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## Assessing HIV acquisition risks among men who have sex with men in the United States of America

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### Abstract

Men who have sex with men (MSM) can reduce their risk of acquiring human immunodeficiency virus (HIV) by using various prevention strategies and by understanding the effectiveness of each option over the short- and long-term. Strategies examined were: circumcision; insertive anal sex only; consistent, 100% self-reported condom use; and pre-exposure prophylaxis (PrEP). PrEP efficacy was based on three levels of adherence. The cumulative HIV acquisition risk among MSM over periods of 1 year and 10 years were estimated with and without single and combinations of prevention strategies. A Bernoulli process model was used to estimate risk.

In the base case with no prevention strategies, the 1-year risk of HIV acquisition among MSM was 8.8%. In contrast, the 1-year risk associated with circumcision alone was 6.9%; with insertive sex only, 5.5%; with 100% self-reported condom use, 2.7%; and with average, high, and very high PrEP adherence, 5.1%, 2.5%, and 0.7%, respectively. The 10-year risk of HIV acquisition among MSM with no prevention strategy was 60.3%. In contrast, that associated with circumcision alone was 51.1%; with insertive sex only, 43.1%; with 100% self-reported condom use, 24.0%; and with average, high, and very high PrEP adherence, 40.5%, 22.2%, and 7.2%, respectively. While MSM face substantial risk of HIV, there are now a number of prevention strategies that reduce risk. Very high adherence to PrEP alone or with other strategies appears to be the most powerful tool for HIV prevention.

### Keywords

HIV; HIV infections; prevention & control; pre-exposure prophylaxis; condoms; unsafe sex; risk reduction behavior; United States

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An estimated 1.2 million people in the United States were living with human immunodeficiency virus (HIV) at the end of 2013; of these, 55% were men who have sex with men (MSM) (1). Of the new HIV diagnoses among adults in 2013, about 68% were in MSM, some of whom were also injection drug users (2). Furthermore, while the annual

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number of HIV diagnoses for all other groups decreased in 2009 – 2013, it increased among MSM, from 27 394 to 30 689 (2).

The majority of HIV infections among MSM occur through sexual transmission. Among males living with HIV, more than 70% of infections were attributable to male-to-male sexual contact (1). A previous analysis (3) reported on the effectiveness of single and combination prevention strategies over time on reducing the risk of HIV transmission among serodiscordant MSM and heterosexual couples. It found relatively high levels of HIV acquisition risk over time, unless prevention strategies were combined.

This analysis evaluated how MSM who are at risk for acquiring HIV and are unaware of their partner's serostatus can reduce their risk by using single and combination prevention strategies. Four strategies were assessed, both singly and combined with the others: circumcision; insertive anal sex only, i.e., no receptive anal sex; consistent (100% adherence) condom use; and pre-exposure prophylaxis (PrEP). For PrEP efficacy, three levels were evaluated—average, high, and very high—based on observed adherence in clinical trials (4). Because HIV prevalence may vary widely in the communities from which MSM choose their partners, the analysis also examined the effectiveness of prevention strategies among varying prevalence rates.

## MATERIALS AND METHODS

The cumulative risk of HIV acquisition among MSM over 1 year and 10 years was estimated. A Bernoulli process model was used to estimate HIV risk without a prevention strategy in the base case (see Supplementary Materials; 3, 5); then the base case estimate was adjusted with each risk-reduction strategy separately and in combination. Risk ratios were assumed to be independent and multiplicative in assessing risk reduction with combination strategies (3, 6). The key input parameters used in the model included per-act HIV transmission probabilities with insertive and receptive anal sex, HIV risk-reduction strategies or risk modifiers, number of sex acts, and HIV prevalence among MSM partners (see Supplementary Materials). The analyses were conducted with Microsoft Excel™ (Microsoft Corp., Redmond, Washington, United States).

