Country-wide distribution of the nitrile female condom (FC2) in Brazil and South Africa: a cost-effectiveness analysis

David W. Dowdy[a], Michael D. Sweat[b] and David R. Holtgrave[c]

Objective: To evaluate the cost-effectiveness and potential impact of expanded female condom distribution.

Design: Cost-effectiveness analysis assessing HIV infections averted annually and incremental cost per HIV infection averted for country-wide distribution of the nitrile female condom (FC2) among sexually active individuals, 15–49 years, with access to publicly distributed condoms in Brazil and South Africa.

Results: In Brazil, expansion of FC2 distribution to 10% of current male condom use would avert an estimated 604 (5–95th percentiles, 412–831) HIV infections at $20 683 (5–95th percentiles, 13 497–29 521) per infection averted. In South Africa, 9577 (5–95th percentiles, 6539–13 270) infections could be averted, at $985 (5–95th percentiles, 633–1412) per infection averted. The estimated cost of treating one HIV-infected individual is $21 970 (5–95th percentiles, 18 369–25 719) in Brazil and $1503 (5–95th percentiles, 1245–1769) in South Africa, indicating potential cost savings. The incremental cost of expanded distribution would be reduced to $8930 (5–95th percentiles, 5864–13 163) per infection averted in Brazil and $374 (5–95th percentiles, 237–553) in South Africa by acquiring FC2s through a global purchasing mechanism and increasing distribution threefold. Sensitivity analyses show model estimates to be most sensitive to the estimated prevalence of sexually transmitted infections, total sexual activity, and fraction of FC2s properly used.

Conclusions: Expanded distribution of FC2 in Brazil and South Africa could avert substantial numbers of HIV infections at little or no net cost to donor or government agencies. FC2 may be a useful and cost-effective supplement to the male condom for preventing HIV.

AIDS 2006, **20**:2091–2098

Keywords: HIV, prevention, female condom, economic evaluation, modeling

Introduction

The male condom is a cornerstone of HIV prevention efforts worldwide. Consistent condom use may reduce HIV incidence by 95% per act [1], and over 700 million condoms are provided annually by donors and governments to sub-Saharan Africa alone [2]. Nevertheless, male condom use remains limited, particularly among women in developing countries [3], thus spurring efforts to identify female-controlled methods of HIV prevention to supplement the male condom [4].

The first female-controlled barrier method for HIV prevention, the polyurethane female condom, has similar efficacy to the male condom in preventing HIV and other sexually transmitted infections (STI) [5–7]. More importantly, simultaneous availability of female and male condoms may lead to higher rates of protected sex than if

From the [a]Department of Epidemiology, the [b]Department of International Health, and the [c]Department of Health, Behavior, & Society, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.

Correspondence to Professor D. Holtgrave, Department of Health, Behavior & Society, Johns Hopkins Bloomberg School of Public Health, 624 Broadway, Suite 280, Baltimore, MD 21205, USA.

E-mail: dholtgra@jhsph.edu
Received: 10 May 2006; accepted: 20 July 2006.

only male condoms are available [8–12]. However, polyurethane female condoms cost 10 to 20 times more than male condoms [13]. Although a hypothetical female condom program for South African sex workers was cost-effective [14], it is uncertain whether these results would generalize to a larger population.

In October 2005, a second-generation nitrile female condom was released under the name FC2. FC2 offers equivalent protection and pricing to the existing polyurethane female condom [15,16]. However, when distributed in larger volumes, FC2 can be manufactured at much lower cost. To evaluate the total cost and potential impact of such distribution, the current study modeled the cost-effectiveness of country-wide FC2 purchase and distribution, from a donor or government perspective, in Brazil and South Africa, two countries representative of different stages in the HIV pandemic.

Methods

Model description

Separate models were constructed for Brazil and South Africa to include the populations aged 15–49 years who were sexually active in the preceding year. Both countries have established public-sector programs that provide male and female condoms, as well as treatment for AIDS. Taking the perspective of a donor or government agency, incremental cost-effectiveness was estimated by comparing FC2 distribution at existing levels in each country (at which the price of FC2 is the same as that of the polyurethane female condom) with hypothetical programs in which FC2 was purchased and distributed at three levels such that FC2 use equalled 3%, 10%, and 30% of estimated male condom use. Measured costs included all costs of acquisition and distribution currently borne by the public sector, and effectiveness was measured as the number of HIV infections averted. The primary outcome was the incremental cost of FC2 expansion per HIV infection averted. This was compared with the estimated cost, per HIV-infected individual, of antiretroviral therapy (ART) in each country. Prevention of pregnancy or other STI, as well as any costs/savings to entities other than the public sector (e.g., patient time to attend clinic, savings owing to averted hospitalizations) were not considered. The incremental costs and effectiveness associated with 1 year of condom distribution were modeled. Costs are reported in 2005 US dollars, with future costs and benefits (i.e., averted cost of treating individuals with incident HIV) discounted at 3%, including sensitivity analysis for 0 and 7% discounting.

