

Cost-Effectiveness of Adult Circumcision in a Resource-Rich Setting for HIV Prevention among Men Who Have Sex with Men

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Background. We examined the effects and cost-effectiveness of 4 strategies of circumcision in a resource-rich setting (Australia) in a population of men who have sex with men (MSM).

Method. We created a dynamic mathematical transmission model and performed an economic analysis to estimate the costs, outcomes, and cost-effectiveness of different strategies, compared with those of the status quo. Strategies included circumcision of all MSM at age 18 years, circumcision of all MSM aged 35–44 years, circumcision of all insertive MSM aged ≥ 18 years, and circumcision of all MSM aged ≥ 18 years. All costs are reported in US dollars, with a cost-effectiveness threshold of \$42,000 per quality-adjusted life-year.

Results. We find that 2%–5% of human immunodeficiency virus (HIV) infections would be averted per year, with initial costs ranging from \$3.6 million to \$95.1 million, depending on the strategy. The number of circumcisions needed to prevent 1 HIV infection would range from 118 through 338. Circumcision of predominately insertive MSM would save \$21.7 million over 25 years with a \$62.2 million investment. Strategies to circumcise 100% of all MSM and to circumcise MSM aged 35–44 years would be cost-effective; the latter would require a smaller investment. The least cost-effective approach is circumcision of young MSM close to their sexual debut. Results are very sensitive to assumptions about the cost of circumcision, the efficacy of circumcision, sexual preferences, and behavioral disinhibition.

Conclusions. Circumcision of adult MSM may be cost-effective in this resource-rich setting. However, the intervention costs are high relative to the costs spent on other HIV prevention programs.

The incidence of human immunodeficiency virus (HIV) infection among men who have sex with men (MSM) has been increasing in many high-income countries, including Australia, over the past decade [1]. The increase in HIV infections has prompted interest in new prevention technologies, along with renewed interest in prevention and education programs.

Adult male circumcision has been shown to be effective for the prevention of HIV acquisition in 3 randomized trials among heterosexual men in Southern and Eastern Africa [2–4]. A meta-analysis of observational data on the effect of circumcision among MSM revealed insufficient recent evidence that male circumcision protects against HIV infection or other sexually transmitted infections, but this meta-analysis did report an association between circumcision and protection against HIV infection in studies of MSM that were conducted before the introduction of highly active antiretroviral therapy [5]. In 2008, a study of a large Australian community-based cohort reported a statistically significantly reduced risk of HIV seroconversion among circumcised MSM who predominantly took the insertive role in anal intercourse, with an 85% reduction in the acquisition of HIV among predominately insertive MSM and a 95% certainty that the true value was between 20% and 97% [6].

Cost-effectiveness models for Southern and Eastern

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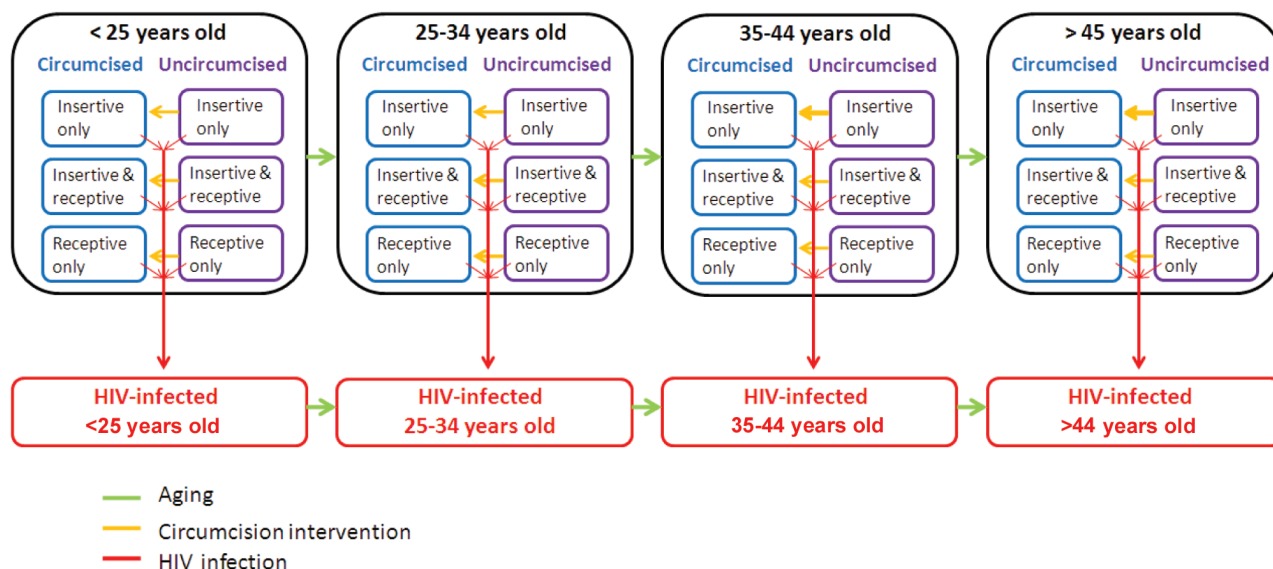


Figure 1. Schematic diagram of the model population of 180,000 men who have sex with men. HIV, human immunodeficiency virus.

Africa have suggested that circumcision is cost-effective [7–9]. However, there have been no economic evaluations of the value of adult male circumcision for the prevention of HIV infection in resource-rich countries that have a relatively high baseline prevalence of circumcision and an HIV epidemic affecting mainly MSM. On the other hand, the popularity of pediatric circumcision has been steadily declining in Australia, from rates of 80% in the 1960s to <10% in the past decade, and hence the prevalence of circumcision among adults has also been decreasing [10].

