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Comparison of Sexual Mixing Patterns for Syphilis in Endemic and Outbreak Settings

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Abstract

Background—In a largely rural region of North Carolina during 1998–2002, outbreaks occurred of heterosexually-transmitted syphilis, tied to crack cocaine use and exchange of sex for drugs and money. Sexual partnership mixing patterns are an important characteristic of sexual networks that relate to transmission dynamics of STIs.

Methods—Using contact tracing data collected by Disease Intervention Specialists, we estimated Newman assortativity coefficients and compared values in counties experiencing syphilis outbreaks to non-outbreak counties, with respect to race/ethnicity, race/ethnicity and age, and the cases' number of social/sexual contacts, infected contacts, sex partners, and infected sex partners, and syphilis disease stage (primary, secondary, early latent).

Results—Individuals in the outbreak counties had more contacts and mixing by the number of sex partners was disassortative in outbreak counties and assortative non-outbreak counties. Whereas mixing by syphilis disease stage was minimally assortative in outbreak counties, it was disassortative in non-outbreak areas. Partnerships were relatively discordant by age, especially among older White men, who often chose considerably younger female partners.

Conclusions—Whether assortative mixing exacerbates or attenuates the reach of STIs into different populations depends on the characteristic/attribute and epidemiologic phase. Examination of sexual partnership characteristics and mixing patterns offers insights into the growth of STI outbreaks that complement other research methods.

Keywords

sexual networks; syphilis; heterosexual transmission; mixing patterns

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Introduction

In a largely rural region of southeastern North Carolina during 1998–2002, outbreaks occurred of heterosexually-transmitted syphilis tied to widespread crack cocaine use and exchanging sex for drugs and money. (1) (2) The outbreaks were concentrated in counties with high endemic syphilis rates before the outbreak that subsequently exceeded incidence levels rarely observed in the United States at the time. The statewide incidence of primary, secondary, and early latent syphilis hovered below 20 cases per 100,000 person-years. Incidence during 1998–2002 in Robeson County grew from 87/100,000 person-years to 116/100,000 and from 8/100,000 to 46/100,000 in Moore County. Columbus County experienced a 600% fold increase in new diagnoses, from 15/100,000 (1998) to a peak of 99/100,000 by 2000 while the incidence in Montgomery County also peaked at nearly 200/100,000, after several years of rates less than 12/100,000.(3)

The trajectory of outbreaks of sexually transmitted infections (STIs) is determined, in part, by the structural characteristics of the social and sexual networks, and risk behaviors of persons within such networks.(4, 5, 6) Sexual mixing patterns are an especially important characteristic of sexual partnerships and networks. Assortative mixing refers to sexual partnerships among people with similar characteristics and risk behaviors. Assortative mixing among high risk persons sustains transmission within the group and impedes STIs from diffusing into the lower risk populations. Discordant or disassortative sexual mixing connects populations with higher prevalence of STIs to those with lower prevalence.(7, 8, 9) The extent of assortative sexual mixing varies by population and by attribute of interest, including age, race/ethnicity, education, number of sex partners, concurrent sex partners, and drug use. (4, 10, 11, 12, 13, 14, 15, 16) For example, adolescent females who have older male sex partners are at greater risk for infections of chlamydia or gonorrhea(17), herpes simplex virus-2(18), and HIV(19). When characteristics of each person and his or her sex partners are known, the extent of assortative mixing can be assessed with quantitative measures.(20, 21, 22)

Using state health department data, previous in-depth analysis of structural and other characteristics of the network that developed in Columbus County demonstrated the contribution of the cases' social contacts to the outbreak.(2) Social contacts and possible cases linked otherwise disconnected cases, creating a dense network conducive to rapid spread of infectious diseases.(2) In this analysis, we assess and compare sexual mixing patterns among persons residing within counties experiencing syphilis outbreaks to patterns of those residing outside the outbreak counties. We hypothesize that mixing patterns in the counties where the outbreak occurred will be more disassortative with respect to age,(17, 18, 19) and number of sex partners (10, 11, 15) and more assortative with respect race/ethnicity (15) than in areas not affected by the outbreak.

Materials and Methods

All newly diagnosed cases of syphilis and HIV infection are reported to the state Division of Public Health and STD/HIV Prevention & Treatment Branch. Disease Intervention Specialists (DIS) routinely interview persons newly diagnosed with syphilis or HIV to

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identify sex partners who are contacted interviewed, tested, and if infected, are brought to health care provided for treatment. DIS also elicit names of the case's friends and others in his or her social network whom the case believes would benefit from testing, might have symptoms suggestive of disease, or engage in behaviors that place them at risk for infection. (23) Some of the people referred to DIS may actually be the sex partners of cases, whom they do not want to disclose as such, because disclosure may implicate them in illegal or proscribed behaviors.(23) The social and sexual connections are tracked electronically, permitting construction of sexual networks among cases and contacts directly and indirectly connected to each other.

