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Linearity and Nonlinearity in HIV/STI Transmission: Implications for the Evaluation of Sexual Risk Reduction Interventions

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Abstract

A mathematical model of HIV/sexually transmitted infections (STI) transmission was used to examine how linearity or nonlinearity in the relationship between the number of unprotected sex acts (or the number of sex partners) and the risk of acquiring HIV or a highly infectious STI (such as gonorrhea or chlamydia) affects the utility of sexual behavior change measures as indicators of the effectiveness of HIV/STI risk-reduction interventions. Findings indicate that the risk of acquiring HIV through vaginal intercourse is essentially a linear function of the number of unprotected sex acts and is nearly independent of the number of sex partners. Consequently, the number of unprotected sex acts is an excellent marker for the risk of acquiring HIV through vaginal intercourse, whereas the number of sex partners is largely uninformative. In general, the number of unprotected sex acts is not an adequate marker for the risk of acquiring a highly infectious STI due to the highly nonlinear per act transmission dynamics of these STIs. The number of sex partners is a reasonable indicator of STI risk only under highly circumscribed conditions. A theoretical explanation for this pattern of results is provided. The contrasting extent to which HIV and highly infectious STIs deviate from the linearity assumption that underlies sexual behavior outcome measures has important implications for the use of these measures to assess the effectiveness of HIV/STI risk-reduction interventions.

Keywords

outcome evaluation (other than economic evaluation); design and evaluation of programs and policies; measurement; methodology (if appropriate)

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Introduction

The effectiveness of HIV prevention and other sexually transmitted infections (STI) risk-reduction interventions often is assessed by measuring changes in risk behavior indicators such as the number of unprotected sex acts or the number of sex partners (Holtgrave and Pinkerton 2000; Oakley, Fullerton, and Holland 1995; Stephenson, Imrie, and Sutton 2000). The primary objective of these interventions is to reduce intervention participants' risks of acquiring HIV or another STI, rather than decreasing risk behaviors per se (Fishbein 1996). Consequently, the validity of using behavioral markers such as changes in the numbers of unprotected sex acts or sex partners to assess intervention effectiveness depends on the extent to which such changes are correlated with actual reductions in the risk of acquiring the target STI (Petersman et al. 2000; Pinkerton et al. 2002).

The number of unprotected sex acts and sex partners are linear measures, in that the difference between one and two unprotected sex acts, for example, is treated in most statistical analyses as being equivalent to the difference between two and three sex acts. STI transmission, in contrast, is a nonlinear process: Decreasing the number of unprotected sex acts from two to one produces a greater reduction in STI risk than does decreasing the number of sex acts from three to two (Chesson and Gift 2000). In particular, the incremental (or added) risk associated with the third unprotected sex act is less than the incremental risk associated with the second unprotected sex act. This deviation from the linearity assumption that underlies behavioral outcome measures such as the number of sex acts or sex partners has important implications for the use of these measures to assess the effectiveness of STI risk-reduction interventions.

The present article explores these implications. Using a mathematical model of STI transmission we demonstrate here that the utility of behavioral change measures such as decreases in the number of unprotected sex acts or sex partners—when viewed as indicators of STI risk-reduction—critically depends on how linear or nonlinear the relationship is between the particular behavioral outcome measure and the risk of acquiring the target STI. The analyses contrast HIV—which is not readily transmitted during vaginal intercourse—with highly infectious STIs such as gonorrhea, chlamydia, and syphilis. The key question addressed in these analyses is whether or not changes in the number of sex acts or sex partners are adequate markers of corresponding changes in the risk of HIV/STI acquisition. A theoretical explication of the modeling results is presented.

Mathematical Model and Parameter Values

A mathematical model of HIV/STI transmission was used to examine the influence of the number of sex acts and the number of sex partners on the likelihood of HIV/STI acquisition. The risk that an uninfected person would acquire a particular STI (including HIV) as a consequence of engaging in unprotected sex with each of m different sex partners is $P = 1 - (1 - \pi_1\beta_1)(1 - \pi_2\beta_2) \dots (1 - \pi_m\beta_m)$, where π_k is the probability that partner k is infected, $\beta_k = 1 - (1 - \alpha)^{n_k}$ is the probability of STI transmission if the partner is infected, α is the per-act STI transmission probability, and n_k is the number of unprotected sex acts with partner k .

