Shifts in condom use following microbicide introduction: should we be concerned?

Anna M. Foss[a], Peter T. Vickerman[a], Lori Heise[b] and Charlotte H. Watts[a]

Objectives: Abandoning condoms for microbicides is termed 'condom migration'. This study estimated the reduction in condom use that can be tolerated following the introduction of an HIV- and sexually transmitted disease (STD)-efficacious microbicide without increasing an individual's risk of HIV infection, and explored how microbicide use affects HIV-risk.

Design: Development of a static mathematical model to compare how different combinations of condom and microbicide use affect individual risk of HIV and STD infection at a particular point in time.

Methods: The model is used to identify the 'break-even point' at which any increased risk associated with condom migration is counter-balanced by the protection afforded with microbicides. Data from Benin is used as a case-example.

Results: Considering a 50% HIV- and STD-efficacious microbicide, groups that use condoms with 25% consistency or less could cease using condoms without increasing their risk if they use microbicides in 50% or more of sex acts. However, migration may increase risk if the initial condom-consistency is high ($>70\%$) and microbicide-consistency is low ($<50\%$ of non-condom-protected acts). For the Benin case-example, if condoms are initially used in 70% or less of sex acts, and if consistency of condom use is sustained following microbicide introduction, there will be a 20% or greater reduction in HIV-risk if the microbicide is used in 50% of non-condom-protected sex acts.

Conclusions: There are likely to be many situations in which the benefits of microbicide use outweigh the negative impact of condom migration, and where microbicides could substantially reduce HIV-risk.

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Introduction

Microbicides are substances capable of reducing the transmission of HIV and other sexually transmitted pathogens when applied vaginally. Currently about 65 compounds are in some stage of development. Of these, 17 are in phase I or II clinical trials and four are expected to enter phase III trials later this year [1,2 (personal communication with Polly Harrison; March 2003)]. The new generation of products being evaluated have different mechanisms of action than nonoxynol-9 (N-9), the spermicidal product that has proven ineffective against HIV [2–4].

At present it is unknown what efficacy we can expect microbicides to have. The first generation of micro-

From the [a]Health Policy Unit, Department of Public Health and Policy, London School of Hygiene & Tropical Medicine, London, UK and [b]Global Campaign for Microbicides, PATH (Program for Appropriate Technology in Health), Washington DC, USA.

Correspondence to Anna Foss, Department of Public Health & Policy, London School of Hygiene & Tropical Medicine, Keppel Street, London, WC1E 7HT, UK.

Tel: +44 (0)20 7612 7891; fax: +44 (0)20 7637 5391; e-mail: anna.foss@lshtm.ac.uk

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bicides are likely to be less efficacious than the male-condom [5]. Because of this, microbicides will be delivered using hierarchical messages that promote the concurrent use of microbicide with a condom as 'best choice', but suggest microbicide use alone as a fallback option when condom use is not possible. This parallels other 'harm reduction' approaches to HIV prevention used with injecting drug users [6]. Studies suggest that women find hierarchical counselling more acceptable than other counselling methods [7,8].

Evidence from many settings strongly suggests that many women will find microbicides easier to use than condoms and that they can be used when condom use is not possible [9–17]. This has raised the concern that women might abandon condoms in favour of microbicides. Indeed, the fear of 'condom migration' has been a major barrier to the widespread endorsement of microbicides as a potential method of HIV prevention [18].

This article presents a mathematical model of HIV transmission developed to estimate the level of protection provided by different combinations of condom and microbicide use. The model is used to identify the 'break-even point' at which any increase in risk associated with condom migration is counter-balanced by the increased protection afforded with microbicides, and to explore how different levels of microbicide use affect an individual's HIV-risk.

Condom efficacy and consistency of use

A meta-analysis of studies evaluating rates of seroconversion among discordant couples who always use condoms estimated that condom HIV-efficacy is approximately 87%, with a potential range from 60% to 96% [19]. Another meta-analysis estimates that consistent condom use reduces HIV incidence by 80% [20]. A review by the US National Institutes of Health concludes that there is insufficient available data to estimate the efficacy of condoms against many STDs, and notes that efficacy is likely to vary by STD pathogen [21].