This study aimed to model the potential costs and benefits, compared with the status quo, of implementing an adult male circumcision program for the prevention of HIV infection among Australian MSM. We also aim to consider the efficiency of targeting intervention to different groups of MSM in the event of budgetary constraints. Finally, we explored the impacts of potential changes in behavior on these estimates.

METHODS

Four main strategies of coverage are considered for implementation of circumcision; these are compared with the status quo or no specific intervention, which is defined as neonatal circumcision that continues at the current rate. The strategies are labeled as follows: (1) sexual debut, which is defined as circumcision of all uncircumcised MSM at age 18, because this approach is being adopted in African circumcision programs; (2) 35–44-year-olds, which is defined as circumcision of all uncircumcised MSM aged 35–44 years in the first year of the program and on entry to the age range thereafter, because this group has the highest incidence of HIV infection in Australia [1] (their baseline circumcision prevalence is 70% [10]); (3)

insertive, which is defined as circumcision of all MSM aged ≥ 18 years who are predominately insertive in their sexual behavior, because circumcision is likely to have the greatest effect in this group; and (4) all MSM, which is defined as circumcision of all MSM aged ≥ 18 years. Each strategy is assumed to start with an intensive phase during the first year in which all men in the target group are circumcised and then to continue with an ongoing program to maintain circumcision rates for individuals entering the targeted age group each year.

We used a dynamic population-level mathematical transmission model composed of mathematical differential equations developed, implemented, and solved with Matlab software (MathWorks) to estimate the number of new HIV infections over a 25-year period starting in 2008 for each strategy in a hypothetical population of 180,000 MSM in Australia [11] (Figure 1). The data on the number of new infections and circumcisions are included in an economic analysis of costs and benefits that was performed from the perspective of the government as a third-party payer. The discounting of costs and outcomes (3%) is consistent with the policy set by the Panel on Cost-Effectiveness in Health and Medicine [12]. Costs are reported in US dollars (2007 prices) with purchasing power parity of 1.43 Australian dollars equal to 1 US dollar [13].

Our model includes data from previous studies of MSM in Australia on age-specific circumcision status (range, 50% for MSM aged 18–25 years to 83% for MSM aged ≥ 45 years) [10, 14–16] and HIV prevalence (range, 0.5% for MSM aged 18–25 years to 18% for MSM aged ≥ 45 years) [11]; probability of HIV acquisition and transmission for different sexual acts (0.008 for receptive anal sex and 0.0008 for insertive anal sex) [17–19]; frequency of sexual acts (125 acts per man per year)

Table 1. Parameters and Values Used in the Mathematical Model

Parameter	Value	Sensitivity, %	Reference(s)
Population	180,000	...	[11]
Effectiveness of circumcision in prevention of HIV acquisition among insertive men, %	60	43–80	[2–4, 32]
Age-specific baseline circumcision status, %			[10, 14–16]
<25-Year-olds	50.3	...	
25–34-Year-olds	59.3	...	
35–44-Year-olds	69.5	...	
≥45-Year-olds	82.6	...	
HIV infection prevalence, %			[11]
<25-Year-olds	0.5	1.5	
25–34-Year-olds	5	6	
35–44-Year-olds	10	12	
≥45-Year-olds	18	20	
Probability of acquisition			[17–19]
Insertive anal	0.0008	...	
Receptive anal	0.008	...	
Frequency of sexual acts, acts/man/year	125	...	[20, 21]
Condom usage, %	65	70	[22, 23]
Condom efficacy, %	90	95	[24, 25]
Use and impact of ART on infectiousness, %			[22, 26–29]
HIV-infected MSM on ART	70–75	...	
MSM on ART who achieve viral suppression	80	...	
Reduction in infectiousness if viral suppression is achieved	95	90	
Strategic positioning and role preference, %			[6, 30]
Insertive only	33	...	
Receptive only	10	...	
Insertive and receptive	57	...	
Cost of HIV management (discounted)	\$342,916	\$171,328–\$513,986	[38]
Cost of intervention circumcision	\$1,767	\$883–\$2,365	[36–38]
Utility loss due to HIV, QALYs (discounted)	7.5	...	[40]
Discount rate, %	3	0–5	[12]

NOTE. Results of the sensitivity analyses are given as percentages except where otherwise indicated. Costs are given in US dollars. QALY, quality-adjusted life-year.

[20, 21]; condom usage (65%) [22, 23] and efficacy (90%) [24, 25]; use and impact on infectiousness of antiretroviral therapy (70%–75% of HIV-infected MSM receive antiretroviral therapy, of whom 80% achieve viral suppression, which reduces infectiousness by 95%) [22, 26–29]; and strategic positioning and role preference (33% of MSM engage only in insertive anal sex) [30]. The model was calibrated to accurately reflect the population of Australian MSM and the HIV epidemic in this population [11]. The simulations used the model input ranges and adjusted the per-act transmission probabilities (to the levels indicated above) to produce estimates of HIV infection incidence (mean, 680 cases per year [95% confidence interval {CI}, 456–963 cases per year]) that matched the HIV epidemic in Australia (681 HIV infection diagnoses in the MSM population in 2006). We assume sexual mixing occurs across all age groups but is primarily assortative within each age group, with 75%

of sexual episodes occurring between men in the same age group [31].

