Delayed Application of Condoms Is a Risk Factor for Human Immunodeficiency Virus Infection among Homosexual and Bisexual Men

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The objective of this analysis was to identify risk factors for recent human immunodeficiency virus (HIV) infection among homosexual and bisexual men in Ontario, Canada, during 1998–2001. Participants were recruited through the provincial HIV diagnostic laboratory and through physicians and community organizations. HIV test results were used to identify recent seroconverters (cases). A subsample of 183 men (62 cases and 121 controls) enrolled in the Polaris HIV Seroconversion Study as of June 2001 was analyzed. This analysis focused on sexual behaviors with partners who were HIV-positive or whose HIV status was unknown. In multiple logistic regression, independent risk factors were identified. Rates of unprotected receptive oral, insertive anal, and receptive anal sex and delayed application of condoms during receptive anal sex (RAS) were significantly higher among cases (97%, 41%, 53%, and 53%, respectively) than among controls (73%, 19%, 14%, and 2%). Independent risk factors for HIV infection were RAS without condoms (odds ratio = 4.4, \( p = 0.0004 \)) and delayed application of condoms during RAS (odds ratio = 5.8, \( p = 0.01 \)). There was an association with condom failure (breakage or slippage) during RAS that approached significance (odds ratio = 2.9, \( p = 0.09 \)). Delayed application of condoms for RAS may result in contact with preejaculatory fluid. This behavior, which to date has received little attention, may pose as much risk for HIV infection as fully unprotected RAS.

Unprotected receptive anal intercourse is a well-documented risk factor for human immunodeficiency virus (HIV) infection (1–7). The use of condoms during anal sex has been widely promoted for the prevention of HIV infection among homosexual and bisexual men. However, condoms may not be used appropriately. In a qualitative study, Quirk et al. (8) identified forms of condom use that involved at least some unprotected intercourse and named the phenomenon “unsafe protected sex.” In addition to condom failure, in which a condom breaks or splits during intercourse, Quirk et al. reported that some participants would begin intercourse without a condom but apply a condom at some time before ejaculation. The authors cautioned that additional epidemiologic studies would be required to determine whether issues involving correct condom use and condom failure were important in HIV transmission.

Homosexual and bisexual men living in Ontario, Canada, experienced a significant increase in the incidence of HIV infection between 1996 and 1999 (9, 10). We examined risk factors for HIV infection in this population, incorporating detailed measures of condom use.

MATERIALS AND METHODS

This analysis was undertaken as part of the ongoing Polaris HIV Seroconversion Study, which was initiated in 1998. The
Condom Use and Risk Factors for HIV Infection

Independent variables of interest were the number of sexual partners and specific sexual behaviors, namely unprotected receptive oral sex (with ejaculation) and unprotected insertive and receptive anal sex (with or without ejaculation). We also examined imperfect condom use for insertive and receptive anal sex: 1) condom failure (breakage and/or slippage); 2) delayed application of a condom, where anal sex is initially unprotected but a condom is applied at some time after anal sex begins; and 3) premature removal of a condom, where a condom is removed and unprotected sex
follows. See the Appendix for the specific phrasing of the questions on sexual behavior.

Statistical analysis was conducted using SAS, version 8 (SAS Institute, Inc., Cary, North Carolina). The \( p < 0.05 \) level was used to evaluate statistical significance. Preliminary exploratory analysis involved a review of distributions of potential independent variables and their crude associations with HIV status using Pearson chi-squared tests, Wilcoxon rank-sum tests, and logistic regression. Independent variables were combined into one multiple logistic regression model (the full model), and all pairwise interactions were examined for significance. Nonsignificant variables were then eliminated from the model, as long as they were not required for adjustment of the remaining variables. The Hosmer-Lemeshow goodness-of-fit test was used to determine model fit (11). Results are reported as odds ratios.

The population attributable risk (PAR) was calculated for each independent risk factor. We used the equation PAR = \[
\frac{p \times (RR - 1)}{1 + p \times (RR - 1)}
\]
where \( p \) is the proportion with the risk factor in the population and \( RR \) is the estimate of the relative risk of infection for that risk factor (12). The odds ratio was used as an estimate of the relative risk; this assumption is valid for rare diseases (12). The prevalence of the risk factor in the control group was used as an estimate of the population prevalence, under the assumption that behavior among controls was generalizable to the population of homosexual and bisexual men in Ontario.

RESULTS

Data obtained from 183 homosexual and bisexual men (62 cases and 121 controls) enrolled as of June 2001 were analyzed. Characteristics of these men are given in table 1. Cases and controls did not differ significantly in terms of sexual orientation, age, education, race, region in Ontario, or HIV testing history.

