

Male circumcision in HIV prevention

The findings of Robert Bailey (Feb 24, p 643),¹ Ronald Gray (p 657)², and their co-workers indicate that male circumcision can have a significant protective effect against HIV infection. Although these results are clearly important for HIV prevention, the benefits of male circumcision could be negated by behaviour that increases HIV risk, especially by a drop in condom use or a rise in sexual partners.

In Bailey and colleagues' trial, circumcised men engaged in riskier sexual behaviour than non-circumcised men. We are concerned about how decreased condom use by circumcised men could increase sexually transmitted infections (STI), and therefore amplify HIV transmission. This concern is especially relevant to those who model the impact of male circumcision, who have so far not taken increases in STIs into account.³ STIs are associated with a two-fold to five-fold increase in HIV transmission.⁴

Herpes simplex virus-2 (HSV-2) is particularly important in HIV transmission and we are not aware of any evidence that circumcision reduces the likelihood of HSV-2 infection. In fact, in Bailey and colleagues' trial, 28% of men were HSV-2 positive and HSV-2 was the only baseline predictor of HIV seroconversion. Failure to account for increases in STIs resulting from less-frequent condom use after circumcision probably inflates estimates of averted HIV infections. Previous cost-effectiveness models of HIV-prevention interventions have accounted for increased STIs after a fall in condom use.⁵ An accurate assessment of the population impact of male circumcision needs to consider both the risk-reducing and potentially risk-enhancing effects of this procedure.

We declare that we have no conflict of interest.

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- 1 Bailey RC, Moses S, Parker C, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet* 2007; **369**: 643–56.
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Recent randomised trials of male circumcision in sterile conditions show substantially reduced HIV incidence in circumcised men.^{1,2} However, the epidemiological mechanism for this effect remains unclear. Although trial investigators have suggested unsubstantiated physiological factors for the apparent protective effect, other mechanisms could account for the results. Circumcision reduces the incidence of genital symptoms.^{2,3} Consequently, circumcised men might receive fewer unsafe injections and other blood exposures during treatment for genital symptoms.⁴ Also, some Africans believe that anal sex has a lower risk of HIV transmission than vaginal sex.⁴ Men who mistakenly practise anal sex as a protective behaviour might feel, after circumcision, less at risk of acquiring HIV and, therefore, shift to vaginal sex, with its lower actual risk of transmission.⁴

In sub-Saharan Africa, circumcised virgins and adolescents are substantially more likely to be HIV-infected than their uncircumcised counterparts.⁴ This result is consistent with repeated observations of unhygienic circumcision procedures. Circumcised adult men, however, are less likely to be infected than uncircumcised

men. The apparent protective effect of circumcision in observational studies of African men could be due to mortality from circumcision-related HIV infections, circumcised men's decreased exposure to contaminated sharps during treatment for genital symptoms, and other factors.⁴

We need studies that involve comprehensive assessment of transmission modes, including tracing of sexual partners and HIV DNA sequencing for incident case-partner pairs, both to determine the mechanism for the observed protective effect and understand whether interventions aside from circumcision would more directly, effectively, and inexpensively activate this mechanism.

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We agree with Robert Bailey and colleagues that a strategy to implement male circumcision will face many problems.^{1,2} A few years ago, in the main sexually transmitted diseases (STI) clinic in Durban, South Africa, we started referring for circumcision people who we thought were at very high risk of acquiring HIV because of deep crevices in the coronal sulcus. We soon gave up because surgeons

The printed journal includes an image merely for illustration

Still Pictures

refused to undertake what they considered to be cosmetic surgery.³

This failure to promote circumcision led us to explore the role of poor genital hygiene as a risk factor for HIV, and we have shown that penile wetness is associated with HIV in uncircumcised men.⁴ We believe that penile wetness is a marker for poor genital hygiene and varies significantly between different populations of uncircumcised men: in Durban penile wetness was identified in 49% of male STI clinic attenders compared with 8% in London.^{4,5} Although the circumcision trials in Kenya and Uganda were rigorous, they did not seem to provide information about genital hygiene. The Uganda² study did report asking questions about male genital hygiene but these results were not shown.

Clearly, undertaking mass male circumcision in selected populations in Africa will be a huge task. We therefore suggest that until any circumcision programme is successfully rolled out, in addition to the usual package of other preventive measures, uncircumcised men are advised to achieve good standards of penile hygiene by keeping the subpreputial space dry.

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Research into circumcision to curtail the HIV pandemic in Africa, such as Robert Bailey and colleagues' work,¹ has been marred by poor science, and the investigators have been criticised by their peers. The rationale for excising foreskins to prevent HIV infection is based on Weiss and colleagues' hypothesis that Langerhans cells in the foreskin are vulnerable to HIV infection.² de Witte and colleagues³ have now proved the opposite: that Langerhans cells produce langerin, which protects against HIV infection. The basis for excising the foreskin to prevent HIV infection now has been overturned. Moreover, Brewer and colleagues have shown that HIV infection is higher in circumcised virgins and adolescents.⁴

All three randomised controlled trials on circumcision against HIV have been terminated early. Mills and Siegfried point out that early termination exaggerates the effects of the studied intervention and call for a meta-analysis of the RCTs.⁵

Male circumcision has long been an operation in search of a disease. Consequently, it is difficult to accept these RCTs at face value. Given the contradictory evidence, whether male circumcision will worsen or improve HIV infection is uncertain. We think more study is needed, including a meta-analysis as proposed by Mills and Siegfried, before mass circumcision programmes are considered.

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Authors' reply

Seth Kalichman and colleagues are concerned that circumcised men might reduce their use of condoms or increase their sexual partners. Men randomised to circumcision in our trial reported an increase in condom use (from 22% to 36%, $p < 0.001$), and the proportion of men who reported two or more sexual partners dropped (from 42% to 33%, $p < 0.001$) between baseline and 6-month follow-up; these reductions in risk behaviours were sustained throughout follow-up. Study groups did not differ in the incidences of syphilis, gonorrhoea, trichomonas, or HSV-2 infections.

Modelling of our study population has shown that the fraction of all HIV infections prevented through circumcision that is attributable to prevention of other sexually transmitted infections (STIs) is likely to be small.¹ Thus, any increase in STI incidence related to risk compensation by circumcised men is likely to have a small effect on HIV infection. Other studies on sexual behaviour and circumcision show no evidence of risk compensation.^{2,3}

Brewer and colleagues suggest that because uncircumcised men have more genital infections, they are exposed to more unsafe injections and blood exposures than circumcised men. During follow-up, genital ulcers were twice as prevalent in the control group, but self-reported injections were equally common in the two groups (36.7% circumcision vs 38.5% control, $p = 0.338$). Brewer and colleagues also suggest that circumcised men might engage in more vaginal and less anal sex, thus accounting for fewer HIV infections. Reports of anal sex were equally uncommon in both groups (1.6%