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SPECIAL THEME: HIV INFECTION

Significant reduction in HIV prevalence according to male circumcision intervention in sub-Saharan Africa

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Background Observations that reduced adult HIV prevalence in sub-Saharan Africa correlated with levels of male circumcision (MC), have suggested that MC could be used as a preventative measure against HIV infection. The exact benefits of this intervention are uncertain. Moreover if MC is not feasible for the whole male population, which groups should be targeted?

Methods A mathematical model simulated observed levels of HIV prevalence under the complete range of current levels of circumcision. Increased MC from 2007 was incorporated in this model and used to simulate HIV prevalence in 2020.

Results Complete coverage by MC could reduce HIV prevalence from 12 to 6% for an average population country in sub-Saharan Africa in 2020. This reduction is scaled proportionally when lower circumcision levels are achieved. These benefits are achieved mostly by circumcising men between 20 and 30 years of age (adult prevalence reduced from 12 to 10%), and those with riskier behaviour (8 to 6.9%). Complete negation of these benefits requires at least 40% of circumcised males to significantly increase risky behaviour.

Conclusions MC provides an effective intervention in sub-Saharan Africa to reduce HIV prevalence. It is most effective when applied to 20–30 year old risky males with diminishing returns with application to the wider male population.

Keywords HIV, circumcision, mathematical model, sub-Saharan Africa, intervention

Introduction

It has been speculated for some time that male circumcision (MC) provides protection against HIV infection.[1–3] Several ecological studies of African populations have shown a correlation between low adult HIV prevalence and a high percentage of circumcised men.[4–7] Additionally, recent randomized trials have demonstrated that circumcision provides a measure of protection against HIV infection in men with mean risk reductions of 51–60%.[8–10]

Although access to antiretroviral drugs is slowly increasing in Sub-Saharan Africa, for the foreseeable

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future their availability will be considerably lower than the demand by ~26 million currently infected with HIV in that region.[11] Experimental HIV vaccines have so far failed to demonstrate sufficient efficacy and this implies that the major means for combating the spread of HIV falls to other prevention strategies. It is of growing interest therefore to assess if increased MC can be effective in reducing HIV prevalence.

Recently published mathematical modelling of MC simulated in Sub-Saharan Africa suggested this intervention could significantly impact HIV incidence and prevalence.[12–14] However that research did not incorporate the skewed age and sex profiles of HIV prevalence or different levels of sexual activity within a population,[15,16] and also assumed complete or partial coverage of the population in each country. Although these results provide a valuable guide to the impact of MC in Sub-Saharan Africa, they do not address the issue of whether complete coverage by MC is possible, and if not which age groups or sexual activity groups should be targeted. In addition to addressing these issues, we assess how well these benefits are maintained under increasing risky behaviour, an important concern as circumcision goes from clinical trials to public interventions.[17]

Methods

Mathematical model

The model developed here is a deterministic, compartmental model, which simulates the HIV/AIDS epidemic spread through heterosexual transmission in sub-Saharan Africa and was based on other models of heterosexual transmission of HIV in sub-Saharan communities.[16,18] The model was used to simulate the effect of different intervention scenarios on the epidemic and population dynamics over a 40-year period from 1980 to 2020, updating the number of infections, births, deaths, etc on a monthly basis. Starting the simulation in 1980 allowed for the model to be validated by comparing the simulated results with historical data from 1980 to 2007. The terminal point of 2020 was chosen in order to investigate the longer term impact of MC on a representative sub Saharan African population without conclusions being nullified by uncertainty in parameters and unrealistic assumptions about behavioural trends. The initial, baseline scenario considered the introduction of HIV into a community with an existing number of circumcised males and no further intervention. The other scenarios examined the effects of circumcising males in different groups once an epidemic had become established within the community. In order to account for the uncertainty in the model's parameters, each scenario was repeated 500 times with the parameters sampled using Latin Hypercube sampling[19] from uniform distributions. The intervals for the distributions were chosen in line with literature estimates and are displayed in Table 1.

