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Heterogeneity in Number and Type of Sexual Contacts in a Gay Urban Cohort

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Abstract

HIV transmission models include heterogeneous individuals with different sexual behaviors including contact rates, mixing patterns, and sexual practices. However, heterogeneity can also exist within individuals over time. In this paper we analyze a two year prospective cohort of 882 gay men with observations at six month intervals focusing on heterogeneity both within and between individuals in sexual contact rates and sexual roles. The total number of sexual contacts made over the course of the study (mean 1.55 per month) are highly variable between individuals (standard deviation 9.82 per month) as expected. At the individual level, contacts were also heterogeneous over time. For a homogeneous count process the variance should scale with the mean; however, at the individual level the variance scaled with the square root of the mean implying the presence of heterogeneity within individuals over time. We also observed a high level of movement between dichotomous sexual roles (insertive/receptive, protected/unprotected, anal/oral, and HIV status of partners). On average periods of exclusively unprotected sexual contacted lasted 16 months. Our results suggest that future HIV models should consider heterogeneities both between and within individuals in sexual contact rates and sexual roles.

Keywords

HIV; behavior; contact rates

1 Introduction

HIV persists despite being well characterized, weakly transmitted (Gray, Wawer, Brookmeyer, Sewankambo, Serwadda, Wabwire-Mangen, Lutalo, Li, vanCott, and Quinn (2001)), highly preventable (Holmes, Levine, and Weaver (2004)), and having well-funded research and prevention programs. Our inability to eliminate HIV may stem from current prevention practices that are fundamentally sound yet are too small in magnitude, or because our theoretical understanding is lacking, leading to inefficient prevention recommendations.

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HIV prevention programs have been effective in reducing, but not eliminating, HIV transmission. For example, the sharp decline of HIV in Uganda in the 1990s was attributed to the implementation of effective, cooperatively designed prevention programs (Green, Halperin, Nantulya, and Hogle (2006)). Since 2005 the prevalence of HIV in Uganda remained stable at about 6.5% (Kim, Hallett, Stover, Gouws, Musinguzi, Mureithi, Bunnell, Hargrove, Mermin, Kaiser, Barsigo, and Ghys (2011)), indicating that these programs are clearly effective in reducing risk behavior, but high-levels of transmission still occur. The question arises, what generates the remaining force of infection?

The determinants of the patterns of HIV infection are complex. However, a large portion of the variance in the patterns of HIV infection are attributed to three broad factors: who does what with whom (Alam, Romero-Severson, Kim, Emond, and Koopman (2010)) (Jacquez, Simon, and Koopman (1989)) (Anderson, Gupta, and Ng (1990)), the distribution and correlation of individual-level sexual risk behavior (Dietz (1988)) (May and Anderson (1987)), and the natural-history of infection (Koopman, Jacquez, Welch, Simon, Foxman, Pollock, Barth-Jones, Adams, and Lange (1997)) (Hyman and Stanley (1988)). In this paper we present evidence for a fourth factor that we believe is important in driving the HIV epidemic: the individual-level change in sexual behavior over time. This kind of heterogeneity is not generally regarded as a key population-level determinant of HIV infection; however, recent theoretical results suggest that changes in both the number of sexual partners (Zhang et al. this issue) or the sexual role that an individual plays over time can greatly increase both the endemic prevalence of HIV but also the acute-stage transmission rate (Alam et al. (2010)).

Often papers that deal with behavior change over time look for changes in the prevalence of high-risk behavior in repeated cross-sectional measures of a single population (Knussen, Flowers, McDaid, and Hart (2011)). These analyses are indisputably valuable for the assessment of behavior change and behavioral intervention efficacy(Blower and McLean (1994)); however, any information about changes in individual-level sexual behavior over time is lost as individuals from multiple cross-sectional samples cannot be readily identified. Such studies can inform us about the average or typical risk profile of an individual, but they cannot tell us about an individual's behavioral history. Behavioral data collected by multiple prospective cohort studies such as Multicenter AIDS Cohort Study and the Western Australian HIV Cohort Study could be analyzed in a way to get at the structure of individual-level behavioral. However, to our knowledge such an analysis has not been published.

