

The Relationship between Condom Use and Herpes Simplex Virus Acquisition

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Background: Few studies have evaluated the relationship between condom use and herpes simplex virus type 2 (HSV-2) and HSV type 1 (HSV-1) acquisition.

Objective: To assess the relationship between condom use and acquisition of HSV-2 and HSV-1 among men and women.

Design: Analysis of data collected as part of a clinical trial of an ineffective candidate vaccine for HSV-2.

Setting: Sexually transmitted disease clinics.

Participants: Men and women at risk for HSV-2 acquisition, defined as having 4 or more sexual partners or having a sexually transmitted disease in the past year.

Measurement: Acquisition of HSV-2 and HSV-1 as measured by viral culture or change to positive HSV serostatus.

Results: Of 1843 participants, 118 (6.4%) became infected with HSV-2. In multivariate analyses, participants reporting more fre-

quent use of condoms were at lower risk for acquiring HSV-2 than participants who used condoms less frequently (hazard ratio, 0.74 [95% CI, 0.59 to 0.95]); categories of increasing condom use were 0% to 25%, 25% to 75%, and greater than 75% of sexual acts. Nineteen (2.9%) of 659 participants at risk for infection with HSV-1 became infected. No statistically significant association between condom use and infection with HSV-1 was found (hazard ratio, 0.79 [CI, 0.48 to 1.31]).

Limitations: Use of condoms was measured by self-report, and persons who used condoms may have differed from those who did not.

Conclusions: Consistent use of condoms is associated with lower rates of infection with HSV-2 and should be routinely recommended.

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Genital herpes is a common sexually transmitted infection that can be transmitted during episodes of recurrent lesions and during subclinical shedding (1). In the absence of an effective vaccine, condoms have been routinely recommended for prevention of transmission, and a recent study showed that daily antiviral therapy also decreases the risk for transmission of herpes simplex virus type 2 (HSV-2) in discordant couples (2, 3). In a previous study of monogamous HSV-2–discordant couples who were enrolled in an ineffective candidate HSV-2 vaccine trial, we showed that condoms protect women from HSV-2 infection (4). However, very few cases of genital HSV-2 occurred among men who were sexual partners of women infected with HSV-2, precluding definitive conclusions about the effectiveness of condoms for prevention of transmission to men. We present data from a concurrent trial of the candidate vaccine among HSV-2–seronegative persons attending sexually transmitted disease clinics (5). A total of 1862 participants were enrolled in this study; 85 cases of genital herpes were documented in men, and 33 cases were documented in women. We analyzed the effect of condom use on HSV acquisition in this prospectively followed cohort of men and women.

METHODS

Study Sample

Participants included in this analysis took part in a randomized, double-blind, placebo-controlled efficacy trial of a candidate subunit HSV-2 vaccine that was subse-

quently shown to be ineffective (5). The trial involved 22 centers located at sexually transmitted disease clinics and enrolled 1862 participants. Initial serologic testing was done at screening; participants who were seronegative for HIV and HSV-2 and reported 4 or more sexual partners in the past year or 1 or more sexually transmitted diseases in the past year were eligible to enroll. The effectiveness of condom use among the 528 discordant couples enrolled in a parallel vaccine study was reported previously (4, 5).

Participants were enrolled and followed for 18 months, during which they were evaluated at 11 study visits. At enrollment, we collected demographic information and information about sexual history. At each study visit, we took blood samples and recorded the following information about sexual history, which described behavior since the last visit: frequency of sexual activities, defined as vaginal or anal intercourse; frequency of condom use; number of partners; number of new partners; and number of partners with a known history of genital herpes. The

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Context

We need other means to reduce the risk for transmitting genital herpes (herpes simplex virus type 2 [HSV-2]). Are condoms effective?

Content

In a trial of an ineffective HSV-2 vaccine, 1843 participants were divided into 3 groups according to the frequency of condom use (for 0% to 25%, 25% to 75%, and >75% to 100% of sexual acts). Frequent condom users had fewer HSV-2 infections. Compared with participants in the next lowest category, participants in a category had a 26% lower risk for HSV-2 infection.