In the model, the population is divided into subpopulations by gender, age groups from 0 to 80 years old in 1-year interval, a more sexually active core group and a less active non-core group and HIV uninfected and infected. Men are further divided into circumcised and uncircumcised groups. The infected population is split into five stages of infection corresponding to acute, asymptomatic, early symptomatic, late symptomatic and AIDS. The fertility and HIV-unrelated death rates are chosen from observed data of sub-Saharan countries, leading to about 4% population growth annually without the presence of HIV.[16] The population is initially distributed with an age-profile that is stable under the given fertility and non-HIV death rates.

Table 1 Model parameters and range of uniform distribution

Parameters	Range
Percentage of men circumcised	0–100%
Relative susceptibility of circumcised men[8–10]	30–70%
Percentage of population in core-group	0–20%
Contacts per year for non-core group divided by annual birth-rate[21]	4–6
Contacts/year of core group divided by contacts/year of non-core group	3–5
Peak number of contacts with FSW for a male[21]	0–2
Average age difference between male and female partners[20]	7–11
Percentage of contacts that used condoms effectively	0–40%
Percentage of contacts with FSW that used condoms effectively[22]	0–40%
Percentage of contacts for a person in acute stage compared with uninfected person	0.5–0.9
Percentage of contacts for a person in late symptomatic stage compared with uninfected person	0.2–0.6
Percentage of contacts for a person in AIDS stage compared with uninfected person	0–0.2
Percentage infectivity of female-to-male transmission compared with male-to-female transmission[25, 26]	0.3–0.5
Peak HIV prevalence in FSW	0–40%
Percentage infectiousness of circumcised men compared with uncircumcised men[8]	80–100%

The number of sexual partnerships per woman per year is proportional to the fertility rate with a peak of one partnership per year for non-core women and two to four partnerships per year for a core group woman. Partner selection for women is based on age alone according to a Poisson distribution specific to each 1-year age group.[20,21] It was assumed that a 15-year-old girl would on average have a partner 9 years older than herself, whilst the mean age difference decreased linearly to 2 years for a 49-year-old woman. In addition, males also have sexual contacts with female sex workers (FSW) with the number of contacts per year increasing for young males and then decreasing as the man ages.[21] The HIV prevalence among FSW was modelled by calculating the average prevalence among young women and increasing that by a constant factor so that it agrees with empirical data from 1980 to 1993.[22]

The probability of transmission per partnership was assumed to vary with viral load which itself varies during the course of infection.[23,24] Also, we assumed that people in the latter stages of HIV infection would have sexual contacts less frequently, leading to a reduction in transmission rates. Male–female transmission was also assumed more likely then female–male transmission, according to several studies and models.[12,25,26] Transmission probability was further affected by circumcision and effective condom use.[8–10] Recruitment to the circumcision group was treated differently in each scenario. In the baseline scenario, only neonatal circumcision existed, with the percentage of babies circumcised being equal to the percentage of currently circumcised adult men, reflecting the link between circumcision and ethnicity/religion. Intervention scenarios also included the circumcision of adult men, starting in 2007. This was modelled by decreasing the numbers of uncircumcised men and increasing the numbers of circumcised men until a specified percentage of men in that age group, irrespective of HIV status, were circumcised.

The remaining parameters, such as HIV-related mortality and mother–child transmission probability were selected from empirical studies.[27–30] For further details about the model, see Supplementary data.

Mean behaviour and confidence intervals

We determined mean behaviour and 95% confidence intervals (CI) for HIV prevalence and incidence under each scenario by Latin Hypercube sampling uniformly over the range of parameter values (Table 1), with 500 model simulations over the 40-year period.

The basic model consisted of 16 parameters (Table 1) representing the uncertainty in sexual behaviour, population demographics and the benefits of MC. The intervention scenarios were: (i) circumcising all adult males until the fraction of circumcised men reached a specified level, (ii) circumcising only men who belong to the more sexually active group, (iii) circumcising only men who belong to the less active group, (iv) circumcising only men of certain age groups, (v) circumcising all adult men but assuming partial recruitment of those men who received MC into the more sexually active group and (vi) similar to the last scenario but recruiting an equivalent percentage of non-core women into the core group. In reality, it is not possible to assign children to either the core or non-core group; however the purpose of these simulations was to estimate the contribution of each group to the overall result of a general intervention.

