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Male circumcision: a new approach to reducing HIV transmission

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Stephen Moses and Michel Le May are the top-ranked winners of the 2008/09 competition for CIHR/CMAJ Top Canadian Achievements in Health Research. Dr. Moses describes his research project in the following essay. Dr. Le May's essay and synopses of the other 6 winning achievements are available at www.cmaj.ca.

Through the first 2 decades of the HIV/AIDS epidemic, numerous observational studies reported significant associations between lack of male circumcision and risk of sexually transmitted HIV infection among men.¹ A meta-analysis of these studies in Africa showed an adjusted reduction in HIV risk of about 45% in the general population and 70% in high-risk groups.² Uncircumcised men may also be at increased risk of certain sexually transmitted infections, particularly ulcerative infections, which may increase susceptibility to HIV infection.³ These data led to calls for male circumcision to be accepted as an important strategy for HIV prevention, especially in areas of high prevalence of HIV infection.

Most researchers and policy-makers, however, felt that evidence from randomized controlled trials showing a protective effect of male circumcision against HIV infection was required before the procedure could be promoted widely as a preventive measure. In the absence of results from randomized controlled trials, it was not possible to rule out the many factors, such as sexual behaviour, that may have confounded the observed relation between male circumcision and HIV infection. Furthermore, there are potentially serious risks associated with circumcision, including infection, trauma and bleeding. The potential for behavioural disinhibition or risk compensation following male circumcision (the adoption of higher risk behaviour out of the mistaken belief that protection is absolute) was also of concern.

The University of Manitoba / University of Nairobi collaborative research group in Kenya was among the first to identify the association between lack of male circumcision and risk of HIV infection after conducting several cross-sectional and prospective studies beginning in the mid-1980s.⁴ In the late 1990s, under the leadership of Dr. Jeckoniah Ndinya-Achola of the University of Nairobi, Dr. Robert Bailey of the University of Illinois at Chicago and me, the group began planning a randomized clinical trial. The main concentration of uncircumcised men in Kenya was in Nyanza Province, in the western part of the country. Not circumcising men is an

Key points

- Three randomized trials in Africa, including one conducted in Kenya by the University of Manitoba, have confirmed that male circumcision reduces the risk of HIV infection among men by more than 55%.
- Male circumcision is now endorsed by the World Health Organization and the Joint United Nations Programme on HIV/AIDS as an effective measure for preventing HIV infection.
- As services for the provision of male circumcision expand, we need to ensure that the procedure is conducted safely and that counselling is provided to minimize risk compensation (the adoption of higher risk behaviour out of the mistaken belief that protection is absolute).

ingrained cultural practice in the Luo community in that area. Therefore, it was uncertain whether it would be acceptable to undertake a randomized trial there. Feasibility studies were undertaken, and the response in the community was positive,⁵ with men indicating their willingness to participate in a trial. Most men agreed to be circumcised if randomly assigned to the treatment group provided that the procedure could be performed safely, without too much pain or inconvenience, and that there was a possibility that it might reduce their risk of HIV infection. After enlisting the support of community political, religious and cultural leaders, funding for a trial was obtained in April 2001 from the Canadian Institutes of Health Research, and later from the US National Institutes of Health.

The principal objective of the trial was to assess the effectiveness of male circumcision in reducing HIV incidence among young men in Kisumu District in western Kenya. Uncircumcised HIV-seronegative men aged 18–24 years were randomly assigned to either the circumcision or the non-circumcision arm of the study. They were followed every 6 months for 2 years with assessments of risk behaviours and testing for sexually transmitted infections, as well as HIV antibody testing and counselling. Intensive counselling about behavioural risk reduction and unlimited free condoms were provided to all participants. The primary outcomes were inci-

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dence of HIV infection and surgical complications of male circumcision. Secondary outcomes were incidence of sexually transmitted infections and behavioural risk.

The first participant was enrolled in February 2002. The recruitment target of 2784 participants was reached in September 2005. The planned completion date of the trial was September 2007; however, the trial was stopped early on Dec. 12, 2006, when the Data Safety and Monitoring Board determined that the observed 53% protective effect of circumcision against HIV infection was so strong that it would be unethical to continue the trial and that circumcision should immediately be offered to the control group. Under the controlled circumstances of a trial, there were relatively few surgical complications, with an overall rate of adverse events of less than 2% and no serious adverse events observed.⁶ The other major concern, risk compensation, did not seem to be an important occurrence: sexual behaviour, including numbers of reported sex partners and reported use of condoms, did not differ significantly between the circumcision and control arms.⁷

The pooled results of this trial and 2 randomized controlled trials conducted in South Africa and Uganda showed that male circumcision decreased the incidence of HIV infection by about 56%.⁸ Male circumcision was subsequently endorsed as a preventive measure by the World Health Organization and the Joint United Nations Programme on HIV/AIDS (UNAIDS). In a report published in March 2007,⁹ these organizations wrote that “The efficacy of male circumcision in reducing female to male transmission of HIV has been proven beyond reasonable doubt. This is an important landmark in the history of HIV prevention.” They went on to recommend that “Promoting male circumcision should be recognized as an additional, important strategy for the prevention of heterosexually acquired HIV infection in men.”

