

How sex acts scale with the number of sex partners: evidence from *Chlamydia trachomatis* data and implications for control

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2 Mathematical models are frequently used to assess the impact of control in-
3 terventions for *Chlamydia trachomatis* and other sexually transmitted infections
4 (STIs). Modeling approaches that stratify the population by the number of sex
5 partners often assume the transmission risk per partner to be constant. How-
6 ever, sexual behavior data suggests that people with many partners share less
7 sex acts per partner than people with fewer partners. This should lower the risk
8 of transmission per partner for highly sexually active individuals and could have
9 important epidemiological consequences for STI transmission. We devise a new
10 epidemiological model that we fit to chlamydia prevalence data from Natsal-2
11 and CSF, two population-based probability sample surveys of sexual behavior in
12 Britain and France. Compared to a standard model where the transmission risk
13 per partner is constant, a model with realistic numbers of sex acts per partner
14 provides a better fit to the data. Furthermore, the improved model provides ev-
15 idence for strong assortative mixing among individuals with different numbers of
16 sex partners. Our results suggest that all chlamydia infected individuals with one
17 or more new heterosexual partners per year contribute significantly to ongoing
18 transmission, underlining that control interventions should be aimed towards all
19 sexually active young adults.

21 The spread of sexually transmitted infections (STIs) crucially depends on the number of
22 sex partners and the number of sex acts within a sexual partnership. Empirical studies
23 have shown that the number of sex partners within a given time period is a strong
24 determinant for the spread of curable STIs such as *Chlamydia trachomatis* (Fenton et al.,
25 2001; Sonnenberg et al., 2013; Althaus et al., 2012c) and *Neisseria gonorrhoeae* (Ison
26 et al., 2013). However, the number of sex acts as an additional factor for transmission has
27 not received as much attention. In particular, mathematical models of STI transmission
28 that are frequently used in guiding public health policy decision making often assume
29 the number of sex acts per partner to be constant and independent of the number of
30 partners an individual has (Hethcote and Yorke, 1984; Anderson and May, 1991; Garnett
31 and Anderson, 1993b; Garnett et al., 1999; Keeling and Rohani, 2008). Neglecting
32 the number of sex acts per partner could lead to inaccurate estimates of the efficiency
33 of public health interventions, for instance when predicting the impact of screening
34 interventions on chlamydia spread.

35 Theoretical studies have shown that taking into account the number of sex acts in
36 models of STI transmission can dramatically alter the results (Kaplan, 1990; Røttingen
37 and Garnett, 2002). An important aspect was illustrated in the study by Nordvik
38 and Liljeros (2006), where they showed that it is not only the number of partners,
39 but also the number of sex acts per partner, that is important for the transmission of
40 an infection. Garnett and Anderson (1996) developed a generic framework to include
41 the heterogeneity in the number of sex acts between individuals and showed that it
42 can enhance the likelihood of persistence of STIs. Still, we lack a solid understanding
43 of the relationship between the number of sex acts and the number of sex partners.
44 Furthermore, it remains to be determined how this relationship can be appropriately
45 integrated into mathematical models of STI transmission that then can be validated
46 with data.

47 The results of probability sample surveys of sexual behavior allow us to formulate
48 some hypotheses on the relationship between the number of sex acts and the number
49 of sex partners. Blower and Boe (1993) analyzed data from 1770 unmarried individuals
50 aged 20–44 years collected in San Francisco (USA) from 1988–1989. They concluded that
51 it may be most appropriate to see the number of sex acts as a ‘budget’ split between
52 sex partners. Nordvik and Liljeros (2006) looked at the total number of sex acts in
53 relation to the total number of sex partners based on data from 1150 individuals aged
54 16–31 years collected in Sweden in 1988. The authors found that the total number of
55 sex acts remains constant in individuals with higher numbers of sex partners (it even
56 decreases in women). In principle, one can directly infer the relationship between sex
57 acts and sex partners from sexual behavior surveys, but there remain potential biases
58 due to the self-reported data. For example, it proves difficult to discriminate between
59 protected and unprotected sex acts in such surveys. A better understanding of the
60 quantitative relationship between the number of sex partners and the number of sex
61 acts could provide useful insights into the epidemiology of STIs and their control.

62 Another important aspect of taking the number of sex acts between sex partners into
63 account is its effect on the topology of the sexual contact network. If the number of sex
64 acts per sex partner is constant, each contact (edge) between susceptible and infected
65 individuals (nodes) is weighted equally, i.e., has the same transmission probability. This
66 is not the case if sex acts are explicitly accounted for (Moslonka-Lefebvre et al., 2012).
67 However, network-based models usually require computationally-intensive simulations

68 Kamp et al. (2013), which is why mathematical models of STIs tend to adopt a simpler
69 approach by stratifying the population into subgroups with varying levels of sexual
70 activity (Hethcote and Yorke, 1984; Garnett and Anderson, 1993b; Garnett et al., 1999).
71 These models are often referred to as ‘risk class models’, although the stratification is
72 based on the partner change rate that does not necessarily correlate with risk. In models,
73 the level of sexual mixing between individuals can vary from fully proportionate (to the
74 number of sex partners individuals have) to completely assortative (individuals within
75 a sexual activity or risk group mix only with themselves). While some studies based on
76 sexual behavior data indicate a certain level of assortative mixing between individuals
77 (Renton et al., 1995; Garnett and Anderson, 1993a; Garnett et al., 1996; Aral et al.,
78 1999), the output of STI transmission models is often only consistent with close to
79 proportionate (or random) mixing (Garnett et al., 1999; Althaus et al., 2012a). This
80 inconsistency illustrates the challenge in estimating the degree of sexual mixing, and
81 we show that considering the number of sex acts per sex partner in models of STI
82 transmission sheds new light on this question.