The last two scenarios were designed to provide lower and upper bounds, respectively for the effects of widespread increases in risky behaviour following a MC intervention caused by overconfidence in the protective effect. We were uncertain if women would increase their rate of partner change in response to increased pressure from men, or whether men would have to change their partner preferences in order to achieve a greater number of contacts. We assumed that demand for FSW increased with increased risky behaviour but a lack of increased contacts with the general female population did not lead to an increase in FSW contacts.

Simulations were performed with Matlab Version 7.0, The MathWorks Inc., Natick MA, USA.

Results

Agreement with ecological studies

The mathematical model produced findings consistent with the range of observed[12] correlations between current HIV prevalence and levels of MC in Sub-Saharan Africa (Figure 1). This agreement between

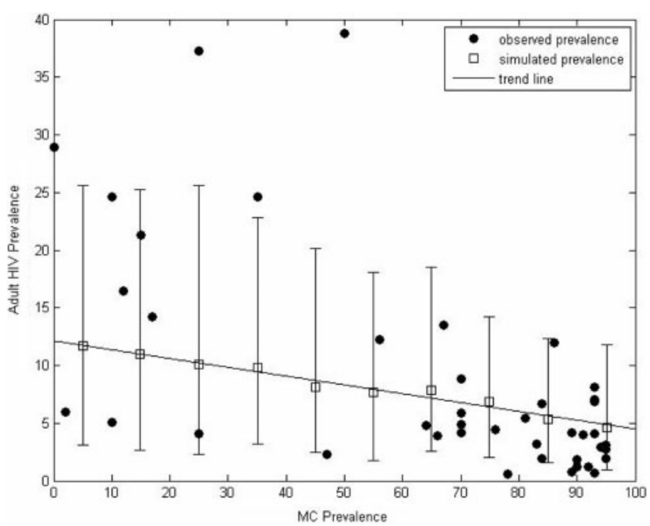

Figure 1 Simulations, mean and 95% CI compared with observed adult HIV prevalence in Sub-Saharan African countries in 2003 and their estimated levels of MC (circles[12])

simulation and observations from 41 sub Saharan countries confirms that the model generates valid estimates of HIV prevalence in a representative sub Saharan population. Simulations showed adult HIV prevalence decreasing from 12% with no circumcised men to 5% with all men circumcised in a country with average levels of MC. The 95% CI generally included the range of countries from ∼25% down to 1% HIV prevalence. However four southern countries, Botswana, Lesotho, South Africa and Swaziland, lie above the 95% CI and seven northern countries, Sudan, Somalia, Gambia, Niger, Sierra Leone, Senegal and Mauritania, lie below the 95% CI of these simulations, suggesting the influence of regional heterogeneities such as correlation between behaviour and MC, migration patterns and starting years of the HIV epidemic.

Circumcision as an intervention with different levels of coverage

Higher levels of MC, when present at the beginning of an HIV epidemic, can lead to greatly reduced adult HIV prevalence (Figure 1). However what impact will increasing MC have on an established epidemic? We simulated increased MC commencing in 2007, with levels of circumcision increasing over the subsequent 5 years and assessed changes in HIV prevalence at year 2020.

For an average population with low initial MC (0–20%), increasing MC to full coverage starting in 2007 would decrease HIV prevalence in 2020 from 12 to 6%. This 6% HIV prevalence decrease with 100% MC intervention scales similarly for lower MC coverage, regardless of initial MC levels (Figure 2a). Hence increasing MC by 50%, from 0 to 50% or from 50 to 100%, will decrease HIV prevalence in 2020 by half of the 6% decrease, namely by 3% (from 12 to 9% for 0 initial MC and from 8 to 5% for 50% initial MC). Similar results were found for the incidence of HIV in 2020 with incidence dropping from 19 new cases per thousand adults to just 7 cases per thousand. Countries with HIV prevalence higher than the mean can experience further decreases as depicted by the 95% CI (Figure 2a). A country like Zimbabwe with 10% MC and 25% adult HIV prevalence could reduce this to 13% if MC coverage were increased to 100%.

Effects on HIV prevalence for women were similar to that for men, with little difference in mean decreases with MC in 2020. As would be expected, the effects on HIV prevalence and incidence among men occur ∼2 years earlier than among women (Figure 2b).

Restricting intervention to certain age groups

To date most models of the effectiveness of MC have only considered circumcising men regardless of their age.[12] However, age is an important factor in the success of an MC intervention (Figure 2c).

