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Interval Estimates for Epidemic Thresholds in Two-Sex Network Models

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Abstract

Epidemic thresholds in network models of heterogeneous populations characterized by highly right-skewed contact distributions can be very small. When the population is above the threshold, an epidemic is inevitable and conventional control measures to reduce the transmissibility of a pathogen will fail to eradicate it. We consider a two-sex network model for a sexually transmitted disease which assumes random mixing conditional on the degree distribution. We calculate interval estimates for the epidemic threshold for stochastic process models in three human populations based on representative surveys of sexual behavior (Uganda, Sweden, USA). For Uganda and Sweden, the epidemic threshold is greater than zero with high confidence. For the USA, the interval includes zero. We discuss the implications of these findings along with the limitations of epidemic models which assume random mixing.

1 Introduction

Epidemic models exhibit critical behavior. When a population is below some critical threshold, a major outbreak of an infectious disease (i.e., an epidemic) can not occur. Classically, epidemic thresholds were seen in terms of a critical number of susceptible hosts: a population with too few susceptible could not support an epidemic (Bailey, 1975). More modern treatments have focused on the threshold parameter R_0, the basic reproduction number (Heesterbeek, 2002). R_0 is defined as the expected number of secondary cases produced by a single (typical) index case in a completely susceptible population (Diekmann et al., 1990). For a homogeneous, one-sex model of a directly-transmitted pathogen and one disease state, this expected number of cases is given simply by the product of the transmissibility of the agent (β), the average contact rate between susceptible and infected members of the population ($\bar{c}$), and the duration of infectiousness, usually defined by the reciprocal of the recovery rate ($\delta = \nu^{-1}$):

$$R_0^{(U)} = \beta \bar{c} \delta, \tag{1}$$

where the superscript (U) indicates that R_0 applies to a homogeneous (uniform) population.

This somewhat schematic definition of R_0 enjoys the great advantage of easy interpretation. Public health campaigns designed to eliminate STIs focus on one of three strategies suggested by (1): (a) reduce transmissibility (β) through vaccines, barrier contraceptive use, or, in the case of non-curable viral infections, therapeutics (e.g., HAART), (b) reduce the contact rate ($\bar{c}$) through education, or (c) increase the recovery rate (ν) through treatment of curable STIs. Some interventions combine strategies. For example, contact-tracing combines contact-reducing and recovery-rate increasing interventions (Janssen et al., 2001; Golden, 2002).

The definition of R_0 in heterogeneous populations is somewhat more complex, though by discretizing "generations" of infections, its calculation is a simple extension of the homogeneous case (Diekmann et al., 1990; Diekmann and Heesterbeek, 2000). For many sexually transmitted infections (STIs) with one disease state, heterogeneity is incorporated into models by way of a mixing matrix in which the population is stratified by sexual activity level and the matrix gives the activity-specific probability of interaction (Gupta et al., 1989; Anderson and Garnett, 2000).

For a population characterized by heterogeneous sexual activity, and and in which there is random mixing linearly proportional to activity levels, Anderson et al. (1986) demonstrate that R_0 becomes:

$$R_0^{(H)} = R_0^{(U)}(1 + CV^2), \tag{2}$$

where CV is the coefficient of variation of sexual activity in the population (i.e., the standard deviation divided by the mean of the number of sexual partners). Clearly, populations characterized by large variance – and particularly large variance relative to the mean – will have higher reproduction numbers and thus, lower epidemic thresholds.

The great majority of epidemic models that followed from the pioneering work of Anderson et al. (1986) are one-sex, either explicitly because they consider homosexual transmission dynamics (e.g., Gupta et al., 1989) or implicitly because they do not model the interaction of the sexes(Newman, 2002b).

Men's and women's sexual behavior differs systematically throughout the world as a function of cultural norms, gender-power relations, and social institutions regulating individual behavior. In

Africa, home to the world's largest fraction of HIV sero-positive people, HIV is sexually transmitted primarily by contacts between men and women. Two-sex models admit the possibility of an epidemic threshold of zero, even if the behavior of either of the sexes alone would yield a non-zero threshold (Newman, 2002b).

A second, related concern is that the partnership distributions' variance, while finite, could still be high enough to impede the effectiveness of transmissibility-based interventions. Since, for example, no vaccine is completely effective (Blower et al., 2001), a non-zero epidemic threshold could still pose a practical barrier to disease eradication if it were low enough.

Pastor-Satorras and Vespignani (2002) note that epidemic thresholds for "bounded scale-free" networks are higher than for homogeneous networks. While this result is not particularly novel in the context of mathematical epidemiology (cf. Hethcote and Yorke, 1984; Anderson et al., 1986; Gupta et al., 1989), it reinforces the need to examine quantitatively the effect of large degrees of behavioral heterogeneity on the epidemic thresholds of STIs.

Furthermore, while the Anderson et al. (1986) result for heterogeneous R_0 helps provide the intuition for why partnership distributions with power-law behavior can yield epidemics without critical behavior (see also May and Lloyd, 2001), this derivation of the epidemic threshold (i.e., at $R_0^{(H)} > 1$) is based on a compartmental model and not on an explicit network epidemic model.