Circumcision is assumed to have an effectiveness of 60%, on the basis of data from 3 randomized controlled trials among heterosexual men in Southern and Eastern Africa [2–4], with sensitivity analyses for a range from 40% to 80% to illustrate the impact of our assumption and the results of a published meta-analysis [32]. The putative direct benefit of circumcision would be only to men practicing insertive sex. In the Health in Men cohort, reported sexual behaviors correlated well with the initial declared preference [6]. Input values, ranges, and sources are reported in Table 1. Costs are reported in Table 2.

We define the probability of HIV acquisition per unprotected penetrative insertive penile-anal act to be β_i^u for an uncircumcised man and β_i^c for a circumcised man. If ϵ_i^c is the effectiveness of circumcision in reducing HIV acquisition per insertive act,

Table 2. Costs of Intervention Circumcision

Procedural item	Patients, %	Unit cost, US\$	Total cost, US\$	MBS item or reference
Consultation with GP, with rebate	100	43.57	43.57	36
Test for HIV antibodies	100	9.37	9.37	69384
Consultation with GP, with rebate	100	43.57	43.57	36
Full blood estimate	100	4.76	4.76	65060
Clotting studies	100	8.36	8.36	65120
Chemistry	100	11.78	11.78	66515
Consultation with counselor	100	20.98	20.98	10994
Consultation with specialist, with rebate	100	81.05	81.05	110
Surgery	100	1,403.50	1,403.50	Code M05Z [35]
Consultation with GP for pain	0.30	22.94	0.07	[36, 37]
Consultation with GP for bleeding	2.40	22.94	0.55	[36, 37]
Consultation with GP for infection	3	22.94	0.69	[36, 37]
Consultation with specialist for bleeding	2	40.56	0.81	[36, 37]
Postoperative consultation with surgeon	100	40.56	40.56	116
Consultation with GP to check healing before resuming sex	100	22.94	22.94	23
Consultation with counselor about importance of safe sex	100	20.98	20.98	10994
Consultation with GP, with rebate	100	43.57	43.57	36
Test for HIV antibodies	100	9.37	9.37	69384
Total	1,766.46	...

NOTE. Procedural items are given in sequential order; some procedures are repeated. We assume that each procedural item in the sequence occurs once. GP, general practitioner; HIV, human immunodeficiency virus; MBS, Medical Benefits Schedule of the Australian Health Insurance Commission.

then $\beta_i^c = (1 - \varepsilon_i^c)\beta_i^u$. We define the probability of HIV acquisition per unprotected penetrative receptive penile-anal act to be β_r for both circumcised and uncircumcised men. We assume that condoms have a protective effectiveness of ε_c for both insertive and receptive penile-anal sex and for both circumcised and uncircumcised men, which leads to a probability of transmission of $(1 - \varepsilon_c)\beta$ if a condom is used. If HIV-negative MSM have an average of n penetrative penile-anal acts per year, and if condoms are used in a proportion p_c^r of receptive acts and p_c^i of insertive acts, then the probability that a circumcised man (in age group k) who practices both insertive and receptive penile-anal sex will acquire HIV each year is

$$\lambda_k^c = \sum_j P_j \left\{ 1 - (1 - \beta_i^c)^{n_k(1-p_r)(1-p_c^i)} [1 - (1 - \varepsilon_c)\beta_i^c]^{n_k(1-p_r)p_c^i} \right. \\ \left. \times (1 - \beta_r)^{n_k p_r(1-p_c^r)} [1 - (1 - \varepsilon_c)\beta_r]^{n_k p_r p_c^r} \right\},$$

where p_r represents the proportion of all acts that are receptive. The probability that an uncircumcised man (in age group k) who practices both insertive and receptive penile-anal sex will acquire HIV each year is

$$\lambda_k^u = \sum_j P_j \left\{ 1 - (1 - \beta_i^u)^{n_k(1-p_r)(1-p_c^i)} [1 - (1 - \varepsilon_c)\beta_i^u]^{n_k(1-p_r)p_c^i} \right. \\ \left. \times (1 - \beta_r)^{n_k p_r(1-p_c^r)} [1 - (1 - \varepsilon_c)\beta_r]^{n_k p_r p_c^r} \right\}.$$

In both cases, P_j denotes the prevalence of HIV infection in

sexual partners of age group j , and we use the standard binomial modeling formula [33, 34], adjusted to include the different protection options. For men who practice only receptive sex, the probability of HIV acquisition each year is

$$\lambda_k^r = \sum_j P_j \left\{ 1 - (1 - \beta_r)^{n_k(1-p_c^r)} [1 - (1 - \varepsilon_c)\beta_r]^{n_k p_c^r} \right\},$$

and the probability of HIV acquisition per year for men who practice only insertive sex is

$$\lambda_k^{IC} = \sum_j P_j \left\{ 1 - (1 - \beta_i^c)^{n_k(1-p_c^i)} [1 - (1 - \varepsilon_c)\beta_i^c]^{n_k p_c^i} \right\}$$

for circumcised men and

$$\lambda_k^U = \sum_j P_j \left\{ 1 - (1 - \beta_i^u)^{n_k(1-p_c^i)} [1 - (1 - \varepsilon_c)\beta_i^u]^{n_k p_c^i} \right\}.$$

for uncircumcised men.