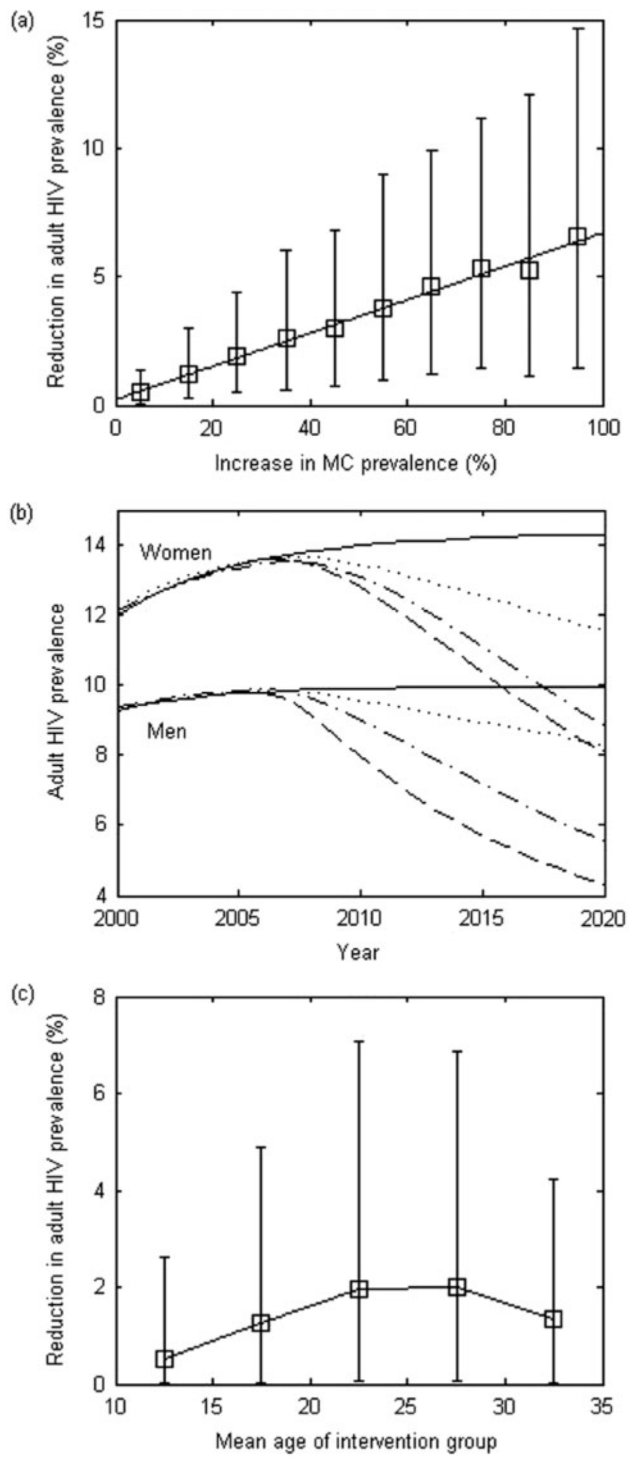

Figure 2 (a) Change in adult HIV prevalence in 2020 due to an intervention of an increase in the percentage of men circumcised. (b) Adult HIV prevalence for males and females over time. Prevalence without intervention (solid), with an intervention commencing in 2007 with full coverage achieved within 5 years (dashed), with an intervention applied only to core group members (dotted) and with an intervention applied only to men between 20 and 30 years of age (dot dashed). (c) Change in adult HIV prevalence in 2020 with increased MC as a function of the age group to be circumcised

Circumcising men between the ages of 20–25 or 25–30 years old caused the greatest decrease in prevalence, 2% on average. Circumcising men older than 30 years from 2007 caused less reduction in HIV prevalence (1.3%) due to declining contact with FSW. Circumcising males, aged 10–15 years also had a small effect (0.5%), since not every member of this group had been sexually active and therefore susceptible to HIV infection by the year 2020. In terms of HIV incidence reduction, circumcising men between the ages of 20 and 25 reduced incidence by 4.9 cases/thousand whereas circumcising 25–30 year old men reduced incidence by 4.4 cases/thousand. Incidence reduction in the other age groups followed a similar pattern to the reduction in HIV prevalence.