(Pinkerton and Abramson 1993). (For simplicity, we assume there is no risk of transmission during condom-protected sex and that $\pi_k = \pi$ is the same for all partners.)

During the asymptomatic phase of HIV infection the per-act transmission probabilities for receptive vaginal and anal intercourse are approximately $\alpha = .001$ and $.02$, respectively (the risk of HIV acquisition associated with insertive vaginal or anal intercourse is even smaller, $\alpha = .0005$; Katz and Gerberding 1998; Mastro and de Vincenzi 1996; Royce et al. 1997). In contrast to HIV, many common STIs (e.g., gonorrhea, chlamydia, syphilis, and trichomonas) are quite easily transmitted, with per-act transmission probabilities that range from approximately $\alpha = .2$ – $.5$ (Bowden and Garnett 2000; Garnett et al. 1997; Holmes, Johnson, and Trostle 1970; Katz, Caine, and Jones 1990; Stone 1994).

The prevalence of HIV and of highly infectious STIs such as gonorrhea, chlamydia, syphilis, and trichomonas varies greatly from one population group to the next. Unless otherwise noted, for illustrative purposes the analyses assume a rather high $\pi = 10\%$ prevalence of infection among sex partners (CDC 2006; Miller et al. 2004). However, all of the findings reported below hold for all prevalence values between 0.1% and 25% .

For purposes of illustration, the analyses generally assume a maximum of 25 unprotected sex acts and 5 sex partners. These values are consistent with the baseline values reported by the high-risk men and women in the national institute of mental health (NIMH) Multisite HIV/STI Intervention Trial, who averaged 25.9 unprotected sex acts and 3.8 partners in the previous 90 days (NIMH Multisite HIV Prevention Trial 1997).

Validity of the Number of Sex Acts as a Marker for Risk Reduction

As illustrated in Figure 1, the risk of acquiring a highly infectious STI is a decidedly nonlinear function of the number of unprotected sex acts at the partnership level. Because the per-act transmission probability is so high ($\alpha \approx .2$), only a relatively small number of acts with a particular partner is required for the per-partner risk to begin to approach its maximum value, which equals the probability that the partner is infected, π . Each additional partner essentially “resets” the risk accumulation process, but at a higher base-line level and with a higher maximum potential risk (equal to $1 - (1 - \pi)^m$, where m denotes the number of partners). Consequently, the risk of acquiring a highly infectious STI critically depends on the number of sex partners and on the distribution of sex acts among sex partners, as well as on the number of unprotected sex acts, as shown in Figure 2. Indeed, it is quite possible to decrease the number of unprotected sex acts but simultaneously to increase risk. For example, when $\alpha = .5$, engaging in just one sex act with each of five different partners (five acts total) is riskier than engaging in 25 acts with a single partner. Thus, the decrease in the number of unprotected sex acts is generally not a reliable marker of STI risk reduction.

By way of comparison, for 25 or fewer sex acts, reductions in the number of unprotected vaginal intercourse acts are *always* accompanied by reductions in the risk of acquiring HIV infection through vaginal intercourse, *regardless of any change in the number of sex partners or the distribution of sex acts among partners*. As such, the decrease in the number of unprotected vaginal intercourse acts is an excellent behavioral marker of HIV risk reduction.

Validity of the Number of Sex Partners as a Marker for Risk Reduction

Because the risk of acquiring HIV through vaginal intercourse is almost entirely determined by the number of unprotected sex acts, HIV acquisition risk is essentially independent of the number of sex partners or the distribution of sex acts among sex partners. For example, the minimum risk (all acts with the same partner) and the maximum risk (each act with a different partner) associated with 25 acts of receptive vaginal intercourse differ by only 1%, despite a 2,400% difference in the number of partners. Consequently, the number of sex partners is largely uninformative as an indicator of the risk of acquiring HIV risk through vaginal intercourse. Risk could increase, despite a substantial decrease in the number of partners, due to just a very slight increase in the number of unprotected sex acts.