Limitation

In this observational cohort study, many unmeasured factors could also contribute to altered rates of HSV-2 acquisition.

Conclusion

Condom use is associated with a lower rate of acquisition of HSV-2.

—The Editors

information regarding number of partners was gender-specific. In addition, participants were counseled routinely about safer sexual behavior and were offered condoms at each study visit. Genitourinary signs and symptoms were evaluated as needed at additional interim visits.

Laboratory Methods

The Western blot assay done at the University of Washington, Seattle, Washington, established HSV serologic status at study entry and was used to document seroconversion (6). Type-specific cultures using standard techniques were done at local study sites.

Statistical Analysis

Acquisition of HSV-2 was defined by seroconversion on the Western blot assay or by a positive culture for HSV-2. Time to HSV-2 acquisition was defined as the number of days from screening to the first positive culture for HSV-2 or as the midpoint between the last negative result of the HSV-2 antibody test and the first positive result of the HSV-2 antibody test. In this analysis of condom use and HSV acquisition, we included the time from screening to enrollment in the study, whereas in the vaccine trial participants were followed beginning at enrollment. Thus, our report includes 109 participants who were not included in the efficacy analysis of the original vaccine trial. Twenty of these participants seroconverted to HSV-2 during the screening period before enrollment, and 89 were lost to follow-up after enrollment.

Participants who did not acquire HSV-2 were censored at the last blood draw taken during the study or at enrollment if they did not report any sexual activity there-

after. Participants who reported no sexual activity for the entire time from screening to study termination were excluded from the analysis because they were not at risk for HSV-2 infection. Participants with follow-up longer than 65 days beyond the 18 months specified in the protocol (3%) were censored at day 605.

Participants who were seronegative for HSV type 1 (HSV-1) and HSV-2 at screening were included in the analysis of HSV-1. Time to HSV-1 acquisition was defined as the number of days from screening to the first positive culture for HSV-1 or the midpoint between the last negative result of the HSV-1 antibody test and the first positive result of the HSV-1 antibody test. Participants who did not acquire HSV-1 were censored at the last blood draw or at enrollment if they did not report any sexual activity thereafter. Participants who reported no sexual activity for the duration of the study were excluded from the analysis of HSV-1.

Kaplan–Meier curves, log-rank tests, and univariate and multivariate Cox regression models were used to determine baseline risk factors associated with HSV-2 acquisition. To relate sexual behavior to HSV-2 acquisition during the study, we constructed time-dependent covariate Cox regression models. The analysis time was divided into four 150-day intervals, and information about sexual history collected at interim visits was used to calculate covariate summaries for each period. Because continuous variables did not satisfy the assumption of a linear effect in the log hazard, they were categorized. Our choice for the cut-points was motivated by maintaining equal numbers of participants in each category (for example, age was split at the median value, 27 years), by consistency with observed risk patterns, or by interpretation considerations. Frequency of sexual activity was expressed as the average number of sexual acts per week in the time period, calculated by averaging the reported estimates over the visits for each interval. This average was then categorized as greater than 2 versus 2 or fewer to correspond to observed risk patterns. Use of condoms during the study period was described categorically in each interval (used for 0% to 25%, for 25% to 75%, or for >75% of sexual acts). This grouped linear parameterization was chosen to remain consistent with published analyses (4) while allowing a dose–response relationship, assuming constant change in the risk with increasing category of condom use. The use of condoms was not evaluated during intervals for which the participants did not report any sexual activity. The number of partners reported was summarized for each period and was modeled in a binary fashion. Partner cut-points were chosen for interpretation reasons to describe ways in which this patient group may differ from monogamous couples who were studied in a previously published report addressing condom use and infection with HSV (4). Total number of partners was modeled as more than 1 versus 1 or fewer, and both new partners and partners with a history of genital herpes were modeled as any versus none. These

Table 1. Incidence of Herpes Simplex Virus Acquisition in Study Participants by Demographic Subgroups*