Circumcising only high-risk individuals

Sexual activity is another aspect that determines the effectiveness of MC intervention but activity is not uniform throughout the population. In our model, we let 0–20% of the population change partners 2–4 times more regularly than the rest of the population. This more active core group is often important as a disease can be endemic within this subpopulation and from there re-infect the rest of the population. We investigated what would happen if the intervention was applied either only to these more sexually active men or to all men, except them. Even though the core group represents on average 10% of the population, only circumcising them leads to approximately one-third the benefits of circumcising every male. For example going from 50% MC to 100% MC in all males reduces adult prevalence in 2020 by 3.0% but by 1.1% if only the smaller core group is targeted. Excluding the core group from the MC intervention also reduces its effectiveness with an average decrease in HIV prevalence in 2020 of 2.2% or about two-thirds of the reduction when applied to all men (Figure 2b). Reduction in HIV incidence followed this trend with a reduction of 2.4 cases/thousand when only the core group was circumcised compared with 4.6 cases/thousand when the core group was excluded.

Sensitivity of intervention to increased risky behaviour

It has been observed that treated individuals can undo benefits arising from treatment by increasing their risky behaviour. For MC this could lead to an increase in prevalence as the new behaviour negates the benefit derived from the intervention. Our analysis considered two scenarios of population-wide changes in sexual behaviour following a MC intervention starting in 2007. The first scenario changed only the number of sexual partnerships per year for men by moving newly circumcised males from the non-core group to the core group (Figure 3a), whereas the second one moved both males and a proportional number of females from the non-core group to the core group (Figure 3b), increasing the overall number of partnerships. The actual behaviour change should lie between these extreme scenarios. Decreased HIV prevalence and incidence with MC in the first intervention seems robust to increases in male risky behaviour with mean change in prevalence and incidence below 0 even when all men join the high-sexual activity group (Figure 3a). However in the second scenario, mean change in adult HIV prevalence and incidence becomes positive when ~43% of treated men engage in riskier behaviour (Figure 3b). These two intervention scenarios provide a rough lower and upper bound, respectively on the sensitivity of MC interventions to increases in risky behaviour. In addition, countries with HIV prevalence higher

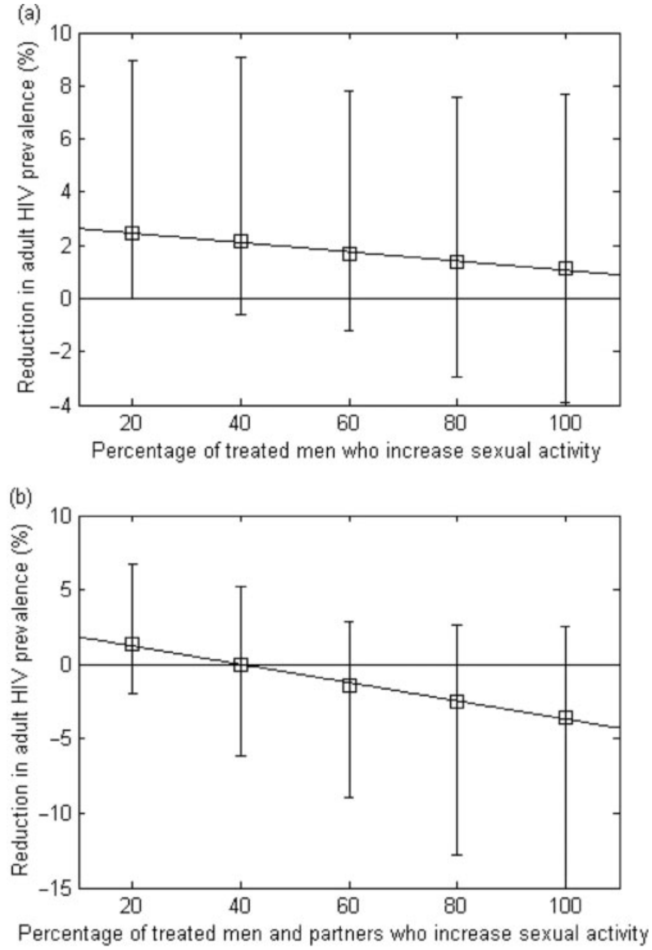

Figure 3 (a) Change in adult HIV prevalence in 2020 with increased MC as a function of the percentage of men who receive the intervention and subsequently engage in riskier behaviour. (b) Change in adult HIV prevalence in 2020 with increased MC as a function of the percentage of men who receive the intervention and their partners who subsequently engage in riskier behaviour

than the mean are more susceptible to increased risky behaviour undoing the benefits of MC, as the 95% CI quickly encompasses a positive change in 2020 prevalence.