83 Our goal is to gain a more detailed picture of the relationship between the number of
84 heterosexual sex acts and the number of heterosexual sex partners and study its effect on
85 the transmission of chlamydia, the most prevalent bacterial STI. To this end, we make
86 use of two datasets of sexual behavior: the British National Survey of Sexual Attitudes
87 and Lifestyles (Natsal-2) (Johnson et al., 2001), and the ‘Contexte de la Sexualité en
88 France’ (CSF 2006) (Bajos and Bozon, 2006, 2008). First, we directly infer the relation-
89 ship between the number of heterosexual sex acts and the number of heterosexual sex
90 partners from Natsal-2. We then fit a novel epidemiological model of STI transmission
91 to chlamydia prevalence data of both datasets and indirectly infer epidemiological pa-
92 rameters as well as the relationship between the number of heterosexual sex acts and
93 heterosexual sex partners. Both methods support the notion that the number of hetero-
94 sexual sex acts per partner decreases with higher number of heterosexual sex partners.
95 This is also consistent with a high level of assortative mixing between individuals with
96 similar number of sex partners. Lastly, we show that taking realistic numbers of sex acts
97 into account when modeling the heterosexual transmission dynamics of chlamydia has
98 a crucial effect on the projected impact of control interventions.

99 **Methods**

100 **Data**

101 **Natsal-2**

102 Natsal-2 is a population-based probability sample survey of sexual attitudes and lifestyles
103 conducted in Britain in 1999-2001 (Johnson et al., 2001). The sample consists of 11,161
104 women and men aged 16–44 years. Urine samples for ligase chain reaction (LCR) testing
105 for chlamydia infection are available for a subset of 3569 sexually active respondents
106 aged 18–44 years (Fenton et al., 2001). We use the following variables: number of new
107 heterosexual sex partners in the last year, number of occasions of heterosexual sex in
108 last 4 weeks, chlamydia test result from urine sample. Individual weights are used for
109 all variables to adjust for unequal selection probabilities and to correct for the age and
110 gender profile in the survey population. The full dataset is available from the UK Data
111 Archive at the University of Essex (<http://data-archive.ac.uk>).

113 ‘Contexte de la Sexualité en France’ (CSF 2006) is a survey conducted in France among
114 12,364 randomly chosen individuals aged 18–69 years (Bajos and Bozon, 2006, 2008).
115 Urine samples testing for chlamydia infection are available for a subset of 7407 sexually
116 active respondents. The two variables we used are the number of new heterosexual sex
117 partners in the last year and the chlamydia test result from urine sample (see Supple-
118 mental Files).

119 Sex acts and sex partners

120 We stratify the population by the reported number of new heterosexual partners in the
121 last year which results in n different sexual activity classes with c_i sex partners. The
122 average heterosexual activity of each individual during one year is assumed to be reflected
123 in the reported number of heterosexual sex acts during the last 4 weeks. For simplicity,
124 and in order to increase sample size, we pool data of women and men together.

125 The reported numbers of sex acts during the last 4 weeks are highly dispersed
126 (Fig. 1A). Therefore, we assume that the observed number of sex acts during the last
127 4 weeks (Z) for a given individual with c_i new heterosexual partners during the last
128 year follows a negative binomial distribution. This distribution is frequently used to
129 describe overdispersed data in biology and epidemiology (Lloyd-Smith, 2007; Hamilton
130 et al., 2008). In the context of data on the number of sex acts, it can be interpreted
131 as a process of sequential Bernoulli trials to reach ‘sexual satisfaction’ with the param-
132 eters (k, p) : for each of Z sex acts there is a probability p that it will not be sexually
133 satisfying and individuals engage in new sex acts until satisfaction has been reached in
134 k of them. The negative binomial distribution can also be interpreted as a mixture of
135 Poisson distributions where the rates at which different individuals have sex are drawn
136 from a gamma distribution with shape parameter k and scale parameter $p/(1-p)$. More
137 generally, a single Poisson distribution is obtained for $k \rightarrow \infty$ and the negative binomial
138 distribution is reduced to a geometric distribution for $k = 1$.

139 We assume that the mean of the negative binomial distribution is given by the
140 following functional relationship:

$$m_i = d_1 + d_2 c_i^{d_3}, \quad (1)$$

141 where m_i and c_i are the average number of sex acts and the number of sex partners for
142 individuals of sexual activity class i , respectively. m_i can then be scaled to obtain the
143 expected number of heterosexual sex acts per year (M_i).

144 We construct a series of nested models by fixing some of the parameters to specific
145 values. For example, if $d_2 = 0$, the total number of sex acts does not increase with
146 higher numbers of sex partners. For $d_3 = 1$, the number of sex acts changes linearly
147 with higher numbers of partners. The nested models then allow to perform hypothesis
148 testing about different functional relationships between the number of sex acts and sex
149 partners.

