Institution: London School of Hygiene & Tropical Medicine (LSHTM)

Unit of Assessment: UoA2 – Public Health, Health Services & Primary Care

Title of case study: Male circumcision as an HIV prevention strategy

1. Summary of the impact

Research carried out by LSHTM into the effects of male circumcision on HIV prevention has led to important policy recommendations by WHO and UNAIDS, the joint UN Programme on HIV/AIDS. The research showed a strongly reduced risk of HIV infection among circumcised men, and modelling studies estimated that male circumcision programmes in 13 priority countries in Africa could avert 4m HIV infections by 2025. Members of the research team serve on key international advisory groups, and these results have been widely used to underpin international policy guidelines.

2. Underpinning research

An estimated 34m people live with HIV, of whom two-thirds live in sub-Saharan Africa. Approximately 2.7m people are newly infected with HIV every year, and despite advances in scaling up antiretroviral treatment, 1.8m per year die of HIV-related causes. Discovering ways to prevent HIV acquisition and transmission therefore remains a primary concern worldwide.

In 1997, researchers from LSHTM – including Helen Weiss, Reader in Epidemiology and International Health (joined LSHTM in 1997, then Lecturer), and Richard Hayes, Professor of Epidemiology and International Health (joined LSHTM in 1978, then Research Fellow) – joined the Study Group on Heterogeneity of HIV Epidemics in African Cities. The group carried out a series of large, population-based cross-sectional surveys in four African cities, investigating why HIV had spread at very different rates in East and West Africa and reached very different prevalence in the two regions. The results showed that two biological variables – herpes simplex virus type 2 (HSV-2) and male circumcision – were independent individual-level risk factors for HIV and differed between low and high HIV prevalence areas.[3.1]

Weiss and Hayes subsequently carried out a systematic literature review of studies published up to April 1999 that included circumcision as a risk factor for HIV-1 infection in males in sub-Saharan Africa, and found strong consistent evidence that circumcised men were at lower risk of HIV.[3.2] Weiss presented the findings at an informal WHO consultation in 2000 in Durban, and an updated meta-analysis at USAID in 2002, and helped provide the justification for three subsequent randomised controlled trials (RCTs) started in 2002/2003 by French and US research teams. These trials showed conclusively that male circumcision reduces the risk of HIV acquisition by between 48 and 60%.[3.3]

LSHTM researchers then went on to examine whether this protective effect of circumcision could be partly due to its protective effect against other STIs, especially those causing ulcers. They conducted the first systematic review and meta-analysis of circumcision and ulcerative STIs,[3.4] quantifying the effect of male circumcision on syphilis, chancroid and HSV-2. Published in 2006, the findings strongly indicated that circumcised men are at lower risk of chancroid and syphilis. In other studies, Weiss and colleagues reviewed the evidence of an association between male circumcision and penile cancer (2011), and circumcision and human papillomavirus (HPV) infection (2011), showing that both conditions could be reduced by the expansion of circumcision services.

In 2008, Weiss and Richard White (Reader in Infectious Disease Modelling, joined LSHTM 1998, then Research Assistant) participated in an Expert Group formed by UNAIDS, the WHO and the South African Centre for Epidemiological Modelling and Analysis (SACEMA), to model the likely population-level impact of male circumcision on the HIV epidemic.[3.5] The resulting modelling statement (2009), itself building on earlier research by White and colleagues,[3.6] predicted that circumcision is capable of yielding large benefits among heterosexual men in low-circumcision, high-HIV prevalence settings, with one HIV infection being averted for every 5 to 15 male circumcisions performed.

3. References to the research

3.1 Buvé, A, Caraël, M, Hayes, RJ, Auvert, B, Ferry, B, Robinson, NJ, Anagonou, S, Kanhonou, L, Laourou, M, Abega, S, Akam, E, Zekeng, L, Chege, J, Kahindo, M, Rutenberg, N, Kaona, F, Musonda, R, Sukwa, T, Morison, L, Weiss, HA and Laga, M for the Study Group on Heterogeneity of HIV Epidemics in African Cities (2001) The multicentre study on factors determining the differential spread of HIV in four African cities: summary and conclusions, *AIDS*, 15(Suppl. 4): s127–S131, doi: 10.1097/00002030-200108004-00014. Citation count: 84

3.2. Weiss, HA, Quigley, MA and Hayes RJ (2000) Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis, *AIDS,* 14(15): 2361–2370, doi: 10.1097/00002030-200010200-00018. Citation count: 293

3.3 Weiss, HA, Halperin, D, Bailey, RC, Hayes, RJ, Schmid, G and Hankins CA (2008) Male circumcision for HIV prevention: from evidence to action?', *AIDS*, 22(5): 567–574, doi: 10.1097/QAD.0b013e3282f3f406. Citation count: 89