Model assumptions: epidemiology

Tables 1 and 2 provide the parameter values used in the Brazilian and South African models, respectively. The modeled population size and HIV prevalence were

Table 1. Model assumptions, Brazil.

Parameter	Base-case estimate	Range	Data source
Epidemiological parameters			
Population size (millions)[a]	25.3		[17]
HIV prevalence (%)			[17]
Male	0.9	0.6–1.1	
Female	0.5	0.4–0.6	
Costs (in US$)			
Unit cost of acquisition			[b]
Present volume	0.69		
Low volume[c]	0.59		
Moderate volume[c]	0.54		
High volume[c]	0.40		
Global purchasing[d]	0.22		
Unit cost of transportation/ insurance	0.025		[b]
Annual cost of HIV treatment, per patient	2500	1875–3125	[21]
Duration of HIV treatment, per patient (years)	10	7.5–12.5	Assumed
Annual discount rate	0.03	0–0.07	
HIV transmission parameters			
STI prevalence (%)			
Ulcerative, male	2.0	0–4.1	[17,26]
Ulcerative, female	2.3	0–4.7	[17,26]
Non-ulcerative, male[e]	0.8	0–1.6	[16]
Non-ulcerative, female[e]	1.5	0–2.9	[16]
HIV transmission probability, per sex act			[25]
No STI, female to male	0.001		
No STI, male to female	0.002		
Non-ulcerative STI, female to male	0.01		
Non-ulcerative STI, male to female	0.02		
Genital ulcerative disease	0.06		
Annual number of sex acts, per person	45.0	33.8–56.2	[11,17]
Annual number of sexual partners			[17]
Male	2.4	1.0–4.1	
Female	1.2	1.0–1.4	
Efficacy in preventing HIV			
Male condom	0.95	0.9–1.0	[1]
FC2	0.95	0.9–1.0	[5–7]
Fraction of distributed FC2s used correctly			Assumed
Low volume[c]	0.95	0.71–1.0	
Moderate volume[c]	0.85	0.64–1.0	
High volume[c]	0.75	0.56–1.0	
Fraction of sex acts protected			
Male condom	0.38	0.29–0.48	[17]
FC2, low volume[c]	0.011	0.009–0.014	
FC2, moderate volume[c]	0.04	0.03–0.05	
FC2, high volume[c]	0.11	0.09–0.14	
Fraction of sex acts protected by FC2 otherwise protected by male condom	0.12	0–0.25	[11]

FC2, second-generation nitrile female condom; STI, sexually transmitted infection.
[a]Age 15–49 years, sexually active in past year, with access to public-sector condom program.
[b]Price estimates provided by the Female Health Company, Chicago, Illinois, USA.
[c]The number of FC2s used was assumed to be 3% (low volume), 10% (moderate volume), or 30% (high volume) of the number of male condoms used.
[d]Assumes high (30%) volume, but a price based on a global purchase of 300 million FC2s.
[e]In patients without ulcerative STI.

Table 2. Model assumptions, South Africa.

Parameter	Base-case estimate	Range	Data source
Epidemiological parameters			
Population size (millions)[a]	16.8		[18]
HIV prevalence (%)			[18]
Male	15.9	13.0–18.8	
Female	21.6	18.5–24.6	
Costs (in 2005 US$)			
Unit cost of acquisition			[b]
Existing volume	0.87		
Low volume[c]	0.59		
Moderate volume[c]	0.54		
High volume[c]	0.40		
Global purchasing[d]	0.22		
Unit cost of distribution, training, education			[b]
Low volume[c]	0.18		
Moderate volume[c]	0.11		
High volume[c]	0.05		
Global purchasing[d]	0.03		
Annual cost of HIV treatment, per patient	208		[22]
Duration of HIV treatment, per patient (years)	8.0	6.0–10.0	Assumed
Annual discount rate	0.03	0–0.07	
HIV transmission parameters			
STI prevalence (%)			
Ulcerative, male	3.0	0–5.9	[29,30]
Ulcerative, female	3.0	0–5.9	[29,30]
Non-ulcerative, male[e]	1.5	0–3.0	[29]
Non-ulcerative, female[e]	2.7	0–5.3	[29]
HIV transmission probability, per sex act			[25]
No STI, female to male	0.001		
No STI, male to female	0.002		
Non-ulcerative STI, female to male	0.01		
Non-ulcerative STI, male to female	0.02		
Genital ulcerative disease	0.06		
Annual number of sex acts, per person	54.9	41.2–68.7	[18]
Annual number of sexual partners			[18]
Male	1.5	1.0–2.2	
Female	1.2	1.0–1.4	
Efficacy in preventing HIV			
Male condom	0.95	0.9–1.0	[1]
FC2	0.95	0.9–1.0	[5–7]
Fraction of distributed FC2s used correctly			Assumed
Low volume[c]	0.95	0.71–1.0	
Moderate volume[c]	0.85	0.64–1.0	
High volume[c]	0.75	0.56–1.0	
Fraction of sex acts protected			
Male condom	0.30	0.23–0.38	[18]
FC2, low volume[c]	0.009	0.007–0.011	
FC2, moderate volume[c]	0.03	0.02–0.04	
FC2, high volume[c]	0.09	0.07–0.11	
Fraction of sex acts protected by FC2 otherwise protected by male condom	0.13	0–0.26	Assumed