In this paper we consider models where individuals are represented as nodes in a network and edges represent heterosexual sexual contact. Disease spreads only through diffusion over the network of sexual contacts. We assume that the network is a realization of a stochastic process characterized by random mixing between individuals conditional on the individual activity levels (i.e., the nodal degrees) (Newman, 2002b). We focus on models for the population degree distributions in which the variance can greatly exceed the mean. One important class are those that exhibit power-law behavior, often loosely referred to as "scale-free" distributions (Liljeros et al., 2001; Dezső and Barabási, 2002). We estimate thresholds for two-sex epidemics that model the contact structure underlying transmission. These thresholds represent for explicitly networked models the analogue of $R_0^{(H)}$ as given in (2) for example.

In Section 2 we develop models for the sexual contact degree distribution. In Section 3, we derive the epidemic thresholds for these models within the random graph model of Newman (2002b). The degree distribution models are estimated for three populations (Section 3.1) and the epidemic thresholds are estimated (Section 3.2). In Section 6, we discuss the epidemiological relevance of these results, and approaches to overcome the limitations of the models.

2 Models for Degree Distributions

Let $P(K = k)$ be the probability mass function of the number of partners within a well defined period that a randomly chosen person in a population has had. We say $P(K = k)$ has *power-law behavior* with scaling exponent $\rho > 1$ if there exist constants c_1, c_2, and M such that $0 < c_1 \leq P(K = k)k^\rho \leq c_2 < \infty$ for $k > M$. Empirical distributions of the number of sex partners, both lifetime and over the past year, show a pronounced right-skew, with the great majority of people having few partners and some having many (Laumann et al., 1994; Lewin, 1996; Hubert et al., 1998; Aral, 1999; Youm and Laumann, 2002). This observation has led a number of authors to suggest that sexual partnership distributions have power law behavior (Liljeros et al., 2001, 2003; Schneeberger et al., 2004). These authors do not consider the wide range of right-skewed

distributions as plausible alternatives.

For $\rho \leq 3$, the variance of a distribution with power-law behavior is infinite. The Anderson et al. (1986) approximation for R_0 therefore suggests that populations characterized by partnership distributions with power-law behavior and $\rho \leq 3$ will lack epidemic thresholds, since with infinite variance $R_0^{(H)} > 1$ for arbitrarily small transmissibility or duration of infectiousness. Note that an actual population will always have finite variance, and hence the extrapolation of mathematical models for the degree distributions that have infinite variance requires a careful assessment of the quality of the approximation provided by the model (Jones and Handcock, 2003; Handcock and Jones, 2004).

We focus on two competing stochastic mechanisms for the formation of sexual contact networks. The first is a variation on a preferential attachment process, such as those advocated by several recent authors (Barabási and Albert, 1999; Pastor-Satorras and Vespignani, 2001; Liljeros et al., 2001). The second process is a non-homogeneous Poisson model for partnership formation. The limiting distributions of both these mechanisms can be characterized by long tails. They have the additional benefit that they have the same number of parameters, facilitating comparison.

2.1 Preferential Attachment Model

A mechanism that has been suggested for the formation of power-law sexual networks is preferential attachment (Albert and Barabási, 2000; Liljeros et al., 2001; Dezső and Barabási, 2002). This and related stochastic processes have a long history in applied statistics (Simon, 1955; Kendall, 1961; Irwin, 1963). Consider a population of r people in in which (1) there is a constant probability p that the $r+1$st partnership in the population will be initiated from a randomly chosen person to a previously sexually inactive person, and (2) otherwise the probability that the $r+1$st partnership will be to a person with exactly k partners is proportional to $kf(k|r)$, where $f(k|r)$ is the frequency of nodes with exactly k connections out of the r total links in the population. The limiting degree distribution of those connected by this process as $r \to \infty$ is known as the Waring distribution (Irwin, 1963). The Yule distribution discussed by Simon (1955) and used by Jones and Handcock (2003) to model degree distributions is a special case of the Waring distribution with $p = (\rho-2)/(\rho-1)$.

The probability mass function (PMF) of the Waring distribution (Johnson et al., 1992) is:

$$P(K = k|K > 0) = \frac{(\rho-1)\Gamma(\rho+\phi)}{\Gamma(\phi+1)} \cdot \frac{\Gamma(k+\phi)}{\Gamma(k+\phi+\rho)}, \qquad \phi > -1, \tag{3}$$

where $\Gamma(\cdot)$ is the Gamma function and the mixing parameter ϕ is related to p via:

$$p = \frac{\rho-2}{\rho+\phi-1}. \tag{4}$$

The Waring distribution has power-law behavior with scaling exponent ρ. The mean and variance of the Waring distribution are:

$$\mathbb{E}(K|K>0) = \frac{1}{p}$$

$$\mathbb{V}(K|K>0) = \frac{(1-p)(\rho-1)}{p^2(\rho-3)}$$

Thus, the expected value of the Waring distribution is simply the inverse of the probability of forming a tie to an individual lacking existing ties. Both the Waring and the Yule distributions have been re-discovered, apparently without awareness of their historical antecedents, by Levene et al. (2002) and Dorogovtsev et al. (2000) respectively in the context of modeling growth of the Internet.

2.2 Non-Homogeneous Poisson Model

A reasonable alternative model to the preferential attachment mechanism is that people form partnerships according to a Poisson process. One possible behavioral mechanism that underlies this model is that people acquire new partners at a constant rate, λ. Clearly, the assumption that all people in the population are characterized by the same rate of partner acquisition is unreasonable. To include heterogeneity, we can model λ as a random draw from some population distribution $P(\lambda)$.

