



The illusive promise of circumcision to prevent female-to-male HIV infection – not the way to go for South Africa

'Circumcision reduces HIV infections 76% in South Africa, researchers find', screamed the headline in the online Bloomberg news, taking its cue from the reported findings of a randomised, controlled intervention trial (RCT) conducted at Orange Farm, Gauteng. The findings were presented by French researcher Bertran Auvert *et al.* in July 2011 at an AIDS conference in Rome, showing that circumcision significantly reduced the risk of female-to-male transmission of HIV. 'We are changing the social norm,' Auvert gushed at a news conference. 'It's the first time in the world that we have a successful intervention in a community to reduce the sexual transmission of HIV between adults.'

University of the Witwatersrand researcher Francois Venter echoed the triumphant tone, telling the *Bulletin of the WHO* that 'Male circumcision is the most powerful intervention we have at this point in time. One of [its] beauties is that it is a one-off operation which takes 15 - 20 minutes but then has a profound effect on the rest of a man's life; whereas to promote condom use or microbicides, repeated long-term promotion is needed.' The most powerful intervention? A lay listener might be forgiven for concluding that circumcision represents a silver bullet that renders conventional prevention strategies obsolete.

Indeed, Marwick Khumalo, a Member of Parliament in Swaziland, was quoted in the local press as saying: 'All male children should be circumcised. To show my seriousness, I have taken all my sons for circumcision.' The KwaZulu-Natal correctional services report a near-stampede by prison inmates across the province demanding to be circumcised, and the authorities are scurrying about to set up circumcision stations in the prisons from their limited HIV prevention resources, apparently oblivious to the absence of any evidence that circumcision prevents male-to-male HIV transmission.

The evidence

The Orange Farm study was one of three independent RCTs conducted in South Africa,¹ Uganda² and Kenya³ to determine whether circumcision reduced the risk of female-to-male transfer of HIV infection during penetrative heterosexual sex. The results showed that the intervention significantly reduced the incidence of HIV infection in the circumcised study group compared with the controls, by 60% in South Africa, 53% in Kenya and 51% in Uganda. In all three studies, the benefits of intervention observed on interim calculations were judged by the researchers to be sufficiently convincing to justify early termination of the RCTs on ethical grounds.

The published conclusion of the South African study is more circumspect, declaring simply that 'Male circumcision provides a degree of protection against acquiring HIV infection, equivalent to what a vaccine of high efficacy would have achieved. Male circumcision may provide an important way of reducing the spread of HIV infection in sub-Saharan Africa.' The comparison to a vaccine has been contested, but the constrained demeanour is probably closer to reality.

The extended claim that circumcision confers lifelong protection seems like a stretch, and cannot be inferred from this or the other RCTs, all of which were terminated at 24 months or less. And because the control group were also offered circumcision at the termination

of the RCT, the opportunity to continue longer-term follow-up was forever extinguished.

The three RCTs sought to test what has long been suggested in many epidemiological studies, dating back to 1987, that enquired into circumcision as a risk factor for HIV-1 infection among men. The studies, though not always consistent, appeared to show that circumcision reduces the risk of HIV infection in men. They were conducted in a wide variety of populations and environments, and a large diversity of research conditions. In 2000, Weiss *et al.*⁴ published a systematic review and meta-analysis of such studies, and concluded that 'Male circumcision is associated with a significantly reduced risk of HIV infection among men in sub-Saharan Africa, particularly those at high risk of HIV.' However, the authors concede that meta-analyses are vulnerable to bias because studies yielding statistically significant findings are more likely to be submitted and published than studies with negative results.

On the other hand, a much-cited Cochrane systematic review from the South African Medical Research Council (MRC) published three years later,⁵ while also finding 'a strong epidemiological association between male circumcision and prevention of HIV, especially among high-risk groups', nevertheless cautioned that there was 'insufficient evidence to support an interventional effect of male circumcision on HIV acquisition in heterosexual men' because 'the observational studies are inherently limited by confounding which is unlikely to be fully adjusted for.'

That was before the three RCTs, publication of which has led to the current drive to inflict mass circumcision on southern African men. Circumcision intervention has now been embraced by the WHO, the Centers for Disease Control, other health-based organisations and some researchers. Even the MRC has since reversed its position, with lead researcher Siegfried declaring on 15 April 2009 that 'Research on the effectiveness of male circumcision for preventing HIV in heterosexual men is conclusive. No further trials are required to establish that HIV infection rates are reduced in heterosexual men for at least the first two years after circumcision.'

However, the three RCTs have not been without detractors. In a scathing critique, Van Howe and Storms⁶ point out that 'In the South African trial, men who reported at least one episode of unprotected sex accounted for 2 498 person-years and 46 HIV infections during the trial. Among the remaining men, who accounted for 2076 person-years, 23 became infected although they either had no sexual contact or always used a condom ... Similarly, in the Ugandan trial, men who consistently used condoms had the same rate of infection as those who never used condoms. Finally, in the first three months of the Kenyan trial, five men became HIV-positive who reported no sexual activity in the period before the seroconversion.' They conclude from their recalculations and statistical reasoning that 'Conservatively for the three trials, 89 of the 205 infections (43.1%) were sexually transmitted. Without knowing which infections were sexually transmitted [and which were not], it is impossible to test the hypothesis of whether circumcision reduces the rate of sexually transmitted HIV.' Such studies, it must be said, depend on subject self-reporting, and, sexuality being a very private matter, the subjects may sometimes be inclined to be less than candid.