Despite such high HIV-efficacy, there is substantial evidence that in many settings levels of consistent condom use is low, especially within primary partnerships [22]. Studies show that even after directed intervention, the percentage of couples that achieve consistent condom use seldom exceeds 20–30%, except where individuals know that one partner is HIV infected [18]. Success in increasing the consistency of condom use has been greatest among sex workers and other vulnerable groups [8,23], but even here, many sex workers do not use condoms consistently with their non-commercial, primary partners [24]. Even when condoms are used consistently they may be used incorrectly [25]. The immense gap between the numbers requiring protection and those using condoms consistently and correctly could potentially be filled by microbicides.

Migration from the condom: current evidence

To date nine studies have examined how the availability of microbicidal-like products such as spermicides affect male-condom use (Table 1). These studies are limited because they focus on nonoxynol-9 spermicides, and tend to involve vulnerable groups of women. Nonetheless, six found that the availability of additional protection options along with counselling resulted in increased condom use [7,8,26–30]. Of the three studies that observed a lower consistency of condom use when both spermicides and condoms were provided [31–33], one was conducted among Kenyan sex workers [32], another among Colombian sex workers [31], and the third among high-risk women in Cameroon [33]. Only two of these [31,33] measured the consistency of condom use, the greatest difference being between the 'male-condom only' and the 'spermicides as a fallback' study arms in the Colombian study (95% versus 78%), illustrating that migration may be a concern under certain circumstances [31]. The Kenyan study used different measures of condom use at baseline and follow-up and so it is hard to accurately assess the amount of migration that occurred since it is difficult to determine if 'consistent condom use' is the same as '100% condom use'.

Methods

This study builds upon previous studies by Sokal *et al.* and Watts *et al.* that used mathematical modelling to identify factors affecting the potential impact of microbicides [34,35]. For this analysis we use an established mathematical equation that describes the probability of HIV transmission between susceptible and infected individuals [36–38]. As in the study by Watts *et al.*, we refine the equation to consider the level of protection provided by different methods, incorporating both how the presence of an STD and the initial high HIV viraemia phase may facilitate HIV transmission [35]. When just one method of protection is used, the probability (π) that a susceptible person becomes HIV infected over a fixed time period is:

$$\begin{aligned}\pi = 1 - [1 - p + s\{ph[1 - \alpha\delta\beta(1 - E)]^n \\ + \ p(1 - h)[1 - \delta\beta(1 - E)]^n\} \\ + \ (1 - s)\{ph[1 - \alpha\beta(1 - E)]^n \\ + \ p(1 - h)[1 - \beta(1 - E)]^n\}]^m,\end{aligned} \quad (1)$$

Table 1. Studies of condom and spermicide introduction.

Study year	Location	Study population	Aims	Study design	Baseline sexual behaviour[a]	Baseline condom use[a,b]	Condom use after[a,b]	Spermicide use after[a,c]	Condom migration	Reference
1992–1993	Santa Fe de Bogota, Colombia	Sex workers at STD clinic	Determine if spermicide use influenced condom use	199 women seen every 2 weeks for 12 weeks. Three arms: condom only (CO); condom with spermicide (CS); spermicide used when condom not (SB). 16% lost to follow-up.	HIGH (60–70 acts and $>$ 2 partners per month)	'Often' use of barrier methods (mainly condoms): $>$ 50% women.	95% in CO 92% in CS 78% in SB	86% in SB 65% in CS	YES[d]	[31]
Early 1990s	Texas, USA	Women at family planning clinic	Compare use of barrier methods following hierarchical vs. condom-only counselling	167 women seen for follow-up three times over 6 months. Two arms: condoms only (CO); condoms and N-9 film (CN-9). 40% CO and 57% CN-9 lost to follow-up.	LOW ($\sim$ 80% had $\leqslant$ 1 partner in past 6 months)	No condom use in past 6 months: 56% in CN-9; 44% in CO.	33% in CN-9; 19% in CO.	3% in CN-9	NO[d]	[29]
1994–1996	Yaounde/ Douala, Cameroon	Sex workers	Determine effect of N-9 vaginal film on rate of STDs including HIV	Randomised controlled trial. 1292 women seen monthly for over 1 year. Two arms: N-9 film (N-9) and placebo film (P). About one-quarter lost to follow-up by end of year 1.	HIGH ($\geqslant$ 4 partners per month)	Use of condom with last client: 49% women in N-9; 48% women in P.	96% in N-9; 95% in P.	74% in N-9 and in P	NO[e]	[28]
1994–1996	Kwazulu Natal, South Africa	STD patients	Reduce STD risk	102 women and 100 men seen over 3 months. Two arms: four counselling sessions on risk behaviour (SCIT); one counselling session on HIV/AIDS (HIT). Both groups received, and were given information on, condoms and vaginal N-9 suppositories. About one-quarter lost to follow-up.	MEDIUM ($>$ 1 partner per 3 months)	Any male condom use:- SCIT: 14% (women and men); HIT: 6% women, 18% men. 100% male condom use:- SCIT: 2% women, 0% men; HIT: 0% (women and men).	Any male condom use:- SCIT: 57% women, 56% men; HIT: 12% women, 29% men. 100% male condom use:- SCIT: 17% women, 11% men; HIT: 0% women, 3% men.	No data on consistency of use (38% of SCIT women and 9% of HIT women ever used N-9)	NO[e] (1 woman in SCIT migrated)	[26]
1995–1996	Philadelphia, USA	Women at STD clinic	Compare use of barrier methods following hierarchical vs. condom-only counselling	292 women seen for follow-up 3 times over 6 months. Three arms: male-condom counselling (MC); female-condom counselling (FC); hierarchical message (HM). 25–50% lost to follow-up.	MEDIUM ($\sim$ 2 partners per month)	28% in MC 26% in FC 32% in HM	62% in MC 74% in FC 66% in HM	No data on consistency of use (48% women ever used spermicide with main partner)	NO[d]	[7,8][f]

