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FULL TITLE:

How much could a microbicide's STI-efficacy contribute to reducing HIV-risk and the level of condom use needed to lower risk? Model estimates

SHORT TITLE:

Importance of STI-efficacy for microbicides

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AUTHOR CONTRIBUTIONS

Anna Foss (AF) took the lead in the analysis and made substantial contributions to the conception, design of the analysis and interpretation of the results presented. Peter Vickerman (PV) and Charlotte Watts (CW) contributed to the conception and design of the analysis, and helped to interpret the findings. PV and CW provided substantial input into several drafts of the paper. Michel Alary (MA) helped with interpreting the data from Cotonou and commented on drafts of the paper.

KEY MESSAGES

1. A microbicide's STI-efficacy may have a substantial impact on STI and HIV incidence among high-risk groups.
2. For highly transmissible STIs, such as gonorrhoea, as the STI prevalence increases the relative reduction in HIV-risk increases at first, due to the proportion of HIV-risk attributable to the STI increasing, but then decreases at higher prevalences as the STI becomes harder to control.
3. For a less transmissible STI, like chlamydia, the STI can still be impacted upon with a moderate/high STI-efficacious microbicide even at high STI prevalences.
4. The variation in the 'condom migration thresholds' (the reduction in condom use following microbicide introduction that can be tolerated without increasing HIV-risk), for different STI-efficacies and STI prevalences, may be difficult to accurately measure.

ABSTRACT

Objective

This study explores the potential contribution of a microbicide's STI-efficacy in reducing a female sex worker's (FSW's) risk of STI and HIV infection. The study then investigates whether the threshold, for the reduction in condom use following microbicide introduction that can be tolerated without increasing HIV-risk, is affected by the STI-efficacy.

Methods

A dynamic model describing the transmission of a bacterial STI between FSWs and their clients was coupled with a static HIV model. The model uses data from Cotonou, Benin (1998-99), for illustration, to estimate the change in risk following the introduction of 50% HIV-efficacious microbicides of different STI-efficacies, used in 50% of sex acts when a condom is not used. The condom migration thresholds were estimated. The degree to which the findings are influenced by STI prevalence was explored.

Results

For highly transmissible STIs, there is a non-monotonic relationship between STI prevalence and microbicide impact on HIV with the relative reduction in HIV-risk first increasing, due to the proportion of HIV-risk attributable to the STI increasing, but then decreasing at high prevalences as the STI becomes harder to control. A less transmissible STI can still be impacted upon with a moderate/high STI-efficacy microbicide even at high STI prevalences. This relationship is also reflected in the condom migration thresholds.

Conclusions

A microbicide's STI-efficacy may have a substantial impact on STI and HIV incidence among high-risk groups. The variation in the condom migration thresholds for different STI-efficacies and STI prevalences may be difficult to accurately measure.

Key words: HIV, sexually transmitted infections, vaginal microbicides, condoms, mathematical models

INTRODUCTION

A microbicide is a substance capable of reducing the transmission of HIV and other sexually transmitted infections (STIs). Studies have shown that many promising candidates prevent infection in the laboratory, and three are in large-scale HIV-effectiveness clinical trials.¹

At present it is unknown what HIV- and STI-efficacy we can expect microbicides to have, where 'efficacy' is defined here as the percentage reduction in the transmission probability per sex act. Two of the products currently in late stage clinical HIV-effectiveness trials have demonstrated STI-efficacy, in-vitro or in animal models, including gonorrhoea, herpes simplex virus and chlamydia, although some products in development have no STI-efficacy.¹⁻³ Mathematical modelling suggests that a microbicide's STI-efficacy could play an important role in HIV transmission, particularly in settings where prevalence is relatively low/moderate, and can be impacted upon.⁴ However, it is not possible to infer from this analysis how important a microbicide's STI-efficacy may be in other epidemiological settings, beyond the two African settings considered.

This paper uses modelling to explore the potential contribution of a microbicide's STI-efficacy in reducing a female sex worker's (FSW's) risk of STI and HIV infection for a range of different STI prevalence and efficacy assumptions. Since there is concern that the introduction of microbicides may result in women who are using condoms switching

to less effective microbicides (termed ‘condom migration’),⁵ the implications of these results for the degree to which condom migration can be tolerated without increasing HIV-risk are explored. The findings are compared with a previous analysis that also estimated the ‘condom migration threshold’, but assumed that microbicides have equal HIV- and STI-efficacy.⁶

METHODS

Foss et al (2003) presented a standard Bernoulli equation describing an individual's risk of becoming HIV infected over a fixed time-period, referred to as the 'static HIV model' (Appendix).⁶ An analogous equation can also be used to describe the probability of STI acquisition (π_s) (Appendix). In both cases, the main assumption is that the probability of transmission per sex act is independent of previous sex acts.