Virus and Subgroup	Participants Acquiring HSV, n/n (%)	Acquisition Rate/ 100 Person-Years (95% CI)	HSV Acquisition Rate/ 10 000 Sexual Acts (95% CI)
HSV-2			
Gender			
Women	33/478 (6.9)	5.7 (4.1–8.1)	6.0 (4.3–8.5)
Men	85/1365 (6.2)	5.1 (4.1–6.3)	5.3 (4.2–6.5)
Race			
White	51/1134 (4.5)	3.5 (2.6–4.6)	3.5 (2.6–4.6)
African American	60/585 (10.3)	9.4 (7.3–12.1)	10.7 (8.3–13.8)
Other†	7/124 (5.7)	4.8 (2.3–10.0)	5.3 (2.5–11.2)
Total	118/1843 (6.4)	5.2 (4.4–6.3)	5.5 (4.6–6.5)
HSV-1			
Gender and sexual orientation			
Women	3/190 (1.6)	1.2 (0.4–3.8)	1.4 (0.4–4.3)
Heterosexual men	12/396 (3.0)	2.3 (1.3–4.1)	2.4 (1.3–4.2)
MSM	4/73 (5.5)	4.2 (1.6–11.3)	8.1 (3.0–21.5)
Total	19/659 (2.9)	2.2 (1.4–3.5)	2.5 (1.6–3.9)

* HSV-1 = herpes simplex virus type 1; HSV-2 = herpes simplex virus type 2; MSM = men who have sex with men.
† Includes Asian, Hispanic, and other races.

analyses did not adjust for receipt of placebo versus receipt of vaccine, because this factor was not statistically significant in acquisition of HSV and did not influence the covariates of interest for this study. An interaction term between condom use and gender was used to check the hypothesis of a difference in the effect of condoms by gender and to provide gender-specific estimates of condom use. Two-sided *P* values for model covariates were calculated by using the likelihood ratio test.

The same methods were used to explore baseline risk factors and time-varying risk factors for time to infection with HSV-1. Poisson regression was used to provide *P* values for comparisons involving incidence rates. Tests for changes in sexual behavior with time used generalized estimating equations. Statistical analyses were done by using Stata statistical software (version 8.1, Stata Corp., College Station, Texas).

Role of the Funding Source

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RESULTS

Of the 1862 participants who enrolled for the vaccine trial, 19 did not report any sexual activity during the entire study and thus were excluded from this analysis. The remaining 1843 participants included 1365 men and 478 women. The median age of the participants was 27 years. Sixty-two percent were white, 32% were African American, and 6% were people of other races; 1184 participants

(64%) were seropositive for HSV-1 at study entry. Most men and women qualified for the study by reporting 4 or more partners in the past year (66% of men, 70% of women); some reported 1 or more sexually transmitted diseases in the past year (12% of men, 19% of women); and the remainder met both criteria (22% of men, 11% of women).

Incidence of HSV-2

One hundred eighteen (6.4%) participants acquired HSV-2 during the study period. The rate of acquisition did not differ between men (5.1 per 100 person-years [95% CI, 4.1 to 6.3 per 100 person-years]) and women (5.7 per 100 person-years [CI, 4.1 to 8.1 per 100 person-years]) (*P* = 0.55) but varied significantly by race. White participants acquired HSV-2 at a rate of 3.5 per 100 person-years (CI, 2.6 to 4.6 per 100 person-years), whereas African-American participants acquired HSV-2 at a rate of 9.4 per 100 person-years (CI, 7.3 to 12.1 per 100 person-years) (*P* < 0.001). The incidence rate for HSV-2 acquisition for participants of other races was 4.8 per 100 person-years (CI, 2.3 to 10.0 per 100 person-years). Similar results were produced by calculating these rates by number of sexual acts (Table 1).

Demographic Characteristics Associated with HSV-2 Acquisition

In multivariate analyses, gender, sexual orientation, race, and age were statistically significantly associated with acquisition of HSV-2. Compared with heterosexual men, women (hazard ratio, 1.79 [CI, 1.13 to 2.83]) and men who have sex with men (hazard ratio, 2.65 [CI, 1.34 to 5.25]) had an increased risk for acquisition. African-American participants acquired HSV-2 at more than 3 times the rate of white participants (hazard ratio, 3.77 [CI, 2.45 to 5.80]), and younger participants were at greater risk than older participants (Table 2).

