HIV prevention policy and programme planning: What can mathematical modelling contribute?
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Chapter 6

Male circumcision and risk of HIV infection in women: a systematic review and meta-analysis

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Male circumcision provides long-term indirect protection to women by reducing the risk of heterosexual men becoming infected with HIV. In this Review, we summarise the evidence for a direct effect of male circumcision on the risk of women becoming infected with HIV. We identified 19 epidemiological analyses, from 11 study populations, of the association of male circumcision and HIV risk in women. A random-effects meta-analysis of data from the one randomised controlled trial and six longitudinal analyses showed little evidence that male circumcision directly reduces risk of HIV in women (summary relative risk 0.80, 95% CI 0.53–1.36). Definitive data would come from a further randomised controlled trial of circumcision among men infected with HIV in serodiscordant heterosexual relationships, but this would involve enrolling about 10 000 couples and is likely to be logistically unfeasible. As circumcision services for HIV prevention are scaled-up in high HIV prevalence settings, rapid integration with existing prevention strategies would maximise benefits for both men and women. Rigorous monitoring is essential to ensure that any adverse effects on women are detected and minimised.

**Introduction**

Three randomised controlled trials and over 40 observational epidemiological studies have provided compelling evidence that male circumcision reduces the risk of heterosexual men becoming infected with HIV. WHO-UNAIDS recommend that circumcision be added to present HIV-prevention strategies for HIV risk reduction in heterosexual men.

Men who are not infected with HIV in high HIV-prevalence settings will directly benefit from expanded access to circumcision services, but the implications for women are less clear. Women are affected by circumcision as sexual partners and as parents. Studies of the acceptability of circumcision in southern and east Africa done before trials showed that a majority of women interviewed (median 69%; range 29–87%) favoured circumcision for their partners, and 81% (range 70–90%) were willing to circumcise their sons, if it were safe and affordable. A study from Mysore, India, also found that most women with uncircumcised sons (457 of 564; 81%) would definitely circumcise them if the procedure was offered safely and free of charge.

A woman’s risk of HIV infection depends on the prevalence of HIV infection among her male partners, the rate of forming partnerships, and the probability of becoming infected with HIV on exposure to an infected partner. Expanded male circumcision services will decrease the HIV prevalence in men, and mathematical modelling confirms that, in high HIV-prevalence settings, women will benefit from expanded circumcision services through a lower risk of exposure to men infected with HIV. In the absence of a direct protective effect of circumcision on male-to-female transmission, these benefits will likely take several years to become evident, and will increase over time, with subsequent reductions in rates of mother-to-child transmission. The effect of circumcision on the probability of becoming infected with HIV on exposure to an infected male partner will depend on whether there is a direct protective effect of circumcision on male-to-female transmission, as well as any effect of circumcision on HIV cofactors (ie, factors that affect HIV transmission probability) in either the man or the woman. Although there are few data on the direct effect of circumcision on male-to-female HIV transmission, randomised controlled trials show that circumcised men are at substantially lower risk of some cofactors (genital ulcer disease and possibly herpes simplex virus type 2). There is increasing evidence that female partners of circumcised men also have a reduced risk of cofactors, including genital ulcer disease and vaginal infections such as bacterial vaginosis and trichomonas infection.

In this Review, we summarise the available epidemiological evidence of a direct effect of circumcision on male-to-female transmission of HIV, and discuss research and public health implications of our findings.