The complete results from the simulations of the different intervention scenarios can be found in the Supplementary data.

Discussion

MC has been shown to be an important factor in HIV epidemics.[4,7–10] Our simulations are consistent with these observations, duplicating the correlation between MC and HIV prevalence from low MC countries [mean observed HIV prevalence in 2003 of 21%, simulation mean 13% (3–26%)] through to countries with high levels of MC [mean observed HIV prevalence in 2003 of 4%, simulation mean 5% (1–13%)]. Although MC is not the sole predictor of levels of HIV prevalence, observations, intervention trials of MC,[8–10] and these and other simulations highlight the role it can play as an intervention in sub-Saharan Africa. A country with low MC and HIV prevalence reflecting current mean values could reduce HIV prevalence from 12 to 6% by 2020. This 6% mean decrease with maximum coverage is reduced on a proportional basis with lower coverage, regardless of initial MC levels. Hence an increase by 50%, from 0 to 50% or from 50 to 100%, would reduce mean HIV prevalence in 2020 by 3%, regardless of starting HIV levels (Figure 2a). Countries where the HIV epidemic reflects behaviour more risky than the norm can expect an even greater reduction. For example, a country like Zimbabwe could reduce adult HIV prevalence from 25 to 13% by 2020 solely due to this intervention.

However complete coverage of MC in a country will be difficult to achieve. Given limited coverage the question is: what groups should then be targeted? Our primary endpoint was HIV prevalence in 2020, with an intervention commencing now. On that time scale there is little benefit in MC for young males. Our calculations also suggest less benefit is obtained circumcising men over 30 years of age (Figure 2c), since it is the young adult age group that is more sexually active.

Women and uncircumcised men will also benefit from circumcising young men due to the decrease in overall HIV prevalence among men. Unfortunately the indirect protection for women is delayed by a few years (Figure 2b) due to the tendency for young women to have contacts with older, already infected men. Other measures such as vaginal microbicides[31] need to be employed alongside circumcision to reduce infection during this period.

Although it would be difficult, the greatest benefit would be achieved by concentrating on MC in high-risk groups. Circumcising this group produces roughly one-third of the benefits of circumcising every man in the same age groups. In terms of cost-effectiveness, circumcising the high sexual activity group, which is ~10% of the population in these calculations, produces the greatest reduction in HIV prevalence for the smallest number of surgical procedures. The converse of this is that omitting this group will greatly reduce the effectiveness of the intervention. Combining these results with those from the different age group simulations suggests that high-risk men in the 20–30 year old age group should receive priority in a MC intervention.

Using MC as an intervention should be accompanied by education on its actual benefits and limitations, as it does not provide complete protection from HIV infection. The intervention's effect on HIV prevalence in an average population can be negated when there are large increases in male and female sexual activity (Figure 3b) and this sensitivity becomes more pronounced in those countries which already exhibit high HIV prevalence. Fortunately recent studies[32] on the sexual behaviour change associated with MC have shown almost no increase in risky activity following circumcision, however whether these observations will apply to a general intervention is unknown.[17] Further modelling is required to examine more accurate scenarios of increased risky behaviour and specific examples of behaviour change such as decrease in condom usage with increasing MC.

These results are also limited in that the population was assumed to be free from other sexually transmitted diseases that are known to be co-factors in HIV infection. As MC has been observed to provide protection against some of these STD, further simulations are necessary before estimating the impact of a MC intervention and subsequent behaviour change in a population with significant STD prevalence.[17]

The model is also limited in that only one intervention roll-out strategy was considered. Within each scenario, uncircumcised men, who belonged to the targeted groups, were circumcised at a rate proportional to their numbers with all such men being circumcised within 5 years of the start of the intervention. Issues such as limitations on the number of circumcisions performed annually and reluctance by men to be circumcised were not considered. These concerns as well as the prioritization of certain groups of men are part of ongoing modelling.