Here we model $P(\lambda)$ as a Gamma distribution with mean μ and standard deviation σ. Let $\lambda_i + 1$ be the expected number of partners for person i in the sub-population of those with at least one partner. The model can then be written:

$$P(K = k|K > 0, \lambda) = \frac{e^{-\lambda}\lambda^{k-1}}{\Gamma(k)} \tag{5}$$

$$P(\lambda_i = \lambda) = \frac{e^{-\lambda/\eta_1}(\lambda/\eta_1)^{\eta_2-1}}{\eta_1\Gamma(\eta_2)} \quad \lambda > 0 \tag{6}$$

where $\eta = (\eta_1, \eta_2) = (\sigma^2/\mu, \mu^2/\sigma^2)$. The conditional distribution of K given $K > 0$ is therefore negative binomial distribution shifted to $k = 1, 2, \ldots$. One interpretation of this distribution is that people are following a search for partners that satisfy a certain criterion and continue to acquire partners until they have η_2 such partners. Partners satisfy the criterion independently and each with probability p_c. This probability defines the scale parameter of the underlying heterogeneity distribution ($\eta_1 = (1 - p_c)/p_c$). The mean and variance of the negative binomial in terms of the gamma mean-standard deviation parameterization are $\mathbb{E}(K|K > 0) = \mu + \mu^2/\sigma^2$ and $\mathbb{V}(K|K > 0) = (\sigma + \mu/\sigma)^2$. If the population heterogeneity distribution $P(\lambda)$ is right-skewed the partner distribution K will also be right-skewed. Thus this model is one plausible alternative to the preferential attachment model that can have heavy tails, but does not have power-law behavior. As we shall see, this leads to different epidemic potentials for the two models even when their ability to describe the observed partnership distributions is similar.

3 Epidemic Models on Random Graphs

The impact of the degree distribution on the spread of STDs on an arbitrarily-defined contact structure has been studied by Newman (2002b), who gives both one-sex and two-sex results. Suppose that the degree distribution of a population has PMF $P_\theta(K = k)$ where θ is the (possibly vector) parameter. For example, for the Waring model $\theta = (\rho, p)$ the scaling exponent and probability of

recruiting a novice parameter. The critical transmissibility of an infectious agent is defined by a quantity we call the *concentration index*, $C(\theta)$, given by:

$$C(\theta) = \frac{\mathbb{E}_\theta(K)}{\mathbb{E}_\theta(K^2) - \mathbb{E}_\theta(K)} = \frac{\mathbb{E}_\theta(K|K>0)}{\mathbb{E}_\theta(K^2|K>0) - \mathbb{E}_\theta(K|K>0)}, \tag{7}$$

where $\mathbb{E}_\theta(K)$ is the expectation of the random variable K with respect to the PMF $P_\theta(K = k)$. Higher values of $C(\theta) \geq 0$ indicate distributions that are more concentrated and a value of zero indicates a distribution with infinite variance. We note that Newman (2002b) refers to this quantity as the critical transmissibility (T_c), which it clearly is for the one-sex case. The concentration index notation, $C(\theta)$, makes specification of the epidemic threshold in the two-sex case much more compact than Newman's original notation, which was in terms of probability generating functions of the nodes and edges of the transmission graph.

As an application, suppose that the degree distribution of a one-sex population follows the Waring model (3) with scaling exponent ρ and recruitment probability p. Then

$$C(\rho, p) = \frac{\mathbb{E}(K)}{\mathbb{E}(K^2) - \mathbb{E}(K)} = \begin{cases} \frac{p(\rho-3)}{2(1-p)(\rho-2)} & \rho > 3 \\ 0 & \rho \leq 3 \end{cases} \tag{8}$$

For the negative binomial model, the concentration index is most parsimoniously represented using the underlying gamma heterogeneity parameter η:

$$C(\eta) = \frac{\mathbb{E}(K)}{\mathbb{E}(K^2) - \mathbb{E}(K)} = \frac{1+\eta_1}{\eta_2(1-\eta_1)^2 - \eta_1^2} \tag{9}$$

Defining the concentration index as in (7), it is simple to explore epidemic thresholds in two-sex, heterosexual transmission models. Suppose that the degree distribution of the men and women in a population have PMFs with parameters θ_m and θ_f respectively. The model in Newman (2002b) assumes a form of random mixing with respect to degree that satisfies the constraints on the degree distributions. We define the *epidemic threshold* of the population to be:

$$T(\theta_m, \theta_f) = C(\theta_m)C(\theta_f) \tag{10}$$

Under this model, and assuming that the disease has mutually positive transmissibilities between men and women, Newman shows that an epidemic will occur with probability approaching 1 as the number of partnerships approaches infinity if either $C(\theta_m)$ or $C(\theta_f)$ is zero (i.e., the variance of either of the distributions is infinite). In this case there is said to be no epidemic threshold ($T(\theta_m, \theta_f) = 0$). Based on his results the probability of an epidemic approaches 0 as the number of partnerships approaches infinity if

$$0 < T_{mf}T_{fm} \leq T(\theta_m, \theta_f) \tag{11}$$

where the *transmissibility* T_{fm} is the average integrated probability of transmission per partnership from females to males. The transmissibility T_{mf} is defined reciprocally. In particular, this means that independently of the transmissibility the probability of an epidemic approaches 0 as the number of partnerships approaches infinity if $T(\theta_m, \theta_f) > 1$. The range of values of the population distributions that allow for a transition to an epidemic following random infection is defined by

$$0 < T(\theta_m, \theta_f) < T_{mf}T_{fm}. \tag{12}$$

In this range, the likelihood that an epidemic occurs can be reduced by interventions that decrease the transmissibilities of the pathogen. Examples of such interventions include vaccination, barrier contraceptive use, or therapeutics (e.g., anti-retroviral therapy).

