

Case-Crossover Analysis of Condom Use and HSV-2 Acquisition

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Previous studies have demonstrated the protective effect of condoms for HIV and other sexually transmitted infections. Surprisingly, however, the effectiveness of condoms in preventing HSV-2 transmission is less well documented. Larger prospective studies have suggested that condom use is moderately efficacious in preventing HSV-2 transmission, but these studies have lacked the ability to control for individual-level characteristics that might be associated with sexual-risk. For these reasons, lead author Jeffrey Stanaway of the University of Washington Epidemiology department, working with Dr. Anna Wald and Dr. Amalia Magaret of the Vaccine and Infectious Disease Division, designed a case-crossover study to deal with these individual-level confounders. Their goal was to produce a more accurate estimate of the effect of condom use on HSV-2 acquisition.

The case-crossover design requires participants to have at least one control visit during which they remain HSV-2 negative, and a case visit during which they were documented to have acquired HSV-2. This design allows for greater control of individual-level confounders, as each case-control set comes from the same person. By having case-control pairs form the same person, factors like sex and age are perfectly matched; other factors that might vary only slightly during the study period, such as education or risk tolerance, can be very closely matched in this study design. For their study, the authors pooled data from 6 earlier prospective studies in which HSV-2 status was measured at enrollment as well as during a follow-up period, and which included self-reports of condom use and sexual activity. After further pooling participants from the original studies that fit the case-control criteria, Stanaway et al. were able to include 191 participants in their analysis.

The researchers found a 3.6% increase in the odds of HSV-2 acquisition with each unprotected act (OR = 1.036; 95% confidence interval [CI]: 1.021-1.052). There was no significant increase in the odds of acquisition for protected acts (OR= 1.008; 95% CI; 0.987-1.030), so the estimated odds of acquiring HSV-2 were significantly lower with a protected act than with an unprotected act. Based on categorical condom use, there was a 3.6% increase in the odds of HSV-2 acquisition when condoms were never used (OR = 1.036, 95% CI: 1.021-1.052), a 2.7% increased in the odds of acquisition with each act when condoms were sometimes used (OR = 1.027; 95% CI: 1.010-1.044), and no significant increase in risk when condoms were always used (OR = 0.989; 95% CI: 0.957-1.023).

This analysis demonstrates a significant protective effect of condoms to prevent HSV-2 transmission, as the odds of HSV-2 acquisition were significantly lower with protected than unprotected acts. Additionally, the categorical descriptions of consistency in condom use demonstrate a dose-response relationship that further supports these findings. Use of the case-crossover design is a major strength of this study. In addition to enhancing statistical power, the outcome of the authors' analysis using this design suggests the likelihood of unmeasured confounding factors in other previous assessments of condom effectiveness against HSV-2. Taken together with these previous findings, the study of Stanaway et al. confirms and strengthens the recommendations for consistent condom use to prevent HSV-2 transmission.

[Stanaway JD, Wald A, Martin ET, Gottlieb SL, Magaret AS](#). 2012. Case-Crossover Analysis of Condom Use and Herpes Simplex Virus Type 2 Acquisition. *Sexually Transmitted Diseases*. May; 39(5):388-93.