Nevertheless this analysis indicates that circumcision has the potential to be an effective intervention against the HIV epidemic in sub-Saharan Africa even if such intervention is limited to a subset of the young male population.

Supplementary Data

Supplementary data are available at *IJE* online.

Conflict of interest: None declared.

KEY MESSAGES

- Mathematical modelling indicates that increased MC can prove an effective intervention against HIV in sub-Saharan Africa.
- Complete coverage by MC could reduce HIV prevalence for an average population country in sub-Saharan Africa in 2020 from 12 to 6%.
- This intervention is most effective when applied to 20–30 year old risky males with diminishing returns with application to the wider male population.

References

1. Halperin DT, Bailey RC. Male circumcision and HIV infection: 10 years and counting. *Lancet* 1999;**354:** 1813–15.
2. Bonner K. Male circumcision as an HIV control strategy: not a 'natural condom'. *Reprod Health Matters* 2001;**9:**143–55.
3. Lagarde E, Dirk T, Puren A, Reathe RT, Bertran A. Acceptability of male circumcision as a tool for preventing HIV infection in a highly infected community in South Africa. *AIDS* 2003;**17:**89–95.
4. Weiss HA, Quigley MA, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. *AIDS* 2000;**14:**2361–70.
5. Urassa M, Todd J, Boerma JT, Hayes R, Isingo R. Male circumcision and susceptibility to HIV infection among men in Tanzania. *AIDS* 1997;**11:**73–80.
6. Baeten JM, Richardson BA, Lavreys L *et al*. Female-to-male infectivity of HIV-1 among circumcised and uncircumcised Kenyan men. *J Infect Dis* 2005;**191:**546–53.
7. Gray RH, Kiwanuka N, Quinn TC *et al*. Male circumcision and HIV acquisition and transmission: cohort studies in Rakai, Uganda. Rakai project team. *AIDS* 2000;**14:** 2371–81.
8. 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.
9. 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.
10. 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.
11. Bulletin from WHO/UNAIDS. Access to HIV treatment continues to accelerate in developing countries, but bottlenecks persist, says WHO/UNAIDS report. *Indian J Med Sci* 2005;**59**:323–26.
12. Williams BG, Lloyd-Smith JO, Gouws E *et al*. The potential impact of male circumcision on HIV in Sub-Saharan Africa. *PLoS Med* 2006;**3:**e262.
13. Nagelkerke NJ, Moses S, de Vlas SJ, Bailey RC. Modelling the public health impact of male circumcision for HIV prevention in high prevalence areas in Africa. *BMC Infect Dis* 2007;**7:**16.
14. 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.
15. Anderson RM. Mathematical models of the potential demographic impact of AIDS in Africa. *AIDS* 1991;**5 (Suppl 1):**S37–44.
16. Anderson RM, May RM, Ng TW, Rowley JT. Age-dependent choice of sexual partners and the transmission dynamics of HIV in Sub-Saharan Africa. *Philos Trans R Soc London B Biol Sci* 1992;**336:**135–55.
17. Kalichman SC, Eaton L, Pinkerton SD. Circumcision for HIV prevention: failure to fully account for behavioral risk compensation. *PLoS Med* 2007;**4:**1.
18. Auvert B, Buonamico G, Lagarde E, Williams B. Sexual behavior, heterosexual transmission, and the spread of HIV in sub-Saharan Africa: a simulation study. *Comp Biomed Res* 2000;**33:**84–96.
19. Blower SM, Hartel D, Dowlatabadi H, Anderson RM, May RM. Drugs, sex and HIV: a mathematical model for New York City. *Philos Trans R Soc London B Biol Sci* 1991;**331:**171–87.
20. Gregson S, Nyamukapa CA, Garnett GP *et al*. Sexual mixing patterns and sex-differentials in teenage exposure to HIV infection in rural Zimbabwe. *Lancet* 2002; **359:**1896–903.
21. Munguti K, Grosskurth H, Newell J *et al*. Patterns of sexual behaviour in a rural population in north-western Tanzania. *Soc Sci Med* 1997;**44:**1553–61.
22. *United Republic of Tanzania Epidemiological Fact Sheet on HIV/AIDS and sexually transmitted infections - 2002 Update:* UNAIDS, UNICEF, WHO. 2002.
23. Quinn TC. Viral load, circumcision and heterosexual transmission. *Hopkins HIV Rep* 2000;**12:**1,5,11.
24. 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:**921–29.
25. Nicolosi A, Correa Leite ML, Musicco M, Arici C, Gavazzeni G, Lazzarin A. The efficiency of male-to-female and female-to-male sexual transmission of the human immunodeficiency virus: a study of 730 stable couples. Italian Study Group on HIV Heterosexual Transmission. *Epidemiology* 1994;**5:**570–75.
26. European Study Group on Heterosexual Transmission of HIV. Comparison of female to male and male to female transmission of HIV in 563 stable couples. *BMJ* 1992;**304**:809–13.
27. John GC, Kreiss J. Mother-to-child transmission of human immunodeficiency virus type 1. *Epidemiol Rev* 1996;**18:**149–57.
28. Morgan D, Maude GH, Malamba SS *et al*. HIV-1 disease progression and AIDS-defining disorders in rural Uganda. *Lancet* 1997;**350:**245–50.