For degree distributions with power-law behavior, such as the Waring, the probability of an epidemic approaches 1 as the number of partnerships approaches infinity if either ρ_m and ρ_f is less than or equal to 3. The probability of an epidemic approaches 0 as the number of partnerships approaches infinity if $(\rho_m - 3)(\rho_f - 3) > 4(\phi_m + 1)(\phi_f + 1)$ regardless of the transmissibilities. The epidemic potential in the intermediate range will depend on the transmissibilities (T_{mf}, T_{fm}) and the scaling parameters (θ_m, θ_f).

3.1 Estimating The Degree Distribution

Much of the empirical work on characterizing the degree distribution of samples from a variety of physical, biological, and social networks is based on regression concepts, in which the scaling parameter is estimated from the regression of the apparently linear region of the plot of the logarithm of the survival function $P(K \geq k)$ against $\log(k)$. OLS regression is not an appropriate inferential tool for this problem as the data violate a variety of assumptions linear regression (Jones and Handcock, 2003). Furthermore, the apparent linearity of the tail can be a spurious visual illusion owing to the cumulative nature of the log-survival plot. In order to move away from ad hoc curve fits, Handcock and Jones (2004) advocate the specification of stochastic process models for network formation. Such stochastic models are amenable to empirical verification and allow estimation of model parameters using Maximum Likelihood.

We estimated the Waring and negative binomial parameters for three populations: (1) Rakai District, Uganda (Wawer, 1992), (2) Sweden (Lewin, 1996), (3) USA (Laumann et al., 1994). Descriptions of these datasets are given in (Handcock and Jones, 2004). We adapt the model to allow for the possibility that the tail behavior (i.e., $k > 1$) of the degree distribution may differ fundamentally from the majority of the observations for which $k = 0$ or 1 (May and Lloyd, 2001). We generalized the models to allow separate parameters to fit the probabilities of lower degrees. The parametric model is fit only to values $K \geq k_{min} > 0$, and we use likelihood-based model selection procedures (e.g., Burnham and Anderson, 2002) to choose the best fitting model. Specifically, we used a corrected Akaike Information Criterion (AIC_C)(Simonoff and Tsai, 1999). Full details of the fitting procedure can be found elsewhere (Jones and Handcock, 2003; Handcock and Jones, 2004).

3.2 Confidence Intervals for Epidemic Thresholds

Uncertainty in the network model parameters, θ will produce uncertainty in the concentration index and, hence, the epidemic threshold of the population. To assess this uncertainty quantitatively, we constructed 95% bootstrap confidence intervals for $C(\theta)$ (Efron and Tibshirani, 1993). For each population of n individuals, the observed values of individual partner counts were re-sampled with replacement to produce 5000 samples of size n and $C(\theta)$ for each replicate sample was calculated to yield the intervals.

Table 1: Parameter estimates for the Waring model. AIC_c is the corrected Akaike Information Criterion for the best fitting Waring model, k_{min} is the lower cutoff degree, ρ is the scaling exponent, p is the second parameter, p is the probability of forming a tie to an individual lacking partners, and $C(\theta)$ is the concentration index for the parameter values.

Country	sex	AIC_c	k_{min}	ρ	ϕ	p	$C(\theta)$
Uganda	women	1061.3	1	8.68	-0.56	0.94	7.64
	men	1576.2	2	4.58	-0.46	0.83	0.97
Sweden	women	2143.9	2	4.45	1.53	0.49	0.75
	men	3025.0	2	6.53	1.87	0.61	1.56
USA	women	3208.7	1	3.11	-0.68	0.77	0.17
	men	3247.8	2	4.47	2.05	0.45	0.24

Table 2: Parameter estimates for the negative binomial model. AIC is the Akaike Information Criterion for the best fitting negative binomial model, k_{min} is the lower cutoff degree, t_e is the expected stopping time of the negative binomial, p_c is the probability a person satisfies the criterion, μ mean of the underlying gamma distribution, σ is the standard deviation of the gamma distribution, and $C(\theta)$ is the concentration index for the parameter values. To aid interpretation of the model we have included the alternative parametrization: t_e is the expected stopping time of the negative binomial, and p_c is the probability a person satisfies the criterion.

Country	sex	AIC_c	k_{min}	t_e	p_c	μ	σ	$C(\theta)$
Uganda	women	1058.3	2	0.27	0.19	0.22	0.96	6.60
	men	1574.4	4	3.58	0.52	1.72	1.26	0.82
Sweden	women	2142.9	1	0.38	0.36	0.24	0.65	2.31
	men	3024.3	1	0.66	0.25	0.49	1.23	1.21
USA	women	3210.0	4	2.86	0.15	2.42	3.68	1.88
	men	3204.3	1	0.78	0.26	0.58	1.30	0.93

4 Results

4.1 Degree Models

The results for the Waring model MLE fits are presented in Table 1. For both men's and women's networks from all three populations $\rho > 3$, indicating finite variance. Nonetheless, the parameter values for the USA yield quite low values of $C(\theta)$.

