

## COMMENTARY





# In developed countries male circumcision prevalence is inversely related to HIV prevalence

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## Abstract

A study by Chemtob and co-workers found significantly lower prevalence of HIV amongst heterosexual men and women in Israel compared with the Netherlands and France. Risk factors for heterosexual HIV infection in these countries were similar, apart from one, namely, a strikingly higher prevalence of male circumcision (MC) in Israel compared with the Netherlands and France. It is now well established that MC protects heterosexual men against becoming infected with HIV during sexual intercourse with an infected woman. In epidemic settings, such as countries in sub-Saharan Africa, in which heterosexual contact is the primary driver for HIV infection, MC is being implemented to reduce HIV prevalence. The results of the new study by Chemtob and co-workers support the evidence and recent polices in the United States advocating MC to reduce the spread of HIV. While prevalence in developed countries is generally low, it is rising. In the long term, neonatal MC is the most desirable option, since not only is it simpler, safer, cheaper and more convenient than MC later, it provides immediate protection from infections, penile inflammation, genital cancers and physical problems. It is also cost-effective. European countries have not supported MC for its public health benefits. The new findings add to calls for European and other countries with low MC prevalence to consider developing evidence-based policies favoring MC in order to reduce HIV and other infections and diseases and at the same time reduce suffering, mortality and the cost of treating these.

Keywords: Circumcision, Male, HIV, Rate, Europe, Israel, Public health, Policy

## Male circumcision protects against HIV infection

The evidence that male circumcision (MC) can substantially reduce HIV infection in men during heterosexual intercourse is now well accepted, leading to its adoption as an HIV prevention strategy in high prevalence settings of sub-Saharan Africa [1]. The policy followed the publication of results from three randomized controlled trials (RCTs) in South Africa [2], Kenya [3] and Uganda [4]. Further support has been provided by meta-analyses [5–8], effectiveness studies in the implementation of MC [9], follow-up of RCT study participants in which protection reached 70 % [10–12], and biological evidence [13]. However, the relevance of MC for HIV prevention in low prevalence settings, as applies to developed nations, has been less clear.

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## New findings for developed countries

A recent article in Israel Journal of Health Policy Research by Chemtob and colleagues has provided much-needed evidence demonstrating that MC was associated with reduced HIV acquisition in heterosexuals in countries in which HIV prevalence is low [14]. The study found the rate of newly diagnosed heterosexual HIV cases in Israel, where MC prevalence exceeds 90 %, was 0.46 (range 0.26–0.70) per 100,000 of the population per year over the period 2004-2010. The annual incidence of HIV infection in men in Israel was on average 6 times lower than in the Netherlands (mean 2.0 annual cases per 100,000 of the population; range 1.9-2.3) and France (mean 3.3; range 2.7-3.5) where the MC prevalence in both is less than 10 %. HIV prevalence was also lower in women in Israel (0.20; range 0.10-0.34), where the number of cases per year were 10 times fewer over that period when compared with the annual number of cases in women in the Netherlands (1.4; range 1.1-2.1) and France (2.6; range

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2.4–3.1). The authors excluded cases originating in men who have sex with men and intravenous drug users, each of which represent high-risk groups. In addition, they also excluded cases of heterosexual HIV transmission originating from countries with generalized HIV epidemics. Migrants were, moreover, unlikely to contribute very much to HIV infections in the general heterosexual populations of each country.

While inter-country comparisons are subject to the influence of confounding factors, including sexual behavior, the three countries examined are fairly similar in just about every aspect of known risk factors for sexually acquired HIV infection, apart from MC prevalence. Those factors included the number of sex partners and condom use. The proportion of people tested for HIV in the past year was highest in Israel. The authors suggest that infection of women by a small proportion of men who engage in sexual intercourse with both women and other men was of very limited impact.

#### HIV was once a rare virus

In those countries, mostly in sub-Saharan Africa, where HIV prevalence is at epidemic levels, HIV was once rare or nonexistent. Had MC been introduced as a preventive measure before the three trials were completed in 2007 then many infections would have been averted and lives could have been saved [15].