In this paper we present an analysis of a longitudinal cohort of gay men observed for two years beginning in 1992. We present evidence for heterogeneity in the number of sexual contacts and the types of those contacts at the population and individual level and both between individuals but also within a single individual over time. We argue that, even over short periods of time, both the number of sexual contacts that an individual makes and the nature of those contacts can be highly variable.

2 Material and Methods

2.1 Behavioral data

The data we use in this chapter comes from the Centers for Disease Control and Prevention Collaborative Seroincidence Study (CSS). In 1992 this multi-site study enrolled three large cohorts of HIV-susceptible men in Chicago, Denver, and San Fransisco. Eligibility criteria included report of any anal sex, report of any non-HIV sexually transmitted infection, or, in San Fransisco, report of receptive oral sex with ejaculation. The study enrolled and followed susceptible individuals for a period of up to 24 months. Observation stopped due to follow-

up loss, a positive HIV test, or completion of the study. At enrollment, individuals were asked the number of times they had sex in the previous six months. Every six months individuals were asked again about their sexual behavior in the previous six months for up to four total interviews. The exact time at which each sexual contact occurred in a observational period is unknown. The dataset that we used was aggregated over partnership status such that our results only reflect sexual frequency rather than partnership dynamics.

Observation stopped either due to attrition or seroconversion. The full dataset included 1883 participants. 111 (6%) individuals were observed for 1 period, 329 (18%) individuals were observed for 2 periods, 561 (30%) were observed for 3 periods, and 882 (47%) individuals were observed for all 4 periods.

Ten types of sexual contacts were measured in the full dataset: unprotected receptive anal (URA), unprotected insertive anal (UIA), unprotected receptive oral with ejaculation (URO), protected receptive anal (PRA), and protected insertive anal (PIA); each type is further subdivided into contacts made with a partner known to be HIV positive (+) and ones of unknown HIV status (?). We aggregated the measured categories into more epidemiologically relevant categories: 'protected' (PRA+, PRA?, PIA+, PIA?), 'unprotected' (URA+, URA?, UIA+, UIA?, URO+), 'with HIV+' (URA+, UIA+, PRA+, PIA+), 'with HIV?' (URA?, UIA?, PRA?, PIA?), 'insertive' (UIA+, UIA?, PIA+, PIA?), 'receptive' (URA+, URA?, PRA+, PRA?), and 'oral with ejaculation' (URO+, URO?).

The data show some evidence for geographic heterogeneity. The 2 sample KolmogorovSmirnov statistic gave evidence (p < 0.05) that the second through fourth observational periods at the Denver site are unlikely to be drawn from the same distribution as the rest of the data. However, the data at the Denver site showed similar levels of heterogeneity both between and within individuals to the rest of the dataset. The robustness of our primary results to geographic heterogeneity in the dataset justified pooling by the study site.

To avoid ambiguity in parameterization of the Negative Binomial and Gamma distributions that arise in our analysis, we define the distributions both in terms of their parameters and in terms of the expectation and standard deviation.

2.2 Sexual roles

The term sexual role is usually used to refer to whether or not an individual exclusively practices insertive sex (tops) or receptive sex (bottoms). An individual who does both is considered 'versatile'. We expand the traditional definition of sexual role to include oral/ anal, protected/unprotected, and HIV+/HIV? in addition to insertive/receptive. Each category defines four exclusive states: abstinence, versatility, and either exclusively one type of contact or the other–only receptive or only insertive for example.

Over very long time periods, most sexually active individuals will be classified as versatile; however, examining sexual roles over shorter periods reveals a dynamic process of changing sexual roles. To examine the stability of sexual roles over the course of the study we calculated the empirical probability of changing roles between observational periods as the probability of observing a given sexual role conditional on the current sexual role. We used the same methods in Blower et al. (Blower, van Griensven, and Kaplan (1995)) to analyze the CSS data in terms of sexual role dynamics.

