

# Evaluating the potential impact of vaginal microbicides to reduce the risk of acquiring HIV in female sex workers



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## BACKGROUND

Vaginal microbicides are chemical compounds, currently under development and clinical testing, which can be applied topically to prevent or reduce the transmission of HIV, including neonatal transmission, and other sexually transmitted diseases.

Currently, condoms are the only method of protection available for individuals who have vaginal sex, but studies suggest that condom use is often low. Current efforts are aimed at developing intravaginal topical formulations to curb mucosal and perinatal HIV transmission by directly inactivating HIV or preventing HIV from attaching, entering or replicating in susceptible target cells as well as dissemination from target cells present in semen or the host cells that line the vaginal wall. Vaginal microbicides may provide an alternative mechanism of protection for women whose partners are unwilling to use condoms, and could also be applied in addition to condoms. The hope is that microbicides can be added to lubricants for convenient use or combined with a contraceptive.

Female sex workers (FSWs) are an obvious behavioral core group with high risk of acquiring HIV infection. This study predicts the potential impact of vaginal microbicides in reducing the risk of acquiring HIV in FSWs.

Here, three questions are addressed: 1) Would the introduction of vaginal microbicides substantially reduce the daily risk of FSWs acquiring HIV infection? 2) Which factor would it be most important to maximize, microbicide efficacy or microbicide use? 3) What level of microbicide efficacy and use would be necessary to counterbalance a possible reduction in condom use? We examine the potential impact of microbicide efficacy by considering both low-to-moderate (30-50%) and moderate-to-high (50-80%) efficacy microbicides. We also evaluate heterogeneity in FSWs by considering FSWs who sometimes use condoms (FSW-Cs) and FSWs who never use condoms (FSW-NCs) with their clients.

## METHODS

We define an FSW's risk as the chance, per day, of becoming infected with HIV. We formulate risk equations for the probability of acquiring HIV, both currently and post-vaginal-microbicide introduction (post-VMI). These risk equations take into account the prevalence of HIV among FSWs' clients ( $P_c$ ), the average number of vaginal sex partners per day ( $\rho$ ), the transmission probability of HIV per vaginal sex act ( $\beta$ ), the number of vaginal sex acts per partner per day ( $n$ ), condom efficacy ( $e_c$ ), and expected microbicide efficacy ( $e_m$ ). Our risk equations also include the proportion of sex acts where: (i) only condoms are used ( $p_c$  currently,  $p_c$  post-VMI), (ii) only microbicides are used ( $p_m$ ), or (iii) both condoms and microbicides are used ( $p_c$ ). See Figure 1 for a schematic on the protection options. The proportion of sex acts where no protection is used currently is  $(1-p_c)$  and will be  $(1-p_c-p_m)$  post-VMI.

According to our model, the probability of HIV acquisition for an FSW currently (when the only protection options are condoms or no protection) is:

$$r_1 = 1 - \left\{ [1 - (1 - e_c)\beta]^{p_c} [1 - \beta]^{(1-p_c)} \right\}^{ncP}$$

and post-VMI (when the available protection options are condoms, microbicides, both condoms and microbicides, or no protection), an FSW's risk per day is

$$r_2 = 1 - \left\{ [1 - (1 - e_c)\beta]^{p_c} [1 - (1 - e_m)\beta]^{p_m} [1 - (1 - e_c)(1 - e_m)\beta]^{p_c} [1 - \beta]^{(1-p_c-p_m)} \right\}^{ncP}$$

To evaluate the potential impact of vaginal microbicides in reducing the risk of HIV acquisition in both groups of FSWs, we analyze our risk equations with uncertainty analysis using Monte Carlo simulations and multivariate sensitivity analysis.

Figure 1: Conceptual Diagram of Protection Options where no condom replacement occurs

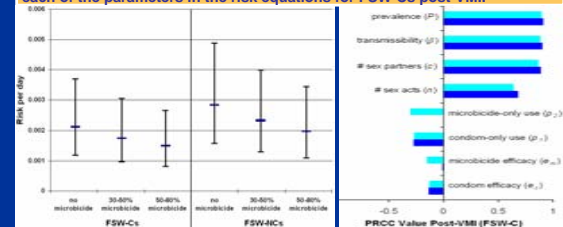
Protection Options	
Before Microbicide Availability	After Microbicide Availability
Condom	Condom only
	Condom + Microbicide
No Protection	Microbicide only
	No Protection

## RESULTS

Microbicides could reduce an FSW's risk significantly, whether her clients currently sometimes (FSW-Cs) or never (FSW-NCs) use condoms. For both groups of FSWs, daily risk would decrease ~17% using 30-50% effective microbicides or ~28% for 50-80% effective microbicides, respectively (Fig. 2a). We note that the median percentage decrease for both FSW-Cs and FSW-NCs is similar in each case; however, median daily risk for each group is quite different. Even if microbicides become available and are used, FSWs will still have ~0.2% chance of acquisition of HIV per day.