Table 2. Risk Factors for Acquisition of Herpes Simplex Virus 2, Adjusted for Sexual Behavior during the Study*

Covariates	Univariate Hazard Ratio (95% CI)	P Value	Adjusted Hazard Ratio† (95% CI)	P Value
Gender and sexual orientation		0.51		0.007
Women vs. heterosexual men	1.30 (0.83–2.02)		1.79 (1.13–2.83)	
MSM vs. heterosexual men	1.07 (0.56–2.04)		2.65 (1.34–5.25)	
Race		<0.001		<0.001
African American vs. white	2.52 (1.68–3.79)		3.77 (2.45–5.80)	
Other vs. white	1.36 (0.58–3.20)		1.49 (0.64–3.46)	
Age, ≤ 27 years vs. > 27 years	1.54 (1.03–2.31)	0.04	1.62 (1.06–2.47)	0.03
Condom use during study (risk for each increased condom use category)‡	0.78 (0.62–0.98)	0.04	0.74 (0.59–0.95)	0.02
Sexual activities per week, > 2 vs. ≤ 2 sexual activities per week	1.81 (1.22–2.69)	0.003	1.77 (1.18–2.67)	0.007
Total partners, >1 vs. ≤ 1	0.93 (0.63–1.39)	0.73		
New partners, any vs. none	0.87 (0.58–1.30)	0.50		
Partner with genital herpes simplex virus, any vs. none	1.63 (0.95–2.78)	0.08	2.30 (1.32–4.01)	0.007

* MSM = men who have sex with men.

† Adjusted for gender/sexual orientation, race, age, condom use, sexual activity, and herpes simplex virus status of partner.

‡ Condom use categories: 0%–25%, 25%–75%, and > 75% of sexual acts.

Sexual Behavior during the Study

Information about sexual history after study enrollment was available for 1721 participants. Overall, the rate of sexual activity declined during the study period. The average number of sexual acts per week reported in the first 150-day interval was 2.2, whereas the averages for the subsequent 3 periods were 2.0, 1.8, and 1.7, respectively ($P < 0.001$ [test for trend]). Overall, 688 (40%) participants reported using condoms 0% to 25% of the time, including 199 (12%) participants who reported never using condoms, whereas 496 (29%) participants reported using condoms more than 75% of the time, including 222 (13%) participants who reported always using condoms. Sixteen (8%) of the 199 participants who reported never using condoms and 12 (5%) of the 222 participants who reported always using condoms acquired HSV-2 (Table 3). In parallel to sexual activity, mean condom use decreased during the study, starting at 49% and ending at 43% for the last interval ($P < 0.001$ [test for trend]). This decrease was mainly observed in participants reporting no new partners (starting at a mean of 42% and ending at a mean of 34%) and remained fairly constant over time for participants who reported having new partners (starting at 54% and ending at 51%). The number of new partners varied

with gender and sexual orientation but did not vary greatly with time. Heterosexual men reported a median of 3 new partners, men who had sex with men reported a median of 7 new partners, and women reported a median of 2 new partners ($P < 0.001$ [Kruskal–Wallis test]). The percentages of heterosexual men, men who had sex with men, and women who reported at least 1 partner with a history of genital herpes were 17.4%, 17.2%, and 14.9%, respectively. These percentages decreased slightly over time (data not shown).

Reporting a partner with a history of HSV was associated with an increased risk for HSV-2 acquisition (hazard ratio, 2.30 [CI, 1.32 to 4.01]) (Table 2). More frequent sexual intercourse was also associated with greater risk for HSV-2 infection. In a multivariate model, an average of more than 2 sexual acts per week was associated with a 77% increase (hazard ratio, 1.77 [CI, 1.18 to 2.67]) in risk for acquiring HSV-2 when compared with 0 to 2 sexual acts per week.