3 Results

3.1 Representativeness of the data

The incidence rate in the dataset is consistent with back calculations of the national incidence in the United States among men who have sex with men (MSM). 52 individuals seroconverted during 35,880 total months of observation for an incidence rate of 0.0174 per person-year. Hall et al. estimated about 19,000 MSM cases of HIV in 1992 (Hall, Song, Rhodes, Prejean, An, Lee, Karon, Brookmeyer, Kaplan, McKenna et al. (2008)). The estimated incidence rate corresponds to an at-risk population of about 1.09 million, which represents 1.3% of the 1992 population of men aged 15-64 in the US. The size of the at-risk MSM population is unknown although this estimate is reasonable. The estimated incidence rate estimate with incidence rates reported in the state of Florida in 2010 (Lieb, White, Grigg, Thompson, Liberti, and Fallon (2010)). The consistency of the incidence rate estimate with other reported incidence in 1992 suggest that the behavioral data do not have an inordinate number of higher or lower risk individuals that would be expected from a random sample.

3.2 Within population temporal heterogeneity

Each contact type shows a decreasing trend in time in both the average number and the standard deviation of the number of contacts. Figure 1 shows plots of the number of contacts made in each observational period. In the first observational period an average susceptible individual made 1.97 contacts of any type per month, while in the final period the average individual made only 1.29 contacts of any type per month, a decrease of 35%. Each contact type decreased by a similar proportion, excluding unprotected contacts which decreased by 47%.

Changes in the standard deviation were mirrored by changes in the average such that the coefficient of variation, the ratio of the standard deviation to the mean, was stable over time with the exception of the third observational period. In the third observational period the coefficient of variation decreased in several contact types including contacts with HIV positive partners and with unprotected contacts. This decrease was largely driven by a single individual reporting an uncharacteristic episode of high activity in the third observational period. The skewness of the total number of contacts likewise increased sharply in the third observational period for both unprotected contacts and for contacts made with partners known to be HIV positive. Excluding the individual who reported a very high number of contacts in the third observational period eliminated the dip in the coefficient of variation and skewness. Oral contacts with ejaculation appear to be an exception to the observed trends. Both the skewness and coefficient of variation of oral contacts with ejaculation increased in each subsequent period.

The secular trend could be a reflection of changing sexual behavior in response to increased social marketing of safer sex practices in the early 1990s. If that theory is true, we should see that unprotected sex decreased more than protected sex. This is supported here where the average reduction in the total number of contacts is 35% while unprotected and protected contacts decreased by 47% and 27% respectively. Alternatively, the effect could be due to enrollment in the study itself (Murray, Swan, Kiryluk, and Clarke (1988)). With the exception of oral contacts, the reduction in the reported number of contacts is greatest between the first and second waves, which is expected if enrollment in the study itself produced a protective effect. Both explanations could produce the observed secular trend. However, without further study, identification of the cause of the apparent secular trend is impossible.

3.3 Between individual contact rate heterogeneity

The aggregate data clearly show contact rate heterogeneity between individuals. On average, individuals reported 1.55 contacts per month, but, the number of contacts was highly heterogeneous between individuals. A large number of individuals (113/882) remained abstinent for the duration of the study, while individuals in the top 10% made 48% of all contacts. In a system with homogeneous contact rates, the variance from stochastic effects is proportional to the contact rate itself and can be quite small. The Negative Binomial can be used as a generalization of a Poisson process where the rate of the process is a Gamma random variable. A population with contact rates distributed as *Gamma*(k, θ) will generate *NegBin*(k, $\frac{\theta}{\theta+1}$) contacts. For any fixed average contact rate, the parameter k can be adjusted to account for between individual heterogeneity in reported number of contacts.

Figure 2 shows a histogram of the data with Poisson and Negative Binomial models. The Negative Binomial model captures both the large number of abstainers and the small number of highly sexually active individuals that are missed by the simple Poisson model. This analysis cannot prove that contact rate heterogeneity is Gamma distributed. However, the poor fit of the Poisson model implies the presence of between individual contact rate heterogeneity, and that Gamma distributed heterogeneity produces a much better fit than the assumption of no heterogeneity.

