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# Male circumcision and risk of HIV-1 infection

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## Male circumcision and risk of HIV-1 infection

Sir — Steven Reynolds and colleagues (Mar 27, p 1039)<sup>1</sup> have recast old data from the Mehendale group in Pune, India, on female-to-male infection with HIV-1. They purport to show a significant reduction in female-to-male infection if the man is circumcised.

The exhaustive Cochrane review<sup>2</sup> of the evidence for possible protection from female-to-male sexual transmission of HIV-1 by circumcision concluded that “insufficient evidence exists to support an interventional effect of male circumcision in heterosexual males”. In reviewing previous studies from the Mehendale group in Pune, the Cochrane review noted a low or unstated participation rate, failure to control for religion, and an imbalance between circumcised and uncircumcised groups. As in these previous studies, Reynolds and colleagues’ report is also affected by selection bias because it involved highrisk groups from sexually transmitted disease clinics rather than the general population.

The present study also contains major statistical flaws. Although Reynolds and colleagues attempt to control for religion, a confounder remains because only three participants in the uncircumcised group (0.6%) were Muslim. As Reynolds and colleagues state, “When non-Muslim men were assessed separately, the protective effect was not significant”.

Furthermore, the discrepancy in sample sizes (191 circumcised men vs 2107 genitally intact men) clearly suggests heterogeneity of variance, such that reported “statistically significant effects” might be little more than statistical artifacts, especially with the large overall sample size (n=2298) and resultant high level of experimental power.

Although multiple univariate effects are reported, the corresponding multivariate effects are not reported (in the absence of a significant multivariate effect, interpretation of univariate effects is likely to be difficult).<sup>3</sup> At the very least, basic Bonferroni corrections should be done to keep to a minimum the risk of claiming “significant effects” that are due to chance alone.<sup>3</sup> Also, I am surprised that no effect sizes are reported.

Researcher bias should not be ignored. There is a strong tendency to defend the culture of origin.<sup>4</sup> The Cochrane review notes: “Circumcision practices are largely culturally determined and as a result there are strong beliefs and opinions surrounding its practice. It is important to acknowledge that researchers’ personal biases and the dominant circumcision practices of their respective countries may influence the interpretation of their findings”.<sup>2</sup>

The study also notes a substantial failure to use condoms during visits with female sex workers. Clearly, irrespective of circumcision status, the HIV-1 infection rate would approach zero in both groups if condom use were universal.

The investigators tacitly acknowledge that circumcision would not be culturally acceptable to Hindu men. In addition, there are other factors to consider before taking any

decision to introduce circumcision. These include potential adverse medical and psychosexual effects, as well as legal, ethical, and human rights issues.<sup>5</sup>

The statistical inadequacies highlighted weaken the validity of Reynolds and colleagues' study. Therefore it would be prudent to await the results of the three randomised controlled trials now underway<sup>2</sup> before any conclusions are drawn about HIV-1 transmission and male circumcision status.

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