Influence of Condom Use on Infection with HSV-2 during the Study

Increasing use of condoms was associated with lower rates of HSV-2 acquisition: Participants who used condoms for 0% to 25% of sexual acts had the greatest risk for infection, those who used condoms for 25% to 75% of sexual acts had a relatively lower risk, and participants who used condoms for more than 75% of sexual acts had an even lower risk in analyses adjusted for sexual behavior and important baseline characteristics (hazard ratio, 0.74 [CI, 0.59 to 0.95] for each category of increased condom use) (Figure). In analyses including an interaction term between gender and condom use, the effect of condom use on HSV-2 acquisition among men (hazard ratio, 0.69 [CI, 0.51 to 0.93]) and women (hazard ratio, 0.87 [CI, 0.58 to 1.30]) did not differ significantly ($P = 0.39$ for interaction).

Table 3. Frequency of Condom Use during the Study among Participants with Follow-up*

Frequency of Condom Use	Acquisition of HSV-2		Total
	Yes†	No	
Never	16	183	199
1%–25% of sexual acts	31	458	489
25%–75% of sexual acts	26	509	535
>75%–99% of sexual acts	11	263	274
Always	12	210	222

* HSV-2 = herpes simplex virus type 2.

† Two cases are missing in this table because the participants did not report any sexual acts for visits included in the analysis.

Incidence of and Risk Factors for HSV-1

Six hundred fifty-nine participants (190 women and 469 men) were seronegative for HSV-1 at study entry. Seventy-six percent were white; 19% were African American; and 5% were Asian, Hispanic, or other races. Nineteen (2.9%) participants, 16 men and 3 women, acquired HSV-1 during the study period. The overall rate for infection was 2.2 per 100 person-years (CI, 1.4 to 3.5 per 100 person-years) and 2.5 per 10 000 sexual acts (CI, 1.6 to 3.9 per 10 000 sexual acts) (Table 1). Men had a higher incidence rate of HSV-1 than did women (2.6 per 100 person-years [CI, 1.6 to 4.3 per 100 person-years] vs. 1.2 per 100 person-years [CI, 0.4 to 3.8 per 100 person-years]), but this difference was not statistically significant ($P = 0.22$). Of the 16 men who became infected, 12 were heterosexual and 4 were men who had sex with men, although the observed incidence rate of infection with HSV-1 was higher among the latter group (4.2 per 100 person-years [CI, 1.6 to 11.3 per 100 person-years]) than among heterosexual men (2.3 per 100 person-years [CI, 1.3 to 4.11 per 100 person-years]).

Twenty-six of the 659 participants available for the baseline HSV-1 analysis were censored at enrollment because they were lost to follow-up or did not report sexual activity after enrollment. Thus, 633 participants provided information about sexual behavior during the study period and were included in the time-dependent analysis. To define correlates of HSV-1 acquisition, we examined the same risk factors as were examined for HSV-2. The only statistically significant predictor for acquiring HSV-1 was any new partners versus no new partners (hazard ratio, 3.15 [CI, 1.08 to 9.17]); greater than 1 versus 1 or fewer total partners showed borderline significance (hazard ratio,

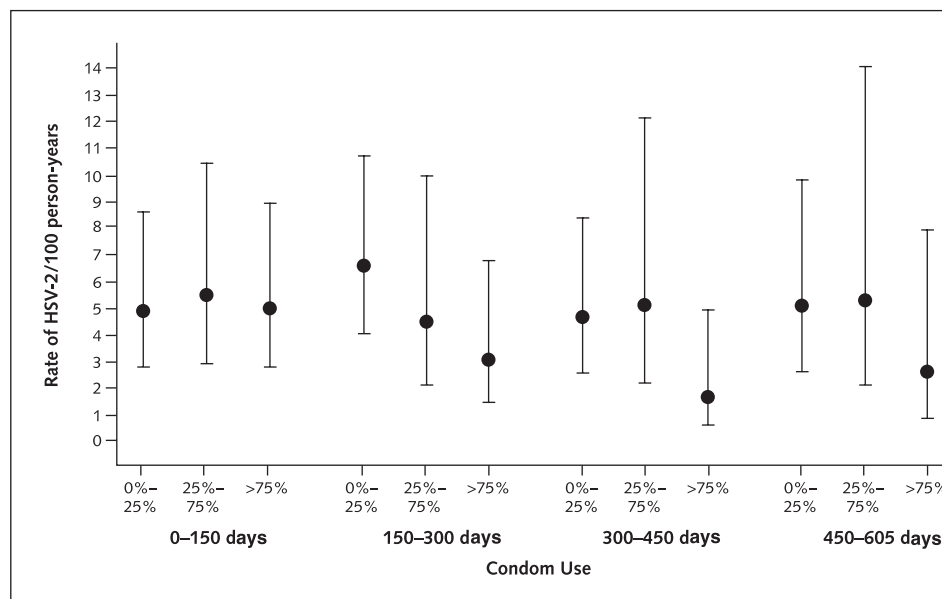
2.65 [CI, 1.00 to 7.05]), and other factors were not statistically significantly associated with increased risk for HSV-1 acquisition (data not shown). Condom use was not significantly associated with HSV-1 acquisition (hazard ratio, 0.79 [CI, 0.48 to 1.31]); however, a relatively smaller number of events precluded firm conclusions.