If α_k is the proportion of men in age group k who are circumcised and N_k is the number of men in age group k , then the expected average number of HIV infections in year t is

$$I(t) = \sum_k \alpha_k(t) N_k (1 - P_k) [q_i \lambda_k^{IC} + q_r \lambda_k^R + (1 - q_r - q_i) \lambda_k^C] \\ + [1 - \alpha_k(t)] N_k (1 - P_k) [q_i \lambda_k^U + q_r \lambda_k^R + (1 - q_r - q_i) \lambda_k^C],$$

where q_i is the proportion of men who engage only in insertive

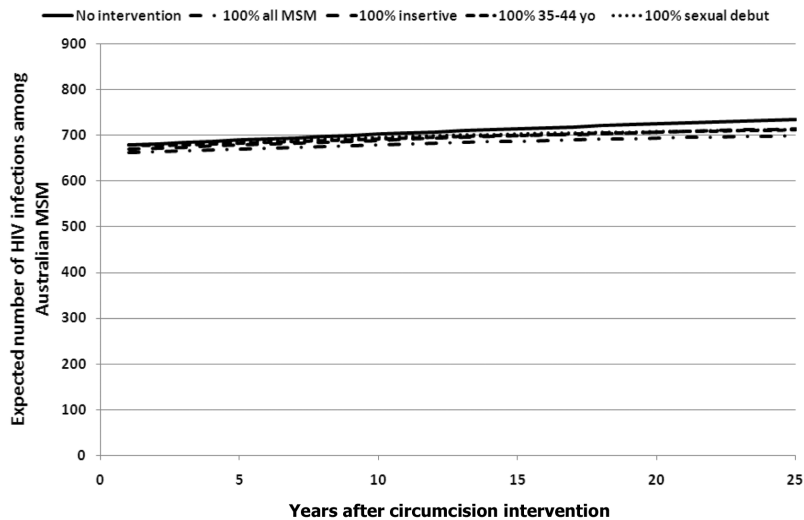


Figure 2. Expected number of human immunodeficiency virus (HIV) infections per year among Australian men who have sex with men (MSM), according to our population-level mathematical transmission model, for the status quo (no intervention) and for strategies of circumcising 100% of MSM prior to sexual debut, circumcising 100% of 35–44-year-old (yo) MSM, circumcising 100% of MSM who practice only insertive penile-anal sex, and circumcising all MSM. Curves show mean trajectories of 1000 model simulations.

sex and q_R is the proportion of men who engage only in receptive sex (thus, $1 - q_I - q_R$ is the proportion of MSM who practice both insertive and receptive sex).

The prevalence of circumcision among Australian men is nonuniformly distributed across age groups, as presented in Table 1 [16]. Because the distribution of circumcision rates is age dependent, the distribution of circumcision with age will change each year. The proportion of men in age group k who are circumcised is adjusted each year according to the formula

$$\alpha_k(t+1) = \frac{\Delta t_k - 1}{\Delta t_k} \alpha_k(t) + \frac{N_{k-1}}{N_k \Delta t_{k-1}} \alpha_{k-1}(t) + \sigma_k(t),$$

where Δt_k is the “length” in years of age group k and $\sigma_k(t)$ represents specific intervention circumcisions in year t to age group k . All parameter values used in our mathematical model are presented in Table 1.

Interventions based on focused circumcisions are simulated, and the outputs from the model include the number of HIV infections over time for each strategy. A detailed uncertainty analysis is performed for each strategy, whereby all input parameters are specified over a plausible range, and 1000 sets of parameter values are sampled and used in 1000 model simulations, producing a range of possible values for all outcome variables.

The population model was developed using inputs relevant to the Australian setting. To assess the outputs of the model, we compare the number of HIV infections in the first year of the model with Australian national surveillance data of HIV infection diagnoses in the year 2007. Although diagnosis may

lag infection by a number of years, MSM in Australia have good access to free testing, so this assumption is likely to be reasonable, especially because the proportion of undiagnosed HIV infections has been estimated to be relatively low [35].

The economic analyses are performed using Excel software (Microsoft). Inputs include the number of circumcisions; the number of HIV infections for each strategy (from the transmission model); the cost of circumcision, including the cost of the operation [36] and the cost of medical visits for adverse-effect management and prevention counseling [37, 38], which are all derived from published cost estimates; the lifetime cost of management of HIV infection (discounted at 3%) [39]; and the lifetime loss of quality-adjusted life-years (QALYs) due to HIV infection (discounted at 3%) [40]. In the analysis, each incident HIV infection accrued a QALY loss and the cost of

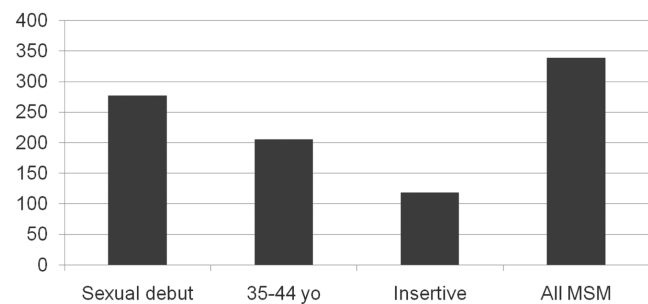


Figure 3. Number of circumcisions needed to prevent 1 human immunodeficiency virus infection for the strategies targeting men who have sex with men (MSM) prior to sexual debut, 35–44-year-old (yo) MSM, MSM who practice insertive penile-anal sex, and all MSM.

Table 3. Discounted Incremental Cost-Effectiveness Ratios

Strategy	HIV infections averted ^a	QALYs gained ^a	Incremental cost, US\$ ^a	Incremental cost per QALY gained, US\$	Upper 95% confidence limit, US\$/QALY
Sexual debut	146	1093	29,332,093	26,841	94,991
35–44-Year-olds	204	1527	14,335,127	9,390	44,332
Insertive	246	1845	21,761,545	Cost-saving	Cost-saving
All MSM	444	3328	25,760,458	7,741	18,224

NOTE. Costs are given in US dollars. HIV, human immunodeficiency virus; MSM, men who have sex with men; QALY, quality-adjusted life-year.