Table 1. (continued)

Study year	Location	Study population	Aims	Study design	Baseline sexual behaviour[a]	Baseline condom use[a,b]	Condom use after[a,b]	Spermicide use after[a,c]	Condom migration	Reference
1996–1998	Mombasa, Kenya	Sex workers	Effect of N-9 gel on acquisition of STDs	Randomised controlled trial. 278 women seen monthly for over 1 year. Two arms: N-9 gel and placebo gel (P). Counselled to use condom with gel. About one-third lost to follow-up by 12 months.	HIGH (~ 2 acts and 1 partner per week)	Consistent condom use: 71% women in N-9; 68% women in P.	100% condom use: 50% women in N-9; 54% women in P.	50% in N-9 57% in P	YES?[e]	[32]
1996–2000	South Africa Thailand Benin	Sex workers	Effect of COL-1492 vaginal gel (N-9) on HIV transmission	Randomised controlled trial with 892 women seen monthly over ~4 years. Two arms: N-9 gel and placebo gel (P). All asked to use condom with gel. About one-third lost to follow-up by 48 weeks.	HIGH (~ 3 clients per day)	Condom use > 50% of sex acts: 67% in N-9; 66% in P.	87% in N-9 90% in P	69% in N-9 90% in P	NO[e]	[30]
1998–2000	Yaounde, Cameroon	High-risk women	Effect of N-9 gel plus condom use vs. condom use alone on HIV transmission	Randomised controlled trial with 1251 women seen monthly for 6 months. Two arms: N-9 gel and condom (GC) or condom only (C). Less than 1% lost to follow-up.	ACTIVE[g] (~ 3 acts per week)	Used condom last sex act: 37% women in GC; 35% women in C.	81% in GC 87% in C	68% in GC	YES[d]	[33]
Late 1990s	Miami, USA	Female drug abusers at medical centre	Compare use of barrier methods following hierarchical vs. condom-only counselling	41 women seen over 3 months. Two arms: male and female condoms (MFC); male and female condoms plus N-9 after initial condom only period (MFCS).	ACTIVE[g] (⩾ 1 act per week)	Male condom use: 19% in MFCS.	Male condom use: 27% in MFCS.	< 45%[h] in MFCS	NO[e]	[27]

[a]Unless otherwise stated, 'acts' and 'partners' in the studies with sex workers refer to those with clients, and condom and spermicide use refers to that used with clients. [b]Unless otherwise stated, the percentages in this column refer to the average percentage of sex acts in which a condom is used. [c]Unless otherwise stated, the percentages in this column refer to the average percentage of sex acts in which a condom is not used but spermicide is used. [d]Comparing condom use after in spermicide/hierarchical message arm with that in condom-only arm. [e]Comparing condom use after with condom use at baseline. [f]Personal communication with Erica Gollub; January 2002. [g]ACTIVE in this column denotes that there was no data on the rate of sexual partner change in the paper but that it did highlight that the people were sexually active. [h]45% of the non-male-condom-protected sex acts were protected by female condom or N-9 products (vaginal suppositories, film, gel).