Protagonists have touted universal neonatal circumcision (proscribed in South Africa under current law) even though, as cogently argued by Sidler *et al.*,⁷ no credible evidence exists linking circumcision to future protection from HIV in adulthood. The scale of the projected implementation is staggering. Kelly Curran, Technical Director of the HIV/AIDS and Infectious Diseases Department affiliated with Johns Hopkins University,⁸ envisages a roll-out aimed at 80% coverage in 13 countries involving approximately 28 million (that's right, 28 million) procedures over 5 years. In Zambia and Swaziland, a partnership has been launched to circumcise 642 000 adolescent boys and men over 5 years, with the support of a start-up grant of \$50 million from the Bill and Melinda Gates Foundation. It is curious and even worrisome that the campaign to circumcise African men seems to be driven by donor funding and researchers from the North.

Why rolling out circumcision is not the way to go for South Africa

For all the drum-beating promotion of universal circumcision prophylaxis in southern Africa, the big question remains: what man would want to accept circumcision and the associated risks, if he were made clearly to understand the need to continue to abstain, be faithful and/or condomise? What then would be the benefit? A UNAIDS statement of 19 March 2009 states categorically that 'The male latex condom is the single most efficient, available technology to reduce the sexual transmission of HIV and other sexually transmitted infections.' Circumcision, on the other hand, is more expensive, more invasive and less effective by itself. As Van Howe and Storms⁶ put it, 'It is not hard to see that circumcision is either inadequate (otherwise there would be no need for the continued use of condoms) or redundant (as condoms provide nearly complete protection).' Circumcision roll-out will divert scarce resources in money, human resources and infrastructure away from essential health services, in a system that is already severely under-provided. Francois Venter is cited by Chris Bateman⁹ as stating quite correctly that circumcision roll-out would require "serious energy, money and resources" for an effective scale-up of what he believed should be a stand-alone service'. In South Africa today, VCT, ART and PMTCT – all of them with a proven impact on prevention – should merit more priority than circumcision in resource allocation.

Several authors have pointed out as well that, without field testing, it is impossible to predict the applicability and repeatability of the RCT findings in real-world situations. That the RCTs were terminated early does not help. Nor does South Africa's experience with the HIV epidemic offer any clues. It is true that the Eastern Cape (EC)'s Xhosa speakers, who traditionally circumcise, have relatively lower prevalence rates (11%) than KwaZulu-Natal's Zulu speakers (16%), who do not. The difference is not huge, and the EC rates are still way too high by any standard. On the other hand, the Western Cape, with a spotty circumcision tradition, has the lowest prevalence (6%) in the country, almost half that of the EC (ASSA2003 Projections for 2010). According to one nationwide demographic survey,¹⁰ 12.3% of circumcised men were HIV-positive, and 12.0% of intact men were similarly HIV-positive. Van Howe and Storms⁶ observe that among developed nations, the USA has the highest rate of (largely neonatal) circumcision and the highest rate of heterosexually transmitted HIV. Within the USA, black Americans have the highest rate of circumcision and the highest rate of heterosexually transmitted HIV.

These data certainly show no distinct pattern relative to circumcision and the risk of HIV infection.

There is a real risk that the roll-out of circumcision will dilute the standard prevention messages and undermine the gains already made in respect of condom use and behaviour modification. This could result from risk compensation – a false sense of security. Risk compensation occurs when people engage in risky behaviour in the mistaken belief that they have acquired assured protection. For example, in their modelling exercise, Blower and McClean¹¹ found that if an HIV vaccine offered 50% protection, but reduced condom use or increased other risky behaviours, it would be likely to result in higher HIV infection rates. The enthusiasm for circumcision among traditionally non-circumcising populations suggests that circumcision is perceived as special and sufficient protection, and there is a risk that medically circumcised men may feel 'liberated' to engage in risky behaviour, putting themselves and their partners in danger of infection. There is already some evidence to this effect. In the survey by Bridges *et al.*¹² assessing determinants of demand for circumcision, South African men listed 'It means that men don't have [to] use a condom' as an advantage of circumcision. It is noteworthy that circumcision does not protect women from infection risk, but may well increase that risk in the event of risk compensation by their partner.

South Africa must take a page from the book of the Australian Federation of AIDS Organisations¹³ which, in rejecting circumcision for Australia, reiterated that 'correct and consistent condom use, not circumcision, is the most effective means of reducing female-to-male transmission, and vice-versa. Circumcision does not prevent HIV – in high prevalence areas it *reduces the risk of* female-to-male transmission. HIV acquisition rates were nevertheless high in both the circumcised and the non-circumcised groups involved in the trials.'

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