3.4 Within individual contact rate heterogeneity

The data show clear evidence that sexual contact rates are not only variable between individuals but are also variable within a single individual over time. Figure 3 shows the relationship between the average and standard deviation of the number of contacts of any type for each individual over time. The data clearly show that individuals with the highest number of contacts also have the most variable number of contacts over time; for many individuals, periods of sexual inactivity are punctuated by episodes of elevated sexual activity. If the contact rates are constant over time, each observation is a Poisson random variate, and the mean should converge to the variance in the limit of the sample size. The small number of observations per individual permits a fair amount of stochasticity in the mean/variance relationship making it difficult to rule out the hypothesis that the data are generated by a simple Poisson process especially at low average contact rates. However, the overall unsuitability of the Poisson model is clear; the expected variance for a given mean contact rate (solid red line figure 3) clearly underestimates the temporal variability of the data for a given average contact rate especially at higher contact rates.

To account for the excess variance we assume an additional source of Gamma distributed heterogeneity among observational periods. In a given interval an individual's contact rate deviates from its long-run average by an amount determined by the shape and scale of the heterogeneity. This assumption allows the variance of the number of contacts over time to be tuned independently of an individual's contact rate over time. Assuming an individual has contact rate χ such that $Pr(\chi) \equiv Gamma(k, \theta)$, then the number of contacts made by a single individual over time is distributed as $NegBin\left(r, \frac{r}{\chi+r}\right)$ where $r \in (0, \infty)$ is an over-dispersion parameter. As $\lim_{r\to\infty} NegBin\left(r, \frac{r}{\chi+r}\right) \to Pois(\chi)$. We estimated the average over-dispersion parameter, r, at 0.55 for the entire population by taking the harmonic mean of the over-dispersion parameter estimated for each individual, assuming a known average contact rate. The over-dispersion parameter showed a small level of heterogeneity as a function of average contact rate. However, the average over-dispersion parameters were robust to multiple different stratifications.

The Negative Binomial model performs better than the simple Poisson model by capturing the apparent linear scaling of the standard deviation to the mean. However, at lower average contact rates, the Negative Binomial model predicts variances that are higher than a simple linear regression of the transformed data (figure 3). This is due to the low number of observations per individual that establishes a relatively low maximum variance at low average contact rates. This phenomena is an artifact of the study design and not necessarily of the contact dynamics in the population. For example, if within individual contact rates are characterized by infrequent high contact rate episodes, then variance at the low end of contact rates would underestimate longer term variance. On the other hand, there may be individuals who have low variance and who would never have a high contact rate period. These possibilities cannot be distinguished from a study design that only has four sequential observations. Nevertheless, at higher average contact rates, the Negative Binomial model captures the scaling of the mean to the variance well.

3.5 Within individual sexual role heterogeneity

The marginal trend in the data over time show rapidly changing sexual roles. The proportion of sexual roles stratified by observational period are presented in table 1. Abstinence becomes more common as the study progress for all sexual roles while versatility dramatically drops for all roles. Both of these phenomena are related to the general trend of decreasing number of average contacts. In general, the number of individuals reporting exclusive behavior remained constant over the study. The number of people reporting only protected sex remained constant, while the number of people reporting sex with partners of unknown HIV status—more likely with a casual partner–decreased, suggesting that individuals were reducing their risk by having fewer sexual contacts rather than increasing the proportion of protected contacts. The number of individuals only having oral sex with ejaculation increased by almost two fold, possibly due to the perception that oral sex is safer than anal sex regardless of semen exposure.

In addition to showing a trend in the marginal distribution of sexual roles, the data also suggest sexual roles are highly dynamic. Table 2 gives the empirical probability of moving into a new sexual role in the next observational period (columns) conditional on one's sexual role in the current observational period (rows). This transition matrix assumes that individuals can move to any of the four possible states, given their current state, with a given probability. This is equivalent to saying the data are generated by a fully connected Markov chain with four states, which appears to be a valid assumption. Figure 4 shows the estimated and observed frequencies of the insertive/receptive sexual roles, assuming the initial state of the system is given by the empirical frequencies in the first observational period.

The Markov model closely fits the trends for all of the defined sexual roles including insertive/receptive role as shown in the figure. Assuming a second-order process (i.e. the predicted values are a function of the two previous observational periods for those where they are available) did not significantly change the predicted values in the third and fourth observational periods ($\chi^2 = 0.13 \text{ p} = 0.99$ and $\chi^2 = 0.40 \text{ p} = 0.94$) for the third and fourth wave respectively).