where E is the average probability that an individual is protected for one sex act, in a partnership. We call this the 'use-effectiveness' against HIV of a method used in a particular partnership. It is given by the product of the clinical efficacy of the method against HIV transmission and the average consistency that it is used in the partnership. Also, p is the probability that a selected sexual partner is HIV infected; h is the probability that an HIV infected partner has high viraemia; s is the probability that within a partnership at least one person has an STD; m is the average number of sexual partnerships the person has over the fixed time-period; n is the average number of sex acts per partnership during the fixed time-period; β is the probability of HIV transmission per sex act; α is the multiplicative increase in the per sex act probability of HIV transmission during the high viraemia phase; and δ is the multiplicative increase in the per sex act probability of HIV transmission in the presence of another STD.

An analogous equation (not including the high viraemia and STD multiplicative co-factors) can also be used to describe the probability of STD transmission. In both cases, the main assumption is that the probability of transmission per sex act is independent of previous sex acts. It is a static model considering only one-way transmission of HIV over a fixed time-period and so is most reliable over short timeframes.

In this paper we use the equation in three ways. Firstly, we compare the protection provided against HIV and STDs by using either condoms only or microbicides only, with various consistencies, to identify when microbicides alone would provide more protection than condoms alone. Secondly, we compare the protection provided by condoms used alone at various consistencies with the protection provided by condoms and microbicides, allowing for the possibility that condom-consistency may decline following microbicide introduction. This is used to identify the 'break-even point' at which an individual is equally protected after microbicide introduction as before, assuming a microbicide HIV- and STD-efficacy of 50%. We choose an efficacy of 50% for illustrative purposes to look at the impact of a low-efficacy microbicide and the effect of migration from a high-efficacy method, namely condoms. We assume that condoms are 95% HIV- and STD-efficacious. This is a high estimate [19,20,39], that will produce conservative estimates of the amount of migration that can be tolerated without increasing risk. Thirdly, we develop a case-example from Cotonou, Benin, to explore how different patterns of condom and microbicide use in a specific setting interact to affect HIV-risk in four different groups: sex workers, the clients of sex workers, women with multiple sexual partners, and women in monogamous HIV-discordant partnerships. For this exercise, we use equation (1) with epidemiological and behavioural data from Cotonou [40–42] and the scientific literature [43–48], and consider the introduction of a 50% HIV- and STD-efficacious microbicide, assuming 10% condom migration. Cotonou was chosen for the case-example because comparable data for different groups were available, and Cotonou has already been a site for a phase II/III microbicide trial and is likely to be involved in future microbicide trials [30].

The estimates of microbicide-consistency are based on those of spermicide-consistency from the studies in Table 1. Two of these studies do not have the required available data. Five of the remaining seven studies report 50–90% of non-condom-protected sex acts being protected by spermicide. The other two studies indicate a low consistency of spermicide use. The reasons for this are uncertain but may be linked to the study populations in these studies being women with relatively low levels of sexual activity attending a family planning clinic in Texas or drug abusers at a medical centre in Miami. Overall, the studies in Table 1 indicate that high microbicide-consistency may be attained in many settings.

E is a measure of how a method of protection alters an individual's HIV-risk. The probability (π) that a susceptible person, using a particular method of protection, becomes HIV infected over a fixed time-period decreases as the use-effectiveness (E) increases. Any comparison of the risk of HIV infection associated with the use of different methods reduces mathematically to a comparison of the use-effectiveness of the different methods. Consequently, microbicides provide more protection than condoms if the use-effectiveness of microbicides is greater than the use-effectiveness of condoms. Within a partnership, for example, the protection provided by a microbicide of 50% HIV- and STD-efficacy used with 40% consistency is greater than that provided by condoms (95% HIV- and STD-efficacy) used with 20% consistency.