**Methods**

**Search strategy and selection criteria**

Inclusion criteria were epidemiological studies of the association of HIV prevalence or incidence in women as the outcome, with male partners’ circumcision status as an exposure. We identified such studies by searching PubMed with the following search string: (“HIV seropositivity/epidemiology”[MeSH] or “HIV sero-positivity/etiology”[MeSH] or “HIV seropositivity/prevention and control”[MeSH] or “HIV seropositivity/transmission”[MeSH] or “HIV infections/epidemiology”[MeSH] or “HIV infections/epidemiology”[MeSH] or “HIV infections/prevention and control”[MeSH]) or “HIV infections/transmission”[MeSH] or HIV[MeSH] or hiv[text word] and (“epidemiologic studies”[MeSH] or “seroepidemiologic studies”[MeSH] or “risk factors”[MeSH] or “odds ratio”[MeSH] or
"prevalence"[MeSH] or “incidence”[MeSH] or “risk”- [MeSH] or “cross-sectional studies”[MeSH] or “epidemiologic methods”[MeSH] or prevalence[text word] or incidence[text word] and [journal article[pt] or letter[pt]] and “humans”[MeSH] and “female”[MeSH] and (“circumcision, male”[MeSH] or circumcision[text word]).

The initial search, done on Nov 27, 2008, identified 121 papers. The abstracts of these 121 papers were read by two reviewers (HA W and Natasha Larke, London School of Hygiene and Tropical Medicine, London, UK), and 41 were potentially relevant (ie, the abstract showed that the study included measures of effect size for HIV risk factors for women). The search was updated on Aug 8, 2009, identifying a further 17 papers, of which one was potentially relevant. Two studies from conference presentations were also included.14,15 Full copies of the 42 potentially relevant papers and two presentations were obtained, and one further paper16 was identified through the reference lists of relevant papers. 33 of these papers were deemed ineligible, with the most common reason being that they did not contain data on circumcision status of the male partner (figure 1). Additional relevant analyses were obtained from two authors (Gray RH, Johns Hopkins University, Baltimore, USA, personal communication; Lingappa J, University of Washington, Seattle, USA, personal communication). Of the 14 eligible studies, two included three subanalyses (Gray RH, personal communication),19 and one included two subanalyses (Lingappa J, personal communication). The final review contained data on 11 distinct study populations, and included 19 analyses.

In addition, we reviewed data from the Demographic and Health Surveys (DHS) project20 to obtain self-reported prevalence of male circumcision, and national population-based surveys done from 2001–05.21

Data extraction and analysis

11 studies contained relevant information and data were extracted by HAW and CAH. The data extracted included study design, study population, location, circumcision prevalence, HIV prevalence among women by circumcision status of their partner, and measures of effect. Unadjusted risk ratios (RRs) and 95% CIs were calculated from data given in the papers. Adjusted measures of effect were also extracted. To our knowledge, none of the studies included men infected with HIV on antiretroviral treatment, either because they were done before availability of treatment, or because such men were ineligible for the studies.

The association of male circumcision and HIV risk in women is best estimated from longitudinal studies, which, unlike cross-sectional studies, are able to distinguish the temporal sequence of exposure and infection with HIV (table 1). Specifically, in cross-sectional studies of couples we do not know which partner was infected first, and such information is essential to estimate the effect of circumcision on male-to-female transmission. For this reason, the primary analysis was restricted to longitudinal studies. Random-effects meta-analysis was used to assess between-study heterogeneity, and to calculate the summary RR and 95% CI. For consistency, unadjusted measures of effect for cross-sectional studies are presented as prevalence ratios, even if an odds ratio (OR) is presented in the original paper. The meta-analysis was done using the adjusted measure of effect ratio if available, otherwise the unadjusted measure was used. All analyses were done with Stata 10.1.
### Results

**Randomised controlled trial data**

Good randomised controlled trials are the gold standard of epidemiological evidence (table 1). Only one trial of male circumcision has investigated the effect on women becoming infected with HIV. This trial, which enrolled men infected with HIV with no evidence of immunosuppression, with uninfected female partners, was done in Rakai, Uganda, in parallel with the trial among men not infected with HIV. Recruitment into the trial was stopped at interim analysis on the recommendation of the data safety monitoring board. This decision was on the basis of the futility of continuing to recruit because fewer numbers are too small to be conclusive. Among the 18 couples in the intervention arm who resumed sex more than 5 days before certified wound healing there were five seroconversions (27·8%), compared with six among 63 couples (9·5%) who first had sex after this time ($p=0·06$). This latter figure is similar to the seroconversion risk among couples in the control arm (six of 68; 8·8%).