150 Epidemiological model

151 We assume the population to be stratified into n different sexual activity classes x_i
152 with c_i new heterosexual partners per year (Hethcote and Yorke, 1984; Garnett and
153 Anderson, 1993b). x_i denotes the proportion of individuals in sexual activity class i . On
154 average, individuals change their sexual activity after one year, and are proportionally

155 redistributed among all sexual activity classes. For simplicity, we assume that sexual
 156 activity and the natural history and transmission of the infection are the same in women
 157 and men. If y_i is the proportion of infected individuals in sexual activity class i , an SIS
 158 (susceptible-infected-susceptible) model (i.e., with no immunity) can then be written as
 159 follows:

$$\frac{dy_i}{dt} = \mu \sum_{j=1}^n x_j y_j + (1 - y_i) c_i \sum_{j=1}^n b_{ij} \rho_{ij} y_j - (\gamma + \mu) y_i, \quad (2)$$

160 where $1/\gamma$ and $1/\mu$ denote the average duration of infection and the average time spent
 161 in one sexual activity class, respectively. ρ_{ij} represents the elements of the mixing matrix
 162 that, following Garnett et al. (1999), can be defined as

$$\rho_{ij} = \epsilon \delta_{ij} + (1 - \epsilon) \frac{c_j x_j}{\sum_{l=1}^n c_l x_l}, \quad (3)$$

163 where δ_{ij} denotes the Kronecker delta (it is equal to 1 if $i = j$ and to 0 otherwise).
 164 Mixing can be varied between proportionate ($\epsilon = 0$) and fully assortative ($\epsilon = 1$).

165 The per partnership transmission probability b_{ij} can be considered as a Bernoulli
 166 process of repeated transmission probabilities per sex act:

$$b_{ij} = 1 - (1 - \beta)^{a_{ij}} \quad (4)$$

167 where β denotes the transmission probability per sex act and a_{ij} the number of sex acts
 168 in a partnership between an individual of sexual activity class i and j . To construct the
 169 matrix a_{ij} , we use the following algorithm to distribute the number of sex acts between
 170 partners:

- 171 1. Define $s_i = \frac{M_i}{c_i}$ as the average number of sex acts per partner for an individual of
 172 sexual activity class i .
- 173 2. Set $i = n$, i.e., start distributing the number of sex acts from individuals of the
 174 highest sexual activity class.
- 175 3. The number of sex acts from an individual of sexual activity class i will be shared
 176 with individuals of the same and lower sexual activity classes $j = [1, i]$. Hence, we
 177 distribute the number of sex acts s_i proportional to the probability of a contact
 178 between an individual of class i and class j (ρ_{ij}) and to what the partners are
 179 willing to share (s_j).
- 180 4. The number of sex acts in individuals of sexual activity class $j = [1, i]$ that remain
 181 to be shared (s_j) need to be updated to only those sex acts that have not been
 182 shared with individuals of sexual activity class i or higher.
- 183 5. If $i > 1$, set $i = i - 1$ and go to step 3. Otherwise, stop.

184 We calculate the basic reproduction number, R_0 , for a given sexual activity class as
 185 follows: $\frac{c_i \sum_{j=1}^n (b_{ij} \rho_{ij})}{\gamma}$. R_0 for the entire population is calculated using the next generation
 186 method (Diekmann et al., 1990; Diekmann and Heesterbeek, 2000). An overview of all
 187 parameters and variables to describe the epidemiological model as well as the sexual
 188 behavior is given in Table 1.

Table 1: Parameters and variables used to describe the sexual behavior and the epidemiological model.

| Notation | Description |
|-----------------|--|
| n | Number of host classes with different sexual activity |
| c_i | Number of new heterosexual sex partners in the last year for individuals of host class i |
| m_i | Average number of heterosexual sex in the last 4 weeks for individuals of host class i |
| M_i | Average number of heterosexual sex in the last year for individuals of host class i |
| d_1, d_2, d_3 | Parameters describing the functional relationship between c_i and m_i |
| x_i | Proportion of the host population in sexual activity class i |
| X_i | Number of individuals in sexual activity class i |
| y_i | Proportion of infected individuals in sexual activity class i |
| μ | Rate at which individuals change their sexual activity |
| γ | Recovery rate of the infection |
| ρ_{ij} | Mixing matrix between individuals of sexual activity classes i and j |
| ϵ | Sexual mixing coefficient (assortative index) |
| δ_{ij} | Kronecker delta (a function equal to 1 if $i = j$, and to 0 otherwise) |
| s_i | Average number of sex acts per sex partner for an individual of host class i ($\frac{M_i}{c_i}$) |
| a_{ij} | Number of sex acts in a partnership between individuals of sexual activity classes i and j |
| β | Transmission probability per sex act |
| b_{ij} | Transmission probability per partnership between individuals of sexual activity classes i and j |

189 Maximum likelihood estimation

190 Direct method

191 We estimate the parameters d_1 , d_2 and d_3 that describe the functional relationship be-
 192 tween the number of sex acts and sex partners (equation 1) and the dispersion parameter
 193 k from the negative binomial distribution using a maximum likelihood approach and the
 194 `mle2` function from the package `bbmle` (Bolker, 2008) for the R software environment
 195 for statistical computing (R Development Core Team, 2009).

196 Indirect method

197 We fit the epidemiological model to chlamydia prevalence data to obtain maximum
 198 likelihood estimates of behavioral and/or infection parameters (Bolker, 2008). Given
 199 a model-predicted prevalence y_i for sexual activity class i , the log-likelihood to find k_i
 200 positive tests in a sample of X_i individuals over all n sexual activity classes is

$$L(\beta, \gamma, \epsilon, d_1, d_2, d_3) = \sum_{i=1}^n \left(\log \binom{X_i}{k_i} + k_i \log y_i + (X_i - k_i) \log(1 - y_i) \right). \quad (5)$$

201 We obtain the model predicted prevalences for each sexual activity class, y_i , by
 202 numerically simulating equation 2 to its steady-state using the function `ode` from the R
 203 package `deSolve` (Soetaert et al., 2010). The parameter inference was performed using
 204 the function `mle2` from the package `bbmle` (Bolker, 2008). We first used the minimization
 205 algorithm by Nelder and Mead (1965) that is very robust in finding local optima. For
 206 those fits where different starting values of the parameters resulted in multiple optima,
 207 we decided to use the method SANN. SANN is a variant of simulated annealing (Bélisle,
 208 1992) and usually performs better on rough likelihood surfaces at the cost of being
 209 computationally expensive.

