ratio (HR) for those who named their partners in the DIS interview was 0.51 (95% CI: 0.225 – 1.170,  $p=0.113$ ), indicating a 49% reduction in risk. The p-value for the model that contained the binary partner treatment variable was also not statistically significant ( $p=0.258$ ), but the HR of 0.48 (95%CI: 0.136 – 1.711) is notable.

### Discussion

None of the Kaplan-Meier analyses or Cox Hazard Proportional models produced p-values  $<0.05$ . However, this was a small pilot study that utilized a convenience sample that was not tested for statistical power. Although elicitation of partners (yes/no) was not significantly associated with time until reinfection ( $p=0.106$ ), the results suggest possible trends in the data. Most notably, in the interviewed subset group, 23.8% of patients who named partners were reinfected during study period, whereas 50% of those who did not name partners were reinfected in that time. Also, the HR for index patients who named partners was 0.51 (96%CI: 0.225 -1.170,  $p=0.113$ ), indicating a 49% reduction in risk. Similarly, partner treatment status was not significantly associated with time to reinfection ( $p=0.258$ ), but the HR of 0.48 (95% CI: 0.136 – 1.711) indicated a substantial reduction in risk. Also, 33.3% of cases with no partners treated were reinfected by the end of the study, and only 20% of cases with some or all partners treated were reinfected. Future studies should be conducted to assess these trends further.

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Public health officials might assume that having anonymous partners or partners met on hook-up apps, would increase the likelihood of reinfection. These partners are likely to be difficult to locate, to inform of possible exposure, and to link to treatment. However, neither of these factors were significantly associated with time to reinfection nor did they demonstrate any statistical trends. They do not appear to have influenced the outcome or have acted as confounding variables.

### Limitations

This exploratory study suffered from several important limitations which future studies should address. Due to its small sample size, this study cannot adequately address the aforementioned trends seen in HRs and time to reinfection in patients from whom partners were elicited and in patients with treated partners. Future studies, with larger sample sizes, should address these relationships.

Another weakness is the limited number of variables included in the study. We did not include demographic variables such as race, income, educational status, or zip code, which might relate to willingness to participate in the interview or willingness to reveal information about partners. Future studies should include these variables, especially since they are often the only available data on the patients who refuse the interview, and the data might provide insight into some of the differences between the interviewed and not-interviewed groups. We also did not include other potential risk variables such as sex and gender of partners, method of partner acquisition, drug use, intravenous drug use, partner intravenous drug use, or participation in transactional sex. Future studies should include these variables, since they are possibly related to the reinfection risk as well as willingness or ability to participate in the interview or to provide partner contact information.

Our study focused on the number of partners named and on how many of those were treated. Future studies should also consider the relationship between the total number of uncontacted partners (named and unnamed) and reinfection risk. In our sample, this number was difficult to assess. In the DIS interview some patients provided an exact number of partners from the interview time period, but

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others provide only a vague estimate, and others refused to answer or do not know. Since many of the unnamed partners are anonymous, we chose to assess the relationship between having anonymous partners and reinfection. As previously noted, we hypothesized that having anonymous partners would make contact tracing difficult, would increase community spread, and would increase the likelihood of reinfection. However, we found no relationship. Addressing the number of uncontactable partners would offer a more nuanced understanding of how the DIS process intervenes or fails to intervene in community spread which then poses increased risk of reinfection to the patient.

Our study did not address characteristics of the sexual partners or characteristics of the partner notification process, DIS collect little information about or from contacts, aside from limited demographic information. However, some information is available, such as if the contacts tested negative and were prophylactically treated, if they tested positive and were treated, if they had already been treated prior to notification, or if they refused testing and treatment. Future studies might include these factors in analyses and might also consider if the partner notification was performed solely by the DIS or was a cooperative effort between DIS and index patient.

We also did not include variables in the DIS interview and partner elicitation process that might lead to behavior change and adoption of risk reduction strategies. One such variable is patient engagement in the interview. Patients who provide partners might be more engaged in the interview and thus with the health education messages the DIS provides. Engagement in the interview might also suggest a readiness to change health-related behaviors. Also, the very act of naming one's partners might help the patient to reassess their own attitudes about hazards, risks to self, risks to others, and health behavior change. Further quantitative and qualitative studies should address how the DIS interview process is related to changes in patients' health literacy, changes in attitudes about sexual health and health risks, readiness to change, and actual behavior change. These studies should then address how these factors are associated with reinfection risk and time to reinfection.