Contact tracing data for a contiguous region of central and eastern North Carolina spanning 64 of the state's 100 counties, over a ten-year period (1993–2002), were initially chosen to maximize the possibility of tying together seemingly unrelated cases into larger sexual network components. Furthermore, Interstate 95, which crosses through the region, is a drug trafficking route from Florida to the northeast, which has been hypothesized to increase drug use, exchange of sex, and elevated STI rates for those live in close proximity to the highway. (24) From this expansive dataset, we selected the observation period of October 1998 – December 2002 and classified Robeson, Columbus, Montgomery and Moore Counties as the *outbreak counties* on the basis of: 1) annual surveillance reports of syphilis incidence (3); 2) the frequency distribution of the month and year of dates of syphilis diagnoses by county; and 3) network analysis that revealed large cyclic connected sexual networks indicative of outbreaks. (25)

The analysis included cases diagnosed with primary, secondary, or early latent syphilis and their sex partners and social contacts irrespective of infection status. We excluded cases younger than 14 years of age (newborns diagnosed with congenital syphilis) and patients with late latent syphilis diagnoses (indicative of prolonged subclinical infection). Non-cases were classified as uninfected if negative syphilis tests were documented. Sex partners and social contacts who either refused testing or could not be located by DIS were classified as having unknown disease status.

In social network analysis, *node degree* refers to the number of connections an individual (i.e., node) has to other people.(26) We calculated four node degree values for the cases: 1) ***All*** types of partnerships including infected, uninfected, and unknown infection status, of sex partners, social contacts and possible cases; 2) ***Infected*** sex partners, social contacts and possible cases; 3) ***Sex partners*** irrespective of disease status; and 4) ***Infected sex partners*** only.

We used Newman's *assortativity coefficient* (21, 22) to measure the extent of assortative sexual mixing.(21, 22) The assortativity coefficient is calculated from the mixing matrix – the proportional cross-tabulation of partnerships by the attribute of interest. The formula is:

$$r = \left(\mathrm{Tr}\,\mathbf{e} - \|\mathbf{e}^2\|\right) / \left(1 - \|\mathbf{e}^2\|\right)$$

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where r is the assortativity coefficient, **e** is the matrix whose elements are the cell values, e_{ij}, of the mixing matrix; Tr **e** is the trace of the matrix; and $||\mathbf{e}^2||$ is the sum of all cells of the square of the mixing matrix.

The assortativity coefficient (r) ranges from −1.0 to 1.0, corresponding from perfectly disassortative mixing (where no one in the population partners with anyone sharing the same characteristic), to completely assortative mixing (i.e., all partnerships are concordant for the characteristic). Although the r value zero refers to random mixing (the characteristic has no influence on pairing), positive r-values close to zero can be interpreted as disassortative mixing because random mixing more likely results in partnering of two individuals who do not share the same attribute.

Before Newman derived the assortativity coefficient, studies assessed sexual mixing patterns with a less robust assessment, referred to as the Q-statistic.(20) Its primary limitation is that it can change dramatically if the rows and columns of the mixing matrix are transposed. We previously computed Q-statistics, which were roughly comparable to Newman's assortativity coefficients, for a case-control study of heterosexual HIV infection(10) to permit comparison of the results to other studies that used Q-statistics.

One analysis of mixing with respect to number of sex partners for the general US population yielded a Q-statistic of approximately 0.35.(11) A study of couples attending an STD clinic in Seattle, Washington was highly assortative (Q=0.44) by age, but less assortative with respect to education (Q=0.23) and number of sex partners (Q=0.16).(8) On the basis of these studies, our past work(10), and the findings from the analysis presented here, we have *broadly* classified assortativity coefficients ≥0.35 as *highly* assortative, 0.15–0.34 as assortative, 0.10–0.15 as *minimally* assortative, and <0.10 as disassortative. (Note: This classification scheme is a modification of our previous publication(10).)

We assessed and compared heterosexual mixing patterns within and outside of the outbreak counties with respect to race/ethnicity, age and race/ethnicity combined, the four measures of node degree, and syphilis disease stage. The analysis was restricted to heterosexual partnerships because they composed 75% of all social and sexual ties documented by DIS; about two thirds of ties between people of the same gender involved social connections. For age mixing, we calculated the age of each person on January 1, 2000 and used five-year age categories 14-19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, and ≥50 years in the cross-tabulations. We assessed mixing with respect to syphilis disease stage (primary, secondary, and early latent) for partnerships in which *both* members were infected.

The NC Department of Public Health granted us access to these data for secondary analysis, which is exempt from approval of the Institutional Review Board at the University of North Carolina at Chapel Hill.