FC2, second-generation nitrile female condom; STI, sexually transmitted infection.
[a]Age 15–49 years, sexually active in past year, with access to public-sector condom program.
[b]Price estimates provided by the Female Health Company, Chicago, Illinois, USA.
[c]The number of FC2s used was assumed to be 3% (low volume), 10% (moderate volume), or 30% (high volume) of the number of male condoms used.
[d]Assumes high (30%) volume, but a price based on a global purchase of 300 million FC2s.
[e]In patients without ulcerative STI.

estimated from population-based surveys that provided data on age, HIV status, and sexual activity in the past year [17,18]. The population size in the Brazilian model was also multiplied by a factor of 0.34 to simulate the proportion of the sexually active population with access to publicly acquired condoms [19]. By contrast, more than 90% of condoms procured in South Africa are provided through the public sector [20], and universal access was assumed.

Model assumptions: costs

The incremental cost of an expanded FC2 program was estimated in Brazil as $[v_e(c_e + i_e) - v_i(c_i + i_i)]$, where c is the unit cost of acquisition (market price), i the unit cost of insurance and transportation, and v the volume of distribution; subscripts e and i refer to the expanded and initial program, respectively. The estimated unit cost for FC2 at different levels of distribution was obtained from the manufacturer (Female Health Company, Chicago, Illinois, USA). The FC2 manufacturer reported that, in Brazil, transportation and insurance comprise the only additional costs of the female condom program funded by the Brazilian government. In South Africa, rather than adding a cost for insurance and transportation, the FC2 unit acquisition cost was multiplied by a percentage to account for distribution, training of program staff, and education/outreach, in accordance with that country's current practices. The 30% increase at low distribution volume reflected the costs associated with the current female condom program in South Africa (Female Health Company). The cost of ART in Brazil was estimated by assuming a constant annual per-person cost, as reported by the Ministry of Health in 2005, for 10 years, starting in 2006 [21]. In South Africa, this estimate was taken as the annual projected cost of a program planned by the Ministry of Health to provide ART to a significant portion of its population [22], divided by the estimated HIV-positive population of that country in 2005, and multiplied (with discounting) by an estimated 8-year lifespan after HIV infection [18,23].

Model assumptions: HIV infections averted

The incremental number of HIV infections averted by FC2 distribution was estimated using the formula [24]: probability of HIV infection $= 1 - \{P[1 - R(1 - FE)]^N + (1 - P)\}^M$, where P is the average HIV prevalence among sexual partners of the target population, R is the risk of HIV transmission per unprotected sex act (infectivity), F is the fraction of sex acts when a condom (male or female) is used correctly, E is the effectiveness of condoms, N is the average number of sex acts per partner, and M the average number of sex partners. Based on previously published models validated to predict HIV incidence [25], it is estimated that the probability of HIV transmission for a single unprotected vaginal sex act is 0.001 (female to male) or 0.002 (male to female). This probability was multiplied tenfold in the presence of non-ulcerative

STI and was estimated to be 0.06 per sex act in the presence of genital ulcerative disease.

In Brazil, the point prevalence of genital ulcerative disease was calculated by multiplying the herpes simplex virus 2 seroprevalence [26] by the average duration of disease and frequency of recurrent symptoms [27], and adding to that the syphilis prevalence in pregnant women [17]. The estimated prevalence of non-ulcerative STI was based on the annual prevalence of symptomatic STI [17], assuming a symptomatic duration of 10 days for men and 18 days for women [28], and that 25% of those infected were infected one additional time in the preceding 3 months. In South Africa, genital ulcerative disease prevalence was estimated as the prevalence of genital ulceration in the past 3 months [29], assuming that 72% of these ulcers represented syphilis or chancroid (with a detection rate of 85% and disease duration of 90 days) and 28% represent herpes simplex virus 2 (detection rate of 30% and disease duration as above) [30]. Non-ulcerative STI prevalence was estimated as for Brazil, using painful urination or discharge as a proxy for disease [29].

To estimate the mean annual number of sexual partners in Brazil, data were used from a population-based survey on lifetime sexual practices [17], assuming that individuals with more than 10 lifetime partners had five partners per year, while other sexually active individuals had one partner per year. The number of sex acts per year was estimated by applying a Poisson distribution to the reported frequency of sexual intercourse in the preceding week among sexually active urban women [11]. In South Africa, 13.5% of men and 3.9% of women reported having sex with more than one partner in the preceding year [18]; these individuals were assumed to have a mean of four partners per year. The annual number of sex acts was reported directly [18]. Our model excluded extreme partnership rates, thus describing a general population where many male-to-female HIV transmissions occur between men with higher partnership rates than women. By contrast, all individuals, regardless of sexual frequency, contributed to the estimate of total sex acts.