Similarly, we can compare an individual's HIV-risk before and after microbicide introduction. The use-effectiveness against HIV of condoms used with average consistency (percentage of sex acts in which a condom is used) f_o in each partnership is $E_c = f_o e$, where e is the per sex act HIV-efficacy of condoms. The use-effectiveness against HIV of condoms, used with average consistency f_R in each partnership after microbicide introduction, and microbicides, used in a proportion M of sex acts in which a condom is not used, is $E_m = f_R e + (1 - f_R)Mb$. Here b is the per sex act HIV-efficacy of microbicides. The level of HIV protection provided by condoms and microbicides will be greater than the protection provided by condoms alone if the use-effectiveness of condoms and microbicides is greater than the use-effectiveness of condoms alone ($E_m > E_c$), which can be written:

$$f_R e + (1 - f_R) Mb > f_o e \quad (2)$$

This inequality can be used to identify the maximum absolute drop in condom-consistency (condom migration) that could be tolerated following microbicide introduction without increasing HIV-risk.

Results

From equation (2) we can identify the minimum consistency of condom use that can be tolerated after microbicide introduction ($f_R{}^*$) without increasing an individual's HIV-risk:

$$f_R{}^* = \frac{f_0 - M\lambda}{1 - M\lambda}, \quad (3)$$

where $\lambda = b/e$ is the ratio of the clinical efficacies against HIV of microbicides to condoms, and f_0 and M are as defined in the Methods. We will refer to this threshold ($f_R{}^*$) as the 'break-even point'.

Likewise, an analogous condition applies for STDs. To ensure that microbicide introduction results in the reduction of an individual's risk of both HIV and STDs we need λ to be the smallest of the relative clinical HIV-efficacy of microbicides to condoms, and their relative clinical STD-efficacy. For the rest of this analysis we assume that the λs are the same and by efficacy we mean efficacy against both HIV and STDs.

It can be seen from equation (3) that while the underlying probability of infection (π) is affected by the number of sexual partners and acts, and the underlying HIV/STD prevalence, these do not affect the break-even point. This suggests that the break-even point will be the same irrespective of the epidemiological setting in which microbicides are introduced. Although HIV-risk varies substantially between settings, the break-even point results from comparing solely the protection provided by different methods within the same risk context; thus, these factors do not determine when microbicide introduction will be beneficial. The break-even point depends only on the relative efficacy of microbicides to condoms, and the consistency with which they are used.

From equation (3), the maximum amount of migration that can be tolerated without increasing HIV-risk is greater for a higher relative clinical efficacy of microbicides to condoms (λ), for a higher consistency of microbicide use when condoms are not used (M), or for a lower initial condom-consistency (f_0).

Finally, equation (3) can be used to identify the consistency of microbicide use required to ensure that total migration (condoms not used) will not increase risk. For this, the consistency of microbicide use must be greater than the ratio of the initial condom-consistency and the relative efficacy of microbicides to condoms $M > f_0/\lambda$.

Further insights can be gained by looking at the relationship between the initial condom-consistency and the break-even point, for a microbicide that is 50% efficacious, for different levels of microbicide use (Fig. 1).

The point where each plot line meets the f_0-axis indicates the initial condom-consistency at which, for a specific microbicide-consistency, total migration can occur without increasing risk. For example, if micro-

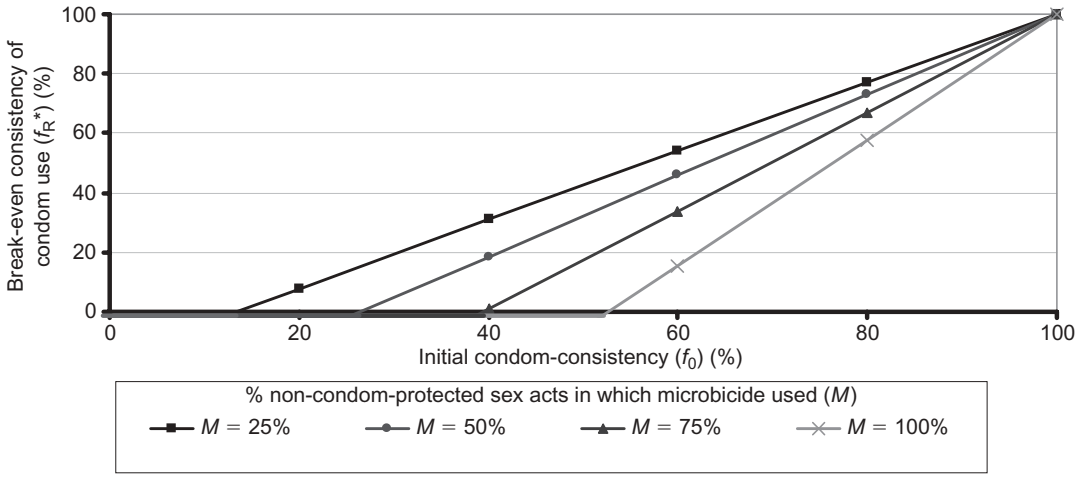

Fig. 1. 'Break-even' consistency of condom use following the introduction of a 50% HIV- and sexually transmitted disease-efficacious microbicide.