Results

DIS identified a total of 5299 cases, uninfected persons, and people with unknown disease status; 37% resided in one of the four outbreak counties. Most cases occurred among African Americans (64%) and they accounted for 50% and 72%, respectively, of persons in

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the outbreak and non-outbreak counties (Table 1). Native Americans composed 31% of cases in the outbreak counties and were virtually absent from non-outbreak counties. (Note: Native Americans and African Americans accounted for approximately 38% and 31%, respectively, of the Robeson County population.(27, 28)) Ten percent were adolescents (14-19 years of age) from the entire region, but they accounted for more people in the outbreak counties (12%) than non-outbreak counties (8%). Furthermore, 45% of the 448 adolescents resided in outbreak counties.

Primary syphilis cases composed 22% of cases in outbreak counties yet only 13% in the non-outbreak counties (Table 2). Of the 329 primary syphilis cases from the entire region, about half (161) resided in one of the four outbreak counties.

Cases residing in the outbreak counties generally had more contacts and sex partners than did those who lived elsewhere (Table 3). The mean All Degree (i.e., all types of partnerships, sex partners, social contacts, and possible cases) was 3.51 partners per case (standard deviation[sd] 3.63) among outbreak county residents, approximately one additional contact per case than cases from non-outbreak counties (2.69, [sd 3.86]). Although the median numbers of sex partners for cases in outbreak and non-outbreak counties were comparable (~ two partners), 27% of cases residing in outbreak counties had at least three sex partners in contrast to 20% of cases living elsewhere (Table 3).

Partnerships and Mixing patterns

Race/ethnicity—Mixing with respect to race/ethnicity was highly assortative in both outbreak (*r*=0.513) and non-outbreak counties (*r*=0.382). The remarkable difference in *r*-values between outbreak and non-outbreak counties is likely driven by 1) the increase in absolute number of partnerships involving at least one Native American in the outbreak counties (n=849) as compared to the non-outbreak counties (n=68); and 2) 54% of the partnerships in the outbreak counties involving at least one Native American were race-concordant, whereas of the total 68 partnerships in the non-outbreak counties, Native Americans primarily partnered with whites (22%) or Blacks (19%).

Age and race/ethnicity—Preliminary analyses indicated that the distribution of age differences between men and women did not vary by residence (outreak vs. non outbreak county) and therefore was not pursued further (results not shown). To assess mixing with respect to age and race/ethnicity simultaneously, we computed assortativity coefficients for age, stratified by the race/ethnicity of the male (Figure 1). Age mixing for all race/ethnicities was minimally assortative (*r*=0.119) and men were an average of 6.6 years older than their women partners. The point estimates for *r* values suggest important variations in age mixing by race/ethnicity. Age mixing among white men was disassortative (*r*=0.088) in contrast to minimally assortative for Black (*r*=0.113), Hispanic (*r*=0.146), and Native American (*r*=0.136) men. Furthermore, the mean age difference for white men and their women partners (10.2 years) is higher (ANOVA p-value <0.001) than Black (6.5 years), Hispanic (4.9 years), and Native American men (5.3 years).

Node degree—Mixing with respect to the number of contacts generally exhibited greater assortativity in the non-outbreak counties (Figure 2). Coefficients for the All Degree

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measure were 0.108 and 0.190 for outbreak and non-outbreak counties respectively. Mixing differences were more pronounced with respect to the number of sexual partnerships. Disassortative mixing describes the outbreak counties for both Sex Partner degree (*r*=0.056) and Infected Sex Partner degree (*r*=0.046). Conversely, non-outbreak counties exhibited assortative mixing for Sex Partner Degree (*r*=0.198) and Infected Sex Partner degree (*r*=0.167).

Disease stage—The proportion of partnerships involving two persons both diagnosed with primary syphilis was higher in the outbreak counties (19%) than non-outbreak counties (5%) (Table 4). In non-outbreak counties, 70% of the partnerships with one secondary case were connected to a case with early latent disease in contrast to 53% of the outbreak county partnerships. Disease stage mixing in outbreak counties was minimally assortative (*r*=0.110) and in non-outbreak counties, very disassortative (*r*=0.005) (Figure 3).

Discussion

We compared characteristics of heterosexual networks and mixing patterns identified in outbreaks of syphilis with characteristics observed in environments with low-level endemic syphilis transmission. Several mixing patterns likely affected syphilis incidence. Individuals in the outbreak counties were connected to more people than individuals in the non-outbreak counties: Each of the node degree assessments (All, Infected, Sex Partner, and Infected Sex Partner) were greater in outbreak than in non-outbreak counties. Mixing by sex partner node degree measures were disassortative in outbreak counties and assortative elsewhere. Whereas mixing by syphilis disease stage was minimally assortative in outbreak counties, it was disassortative in non-outbreak areas. Partnerships were relatively discordant by age, especially among older white men, who often chose considerably younger female partners.

Assortative mixing for the number of sex partners in non-outbreak counties suggests monogamous/lower risk individuals tended to form sexual partnerships with other lower risk people, and those with many partners tended to have other high risk partners, thereby obstructing widespread transmission between groups. In contrast, disassortative mixing for Sex Partner and Infected Sex Partner degree in the outbreak counties suggests frequent cross-over partnering between lower and higher risk individuals that created numerous bridges extending transmission into otherwise low risk sexual networks.

