



## Review

## Pros and cons of circumcision: an evidence-based overview

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## ABSTRACT

Based on three large randomized controlled trials (RCTs) conducted in Africa, it can clearly be stated that circumcision lowers the risk of infection with the human immunodeficiency virus (HIV) and some sexually transmitted infections (STIs) among males in settings of high HIV and STI endemicity. Similar effects on STI risk may exist for females, although this may result from an indirect effect of decreasing risk of infection among male partners. It is unknown whether circumcision prevents HIV acquisition in men who have sex with men (MSM), although there might be a protective effect for men who engage mainly in insertive anal intercourse. When the effects of adult circumcision on sexual function and satisfaction of men are examined, high-quality evidence strongly supports lack of harm. Whether circumcision alters sexual satisfaction of female partners is not known as fewer and smaller studies reported conflicting results. Circumcision rarely causes serious complications if practiced by trained practitioners, in a sterile setting, and with a proper follow-up. These conclusions are limited by the lack of high-quality data from areas outside of Africa. RCTs have not been conducted to assess the effects of circumcising infants or MSM. Circumcision has well-proven benefits for people residing in areas with high prevalence of STIs, including HIV, and is not unethical for those who choose to be circumcised or have their children circumcised on religious, social, or cultural grounds. For many others, a definite pro or con recommendation, based on a risk-benefit ratio, cannot be made. **B. Friedman, CMI 2016;22:768**

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## Introduction

Few procedures generate as much controversy as male circumcision. While religious and social factors strongly influence the decision of many adults and parents about circumcision, others seek to understand in what ways, medically speaking, this procedure can bring benefits or cause harm. While reviewing the literature for this review we have made two observations: first, the abundance of very low-quality research, some of which is clearly biased unreservedly for or against circumcision; second, the bulk of trials and systematic reviews concentrate on one aspect of possible benefits or harms, but do not provide a general overview [1]. Thus, we have tried to filter out bad science, and provide a balanced

discussion of the pros and cons of circumcision for those who have to make a very personal decision.

## Methods

We searched PubMed and the Cochrane Library for the term 'circumcision', filtering in PubMed for clinical trials and systematic reviews. We addressed primarily systematic reviews of randomized controlled trials (RCTs). Where unavailable, we searched for RCTs, and when RCTs were unavailable or insufficient we included observational studies in the literature review. We rated the quality of the evidence as very low, low, moderate, or high. We based the rating primarily on the study design (high quality for RCTs and low quality for observational studies) and then downgraded or upgraded according to the internal validity of each study, following the GRADE recommendations [2]. We accepted the quality rating from systematic reviews using the GRADE system and risk of bias assessment from other systematic reviews. We used the

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terminology ‘affected’ for high-quality evidence, ‘probably affected’ for moderate-quality evidence, ‘may be affected’ for low-quality evidence, and ‘effect not known’ for very low-quality or no evidence [3].

## Circumcision and the risk of HIV acquisition

### Heterosexual men

The inner surface of the foreskin contains Langerhans cells with human immunodeficiency virus (HIV) receptors, which explains the biological rationale for using male circumcision to decrease rates of HIV acquisition among men [4]. Early non-randomized studies attempting to assess the effects of circumcision on HIV could not control for religion and tradition as confounding factors. Three major RCTs comparing immediate and delayed (21–24 months) circumcision, and assessing HIV acquisition in the interval, were conducted in South-Africa, Kenya, and Uganda in the 2000s. All were stopped early when male circumcision was shown to decrease the rates of HIV acquisition in planned interim-analysis [5–7] (Table 1). A Cochrane review of these RCTs, which included a total of 11 500 men, showed that circumcision reduced HIV acquisition with an incidence risk ratio (IRR) of 0.46 (95% CI 0.34–0.62) at the end of follow-up. The number needed to treat (NNT) at 21–24 months was 56 (95% CI 41–90). Circumcision prevented 17 HIV infections (95% CI 11–24) over 2 years per 1000 men, with a control event rate of 2.5% translating to a population yearly incidence of HIV acquisition of 1.25% [8]. The quality of the evidence was moderate to high, downgraded for unreliable randomization methods in two of the trials and early discontinuation in all three trials (although discontinuation rules were defined in all three).