3.4 Weiss, HA, Thomas, SL, Munabi, SK and Hayes RJ (2006) Male circumcision and risk of syphilis, chancroid, and genital herpes: a systematic review and meta-analysis, *Sexually Transmitted Infections*, 82(2): 101–110, doi: 10.1136/sti.2005.017442. Citation count: 161

3.5 UNAIDS/WHO/SACEMA Expert Group on Modelling the Impact and Cost of Male Circumcision for HIV Prevention (2009) Male circumcision for HIV prevention in high HIV prevalence settings: what can mathematical modelling contribute to informed decision making?, *PLoS Medicine*, 6(9), e1000109, doi: 10.1371/journal.pmed.1000109. Citation count: 5

3.6 White, RG, Glynn, JR, Orroth, KK, Freeman, EE, Bakker, R, Weiss, HA, Kumaranayake, L, Habbema, JDF, Buvé, A and Hayes RJ (2008) Male circumcision for HIV prevention in sub-Saharan Africa: who, what and when?, *AIDS*, 22(14): 1841–1850, doi: 10.1097/QAD.0b013e32830e0137. Citation count: 33

Key grants

Weiss, A Systematic Review and Meta-analysis of the Association Between Male Circumcision and HIV Infection in sub-Saharan Africa, UNAIDS, 4/1999–6/1999, £3,100.

Weiss, Neonatal Circumcision Landscaping, Bill & Melinda Gates Foundation, 11/2007–4/2008, $132,585.

Weiss, Health Risks and Benefits of Male Circumcision for Women and HIV Infected Men: Summary of Evidence to Date, WHO, 10/2008–2/2009, £26,324.

Weiss and Larke, Systematic Reviews of the Associations of Male Circumcision with Infectious Diseases in Males, Other than HIV, WHO, 3/2009–9/2009, £36,256.

4. Details of the impact

LSHTM's research into the effects of male circumcision as a strategy for HIV prevention, as well as the prevention of other STIs, has been widely used to underpin international policy recommendations on male circumcision, in particular for sub-Saharan Africa. Its key contribution was to use systematic reviews, meta-analyses and modelling to draw clear conclusions from a wide body of research.

In March 2007, WHO/UNAIDS convened a pivotal meeting bringing together stakeholders, policy-makers and researchers. Weiss and Hayes presented a meta-analysis of the three trials, providing a point estimate that underscored the strength of the evidence and underpinned the document issued by the meeting recommending male circumcision as an HIV prevention strategy in combination with other methods like condom promotion.[5.1] This key document laid the foundations for subsequent guidelines and policy statements published after January 2008 and may be found at www.malecircumcision.org.

In 2008, WHO/UNAIDS' operational guidance for countries wishing to scale up male circumcision for HIV prevention cited the research conducted by Weiss and colleagues as evidence of a strong link between male circumcision and reduced HIV prevalence, as well as evidence of male circumcision providing protection against ulcerative STIs and penile cancer.[5.2] In the same year, the US Centers for Disease Control and Prevention (CDC) made reference to the research in a paper laying out the implications of the findings on male circumcision for the USA.[5.3] In August 2012, the American Academy of Pediatrics published new guidelines for infant male circumcision in the US (see http://pediatrics.aappublications.org/content/early/2012/08/22/peds.2012-1990), which also cited the underpinning research.

In June 2009, Weiss chaired the first session of an international consultation convened by WHO and UNAIDS on male circumcision and HIV prevention, which focused on how to scale up male circumcision services in sub-Saharan Africa following the March 2007 WHO/UNAIDS recommendation.[5.4]

The UNAIDS/WHO/SACEMA expert group (including White and Weiss) on modelling the impact and cost of male circumcision for HIV prevention published a consensus statement aimed at policy-makers in September 2009, building on earlier research including that by White and colleagues.[3.5] This work helped estimate the number of circumcisions needed for maximum impact, and the costs of scale-up.[5.5] The paper cites our work,[3.2, 3,3. 3.4, 3.5] and Hankins and colleagues show that an investment of US$1.5bn between 2011 and 2015 could achieve 80% coverage in 13 priority countries in southern and eastern Africa and would avert 3.4m new HIV infections, resulting in net savings of US$16.5bn. In November 2011, WHO/UNAIDS published a joint strategic five-year action framework to accelerate the scale-up of voluntary medical male circumcision for HIV prevention in eastern and southern Africa.[5.6] Intended for use by country, regional and global stakeholders, this highlights the consensus modelling paper[3.5] demonstrating the cost effectiveness of medical male circumcision. The Framework set a goal of circumcising 80% of males (20m circumcisions) in 14 priority countries by 2015, and an additional 8.4m circumcisions between 2016 and 2025.[5.6] The most recent data available from WHO is to the end of 2011, by which time an estimated 1.4m male circumcisions had been conducted since the beginning of 2008 in the priority countries.[5.7]