We examined sexual behavior with all partners during the time period, including HIV-negative regular partners, Wilcoxon rank-sum tests, and logistic regression. Independent variables were combined into one multiple logistic regression model (the full model), and all pairwise interactions were examined for significance. Nonsignificant variables were then eliminated from the model, as long as they were not required for adjustment of the remaining variables. The Hosmer-Lemeshow goodness-of-fit test was used to determine model fit (11). Results are reported as odds ratios.

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### TABLE 2. Distribution of sexual behaviors* among homosexual and bisexual men in the Polaris HIV† Seroconversion Study, Ontario, Canada, 1998–2001

<table>
<thead>
<tr>
<th>Cases (%) (n = 62)</th>
<th>Controls (%) (n = 121)</th>
<th>p value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unprotected receptive oral sex with HIV+/UK† partner</td>
<td>97</td>
<td>73</td>
</tr>
<tr>
<td>With exposure to ejaculate</td>
<td>55</td>
<td>27</td>
</tr>
<tr>
<td>Any anal sex with HIV+/UK partner</td>
<td>95</td>
<td>61</td>
</tr>
<tr>
<td>Unprotected insertive anal sex with HIV+/UK partner</td>
<td>41</td>
<td>19</td>
</tr>
<tr>
<td>Imperfect condom use for insertive anal sex with HIV+/UK partner</td>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>Condom failure</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>Delayed application of condom</td>
<td>20</td>
<td>7</td>
</tr>
<tr>
<td>Premature removal of condom</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Unprotected receptive anal sex with HIV+/UK partner</td>
<td>53</td>
<td>14</td>
</tr>
<tr>
<td>Imperfect condom use for receptive anal sex with HIV+/UK partner</td>
<td>44</td>
<td>8</td>
</tr>
<tr>
<td>Condom failure</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Delayed application of condom</td>
<td>32</td>
<td>2</td>
</tr>
<tr>
<td>Premature removal of condom</td>
<td>17</td>
<td>3</td>
</tr>
</tbody>
</table>

* Reported behavior during the time period of infection for cases and a comparable time period for controls (mean = 10.2 months; median, 6; range, 3–27).
† HIV, human immunodeficiency virus; HIV+/UK, HIV-positive/serostatus unknown.
‡ The p values were estimated using the Pearson chi-squared test.

Prevalence of all behavior was higher among cases than among controls. Although 5 percent of cases did not report having anal sex with HIV-positive or status-unknown partners, all cases reported engaging in anal sex with any partner, including regular partners thought to be HIV-negative.

We also measured the proportion of men having unprotected anal sex through imperfect condom use that would have been missed had we used only measures of anal sex without condoms. Forty-one percent of cases and 19 percent of controls reported having insertive anal sex without condoms, yet an additional 15 percent of cases and 7 percent of controls reported either condom failure, delayed application, or premature removal of condoms for this activity but not sex without condoms. Similarly, 53 percent and 14 percent of cases and controls, respectively, reported having receptive anal sex without condoms, and a further 12 percent of cases and 4 percent of controls reported some form of imperfect condom use for this activity but not sex without condoms.

Rates of condom failure, delayed application of condoms, and premature removal of condoms were compared for the 45 cases and 44 controls who used condoms during receptive anal sex with HIV-positive or status-unknown partners. There were 1,745 and 782 episodes of receptive anal sex with condoms among these cases and controls, respectively. Rates of condom failure were significantly higher among cases than among controls (8.0 percent vs. 2.6 percent; p < 0.0001), as were rates of delayed application of condoms (9.8 percent vs. 1.8 percent; p < 0.0001). However, rates of premature removal of condoms did not differ significantly between cases and controls (2.6 percent vs. 3.1 percent; p = 0.54).

Behavior with regular partners thought to be HIV-negative was also examined. Among cases and controls who had an HIV-negative regular partner, there were no statistically significant differences in rates of specific sexual behaviors (data not shown), with the exception of premature removal of condoms. More cases than controls prematurely removed condoms for insertive anal sex (11 percent vs. 1 percent; p = 0.02 in Fisher’s exact test) and receptive anal sex (8 percent vs. 0 percent; p = 0.02 in Fisher’s exact test). Because of the small number of controls who prematurely removed condoms, such behavior with regular HIV-negative partners was not analyzed further.

