Prevention strategies for sexually transmitted infections: importance of sexual network structure and epidemic phase

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This article explores the relationship between sexual network structure and epidemic phase in sexually transmitted disease epidemiology, and discusses how this may be used to inform prevention strategies at the population level. There are relatively few empirical studies of sexual networks, and even fewer that track the evolution of networks over time. Most studies focus on networks in the context of disease transmission and will miss the network structure in the wider population. Results from disease-related studies in the early epidemic phase show densely connected networks with multiple short loops. In later hyperendemic phases, networks appear more loosely connected with a dominance of long branching structures. The latter structure has also been described from non-diseased populations. These structures evolve over time, both of the epidemic curve and as a cohort ages and undergoes demographic change. Population strategies for prevention should vary depending on network structure and epidemic phase. In early and late epidemic phases, interventions focusing on high-risk populations—that is, dense areas of a sexual network—will have a large population effect. In contrast, for established endemic diseases a smaller change (of behaviour or interruption of transmission through screening) in a larger proportion of the population could have the largest population impact. Further empirical work on the way network structures relate to epidemic phase, and how this changes with age and social development will help to inform intervention strategies at the population level.

Sexual networks are the structures through which organisms are transmitted. They are extremely difficult to explore through research as they remain hidden from the view—individuals can only see their own links or egocentric networks. They may think they also know their partner’s partner’s partner (and beyond) and that the network fades from view. Researching sexual networks to go beyond the individual (egocentric) to the group (sociocentric) level is fraught with practical and ethical difficulties. Interest in sexual network research started to grow in the mid-1980s, with the aim of improving our understanding of HIV transmission and thereby informing informing control strategies, and was followed by much empirical research and theoretical research. Some of this led to suggestions of interventions, such as the use of social networks to track syphilis outbreaks, but it does not seem to have delivered widely on improved intervention, beyond that already used in partner notification strategies, or to a generalised advance in epidemiological theory of transmission of sexually transmitted infections (STIs).

Sexual network research takes place alongside a growing understanding of the different phases of epidemics. Wasserheit and Aral described the major stages in an STI epidemic, starting with the growth (I) phase, then passing through the hyperendemic (II), the decline (III) and finally the endemic or equilibrium (IV) phase; in theory this could lead to a final elimination (V) phase. Following the initial theoretical exposition of these phases, further theoretical and empirical work has been carried out to undermine the importance of this framework for interpretation and intervention. There are several examples in which this model has helped to interpret secular trends and guide responses (see Aral).

There are clear links between conceptualisation of epidemic phase and sexual networks. Introduction and growth phases require “spread” networks in which the reproductive rate of the infection is greater than 1 and incidence exceeds recovery. In a stable hyperendemic (II) or final endemic (IV) phase there is a relative equilibrium and infection transmits through “maintenance” networks where $R_0$ approximates to 1. In this article I explore this relationship further through empirical examples of sexual networks, and ask what implications this body of work has for future theory, interventions and research.

DO NETWORKS MATTER?

The limited application of network theory to improved sexual health begs the question whether networks really are important in determining the spread and, therefore, control, of STI. Are network size, structure and evolution really key features of transmission? A study of HIV in women in Peru elegantly showed the importance of network size. Seventy-five pregnant women with HIV were compared with 137 HIV-negative pregnant controls. Fifty of the 75 infected women were reported as having no personal risk factor for HIV, and their median number of sexual partners in the previous five years was 1. The authors estimated second and then third generation sexual network size—the sum of the individual’s sexual partners plus their partners’ partners (and then beyond) over a five-year period. The mean second generation size was 8.4 for cases and 2.5 for controls; taken to the third generation the network size was 672 in cases and 160 in controls. This confirms the common sense, but little documented, observation that it is not just an individual’s number of partners that determines their risk of STI acquisition, but their partners’ partners and beyond.

Although the above example neatly shows the influence of a local network on an individual’s risk it does not address how network size or structure affects the transmission of infection at a population level. One of the unusual characteristics of sexually transmitted pathogens according to Anderson and May is the effective lack of a density threshold, in contrast with diseases such as measles in which transmission is strongly associated with population density. STIs are consequently able to persist in very small populations. Given this, does the size of a sexual network make any difference to transmission? Clearly at the extremes this must be true, because in a mutually monogamous couple, neither of whom is infected, there can be

Abbreviation: STI, sexually transmitted infection
no transmission. Where there are large numbers of individuals connected through sexual contact there is the possibility of transmission but again, only if the organism is already present. So although size clearly does make a difference it will probably not be linear beyond a particular threshold density, and therefore the exact relationship between network size and transmission is not clear. What is clear is that many of the assumptions of simple models do not apply in the case of sexual mixing. This is because numbers of partners are not normally distributed, and partners are selected non-randomly, undermining the inclusion of average rate of partner change in the basic differential equation for the reproductive number.24