211 Sex acts and sex partners (direct method)

212 The reported numbers of heterosexual sex acts during the last 4 weeks in Natsal-2 show
 213 an increasing trend for higher number of new heterosexual partners during the last year
 214 (Fig. 1A). Fitting a series of nested models to the data suggests that a *linear* relationship
 215 between the number of sex acts, m_i , and the number of sex partners, c_i , describes the
 216 data best (Table 2 and Fig. 1B, solid line). The model where the number of sex acts
 217 for individuals with different numbers of sex partners is *constant* also fits the data
 218 well (Fig. 1B, dashed line). In contrast, the commonly used assumption where the total
 219 number of sex acts is strictly *proportional* to the number of sex partners is not consistent
 220 with the data (Fig. 1B, dotted line). We also fit an exponential relationship between the
 221 number of sex acts and sex partners (as suggested by Garnett and Anderson (1996)) to
 222 the data, but this resulted in a poorer fit (AIC = 17380.1) compared to the models in
 223 Table 2.

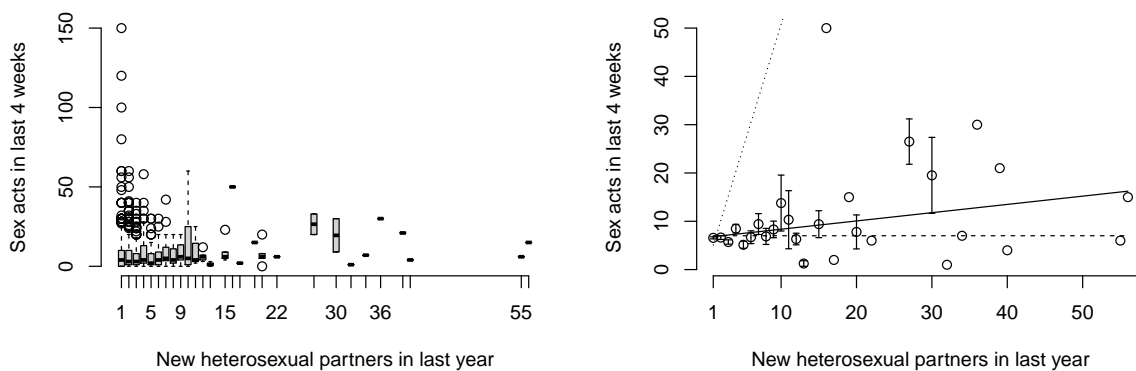


Figure 1: Number of heterosexual sex acts during the last 4 weeks as a function of the number of new heterosexual partners during the last year. (A) Boxplot of the reported data in Natsal-2 ($n = 2824$). The number of sex acts are positively correlated with the number of sex partners (Pearson's $r = 0.07$; $p < 10^{-3}$). (B) Functional relationship between the number of sex acts and the number of sex partners together with the means and standard errors of the reported data. The best fit model (*Linear*, solid line) is shown together with the models assuming the total number of sex acts (*Constant*, dashed line) or the number of sex acts per partner (*Proportional*, dotted line) to be constant.

224 Parameter inference (indirect method)

225 We perform two series of model fitting to indirectly infer parameters from chlamydia
 226 prevalence data. First, we only consider epidemiological parameters: the per sex act
 227 transmission probability β , the infectious duration $1/\gamma$ and the sexual mixing coefficient
 228 ϵ . Second, we focus on inferring the shape of the functional relationship between the
 229 number of sex acts and the number of sex partners (equation 1) and estimate d_1 , d_2 , d_3
 230 and ϵ . For the second approach, we assume that β and γ are fixed and informed by the
 231 literature. The rationale for choosing two separate approaches is that estimating all six
 232 parameters simultaneously would result in overfitting of the model.

Table 2: Maximum likelihood estimates of the functional relationship between the number of sex acts and the number of sex partners (direct method). Fixed parameters are given in squared brackets and estimates are shown together with 95% confidence intervals. The six different models were sorted in increasing order of their AIC. Only models whose AIC were within 10 from the best fit (*Linear*) model are shown together with the classical model where the number of sex acts increases strictly *proportional* to the number of sex partners. Based on likelihood ratio tests, the linear model is superior to the constant and full model ($p < 0.05$).

| Model | Parameters | | | | No. of free parameters | -2LogLik | Δ AIC |
|--------------|-------------------|--------------------|--------------------|-------------------|------------------------|----------|--------------|
| | d_1 | d_2 | d_3 | k | | | |
| Linear | 6.64 (6.20, 7.09) | 0.17 (0.01, 0.33) | [1.00] | 0.65 (0.61, 0.69) | 3 | 16821.9 | 0.0 |
| Full | 6.77 (6.29, 7.25) | 0.07 (-0.14, 0.28) | 1.34 (0.31, 2.36) | 0.65 (0.61, 0.69) | 4 | 16821.4 | 1.6 |
| Exponent | 5.77 (5.40, 6.15) | [1.00] | 0.39 (0.13, 0.65) | 0.65 (0.61, 0.69) | 3 | 16824.3 | 2.4 |
| No intercept | [0.00] | 6.81 (6.42, 7.20) | 0.06 (-0.01, 0.13) | 0.65 (0.61, 0.69) | 3 | 16825.6 | 3.7 |
| Constant | 7.01 (6.67, 7.34) | [0.00] | – | 0.65 (0.61, 0.69) | 2 | 16828.4 | 4.6 |
| Proportional | [0.00] | 5.08 (4.81, 5.35) | [1.00] | 0.54 (0.51, 0.57) | 2 | 17296.0 | 472.2 |