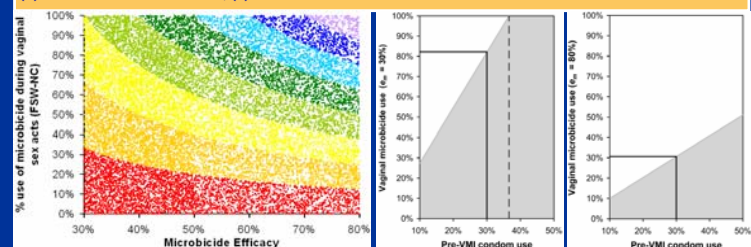
We determined that increasing microbicide usage would have a greater impact on reducing HIV acquisition in FSWs than increasing microbicide efficacy; results shown for 30-50-80% efficacy (Fig. 2b).

Figure 2: (a) Box-plots resulting from 1000 Monte Carlo simulations of our model for the reduction in risk of HIV acquisition for FSW-Cs and FSW-NCs in the cases of a 30-50% effective microbicide and a 50-80% effective microbicide. (b) Tornado plots of partial rank correlation coefficients for each of the parameters in the risk equations for FSW-Cs post-VMI.



We also quantify the relationships among potential microbicide efficacy, potential microbicide use, and the percent reduction in daily risk for FSW-NCs (Fig. 3a). Here, for example, if a 70% effective microbicide were introduced, a FSW-NC who used this microbicide only 50% of the time would reduce her risk by 30-40% (yellow data). However, if she used this microbicide 100% of the time, she would reduce her risk by 60-70% (dark blue). Slopes of the bands indicate that percentage changes in microbicide use would have a greater effect on reducing risk than the same percentage change in microbicide efficacy. Figures 3b,c show how much microbicide usage would be required to reduce risk (i.e., produce a beneficial outcome) if "condom replacement" occurs and if a: 30% (Fig. 3b), or 80% (Fig. 3c) effective microbicide was available. The necessary frequency for the usage of microbicides will depend upon pre-microbicide condom usage and microbicide efficacy. For example, if pre-microbicide condoms were used in 30% of acts and a 30% effective microbicide became available, then the FSW would have to use the microbicide in at least 82% of sex acts to ensure that her risk did not increase (Figure 3b). However, if an 80% effective microbicide became available, her risk would not increase if she used the microbicide only slightly more often than she had used condoms (Figure 3c).

Figure 3: (a) The relationship between microbicide efficacy and microbicide use for FSW-NCs. The bands of color represent grades of percentage reduction in an individual's daily risk of acquisition of HIV (red=0-10%, orange=10-20%, yellow=20-30%, light green=30-40%, dark green=40-50%, light blue=50-60%, dark blue=60-70%, purple=70-80%). The level of microbicide use required to produce a beneficial outcome (i.e., to decrease risk of HIV acquisition) when "condom replacement" occurs, for a (b) 30% effective microbicide, (c) 80% effective microbicide.



## DISCUSSION AND CONCLUSIONS

We have used an individual-level model to examine the potential daily impact of vaginal microbicides on reducing the risk of HIV acquisition in FSWs, a high risk group of women. We considered FSWs whose clients had HIV prevalence ranging from 10-60%, reflecting data from high risk clients in the developing world. We considered two groups of FSWs (as defined by their condom usage) and two ranges of microbicide efficacy (30-50% and 50-80%).

Behavioral scientists will need to explore the acceptability and perceived ease of use of microbicides; the introduction of microbicides should be linked to education campaigns promoting both condom and microbicide use. We have shown that (even low/moderate efficacy) microbicides could substantially decrease the risk of HIV infection in a group of women (FSWs) who are at great risk for HIV, particularly in high-prevalence regions.

Microbicides could substantially reduce FSWs' risk of acquiring HIV; absolute decrease in risk would be greatest in high-prevalence regions. Public health impact of microbicides will depend upon usage and efficacy. We found that risk reduction is more sensitive to increases in microbicide usage than microbicide efficacy. Even if the microbicides that become available are only low-to-moderately effective, the probability that risk in FSWs will increase (due to replacing condoms with microbicides) is low.