The estimates of male and female condom effectiveness assumed that the devices are equally effective in preventing HIV infection when used correctly [1,5–7], regardless of the presence or absence of other STI, including genital ulcerative disease. Rates of male condom use were obtained from population-based surveys [17,18]; rates of FC2 distribution were calculated such that the number of FC2s correctly used would equal 3%, 10%, and 30% of the total volume of male condoms correctly used in each country. Condoms used incorrectly were assumed to have no effectiveness. It was assumed that the percentage of FC2s purchased at the government or donor level correctly used would be 95%, 85%, and 75%, respectively, at these three distribution levels. A pilot study in Brazil [11] suggested that 12% of sex acts protected by female condoms would have been protected by male condoms in the absence of available female condoms; no such data are available from South Africa, and a similar rate was assumed in that country.

Sensitivity analysis

Sensitivity analysis on the incremental cost per HIV infection averted was performed by simultaneously varying the model parameters in Tables 1 and 2, as shown. Triangular probability distribution functions were applied to each parameter for sensitivity analysis. When data from the literature were unavailable to suggest a high and low range, these values were taken to be 125% and 75%, respectively, of the most likely value. Parameters with higher degrees of uncertainty (e.g., rate of correct FC2 use) were varied over a wider range. The model was simulated using the Latin hypercube algorithm (@Risk; Palisade Corp., Newfield, New York, USA), which systematically generates values of model parameters that are similar to the defined probability distribution across simulation iterations. Iterations of the model were performed until variations in the output parameters (total cost or HIV infections averted) were less than 1.5% in both mean and standard deviation, a process that required thousands of simulations per model iteration. The results of this process were used to perform multivariate sensitivity analysis, and to estimate variability by generating intervals bounded by the 5th and 95th percentiles of all simulations on each given parameter (i.e., 90% of simulations will fall in this interval), assuming that underlying probability functions as described. One-way sensitivity analyses were performed by varying each parameter of interest and recording the resulting model outcome.

Results

The number of sex acts protected by publicly distributed male condoms in 2005 was estimated by our models at 219 million in Brazil and 138 million in South Africa. The estimated incremental cost (excluding savings from averted HIV treatment) to protect one-tenth as many sex acts with FC2 was $12.1 million [5–95th percentiles (90% of simulations), 8.1–16.9 million) in Brazil and $9.1 million (5–95th percentiles, 6.3–12.5 million) in South Africa (Table 3). Distributing FC2 at 30%, rather than 10%, of male condom volume was estimated to cost $33.5 million (5–95th percentiles, 23.2–45.7 million) in Brazil and $22.5 million (5–95th percentiles, 15.6–30.4 million) in South Africa, although these incremental costs could be reduced by nearly 50% by joining a global purchasing scheme with a total FC2 volume of 300 million units. All analyses below refer to the models of expanded FC2 distribution at 10% of male condom volume.

Table 3. Cost-effectiveness of country-wide FC2 distribution, versus existing programs[a].

Country/ distribution level[b]	FC2 volume distributed [$\times 10^6$] (5–95th percentiles[c])	Incremental program cost[c] [$\$ \times 10^6$] (5–95th percentiles[c])	Incremental HIV infections averted [$\times 10^3$] (5–95th percentiles[c])	Incremental cost[d] per infection averted [$\$ \times 10^3$] (5–95th percentiles[c])	Cost of ART, initiated in 2006 [$\$ \times 10^3$] (5–95th percentiles[c])[e]
Brazil					
Low	7.4 (5.6–9.2)	1.8 (0.6–3.2)	0.1 (0–0.2)	19.0 (8.8–31.6)	22.0 (18.2–25.8)
Moderate	26.2 (20.0–32.9)	12.1 (8.1–16.9)	0.6 (0.4–0.9)	20.7 (13.4–29.6)	22.0 (18.3–25.8)
High	84.8 (66.1–105.1)	33.5 (23.2–45.7)	2.0 (1.4–2.8)	16.9 (11.2–23.8)	22.0 (18.2–25.8)
Global[f]	84.2 (64.4–104.9)	17.8 (12.1–24.7)	2.0 (1.4–2.8)	8.9 (5.8–13.2)	21.9 (18.3–25.8)
South Africa					
Low	4.7 (3.5–5.9)	1.9 (0.9–3.0)	1.9 (1.1–2.8)	1.0 (0.5–1.7)	1.5 (1.2–1.8)
Moderate	16.6 (13.0–20.9)	9.1 (6.3–12.5)	9.6 (6.5–13.3)	1.0 (0.6–1.5)	1.5 (1.2–1.8)
High	53.7 (41.5–67.4)	22.5 (15.6–30.4)	32.0 (21.9–44.6)	0.7 (0.4–1.1)	1.5 (1.2–1.8)
Global[f]	53.3 (40.3–66.8)	11.3 (7.7–15.4)	31.4 (21.3–43.7)	0.4 (0.2–0.6)	1.5 (1.2–1.8)

FC2, second-generation nitrile female condom.
[a]Costs are expressed in 2005 US$.
[b]FC2 use estimated as 3% (low), 10% (moderate), or 30% (high, global) of male condom use.
[c]Bounded by the 5th and 95th percentiles of all multivariate simulations, as described in the Methods.
[d]Excludes savings from averted HIV infections.
[e]Results differ slightly between rows because of random variation across simulations.
[f]Assumes high volume, but a price based on a global purchase of 300 million FC2s.