Several published analyses describe how the epidemiology of primary, secondary, and early latent syphilis infections relate to sexual networks and epidemic phase. (29, 30, 31, 32, 33, 34, 35, 36, 37, 38) We build on this literature with analysis of sexual mixing with respect to syphilis stage. The assortative mixing among cases in outbreak counties supports the role of people with early stage, highly infectious syphilis in propagating the outbreak. Additional analyses of the dates of sexual contact relative to disease stage and diagnosis date, however, are needed to confirm this hypothesis. The high proportion and large absolute number of primary infections in the outbreak counties coupled with (albeit) minimally-assortative mixing suggest that highly infectious primary syphilis amplified transmission.

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Consistent with other studies of sexual (8, 15) and social networks(39), mixing with respect to race/ethnicity was quite assortative; whites exhibited the least- and Blacks exhibited the greatest assortative partnering. With the exception of national surveillance reports, Native Americans are typically excluded from sexual behavioral and STI research in the United States because the sample sizes are often too small to make meaningful comparisons to other race/ethnicities. Race/ethnicity mixing was substantially more assortative in the outbreak counties, because syphilis seeped into the Native American community. More than half of the partnerships involving at least one Native American in the outbreak counties were concordant for race/ethnicity, a level similar to African Americans.

The average age differential between men and their women sex partners diverged significantly between white and non-white men (in outbreak and non-outbreak counties combined). White men were an average of 10 years older than their partners, whereas non-white men were between five and 6.5 years older. The mean age difference for men of all race/ethnicities at least age 45 was 17 years, skewing the right tail of the distribution. In other words, as the men aged, the age differential became wider, a pattern similar to a national survey of adults in the United Kingdom.(40) A greater proportion of white men were at least age 60 (14%) than the other racial/ethnic groups (between 2% and 5%). The disproportionate participation of older white men in these sexual networks merits further examination.

Although available data for this analysis were extensive, the network is undoubtedly incomplete because: 1) some cases may have chosen not to name partners; 2) DIS were not provided with enough information to locate some named partners; 3) named partners may have refused to speak to DIS; 4) named partners living in another state could not be traced; and 5) named contacts' identities may not have been correctly matched to those of other persons in the network, effectively negating the existence of ties between people. The US Centers for Disease Control recommends conducting cluster interviews among people in the same social networks to identify others who may be infected. (23) The DIS in NC routinely perform cluster interviewing during outbreaks. Limited resources usually prohibit DIS from performing additional contact tracing for uninfected partners, who may be directly or indirectly connected to other cases. For these reasons, incomplete network ascertainment is common to all network studies of STIs. Nonetheless, missing information is unlikely to fundamentally change the interpretation of the findings. ((41), page 107)

Because these data were collected as part of disease control measures, rather than for research, uniform information for all cases was not available. DIS may exert greater efforts towards contact tracing during outbreaks. DIS may not be able to confirm that some social relationships were actually sexual partnerships. Moreover, DIS may document some risk behaviors relevant to the outbreak (e.g., crack use), but they do not routinely administer standardized questionnaires.

Although this analysis is retrospective, development of tools to examine sexual networks in real time is foreseeable in the near future. Software needs to be developed to generate network images quickly and describe other information such as venues where people met, that facilitate public health interventions. Ideally, DIS would be able to add information to

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case files including contact identities to generate network visualizations, possibly highlighting connections between previously unrelated cases.

We assessed mixing patterns in different geographical areas during one time period. An alternative approach is to compare mixing patterns over time in only the outbreak counties to determine if the patterns before and after the outbreak were markedly different than during the outbreak. Cunningham *et. al.* employed this method using DIS data to investigate structural differences in the sexual networks during and after a large outbreak of syphilis in Baltimore. (30) The results were consistent with these findings. Fewer and smaller network components were present after the outbreak.(30) The data for the time preceding the outbreak in North Carolina is less complete and data following the outbreak is not available to perform a similar analysis here.

Comparison of sexual partnership patterns between outbreak and non-outbreak environments elucidate in part how assortative and disassortative mixing mitigate or facilitate disease transmission. Assortative mixing by race/ethnicity likely contributed to the disproportionate involvement of Blacks and Native Americans, who already experience disparities of STIs.(42, 43) These partnership patterns underscore the need for increased syphilis screening within minority communities and for prevention efforts that accommodate the cultural diversity of affected subpopulations. Involvement of men over age 45 contributed to discordant age mixing regardless of race/ethnicity, but was highest among white men. Additional qualitative and quantitative research among middle-aged white men and young women may illuminate determinants of large age differentials.

Use of public health contact tracing data in other jurisdictions has shown how structural and other characteristics of sexual networks relate to the spread of STIs.(36, 44, 45, 46, 47, 48, 49, 50) By evaluating partnership dynamics from routine data collected by DIS as part of public health control activities, we discovered differences in the extent of assortative mixing in low level endemic and in outbreak settings. Whether assortative mixing exacerbates or attenuates the reach of STIs depends on the characteristic or attribute and epidemiologic phase. Examination of sexual partnership characteristics and mixing patterns offers insights into the growth of STI outbreaks that complement other research methods.