Subsequently, several mathematical modelling studies have been conducted to investigate the potential effect of male circumcision on HIV transmission at the population level. All have shown that the incidence of HIV infection can be decreased substantially, especially in areas where HIV prevalence is high and rates of male circumcision are low. In such settings, typical of many countries in eastern and southern Africa, the provision of male circumcision to the majority of adult men could result, over a period of years, in a reduction of 45%–67% in the prevalence of HIV infection in the general population, including a significant reduction among women.¹⁰ Male circumcision in sub-Saharan Africa could prevent more than 7.7 million people from acquiring HIV infection and 3 million from dying of AIDS over the next 20 years.¹¹ With an estimated cost of US\$181 per HIV infection averted, male circumcision would be highly cost-effective in a country such as South Africa.¹² A study from Uganda suggests that as few as 19 circumcisions would be needed to prevent 1 case of HIV infection.¹³

Many countries in eastern and southern Africa, including Kenya, have now developed plans to expand services for male circumcision. The Government of Kenya has established a National Task Force on Male Circumcision within the Ministry of Public Health and Sanitation and has adopted national policy guidelines for voluntary male circumcision.¹⁴ In addition to being supported by the Government of Kenya, this initiative has received considerable external support from the Bill &

Melinda Gates Foundation and the US President’s Emergency Plan for AIDS Relief (PEPFAR). PEPFAR has also provided \$26 million for expanding services for male circumcision in 12 other countries in eastern and southern Africa. It is still early days, but reports suggest that the demand for male circumcision in many of these countries is rising rapidly. The challenge will be for health care systems to ensure the availability and accessibility of high-quality services to meet this demand.

As services for male circumcision expand, steps need to be taken to ensure that the procedure is conducted safely and that adequate counselling is offered to reduce the likelihood of risk compensation. In addition, risk compensation behaviour will need to be monitored, because experiences with the general population who access regular health care services may differ from those observed in clinical trials. Finally, the sustainability of the strategy will need to be evaluated over time in different countries and health care settings.

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REFERENCES

- Moses S, Bailey RC, Ronald AR. Male circumcision: assessment of health risks and benefits. *Sex Transm Inf* 1998;74:368-73.
- Weiss HA, Quigley MA, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. *AIDS* 2000;14:2361-70.
- Weiss HA, Thomas SL, Munabi SK, et al. Male circumcision and risk of syphilis, chancroid, and genital herpes: a systematic review and meta-analysis. *Sex Transm Infect* 2006;82:101-9.
- Cameron DW, Simonsen JN, D’Costa LJ, et al. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *Lancet* 1989;2:403-7.
- Bailey RC, Muga R, Poulussen R, et al. The acceptability of male circumcision to reduce HIV infections in Nyanza Province, Kenya. *AIDS Care* 2002;14:27-40.
- Krieger JN, Bailey RC, Opeya JC, et al. Adult male circumcision outcomes: experience in a developing country setting. *Urol Int* 2007;78:235-40.
- Mattson CL, Campbell RT, Bailey RC, et al. Risk compensation is not associated with male circumcision in Kisumu, Kenya: a multi-faceted assessment of men enrolled in a randomized controlled trial. *PLoS One* 2008;3:e2443.
- Mills E, Cooper C, Anema A, et al. Male circumcision for the prevention of heterosexually acquired HIV infection: a meta-analysis of randomized trials involving 11,050 men. *HIV Med* 2008;9:332-5.
- World Health Organization (WHO) and Joint United Nations Programme on HIV/AIDS (UNAIDS). *New data on male circumcision and HIV prevention: policy and programme implications*. Geneva (Switzerland): WHO; 2007. Available: http://data.unaids.org/pub/Report/2007/mc_recommendations_en.pdf (accessed 2009 Aug. 26).
- Nagelkerke NJD, Moses S, de Vlas S, et al. Modelling the public health impact of male circumcision for HIV prevention in high prevalence areas in Africa. *BMC Infect Dis* 2007;7:16.
- Williams BG, Lloyd-Smith JO, Gouws E, et al. The potential impact of male circumcision on HIV in Sub-Saharan Africa. *PLoS Med* 2006;3:e262.
- Kahn JG, Marseille E, Auvert B. Cost-effectiveness of male circumcision for HIV prevention in a South African setting. *PLoS Med* 2006;3:e517.
- Gray RH, Li X, Kigozi G, et al. The impact of male circumcision on HIV incidence and cost per infection prevented: a stochastic simulation model from Rakai, Uganda. *AIDS* 2007;21:845-50.
- National AIDS/STD Control Programme. *National guidance for voluntary male circumcision in Kenya*. Republic of Kenya: Ministry of Health; 2008. Available: www.malecircumcision.org/programs/documents/KenyaMCguidance.pdf (accessed 2009 Aug. 31).

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