Since the trial was stopped early, the effect of circumcision on new HIV infections in female partners might have become stronger over time as the relative effect of any increased transmission among couples resuming sex before complete wound healing would be greatest in the first few months after circumcision. However, overall, this trial provides no evidence of benefit or harm of male circumcision on women becoming infected with HIV.

### Population-based longitudinal studies among serodiscordant couples

The most informative observational designs to detect an effect of circumcision on women becoming infected are...
longitudinal studies among monogamous HIV-serodiscordant couples with the male partner infected with HIV and the female partner uninfected. To our knowledge, data from only two such studies are available.15,16 In the Rakai community cohort study of 343 HIV-serodiscordant couples with the male partner infected with HIV, participants were followed from 1994 to 2004.17 An updated analysis of data presented in a previous publication17 found that circumcision was associated with a borderline lower risk of women becoming infected with HIV (RR 0·67, 95% CI 0·45–1·00; table 2). In an earlier analysis of the cohort, based on 224 couples, the overall RR was 0·41 (95% CI 0·20–1·2) and circumcision had a substantially greater protective effect in couples where the men had viral loads below 50 000 copies per mL. However, there was no difference by viral load in the updated analysis (Gray RH, personal communication).

The recently completed Partners in Prevention trial18 of herpes suppressive treatment also provides data on the effect of male circumcision on HIV transmission to female partners. This multicentre study recruited 3408 HIV-serodiscordant couples in 14 African sites. Among these, 1096 couples had a male partner who was infected with HIV and there was at least one follow-up visit of the female partner. Viral sequencing was used to determine whether incident HIV infections had happened within the partnership. There was some evidence that the female partners of circumcised men had less likely to become infected with HIV, although this was not statistically significant (adjusted RR 0·60, 95% CI 0·31–1·36; table 2).

We included the trial data and the longitudinal observational studies15,18,16,19 in a random-effects meta-analysis. The summary RR was 0·80 (95% CI 0·54–1·21; figure 2). Since there was some evidence of heterogeneity (p=0·05), this summary estimate should be interpreted cautiously.

Population-based observational studies among women

We identified seven observational analyses among women that included their male partners’ circumcision status as a risk factor for infection with HIV (table 2). All studies were from sub-Saharan Africa, three studies were cross-sectional, and four were longitudinal. Each of these studies relied on the women’s reports of their partners’ circumcision status, and hence the studies are susceptible to misclassification of circumcision status. Results were inconsistent, with two studies finding a significant protective effect of having a circumcised partner,19,20 one finding a significant adverse effect,19 and four not finding a significant association.16,18 The adjusted measures of effect are generally similar to the unadjusted measures, indicating relatively little confounding. The study found a significantly increased HIV prevalence among 5690 partners of circumcised men that attended antenatal clinics in the Butare region, Rwanda, revealing an HIV prevalence of 7·5 (24·4%) of 307 among women with circumcised partners and 442 (8·4%) of 5286 among women with uncircumcised partners (adjusted OR 2·1, 95% CI 1·5–2·9).16 The association was similar in higher-risk and lower-risk women, with higher-risk women defined as those who reported having more than one sexual partner in the past 5 years or having had sex to support themselves. Notably, the 2005 Rwanda DHS survey16 also found slightly higher HIV prevalence among self-reported circumcised men (3·5% prevalence among circumcised men, 2·1% prevalence among uncircumcised men).

Including these cross-sectional studies in women16,18,20 made little difference to the summary RR (OR 0·81, 95% CI 0·54–1·22) but increased the between-study heterogeneity (p<0·001) as expected, since it is to be expected that estimates from longitudinal studies would be more accurate, since partners’ reported (or observed) circumcision status at the time of HIV seroconversion is known.