The public health implications of male circumcision have not been studied adequately, as all RCTs assessed the effects of the intervention on individuals rather than on populations. A few mathematical models have been proposed aiming at estimating the potential impact of increased circumcision coverage on the incidence of HIV in Africa. A dynamical simulation model, for example, suggested that full coverage of circumcision could avert 0.3 (0.1–0.5) million deaths in the first 10 years and a further 2.7 (1.5–5.3) million in the next 10 years, in sub-Saharan Africa [9]. However, by definition, models can never account for all additional factors that can influence the impact of a specific intervention on disease incidence [10]. Increasing rates of antiretroviral coverage make impossible long-term assessment of the procedure itself, and the effect of circumcision on sexual risk-taking is unknown. In the three RCTs described above, circumcised males practiced riskier sex behaviours, leading to concerns about disinhibition and higher transmission rates of HIV. Other observational studies from Africa

showed mixed results regarding the possibility of disinhibition following circumcision. Recently, a cohort study from Uganda found that, while the circumcision programme attracts more sexually active males, it does not alter their sexual behaviour [11–13].

Evidence outside of Africa comes mostly from observational studies. Such studies were conducted in the USA and Israel, where circumcision rates are high and HIV burden is relatively low, and similarly showed an inverse association between circumcision and HIV acquisition [14,15]. A systematic review of studies conducted in India included 13 observational studies, showing that circumcision may reduce HIV acquisition by approximately 40% (OR 0.66; 95% CI 0.53–0.83) [16]. As circumcision in India is almost exclusively practiced by Muslims, bias is likely (low-quality evidence).

Following the publication of the RCTs from Africa, the Center for Disease Control and Prevention (CDC) announced in 2007 that there is ‘sufficient evidence to inform heterosexually active males about the significant, albeit partial, efficacy of medical circumcision in reducing the risk of HIV infection’ [17]. Similarly, the WHO/UNAIDS recommends male circumcision as an efficacious intervention for HIV prevention in countries with high HIV incidence and low male circumcision prevalence [18].

### Women

As male circumcision reduces the incidence of HIV among men, it may indirectly reduce the risk of exposure to women. Whether circumcision can directly prevent the acquisition of HIV by female partners of HIV-infected men is uncertain. Only one RCT, conducted in Uganda in 2009, addressed this issue and was discontinued early because of futility [19]. In this trial 922 discordant couples were enrolled and randomized either to circumcision or control (delayed circumcision for 24 months). Surprisingly, there was a small increase in the risk of HIV acquisition among women in the intervention group, mainly because of early resumption of sexual activity before wound healing, and an increase in the viral load shortly after circumcision (high-level evidence). A systematic review summarizing this RCT and a few longitudinal observational studies showed that male circumcision probably does not reduce the risk for HIV among women (relative risk 0.80, 95% CI 0.53–1.36) [20].

### Men who have sex with men (MSM)

To the best of our knowledge, no RCT assessed the impact of circumcision on the risk of HIV acquisition among MSM. A Cochrane systematic review published in 2011 included 20 observational studies in high- and middle-income countries with a total of 65 784 participants. The meta-analysis showed that circumcision

**Table 1**  
Randomized controlled trials of immediate vs. delayed surgical circumcision in Africa

	Auvert 2005 [5]	Bailey 2007 [6]	Gray 2007 [7]
Location	Orange Farm, South Africa	Kisumu, Kenya	Rakai, Uganda
Study years	2002–2005	2002–2005	2002–2006
Age range (years)	18–24	18–24	15–49
N patients	3274	2784	4996
Duration of follow-up	21 months	24 months	24 months
Risk of bias <sup>a</sup>			
Selection bias <sup>b</sup>	High risk	Unclear	High risk
Other	None	None	None

<sup>a</sup> All trials stopped early based on pre-defined stopping rules. As the primary outcome (HIV acquisition) was objective, blinding was deemed less relevant and is not addressed.

<sup>b</sup> Based on the highest risk of random sequence generation and allocation concealment.

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