The results for the negative binomial model MLE fits are presented in Table 2. For all samples but the American women, the negative binomial model fits better than the Waring, as indicated by the AIC_c values. Figure 1 plots the inferred distribution of the Poisson parameter λ for the three populations. As expected, all three populations show a great deal of right-skew. The heterogeneity in propensity to have additional partners is very similar for men and women and for the Western countries. In Uganda the women are much less likely to form additional partners than the men.

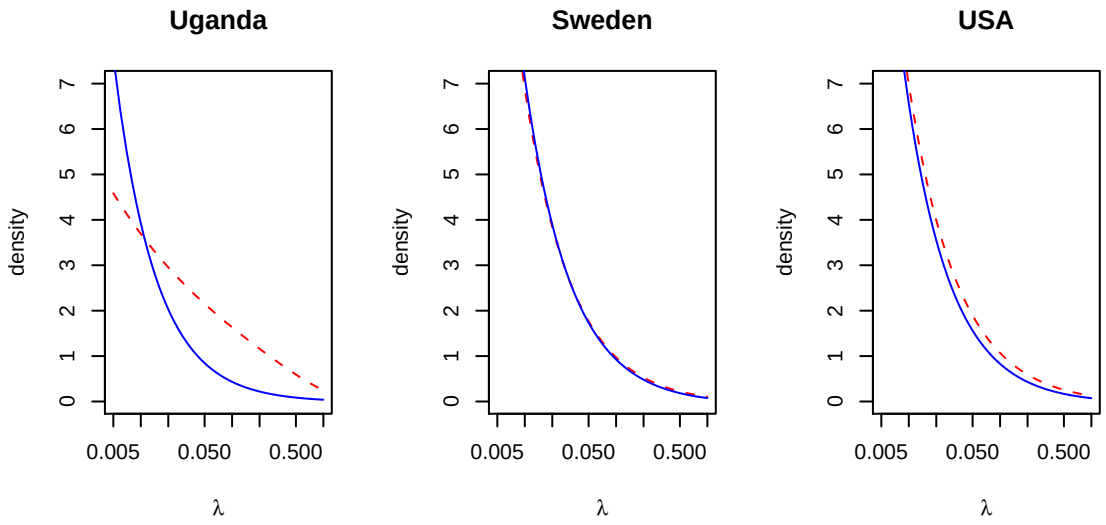

Figure 1: Gamma heterogeneity in the rate of partner acquisition in the three populations. Women are solid blue lines, men are dashed red lines.

4.2 Confidence Intervals on Epidemic Thresholds

We estimated 95% confidence intervals of the epidemic threshold (equation 12) for each population using each of the four combinations of underlying degree models (e.g., male Waring, female Waring, etc.) The confidence intervals for the Waring and negative binomial models are compared in figure 2. The intervals for the negative binomial model tend to be higher than those of the Waring for the Sweden and the USA. In Uganda the epidemic threshold is much higher and more uncertain than the two countries in the developed world. Figure 3 plots the confidence intervals for the best fitting models. For all populations but the USA, all models yielded bounds on the epidemic threshold which did not overlap with zero. In the USA, the confidence interval for the joint-Waring model included zero. (The test of the hypothesis that the threshold is zero again the alternative that it is positive has p-value = 0.69). The USA epidemic threshold confidence intervals for different k_{min} values are presented in Figure 4. For all higher cutoffs the intervals do not include zero.

5 Empirical Concentration Indices and Epidemic Thresholds

Gray et al. (2001) estimate the probability of HIV transmission per coital act for the same population represented in our sample from the Rakai District, Uganda. To calculate a maximally conservative estimate, we can use the upper quintile of their estimate per act ($\gamma = 0.0015$), multiplied by both the mean number of coital acts reported per month, and the number of months over which the local network data were collected (i.e., 12). This yields an estimate of $T_{mf} = T_{fm} = 0.162$. For an epidemic to occur with any probability under this model it is required that

$$T(\theta_m, \theta_f) > T_{mf}T_{fm} = 0.026244,$$

or the mean concentration index be $\sqrt{0.026244} = 0.162$. It is clear that this is not consistent

with the Rakai data where the estimated values of the epidemic thresholds are $T(\theta_m, \theta_f) = 7.18$ for the Waring model and $T(\theta_m, \theta_f) = 5.41$ for the negative binomial model. Rakai is home to a mature AIDS epidemic. The current estimate of HIV/AIDS prevalence in Rakai is 16%, a generalized epidemic by any definition. If the random mixing model is roughly correct, then for the Gray et al. (2001) estimate of the transmissibility of HIV-1 in Uganda, an epidemic would not be possible. This disjunction between the epidemiology in Rakai and the model predictions is clearly problematic and will be taken up in the discussion.

For Sweden, the MLEs for the Waring model lead to the condition

$$0 < T_{mf} T_{fm} < 0.18$$

to ensure an epidemic does not occur. Thus transmissibility would need to be very high for an epidemic to occur (it would need to be at least 2.5 times higher than that observed in Uganda). Thus this model correctly predicts that there is not a general epidemic in Sweden.

For the United States, the MLEs for the scaling parameters of the Waring model are $\rho_m = 3.03$ and $\rho_f = 3.84$. Substituting these values into (11) and (8) leads to the condition

$$0 < T_{mf} T_{fm} < 0.22$$

for an epidemic not to occur. For an epidemic to occur the transmissibility needs to be nearly three times the value of that observed by Gray et al. (2001).