Model adaptations

To investigate the role of microbicide STI-efficacy in HIV-risk, the static model was revised by coupling it with a simple dynamic STI model, to reflect possible changes in STI prevalence. This was required so that the benefit of any STI-efficacy of the microbicide, and any potential negative impact of condom migration, are incorporated as effects on STI transmission.

The model simulated the transmission of a curable STI between FSWs and their male clients, and their risk of acquiring HIV. In order to represent, in a simple way, infection from those beyond the closed intervention populations modelled, a seeding term was included in the model equations for males. Since microbicides would be targeted only to FSWs in contact with an intervention, this seed represents infections from others who do not have access to microbicides. The seed acts as a sustaining force so that the STI is not eradicated, but contributes little to the overall client prevalence (0.8%).

The dynamic STI model was used to estimate the equilibrium STI prevalence before and after the introduction of microbicides, assuming that HIV does not affect the equilibrium STI prevalence over a short timeframe. Numerical methods were used to approximate the change in STI prevalence over time. For this, a dynamic deterministic compartmental model of the transmission of a curable STI was built in Microsoft® Excel (Appendix).

Parameterisation and microbicide efficacy scenarios

As in Foss et al (2003),⁶ data collected in a cross-sectional survey (1998-99) from Cotonou, Benin, is used as an illustrative case-example, to reflect a setting with an ongoing intervention that, at this time, had achieved moderate levels of condom use during commercial sex. Four scenarios are considered for the STI-efficacy of the microbicide: 0%, 25%, 50% and 75%. For illustration, microbicides are assumed to have 50% HIV-efficacy and be used in 50% of non-condom-protected sex acts, to reflect the statistical power of the microbicide efficacy trials and using data from the spermicide trials on levels of use.^{6 7} It is assumed that if a microbicide is used with a condom in a sex act then the additional protection offered by the microbicide is negligible compared to that provided by the condom. Using the input parameters listed in Table 1, the STI model simulated an epidemic, to reach equilibrium STI prevalence values, giving an indication of how changes in condom and microbicide use affect STI prevalence.

[INSERT Table 1]

Model fitting and STI prevalence scenarios

The model was fit to data on the prevalence of gonorrhoea among FSWs and clients collected in the 1998-99 survey in Cotonou. Gonorrhoea prevalence values were used since this was the most prevalent STI in Cotonou for which there were available data for the groups considered.^{8 10 11 28} The fitting procedure involved using the 'Solver' add-in to Microsoft® Excel to fit to these STI prevalences by adjusting specific parameters, namely the duration of the STI, the STI transmission probabilities, and the sustaining seed. These parameters were varied within ranges based on data from the literature for the duration of gonorrhoea²⁵ (incorporating the effects of treatment²⁶, see Table 1) and its transmissibility^{15 16}, and assuming that the sustaining seed for the STI was $\leq 1\%$ (Appendix).

The values used and obtained through the fitting procedure, along with the equilibrium STI prevalence estimates before and after microbicide introduction, were then used in the static HIV model. The HIV model incorporates the facilitating effect of the STI on HIV transmission.^{23 24}

Using data on the number of clients reported by FSWs in Cotonou (1998-99) gave the 'medium' STI prevalence scenario (21.0% among FSWs and 5.4% among clients). In order to consider the generalisability of the findings to other times and settings, the number of clients per FSW per month was adjusted to generate a reasonable range of STI prevalences. Within this range, specific 'low' and 'high' curable STI prevalence scenarios were obtained by, respectively, halving and doubling the number of clients per

FSW per month. The ‘low’ and ‘high’ STI prevalence scenarios obtained for FSWs (and their clients) were 5.5% (2.1%), and 38.6% (8.8%), respectively.

Steps of analysis

In the analysis, the revised model (dynamic STI-static HIV coupled model) is first used to explore to what degree a microbicide’s STI-efficacy can reduce an individual’s risk of STI and HIV infection per month. Then, allowing for condom migration, this model is used to compare the ‘condom migration thresholds’ for microbicides of different STI-efficacies, introduced into settings with various STI prevalence profiles.

A sensitivity analysis was also conducted to explore the effect on the findings of increasing from 2 to 6 the multiplicative STI cofactor facilitating HIV transmission per sex act. In order to investigate the generalisability of the findings to other curable STIs, such as chlamydia in other settings,²⁹⁻³¹ an additional model refit to the same prevalences was identified manually by assuming a longer duration of the STI and lower transmissibility,^{17 18 25 27 32} and the analysis was repeated using this refit. The duration of the STI was then varied, rather than the number of clients per FSW, as an alternative method of exploring the same range of STI prevalences with this refit, to reflect different levels of STI treatment.