Network structure is also important. In a simple illustrative model (fig 1), clearly a small restructuring of links between eight individuals can alter the final prevalence of infection within the group. The figure shows two configurations of eight individuals with a set number of partners (six individuals have two partners and two have three partners). A different network structure alters the final prevalence of infection and one structure is more amenable to disruption of transmission through intervention. Based on a simple transmission probability of 0.5/contact, structure NI produces a final prevalence of 0.39 (3.125/8) compared with 0.45 (3.625/8) in structure NII, a 16% increase.

Thus structure has, in theory, a relationship to likelihood of transmission and thus to opportunities for intervention. Rothenberg provides another example of the importance of network structure for transmission, showing that relatively small changes to the links within a network can have a large impact on the final prevalence of transmission.19 Rothenberg uses this more complex example to show how knowledge of links could inform interventions by prioritising those that permit the widest, or most rapid, dissemination of infection.

These theoretical examples are fascinating. Unfortunately, they are difficult to translate into practice for two reasons. First, there are few empirical studies of actual sexual networks, and, second, where they are described it is generally post festum—that is, they can only be constructed after the event. To be useful in practice we need to build on the evidence of real networks to develop some “typology” that would inform future interventions in the absence of surveillance of actual networks.

**GONORRHOEA IN LONDON**

In 1995, as part of a larger study of transmission of gonorrhoea in London, we used ethnographic methods to explore one sexual network in detail.7 The index patient was a 20-year-old man with gonorrhoea and HIV who reported recent contact with four men who also had HIV infection. The contacts were traced and invited to participate in a wider study of sexual networks. Over the next 12 months, 53 interviews were conducted with 18 men and 1 woman, all of whom had direct or indirect sexual links. They described a linked network of 138 individuals plus over 1200 “unknown” contacts (fig 2). The structure is one of several dense areas which appear as “starbursts”—people with multiple links to other people—some of which are very close to each other making the overall network seem densely connected. There are also several “cycles”—where people are linked in two directions forming a closed loop. Of particular interest from the point of view of transmission of infection are (1) the location of seven women within this dense network of predominantly gay men, (2) the proximity of everyone on the network to one or more people with HIV (everyone was a maximum of five steps from HIV) and (3) the large numbers of anonymous and commercial contacts reported, many of whom may overlap.

This study revealed many of the inherent challenges for empirical network research, including bias in sampling towards known contacts, lack of certainty about the identity of some members, and therefore the possibility that loops may be missed (ie, one person’s contact may be the same individual as another person’s contact but reported with a different name or other identifier). The labour-intensive nature of network research is shown by the need for more than 50 interviews to define this relatively small network.1 We found that some participants revealed more and different partners on subsequent interviews, including relationships that occurred before the first interviews but were not, for various reasons, reported.

If the structure of this network was representative of wider links among gay men in London at the time, it is of little surprise that in the subsequent decade there has been a large increase in gonorrhoea, outbreaks of syphilis and lymphogranuloma venereum, and a continued high incidence of HIV.31 32 The network study took place at the nadir of gonorrhoea and syphilis in the UK, with rates of both infections reaching the lowest levels ever recorded (fig 3). Sexual behaviour changes in response to HIV had led to a dramatic fall in the incidence of these bacterial STIs in the 1980s. The network study was carried out during phase IV with a low endemic level for gonorrhoea, and possibly an elimination phase (V) for syphilis. In such periods these infections are thought to persist in densely connected but isolated networks with limited access to diagnostic and treatment services.33 34 These conditions will allow for a relative balance between incidence and recovery. From this low endemic level infection may decline further towards elimination or a new growth phase may occur if the network links to wider groups. The network identified in the

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**Figure 1** How the structure of a network can influence transmission. (Adapted from Klovdahl et al27 and Center for AIDS Prevention Studies.29) [A] NI and NII are two networks with the same numbers of individuals (8) with the same numbers of links, six individuals have two links (partners) and two individuals have three links. [B] The figure shows the probabilities of infection in each individual if the individual on the far left is infected, and there is a transmission probability of 0.2. The final prevalence is given by the sum of these probabilities. Structure NII has 3.125 times higher final prevalence than structure NI. [C] The figure identifies points for intervention (shown with X) which would stop transmission (eg condoms, vaccination). In NI one intervention at the correct point will “protect” half of the network from infection, whereas three such points are needed in NII.
London study showed the density and loops required for persistence within the group, and also the potential for reintroduction into a wider group through the large numbers of anonymous and commercial contacts. A relatively small increase in risk behaviour, with a decline in condom use, or a delay in access to treatment services, could have a large impact on the ability of the organism to enter a more successful growth phase. This example illustrates that there is no simple relationship between network structure and epidemic phase, given that this same structure appeared to support a low endemic level of infection (IV) but could easily lead to a growth (I) phase, and that this may be different for bacterial and viral STIs.