^a Discounted.

HIV care; both cost and QALY loss are discounted amounts that are discounted again at the time in the model that the infection is assumed to occur. The time horizon of the economic analysis is 25 years in 1-year cycles.

The costs (intervention and disease-related costs) and outcomes (HIV infections and QALYs) are estimated and the incremental cost-effectiveness ratios (ICER) are calculated by comparing the net costs and net outcomes of each strategy with the status quo. We assume that a strategy is cost-effective compared with the status quo when the ICER is <\$42,000 (equivalent to A\$60,000) per QALY gained, which is a shadow price used in a government-published economic analysis of public-sector interventions, including HIV-related interventions [41].

For each strategy, we entered the 95% CIs for the number of HIV infections from the results of the population model into the Excel spreadsheet used for the economic analyses and then ran 2000 simulations and compared them with the status quo by means of the @Risk software program (Palisade). We report 95% CIs and probabilities that the ICER will be less than the cost-effectiveness threshold of \$42,000 per QALY or <0, and simulations with a loss of QALYs counted as dominated.

We performed 1-way sensitivity analyses to account for other important model assumptions and uncertainties in the input parameters, including the impact of risk disinhibition. For variables without a range of published estimates, the ranges for the sensitivity analyses represent our judgement of the variations likely to be encountered in the implementation of the intervention. In the baseline analysis, we included the costs of the management of postoperative complications of circumcision; in a sensitivity analysis, we also included a 10% loss of quality of life in a 4-week postoperative period, which was extrapolated from the literature on quality of life in men with erectile dysfunction [42]. We also explored the inclusion of program costs such as marketing, administration, monitoring, and evaluation.

RESULTS

Over the 25-year period of the population model and compared with the status quo, there were 241 (1.4%) fewer infections

with the strategy of ensuring that all MSM are circumcised prior to sexual debut (sexual debut strategy), 318 (1.8%) fewer infections with the strategy of circumcising all men in the 35–44-year-old age group (35–44-year-olds), 363 (2.0%) fewer infections in the strategy of circumcising men who practice predominantly insertive penile-anal sex (insertive strategy), and 655 (3.7%) fewer infections in the strategy of circumcising all MSM (all MSM strategy). Our model indicates that, after 25 years, 3%–5% of HIV infections per year would be averted (Figure 2). In the insertive strategy, 118 circumcisions would be required to prevent 1 HIV infection, and in the all MSM strategy, 338 of the circumcisions would prevent 1 HIV infection (Figure 3). We found that 10–27 quality-adjusted days (undiscounted) would be gained per circumcision performed, depending on the strategy. The expected change in incidence due to any of the intervention circumcisions is relatively modest, and thus the overall prevalence was not found to change substantially over 25 years as a result of circumcision (a maximum change of 0.15% in absolute prevalence).

Circumcision and medical costs for the first year of the intervention would be \$3.6 million for the sexual debut strategy, \$20.6 million for the strategy targeting 35–44-year-old MSM, \$33.3 million for the strategy targeting insertive MSM, and \$95.1 million for the all MSM strategy. Once the initial startup phase had passed, the yearly costs would range from \$2.0 million to \$5.5 million.

The insertive strategy would save \$21.7 million over 25 years, compared with the status quo, for an overall investment of \$62.2 million (discounted), with 2% likelihood that it would not be cost-saving and a 0.4% likelihood of not being cost-effective. All other strategies would be cost-effective with an ICER of <\$42,000 (A\$60,000) per QALY gained (Table 3), with 1% likelihood that the all MSM strategy would not be cost-effective, but with a 3.6% and 25% likelihood that the 35–44 year old and sexual debut strategies, respectively, would not be cost-effective. The insertive strategy was cost-effective after 7 years of the model, whereas the sexual debut strategy proceeded for 21 years until becoming cost-effective. The total investment over 25 years for the 35–44 year old strategy would be \$83.9

million (discounted), and that for the all MSM strategy would be \$177.6 million.

If men who have been circumcised as part of the intervention reduce their use of condoms by 10%, then none of the interventions are effective, and therefore, none could be cost-effective. If only 80% of all MSM are circumcised, the intervention costs \$14,700 per QALY, and if 90% of all MSM are circumcised, the intervention costs \$9,000 per QALY.

The results of sensitivity analyses of cost and discounting are presented in Figure 4 for the all MSM strategy. The results are similar for the other strategies (not shown). The model is most sensitive to the effectiveness of circumcision, the proportion of predominately insertive men, and the costs of circumcision and of the management of HIV infection: the intervention is cost-saving for all strategies if circumcision is 50% cheaper, it remains cost-effective for 3 of the 4 strategies if the cost doubles due to program and marketing costs, and it would remain cost-effective in most scenarios if HIV infection in Australia cost 50% less than the baseline assumption. The ICER is less affected by the discount rate. If men being circumcised have a temporary loss of quality of life, then there is little effect on cost-effectiveness (Figure 4).

DISCUSSION

This study explores the cost-effectiveness of circumcision as a technology to prevent HIV infection in MSM in a resource-rich setting. Our model suggests that a range of different strategies to implement circumcision could be cost-effective or cost-saving as an intervention to prevent the spread of HIV among MSM. The investment required for a circumcision program would be considerable for its limited impact on the epidemic.