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REFERENCES

1. Foust, EM.; Leone, PA.; Ashby, RM. National STD Conference. San Diego, California: 2002. The impact of prostitution and drugs on a rural syphilis outbreak.
2. Sena AC, Muth SQ, Heffelfinger JD, et al. Factors and the sociosexual network associated with a syphilis outbreak in rural North Carolina. Sex Transm Dis. 2007; 34:280–7. [PubMed: 17139235]
3. North Carolina HIV/STD Surveillance Report. North Carolina Department of Health and Human Services, HIV/STD Prevention and Care Branch, Epidemiology and Special Studies Unit; Raleigh, NC: 2002.

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4. Aral SO. Sexual network patterns as determinants of STD rates: paradigm shift in the behavioral epidemiology of STDs made visible. Sex Transm Dis. 1999; 26:262–4. [PubMed: 10333278]
5. Doherty IA, Padian NS, Marlow C, et al. Determinants and consequences of sexual networks as they affect the spread of sexually transmitted infections. J Infect Dis. 2005; 191(Suppl 1):S42–54. [PubMed: 15627230]
6. Rothenberg R, Muth SQ. Large-network concepts and small-network characteristics: fixed and variable factors. Sex Transm Dis. 2007; 34:604–12. [PubMed: 17325619]
7. Aral SO. Patterns of sexual mixing: mechanisms for or limits to the spread of STIs? Sex Transm Infect. 2000; 76:415–6. [PubMed: 11221121]
8. Aral SO, Hughes JP, Stoner B, et al. Sexual mixing patterns in the spread of gonococcal and chlamydial infections. Am J Public Health. 1999; 89:825–33. [PubMed: 10358670]
9. Doherty IA, Shiboski S, Ellen JM, et al. Sexual bridging socially and over time: a simulation model exploring the relative effects of mixing and concurrency on viral sexually transmitted infection transmission. Sex Transm Dis. 2006; 33:368–73. [PubMed: 16721330]
10. Doherty IA, Schoenbach VJ, Adimora AA. Sexual mixing patterns and heterosexual HIV transmission among African Americans in the southeastern United States. J Acquir Immune Defic Syndr. 2009; 52:114–20. [PubMed: 19506485]
11. Garnett GP, Hughes JP, Anderson RM, et al. Sexual mixing patterns of patients attending sexually transmitted diseases clinics. Sex Transm Dis. 1996; 23:248–57. [PubMed: 8724517]
12. Gorbach PM, Drumright LN, Holmes KK. Discord, discordance, and concurrency: comparing individual and partnership-level analyses of new partnerships of young adults at risk of sexually transmitted infections. Sex Transm Dis. 2005; 32:7–12. [PubMed: 15614115]
13. Haraldsdottir S, Gupta S, Anderson RM. Preliminary studies of sexual networks in a male homosexual community in Iceland. J Acquir Immune Defic Syndr. 1992; 5:374–81. [PubMed: 1548573]
14. Kottiri BJ, Friedman SR, Neaigus A, et al. Risk networks and racial/ethnic differences in the prevalence of HIV infection among injection drug users. J Acquir Immune Defic Syndr. 2002; 30:95–104. [PubMed: 12048369]
15. Laumann EO, Youm Y. Racial/ethnic group differences in the prevalence of sexually transmitted diseases in the United States: a network explanation. Sex Transm Dis. 1999; 26:250–61. [PubMed: 10333277]
16. Rothenberg R, Peterson J, Brown M, et al. Heterogeneity of risk among African-American men who have sex with men. Int J STD AIDS. 2007; 18:47–54. [PubMed: 17326863]
17. Boyer CB, Shafer MA, Teitle E, et al. Sexually transmitted diseases in a health maintenance organization teen clinic: associations of race, partner's age, and marijuana use. Arch Pediatr Adolesc Med. 1999; 153:838–44. [PubMed: 10437757]
18. Catania JA, Binson D, Stone V. Relationship of sexual mixing across age and ethnic groups to herpes simplex virus-2 among unmarried heterosexual adults with multiple sexual partners. Health Psychol. 1996; 15:362–70. [PubMed: 8891715]
19. Gregson S, Nyamukapa CA, Garnett GP, et al. Sexual mixing patterns and sex-differentials in teenage exposure to HIV infection in rural Zimbabwae. Lancet. 2002; 359:1896–903. [PubMed: 12057552]
20. Gupta S, Anderson R, May R. Networks of sexual contacts: implications for the pattern of spread of HIV. AIDS. 1989; 3:807–17. [PubMed: 2517202]
21. Newman M. Assortative mixing in networks. Physical Review Letters. 2002; 89:208701. [PubMed: 12443515]
22. Newman M. Mixing patterns in networks. Physical Review E. 2003; 67:026126.
23. CDC. MMWR Early Release. 2008. Recommendations for Partner Services Programs for HIV Infection, Syphilis, Gonorrhea, and Chlamydial Infection.
24. Thomas JC, Kulik AL, Schoenbach VJ. Syphilis in the South: rural rates surpass urban rates in North Carolina. Am J Public Health. 1995; 85:1119–22. [PubMed: 7625508]
25. Doherty, IA.; Muth, SQ.; Adimora, AA., et al. Where is the syphilis outbreak? Use of number of cases, incidence rates, and sexual networks to assess a syphilis outbreak in North Carolina. International Society of Sexually Transmitted Diseases Research Conference; London. 2009.