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Furthermore, our study did not assess if behavior change occurred. Assessment of the data gathered at patient interviews at the point of reinfection might provide some insight into whether or not reinfected patients had made changes in sexual behavior, changes in sexual partners or networks, changes in partner typology, or changes in methods of acquiring partners. Any of these changes might increase or decrease reinfection risk. However, this data was not available for much of 2020, as Suffolk County DIS workers were reallocated to COVID investigations and were not conducting syphilis investigations.

Another limitation is the unknown amount of variation in DIS workers and in the individual DIS interviews. Although the CDC standardizes training for all DIS workers, and although supervisory staff in Suffolk County in 2016 was consistent, individual DIS capability and style vary. Also, although DIS seek out the same information for each interview and provide the same education, individual interviews can also vary. DIS tailor their interviews based on the index patient's knowledge, health literacy, personality, mood, and affect, as well as the patient's self-identified sexual orientation and reported sexual networks. Furthermore, by 2016, DIS workers across the country experienced multiple increased workplace demands and burdens, most notably, increases in syphilis cases and case load.<sup>16</sup> These stressors might have influenced the amount of time DIS could devote to locating patients and their partners, and it might have affected how much time and attention DIS workers could devote to establishing trust, conducting interviews, or following up with patients for additional partner information. Future studies should address how individual DIS characteristics, such as years of experience, education level, caseload, and level of workplace satisfaction, are related to likelihood of patients being interviewed, numbers of partners elicited, and patient reinfection. Qualitative or mixed methods studies could assess the variation between interviews and observe how these variations are related to reinfection risk.

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Finally, this study might not be generalizable to other counties in the United States. Individual health departments and DIS workers vary from year to year and from county to county, as do demographic, socioeconomic, and cultural characteristics of the counties. A greater number of health departments should be included, across geographic areas and socioeconomic statuses, and across a longer time period. Although this study is small and suffers limitations, it is a pilot study that points to the need for further evaluation the role of the DIS interview and partner elicitation in the reduction of risk of syphilis reinfection.

### Conclusion

Although the CDC and local health departments rely heavily on the DIS interview to prevent the spread of syphilis and to reduce incidence rates, infection rates continue to rise.<sup>1,7</sup> Therefore it is essential to understand what aspects and elements of the DIS interview and partner services are most effective and produce the best public health outcomes. One important outcome is a reduction in index patient reinfections. Reduced risk of reinfection and reduced time to reinfection benefit not only the index patient but also their sexual partners, sexual networks, and communities.

In addition, previous studies demonstrate that DIS workers are overwhelmed and are struggling to elicit partner information.<sup>16,17</sup> If there is a statistically significant association between partner elicitation or percentage of partners treated and reinfection risk, this information can help motivate index patients to name more partners and to provide more detailed information, which may, in turn, reduce syphilis infection rates in the community.

Previous studies have addressed or analyzed DIS efforts and the DIS interview as an intervention,<sup>8-12,16</sup> and some previous studies have looked at reinfection rates in relation factors such as index patient demographics,<sup>3-6</sup> but few have even considered the relationship between the DIS interview and reinfection of index patients. Our study addressed this subject and observed a trend in the data that suggests that partner elicitation and partner treatment outcomes could be associated with a reduction

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in risk of syphilis reinfection. Future studies should address this relationship to better understand how the DIS interview functions as a public health intervention.