In Brazil, a country with HIV prevalence $< 1\%$, the expanded FC2 program averted 604 (5–95th percentiles, 412–831) new HIV infections annually, compared with FC2 distribution at present levels. In South Africa, where HIV prevalence in the modeled population was 19%, the expanded program was estimated to avert 9577 (5–95th percentiles, 6539–13 270) new HIV infections annually. Thus, the incremental cost of expanded FC2 distribution per HIV infection averted was $20 683 (5–95th percentiles, 13 497–29 521) in Brazil and $985 (5–95th percentiles, 633–1412) in South Africa. By comparison, the estimated per-person cost to provide antiretroviral therapy was $21 970 (5–95th percentiles, 18 369–25 719) in Brazil and $1503 (5–95th percentiles, 1245–1769) in South Africa. Assuming that therapy begins in 2010 rather than 2006 reduced the per-person cost of ART by $3018 in Brazil and $206 in South Africa.

In univariate analysis, the incremental cost per HIV infection averted was most sensitive to the estimated prevalence of STI, total sexual activity, and the fraction of FC2s distributed that are used correctly (Table 4). Similar results were found in multivariate sensitivity analysis, and there was little difference across countries (Table 5). Under 'best-case' and 'worst-case' scenarios, in which all parameters were set to the values that were most or least favorable to expanded FC2 distribution, the incremental cost of expanded distribution per HIV infection averted varied from $8901 to $43 283 in Brazil and from $459 to $2102 in South Africa.

Discussion

From the perspective of a payor agency, country-wide distribution of FC2 at higher volumes appears to be cost-saving relative to distribution at existing volumes. In Brazil, successful implementation of an expanded FC2 distribution program could avert over 600 new HIV infections annually, at an estimated incremental cost of $20 683 per infection averted, a figure that compares favorably with the estimated per-person cost of ART ($21 970). A similar program in South Africa was

Table 4. One-way sensitivity analysis.

Parameter/scenario	Range of incremental cost per HIV infection averted [$\$ \times 10^3$][a]	
	Brazil	South Africa
Base case[b]	20.0	0.94
STI prevalence		
Ulcerative, male	16.4–26.1	0.81–1.14
Ulcerative female	17.2–24.1	0.73–1.35
Non-ulcerative male	19.5–20.6	0.91–0.96
Non-ulcerative female	19.7–20.4	0.90–0.98
Annual number of sex acts, per person	13.9–26.2	0.66–1.21
Annual number of sexual partners		
Male	16.7–24.6	0.77–1.17
Female	17.5–23.1	0.86–1.02
Efficacy in preventing HIV		
Male condom	19.7–20.4	0.92–0.95
FC2	18.7–21.6	0.88–1.00
Fraction of distributed FC2s that are used correctly	16.4–26.4	0.77–1.23
Fraction of sex acts protected by male condom	19.9–20.0	0.93–0.94
Fraction of sex acts protected by FC2 otherwise protected by male condom	17.5–23.3	0.81–1.10

STI, sexually transmitted infection; FC2, second-generation nitrile female condom.
[a]Based on the range of values for each parameter as shown in Tables 1 and 2, using the moderate distribution model described in the text; costs are expressed in 2005 US$.
[b]Derived using the base-case estimate for each model parameter in Tables 1 and 2, thus differing slightly from results from the moderate distribution model in Table 3, which represent the means of multiple simulations across probability distributions.

Table 5. Multivariate sensitivity analysis.

Parameter	Association with incremental cost per HIV infection averted[a]	
	Brazil	South Africa
Annual number of sex acts, per person	0.54	0.47
Fraction of distributed FC2s that are used correctly	−0.41	−0.39
STI prevalence		
Ulcerative, female	−0.29	−0.49
Ulcerative, male	−0.41	−0.30
Annual number of sexual partners		
Male	−0.33	−0.33
Female	0.24	−0.15
Fraction of sex acts protected by FC2 otherwise protected by male condom	0.25	0.26
Efficacy in preventing HIV, FC2	−0.13	−0.12

STI, sexually transmitted infection; FC2, second-generation nitrile female condom.
[a]Reported as standardized β coefficients (total $r^2 = 0.97$ in Brazil and 0.99 in South Africa) from country-specific multivariate regression models. Parameters are not shown for which the absolute value of standardized β coefficient was < 0.10 in both models.

estimated to avert over 9500 new HIV infections, at an incremental cost of $985 per infection averted (versus $1503 for ART). Consequently, although expanded distribution of FC2 would avert fewer HIV infections in Brazil than in South Africa, it could be cost-effective owing to the high cost of treating a single HIV case in Brazil. In South Africa, expanded FC2 distribution would avert a larger number of infections, while the cost of ART from a government or donor perspective is relatively low. The variability in these cost-effectiveness estimates is large; the interval between the 5th and 95th percentiles often includes scenarios in which expanded FC2 distribution is more costly than ART, particularly at lower distribution volumes and in Brazil.