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26. Wasserman, S.; Faust, K. Social network analysis : methods and applications. Cambridge University Press; Cambridge New York: 1994.
27. Census 2000 Summary File 3. US Census Bureau; 2000.
28. Census 2000 Summary File 2. US Census Bureau; 2000.
29. Choi KH, Ning Z, Gregorich SE, et al. The influence of social and sexual networks in the spread of HIV and syphilis among men who have sex with men in Shanghai, China. J Acquir Immune Defic Syndr. 2007; 45:77–84. [PubMed: 17325608]
30. Cunningham SD, Michaud JM, Johnson SM, et al. Phase-specific network differences associated with the syphilis epidemic in Baltimore city, 1996–2000. Sex Transm Dis. 2004; 31:611–5. [PubMed: 15388999]
31. Cunningham SD, Olthoff G, Burnett P, et al. Evidence of heterosexual bridging among syphilis-positive men who have sex with men. Sex Transm Infect. 2006; 82:444–5. [PubMed: 17151030]
32. Farley TA, Kahn RH, Johnson G, et al. Strategies for syphilis prevention: findings from surveys in a high-incidence area. Sex Transm Dis. 2000; 27:305–10. [PubMed: 10907903]
33. Klausner JD, Wolf W, Fischer-Ponce L, et al. Tracing a syphilis outbreak through cyberspace. JAMA. 2000; 284:447–9. [PubMed: 10904507]
34. Paz-Bailey G, Meyers A, Blank S, et al. A case-control study of syphilis among men who have sex with men in New York City: association with HIV infection. Sex Transm Dis. 2004; 31:581–7. [PubMed: 15388994]
35. Peterman TA, Kahn RH, Ciesielski CA, et al. Misclassification of the stages of syphilis: implications for surveillance. Sex Transm Dis. 2005; 32:144–9. [PubMed: 15729150]
36. Rothenberg RB, Sterk C, Toomey KE, et al. Using social network and ethnographic tools to evaluate syphilis transmission. Sex Transm Dis. 1998; 25:154–60. [PubMed: 9524994]
37. Schumacher CM, Ellen J, Rompalo AM. Changes in demographics and risk behaviors of persons with early syphilis depending on epidemic phase. Sex Transm Dis. 2008; 35:190–6. [PubMed: 18216726]
38. Simms I, Fenton KA, Ashton M, et al. The re-emergence of syphilis in the United Kingdom: the new epidemic phases. Sex Transm Dis. 2005; 32:220–6. [PubMed: 15788919]
39. Mollica K, Gray B, Trevino LK. Racial homophily and its persistence in newcomers' social networks. Organization Science. 2003; 14:123–36.
40. Mercer CH, Copas AJ, Sonnenberg P, et al. Who has sex with whom? Characteristics of heterosexual partnerships reported in a national probability survey and implications for STI risk. Int J Epidemiol. 2009; 38:206–14. [PubMed: 19001667]
41. Potterat, JJ.; Woodhouse, DE.; Muth, SQ., et al. Network Dynamism: History and Lessons of the Colorado Springs Study. In: Morris, M., editor. Network Epidemiology A Handbook for Survey Design and Data Collection. Oxford University Press; New York: 2004.
42. Kaufman CE, Shelby L, Mosure DJ, et al. Within the hidden epidemic: sexually transmitted diseases and HIV/AIDS among American Indians and Alaska Natives. Sex Transm Dis. 2007; 34:767–77. [PubMed: 17538516]
43. Newman LM, Berman SM. Epidemiology of STD disparities in African American communities. Sex Transm Dis. 2008; 35:S4–12. [PubMed: 18971796]
44. Jolly AM, Muth SQ, Wylie JL, et al. Sexual networks and sexually transmitted infections: a tale of two cities. J Urban Health. 2001; 78:433–45. [PubMed: 11564847]
45. Jolly AM, Wylie JL. Gonorrhoea and chlamydia core groups and sexual networks in Manitoba. Sex Transm Infect. 2002; 78(Suppl I):i145–i51. [PubMed: 12083435]
46. Potterat JJ, Muth SQ, Rothenberg RB, et al. Sexual network structure as an indicator of epidemic phase. Sex Transm Infect. 2002; 78(Suppl 1):i152–8. [PubMed: 12083436]
47. Potterat JJ, Phillips-Plummer L, Muth SQ, et al. Risk network structure in the early epidemic phase of HIV transmission in Colorado Springs. Sex Transm Infect. 2002; 78(Suppl 1):i159–63. [PubMed: 12083437]
48. Potterat JJ, Rothenberg RB, Woodhouse DE, et al. Gonorrhea as a social disease. Sex Transm Dis. 1985; 12:25–32. [PubMed: 4002091]