The input values used in the analysis for the per-act HIV transmission probability associated with unprotected (no condom use) insertive and receptive anal sex, the average number of sex acts per month (three insertive and three receptive anal sex acts per month), and the efficacy of male circumcision applied to only insertive anal acts have been described by Lasry and colleagues (3). An 18% (3% – 43%) HIV prevalence among sex partners was used—based on anonymous HIV testing of MSM in the 2011 National HIV Behavioral Surveillance System, a survey of MSM recruited through venue-based sampling in metropolitan statistical areas of the United States (7). The analysis assumed that 30% of MSM living with HIV would adhere to antiretroviral therapy (ART) and have a suppressed HIV ribonucleic acid (RNA) viral load, conferring on this model a 96% reduction in HIV transmission (8, 9).

An efficacy of 70% (95% Confidence Interval [95% CI]: 58% – 79%) was applied to 100% condom use, based on analyses of data from two HIV prevention trials in the United States that enrolled HIV- uninfected MSM (10). No efficacy was assumed if condoms were used less than 100% of the time, based on results from the same study. Three levels of adherence to PrEP were used based on the iPrEX trial results (4): average, as reported in an intention-to-treat analysis; high, based on pill count; and very high, based on study drug (emtricitabine and tenofovir disoproxil fumarate [FTC/TDF]) detection in blood samples. The corresponding efficacies were 44% (95% CI: 15% – 63%), 73% (95% CI: 41% – 88%), and 92% (95% CI: 40% – 99%), respectively (4).

Univariate sensitivity analysis on two parameters were conducted to explore potential variation in the risk estimates (see Supplementary Materials). The possibly wide variation in prevalence among the communities from which MSM may select their partners was explored. In addition, previous analyses have demonstrated that the number of HIV exposures—sex acts in this analysis—has a large effect on the risk of acquiring HIV. Therefore, similar to Lasry and colleagues (3), in this study the number of sex acts was assumed to vary from 2 – 20 per month, compared to the base case value of 6.

## RESULTS

In the base case with no prevention strategies, the 1-year risk of HIV acquisition among MSM was 8.8% (Figure 1). In contrast, the 1-year risk associated with circumcision alone was 6.9%; with insertive sex only, 5.5%; with 100% self-reported condom use, 2.7%; and with average, high, and very high PrEP adherence, 5.1%, 2.5%, and 0.7%, respectively.

In the base case with no prevention strategies, the 10-year risk of HIV acquisition among MSM was 60.3% (Figure 2). In contrast, the 10-year risk associated with circumcision alone was 51.1%; with insertive sex only, 43.1%; with 100% self-reported condom use, 24.0%; and with average, high, and very high PrEP adherence, 40.5%, 22.2%, and 7.2%, respectively.

The most effective prevention combination—very high PrEP adherence, 100% condom use, circumcision, and insertive sex only—reduced 1-year acquisition risk to 0.04% and 10-year risk to 0.4%. The efficacy of other combinations of prevention strategies are presented in Figures 1 and 2.

When the adjusted HIV prevalence varied from 3% – 43% (base case: 18%), the 1-year HIV acquisition risk without prevention strategies ranged from 1.5% – 19.9% (base case risk: 8.8%; data not shown). With high adherence to PrEP, the 1-year acquisition risk ranged from 0.4% – 5.8% (base case risk: 2.5%).

When the number of sex acts per month varied from 2 – 20 (base case: 6), the 1-year HIV acquisition risk without prevention strategies ranged from 3.1% – 25.7% (base case risk: 8.8%). With high adherence to PrEP, the 1-year acquisition risk ranged from 0.8% – 8.0% (base case risk: 2.5%).

## DISCUSSION

The risk of HIV acquisition was high among MSM in this analysis when no prevention strategies were employed, reaching 60% after 10 years of continuous exposure. At the highest level of adherence, PrEP was the single most protective strategy. However, at the average level of adherence—the level of adherence associated with the modified intention-to-treat analysis in the iPrEX trial (4)—PrEP was less protective than condoms alone when condoms were used to cover all sex acts. Combinations of strategies also were usually very protective, even among those not based on PrEP; for instance, circumcision among men who also practiced only insertive sex, decreased risk substantially.