233 Epidemiological parameters

234 We fit two models to the Natsal-2 and CSF chlamydia prevalence data to estimate the
 235 epidemiological parameters. In one model, the average number of sex acts for individuals
 236 with a specific number of sex partners is given by the best fit model from the direct
 237 method (*Linear*). In the other model, we use the classical assumption where the number
 238 of sex acts increases strictly *proportional* with the number of sex partners. Both models
 239 fit the data well (Fig. 2) but vary in their estimates of the sexual mixing coefficient (Table
 240 3). While the *proportional* model suggests that sexual mixing is proportionate ($\epsilon = 0$),
 241 the *linear* model estimates the mixing coefficient to be more assortative and significantly
 242 different from zero ($\epsilon = 0.83$ (95% CI: 0.46–0.96) and $\epsilon = 0.53$ (95% CI: 0.38–0.68) for
 243 Natsal-2 and CSF, respectively). The estimated recovery rates are consistent with an
 244 average infectious duration of about 1 year (Althaus et al., 2010; Price et al., 2013;
 245 Davies et al., 2014). The per sex act transmission probabilities for the *linear* model
 246 are somewhat lower than previous estimates (9.5%, interquartile range: 6.0%–16.7%)
 247 (Althaus et al., 2012b). This could be explained by the fact that the transmission
 248 probabilities in our model include protected and unprotected sexual intercourse. In
 249 contrast, the estimates of the per sex act transmission probability for the *proportional*
 250 model are very low, indicating that the number of sex acts are not realistically taken
 251 into account.

Table 3: Maximum likelihood estimates of epidemiological parameters. The relationship between the number of sex acts and the number of sex partners is either based on the best fit model from the direct method (*Linear*) or the classical assumption where the number of sex acts increases strictly *Proportional* to the number of sex partners. Estimates are shown together with 95% confidence intervals.

| Model | Data | Parameters | | | No. of free parameters | -2LogLik | AIC |
|--------------|----------|-------------------|---------------------|-------------------|------------------------|----------|-------|
| | | β | $1/\gamma$ | ϵ | | | |
| Linear | Natsal-2 | 3.0% (1.9%, 4.1%) | 1.12 y (0.83, 1.42) | 0.83 (0.46, 0.96) | 3 | 39.3 | 45.3 |
| Linear | CSF | 3.4% (NA, NA) | 0.96 y (NA, NA) | 0.53 (0.38, 0.68) | 3 | 85.2 | 91.2 |
| Proportional | Natsal-2 | 0.7% (0.3%, 1.1%) | 1.16 y (0.44, 1.88) | 0.00 (0.00, 0.00) | 3 | 41.0 | 47.0 |
| Proportional | CSF | 0.4% (0.2%, 0.5%) | 1.04 y (0.45, 1.63) | 0.00 (0.00, 0.00) | 3 | 105.7 | 111.7 |

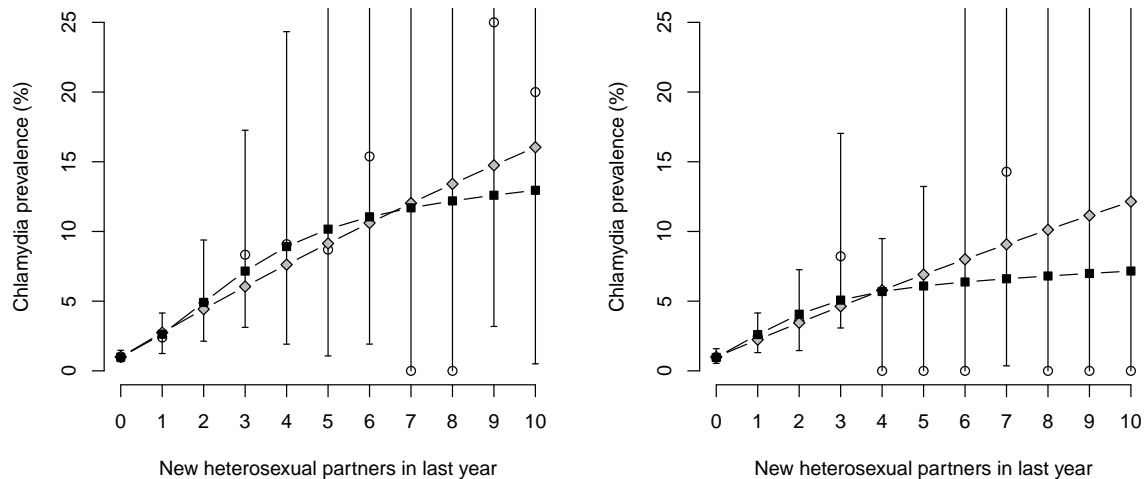


Figure 2: Chlamydia prevalence and model fits. For both datasets, the model where the total number of sex acts increases *linearly* with the number of sex partners (black squares) provides a better fit to the data compared to the classical model where the number of sex acts increases strictly *proportional* with the number of sex partners (gray diamonds). Data points (circles) are shown together with the 95% binomial proportion confidence intervals.