6 Discussion

Capitalizing on the graph-theoretic epidemic formalism of Newman (2002b), we are able to calculate confidence bounds for epidemic thresholds in three populations. Our results indicate that there is very high probability that two of the populations, Uganda and Sweden, are characterized by non-zero epidemic thresholds. Confidence intervals for the epidemic threshold in the USA include the zero value (i.e., the epidemic threshold may not be positive). The best fitting model suggests that there could be no epidemic threshold in the United States. However, the models close to it in terms of model fit all indicate confidence intervals for the critical transmissibility does not include zero.

The model predicts no epidemic in Uganda, despite Rakai having one of the most mature HIV/AIDS epidemics in the world. Four points may help to explain this apparent paradox. First, Rakai is characterized by a declining epidemic and our finding that the concentration index exceeds critical transmissibility may simply reflect the contracting epidemic. This seems somewhat unlikely however, since the HIV/AIDS prevalence is still 16%, higher than most other regions in the world. A second possibility which is closely related to the first is that there is potential censoring of highest-activity people due to premature mortality. The inclusion of more highly active individuals would have made the contact pattern less concentrated, making an epidemic more likely. A third intriguing possibility is that epidemiological assumptions underlying the HIV/AIDS epidemic in Africa are incorrect. Specifically, some recent research has suggested that the role of heterosexual transmission of HIV in Africa has been greatly over-estimated and that a large fraction of HIV is attributable to contaminated needles (Brewer et al., 2003; Gisselquist and Potterat, 2003). Finally, the epidemic model may simply fail to capture the actual risk structure of Rakai.

While Newman's two-sex random graph epidemic model is a great advance in realistically representing the contact structure of pathogens transmitted by intimate contact, it still contains a major weakness which ultimately limits its utility. Specifically, it assumes random mixing conditional on degree. For compartmental epidemic models structured by activity class, departures from random mixing can either slow (if mixing is disassortative) or accelerate (if mixing is assortative) epidemic growth (Morris, 1991; Marschner, 1992; Garnett and Anderson, 1996). In either case, models with heterogeneous activity will yield lower equilibrium prevalence (Anderson and May, 1991). This point is made clear by the final-size equation given by Anderson and May (1991, 272) under heterogeneity:

$$I = 1 - (1 + \Theta)^{-1/CV^2}, \tag{13}$$

where I is the overall fraction of the host population ever infected, Θ is an integrated measure of the force of infection over the course of the epidemic, and CV is the coefficient of variation of sexual activity in the population - see (2). Clearly, as $CV \to \infty$, $I \to 0$, a point recently re-emphasized by May and Lloyd (2001).

While the effects of heterogeneity on the classical compartmental models for STIs are well understood, the implications of heterogeneity in the graph-theoretic epidemic models is less obvious. Through analogy to critical phenomena in percolation theory, the intuition appears to be that degree-based non-random interactions will produce lower epidemic thresholds and larger final sizes of epidemics.

Newman (2002a) notes that correlations in the connectivity of nodes in a network can reduce epidemic thresholds. The extent of assortative mixing by degree in sexual networks is an open empirical question in epidemiology. While Newman (2002a) notes the implications of such correlations for epidemic processes on social networks, the social network data he analyzes come from various professional collaboration networks (e.g., scientific co-authoring, business board membership, movie co-starring) and not from epidemiologically relevant network samples. There is no reason to believe that the structure of a sexual contact network resembles the collaboration network of mathematics papers.

Empirical work in epidemiology indicates that some networks show assortativeness by degree, some do not (Stoner et al., 2000), while some show it weakly (Garnett et al., 1996; Barlow et al., 1997). Degree-based correlations based on standard local network sampling procedures (Morris, 1997) are subject to considerable error. Respondents typically have accurate knowledge of their partners' behavior when they believe their partners have other partners (i.e., high specificity). However, respondents appear to be much worse judges of their partners' behavior when they report that their partners do not have other partners (i.e., low sensitivity) (Stoner et al., 2003). Unbiased estimates of assortative mixing by degree are further complicated by the fact that when sampling networks, a random sample of graph nodes does not yield a random sample of the graph's edges, and for STIs, the clear unit of epidemiological analysis is the partnership.

The answer to the question of degree-based correlations depends on the availability of quality data on the structure of the network that is not present in most sexual history surveys. Such surveys typically only ask questions about the number of sex partners. However the information necessary for evaluating degree-based correlations is available from link-tracing designs and related adaptive designs (Goodman, 1961; Thompson and Seber, 1996). These observations emphasize the need for partner enrollment studies (e.g., Johnson et al., 2003) to facilitate improved inference on the contact structures which support STI epidemics.

In contrast with the recent network research suggesting that properties of sexual networks may facilitate STI spread and persistence – effectively lowering epidemic thresholds – the spatially-motivated work of Sander et al. (2002) suggests that social networks can actually impede the spread of an STI. Whether or not the spatial lattice metaphor applies in any way to human intimate contacts, the point that *localization effects*, by partitioning sexual networks, could slow the spread of an STI (Keeling, 1999). The localization effects could be, literally, geographic or they could be social. For example, Laumann et al. (1994) report effective structural zeros in the NHSLS mixing-by-race matrix. African American women are exceptionally unlikely to have white male partners, making direct transmission between these compartments rare.