High levels of adherence can be difficult to achieve. In the iPrEX trial on pre-exposure prophylaxis among MSM in several countries, only 51% of participants had a detectable level of the study drug in their blood sample, and for that group, PrEP was 92% efficacious (4). The overall efficacy of PrEP in iPrEX was 44% among participants with and without detectable drug in their blood sample. An iPrEX subgroup analysis evaluated adherence to the study drug among 510 participants. Of the 56 participants from the United States, 95% had any detectable levels of the study drug, and 57% had drug levels associated with consistent dosing (11). A multi-site demonstration project implemented in sexually-transmitted disease and community health clinics in the United States found 65% of the study participants had drug levels consistent with taking four or more doses per week, at all visits (12).

Furthermore, MSM frequently report less than 100% condom use. In the 2011 National HIV Behavioral Surveillance System (13), 57% of MSM who reported being HIV-negative or of unknown status, also reported having had anal sex in the prior 12 months without a condom and with a partner of any HIV status, i.e., positive, negative, or unknown (13). Among MSM who considered themselves HIV-negative, but tested positive, 33% reported that their most recent sex act was anal sex, unprotected by a condom and with a male partner of HIV-negative or unknown status. Among MSM who tested HIV-negative, 12% reported that their most recent sex act was anal sex unprotected by a condom with a male partner of HIV-positive or unknown status. Smith and colleagues found in their analyses of condom use and efficacy in 3 490 HIV-negative MSM, 35% of those having anal sex with a male partner of any HIV status reported sex without a condom at least once during any 6-month interval, as did 84% over all 6-month intervals assessed (10). In theory, use of condoms for some, even if not all sex acts should provide some protection from HIV. However, trials of condom effectiveness, where adherence can only be measured through self-report, have not demonstrated partial effectiveness.

Sensitivity analyses showed that the study results would be affected by the prevalence of HIV in the communities from which men choose partners, and the average number of sex acts. Higher prevalence and more sex acts both resulted in greater risk.

### Limitations

This analysis has several limitations. Although the relative magnitude of effect would remain unchanged for the single and combination strategies assessed, a number of factors could

alter absolute risk levels, including a change in the proportion of MSM in a community who have achieved viral load suppression and the increase or decrease in number and type of sex acts over time. In assessing combination strategies, we assumed that risk ratios were independent and multiplicative (3, 6). While it is possible that the efficacy of combined interventions would not be multiplicative, insufficient data were available to assess other possibilities. Furthermore, we assumed no change in risk behavior for the individual base case when estimating 10-year HIV acquisition risks under single or combinations of prevention strategies.

We attributed the protective effect of male circumcision to insertive sex acts, assuming a biological equivalence with insertive vaginal sex. However, because none of the randomized controlled trials of male circumcision included many MSM, definitive statements regarding the effect of male circumcision on the risk of acquiring HIV or other sexually transmitted infections cannot be made. In this analysis, where 50% of anal sex acts were assumed to be insertive and 50% receptive, the greater per-act transmission risk associated with receptive anal sex dwarfed the effect of circumcision, and circumcision alone reduced the 10-year risk of HIV acquisition from 60.3% to only 51.1%.

Lastly, this analysis does not factor in access, affordability, or cost differences between the different strategies, which could affect uptake among MSM. This analysis was designed to provide MSM with a measure of the potential benefits of HIV prevention strategies. However, individual decisions regarding these strategies could also be shaped by perceptions and understandings of HIV risk, potential stigma associated with engaging in HIV prevention efforts, perceived side effects, and adherence challenges.

## Conclusions

In conclusion, while MSM face a substantial risk of acquiring HIV, they also may be able to access a number of prevention strategies to reduce that risk. Combinations of strategies generally work better than single strategies. Very high adherence to PrEP, either alone or combined with other strategies, may be the most powerful tool for HIV prevention. Analyses such as this one improve our understanding of HIV acquisition risk over the short- and long-term, and assist MSM in choosing prevention strategies best suited to personal preferences and circumstances.