Cross-sectional observational studies among couples

We identified nine cross-sectional analyses on circumcision prevalence among HIV-serodiscordant couples (Gray RH, personal communication; Lingappa J, personal communication).16,20 These cross-sectional data provide weaker evidence than randomised controlled trials or longitudinal studies because it is unknown which partner in seroconcordant couples became infected first, and whether transmission happened within the partnership. Table 1 summarises circumcision prevalence in seroconcordant couples infected with HIV (M+F+), serodiscordant couples with a female partner that is infected (M–F+), and serodiscordant couples that are not infected with HIV (M–F–). Given the partial protection of male circumcision against men becoming infected with HIV, we would expect a higher prevalence of circumcision in serodiscordant couples with a female index case (M–F+) than in serodiscordant couples that are infected with HIV. Similarly, if circumcision protects against women becoming infected by male partner...
infected with HIV, one would expect a higher circumcision prevalence in M+F– couples than in concordant couples infected with HIV.

Circumcision prevalence in both M+F+ and M–F+ couples was available for only four studies, of which three were cross-sectional analyses from the Rakai population-based cohort (Gray RH, personal communication). In Rakai, the prevalence of circumcision is higher in M–F+ couples than among seroconcordant couples infected with HIV, as expected, but there is little difference in circumcision prevalence between M+F– couples and seroconcordant couples infected with HIV, suggesting little effect of circumcision on women becoming infected with HIV. The fourth informative study, from Trinidad and Tobago, was a small study, but found circumcision prevalence similar in M+F+ (four of 34; 12%) and M–F+ (two of 20; 10%) couples, and circumcision prevalence higher in M+F– couples (five of 16 [31%]; RR 2·66, 95% CI 0·82–8·58) compared with M+F+ couples; de Gourville, WHO, Geneva, Switzerland, personal communication.

In summary, the cross-sectional studies of circumcision status in couples are not informative with regard to the effect of circumcision on women becoming infected with HIV.

### Ecological data

Figure 3 shows the correlation of country-level male circumcision prevalence with national HIV prevalence (2001–05) among men and women aged 15–49 years, for all countries in sub-Saharan Africa with available data.20–22 HIV prevalence in both men and women is highest in countries in southern Africa where fewer men are circumcised (Zimbabwe, Zambia, South Africa, and Malawi). HIV prevalence is also high in Lesotho, where 48% of men report being circumcised but the true figure is thought to be much lower than this since generally the foreskin is not removed during initiation.23 In other countries, the correlation between the prevalence of HIV in adult women and male circumcision suggests a clear population-level benefit of circumcision to women, most likely through a reduced HIV prevalence in men and hence low risk of exposure.24–26

### Discussion

Our Review finds little epidemiological evidence of a direct protective effect of male circumcision on women becoming infected with HIV, although such an effect cannot be ruled out. We do, however, see that in sub-Saharan Africa, HIV prevalence in women is lower in countries with high levels of male circumcision. This is likely due to reduced exposure to HIV among women in settings where male circumcision is widespread.

The most rigorous study designed to directly estimate the effect of circumcision on women becoming infected is the randomised controlled trial from Rakai, Uganda.27 However, because of the small numbers of partners enrolled concurrently and early termination of the trial, this trial does not provide evidence for or against an effect of circumcision on women becoming infected with HIV. Nevertheless, this trial does indicate a biologically plausible potential increased risk to female partners of circumcised men infected with HIV if sexual intercourse resumes before complete wound healing. Although mathematical modelling shows that this will have little population-level adverse effect because of the brevity of this healing period,4 this finding is clearly of concern for individual women, highlighting the need for careful counselling about the importance of abstaining from sex until complete wound healing. Whenever possible, female partners should also attend pre-circumcision counselling to reinforce this message. Another potential concern for women is that circumcised men might increase their risk-taking behaviour if they believe