However, the effectiveness of circumcision could be nullified if it leads to increases in risk behavior, which is a plausible outcome.

An estimated one-third of the MSM in Sydney predominantly take the insertive role in anal intercourse [6]. Circumcision of predominately insertive MSM would save \$21.7 million over 25 years with a \$62.2 million investment. However, our model assumes that the sexual preferences of MSM would remain stable over 25 years. This assumption is contestable, because sexual behavior and preference may depend on emotions, setting, partnership dynamics, age, and culture and hence be fluid in the long run.

Globally, circumcision programs to prevent HIV infection are being targeted at young men, on the basis of data from randomized controlled trials in Africa on effectiveness [2–4, 32] and cost-effectiveness [7, 8]. In our model, circumcision of young men close to sexual debut was the least cost-effective strategy. The implementation of the sexual debut strategy could also pose significant challenges because of difficulties in identifying large numbers of young MSM early in their sexual lives. Circumcision of men in the age group with the highest incidence of HIV infection in Australia (35–44 years old) [1] was almost as cost-effective as circumcision of all MSM, but the former strategy involved a much smaller initial investment. If circumcision were to be adopted as a public health intervention in Australia, our study suggests that the intervention would be best targeted at this age group.

The scale and effectiveness of a circumcision program could be limited by resource constraints and fiscal burden [43]. In Australia, adult male circumcision is currently usually performed by a surgeon as a day case or with an overnight hospital

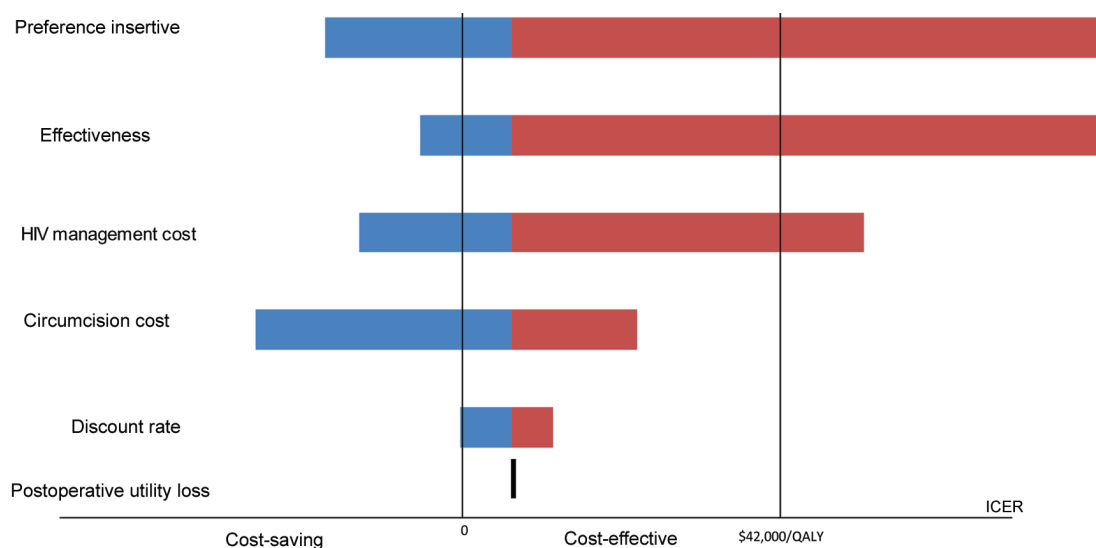


Figure 4. Tornado plot of the impact of varying the input parameters on the incremental cost-effectiveness ratio (ICER) of the strategy of circumcising all men who have sex with men. HIV, human immunodeficiency virus; QALY, quality-adjusted life-year.

stay. Hospitals have significantly long waiting lists because of limited human and other resources, especially in regional and remote settings. Primary care practitioners would require extra training to perform the procedure and funding for higher levels of indemnity insurance. Australian federal and state governments spend different amounts of money on HIV prevention and education campaigns, but none exceed \$7 million per year [44]. The likelihood that governments would decide to invest a large amount of money in a single prevention technology is low.

One could argue that a focus on circumcision might also reduce the funding and attention that is available to other cost-effective programs to prevent the spread both of HIV and of other diseases [45] and might have other negative externalities. For example, our model showed that a 10% decrease in the level of condom use would render the intervention ineffective. However, there was no evidence of disinhibition among participants in the African randomized trials [46].

Circumcision is a unique prevention intervention: it is delivered only once; requires no further adherence, cognition, or purchases; and is present at every sexual encounter for the lifetime of the individual. But the impact of circumcision was estimated to be low in the population of MSM; circumcision averted only 2%–5% of HIV infections in our model. Prevention of 1 HIV infection would require 118–338 circumcisions, a substantially higher number than the estimated 72 circumcisions required to prevent 1 HIV infection among African heterosexual men [32].

In our model, we assumed that all members of the population would accept circumcision and would have equal access to health services. However, acceptance of circumcision may be reduced by personal and cultural beliefs. Although there are no data on Australian MSM, a study from the United States suggested that MSM would consider adult circumcision if it reduced sexual transmission of HIV [47]. Men may believe that sexual pleasure is reduced without a foreskin, despite evidence to the contrary from the African setting.

The analyses of the uncertainty related to the population model inputs suggest that there is only a 75% likelihood that a strategy of circumcising young MSM would be cost-effective, although there was less uncertainty about the cost-effectiveness of a strategy of circumcising all MSM. Lower levels of coverage for the all MSM strategy would still be cost-effective and would have smaller initial budget impacts. The 1-way sensitivity analyses also demonstrate that the results are very sensitive to assumptions about the effectiveness of circumcision, the proportion of men who are predominately insertive, and the costs of circumcision and HIV-related health care.