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49. Wylie JL, Cabral T, Jolly AM. Identification of networks of sexually transmitted infection: a molecular, geographic, and social network analysis. J Infect Dis. 2005; 191:899–906. [PubMed: 15717265]

50. Wylie JL, Jolly A. Patterns of chlamydia and gonorrhea infection in sexual networks in Manitoba, Canada. Sex Transm Dis. 2001; 28:14–24. [PubMed: 11196040]

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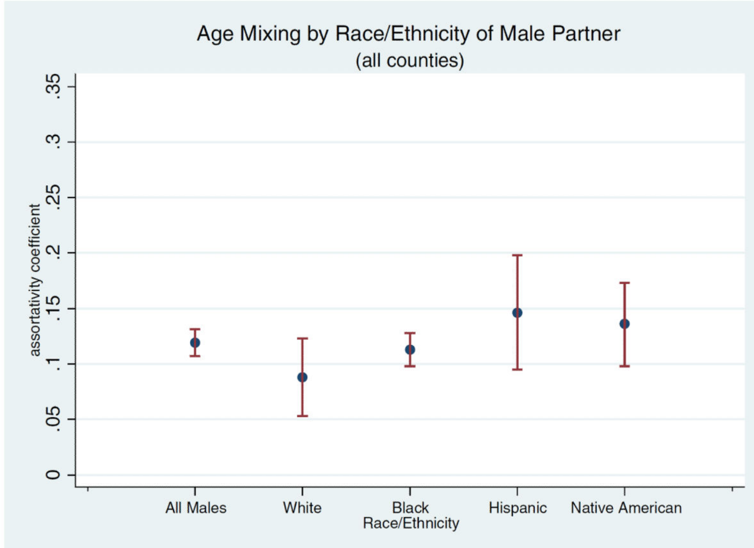

Figure 1.
Age mixing by race/ethnicity of male partner

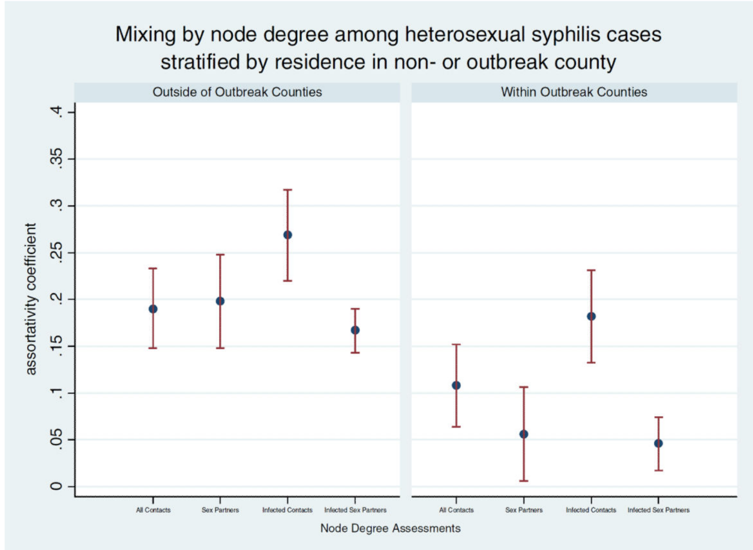

Figure 2.
Mixing by node degree among heterosexual syphilis cases stratified by residene in non- or outbreak county

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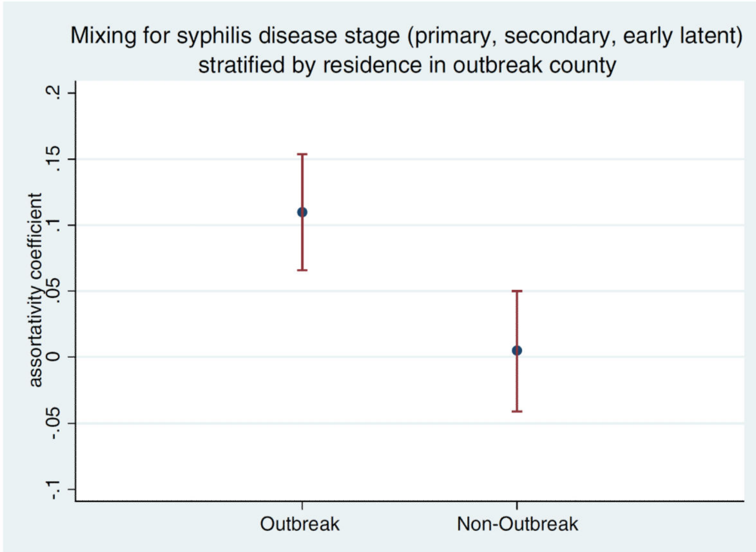