RESULTS

Reduction in STI-risk

Assuming that the consistency of condom use remains at 56%, in low STI prevalence settings, it is relatively easy to have an impact on the STI with a reasonably low or medium STI-efficacy microbicide that is used in 50% of non-condom-protected sex acts, and so increasing STI-efficacy further has limited added value. In higher STI prevalence settings it is harder to control the STI since the risk of infection and re-infection is also high, and so the incremental benefit increases steadily as STI-efficacy increases.

Reduction in HIV-risk

For the ‘medium’ STI prevalence scenario (21% among FSWs), a zero HIV-efficacy microbicide with 50% STI-efficacy reduces HIV-risk by 11%, while a 50% HIV-efficacy microbicide with zero STI-efficacy reduces risk by 23%. So a microbicide that is only 50% efficacious against STI (with no HIV-efficacy) may still have 47% of the HIV-impact that a 50% HIV-efficacious microbicide has without STI-efficacy.

Figure 1 illustrates the reduction in HIV-risk from a 50% HIV-efficacious microbicide (for various STI-efficacies), introduced into a range of STI prevalences, with condom-consistency remaining at 56%, and with other parameters as in Table 1.

[INSERT Figure 1]

In the original model fit (Figure 1a), the potential relative reduction in HIV-risk among FSWs for a 50% HIV-efficacious microbicide with 50% STI-efficacy varies from 25-33% depending on the STI prevalence. There is a non-monotonic relationship between STI prevalence and microbicide impact, with the relative reduction in HIV-risk first increasing as the STI prevalence increases, due to the proportion of HIV-risk attributable to the STI increasing, but then decreasing at higher prevalences as the STI becomes harder to control.

The same pattern is observed if the multiplicative STI cofactor facilitating HIV transmission per sex act is increased from 2 to 6, but the reduction in HIV-risk is greater for each STI-efficacy scenario and there is more variation across the STI prevalences. For a 50% HIV-efficacious microbicide with 50% STI-efficacy the potential relative reduction in HIV-risk varies from 28-47%, depending on the STI prevalence, if an STI cofactor of 6 is used.

If the model is refit assuming a longer duration of the STI and lower transmissibility, the potential relative reduction in HIV-risk is shown in Figure 1b. If the duration of the STI in the refit is adjusted to vary the STI prevalence across the same range as in Figure 1a, the non-monotonic relationship is less pronounced in the 0% and 25% STI-efficacy scenarios and the relationship is actually monotonic for the 50% and 75% STI-efficacy scenarios in this STI prevalence range. This difference between Figure 1a and Figure 1b is due to the different STI transmissibilities assumed in each. In Figure 1a the STI is

highly transmissible, meaning it is hard to control the STI when the STI prevalence is high, resulting in the microbicide achieving less impact on HIV-risk, while in Figure 1b the STI is half as transmissible and this means that the STI can be controlled, even at high prevalences, if the microbicide's efficacy is 50% or more.

Condom migration thresholds

Based on the parameters in Table 1, where the condom consistency was 56% before microbicide introduction, Table 2 shows that more condom migration can be tolerated as the microbicide STI-efficacy is increased.

In the original model fit, the thresholds are more sensitive to changes in the microbicide's STI-efficacy (0-75%) in the medium STI scenario (10-20% with STI cofactor of 2 or 6-23% with STI cofactor of 6), than in the 'low' or 'high' STI prevalence scenarios. The values in Table 2 change by at most 1% for the refit compared to the original fit.

[INSERT Table 2]

The thresholds are also fairly similar across the different STI prevalence scenarios. The small differences are due to the interplay between increasing STI prevalence acting to increase the proportion of HIV-risk attributable to the STI while also potentially making it harder to control the STI, particularly if it is highly transmissible, as observed in Figure 1. At the threshold level of 16% condom migration for a 50% HIV- and 50% STI-efficacious microbicide, a higher STI-efficacy microbicide will reduce HIV-risk and a

lower STI-efficacy microbicide will increase HIV-risk. The magnitude of this decrease or increase in HIV-risk corresponds to the degree to which any more or less condom migration can be tolerated without increasing risk (Figure 2).

[INSERT Figure 2]

DISCUSSION

The findings build on previous modelling that have either explored the importance of STI-efficacy for the HIV-impact of a microbicide in two settings,⁴ or have estimated the degree of condom migration that can occur without increasing risk following microbicide introduction.^{6 33 34} The modelling presented here extends the former analysis because it gives projections for a wide range of STI prevalences and STI-efficacies, and extends the latter analysis by exploring the effect of a microbicide's STI-efficacy on the migration thresholds.