A large body of research suggests that human sexual relations, like other forms of social interaction, are anything but random (e.g., Morris, 1991; Laumann et al., 1994; Youm and Laumann, 2002; McPherson et al., 2001). Modeling epidemics on contact structures which reflect, for example, differential homophily by age and race, and low levels of transitivity is a challenging task. Nonetheless, strong statements regarding optimal control and eradication strategies must be predicated on the best models for the system in question.

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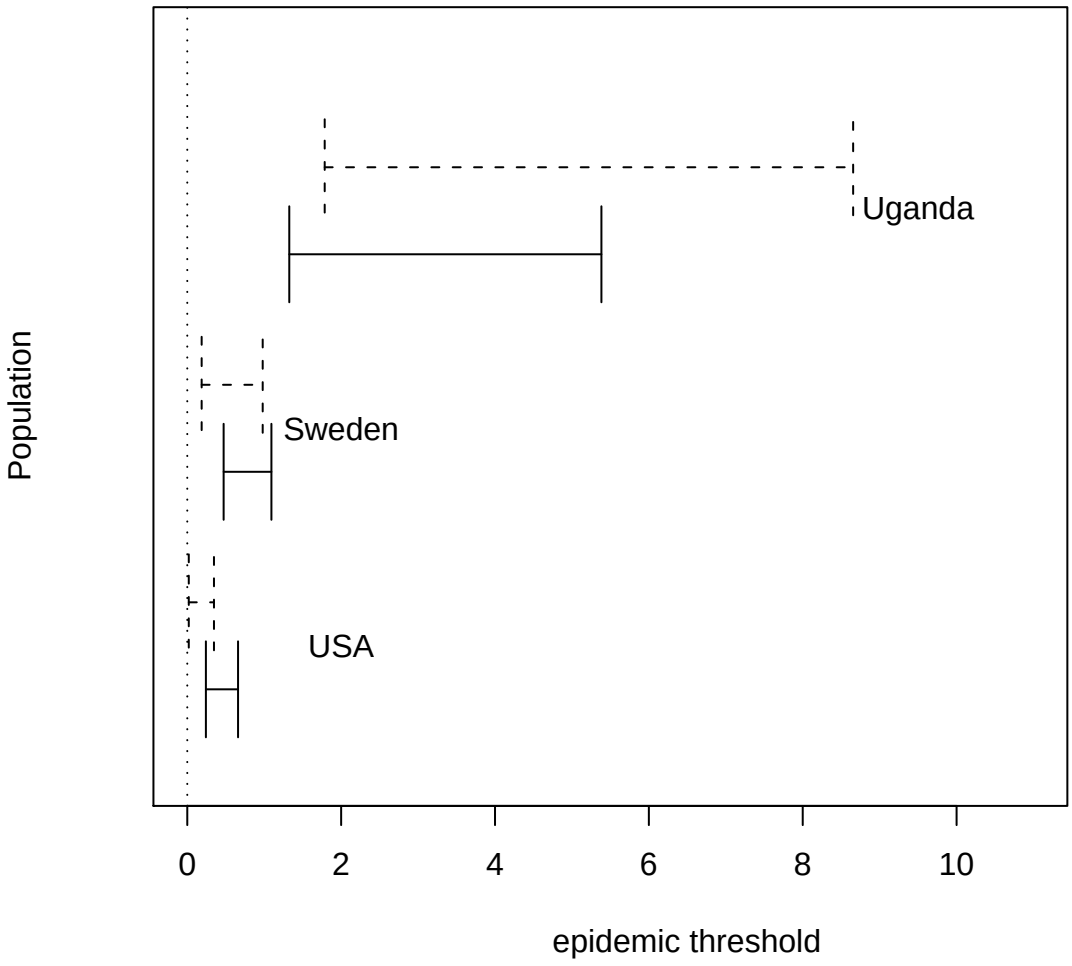

Figure 2: Comparison of the 95% bootstrap confidence intervals for the epidemic threshold given by the negative binomial model (solid lines) and the Waring model (dashed lines) for each population.