**CHLAMYDIA AND GONORRHOEA IN COLORADO SPRINGS**

Some of the best described networks for STIs were reported by Potterat and colleagues, working in Colorado Springs in the USA. They explicitly considered the question of how network structure relates to epidemic phase by comparing sexual network structures among people with chlamydia infection in the late 1990s with those in an outbreak of gonorrhoea from a decade earlier. An observed increase in chlamydia infection locally led to suggestions of an outbreak. However, this could not be verified because diagnostic methods had changed, with the introduction of more sensitive tests, and screening was more widely available, both of which would lead to an increase...
in reported cases whether or not there was an underlying increase in incidence. The authors described the sexual network patterns for 6067 cases of chlamydia between 1996 and 1999. Just over half the cases were in isolated dyads or triads, but there were several large components with up to 141 individuals. They report that: “Visualisation of the 10 largest components (those exceeding 30 individuals) revealed a linear branching structure virtually devoid of closed loops.” The authors then contrasted the structures observed in a study of gonorrhoea between 1988 and 1991 involving 578 individuals. A single large component linked 71% of these individuals. “The dense interconnections in this group reveal a predominantly cyclic pattern ...”. These two contrasting networks are shown in figure 4.

In these two examples the dense network characteristic of an outbreak, or growth phase, contrasts with the predominantly dendritic structure of an endemic infection. Potterat and colleagues suggest that this provides a mechanism for identifying epidemic phase; networks constructed from partner notification data can distinguish phases in equilibrium from spread networks. This is an attractive proposition, but it needs further exploration because similar data could also be produced by different sampling and by organism-specific characteristics. In hyperendemic equilibrium the disease, in this case chlamydia, is widespread in the population and many of the cases will be in slowly propagating networks or transmission “dead ends”. Dense areas will still exist but are less likely to be sampled than where they are the dominant structure. In contrast with a growth phase the probability of sampling one of the dense areas of the network is greater because these will probably predominate. Few cities have the level of partner notification coverage achieved in Colorado Springs, and therefore interpretation of data would be more challenging.

Consideration also needs to be given to the network structures that will support infections with different adaptations to the host. Chlamydia is a more chronic infection with a high proportion of asymptomatic cases. The long duration of infectiousness will permit continued slow propagation, even in a growth phase, as infection may persist through one or more changes in sexual partners, even in a relatively low-density network. Chlamydia may therefore be more effectively adapted to the predominant sexual networks in—for example, the UK or USA, where many young people have a few serial or temporarily overlapping relationships. These structures permit the persistence and spread of infections with a long duration, such as chlamydia or herpes, whereas a more acute infection with fewer asymptomatic cases requires the dense structures to persist or grow. Although the proposition that network structure can indicate epidemic phase is not fully met in these examples, the chlamydia example shows that a hyperendemic phase may be characterised by relatively loose networks, for this infection at least.

**TEENAGE ROMANCE**

The final example is distinct in that it does not start from a sample of people with an STI, but on the formation of partnerships in a high school in the USA. Briefly, data were collected on high school students as part of a National Longitudinal Study of Adolescent Health (Add Health), starting in 1994. In one sub-study, adolescents in the tenth to twelfth grades (aged 16–18 years) in a large school were asked to identify their sexual and romantic partners over an 18-month period. The analysis is based on data from 832 respondents in a single school, identified with the pseudonym “Jefferson High School”. This remarkable study, with a response rate of 90%, provides a wealth of insight into sexual networks during the initiation of sexual activity. The network includes romantic links that are not necessarily sexual, but it is these types of relationship that will probably become sexual over time, and therefore the structure explores potential for transmission. In addition, “romantic” links may not be free from risk of transmitting infection, given that a third of self-defined virgins reported genital contact to orgasm with a partner in the past 12 months. The overall network structure of the students reporting romantic or sexual contacts is reproduced in figure 5. A single large component is shown linking 52% (288) students, and the remainder are in isolated smaller groups, including 126 (22%) in dyads. The large component is composed of a long branching structure that eventually completes a large loop. It includes only one short cycle (of six people), and the remainder are in long branches, with the most distant individuals 37 steps apart.