<table>
<thead>
<tr>
<th>Setting (year of study)</th>
<th>Circumcision prevalence in HIV seroconcordant couples</th>
<th>Circumcision prevalence in M+F+ seroconcordant couples</th>
<th>Circumcision prevalence in M+F– seroconcordant couples</th>
<th>RR for circumcision among M+F+ vs M+F– couples (95% CI)</th>
<th>RR for circumcision among M+F+ vs M+F+ couples (95% CI)</th>
<th>RR for circumcision among M+F– vs M+F– couples (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rakai cohort 1994-98b</td>
<td>Rakai, Uganda (1999)</td>
<td>30/116 (27%)</td>
<td>29/122 (24%)</td>
<td>–</td>
<td>2·67 (1·36–3·13)</td>
<td>0·82 (0·44–1·53)</td>
</tr>
<tr>
<td>Rakai cohort 2003 (Gray)</td>
<td>Rakai, Uganda (2003)</td>
<td>22/56 (14%)</td>
<td>12/47 (27%)</td>
<td>1·18 (0·62–2·25)</td>
<td>0·87 (0·46–1·63)</td>
<td>1·32 (0·65–2·69)</td>
</tr>
<tr>
<td>Rakai cohort 2004 (Gray)</td>
<td>Rakai, Uganda (2004)</td>
<td>29/56 (17%)</td>
<td>22/50 (44%)</td>
<td>1·71 (0·95–2·77)</td>
<td>0·86 (0·46–1·58)</td>
<td>1·50 (0·86–2·67)</td>
</tr>
<tr>
<td>Rakai cohort 2005 (Gray)</td>
<td>Rakai, Uganda (2005)</td>
<td>38/184 (21%)</td>
<td>24/155 (16%)</td>
<td>1·63 (0·99–2·64)</td>
<td>1·01 (0·54–1·89)</td>
<td>1·64 (0·98–2·65)</td>
</tr>
<tr>
<td>Partners in Prevention baseline data (Lingappa)</td>
<td>–</td>
<td>300/816 (37%)</td>
<td>81/346 (23%)</td>
<td>–</td>
<td>1·57 (1·27–1·94)</td>
<td>0·90 (0·56–1·43)</td>
</tr>
<tr>
<td>Partners in Prevention baseline data (Lingappa)</td>
<td>Eastern Africa (2004-05)</td>
<td>–</td>
<td>956/1488 (64%)</td>
<td>300/763 (39%)</td>
<td>–</td>
<td>1·63 (1·48–1·80)</td>
</tr>
<tr>
<td>Carael</td>
<td>Kigali, Rwanda (1986)</td>
<td>34/124 (27%)</td>
<td>Unknown/10</td>
<td>Unknown/4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>De Gourville</td>
<td>Trinidad and Tobago (1992-94)</td>
<td>4/34 (12%)</td>
<td>2/20 (10%)</td>
<td>0·85 (0·17–4·23)</td>
<td>2·66 (0·82–8·58)</td>
<td>0·32 (0·07–1·44)</td>
</tr>
<tr>
<td>Malamba</td>
<td>Kampala, Uganda (1998)</td>
<td>3/49 (6%)</td>
<td>24/102 (24%)</td>
<td>2·4/102 (24%)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*Data are for all serodiscordant couples, since the sex of the index partner was not given.

Table 3: Summary of studies of male circumcision status among cross-sectional studies of serodiscordant HIV couples.
themselves to be fully, rather than partly, protected. To our knowledge, there are no data on risk behaviour after circumcision among men infected with HIV and there is no evidence of risk compensation in newly circumcised men that are not infected.1–3,32