Even fairly low STI-efficacy microbicides can have a large effect on the STI in settings with a low prevalence of curable STI. For highly transmissible STIs, such as gonorrhoea, there is a non-monotonic relationship between STI prevalence and microbicide impact on HIV with the relative reduction in HIV-risk first increasing, due to the proportion of HIV-risk attributable to the STI increasing, but then decreasing at higher prevalences as the STI becomes harder to control. For a less transmissible STI, like chlamydia, the STI can still be impacted upon with a moderate/high STI-efficacious microbicide even at high STI prevalences. This implies that, if the introduction of the microbicide leads to a change in the STI prevalence, the HIV-impact of the same microbicide will likely vary by setting. Additionally, the previous static HIV model estimates of the microbicide's impact on HIV-risk will be conservative in this case.

Increasing the STI-efficacy of a microbicide from zero to 75% also increases the amount of condom migration that can be tolerated without increasing HIV-risk, but only by as much as 10 percentage points if the STI increases 2-fold the probability of HIV transmission per sex act. It may be hard to measure condom use differences to this degree of accuracy.

Limitations

As in the earlier work, using a static HIV model, even when coupled with a dynamic STI model, means it is not possible to estimate how a microbicide may impact on the HIV epidemic over longer time-periods. However, coupling a dynamic STI model with a static HIV model was a simpler intermediate step, using an appropriate level of complexity to address the questions posed, and has provided several key insights.

More recent data from Cotonou (2005) suggest that condom use during commercial sex has increased, and gonorrhoea and HIV prevalences have decreased substantially.^{35 36} As a result, the present-day situation in Cotonou may more closely resemble the low STI prevalences presented here (in Figure 1) than the 'medium' STI prevalence scenario. At the new very high level of reported condom use (95% at last sex), little if any condom migration can be tolerated without increasing HIV-risk. The findings from considering moderate and high STI prevalences have particular relevance to FSW populations in which moderate or high prevalences of curable STI remain, such as in the Philippines²⁹, Vietnam³⁷ and China^{30 31 38}

Only commercial sex was modelled since these were the partnerships of concern in terms of condom migration in the previous static modelling,⁶ and analysis of long-term partnerships in the general population concluded that the estimates from the static model were insensitive to variations in STI-efficacy explored using the revised model.³⁹ Dynamic population-level HIV/STI modelling has been used to investigate this further, with data from Benin and South Africa.⁴ Using a slightly different parameterisation and scenarios from this analysis (in order to fit the more complex model), they agree with our finding that the sensitivity of a microbicide's HIV-impact to increases in STI-efficacy may reduce at very high STI prevalences.

Desai et al (2006) predicted that the fraction of HIV infections prevented in circumcised males that were attributable to STI was unlikely to be more than 10-20% in a population of low- and high-risk groups.⁴⁰ This is lower than what is predicted here for a 50% HIV- and STI- efficacious microbicide used in commercial sex, where up to 28% of the relative reduction in HIV-risk among FSWs was attributed to its STI-efficacy. However, for long-term partnerships in Cotonou, our modelling suggests that less than 10% of a microbicide's HIV-impact can be attributed to the microbicide's STI-efficacy. Additionally, unlike Desai et al (2006), who assumed male circumcision offered no direct protection to females, microbicides are here assumed to provide the same degree of protection to both males and females, which may not be the case. Currently, the phase 3 trials are focusing on measuring the effectiveness of microbicides in reducing the risk of HIV transmission from males to females only.^{1 41} Recent modelling work has investigated this issue of uni- versus bi-directional protection in exploring the potential contribution of

a microbicide's STI-efficacy on the reduction in HIV incidence (effectiveness) observed in a phase 3 trial.⁷ The difference in the reduction in HIV incidence in a trial or HIV-risk among women from a bi-directional versus a uni-directional microbicide may be fairly small initially, since any change in the HIV prevalence among males is likely only to be observable over a longer timeframe.

Conclusions

The findings illustrate that a microbicide's STI-efficacy may have a substantial impact on the incidence of HIV and curable STIs among high-risk groups, particularly in settings where the STI is relatively easy to control and a substantial proportion of HIV-risk is attributable to the STI. Although incorporating microbicide STI-efficacy into the model provided improved estimates of the migration threshold for FSWs, whether this adds important additional policy insights depends on whether the differences between the thresholds for different STI-efficacies are large enough to be measurable.

The analysis presented here highlights the importance of developing and evaluating microbicides with STI-efficacy, and so supports the Microbicide Development Programme trial having some STIs as secondary outcomes. Combination products, such as those based on antiretrovirals added into microbicides with STI-efficacy, should also be pursued.