DISCUSSION

In this study of a relatively large, diverse, sexually active population at risk for HSV-2 acquisition, we showed that condom use was substantially and significantly associated with lower rates of acquisition. Although some participants became infected with HSV-2 despite using condoms, the risk for transmission was substantially reduced with more frequent condom use. The inability of condoms to protect absolutely, even when used for every sexual act, is demonstrated by the occurrence of infection among those participants who reported using condoms 100% of the time. However, we did not have information on whether the condoms were used correctly, as has been recently recommended for assessment of condom use (7). Although evidence for a difference in the effect of condom use between men and women was not significant, gender-specific estimates suggested that condoms might offer protection for men. Their effect among women, however, was inconclusive. Additional risk factors for HSV-2 acquisition included African-American race, younger age, and more frequent sexual activity.

The results of this study contrast with the findings of a previous analysis that examined the effect of condom use among HSV-2-discordant couples who participated in a parallel clinical trial of the same candidate vaccine (4). In

Figure. Frequency of herpes simplex virus (HSV)-2 acquisition in each study interval stratified by condom use.



Solid circles represent the HSV-2 incidence rate per 100 person-years, and bars represent 95% CIs for these rates.

that analysis, we found that condom use was associated with a substantial and statistically significant reduction in HSV-2 acquisition among women with an adjusted hazard ratio of 0.085 (CI, 0.011 to 0.67). Too few events precluded conclusions about men, but the point estimate did not suggest a protective effect. Do the results of the 2 studies tell a different story? Different groups of participants with different risks for HSV-2 exposure and different patterns of sexual behavior and condom use were enrolled in the 2 clinical trials. However, the reduced risk for HSV acquisition among those participants who used condoms was observed in the subgroups that had a higher incidence of HSV-2 acquisition: women in the discordant couples study and men in the sexually transmitted disease clinic study. It is possible that at the lower incidence of HSV-2 acquisition, the effect of misclassification of exposure to HSV-2 and condom use dilutes the association between HSV-2 and condom use. Studies about condoms are difficult to do, because condom use cannot ethically be used as an intervention in a randomized clinical trial. Thus, information can only be derived from observational studies, often originally done for other reasons. As such, the results are subject to confounding by the sexual behavior of the persons studied, by improper use of condoms, and by the infection status of partners. These measurement errors underestimate the effectiveness of condoms (8, 9). Recent analyses of data from Project RESPECT, a study of high-risk men and women, showed that condoms are effective for preventing gonorrhea and chlamydia, if the analyses are limited to people whose partners are known to be infected (10). Thus, similar to our study, the effect of condoms was more pronounced when the analyses focused on high-risk populations, in this case those with known infection. For similar reasons, analysis of data using a case-crossover design found that condoms offered protection against infection with bacterial sexually transmitted diseases, although a cohort analysis of the same data did not find an association between condom use and the incidence of sexually transmitted disease (11). Social desirability bias, defined as over-reporting of condom use because that is what is perceived to be desired by the interviewer, also contributes to reduced estimates of the effectiveness of condoms.