Multiple logistic regression modeling was used to examine the effects of behavior with HIV-positive/status-unknown partners on risks of HIV infection. Results are shown in table 3. No significant two-way interactions were detected in either the full model or the final model. Results of Hosmer-Lemeshow goodness-of-fit tests were nonsignificant for both the full model and the final model, indicating that the models fitted the data well. We increased statistical power by removing nonsignificant variables from the full model, since none were needed for adjustment. Independent risk factors for HIV infection were unprotected receptive anal sex (odds ratio = 4.4, p = 0.0004) and delayed application of condoms for receptive anal sex (odds ratio = 5.8, p = 0.01). Condom failure during receptive anal sex was marginally associated with HIV infection (odds ratio = 2.9, p = 0.09).

No behaviors with regular partners thought to be HIV-negative were statistically significant when added to the models containing behavior with HIV-positive/status-unknown partners (data not shown).

We carried out further analysis to investigate receptive oral sex as a risk factor. When the analysis was restricted to
the 16 cases and 70 controls who had not engaged in unprotected anal sex with HIV-positive/status-unknown partners (through either sex without condoms or imperfect condom use), we found that cases were 2.2 times more likely to have reported receptive oral sex with ejaculation, but this was not statistically significant ($p = 0.25$ in Fisher’s exact test).

The PAR is the estimated proportion of infections that result from a given risk factor. The PAR was calculated for behaviors that were independent risk factors for HIV infection. For estimates of population prevalence, we used the prevalence of behaviors with any partner (regardless of HIV status) among controls. These rates were $44\%$ for unprotected anal sex, $10\%$ for condom failure during receptive anal sex, and $9\%$ for delayed application of condoms during receptive anal sex. The PAR was highest for unprotected receptive anal sex (PAR = 60 percent), followed by delayed application of condoms for receptive anal sex (PAR = 30 percent) and condom failure during receptive anal sex (PAR = 16 percent).

**DISCUSSION**

We compared the sexual risk behaviors of homosexual and bisexual men who became infected with HIV to that of HIV-negative controls. Independent risk factors for HIV infection were unprotected receptive anal sex and delayed application of condoms for receptive anal sex with HIV-positive or status-unknown partners. We also observed a marginally significant association between condom failure during receptive anal sex and HIV infection.

The finding that unprotected receptive anal sex was a risk factor was expected and is consistent with the findings of other studies (1–7). However, we are not aware of any previous studies that examined delayed condom use in the risk of HIV infection. Our analysis found a strong association. The delayed application of condoms may result in exposure to urethral secretions or preejaculatory fluid, both of which have been shown to harbor HIV (13–15). We could find no research that measured HIV transmission through exposure to these fluids in the absence of contact with ejaculated semen, yet there is indirect evidence that such transmission is biologically plausible. In one epidemiologic study (14), urethritis and gonococcal infection were risk factors for the detection of HIV in urethral secretions, and Cohen (16), in a review of laboratory and clinical studies, concluded that there is considerable evidence that concurrent sexually transmitted infections result in higher HIV transmission. Preejaculatory fluid is a product of the bulbourethral (Cowper) glands and the glands of Littré, which secrete into the male urethra (17). Little is known about the role and function of these glands. Preejaculatory fluid is thought to act as a lubricant to facilitate intercourse (18), and it may also be involved in the prevention of urogenital infection (19, 20). In contrast to preejaculatory fluid, ejaculated semen consists of spermatozoa suspended in seminal plasma from the seminal vesicles and prostate, as well as smaller contributions from the
bulbourethral glands and glands of Littré (18). If a significant proportion of HIV is transmitted through secretions of these urethral glands, this could explain why exposure to preejaculatory fluid in the absence of exposure to ejaculated semen results in a transmission risk similar to that of exposure to ejaculated semen. More basic science and epidemiologic research is needed to improve our knowledge of the mechanisms of possible HIV transmission through urethral secretions and preejaculatory fluid.

The delayed application of condoms may also result in heightened risk if men selectively make decisions about condom use on the basis of perceptions of their partner’s risk. If a partner is perceived to be at high risk, a man may decide to use condoms, although a limited amount of unprotected penetrative sex may occur before condoms are actually applied. An Australian study found that “believing withdrawal to be safe” was a significant independent predictor of seroconversion (3). Withdrawal, the practice of engaging in unprotected intercourse without ejaculation, is similar to the delayed application of condoms, as both activities could involve contact with preejaculatory fluid but not ejaculate.