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TABLES AND FIGURES

Table 1: Input parameters used in the static HIV-dynamic STI revised model for microbicides

Parameter definition	Value	References and notes
% of sex acts in which condom is used before microbicide introduction	56%	Condom use at last commercial sex reported by client was 55.8%. ⁸
% of non-condom-protected sex acts in which microbicide is used	50%	Scenario, based on levels of spermicide use observed in trials. ⁶
Per sex act HIV-efficacy of condom	95%	Model-based estimate suggests condom use reduces male-to-female transmission of HIV by 95% per sex act. ⁹
Per sex act STI-efficacy of condom	95%	Assumed equal to HIV-efficacy of condoms. High-end estimate used here so that model findings about effect of microbicide are conservative.
Per sex act HIV-efficacy of microbicide	50%	Scenarios
Per sex act STI-efficacy of microbicide	50%	Scenarios
	(0, 25%, 50%, 75%) [0-100%]	
	56 clients per FSW (<i>m</i>)	FSWs reported a mean of 13 clients in previous week. ^{10 11} Clients reported a mean of
Average number of sexual partnerships per month	(28, 56, 112) [20-112], 2.7 FSWs per client (<i>M</i>)	2.7 visits to FSWs per month. ⁸ Assumed any regular/repeat clients visit the same FSW no more than once per month.
Average number of sex acts per partnership per month	1	Fitted parameter/scenarios
Per sex act transmission probability of HIV	0.002 male-to-female	Reviews suggest male-to-female transmission probability is ~0.002 ¹² (in developing countries ¹³).

Parameter definition	Value	References and notes
Per sex act transmission probability of STI	0.225 male-to-female (B_{MF}), 0.19 female-to-male (B_{FM}) (0.1 in refit for both B_{MF} and B_{FM})	Range (0.19-0.53) based on values for gonorrhoea. ¹⁴⁻¹⁶ Model fit using Solver with range 0.19-0.53 and constraint that male-to-female > female-to-male. 0.1 for refit is based on chlamydia literature. ¹⁷⁻¹⁹
HIV prevalence	FSWs: 40.7%, Clients: 8.4%	¹¹
Probability that an HIV infected partner has initial high viraemia	0.05	Data from Malawi and India suggests range 0.04-0.06. ^{20 21}
Multiplicative increase in the per sex act probability of HIV transmission during the high viraemia phase	10	8-10 fold increase in probability of HIV transmission at peak of acute initial high viraemia phase compared to later low viraemia phase. ²²
STI prevalence	21.0% for FSWs (γ) (5.5%, 21.0%, 38.6%) [3.0-38.6%], 5.4% for clients (Y) (2.1%, 5.4%, 8.8%) [1.5-8.8%]	Based on values for gonorrhoea ¹¹
Multiplicative STI cofactor facilitating HIV transmission if FSW and/or her client is infected with the STI	2 (6 used in sensitivity analysis)	Systematic review found effect estimate on HIV susceptibility of gonorrhoea = 2.1. ²³ Pooled effect estimates of gonorrhoea ~2.3-3.4(1.7-5.5) from meta-analysis and meta-regression. ²⁴ Similar range 2-6 for chlamydia. ^{23 24}
Duration of STI infection	1 month for both FSWs and clients ($1/\gamma$ and $1/T$) (1-3 in refit)	Range 1-6 months duration based on gonorrhoea literature ²⁵ and incorporates effects of treating FSWs in the project clinic and conducting outreach activities to encourage FSWs to attend the clinic for regular STI check-ups, irrespective of symptoms. ²⁶ Model fit using Solver with range 1-6 months. Refit based on chlamydia literature. ^{25 27}
Rate leave population (approximated as 1 / (duration in population))	0.0336 per month for FSWs (ω), 0.0225 per month for clients (Ω)	In 1998-99, FSWs currently selling sex had done for mean of 2.6 years ¹⁰ and current clients had bought sex for a mean of 4 years ¹¹ . Life expectancy from WHO (2004).
Seed into clients, sustaining STI	0.855%	Parameter to sustain infection. Model fit using Solver with range 0-1%.

Table 2: ‘Migration thresholds’ (the maximum absolute reduction in condom-consistency that can be tolerated following microbicide introduction without increasing an individual’s risk of HIV acquisition) in commercial sex for different STI prevalence scenarios and microbicide STI-efficacies (combined with the effect of the microbicide’s 50% HIV-efficacy)