This analysis does not include savings from averted transmission of STI other than HIV, nor does it account for savings in HIV treatment costs other than for ART (e.g., hospitalization or treatment for opportunistic infections). Therefore, it may underestimate the savings associated with expanded FC2 distribution. However, other model assumptions may overestimate FC2 cost-effectiveness, particularly at high distribution volumes. For example, as FC2 distribution programs are expanded and reach remote populations, the proportion of FC2s not used or used to replace male condoms, as well as the cost to scale up and market FC2, may increase. Nevertheless, this analysis suggests that program effectiveness and cost-effectiveness increase substantially with increased volume. Specifically, increasing the volume of FC2s distributed from 3% to 30% of current male condom volume multiplies incremental HIV infections averted approximately 20-fold while reducing the incremental cost per infection averted. Furthermore, the incremental cost of expanded distribution could be further reduced by 45–50% if FC2s were acquired through a global purchasing mechanism with a total volume of 300 million units. These findings argue for further research to determine whether and how female condoms would be used if made available in such volume.

Sensitivity analyses suggest that the cost-effectiveness of expanded FC2 distribution depends as much on population factors driving HIV incidence (e.g., STI prevalence and sexual frequency) as on parameters describing the uptake and use of FC2 (e.g., FC2 effectiveness and fraction of FC2-protected sex acts otherwise protected by male condoms). As a result, one potential criticism of this model is its assumption that genital ulcer disease increases HIV transmission rates. To illustrate the impact of this assumption on our model results, removing the added impact of STI on HIV transmission reduces the number of HIV infections averted by 44%. However, this modification also results in modeled HIV incidence rates that would not sustain the existing prevalence of HIV [17,18] over time. In any case, this model suggests that accurate characterization of current sexual practices is critical for agencies considering the cost-effectiveness of large-scale acquisition and distribution of FC2.

Comparing expanded FC2 distribution with other interventions is difficult because the lack of available data precludes a comprehensive analysis from the societal perspective. Nevertheless, it is important to consider other HIV-prevention activities and other potentially cost-effective or cost-saving healthcare interventions [31–34] as alternatives or complements to FC2. On a gross level, a single case of HIV prevented (without ulcers, non-core group) is expected to save 54.6 disability-adjusted life years (DALY) [35]; therefore, FC2 expansion to moderate volume in South Africa would be expected to cost a donor or government $18 (5–95th percentiles, 11–26) per DALY saved, ignoring any cost-savings from averted HIV treatment. This figure compares with an estimated $1–74 to society per DALY saved for peer-based education, $14–261 for voluntary counseling and testing, and $350–500 for ART in the most favorable settings [36]. However, our payor-perspective analysis ignores both important societal costs (e.g., marketing and promotion) and savings (e.g., averted productivity losses from HIV disease) of expanded FC2 distribution. Therefore, while expanded FC2 distribution may be cost saving, this analysis is not designed to test this hypothesis from a societal perspective or to compare FC2 with other interventions.

An important limitation of this analysis involves our inability to estimate precisely certain variables to which the model is sensitive. For example, variation in the fraction of distributed FC2s that are correctly used (from 64 to 100%) changes the estimated cost of country-wide FC2

distribution in Brazil from $26 351 to $16 424 per HIV infection averted (Table 4). We have attempted to account for variation in parameter values by reporting only population-averaged results with wide sensitivity analysis around those parameters associated with greatest uncertainty. Nevertheless, mis-specification of parameter values and corresponding probability distributions may bias our results, particularly at high volumes of distribution.

The model used in this analysis may also oversimplify the underlying processes of HIV infection and protection from condoms. By adopting a 1-year analysis period, assigning equivalent sexual activity to all members of the population, and assuming constant transmission risk per partner per sexual act, the model fails to account for such processes as differential condom use among a 'core' of highly sexually active individuals [37] or differential likelihood of transmission across partnerships or within partnerships over time [38]. Other proposed models [39] characterize HIV transmission in greater detail; however, these models are less widely validated than the transmission model used here [25]. Nevertheless, this transmission model was not specifically validated for the present study and, therefore, may result in over- or underestimation of FC2 impact.

Our findings suggest a number of future research directions. At present, no country distributes female condoms free of charge to a large population. Therefore, future studies should reexamine FC2 cost-effectiveness after field implementation, paying particular attention to sustained patterns of FC2 and male condom use, as well as marketing costs, in areas where FC2 becomes widely available. Second, although the World Health Organization currently recommends a new female condom for every sex act [40], studies of the safety and acceptability of FC2 reuse might further enhance cost-effectiveness. Third, the impact of country-wide FC2 distribution on STI other than HIV remains unclear. Finally, further analyses are needed to compare FC2 cost-effectiveness with other HIV/AIDS interventions, using a common reference scenario and a societal perspective.