This network, not based on disease transmission or necessarily sexual contract, has more similarities with the chlamydia network in figure 4A than with the gonorrhoea networks in figures 2 and 4B, suggesting the possibility for slow propagation but without the characteristics of a classic “core group” associated with the introduction and growth phases of an epidemic. However, the authors note that (p. 60):
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The particular structure of any network will be the result of stochastic processes but these will take place in the context of social and cultural norms and constraints of partnership formation. In mathematical models, Bearman and colleagues were unable to replicate the observed network structure with random mixing. They achieved a better approximation by introducing assortative mixing by partner numbers, a homophily that they related to some of the data. However, that model produced a more densely connected network with frequent cycles. Introducing certain partner prohibitions into the model improved the fit. This was based on adolescents avoiding "seconds partnerships". By this they mean that after a relationship ended, an individual would not start a new relationship with their former partner's new partner's previous partner. Put simply, for heterosexual relationships, people did not "swap" partners, and therefore cycles of four steps were not seen. By introducing such rules into models they were able to replicate the observed network structure. They concluded that this type of norm leads to large loose networks that facilitate the spread and persistence of bacterial STIs in adolescents and therefore interventions to "high-risk" or "core group" individuals will fail to interrupt transmission.

DISCUSSION

This brief exploration of sexual networks raises questions about the generalisability of core group theory for STI transmission. Classically, epidemiologists have used models to argue that STI transmission in the population is sustained by a core group of highly sexually active individuals, without whom infection would die out. The concept of a core group was outlined in the theoretical literature on STIs by Yorke et al in 1978, who found it a possible explanation of the relative equilibrium state of gonorrhoea in the USA. Yorke postulated that in the absence of any acquired immunity there must be another density-dependent mechanism limiting the spread of gonorrhoea, suggesting that pre-emptive saturation could have a key role. Pre-emptive saturation means that the onward transmission of gonorrhoea is limited by contact between already infected individuals. This could not be the case in the population as a whole, because the prevalence of infection was insufficient, and therefore there must be sub-strata of the population with higher sexual activity and higher prevalence of disease. This relatively abstract notion has had a major influence on subsequent epidemiological thinking, and on programme planners.

The concept of a core group of "superspreaders" of disease is also attractive to dominant morality, fitting well with deeply held social beliefs and images of reservoirs of infection and diseased swamps. Parent du chatellet, a public health doctor in nineteenth-century Paris wrote: "Prostitutes are as inevitable in a great conurbation as sewers, cesspits and refuse dumps. The conduct of the authorities should be the same with regard to each." He advocated targeted interventions (mandatory examination and regulation) for prostitutes to control syphilis. In 1911, a "vice commission" in Chicago wrote: "Prostitution is pregnant with disease, a disease infecting not only the guilty but contaminating the innocent wife and child in the home with sickening certainty almost inconceivable."

The work of Yorke and others chimes in well with such approaches. The attraction of the concept is summarised by Anderson and May who write of Yorke's work on gonorrhoea (p. 230):

"If the core individuals could all be identified and kept free of gonorrhoea (by persistent surveillance and treatment, or by use of an as-yet hypothetical vaccine), the disease would die out, because its basic reproductive rate in the remaining non-core population is less than unity."

The importance of this theory is that if core groups are necessary for introduction, spread and maintenance of STIs in the population, then clearly effective control at the population level would be based on targeting core groups. This contrasts with approaches to many other conditions in which interventions for the whole population are more effective that those restricted to the non-core population is less than unity. In the classic example of stroke, Rose argues that a high-risk approach, identifying those with the highest blood pressure and treating them, will substantially reduce risk in those individuals, but this will have relatively little effect on the rate of stroke in the population because more cases occur in the larger number of people with a small increase in risk. Rose concludes that the most effective strategy for the population is to try to shift the population distribution of blood pressure to the left. The reasoning does not apply directly to infectious disease as the risk of the individual is a function of the risk of others, and conversely reducing the risk of others can protect otherwise susceptible people, as in the case of herd immunity. In STI control we generally use multiple approaches that aim for a shift in population risk—for example, through widespread condom promotion—with high-risk interventions through partner notification, screening of behavioural risk groups and outreach.

The promise of sexual network research is to identify risk networks, more refined than core groups, to hone in on areas of most transmission rather than on those based simply on acquisition. Interventions for core groups based on numbers of sexual partners may miss key individuals who have repeated sex acts with more than one partner, for example. The
different structures identified in the examples above suggest that this may be more effective for certain infections, and at certain epidemic phases, than others. If chlamydia is well adapted to persistence in loose branching networks then this may be more effective for certain infections, and at different structures identified in the examples above suggest that could have the largest population impact.

More research in needed to unravel the way sexual networks relate to epidemic phase and how the relationship changes with age and social development. This will help inform intervention strategies at the population level.

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