		STI-efficacy			
		0%	25%	50%	75%
Original model fit:					
STI prevalence scenario	‘Low’	11%	14%	<i>16%</i>	17%
	‘Medium’	10%	13%	<i>16%</i>	20%
	‘High’	13%	14%	<i>16%</i>	19%
Additional model refit:					
STI prevalence scenario	‘Low’	13%	15%	<i>16%</i>	17%
	‘Medium’	10%	13%	<i>16%</i>	19%
	‘High’	11%	13%	<i>16%</i>	20%
<p>In all scenarios it is assumed that a microbicide provides this degree of protection (efficacy) in 50% of non-condom-protected sex acts.</p> <p>The 16% in the 50% STI-efficacy column is in italics to highlight that this is the migration threshold obtained using the simple static HIV model, which assumed equal HIV-efficacy and STI-efficacy.</p>					

Figure 1: Reduction in HIV-risk among sex workers (from the combined effect of a 50% HIV-efficacy microbicide with four different STI-efficacies) for different STI prevalences

1a: Original model fit using transmission probabilities of 0.2 per sex act, with different STI prevalences obtained by varying the number of clients per FSW

1b: Additional model refit using transmission probabilities of 0.1 per sex act, with different STI prevalences obtained by varying the duration of the STI

Figure 2: Reduction in HIV-risk among sex workers (from the combined effect of a 50% HIV-efficacy microbicide with different STI-efficacies) for three different STI prevalences, assuming a reduction in condom consistency of 16%

2a: Original model fit using transmission probabilities of 0.2 per sex act, with different STI prevalences obtained by varying the number of clients per FSW

2b: Additional model refit using transmission probabilities of 0.1 per sex act, with different STI prevalences obtained by varying the duration of the STI

Figure 1: Reduction in HIV-risk among sex workers (from the combined effect of a 50% HIV-efficacy microbicide with four different STI-efficacies) for different STI prevalences

a: Original model fit using transmission probabilities of 0.2 per sex act, with different STI prevalences obtained by varying the number of clients per FSW