The two longitudinal observational studies among serodiscordant couples suggest a modest reduced risk of becoming infected with HIV (RR 0·67, 95% CI 0·45–1·00; RR 0·60, 95% CI 0·31–1·16), and further data from similar study designs are needed, for example from HIV-vaccine studies in serodiscordant couples. Observational studies that follow women but not their male partners have several fundamental limitations to exploring the association of male circumcision and female risk of becoming infected with HIV. First, there is the likely misclassification of reported circumcision status of the partner where this has not been directly observed. Several studies have shown that self-reported circumcision status by men can be inaccurate.13,14 If such misclassification was non-differential with respect to HIV status of the female partner, this would tend to bias any true association towards the null. With respect to how true the reports are of partners’ circumcision status, one study did sensitivity analyses to adjust for misclassification of circumcision status, and found that reporting errors were unlikely to have obscured an association between male circumcision and women’s risk of HIV.19 Second, female partners of circumcised men are less likely to be exposed to HIV infection because of lower prevalence in circumcised men, and hence an observed lower risk of HIV incidence in female partners of circumcised men might simply reflect a lower HIV prevalence in their male partners. Third, the cross-sectional studies provide limited information because when each woman became infected with HIV is unknown, so the present partner might not be the one who infected her. This is less of a problem in longitudinal studies where few women reported multiple partners during the period of seroconversion, and analyses can be restricted to women reporting one partner during follow-up. For example, when women with multiple partners were excluded from one study, there was little change in effect.19 In our Review, these studies found inconsistent results, and this is likely because of these limitations.

Possible biological mechanisms for an effect of circumcision on reducing HIV transmission between

Figure 3: Correlation of HIV prevalence in adult men and women with male circumcision prevalence

Male circumcision prevalence from DHS data20 and HIV prevalence in adults from population-based surveys.21 DRC=Democratic Republic of Congo.
men and women include an effect of circumcision through reduced risk of HIV cofactors such as genital ulcer disease and other sexually transmitted infections in men infected with HIV or the female partner uninfected with HIV, or a direct biological mechanism (eg, if HIV were transmitted directly from the foreskin). However, most transmission of HIV between men and women is thought to happen through seminal fluid, and recent data from a study among men who have sex with men indicate that cell-free HIV RNA in the seminal fluid, rather than proviral DNA within lymphocytes in the semen might lead to HIV transmission. Although it seems unlikely that circumcision will affect seminal HIV viral load, this hypothesis could be investigated further. For example, seminal viral load could be compared among circumcised and uncircumcised men. Several studies have collected semen samples, including studies of human papillomavirus and circumcision status. Data from the three male circumcision HIV acquisition trials can also be used to investigate the role of circumcision in modifying the natural history of HIV infection, and subsequent male-to-female infectivity. For example, men who are circumcised before becoming infected with HIV might have a lower bolus of exposure because of a smaller mucosal surface area susceptible to infection, and hence lower blood plasma viral set point and seminal viral load compared with uncircumcised men or men who became infected with HIV before circumcision. Unfortunately, seminal viral loads are not available from these trials, but plasma viral setpoint could be compared with circumcision status among HIV seroconvertors.

Given the limited evidence of a possible direct effect of circumcision on women becoming infected with HIV, it is worth considering whether another randomised controlled trial of circumcision among men infected with HIV and their uninfected partners is warranted and feasible. There are several reasons why it would be desirable to know whether male circumcision provides partial protection against male-to-female transmission of HIV, and if so, by how much.

First, without this information, it is not possible to provide fully informed advice on benefits or harms of circumcision to men infected with HIV and their partners. Second, in terms of public policy, the size of the cost-saving and long-term health benefits of circumcision depend on the likely protection afforded to women. Third, further data are needed on personal risks and benefits of circumcision in men infected with HIV who choose to become circumcised.

However, a randomised controlled trial of circumcision among men infected with HIV and their uninfected female partners will be challenging, and sample size calculations on the basis of the summary efficacy of 20% from our meta-analysis suggests that it would need to identify, recruit, and retain about 10,000 HIV serodiscordant couples in a stable partnership with the man’s CD4 count above 250 cells per µL, and both partners willing for the man to be circumcised, willing to participate in the trial, of legal age to provide informed consent, and intending to remain in study area for 2 years (table 4). This would involve screening many tens of thousands of couples to identify those eligible, which might not be logistically feasible. Further, it could be argued that another randomised controlled trial of circumcision, albeit in men infected with HIV, would potentially cause confusion if it is not understood that the new trial intends to answer a different scientific question. Such confusion could possibly delay scale-up of services if people perceive that male circumcision is still being tested as a strategy to prevent HIV.