Our study had a number of limitations. First, models are only approximations of the real world, and simplifying assumptions must be made. For example, there are no data avail-

able on the degree of assortative-disassortive mixing across age groups; we used estimates consistent with a recent modeling study that estimated mixing patterns across age groups of Australian MSM [31]. Second, we used the efficacy of circumcision that was determined from the randomized controlled trials involving heterosexual men in Southern and Eastern Africa [2–4]. However, this estimate fell within the CIs of the estimated reduction of HIV risk that was conferred by circumcision in a large prospective study involving MSM [6]. Third, we used estimates of the discounted QALYs lost and of the costs associated with a lifetime of HIV infection, but these were derived and valued in the United States, which has a health system that is very different from the health system in Australia [40]. However, the cost estimates used in our model were consistent with the costs of HIV-related health care that were derived using an activity-based approach with local costs and data in an Australian economic evaluation of needle and syringe programs [48]. Finally, we did not consider the potential additional benefits associated with circumcision in the reduction of other sexually transmitted infections, which may have underestimated the potential benefits.

In conclusion, our study is the first cost-effectiveness analysis of adult male circumcision among MSM and uses data from rigorously conducted studies in the population. We showed that circumcision could be cost-effective and even cost-saving for a range of implementation strategies. However, the investment required would be considerable, and the impact on the overall epidemic would be limited. In addition, if a perception of being protected from HIV led to increased HIV risk behavior, then the effectiveness of the intervention could easily be overcome. In such a setting, it is not inconceivable that the intervention could lead to an increase rather than a decrease in new HIV infections. A single technology such as circumcision is unlikely to be effective in a complex epidemic; combinations of new and classical health promotion actions are likely to be needed [49].

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References

1. National Centre in HIV Epidemiology and Clinical Research (NCHECR). HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia annual surveillance report. Sydney: NCHECR, 2008.
2. 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.
3. Bailey RC, Moses S, Parker CB, et al. Male circumcision for HIV

- prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet* **2007**; 369:643–56.
4. Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet* **2007**; 369:657–66.
 5. Millett GA, Flores SA, Marks G, Reed JB, Herbst JH. Circumcision status and risk of HIV and sexually transmitted infections among men who have sex with men: a meta-analysis. *JAMA* **2008**; 300:1674–84.
 6. Templeton DJ, Jin F, Mao L, et al. Reduced risk of HIV seroconversion among circumcised homosexual men who report a preference for the insertive role in anal intercourse. In: Program and abstracts of the 20th Australasian Society for HIV Medicine (ASHM) Conference (Perth). Darlinghurst, NSW: ASHM, **2008**:98.
 7. Gray RH, Li X, Kigozi G, et al. The impact of male circumcision on HIV incidence and cost per infection prevented: a stochastic simulation model from Rakai, Uganda. *AIDS* **2007**; 21:845–50.
 8. Kahn JG, Marseille E, Auvert B. Cost-effectiveness of male circumcision for HIV prevention in a South African setting. *PLoS Med* **2006**; 3:e517.
 9. Fieno JV. Costing adult male circumcision in high HIV prevalence, low circumcision rate countries. *AIDS Care* **2008**; 20:515–20.
 10. Australian College of Paediatrics. Position statement: routine circumcision of normal male infants and boys. Parkville, Victoria: Australian College of Paediatrics, **1996**.
 11. Prestage G, Ferris J, Grierson J, et al. Homosexual men in Australia: population, distribution and HIV prevalence. *Sexual Health* **2008**; 5: 97–102.
 12. Gold M, Seigel J, Russell L, Weinstein MC. Cost-effectiveness in health and medicine. New York: Oxford University Press, **1996**.
 13. Organisation for Economic Co-operation and Development (OECD). Purchasing power parity 2008. Paris: OECD, **2008**.
 14. Richters J, Smith AM, de Visser RO, Grulich AE, Rissel CE. Circumcision in Australia: prevalence and effects on sexual health. *Int J STD AIDS* **2006**; 17:547–54.
 15. O'Donnell H. Circumcision incidence in Australia. Circumcision Reference Library Web site. <http://www.cirp.org/library/statistics/Australia/>. Created February **2004**. Revised 10 September 2006. Accessed 23 November 2008.
 16. Templeton DJ, Mao L, Prestage G, Kaldor JM, Kippax S, Grulich AE. Demographic predictors of circumcision status in a community-based sample of homosexual men in Sydney, Australia. *Sex Health* **2006**; 3: 191–3.
 17. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med* **2000**; 342:921–9.
 18. Koblin BA, Husnik MJ, Colfax G, et al. Risk factors for HIV infection among men who have sex with men. *AIDS* **2006**; 20:731–9.
 19. Read TR, Hocking J, Sinnott V, Hellard M. Risk factors for incident HIV infection in men having sex with men: a case-control study. *Sexual Health* **2007**; 4:35–9.
 20. Mao L, Crawford JM, Hoppers HJ, et al. “Serosorting” in casual anal sex of HIV-negative gay men is noteworthy and is increasing in Sydney, Australia. *AIDS* **2006**; 20:1204–6.
 21. Crawford JM, Kippax SC, Mao L, et al. Number of risk acts by relationship status and partner serostatus: findings from the HIM cohort of homosexually active men in Sydney, Australia. *AIDS Behav* **2006**; 10:325–31.
 22. National Centre in HIV Epidemiology and Clinical Research. Gay Periodic Surveys, 1998–2006. University of New South Wales Web site. Available at http://nchr.arts.unsw.edu.au/nchr_library/search_results.php?sprch=PeriodicSurveys&call=y. Accessed 23 November 2008.
 23. Grierson J, Thorpe R, Pitts M. HIV futures 5: life as we know it. Australian Research Centre in Sex, Health and Society monograph series no. 60. Melbourne: Latrobe University, **2006**.
 24. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* **2002**:CD003255.
 25. Fitch JT, Stine C, Hager WD, Mann J, Adam MB, McIlhaney J. Condom effectiveness: factors that influence risk reduction. *Sex Transm Dis* **2002**; 29:811–7.
 26. Van de Ven P, Mao L, Fogarty A, et al. Undetectable viral load is associated with sexual risk taking in HIV serodiscordant gay couples in Sydney. *AIDS* **2005**; 19:179–84.
 27. Blower S, Bodine E, Kahn J, McFarland W. The antiretroviral rollout and drug-resistant HIV in Africa: insights from empirical data and theoretical models. *AIDS* **2005**; 19:1–14.
 28. Zhang H, Dornadula G, Beumont M, et al. Human immunodeficiency virus type 1 in the semen of men receiving highly active antiretroviral therapy. *N Engl J Med* **1998**; 339:1803–9.
 29. Wilson DP, Law MG, Grulich AE, Cooper DA, Kaldor JM. Relation between HIV viral load and infectiousness: a model-based analysis. *Lancet* **2008**; 372:314–20.
 30. Jin F, Crawford J, Prestage G, et al. Unprotected anal intercourse, risk reduction behaviours, and subsequent HIV infection in a cohort of homosexual men. *AIDS* **2009**; 23:243–52.
 31. Wilson DP. Modelling based on Australian HIV notifications data suggests homosexual age mixing is primarily assortative. *J Acquir Immune Defic Syndr* **2009**; 51:356–60.
 32. Mills E, Cooper C, Anema A, Guyatt G. Male circumcision for the prevention of heterosexually acquired HIV infection: a meta-analysis of randomized trials involving 11050 men. *HIV Medicine* **2008**; 9: 332–5.
 33. Rottingen JA, Garnett GP. The epidemiological and control implications of HIV transmission probabilities within partnerships. *Sex Transm Dis* **2002**; 29:818–27.
 34. Kaplan EH. Modeling HIV infectivity: must sex acts be counted? *J Acquir Immune Defic Syndr* **1990**; 3:55–61.
 35. Wilson DP, Hoare A, Regan DG, Law MG. Importance of promoting HIV testing for preventing secondary transmissions: modelling the Australian HIV epidemic among men who have sex with men. *Sexual Health* **2009**; 6:19–33.
 36. Australian Government Department of Health and Ageing. Public sector costs, 2006–2007. Canberra: Australian Government Department of Health and Ageing, **2008**.
 37. Medicare Australia. Medicare benefits schedule, 2008. Australian Government Department of Health and Ageing Web site. <http://www.health.gov.au/internet/mbsonline/publishing.nsf/Content/Medicare-Benefits-Schedule-MBS-1>. Accessed 23 November 2008.
 38. Kigozi G, Gray RH, Wawer MJ, et al. The safety of adult male circumcision in HIV-infected and uninfected men in Rakai, Uganda. *PLoS Med* **2008**; 5:e116.
 39. Schackman BR, Gebo KA, Walensky RP, et al. The lifetime cost of current human immunodeficiency virus care in the United States. *Med Care* **2006**; 44:990–7.
 40. Hornberger J, Holodniy M, Robertus K, Winnike M, Gibson E, Verhulst E. A systematic review of cost-utility analyses in HIV/AIDS: implications for public policy. *Med Decis Making* **2007**; 27:789–821.
 41. Applied Economics. Returns on investment in public health: an epidemiological and economic analysis. Canberra: Australian Government Department of Health and Ageing, **2003**.
 42. Ventegodt S. Sex and the quality of life in Denmark. *Arch Sex Behav* **1998**; 27:295–307.
 43. Fieno JV. Costing adult male circumcision in high HIV prevalence, low circumcision rate countries. *AIDS Care* **2008**; 20:515–20.
 44. Bernard D, Kippax S, Baxter D. Effective partnership and adequate investment underpin a successful response: key factors in dealing with HIV increases. *Sex Health* **2008**; 5:193–201.
 45. Kigozi G, Watya S, Polis CB, et al. The effect of male circumcision on sexual satisfaction and function, results from a randomized trial of male circumcision for human immunodeficiency virus prevention, Rakai, Uganda. *BJU Int* **2008**; 101:65–70.
 46. Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet* **2007**; 369:657–66.
 47. Begley E, Jafa K, Voetsch A, Heffelfinger J, Sullivan P. Willingness of

- men who have sex with men in the US to be circumcised as adults to reduce risk of HIV infection [abstract 983]. In: Program and abstracts of the 14th Conference on Retroviruses and Opportunistic Infections (CROI) (Los Angeles). Alexandria, VA: CROI, **2007**.
48. Wilson DP, Kwon A, Anderson JS, Law MG, Kaldor J. Return on investment 2: evaluating the cost-effectiveness of needle and syringe programs among injecting drug users in Australia. Sydney: National Centre in HIV Epidemiology and Clinical Research, **2009**.
49. Merson M, Padian N, Coates TJ, et al. Combination HIV prevention. *Lancet* **2008**;372:1805–6.