Although STI risk clearly depends on the number of sex partners, the relationship between the number of partners and the risk of acquiring a highly infectious STI grows increasingly nonlinear as the number of sex partners increases (see Figure 3). This nonlinearity limits the utility of decreases in the number of sex partners as a marker for STI risk reduction. More importantly, perhaps, the risk of STI acquisition still depends on both the number of sex acts and the distribution of sex acts among sex partners. For example, engaging in five acts of intercourse with each of five partners (25 acts total) is riskier than engaging in two acts with each of six partners (12 total acts), despite the smaller number of sex partners in the first scenario. Even if the number of sex acts is held constant, risk could increase despite a reduction in the number of sex partners. Evenly dividing 25 sex acts among five partners is riskier than engaging in 20 acts with one partner and one act each with five additional partners.

Theoretical Considerations: Act Linearity

As above, the risk of acquiring a particular STI can be estimated as: $P = 1 - (1 - \pi\beta_1)(1 - \pi\beta_2) \dots (1 - \pi\beta_m)$, where π is the prevalence of infection among partners, $\beta_k = 1 - (1 - \alpha)^{n_k}$ is the probability of STI transmission if partner k is infected, α is the per-act transmission probability, and n_k is the number of unprotected sex acts with partner k . If αn_k is sufficiently small, the per-partnership risk can be approximated by the linear estimator, $\beta_k \approx \alpha n_k$. Likewise, when π and each β_k are small, $P \approx \pi[\beta_1 + \beta_2 + \dots + \beta_m]$. When these conditions are jointly satisfied (notably, the smaller α is, the smaller each β_k is), the overall probability of STI acquisition is approximately $P \approx \pi[\beta_1 + \beta_1 + \dots + \beta_m] = \pi[\alpha n_1 + \alpha n_2 + \dots + \alpha n_m] = \pi\alpha n$, where $n = n_1 + n_2 + \dots + n_m$ is the total number of unprotected sex acts, summed across partners.

This leads us to define a “perfectly act-linear” STI to be an (idealized) STI that *exactly* satisfies the equation $P = \pi\alpha n$. For a perfectly act-linear STI the risk of infection is proportional to the number of unprotected sex acts and is independent of the number of sex partners and the distribution of sex acts among those partners. Moreover, decreasing the number of unprotected sex acts from n to $(n - \Delta n)$ reduces STI risk from $P(n) = \pi\alpha n$ to $P(n - \Delta n) = \pi\alpha(n - \Delta n)$, an overall reduction of $P(n) - P(n - \Delta n) = \pi\alpha \Delta n$. Thus, for a perfectly act-linear STI the reduction in risk is proportional to the decrease in the number of unprotected sex acts, Δn , and is independent of the baseline number of sex acts, the number

of sex partners, or the distribution of sex acts among sex partners. As demonstrated above, HIV transmission during vaginal intercourse is highly act-linear, but transmission of highly infectious STIs is not.

An STI need not be perfectly act-linear for preintervention to postintervention reductions in the number of unprotected sex acts to serve as a valid measure of HIV/STI risk reduction across a study sample. Validity requires only that larger decreases in the number of unprotected sex acts are reliably associated with greater reductions in the risk of HIV/STI acquisition, independent of the preintervention and postintervention numbers of sex partners and the distribution of sex acts among these partners. This is a stringent criterion, but an important one: When met, one can confidently attribute the reduced risk of HIV/STI acquisition to the decrease in the number of unprotected sex acts.