bicides are used in 75% of non-condom-protected sex acts, then total migration can be tolerated if before microbicide introduction condoms are used less than 39% of the time.

The case study from Cotonou, Benin, illustrates how microbicide introduction may affect HIV-risk in four different groups. The most prevalent STD in Cotonou, for which there is available data, is *Neisseria gonorrhoeae* [24,41,42]. Table 2 compares an individual's monthly risk of HIV infection (π) before and after the introduction of a 50% efficacious microbicide, assuming a 10% absolute reduction in the consistency of condom use afterwards. The results show that the percentage reduction in the probability of HIV transmission increases for a lower initial condom-consistency and as microbicide use increases.

Table 2 illustrates that, under most conditions, the introduction of microbicides in this setting would be beneficial. The only scenarios of potential concern are where condom use is initially very high (90%) and microbicides are used in 50% or 75% of non-condom-protected sex acts. In these cases there is an increase in π, indicating an increased risk. However, if a microbicide is used in all acts not protected by a condom, this increased risk disappears.

We conducted a sensitivity analysis on these projections for different microbicide efficacies and found that if the efficacy is 30% then the scenarios that cause an increase in HIV-risk include those where initial condom-consistency is moderate ($\sim$ 50%), and not just when it is very high (90%) which was the case for a microbicide efficacy of 50%. Similarly, if the efficacy is 70% then the initial condom-consistency has to be very high (90%) and microbicide use has to be moderate or lower ($\leqslant$ 50% of non-condom-protected sex acts) for there to be an increase in HIV-risk.

Although the negative numbers in Table 2 highlight that care is needed when counselling consistent condom-users about microbicides, the results do not imply that introducing microbicides at a population level will not be beneficial. Using figures from Table 2, we can estimate the number of 'new recruits' (non-condom-users who start to use microbicides) that are required to balance any shifts away from condom use among high-consistency condom-users. Assuming microbicides are used in 50% of non-condom-protected sex acts, the static model suggests the following. For every four high-consistency condom-users who reduce from 90% to 80% consistency, only one new recruit is required in order to have a positive impact on HIV at a population level.

Equation (1) and the context specific data from Benin can be used to identify, for this setting, what level of condom- and microbicide-consistency must be achieved after microbicide introduction to reduce HIV-risk by various degrees. Table 3 shows the condom- and microbicide-consistency required to break-even or reduce the risk of HIV infection by 20%.

The results provide several important insights about whether migration should be a concern amongst sub-populations with different levels of condom use. Under most circumstances, there will be no increase in HIV-risk if moderate microbicide use is achieved. For example, if a 50% efficacious microbicide is used in 50% of sex acts not protected by condoms then for all partnerships:

- low-consistency condom-users (30%) could reduce condom-consistency to 5% without increasing HIV-risk;
- medium-consistency condom-users (50%) could reduce to 32% consistency and still break-even;
- high-consistency condom-users (70%) could reduce condom use to 59%; and
- very high-consistency condom-users (90%) could reduce condom use to 86%.

If microbicides are used in all non-condom-protected sex acts then for all partnerships:

- low- and medium-consistency condom-users could cease condom use and still break-even;
- high-consistency condom-users could reduce condom use to 37%; and
- very high-consistency condom-users could reduce condom use to 79%.

For the partnerships considered, if condoms are initially used in 70% or less of sex acts, and if there is no reduction in condom-consistency following microbicide introduction, there will be a 20% or greater reduction in HIV-risk as long as microbicides are used in 50% of non-condom-protected sex acts. If microbicides are used more consistently, a 20% reduction in HIV-risk can be achieved even with substantial condom migration, particularly if condoms are used with 50% consistency or less before microbicide introduction.