The rate of HSV-2 infection decreased during the study period. Measures of sexual activity also decreased, including the mean number of sexual acts per week, rate of acquisition of new partners, and number of partners with known genital herpes. Despite regular counseling, condom use also decreased somewhat, especially among participants who did not have new partners. These findings suggest that persons who elect to participate in a vaccine study may be at particularly high risk for HSV-2 acquisition, and this risk wanes with time (regression to the mean). The study of discordant couples also noted a decrease in acquisition rates over time, although the partner without HSV-2 infection remained with the same HSV-2-infected partner (4). Some data suggest that persons who are repeatedly exposed

to HSV-2 have evidence of an immune response despite persistent seronegative antibody status and may have diminished susceptibility (12).

Studies of the incidence of HSV-2 infection consistently show that women are at higher risk for HSV-2 acquisition, as also suggested by the higher risk for HSV-2 among women reported in seroprevalence studies (1, 13–15). In contrast to most published studies, the incidence rate of HSV-2 in our study was similar among men and women (3). One potential explanation is that female and male participants had different risk behaviors and partners with different HSV-2 prevalences. For example, women reported fewer new partners during the study period and fewer partners with genital herpes than did men. In fact, in multivariate models adjusted for sexual behavior during the study, we found that women had an increased risk for HSV-2 acquisition compared with heterosexual men. Thus, the increased susceptibility of women to HSV-2 acquisition was balanced by the higher-risk behavior of men.

Because HSV-2 is sexually transmitted, higher levels of sexual exposure, defined as more frequent sexual activity, having a partner with genital herpes, or having other sexually transmitted diseases, are risk factors for HSV-2 acquisition. Two studies have also shown that persons with HIV infection are at higher risk for HSV-2 acquisition than those without (16, 17). It is not clear whether this represents increased susceptibility or an increased risk for exposure to dually infected partners who have higher rates of shedding of HSV-2. Collectively, studies of the incidence of HSV-2 infection indicate what populations can be enrolled in trials of preventive methods, including vaccines, and are likely to yield a substantial number of events. Of note, the rate of HSV-2 acquisition was much higher among men in the study that enrolled sexually active adults recruited at sexually transmitted disease clinics than in the study that enrolled HSV-2-discordant couples (5.1 per 100 person-years versus 1.5 per 100 person-years) (4). In addition, the study that showed the efficacy of valacyclovir in interrupting sexual transmission of HSV-2 also found a low rate of HSV-2 acquisition among men whose sexual partners had genital herpes (1.8% during 8 months of follow-up) (3). In contrast, in the Project RESPECT study of high-risk adults, the rates of acquisition were 9.9 per 100 person-years for men and 14.8 per 100 person-years for women (14). These findings suggest that future studies of preventive measures among men should be conducted among sexually active men recruited from sexually transmitted disease clinics rather than men who are partners of HSV-2-infected women. Rates of HSV-2 acquisition are high among women recruited from sexually transmitted disease clinics and those who have HSV-infected partners.

We also examined risk factors for HSV-1 acquisition. We saw inconclusive evidence of the ability of condoms to protect participants from HSV-1 infection. Clinical studies from several centers have indicated a recent shift to more frequent genital acquisition (18–21). Although almost all

HSV-2 infections are acquired coitally and, hence, can be prevented by condoms reducing exposure to infectious secretions, most HSV-1 acquisition seems to occur from oral-genital contact, where condoms are less likely to be used (22, 23). The higher incidence of HSV-1 infection among men who have sex with men is consistent with these data and probably reflects the use of barrier protection for genital-genital contact but not for oral-genital contact. The difference in the protective effects of condoms for HSV-2 and not HSV-1 supports the causal role of condoms in reducing HSV-2 acquisition.

We found that using condoms protected participants from HSV-2 acquisition. Consistent use of condoms can decrease the risk for HSV-2 acquisition as well as for several other sexually transmitted diseases, including HIV infection. Although antiviral therapy is likely to be important in terms of managing infection and the risk for HSV-2 transmission from persons who know that they have genital herpes, the use of condoms remains an important preventive strategy for sexually active persons who are at risk for HSV-2 infection.

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