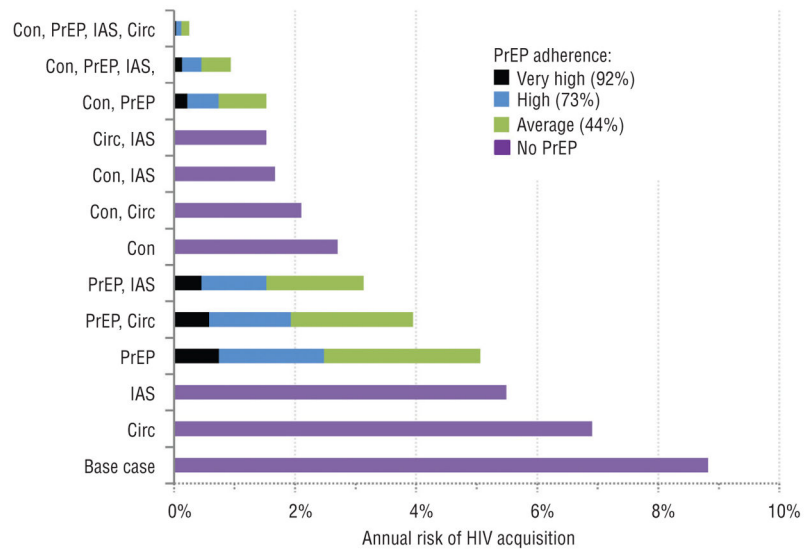
## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

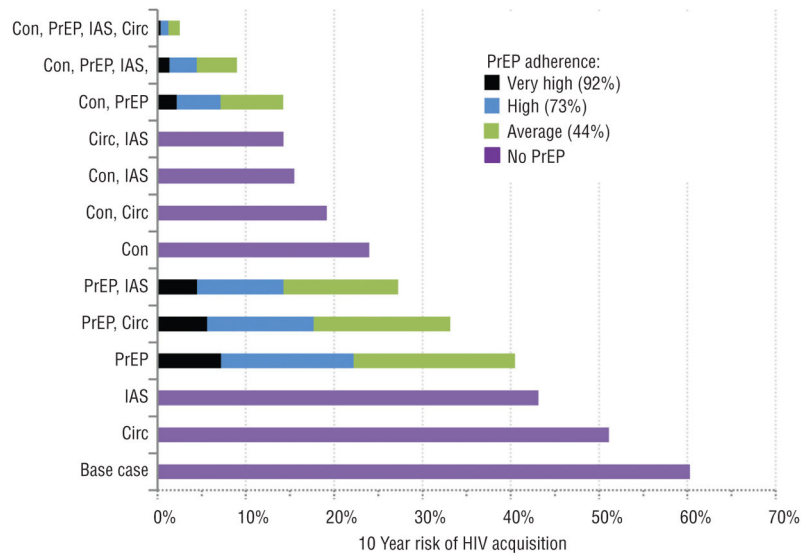
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**FIGURE 1.** Annual risk of Human Immunodeficiency Virus (HIV) acquisition among HIV-uninfected males who have sex with males, using combinations of prevention strategies—condom (CON), pre-exposure prophylaxis (PrEP), circumcision (Circ), insertive anal sex only (IAS)—or no strategy (base case), United States of America, 2015  
**Source:** Prepared by the authors from the study data.



**FIGURE 2.** The 10-year risk of Human Immunodeficiency Virus (HIV) acquisition among HIV-uninfected males who have sex with males, using combinations of prevention strategies—condom (CON), pre-exposure prophylaxis (PrEP), circumcision (Circ), insertive anal sex only (IAS)—or no strategy (base case), United States of America, 2015  
**Source:** Prepared by the authors from the study data.