Conversely, a minimum requirement for validity is that, *for a single partner*, larger decreases in the number of unprotected sex acts should be associated with greater reductions in the risk of HIV/STI acquisition. (In this situation, risk depends only on the number of sex acts. If one study participant can decrease his or her number of sex acts by more than another participant, yet reduce his or her risk by less, mean changes in the number of sex acts become uninterpretable with respect to risk reduction.) Otherwise, the decrease in the number of sex acts is clearly an invalid marker of HIV/STI risk reduction across a study sample.

As shown in Table 1, the decrease in the number of unprotected sex acts is a valid marker of reductions in the risk of HIV acquisition during receptive vaginal intercourse (larger decreases are always associated with reductions in risk) whenever the number of sex acts is less than 46 and the prevalence of infection is 0.1% or greater. In contrast, for highly infectious STIs ($\alpha = .2$), the decrease in the number of unprotected sex acts is an invalid marker of risk reduction when the number of sex acts exceeds four and the prevalence of infection is less than or equal to 25%; this is due to the decidedly nonlinear nature of highly infectious STI transmission at the partnership level (see Figure 1).

Theoretical Considerations: Partner Linearity

As Figure 1 illustrates, for highly infectious STIs the per-partnership risk of STI acquisition approaches the maximum value of $\beta_k = 1$ after only a relatively small number of unprotected sex acts. When each β_k is very close to 1, the overall risk of acquiring a highly infectious STI, $P = 1 - (1 - \pi\beta_1)(1 - \pi\beta_2) \dots (1 - \pi\beta_m)$, is approximately $1 - (1 - \pi)^m$, which in turn can be approximated by πm , provided that both π and m are small.

We therefore define a “perfectly partner-linear STI” to be an idealized STI for which the probability of infection exactly equals πm . For a perfectly partner-linear STI, the risk of STI depends only on the number of sex partners (m) and the probability of encountering an STI-infected partner (π), hence there is a perfect correlation between the number of sex partners and the risk of STI acquisition.

A highly infectious STI with a per-act transmission probability of 0.5 comes close to this ideal, provided that the number of acts with each partner, hence the per-partnership

transmission probability, is relatively large both preintervention and postintervention. For example, the risk associated with five acts of intercourse with each of five partners differs from the “perfectly partner-linear” prediction of 5π by only 4–5% when $\pi = 0.1$ – 1% (but by 20% when π is 10%). However, the requirement of large numbers of sex acts per partner severely limits the utility of the decrease in the number of sex partners as a marker of STI risk reduction. In a typical STI risk-reduction intervention study one would expect some persons with few sex partners and few total acts; some with few partners but many sex acts; and some with many sex acts and sex partners. It is only for the second group that the decreases in the number of sex partners is a reliable marker of risk reduction—and even then, only if members of this group remain in this group postintervention. Thus, in a study sample of persons with varied sexual behavior patterns, one should not expect a strong correlation between the number of sex partners and the risk of STI acquisition.

HIV Transmission Through Anal Intercourse

The above analyses addressed HIV transmission during receptive vaginal intercourse but not receptive anal intercourse. The per-act transmission probability for receptive anal intercourse is approximately $\alpha = .02$, which is much larger than the transmission probability for receptive vaginal intercourse ($\alpha = .001$), but much smaller than for a highly infectious STI ($\alpha = .2$) (Katz and Gerberding 1998). As such, HIV transmission during receptive anal intercourse occupies a gray zone. When the number of sex acts is less than 11 or 12, decreasing the number of sex acts always reduces risk. Conversely, the decrease in the number of sex acts is clearly an invalid indicator of risk reduction when the number of sex acts exceeds 35 (see Table 1). Between 11 and 35 sex acts, the decrease in the number of sex acts might or might not be a valid indicator of reductions in the risk of acquiring HIV through receptive anal intercourse. Although the per-partnership risk of acquiring HIV through receptive anal intercourse is essentially a linear function of the number of sex acts (Figure 1), the per-partnership risk is itself rather large ($\beta \approx 0.1$ after five unprotected sex acts). Consequently, HIV transmission during receptive anal intercourse generally is not linear across partners.