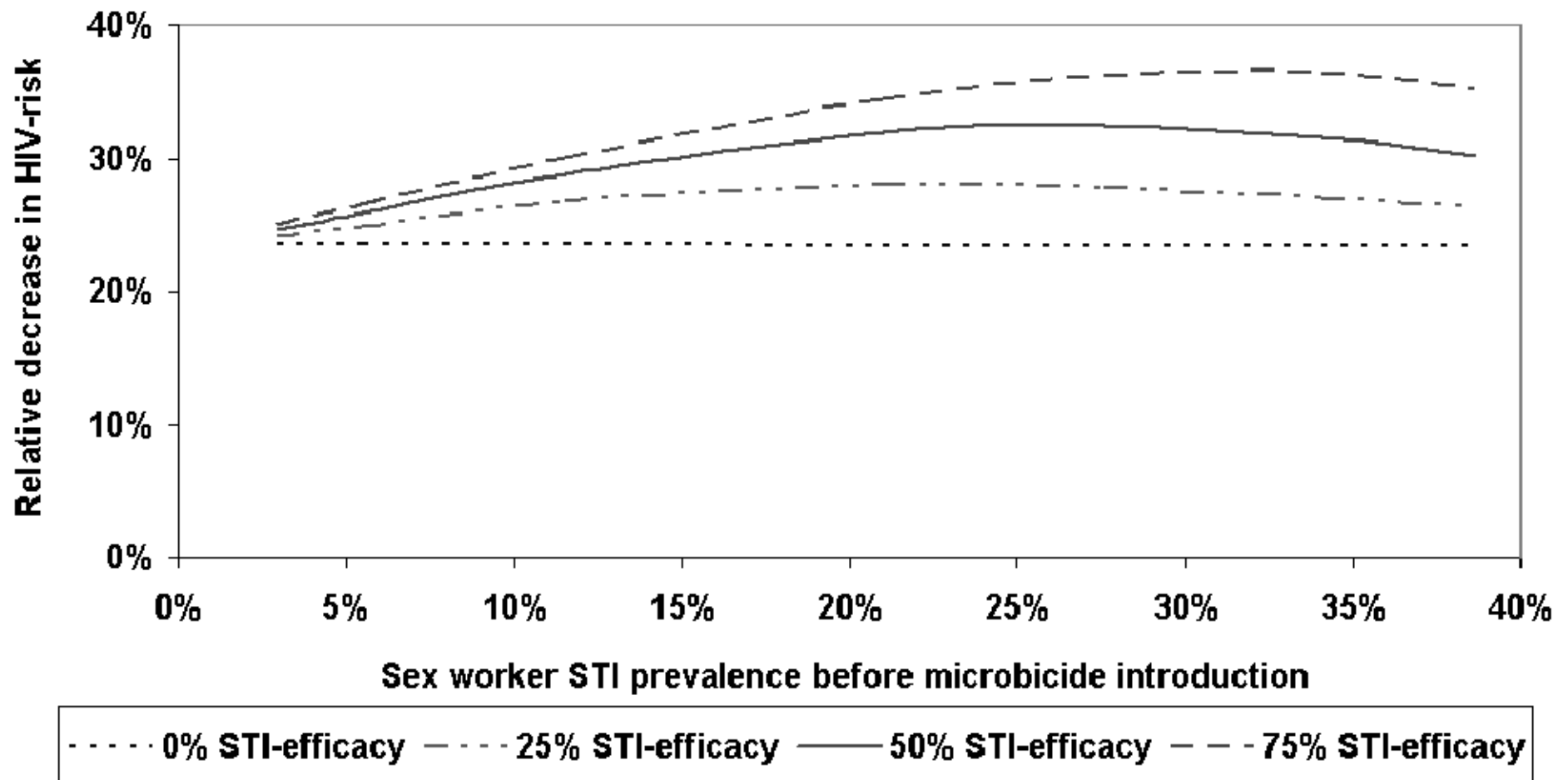


Figure 1: Reduction in HIV-risk among sex workers (from the combined effect of a 50% HIV-efficacy microbicide with four different STI-efficacies) for different STI prevalences

b: Additional model refit using transmission probabilities of 0.1 per sex act, with different STI prevalences obtained by varying the duration of the STI

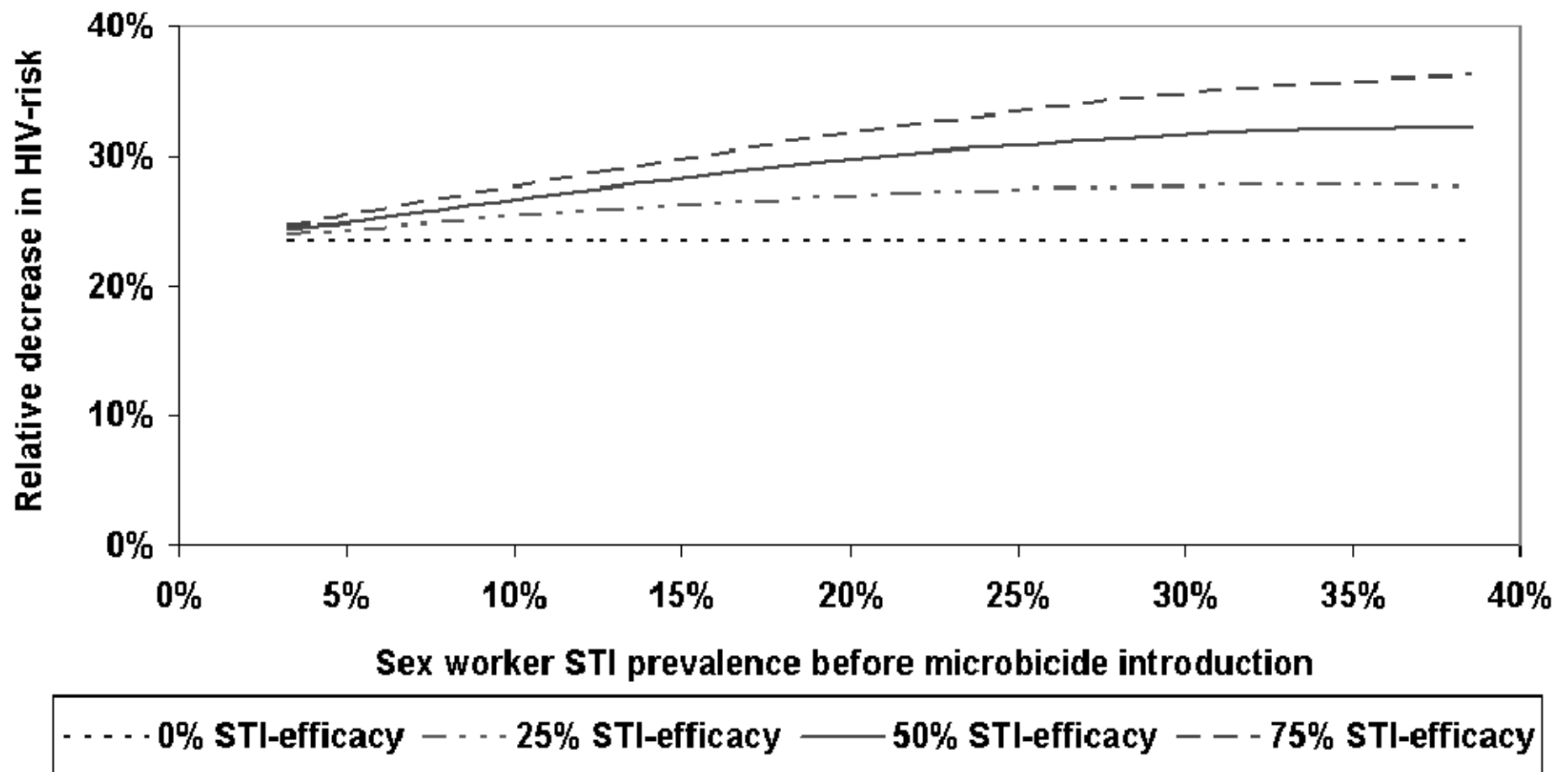


Figure 2: Reduction in HIV-risk among sex workers (from the combined effect of a 50% HIV-efficacy microbicide with different STI-efficacies) for three different STI prevalences, assuming a reduction in condom consistency of 16%