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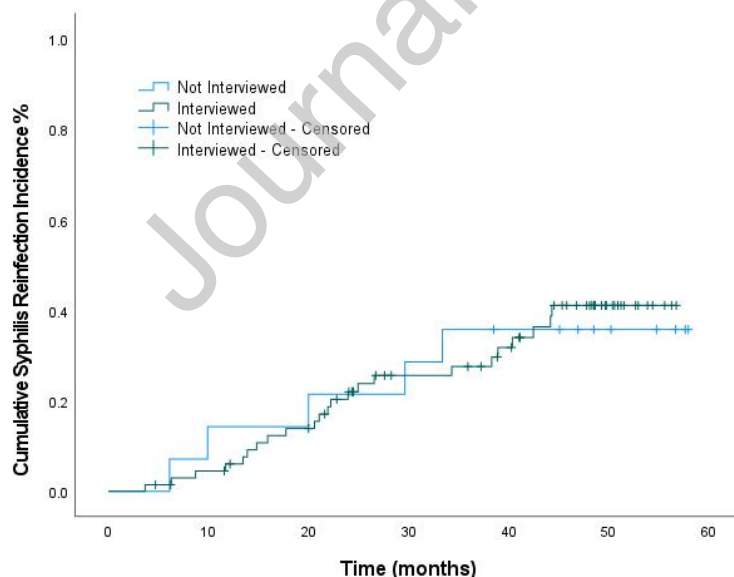
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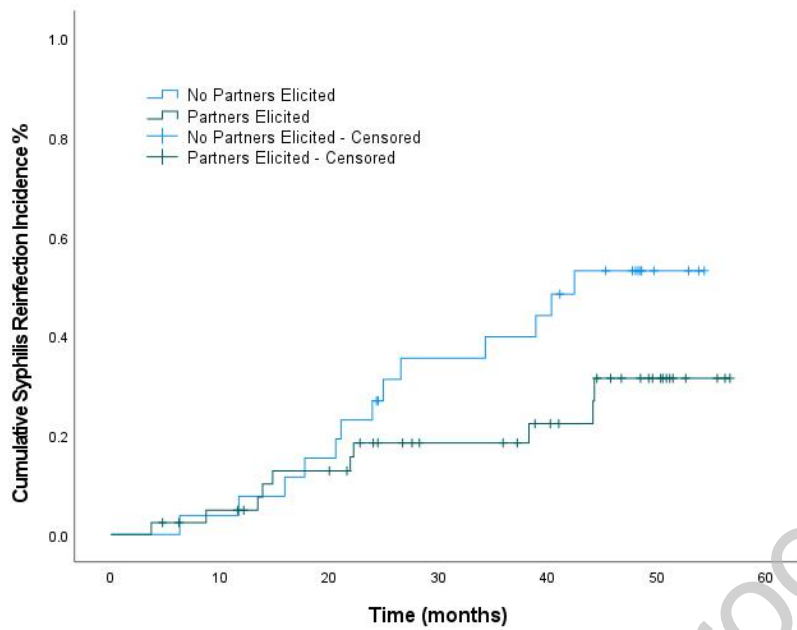
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## LIST OF FIGURES

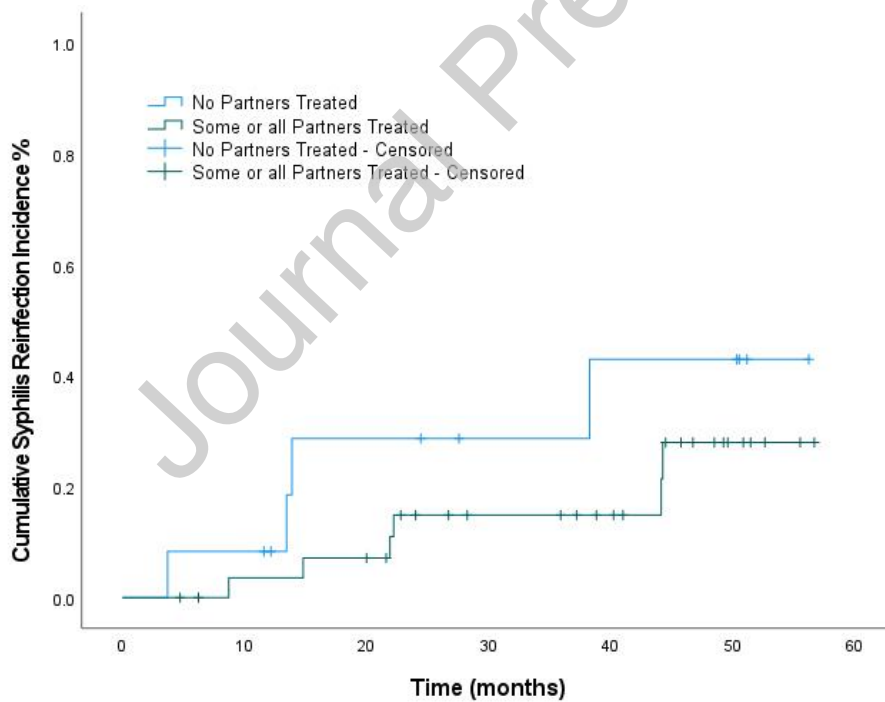


**Figure 1**  
Cumulative Syphilis Reinfection Incidence by Interview Status

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**Figure 2**

*Cumulative Syphilis Reinfection Incidence by Partner Elicitation Status in Patients Interviewed by DIS*