Figure 3.
Mixing for syphilis disease stage (primary, secondary, early latent) stratified by residence in outbreak county

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Table 1

Demographic characteristics of cases, uninfected, and unknown status by residence in non- and outbreak counties, North Carolina 1998–2002

	Non-outbreak counties		**Outbreak counties**		**Total**	
	n	**(%)**	**n**	**(%)**	**n**	**(%)**
Total	**3366**	**(63.5)**	**1933**	**(36.5)**	**5299**	**(100)**
male	1,883	(56)	1,068	(55)	2,951	(56)
female	1,482	(44)	864	(45)	2,346	(44)
Race/ethnicity	3,205		1,906		5,111	
White	575	(18)	273	(14)	848	(17)
Black	2,303	(72)	951	(50)	3,254	(64)
Hispanic	250	(8)	79	(4)	329	(6)
Native American	64	(2)	588	(31)	652	(13)
Asian/Pacific Islander	11	(<1)	13	(1)	24	(<1)
Other	2	(<1)	2	(<1)	4	(<1)
Age on Jan 1, 2000[†]	2,823		1,743		4,566	
14–19	234	(8)	214	(12)	448	(10)
20–29	869	(31)	537	(31)	1,406	(31)
30–39	888	(31)	475	(27)	1,363	(30)
40–49	566	(20)	334	(19)	900	(20)
50–59	175	(6)	114	(7)	289	(6)
≥60	91	(3)	69	(4)	160	(4)

[†]Age was missing for 14% of the records

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Table 2

Syphilis morbidity by residence in non- and outbreak counties, North Carolina 1998–2002

	Non-outbreak counties		**Outbreak counties**		**Total**	
	n	**(col %)**	**n**	**(col %)**	**n**	**(col %)**
Total	**3366**		**1933**		**5299**	
Infected	1,311	39%	744	38%	2,055	39%
Confirmed negative	1,530	45%	967	50%	2,497	47%
Unknown[†]	525	16%	222	11%	747	14%
Disease stage						
Primary	168	13%	161	22%	329	16%
Secondary	361	28%	211	28%	572	28%
Early latent	782	60%	372	50%	1,154	56%

[†]includes named sex partners and contacts who could not be identified or located, or refused testing

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Table 3

Distribution of node degree among cases by residence non- and outbreak counties, North Carolina 1998–2002

	Non-outbreak counties		Outbreak counties		Total	
Total	**1311**		**744**		**2055**	
All degree †	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
1	627	(48)	233	(31)	860	(42)
2	298	(23)	162	(22)	460	(22)
3–5	274	(21)	225	(30)	499	(24)
≥6	112	(9)	124	(17)	236	(11)
mean (sd)	2.69	(3.86)	3.51	(3.63)	2.99	(3.80)
median	2		2		2	
Infected degree ‡	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
0	408	(31)	137	(18)	545	(27)
1	653	(50)	318	(43)	971	(47)
2	159	(12)	148	(20)	307	(15)
≥3	91	(7)	141	(19)	232	(11)
Mean (sd)	1.06	(1.36)	1.60	(1.55)	1.26	(1.46)
median	1		1		1	
Sex partner degree £	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
0	41	(3)	21	(3)	62	(3)
1	713	(54)	314	(42)	1,027	(50)
2	290	(22)	205	(28)	495	(24)
≥3	267	(20)	204	(27)	471	(23)
Mean (sd)	1.90	(1.80)	2.10	(1.56)	1.97	(1.72)
median	1		2		1	
Infected sex partner degree €	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
0	463	(35)	181	(24)	644	(31)
1	677	(52)	380	(51)	1,057	(51)
≥2	171	(13)	183	(25)	354	(17)
Mean (sd)	0.85	(0.83)	1.10	0.92	0.94	(0.90)
median	1		1		1	

† ***All*** types of partnerships including sex partners, social contacts and possible cases, irrespective of disease status;

‡ ***Infected*** sex partners and social contacts;

£ ***Sex partners*** irrespective of disease status;

€ ***Infected sex partners*** only;

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Table 4

Comparison of syphilis disease stage concordance among partnerships where both partners were infected in outbreak and non-outbreak counties, North Carolina 1998–2002

		Primary		Secondary		Early Latent	
	Total†	n	row %	n	row %	n	row %
Outbreak counties							
Primary	245	47	19%	39	34%	76	47%
Secondary	312	44	27%	65	21%	90	53%
Early latent	444	39	26%	74	37%	165	37%
Non-outbreak counties							
Primary	102	5	5%	21	41%	32	54%
Secondary	360	21	12%	65	18%	110	70%
Early latent	544	23	10%	143	47%	236	43%

†Number of partnerships in which at least one person is diagnosed with Primary, Secondary, or Early latent syphilis