a: Original model fit using transmission probabilities of 0.2 per sex act, with different STI prevalences obtained by varying the number of clients per FSW

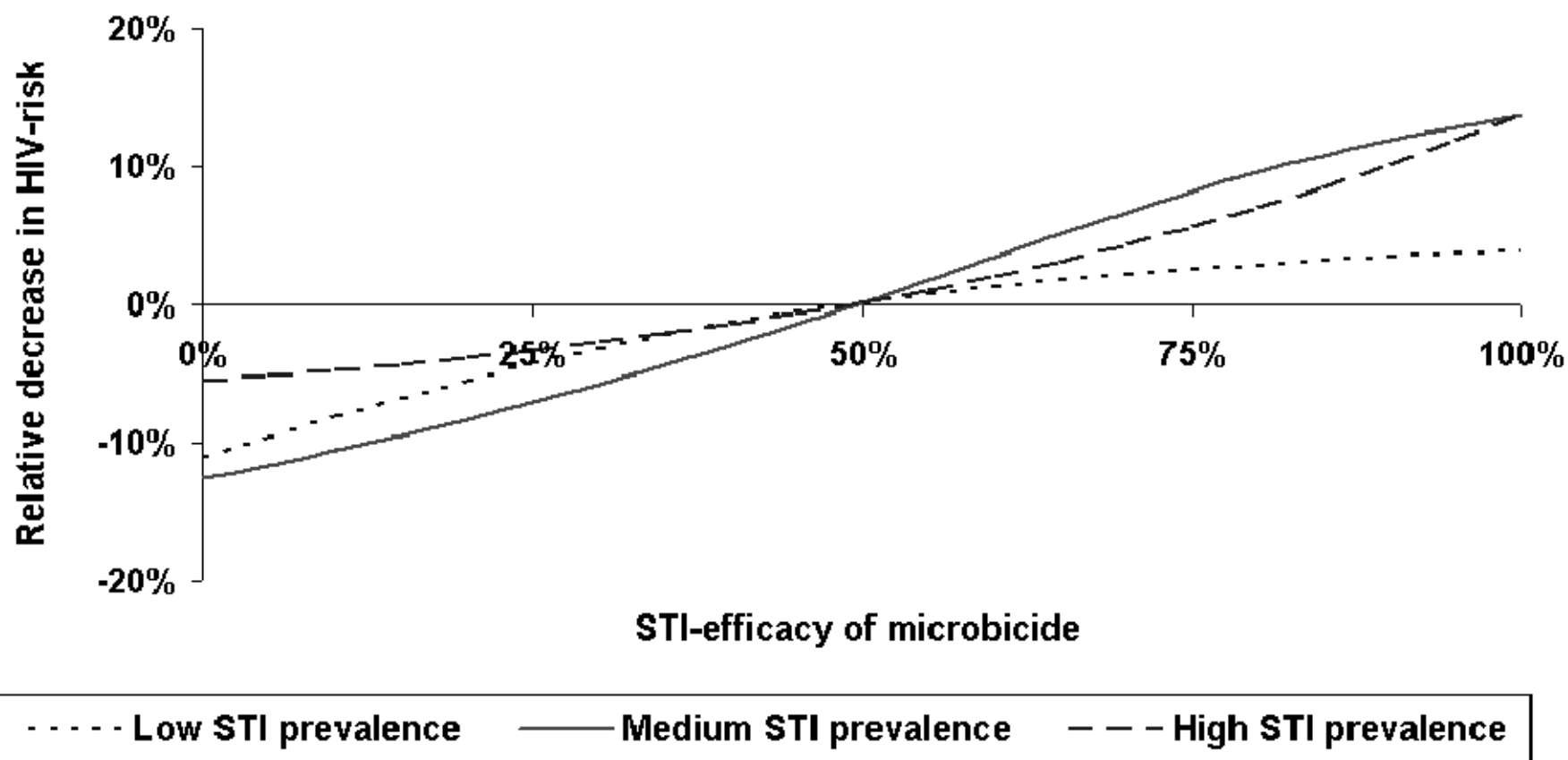


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