The delayed application of condoms has been documented among heterosexual couples (8, 21, 22). Quirk et al. (8) concluded that this behavior occurred either because condoms were perceived more to prevent pregnancy than to prevent sexually transmitted infections or because it was a coerced or collaborative transgression from usual safer sexual practices. To our knowledge, this is the first time the extent of delayed condom application has been systematically examined in homosexual and bisexual men. Qualitative interviews with 17 men in our study revealed that this behavior was related to several factors: having sex in the “heat of the moment,” particularly while under the influence of alcohol or drugs; the perception that preejaculatory fluid poses no risk or minimal risk; and the perception that early penetration poses no risk since rectal trauma or rough sex is necessary for HIV transmission (23).

Although it did not reach statistical significance, the magnitude of the association between condom failure during receptive anal sex and HIV infection was large (odds ratio = 2.9, p = 0.09). Previous reports have identified condom failure as a risk factor (1, 7). Predictors of condom failure include infrequent condom use, infrequent lubricant use, lower socioeconomic status, amphetamine and heavy alcohol use, and greater penile circumference (24–26).

The premature removal of condoms was not found to be an independent risk factor for HIV infection. This was somewhat surprising, since we defined the behavior as the removal of a condom followed by unprotected sex, which presumably would end in ejaculation. It is possible that men who engaged in such behavior tended not to ejaculate but rather practiced withdrawal (3, 27). Alternatively, men may prematurely remove condoms because of difficulties maintaining an erection (28); these men may have resumed intercourse briefly but were unable to complete the act.

A significant degree of unprotected anal sex would have been missed had we not used measures of imperfect condom use. Between 4 percent and 15 percent of men reported some imperfect condom use but not anal sex without condoms. Therefore, studies that do not incorporate these measures may underestimate the prevalence of unprotected anal sex by up to one third. Future studies of condom use should incorporate measures of condom failure, delayed application of condoms, and premature removal of condoms. Physicians and counselors should ask more detailed questions about patterns of condom use when assessing a patient’s risk of HIV and sexually transmitted infections.

Some studies have found that receptive oral sex poses a risk for HIV infection, although much less so than receptive anal sex (5–7, 29; also see reviews by Hawkins et al. (30), Scully and Porter (31), and Rothenberg et al. (32)). Our data did not support this; rather, they suggested that the vast majority of infections among seroconverters in our study occurred through some form of unprotected receptive anal sex. Since all HIV-infected men in our sample practiced anal sex, it is possible that we had insufficient statistical power to detect an association with oral sex.

Similarly, we found no independent association between the number of sexual partners or insertion anal sex and HIV infection. Other investigations have found that the number of partners does not independently predict infection after adjustment for specific sexual practices (1–3). The per-contact risk of unprotected insertive anal sex with an HIV-positive or status-unknown partner has been modeled to be 0.06 percent, substantially lower than the per-contact risk of 0.82 percent for unprotected receptive anal sex (7).

Our investigation had some limitations. Enrollment rates for participants recruited through the Central Public Health Laboratory were 24 percent for cases and 15 percent for controls. Although participants were not significantly different from all of those eligible in terms of geographic region, there may have been other differences that could have introduced bias into our results. The low enrollment rate may have been partially due to seroconverters’ not being psychologically ready to participate in a research study at the time of diagnosis. Seroconverters who choose to enroll in a study at such a time may have expected their positive diagnosis; if this were true, because of ongoing high-risk behavior, it could lead to overestimation of the odds ratios for behavioral risk factors. This potential bias is reduced in our study, since more than one third of seroconverters were recruited through other sources. This alternate recruitment strategy provides a second opportunity for those who require more time to adjust to their diagnosis to enroll. In addition, it serves to reach seroconverters who might have been undetected by the Central Public Health Laboratory.

This analysis was conducted under the assumption that controls were representative of the general population of self-identified homosexual and bisexual men in Ontario. Only controls who sought testing for HIV were eligible, though available information suggests that the majority of homosexual and bisexual men have been tested for HIV at least once (33–35). People who seek HIV testing tend to have greater risk for HIV (33, 34, 36). The impact of this bias would be to underestimate the odds ratios, reduce statistical power to detect significant differences between seroconverters and controls, and overestimate PARs.

The use of a retrospective case-control study design may have led to recall bias. Newly infected HIV-positive cases may have recalled their sexual behavior differently from
HIV-negative controls. For example, cases may have been more likely to report that their regular partner was HIV-positive or that his HIV status was unknown, given information gained upon diagnosis. Another possible limitation is the self-reported nature of the information on sexual behavior, which was not corroborated with reports from sexual partners (37). In particular, men who had receptive anal sex may have been unaware of imperfect condom use by the insertive partner, and these behaviors may have been underreported.