252 Functional relationship

253 We infer the functional relationship of the number of sex acts and sex partners by fitting
 254 the model to the Natsal-2 and CSF chlamydia prevalence data simultaneously (Table 4).
 255 To this end, we set the per sex act transmission probability and the infectious duration
 256 to values similar as estimated in Table 3 ($\beta = 3\%$ and $1/\gamma = 1$ year). We find that
 257 the model where the number of sex acts does not increase with the number of partners
 258 (*Constant*) describes the data best. As in section , we again find evidence for assortative
 259 mixing ($\epsilon = 0.60$, 95% CI: 0.28–0.85). The estimates of d_2 or d_3 are close to zero for the
 260 model with *no intercept*, the *linear* model and the *full* model. This indicates that the
 261 number of sex acts does not substantially increase with higher numbers of partners. The
 262 *proportional* model clearly provides the worst fit to the data, and is the only model that
 263 suggests random sexual mixing. Interestingly, the number of estimated sex acts in the
 264 last four weeks is slightly higher than the estimate from the direct method (10.6 *vs.* 7.0
 265 for the constant model, respectively). This could either reflect an under-estimation of
 266 the per sex transmission probability (set to $\beta = 3\%$) or an under-reporting of sex acts
 267 in Natsal-2.

268 Overall, our indirect method to infer the functional relationship between the number
 269 of sex acts and sex partners corroborates the results from the direct method. Models
 270 where the number of sex acts is *constant* or shows a slight *linear* increase with the
 271 number of sex partners provide the best and most parsimonious fit to the data. In
 272 contrast, the classical assumption of a strict *proportionality* between the total number
 273 of sex acts and the number of sex partners is clearly at odds with the data.

Table 4: Maximum likelihood estimates of the functional relationship between the number of sex acts and sex partners (indirect method). Fixed parameters are given in squared brackets and estimates are shown together with 95% confidence intervals. The five different models are sorted in increasing order of their AIC. Likelihood ratio tests show that the *constant* model is superior to all models with more parameters. The *linear* and *no intercept* model are favored over the *full* and *proportional* model. The models are fitted with initial parameter values from Table 2 and $\epsilon = 0.5$.

| Model | Parameters | | | | ϵ | No. of free parameters | -2LogLik | AIC |
|--------------|-------------------|-------------------|------------------|--|-----------------------|------------------------|----------|-------|
| | d_1 | d_2 | d_3 | | | | | |
| Constant | 10.6 (8.54, 12.9) | [0.0] | [1.0] | | 0.60 (0.28, 0.85) | 2 | 125.4 | 129.4 |
| No Intercept | [0.0] | 10.4 (6.44, 15.2) | 5.1e-4 (0, 1.46) | | 0.63 (0.16, 0.94) | 3 | 125.4 | 131.5 |
| Linear | 10.0 (7.92, 12.4) | 4.6e-3 (0, 0.15) | [1.0] | | 0.69 (0.34, 0.89) | 3 | 125.8 | 131.8 |
| Full | 6.72 (2.54, 12.8) | 3.97 (0.59, 10.2) | 1.1e-4 (0, 0.17) | | 0.59 (0.31, 0.82) | 4 | 125.4 | 133.4 |
| Proportional | [0.0] | 1.28 (1.23, 1.34) | [1.0] | | 7.6e-3 (9.8e-5, 0.38) | 2 | 153.2 | 157.2 |

274 Chlamydia transmission and control

275 We now investigate the effects of different assumptions about the number of sex acts
 276 between partners on chlamydia transmission and control. We focus on the general pop-
 277 ulation in Britain (Natsal-2) and use the *linear* relationship for the number of sex acts
 278 as a function of sex partners from Table 2. This ‘realistic’ model is contrasted to the
 279 classical assumption where the number of sex acts increases strictly *proportionally* with
 280 the number of sex partners. For both models, we use the best-fit estimates of the per
 281 sex act transmission probability β , the recovery rate γ and the sexual mixing coefficient
 282 ϵ from Table 3.

283 For the *linear* model, distributing the number of sex acts to sex partners of different
 284 sexual activity classes generates the sex acts matrix a_{ij} (Fig. 3A). From a_{ij} , we can then
 285 calculate the per partnership transmission probabilities b_{ij} (equation 4), which range
 286 from 19.8% to 93.9% for partnerships between individuals with 10 and one partner(s),
 287 respectively (Fig. 3B). In contrast, the proportional model with a constant number of
 288 sex acts per partner results in a single per partnership transmission probability of 37.0%,
 289 which is close to what has been estimated for mid-risk populations Althaus et al. (2012b).

290 Differences in the per partnership transmission probability affect the transmission
 291 potential of individuals from different sexual activity classes, as reflected in the basic
 292 reproduction number (R_0) of each sexual activity class. In the classical scenario, where
 293 the number of sex acts per partner is constant and the sexual mixing between partners is
 294 fully *proportional*, R_0 is a linearly increasing function of the number of new heterosexual
 295 partners per year (Fig. 4A, gray diamonds). The *proportional* model further suggests
 296 that only individuals with three or more new heterosexual partners per year, or 21.2%
 297 of the individuals who had a new partner in the previous year, will infect more than
 298 one person ($R_0 > 1$). In the more ‘realistic’ *linear* model, the value of R_0 exceeds the
 299 threshold of one for all individuals with one or more new heterosexual partners in the
 300 last year, and saturates around three for higher number of partners (Fig. 4A, black
 301 squares). The differences between the models is also reflected in the value of R_0 for the
 302 entire population. In the classical model, the R_0 for chlamydia is 1.26 while it is 1.12
 303 for the more ‘realistic’ model.