There would also be some ethical concerns around a randomised controlled trial. In settings where circumcision is becoming the norm, asking half the men to remain uncircumcised until the end of the trial could be stigmatising. By contrast with other studies of serodiscordant couples, the trial would enrol only men infected with HIV with female partners that are uninfected. Participation would then imply that the men were infected with HIV, which again could be potentially stigmatising for them. These issues were less pertinent for the Rakai trial as it happened at the same time as the new trial intends to answer a different scientific question. Such confusion could possibly delay scale-up of services if people perceive that male circumcision is still being tested as a strategy to prevent HIV.

<table>
<thead>
<tr>
<th>Rate ratio</th>
<th>Person-years needed</th>
<th>Number of M+F– HIV-serodiscordant couples to recruit</th>
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<tbody>
<tr>
<td>3</td>
<td>0·80</td>
<td>35·522</td>
</tr>
<tr>
<td>4</td>
<td>0·80</td>
<td>22·641</td>
</tr>
<tr>
<td>6</td>
<td>0·80</td>
<td>18·761</td>
</tr>
<tr>
<td>8</td>
<td>0·80</td>
<td>11·821</td>
</tr>
<tr>
<td>3</td>
<td>0·75</td>
<td>19·413</td>
</tr>
<tr>
<td>4</td>
<td>0·75</td>
<td>14·730</td>
</tr>
<tr>
<td>6</td>
<td>0·75</td>
<td>9·816</td>
</tr>
<tr>
<td>8</td>
<td>0·75</td>
<td>7·355</td>
</tr>
</tbody>
</table>

*Sample size needed for individually randomised trials of male circumcision to reduce HIV incidence in women. Assuming 90% power, 95% significance level, 2 years follow-up, 20% loss of person-years. In the Rakai trial, the retention rate in men infected with HIV was 87% in the intervention arm and 96% in the control arm. Retention of female partners was 92%. Retention was probably assisted as many participants were in the Rakai Community Cohort Surveillance Study.

Table 4: HIV incidence per 100 person-years in placebo group translated into sample size needed for randomised trials*
circumcision status with HIV serostatus in the community.

Male circumcision for the prevention of HIV is at present being expanded in several settings, and evidence of a direct benefit to women would potentially increase funding, commitment, acceptance, and support for scale-up. Women will benefit both from a reduced HIV prevalence in men, and lower rates of some other sexually transmitted infections, but also likely lower risks of human papillomavirus, cervical cancer, and vaginal infections. Although any direct reduction in the risk of women becoming infected with HIV because of circumcision would substantially enhance the overall effect of male circumcision programmes and lead to faster reductions in the incidence of HIV in women, this Review found no firm evidence for such a direct effect.

Conclusions

Although at a population-level, widespread male circumcision will benefit women by reducing their risk of exposure to HIV, there are insufficient data to know whether circumcision directly reduces risk of women becoming infected with HIV. A definitive answer would come from a randomised controlled trial of circumcision among heterosexual men infected with HIV in serodiscordant relationships, but such a trial is likely to be unfeasible. At present, circumcision services are being expanded for the prevention of HIV in several settings in southern and eastern Africa, and rapid scale-up of these services, integrated with existing prevention options (male and female condoms, treatment for sexually transmitted infections, testing, and counselling) would maximise the benefits to both men and women. Expansion of male circumcision services needs to include rigorous monitoring and evaluation to ensure that there are no adverse consequences for female partners of circumcised men.

Contributors

HAW designed the search strategy, did the systematic review and meta-analysis, and wrote the first draft of the paper. CAH and HAW extracted the data. KD and CAH commented in detail on the drafts and approved the final version.

Conflicts of interest

We declare that we have no conflicts of interest.

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