Despite these possible limitations, we are confident of the validity of our findings and their importance in guiding future prevention and research. These results come at a time when we are being challenged by increases in HIV incidence among homosexual men in many countries (9, 10, 38–41). Now more than ever, there is a need to understand why the message of using condoms for anal sex, which had been relatively successful, seems to be becoming less effective. Although the quantification of attributable risk confirmed that the majority of HIV infections among homosexual men are still due to receptive anal sex without the use of a condom, delayed application of condoms and condom failure during receptive anal sex also appear to play important roles. In particular, our study demonstrated that a considerable proportion of homosexual men do not apply the condom prior to penetration and that this practice results in HIV transmission. Further studies are necessary to better understand why condoms are not always being used properly and how to effectively ensure correct usage. Preventive counseling must continue to focus on ensuring that condoms are always used during anal sex, but it must also emphasize the potential risks of exposure to pre-ejaculatory fluid and reinforce the importance of applying the condom before any penetration.

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REFERENCES


Questions asked for measures of engaging in receptive anal sex are shown below, using casual partners as an example. A similar format was used for other types of partners and for insertive anal sex. Sexual activity was defined as deep kissing, mutual masturbation, and oral, vaginal, and/or anal sex. Questions 3–5 used a prompt card with the following categories: never (0 percent), rarely (1–25 percent), some of the time (26–75 percent), most of the time (76–99 percent), or always (100 percent).

1. During the time period, with how many casual partners did you engage in sexual activity? By casual partner, I mean a one-night stand, someone you just met, or someone else with whom you did not have an ongoing relationship (does not include paid sex).

2. Thinking about these (insert number) partners, how many different times did you engage in sexual activities with them during the time period?

3. Of all your sexual encounters in that period, how often did they put their penis in your rectum?

4. How often did they put the condom on before they engaged in sexual activity?

5. How often did they put the condom on after they engaged in sexual activity?

6. How often did the condom slip off?

7. How often did they put the condom on after the first time they engaged in sexual activity?

8. How often did they put the condom on after the second time they engaged in sexual activity?

9. How often did they put the condom on after the third time they engaged in sexual activity?

10. How often did they put the condom on after the fourth time they engaged in sexual activity?

11. How often did they put the condom on after the fifth time they engaged in sexual activity?

12. How often did they put the condom on after the sixth time they engaged in sexual activity?

13. How often did they put the condom on after the seventh time they engaged in sexual activity?

14. How often did they put the condom on after the eighth time they engaged in sexual activity?

15. How often did they put the condom on after the ninth time they engaged in sexual activity?

16. How often did they put the condom on after the tenth time they engaged in sexual activity?

17. How often did they put the condom on after the eleventh time they engaged in sexual activity?

18. How often did they put the condom on after the twelfth time they engaged in sexual activity?

19. How often did they put the condom on after the thirteenth time they engaged in sexual activity?

20. How often did they put the condom on after the fourteenth time they engaged in sexual activity?

21. How often did they put the condom on after the fifteenth time they engaged in sexual activity?

22. How often did they put the condom on after the sixteenth time they engaged in sexual activity?

23. How often did they put the condom on after the seventeenth time they engaged in sexual activity?

24. How often did they put the condom on after the eighteenth time they engaged in sexual activity?

25. How often did they put the condom on after the nineteenth time they engaged in sexual activity?

26. How often did they put the condom on after the twentieth time they engaged in sexual activity?

27. How often did they put the condom on after the twenty-first time they engaged in sexual activity?

28. How often did they put the condom on after the twenty-second time they engaged in sexual activity?

29. How often did they put the condom on after the twenty-third time they engaged in sexual activity?

30. How often did they put the condom on after the twenty-fourth time they engaged in sexual activity?

31. How often did they put the condom on after the twenty-fifth time they engaged in sexual activity?

32. How often did they put the condom on after the twenty-sixth time they engaged in sexual activity?

33. How often did they put the condom on after the twenty-seventh time they engaged in sexual activity?

34. How often did they put the condom on after the twenty-eighth time they engaged in sexual activity?

35. How often did they put the condom on after the twenty-ninth time they engaged in sexual activity?

36. How often did they put the condom on after the thirtieth time they engaged in sexual activity?

37. How often did they put the condom on after the thirty-first time they engaged in sexual activity?

38. How often did they put the condom on after the thirty-second time they engaged in sexual activity?

39. How often did they put the condom on after the thirty-third time they engaged in sexual activity?

40. How often did they put the condom on after the thirty-fourth time they engaged in sexual activity?

41. How often did they put the condom on after the thirty-fifth time they engaged in sexual activity?