[29] Morgan D, Mahe C, Mayanja B, Whitworth JA. Progression to symptomatic disease in people infected with HIV-1 in rural Uganda: prospective cohort study. *BMJ* 2002;**324:**193–96.

[30] Bobat R, Moodley D, Coutsoudis A, Coovadia H, Gouws E. The early natural history of vertically transmitted HIV-1 infection in African children from Durban, South Africa. *Ann Trop Paediatr* 1998;**18:** 187–96.

[31] Klasse PJ, Shattock R, Moore JP. Antiretroviral drug-based microbicides to prevent HIV-1 sexual transmission. *Annu Rev Med* 2008;**59:**455–471.

[32] Agot KE, Kiarie JN, Nguyen HQ, Odhiambo JO, Onyango TM, Weiss NS. Male circumcision in Siaya and Bondo districts, Kenya: prospective cohort study to assess behavioral disinhibition following circumcision. *J Acquir Immune Defic Syndr* 2007;**44:**66–70.

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Commentary: Disease modelling to inform policy on male circumcision for HIV prevention

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The findings from three randomized trials[1–3] and multiple observational studies[4] that male circumcision prevents HIV acquisition in men has been welcomed as an historic opportunity to control the HIV epidemic, particularly in sub-Saharan Africa.[5] However, the challenges are daunting because we have never attempted to use surgery as a means of controlling an infectious disease, the African health infrastructure is weak and trained personnel required to provide circumcision surgery on a massive scale are limited. Therefore, modelling the impact of circumcision on the future course of the HIV epidemic is needed to persuade health authorities and donors to invest resources in this unprecedented initiative.

The paper by Londish and Murray in this volume[6] adds to the growing body of models, all of which suggest that circumcision has the potential to abate but not abolish the African HIV epidemic over a period of 10-20 years.[7–10] A variety of model projections were reviewed at a recent Joint United Nations Programme on AIDS (UNAIDS) meeting at Imperial College, London (March 5–6, 2008). A report will be forthcoming. The models have varied in their assumptions and structures, and in the endpoints used (e.g. HIV prevalence or incidence over time, HIV infections or AIDS deaths prevented, the number of surgeries needed to avert one HIV infection and the costs per infection averted). Irrespective of these differences in modelling methods and outputs, the direct biological effect of circumcision on reducing HIV acquisition in men by ~60%, and the secondary protection afforded to women via reduced exposures to HIV infected men, are so overwhelming that, under most plausible scenarios, the impact of circumcision on the African HIV epidemic is clear and substantial. The impact of circumcision will likely be greatest in settings, such as those in southern Africa, where HIV incidence is high and the prevalence of circumcision is low.

The circumcision trials provide an estimate on the numbers needed to treat per HIV infection over a short period of two years. However, since the efficacy of circumcision is likely to be life long, models can estimate the number of surgeries needed to prevent one HIV infection over a period of 10–20 years. In most sub-Saharan African settings, the number of surgeries per HIV infection averted over a decade ranges from 5–15, depending on male HIV incidence. This makes circumcision a highly cost effective intervention, particularly when costs are discounted by savings for future antiretroviral care due to prevention of HIV acquisition.

Other policy relevant questions addressed by modelling include whether to provide services to all men or to focus on specific segments of the population such as limited age groups or subgroups with higher sexual

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