Discussion

First, the analysis illustrates how the level of protection provided by a product is determined by its use-effectiveness. Therefore, if an 'easy to use' method is used twice as often as a method that is twice as HIV- and STD-efficacious, then both methods will provide the same amount of protection against HIV and STD

Table 2. Comparison of the percentage of susceptibles becoming HIV infected per month before and after microbicide introduction, assuming a 10% absolute reduction in condom-consistency.

Initial condom-consistency (f_0) (%)	Condom-consistency after microbicide introduction (f_R) (%), assuming a 10% absolute drop in condom-consistency	Non-condom-protected sex acts in which microbicide used (M) (%)	%π: Percentage of susceptibles becoming HIV infected per month before microbicide introduction (CO) and after microbicide introduction (CM) for different hypothetical scenarios of microbicide introduction											
			Sex workers			Clients			Women with multiple partners			Women in monogamous discordant partnerships		
			%π CO	%π CM	% reduction in π	%π CO	%π CM	% reduction in π	%π CO	%π CM	% reduction in π	%π CO	%π CM	% reduction in π
0	0	50	14.0	10.7	**24**	1.8	1.3	**25**	0.22	0.17	**22**	0.85	0.66	**23**
0	0	75	14.0	9.0	**36**	1.8	1.1	**37**	0.22	0.15	**33**	0.85	0.56	**34**
0	0	100	14.0	7.3	**48**	1.8	0.9	**50**	0.22	0.12	**45**	0.85	0.46	**46**
30	20	50	10.2	8.8	**14**	1.3	1.1	**15**	0.17	0.14	**13**	0.63	0.55	**13**
30	20	75	10.2	7.4	**28**	1.3	0.9	**29**	0.17	0.12	**6**	0.63	0.47	**26**
30	20	100	10.2	6.0	**41**	1.3	0.7	**43**	0.17	0.10	**39**	0.63	0.38	**40**
50	40	50	7.6	6.9	**10**	0.9	0.8	**10**	0.13	0.11	**9**	0.48	0.43	**10**
50	40	75	7.6	5.8	**24**	0.9	0.7	**25**	0.13	0.10	**22**	0.48	0.37	**23**
50	40	100	7.6	4.7	**38**	0.9	0.6	**39**	0.13	0.08	**36**	0.48	0.30	**37**
70	60	50	4.9	4.9	**1**	0.6	0.6	**1**	0.08	0.08	**1**	0.32	0.31	**1**
70	60	75	4.9	4.1	**16**	0.6	0.5	**16**	0.08	0.07	**15**	0.32	0.27	**15**
70	60	100	4.9	3.4	**31**	0.6	0.4	**31**	0.08	0.06	**30**	0.32	0.22	**30**
90	80	50	2.2	2.8	**−31**	0.3	0.3	**−31**	0.04	0.05	**−29**	0.14	0.19	**−30**
90	80	75	2.2	2.5	**−14**	0.3	0.3	**−14**	0.04	0.04	**−13**	0.14	0.16	**−13**
90	80	100	2.2	2.1	**3**	0.3	0.2	**3**	0.04	0.04	**3**	0.14	0.14	**3**

Parameters: Sex workers (prevalence values and number of clients per sex worker based on data from Benin): p = 0.084; gonorrhoea prevalence in sex workers = 0.21 and in clients = 0.054 (s = 0.253); m = 55.3 per month; n = 1 per partner per month. Clients (prevalence values and number of sex workers per client based on data from Benin): p = 0.407; gonorrhoea prevalence in sex workers = 0.21 and in clients = 0.054 (s = 0.253); m = 2.7 per month; n = 1 per partner per month. Women with multiple partners (HIV prevalence value based on data from Benin STD clinics): p = 0.028; estimated gonorrhoea prevalence in STD clinics ∼ 0.02 (s = 0.040); m = 2 per month; n = 5 per partner per month. Women in monogamous discordant partnerships (STD prevalence value based on data from Benin general population): p = 1, gonorrhoea prevalence in general population = 0.01 (s = 0.020); m = 1/6 per month; n = 8 per month. Condom-efficacy against HIV and STDs (e) = 95%; microbicide-efficacy against HIV and STDs (b) = 50%; average percentage of HIV infected individuals with high viraemia (h) = 20%; probability of HIV transmission per sex act (β) = 0.002 (0.001 for transmission to clients); multiplicative increase in the per sex act probability of HIV transmission during the high viraemia phase (α) = 10; multiplicative increase in the per sex act probability of HIV transmission during the presence of an STD (δ) = 20.