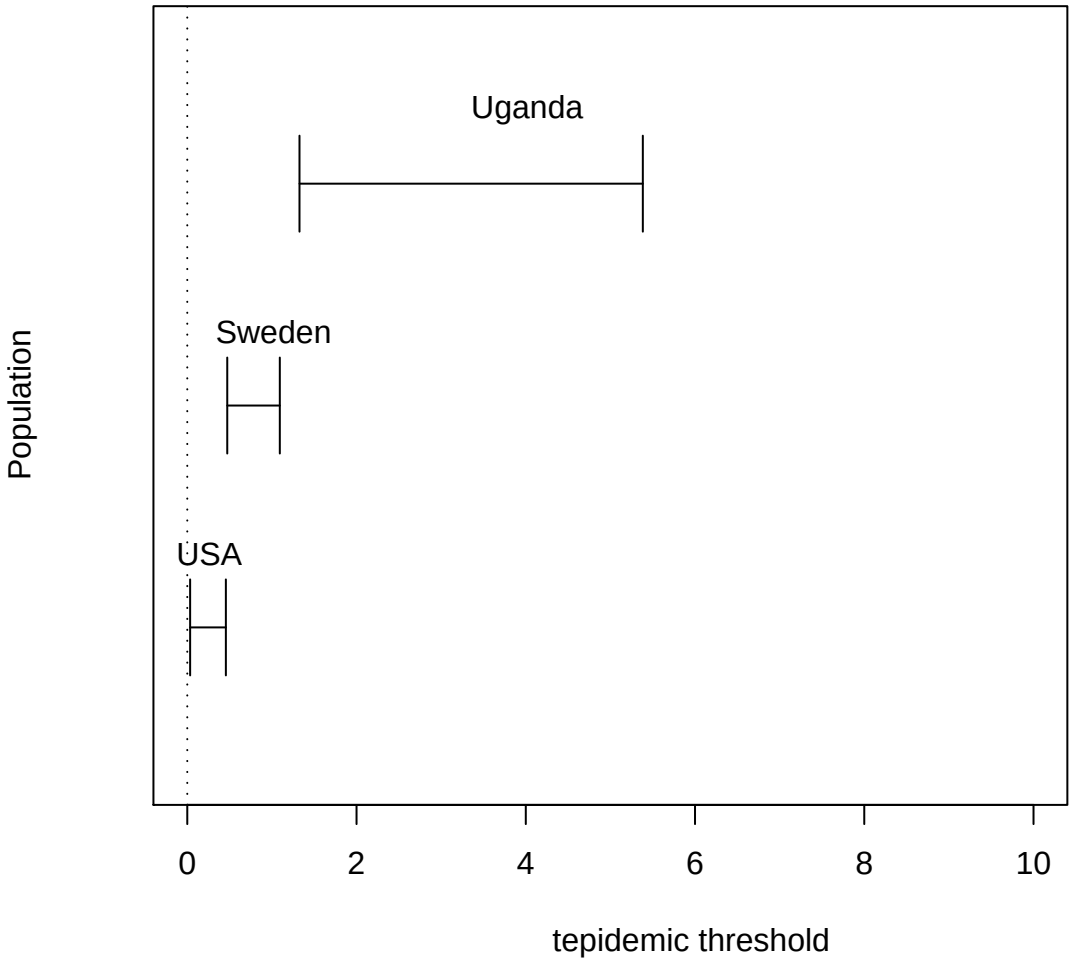

Figure 3: 95% bootstrap confidence intervals for the epidemic threshold given by the best fitting model in each population.

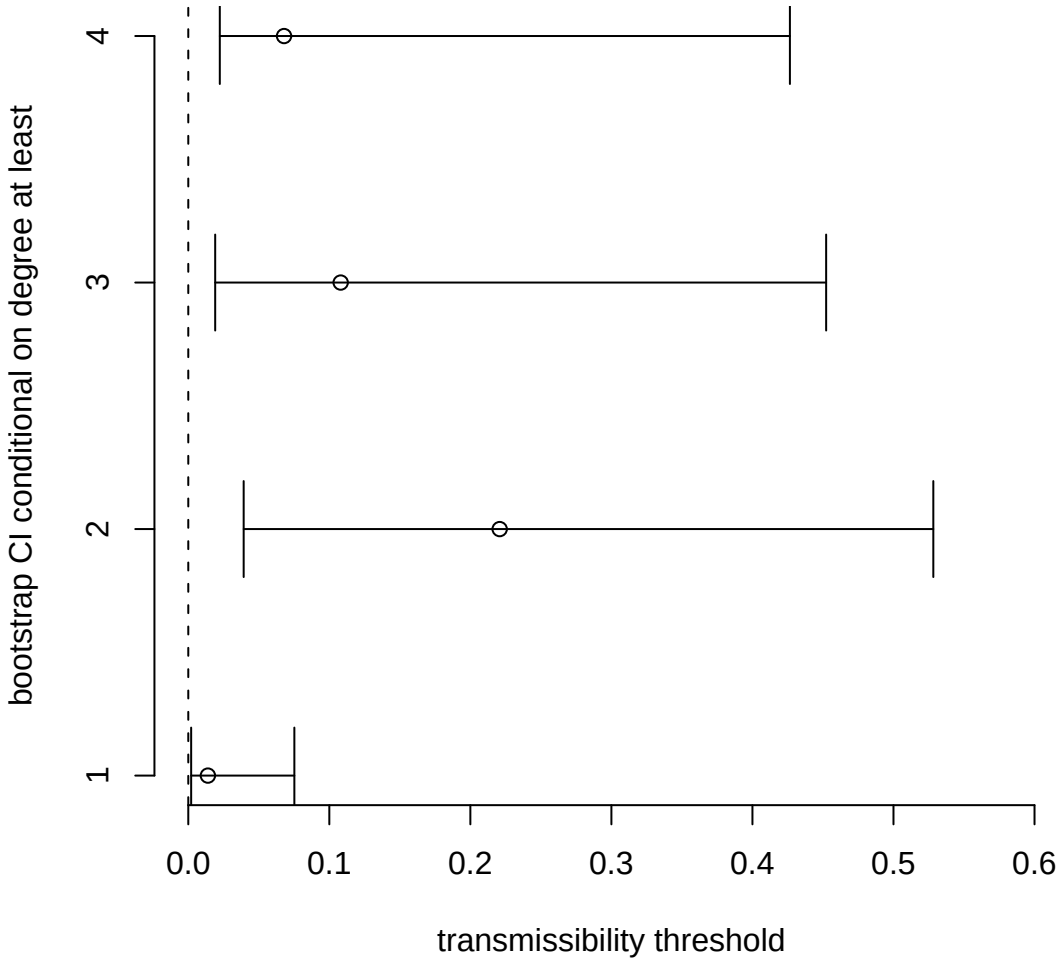

Figure 4: Confidence bounds on the epidemic threshold of the Waring model for the USA.