A similar analysis by Blower et al. (Blower et al. (1995)) using data collected from 8 years earlier from a Netherlands cohort, came to very similar conclusions concerning sexual role dynamics. The increased in abstinence coupled with a decrease in versatility observed in both studies suggests that enrollment in a study may produce a reduction in the total number of sex partners on average. However, the similarity of the transition matrix for the insertive/ receptive dynamics found in this study and Blower et al. suggests that, although the system might not be in equilibrium, the underlaying process of behavior change is constant over longer periods. The consistence of the underlying process of change should not be confused

with the consistency of sexual roles over time; even over short periods of time sexual roles are highly dynamic.

4 Discussion

In this paper we found evidence of heterogeneities in sexual behavior at the population-level over time and at the individual-level both between and among individuals. Heterogeneities in sexual behavior between individuals and populations have been widely accepted, however, most transmission models make the implicit assumption that one's behavior is constant over time. We have shown that over short periods individuals change both the number of sexual contacts that they make, and also the nature of those contacts. The implications of temporal heterogeneity in sexual behavior are just now being appreciated, especially with respect to HIV risk and the acute-stage HIV incidence rate.

Understanding the timing of transmission events over the course of an HIV infection is essential to predicting the efficacy of prevention programs (Stover (2011)) (Miller, Rosenberg, Rutstein, and Powers (2010)). Early HIV infection is characterized by high contagiousness (Wawer, Gray, Sewankambo, Serwadda, Li, Laeyen-decker, Kiwanuka, Kigozi, Kiddugavu, Lutalo et al. (2005)) (Hollingsworth, Anderson, and Fraser (2008)) (Pinkerton (2007)) and lasts for approximately 2 months following infection (Pilcher, Joaki, Hoffman, Martinson, Mapanje, Stewart, Powers, Galvin, Chilongozi, Gama, Price, Fiscus, and Cohen (2007)). The acute stage is followed by a much less contagious period and, if untreated, finally by a highly contagious pre-AIDS stage. Determining which infection stage is responsible for the plurality of transmissions is well studied but contentious (Koopman et al. (1997)) (Rapatski, Suppe, and Yorke (2005)) (Rapatski, Suppe, and Yorke (2006)) (Koopman and Simon (2006)). Most of the studies in a review paper modeling sequence evolution in acute HIV-1 infection on the topic did not include mechanisms that could account for heterogeneity at both levels. Lack of converging opinion on this topic could be due to lack of consensus on the heterogeneities that should be modeled.

Also appearing in this issue, Zhang et al. show that individual-level change in the number of contacts over time can greatly increase the population risk of HIV and the acute stage transmission rate. In that model, individuals experience brief episodes of high risk behavior sequentially followed by longer periods of low risk behavior. The movement between high and low contact rate states produces heterogeneity at both the population and individual levels. However, moving back and forth between only two discreet contact rates states is almost certainly a poor model of the data presented here; the fact remains that including heterogeneity at both the population and individual levels increases the rate of acute stage HIV transmission. Although there is no consensus yet on a proper statistical model of both population and individual-level heterogeneity, we have growing evidence that both levels are theoretically relevant and a empirically verifiable.

A small number of studies have examined change in sexual and social behavior over time in the context of HIV. For instance, Colfax et al. (2005) used a proportional odds model to study change in drug use and its association with sexual behavior among participants in San Francisco. They found that drug use was positively associated with unprotected anal sex with a serodiscordant partner and that individual-level patterns of drug used changed over time. Celentano et al. (2001) also reported statistically significant temporal variability in the adjusted odds ratio for both drug use and needle sharing in a six year longitudinal study. Halkitis et al (2009) measured drug use and risky sexual behavior in a cohort of 232 men recruited from bars and dance clubs. Their multivariate analysis found statistically significant random effects at baseline (intercept) and over time (slope) for the relationship between methamphetamine use and unprotected receptive anal intercourse.

A key limitation of the CSS data that we used is that the relationship status of the partner is not specified. Partnership dynamics are known to have strong effects on both the spread of HIV and on the proportion of infections due to acute stage infectors (Kim, Riolo, and Koopman (2010)). The high levels of temporal variance in contact rates in the CSS data could reflect either an increased number of contacts within a partnership, or an increased number of partners. If each contact rates greatly increases the risk of infection beyond the risk implied by their mean contact rate; individuals experience periods of above average sexual activity and, by extension, are potentially exposed to more HIV infected partners. The effects of individual-level variation in contact rates in the context of enduring partnerships is very complex and deserves further study. The epidemiological implications of these two extremes are very different and cannot be distinguished from this data. Future prospective cohort studies of sexual behavior should include information on the partnership status of each sexual contact.