304 Screening for and treating of asymptomatic chlamydia infection is the primary strat-
 305 egy to prevent disease transmission (Althaus et al., 2014). In England, screening for
 306 women and men is recommended annually and after a change of sexual partner (De-
 307 partment of Health, 2004). Ideally, screening will decrease R_0 below the threshold of

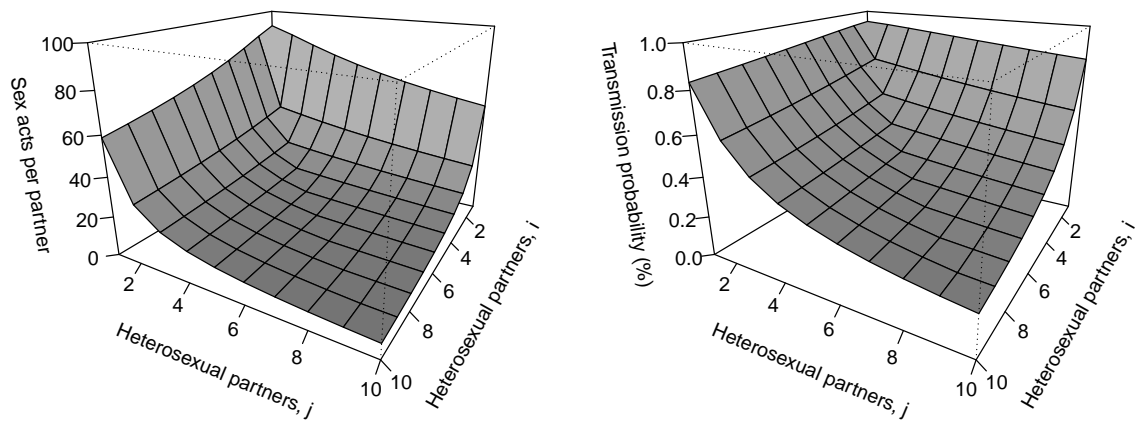


Figure 3: Average number of sex acts (left panel) and per partnership transmission probabilities (right panel) between individuals of sexual activity class i and j . The matrices correspond to the best-fit (*Linear*) model from section .

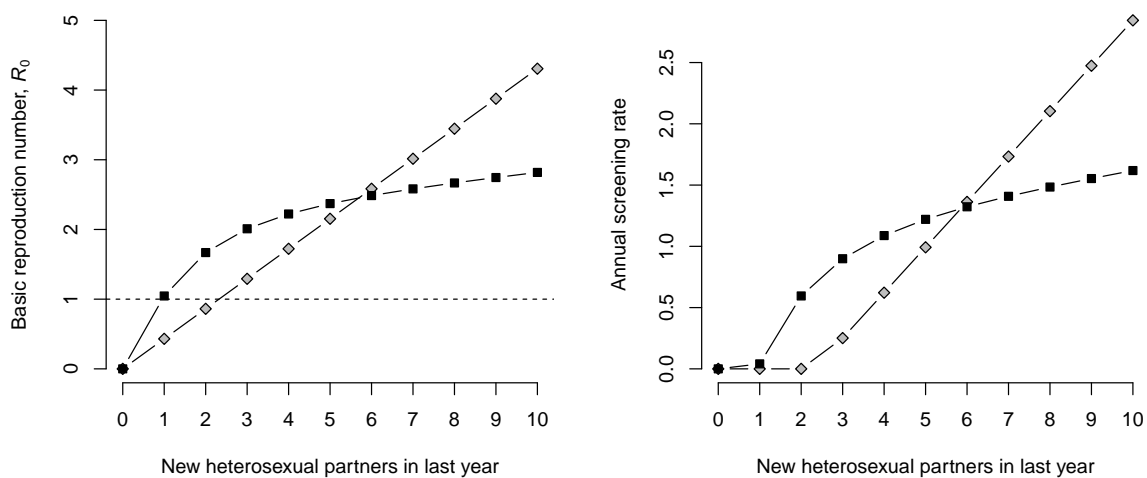


Figure 4: Host-specific basic reproduction number (left panel) and required screening rate to push R_0 below one (right panel). The results from the best-fit *linear* model (black squares) are compared to the classical model where the number of sex acts increases strictly *proportional* with the number of sex partners (gray diamonds). Data are from Natsal-2 only.

308 one. The classical model predicts that low screening rates are sufficient to prevent trans-
 309 mission in individuals with low numbers of partners but that more than three tests per
 310 year on average would be necessary to prevent transmission in individuals with many
 311 partners (right panel of Fig. 4, gray diamonds). Conversely, the ‘more realistic’ model
 312 illustrates that substantial screening (up to once every year) is already necessary to pre-
 313 vent transmission in individuals with low numbers of partners per year (right panel of

315 Discussion

316 This study provides insights into the relationship between the number of sex acts and
317 the number of heterosexual partners, and how it affects the transmission dynamics of
318 chlamydia and the projected impact of control interventions. We use direct and indi-
319 rect methods to infer this relationship from two population-based probability sample
320 surveys. Using a direct method based on self-reported values, we find evidence that the
321 number of sex acts increases only marginally with the number of sex partners. This
322 finding is corroborated using an indirect method based on chlamydia prevalence data,
323 which allows us to show that a standard model where the number of sex acts increases
324 strictly proportionally with the number of sex partners is less consistent than most other
325 models. Noticeably, the most ‘realistic’ model, where the number of sex acts are taken
326 into account, provides strong evidence for assortative mixing between individuals with
327 different numbers of heterosexual partners. The improved model also suggests that all
328 individuals with one or more new heterosexual partners in the last year contribute to
329 chlamydia transmission ($R_0 > 1$).