Discussion

The results of this modeling study indicate that the number of unprotected sex acts is an excellent marker for the risk of acquiring HIV through vaginal intercourse and, to a lesser extent, through receptive anal intercourse. In contrast, the decrease in the number of unprotected sex acts is not a valid marker of STI risk reduction for highly infectious nonviral STIs such as gonorrhea, chlamydia, syphilis, and trichomonas. The results of this analysis also suggest that the risk of acquiring HIV through vaginal intercourse is largely independent of the number of sex partners. Moreover, the number of sex partners generally is not a reliable indicator of reductions in the risk of acquiring a highly infectious STI unless the number of acts with each partner is relatively large at both baseline and follow-up, the prevalence of infections is relatively low, and the per-act transmission probability is quite high.

These findings are consistent with the results of a previous study that used sexual behavior data collected in the NIMH Multisite HIV/STI Intervention Trial (National Institute of Mental Health Multisite HIV Prevention Trial Group 1998; NIMH Multisite HIV Prevention Trial 1997) to model the relationship between changes in the number of unprotected sex acts and sex partners and the risk of acquiring HIV or a highly infectious STI with a presumed per-act transmission probability equal to 0.1 (Pinkerton, Chesson, et al. 2002). For the men and women in that study, a nearly perfect correlation was found between decreases in the number of unprotected sex acts and reductions in the risk of acquiring HIV through vaginal intercourse, but there was essentially no relationship between changes in the number of sex partners and the risk of HIV acquisition. Conversely, reductions in the risk of acquiring a highly infectious STDs were only weakly correlated with decreases in the number of unprotected sex acts and decreases in the number of sex partners. The present analysis provides a theoretical explication for this pattern of results based on the degree of linearity of different STIs with respect to the number of unprotected sex acts or the number of sex partners.

The results presented above are based on a relatively simple, individual-level model of HIV transmission. For simplicity, this model assumes that the prevalence of infection among sex partners is the same for all partners. Clearly some partners are riskier than others. Findings from the model were consistent over a wide range of potential infection prevalence values and would be expected to hold in a mixed-prevalence model. The model examined a range of possible sex act distribution patterns, ranging from the least risky scenario in which sex acts are evenly distributed among sex partners, to the riskiest distribution pattern in which most sex acts are with a “main” partner, with one sex act each for additional partners (Pinkerton and Abramson 1993). Little empirical research has examined actual sex act distribution patterns in high-risk populations, so it is not known whether sex act distributions tend toward the more or less risky end of the spectrum. Finally, although the model functions at the individual level, findings are applicable at the study sample level (e.g., to participants in an intervention trial), as indicated in the analysis of the validity of decreases in the number of sex acts as a measure of HIV/STI risk reduction.

The main findings from our individual-level model generally are consistent with those of Garnett and colleagues, who used a standard compartmental model of STI transmission to explore the population-level impacts of changes in the number of partners and changes in the number of unprotected sex acts (Garnett, White, and Ward 2008). For example, both models found that, in the case of highly infectious bacterial STIs, changes in the number of partners matter more than changes in the number of sex acts.

The very different transmission dynamics of HIV, which is relatively noninfectious during the nonacute phase of infection, and highly infectious STIs such as gonorrhea and chlamydia, calls into question the use of the latter as a “surrogate marker” of the former (Pinkerton, Layde, and NIMH Multisite HIV Prevention Trial Group 2002). Because acquisition of a highly infectious STI is likely after only a few unprotected sex acts with an infected partner, decreasing the number of unprotected sex acts to some nonzero value generally does little to reduce the risk of acquiring a highly infectious STI. The risk of acquiring HIV, in contrast, is highly responsive to any change in the number of unprotected

sex acts. Thus, an intervention participant could substantially reduce his or her risk of acquiring HIV without noticeably affecting his or her risk of acquiring a highly infectious STI.