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Figure 1. Temporal trend of sexual contact rates stratified by type

This figure shows the average (black 'x'), median (red bar), and interquartile range (blue box) for each contact type. The y-axis is the number of reported contacts per 6 month period (x-axis). Data above the 75^{th} or below the 25^{th} percentile were omitted for clarity. Only men who remained susceptible and were observed for all four observational periods were included (n=882).

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Figure 2. Poisson and negative binomial count models of the population-level data This figure shows the total number of contacts of any type made by each individual over the course of the study. The data are represented in black, each bin corresponds to a difference of one contact. The expected number of contacts for the *Pois*(37) and *NegBin*(0.49,0.013) [mean=37, standard deviation=54] models are indicated in green and red respectively. The Negative Binomial model corresponds to a *Gamma*(0.49,77)[mean=38, standard deviation=54] distribution of contact rates. The data are stratified into low (< 100, top) and high (> 100, bottom) for clarity.



Figure 3. Over-dispersion of the individual-level data

This figure shows the mean and standard deviation of the total number of contacts for each of the 882 individuals in the study. The square roots of the mean and standard deviation were calculated for contacts of any type over four equally spaced observational periods comprising two years of total observation. The square root transformation was used to reduce the spread of the data and make the figure more readable. The solid red line indicates the expected variance for a Poisson process with a given mean, the solid black line is the maximum variance for a sequence of four observations at a given mean, the dashed black line is a linear model of the transformed data, and the red dashed line is the Negative Binomial model of the data.

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This figure shows the model predicted (lines) and the empirical (marks) frequencies of the insertive/receptive sexual roles. The black line with 'x' marks indicate abstinence in the proceeding six months, the magenta line with '+' marks indicate versatility, the red line with solid circles indicate insertive-only behavior, and the blue line with solid diamonds indicate receptive-only behavior. The x-axis indicates for which six month observational period the frequencies are calculated.

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period

Frequency (of sex	aal roles si	tratified	by obse	ervation	lal
	type	abstinent	only A	only B	A&B	
A=insertive						
B=receptive						
	total	113	110	72	587	
	-	236	176	118	352	
	2	302	168	113	299	
	ю	340	157	114	271	
	4	343	162	96	281	
A=oral						
B=anal						
	total	113	10	475	284	
	-	236	17	476	153	
	2	302	32	436	112	
	з	340	24	420	98	
	4	343	30	419	90	
A=protected						
B=unprotecte	q					
	total	113	234	48	487	
	-	236	297	LL	272	
	2	302	304	81	195	
	ю	340	282	75	185	
	4	343	287	76	176	
A=HIV+						
B=HIV?						
	total	113	20	590	159	
	-	236	42	555	49	

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Table 2

Empirical probability of sexual role given current role

This table gives the proportion of individuals switching sex roles given their current role. The current role is listed in columns while the proportion of individuals switching to other roles are listed in rows.

type	abstinent	only A	only B	A&B
A=insertive				
B=receptive				
abstinent	0.73	0.08	0.07	0.12
Υ	0.22	0.45	0.05	0.28
В	0.28	0.08	0.40	0.24
A&B	0.15	0.17	0.11	0.60
A=oral				
B=anal				
abstinent	0.73	0.02	0.22	0.04
Α	0.26	0.32	0.15	0.27
В	0.21	0.02	0.70	0.08
A&B	0.14	0.08	0.39	0.39
A=protected				
B=unprotected				
abstinent	0.73	0.16	0.05	0.06
Α	0.23	0.55	0.05	0.18
В	0.25	0.13	0.38	0.24
A&B	0.14	0.32	0.10	0.44
A=HIV+				
B=HIV?				
abstinent	0.73	0.17	0.25	0.01
Α	0.07	0.57	0.19	0.17
В	0.22	0.01	0.73	0.04
A&B	0.10	0.13	0.48	0.30