In conclusion, this cost-effectiveness analysis suggests that expanded distribution of FC2 in Brazil and South Africa may avert hundreds to thousands of HIV infections annually at an incremental cost to governments or donors that is less than that of ART. These models do not include additional savings from averted hospitalization or other treatment costs, but they assume that demand for FC2 exceeds supply at all distribution volumes. Although confidence intervals are wide, and future studies are needed to assess the cost-effectiveness of FC2 after actual field implementation, these preliminary findings suggest that FC2 may be an effective and cost-saving supplement to the male condom as a preventive tool in the fight against HIV/AIDS.

Sponsorship: This research was supported by the Female Health Company, Chicago, Illinois, USA, which had no role in the design of the study or its analysis (other than by provision of some input parameter estimates as stated). DWD was primarily supported in this work by the National Institutes of Health, Medical Scientist Training Program Award 5 T32 GMO7309.

References

1. Pinkerton SD, Abramson PR. **Effectiveness of condoms in preventing HIV transmission.** *Soc Sci Med* 1997; **44**:1303–1312.
2. Shelton JD, Johnston B. **Condom gap in Africa: evidence from donor agencies and key informants.** *Br Med J* 2001; **323**:139.
3. MeasureDHS. *HIV/AIDS Survey Indicators Database*. Calverton, MD: MeasureDHS; 2005. http://www.measuredhs.com/hivdata/data/start.cfm.
4. Minnis AM, Padian NS. **Effectiveness of female controlled barrier methods in preventing sexually transmitted infections and HIV: current evidence and future research directions.** *Sex Transm Infect* 2005; **81**:193–200.
5. Trussell J, Sturgen K, Strickler J, Dominik R. **Comparative contraceptive efficacy of the female condom and other barrier methods.** *Fam Plann Perspect* 1994; **26**:66–72.
6. French PP, Latka M, Gollub EL, Rogers C, Hoover DR, Stein ZA. **Use-effectiveness of the female versus male condom in preventing sexually transmitted disease in women.** *Sex Transm Dis* 2003; **30**:433–439.
7. Farr G, Gabelnick H, Sturgen K, Dorflinger L. **Contraceptive efficacy and acceptability of the female condom.** *Am J Public Health* 1994; **84**:1960–1964.
8. Fontanet AL, Saba J, Chandelying V, Sakondhavat C, Bhiraleus P, Rugpao S, *et al*. **Protection against sexually transmitted diseases by granting sex workers in Thailand the choice of using the male or female condom: results from a randomized controlled trial.** *AIDS* 1998; **12**:1851–1859.
9. Artz L, Macaluso M, Brill I, Kelaghan J, Austin H, Fleenor M, *et al*. **Effectiveness of an intervention promoting the female condom to patients at sexually transmitted disease clinics.** *Am J Public Health* 2000; **90**:237–244.
10. Choi KH, Gregorich SE, Anderson K, Grinstead O, Gomez CA. **Patterns and predictors of female condom use among ethnically diverse women attending family planning clinics.** *Sex Transm Dis* 2003; **30**:91–98.
11. Barbosa RM, Berqu E, Kalckmann S. *Acceptability of the Female Condom in Different Social Contexts: Final Research Report*. 1st edn. Brasilia: Ministry of Health, Secretariat for Health Policies, National STD/AIDS Coordinating Office; 1999.
12. Welsh MJ, Feldblum PJ, Kuyoh MA, Mwarogo P, Kungu D. **Condom use during a community intervention trial in Kenya.** *Int J STD AIDS* 2001; **12**:469–474.
13. Schwartlander B, Stover J, Walker N, Bollinger L, Gutierrez JP, McGreevey W, *et al*. **AIDS Resource needs for HIV/AIDS.** *Science* 2001; **292**:2434–2436.
14. Marseille E, Kahn JG, Billinghurst K, Saba J. **Cost-effectiveness of the female condom in preventing HIV and STDs in commercial sex workers in rural South Africa.** *Soc Sci Med* 2001; **52**:135–148.
15. Beksinska M, Smit J, Mabude Z, Vijayakumar G, Joanis C. **Performance of the Reality polyurethane female condom and a synthetic latex prototype: a randomized crossover trial among South African women.** *Contraception* 2006; **73**:386–393.
16. Smit J, Beksinska M, Vijayakumar G, Mabude Z. **Short-term acceptability of the Reality polyurethane female condom and a synthetic latex prototype: a randomized crossover trial among South African women.** *Contraception* 2006; **73**:394–398.
17. Ministry of Health, Brazil. *MonitorAIDS: The National STD/AIDS Program Monitoring System*, version 2.1. Brasilia: Ministry of Health; 2004.
18. Human Sciences Research Council. *Nelson Mandela HSRC Study of HIV/AIDS*. Cape Town: Human Science Research Council; 2002.