As a direct result of her research expertise, Weiss serves on the WHO Technical Advisory Group on Innovations In Male Circumcision. Following a meeting in January 2012, in which Weiss participated, the Group recommended the use of an elastic ring-controlled radial compression device for adult male circumcision in preference to traditional surgery (March 2012).[5.8]

Also as a direct result of her research, Weiss has frequently attended other WHO/UNAIDS meetings to present research findings and discuss policy issues. She and members of LSHTM were commissioned by WHO to conduct several further systematic reviews as input to their policy deliberations (e.g. on male circumcision and the risk of HIV infection in women, 2009),[5.9] presented at a meeting on implications of the research findings for women in Nairobi in June 2008; and provided model projections on combining microbiocide and male circumcision interventions in rural Uganda (2011).[5.10]

Weiss has raised the profile of male circumcision for HIV prevention in public discourse in the UK through appearances in the media. In August 2008, she discussed the impact of male circumcision on their female partners on *Woman's Hour* on BBC Radio 4. In July 2011, she appeared on *The Health Show* on BBC World News to discuss the new device for bloodless circumcision mentioned above.

5. Sources to corroborate the impact

5.1 WHO/UNAIDS (2007) *New Data on Male Circumcision and HIV Prevention: Policy and Programme Implications: Conclusions & Recommendations* (WHO/UNAIDS Technical Consultation on Male Circumcision and HIV Prevention: Research Implications for Policy &

Programming, 6–8 March. Montreux: WHO/UNAIDS, http://whqlibdoc.who.int/publications/2007/9789241595988_eng.pdf (accessed 16 October 2013) (although published in 2007, this document continues to underpin the ongoing expansion and scale-up of male circumcision in southern and eastern Africa).

5.2 WHO/UNAIDS (2008) *Operational Guidance for Scaling Up Male Circumcision Services for HIV Prevention*. Geneva: WHO, http://www.malecircumcision.org/programs/documents/MC_OpGuideFINAL_web.pdf (accessed 16 October 2013) (see refs 7, 11).

5.3 Centers for Disease Control and Prevention (2013) *Male Circumcision,* http://www.cdc.gov/hiv/prevention/research/malecircumcision/index.html (accessed 16 October 2013) (see refs 6, 12, 21, 44, original guidance published 2008).

5.4 WHO/UNAIDS (2009) *Male Circumcision and HIV Prevention: Operations Research Priorities, An International Consultation* (1–2 June). Nairobi: WHO/UNAIDS, http://www.malecircumcision.org/resources/documents/MeetingObjectivesandAgendaNairobiJune20093Junefinal.pdf (accessed 16 October 2013).

5.5 Hankins, CA, Forsythe S and Njeuhmeli E (2011) Voluntary male circumcision: an introduction to the cost, impact and challenges of accelerated scaling up, *PLoS Medicine*, 8(11), e1001127, doi:10.1371/journal.pmed.1001127.

5.6 WHO/UNAIDS (2011) *Joint Strategic Action Framework to Accelerate the Scale-up of Voluntary Medical Male Circumcision for HIV Prevention in Eastern and Southern Africa: 2012–2016*. UNAIDS, http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/JC2251_Action_Framework_circumcision_en.pdf (accessed 16 October 2013).

5.7 WHO (2011) *Progress in Scaling Up Voluntary Medical Male Circumcision for HIV Prevention in Eastern and Southern Africa: January – December 2011*. Geneva: WHO, http://www.malecircumcision.org/country_updates/documents/FINAL%20VMMC%20Progress%20Report%20Jan-Dec%202011%20WHO.pdf (accessed 16 October 2013).

5.8 WHO (2012) *Use of Devices for Adult Male Circumcision in Public Health HIV Prevention Programmes: Conclusions of the Technical Advisory Group on Innovations in Male Circumcision*. Geneva: WHO, http://www.malecircumcision.org/documents/Use_of_MC_devices_conclusions.pdf (accessed 16 October 2013).

5.9 Weiss, HA, Hankins, CA and Dickson, K (2009) Male circumcision and risk of HIV infection in women: a systematic review and meta-analysis, *Lancet Infectious Diseases*, 9(11): 669–677, doi: 10.1016/S1473-3099(09)70235-X.

5.10 Cox, AP, Foss, AM, Shafer, LA, Nsubuga, RN, Vickerman, P, Hayes, RJ, Watts, C and White, RG (2011) 'Attaining realistic and significant reductions in HIV incidence: model projections of combining microbiocide and male circumcision interventions in rural Uganda, *Sexually Transmitted Infections*, 87(7): 635–639, doi: 10.1136/sti.2010.046227.