Beyond assessment issues, the important differences between HIV and more readily transmitted STIs should inform the behavioral targets of HIV/STI risk-reduction interventions (Pinkerton et al. 2003). For HIV, a risk-reduction approach that encourages intervention participants to decrease the number of unprotected sex acts but does not demand the complete elimination of unprotected sex may be effective at reducing risk (Cates and Hinman 1992; Odets 1994); for example, a 50% reduction in the number of unprotected vaginal intercourse acts is associated with approximately a 50% reduction in the risk of acquiring HIV (Pinkerton and Abramson 1996). For highly infectious STIs, in contrast, simply decreasing the number of unprotected sex acts to some nonzero value generally may be insufficient to significantly reduce the risk of infection. Interventions that target highly infectious STIs should encourage abstinence from unprotected sexual activity and should make clear the significant risks associated with engaging in unprotected sex with multiple partners.

In conclusion, it is important that HIV/STI prevention researchers understand the strengths and limitations of the behavioral outcome measures used to assess the effectiveness of HIV/STI risk-reduction interventions. Differences in the transmission dynamics of HIV and much more infectious STIs must be considered both when designing targeted risk-reduction interventions and when assessing the efficacy of these interventions.

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Figure 1.

Risk (probability) of acquiring HIV or a highly infectious STI from a single, potentially infected partner, as a percentage of the risk associated with the maximum of 25 unprotected sex acts. For highly infectious STIs ($\alpha = .2, .5$), the perpartnership risk grows rapidly in the first several sex acts, then more slowly as saturation is approached. For HIV transmission during receptive vaginal ($\alpha = .001$) or anal ($\alpha = .02$) intercourse, the per-partnership risk is essentially a linear function of the number of unprotected sex acts with the partner.

Figure 2.

Risk of acquiring a highly infectious STI ($\alpha = .5$) as a function of the number of unprotected sex acts, the number of partners, and the distribution of sex acts among sex partners. (Sex acts are evenly divided among sex partners in the least risky distribution, whereas in the riskiest distribution there is one sex act with each of four partners and $n - 4$ sex acts with the remaining partner.) For highly infectious STIs, the risk of acquisition critically depends on all three of the above factors. The arrow indicates that it is quite possible to substantially decrease the number of unprotected sex acts but simultaneously to increase risk. Notice that engaging in a single act of intercourse with each of five different partners (five acts total) is riskier than engaging in 25 acts with a single partner.

Figure 3.

Risk of acquiring HIV or a highly infectious STI as a function of the number of sex partners assuming 25 unprotected sex acts divided evenly among these partners. (Maximum risk would occur if there were 10 partners.) For HIV transmission (receptive vaginal intercourse: $\alpha = .001$; receptive anal intercourse: $\alpha = .02$) near-maximum risk is reached in the first few partners and therefore the number of sex partners is not strongly correlated with HIV acquisition risk. For highly infectious STIs ($\alpha = .2, .5$), the number of partners clearly matters. However, risk is not a strongly linear function of the number of sex partners unless the number of acts with each partner is relatively large.

Table 1

Validity of Decreases in the Number of Unprotected Sex Acts as an Indicator of HIV/STI Risk Reduction

	Invalid if $n >$	Definitely Valid if n		
		$\pi = 25\%$	$\pi = 10\%$	$\pi = 1\%$
HIV: Receptive vaginal intercourse ($\alpha = .001$)	694	52	47	45
HIV: Receptive anal intercourse ($\alpha = .02$)	35	11	11	10
Highly infectious STI ($\alpha = .2$)	4	4	3	3
Highly infectious STI ($\alpha = .5$)	2	2	2	2

Note. STI = sexually transmitted infections. n denotes the number of unprotected sex acts before any decrease and π denotes the HIV/STI prevalence among sex partners. If n is less than or equal to the validity threshold, a larger decrease in the number of unprotected sex acts will always result in a larger decrease in STI risk, irrespective of the number of sex partners or the distribution of sex acts among partners. In contrast, if n exceeds the invalidity threshold it is possible for a study participant to decrease his or her number of sex acts by more than another participant, yet reduce his or her risk by less. For values of n between the two threshold indicators, the decrease in the number of sex acts might or might not be a reasonable indicator of risk reduction.