Table 3. Minimum consistency of condom use to achieve a 20% reduction in HIV-risk (π) following the introduction of a 50% HIV- and STD-efficacious microbicide.

		Minimum consistency of condom use following microbicide introduction (%)		
		Break-even (absolute drop in condom-consistency)	20% reduction in π, HIV-risk (absolute drop in condom-consistency)	
Initial condom-consistency f_0 (%)	Non-condom-protected sex acts in which microbicide is used M (%)	All partnerships f_R* (%)	Client and SW partnerships (Benin) f_R (%)	Monogamous discordant and multiple partners (Benin) f_R (%)
30	50	5 (25)	26 (4)	28 (2)
30	75	0 (30)	10 (20)	12 (18)
30	100	0 (30)	0 (30)	0 (30)
50	50	32 (18)	48 (2)	49 (1)
50	75	17 (33)	36 (14)	38 (12)
50	100	0 (50)	19 (31)	20 (30)
70	50	59 (11)	69 (1)	70 (0)
70	75	50 (20)	63 (7)	63 (7)
70	100	37 (33)	52 (18)	53 (17)
90	50	86 (4)	91 (−1)	91 (−1)
90	75	83 (7)	89 (1)	89 (1)
90	100	79 (11)	86 (4)	86 (4)
		Parameter values (for efficacy) as in Table 2	Parameter values as in Table 2 (based on data from Benin)	

π is an individual's per month risk of HIV infection.
SW, sex worker.

infection. This highlights that both efficacy and factors affecting consistency need to be considered and given equal weighting in the process of microbicide development. For example, a vaginal ring which gradually releases microbicide over many sex acts may have an advantage over a higher efficacy microbicide that needs to be applied before every sex act [49].

Second, the analysis shows that the maximum amount of condom migration that can be tolerated is greater for higher levels of microbicide efficacy and consistency of use but also for lower initial levels of condom-consistency. If few sex acts were previously protected by condoms, microbicides will have a greater potential to reduce HIV transmission and so it is worse for a high condom-consistency-user than for a low condom-consistency-user to migrate by 10%.

The results indicate that there are likely to be many situations in which the benefits of microbicide use outweigh the negative impact of condom migration. For a 50% efficacious microbicide, if the initial condom-consistency is moderate (50%), and microbicides are used in 50–100% of non-condom-protected sex acts, 18–50% fewer sex acts can be protected by condoms with no increase in risk. Migration from the condom may, however, be a potential problem among groups who initially use condoms with high levels of consistency ($> 70\%$), and use microbicides with low consistency ($< 50\%$ of non-condom-protected acts). This highlights the importance of microbicides for women who use condoms inconsistently but could use microbicides consistently, such as women whose partners do not object to methods of protection being used but dislike condoms.

The break-even point is exclusively determined by the relative efficacy of microbicides to condoms, and the consistency with which they are used. Therefore, the decision whether to introduce microbicides into a population can be made independently of the prevalence of HIV/STDs and the number of sexual partners and acts people have in that setting. This is an important finding since accurate sexual behaviour data is hard to obtain due to its sensitive nature and the collection of epidemiological data is a costly process.

We were concerned in this analysis with whether migration from the condom would lead to an increased HIV-risk. These results illustrate that there are many situations where we would break-even. However, we do not want to just break-even, but to reduce HIV-risk. For the scenarios considered in the Benin case-study, if condoms are used in 70% or less of sex acts before microbicide introduction and their consistency does not decrease afterwards, then the

introduction of a 50% efficacious microbicide will result in at least a 20% reduction in HIV-risk if it is used in half of the non-condom-protected sex acts. These results give insights into the likely impact of microbicides in different settings, which can be used to guide trial design.

The analysis provides insights into the extent to which migration from the condom could potentially be a concern at an individual level. Using a static model, however, means we cannot estimate how a microbicide may impact on the HIV epidemic. For this, dynamic modelling is required. Dynamic modelling could also be used to estimate the break-even point for a microbicide that is only efficacious against HIV and not other STDs, and to explore the potential impact and cost-effectiveness of microbicide introduction in different settings [50,51]. Future work will examine these issues.

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