19. IBOPE Group. *Use, Purchase Pattern, and Access of Male Condoms in the Public Health System*. [Private research conducted for the evaluation unit of the Network Access Point (NAP) do Brasil.] Brasilia: IBOPE; 2003.
20. Myer L, Mathews C, Little F. **Condom gap in Africa is wider than study suggests.** *Br Med J* 2001; **323**:937.
21. Chequer P. **Access to treatment and prevention: Brazil and beyond**. *Third International AIDS Society Conference on HIV Pathogenesis and Treatment*. Rio de Janeiro, July 2005 [Monday plenary].
22. Geffen N, Nattrass N, Raubenheimer C. *Centre for Social Science Research Working Paper No. 28: The Cost of HIV Prevention and Treatment Interventions in South Africa*. Cape Town: University of Cape Town; 2003.
23. US Census Bureau. *International Data Base,* April 2005 version. Washington, DC: US Census Bureau; 2005.Available at http://www.census.gov/cgi-bin/ipc/idbsum.pl?cty=SF; 2005.
24. Weinstein M, Graham J, Siegel J, Fineberg H. *Cost-effectiveness Analysis of AIDS Prevention Programs: Concepts, Complications and Illustrations*. Washington, DC: National Academies Press; 1989.
25. Rehle TM, Saidel TJ, Hassig SE, Bouey PD, Gaillard EM, Sokal DC. **AVERT: a user-friendly model to estimate the impact of HIV/sexually transmitted disease prevention interventions on HIV transmission.** *AIDS* 1998; **12 (Suppl 2)**:S27–S35.
26. Cowan FM, French RS, Mayaud P, Gopal R, Robinson NJ, de Oliveira SA, *et al*. **Seroepidemiological study of herpes simplex virus types 1 and 2 in Brazil, Estonia, India, Morocco, and Sri Lanka.** *Sex Transm Infect* 2003; **79**:286–290.
27. Wald A, Zeh J, Selke S, Warren T, Ryncarz AJ, Ashley R, *et al*. **Reactivation of genital herpes simplex virus type 2 infection in asymptomatic seropositive persons.** *N Engl J Med* 2000; **342**: 844–850.
28. Wilkinson D, Connolly AM, Harrison A, Lurie M, Karim SS. **Sexually transmitted disease syndromes in rural South Africa Results from health facility surveillance.** *Sex Transm Dis* 1998; **25**:20–23.
29. Department of Health, Republic of South Africa. *South Africa Demographic and Health Survey 1998*. Washington, DC: Macro International; 1998. http://www.measuredhs.com/pubs/pdftoc.cfm?ID=360&PgName=country.cfm0ctry_id=55.
30. Korenromp EL, Bakker R, de Vlas SJ, Robinson NJ, Hayes R, Habbema JD. **Can behavior change explain increases in the proportion of genital ulcers attributable to herpes in sub-Saharan Africa? A simulation modeling study.** *Sex Transm Dis* 2002; **29**:228–238.
31. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. **Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 trial.** *PLoS Med* 2005; **2**:e298.
32. Adam T, Lim SS, Mehta S, Bhutta ZA, Fogstad H, Mathai M, *et al*. **Cost effectiveness analysis of strategies for maternal and neonatal health in developing countries.** *Br Med J* 2005; **331**:1107.
33. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahe C, *et al*. **Cost-effectiveness of cervical-cancer screening in five developing countries.** *N Engl J Med* 2005; **353**: 2158–2168.
34. Harris GT, Olukoga IA. **A cost benefit analysis of an enhanced seat belt enforcement program in South Africa.** *Inj Prev* 2005; **11**:102–105.
35. Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, *et al*. (eds.). *Disease Control Priorities in Developing Countries,* 2nd edn. New York: Oxford University Press; 2006.
36. Laxminarayan R, Mills AJ, Breman JG, Measham AR, Alleyne G, Claeson M, *et al*. **Advancement of global health: key messages from the Disease Control Priorities Project.** *Lancet* 2006; **367**: 1193–1208.
37. Boily MC, Lowndes C, Alary M. **The impact of HIV epidemic phases on the effectiveness of core group interventions: insights from mathematical models.** *Sex Transm Infect* 2002; **78 (Suppl 1)**:i78–i90.
38. Rottingen JA, Garnett GP. **The epidemiological and control implications of HIV transmission probabilities within partnerships.** *Sex Transm Dis* 2002; **29**:818–827.
39. Baggaley RF, Ferguson NM, Garnett GP. **The epidemiologic impact of antiretroviral use predicted by mathematical models: a review.** *Emerg Themes Epidemiol* 2005; **2**:9.
40. World Health Organization. *WHO Information Update: Considerations Regarding Reuse of the Female Condom*. Geneva: World Health Organization; 2002. http://www.who.int/reproductive-health/stis/docs/reuse_FC2.pdf.