**Figure 3**

*Cumulative Syphilis Reinfection Incidence by Partner Treatment Status in Patients who Provided Partner Information to DIS Workers*

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**Table 1**

*DIS Interview Characteristics Associated with Syphilis Reinfection in Men in Suffolk County, including those who were Interviewed and not Interviewed*

	<b>Number of Cases</b>	<b>Percent of Cases</b>	<b>Number of Cases Reinfected</b>	<b>Percent Reinfected</b>	<b>Mean Time to Re-infection</b>	<b>Log Rank P-value</b>
<b>N</b>	82	100.0%	28	34.1%	44.73 months (95% CI: 40.64 - 48.83)	
<b>Interviewed</b>	68	82.9%	23	33.8%	44.09 months (95% CI: 39.74 - 48.41)	p=0.899
<b>Not Interviewed</b>	14	17.1%	5	35.7%	44.31 months (95% CI: 34.18 - 54.44)	

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**Table 2**

*DIS Interview Characteristics Associated with Syphilis Reinfection in Men in Suffolk County amongst those who were Interviewed*

	Number of Cases	Percent of Interviewed Cases	Number of Cases Reinfected	Percent Reinfected	Mean Time to Re-infection	Log Rank P-value
<b>N</b>	68	100.0%	23	33.8%	44.08 months (95% CI: 39.74 - 48.41)	
<b>Partner Info Elicited</b>	42	61.6%	10	23.8%	47.07 months (95% CI: 41.72 - 52.42)	p=0.106
<b>No Partner Info Elicited</b>	26	38.2%	13	50.0%	39.09 months (95% CI: 32.67 - 45.51)	
<b>Some or All Partners Treated</b>	30	45.6%	6	20.0%	49.19 months (95% CI: 42.67 - 45.5)	p=0.248
<b>Partners Elicited but none Treated</b>	12	17.6%	4	33.3%	40.64 months (95% CI: 28.23 - 53.06)	
<b>All Partners Treated</b>	17	25.0%	3	17.6%	51.34 months (95% CI: 45.50 - 57.20)	p=0.469
<b>Some Partners Treated</b>	13	19.1%	3	23.1%	45.78 months (95% CI: 36.16 - 55.40)	
<b>Partners Elicited but none Treated</b>	12	17.6%	4	33.3%	40.64 months (95% CI: 28.23 - 53.06)	
<b>Has Anonymous Partners</b>	46	67.60%	16	34.8%	43.11 months (95% CI: 37.78 - 48.44)	p=0.781
<b>No Anonymous Partners</b>	21	30.9%	7	33.3%	45.04 months (95% CI: 37.55 - 52.53)	
<b>Anonymous Partner Data Missing</b>	1	1.5%				
<b>Uses Hook-up Apps</b>	22	32.4%	4	18.2%	49.06 months (95% CI: 42.05 - 56.07)	p=0.071
<b>Does not Use Hook-up Apps</b>	43	63.2%	19	44.2%	40.62 months (95% CI: 35.14 - 46.10)	
<b>Hook-up App Data Missing</b>	3	1.0%				

REDUCED RISK OF SYPHILIS REINFECTION IN MEN

**Credit Author Statement for “Reduced Risk of Syphilis Reinfection in Men Interviewed by Disease Intervention Specialists: A Pilot Study**

**Laura McKellar:** Conceptualization; Data curation; Formal analyses; Investigation; Methodology; Project administration; Resources; Software; Validation; Visualization; Writing – original draft preparation; Writing – review & editing. **Wei Hou, PhD:** Conceptualization; Formal analyses; Methodology; Software; Supervision; Visualization; Writing – review and editing.

**Declaration of interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Laura McKellar reports a relationship with Suffolk County Department of Health Services that includes: employment. Co-author serves as a Statistical Editor for AJPM Focus. -W.H.

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