330 A major strength of our approach is that our model formulation allows us to exploit
331 two large datasets of sexual behavior. This gives us more power to perform model
332 comparison and reject those models that are not consistent with the data. It is also
333 encouraging that the two methods for inferring the relationship between the number of
334 sex acts and the number of sex partners (one based on chlamydia prevalence data and the
335 other on self-reported number of sex acts) are in general agreement with one another.
336 Note that an advantage of the indirect method is that it only estimates potentially
337 infectious, or unprotected, sex acts.

338 There are several limitations to our study. First, we pool heterosexual women and
339 men together, and do not take age-specific sexual behavior and different ethnic groups
340 into account. While the average number of heterosexual partners in women and men
341 should be the same, men typically show a higher variability in the number of sex partners
342 compared to women (Gouveia-Oliveira and Pedersen, 2009). Our simplifying assumption
343 is driven by the aim to keep the number of parameters small and the number of data
344 points large enough to be able to statistically compare different models. This is also the
345 reason why our analysis is focused on heterosexuals only. Data from larger probability
346 sample surveys could potentially improve these limiting aspects. However, stratifying
347 the population into women and men in the analysis using the direct method does not
348 reveal significant differences between the two sexes (results not shown). Some other
349 known important factors that we do not include in the model are concurrency of sexual
350 partnerships, condom use and potential sex-specific differences in infection parameters.

351 We extend a commonly used STI transmission model, that stratifies the population
352 into different sexual activity classes, with a sex acts matrix that describes the average
353 numbers of sex acts between individuals of different sexual activity classes. The entries
354 of our sex act matrix are either directly or indirectly inferred from data. Others have
355 used similar models but could not derive the number of sex acts per partner in such de-
356 tail Regan et al. (2008); Garnett et al. (2008). Somewhat different modeling frameworks
357 that investigate the importance of sex acts by means of weighted contact networks have
358 been developed by Britton et al. (2007) and Moslonka-Lefebvre et al. (2012). These mod-
359 els are arguably more realistic than the more commonly used transmission models that
360 stratify the population into different sexual activity classes. However, network models

361 have two major disadvantages. First, the heterosexual contact networks for large popu-
362 lations are usually not known. Second, we currently lack meaningful summary statistics
363 for weighted networks, and model results tend to rely on computationally expensive sim-
364 ulations. An alternative extension of our analyses would be to use a recently developed
365 framework, that manages to derive analytical results for weighted networks by adopting
366 a configuration network approach and using joint probability distributions of number of
367 sex partners and number of sex acts Kamp et al. (2013).

368 This work also brings new elements to the ongoing debate on the level of assortative
369 mixing between heterosexual individuals of different sexual activity classes in the gen-
370 eral population. Using the *linear* relationship between the number of sex acts and sex
371 partners from the direct method, we estimate a sexual mixing coefficient of $\epsilon = 0.83$ for
372 Natsal-2 (Table 3). An early study based on partner notification data indicated that a
373 proportional mixing model is not an adequate description of the observed sexual mixing
374 pattern Granath et al. (1991). Later, Renton et al. (1995) indicated that individuals
375 with high rates of sexual partners preferentially select other individuals with high rates
376 as partners. Garnett et al. (1996) also found that sexual mixing was weakly assortative
377 in patients attending sexually transmitted diseases (STDs) clinics. In contrast, Stoner
378 et al. (2000) did not find evidence for assortative mixing in members of gonorrhea and
379 chlamydia networks. Finally, it is worth noting that we do not include age as an addi-
380 tional factor for assortative mixing. Young adults typically have more new sex partners
381 than older individuals, and people prefer sex partners not too different in age. This au-
382 tomatically introduces a level of assortative mixing in sexual behavior. This illustrates
383 the difficulties in quantifying the degree of sexual mixing, and that the estimates are
384 likely to depend on the population studied.

385 Our estimates of the basic reproduction number (R_0) for chlamydia are consistent
386 with values that were investigated in a recent theoretical study that introduced the
387 concepts of case and partnership reproduction numbers Heijne et al. (2013). Another
388 study based on contact tracing data showed that individual reproduction numbers for
389 chlamydia rarely exceed 3.0 Potterat et al. (1999). Interestingly, this is in line with what
390 we find for the host-specific basic reproduction numbers from the *linear* model (Fig. 4A,
391 black squares), where R_0 saturates around 3.0 for those individuals with a high number
392 of sex partners.

393 Finally, we show that taking into account the number of sex acts between part-
394 ners with different levels of sexual activity can be important in guiding public health
395 interventions, such as chlamydia screening programs. Indeed, a high level of assorta-
396 tive mixing between individuals of different heterosexual activity classes means that
397 chlamydia can easily persist in those sub-populations that are difficult to reach through
398 screening. Furthermore, our results also underline that chlamydia control interventions
399 should be aimed towards all sexually active young adults as they are likely to contribute
400 to ongoing transmission.

401 Competing interests

402 We declare no competing interests.

404 CLA and SA designed the study, carried out the analysis, interpreted the results and
405 drafted the manuscript. MC contributed to the analysis. All authors contributed to
406 revising the manuscript and gave final approval for publication.

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