#### HIV is rising in developed countries

In confirmation of the basis of the findings by Chemtob et al., the protective effect of MC against acquisition of HIV in heterosexual men applies just as well in another low prevalence country, the USA [16]. The proportion of HIV cases attributable to heterosexual contact has, moreover, risen substantially with time in developed countries [17, 18]. National statistics for Australia show that 25 % of cases involved heterosexual contact [18]. After excluding cases from a high prevalence country, the number of cases whose exposure to HIV was attributed to heterosexual contact has increased by 28 % over the past decade [18], 29 % of these being in individuals born in Australia [18, 19]. There has been a steady rise in HIV prevalence in the WHO European Region [20], notably in some non-drug injecting, heterosexual populations in Eastern Europe, as well as in Central Asia [21]. In African Americans in the USA, HIV rates are rising faster than almost all other groups in that country [22]. The US Centers for Disease Control and Prevention (CDC) has recommended MC for HIV prevention in high prevalence groups such as those [23]. Protection against HIV infection was an important component of recent MC policy recommendations by the US CDC [24] and the American Academy of Pediatrics [25].

#### The looming treatment burden

A recent study in the Netherlands highlighted the looming medical burden as a result of an anticipated enormous increase in multiple morbidities and drug interactions in aging HIV-infected patients on combination antiretroviral therapy [26].

#### Neonatal circumcision preferable

In the long term, neonatal MC appears to offer advantages over adult MC for prophylaxis against HIV and other infectious diseases globally [27]. That is because neonatal MC is cheaper, simpler, safer, more convenient, averts concerns about premature resumption of sex during wound healing and provides a risk-benefit ratio of 100:1 in favor [28], as noted by the US CDC [24]. Adverse events are uncommon, virtually all being minor, easy to treat and with complete resolution [25, 28, 29].

#### **Effectiveness against HIV**

The 60 % or higher efficacy of MC in protecting heterosexual men against HIV infection [5, 9–12] makes MC more effective than condoms. That is because, even though condoms are 80 % protective against HIV infection *if used consistently and correctly* [30, 31], a Cochrane systematic review of RCTs of condom use found, "little clinical evidence of effectiveness" and no "favorable results" for HIV prevention [32]. Unlike condoms, MC is a one-off procedure that does not require an item to be applied or administered each time a man has sexual intercourse. Nevertheless both MC and condom use should be advocated.

By reducing HIV prevalence in heterosexual men, MC will help reduce HIV prevalence in women [33] and children [34]. It will also help lower risks for other sexually transmitted infections [28, 35–58], including those that exacerbate HIV risk [41–44].

Finally, MC has been shown to be the most costeffective of all the available interventions for HIV prevention [59]. Calculations for the US have shown that if MC prevalence were to fall from the current high levels of 80 to 10 %, as typically seen in Europe, direct costs for treatment of urinary tract and sexually transmitted infections, including HIV, would increase by US\$4.4 billion for 10 annual birth cohorts [60].

#### Conclusion

The new findings by Chemtob *et al.* have broad implications for efforts to arrest the continued spread of HIV in the heterosexual community of developed countries in which HIV prevalence is currently low. While routine MC will be easier in countries such as Israel and the US that already enjoy a cultural or religious tradition of infant MC, it presents a challenge in countries such as those in Europe in which a cultural bias against MC exists amongst the majority [61].

#### **Commentary on**

Chemtob D, Op de Coul E, Van Sighem A, Mor Z, Cazein F, et al. Impact of male circumcision among heterosexual HIV cases: comparison between three low prevalence countries. Israel J Health Policy. 2015;4:36.

#### Abbreviations

MC: Male circumcision; HIV: Human immunodeficiency virus; CDC: Centers for Disease Control and Prevention; US: United States of America; WHO: World Health Organization.

#### Competing interests

The authors have no competing interests relevant to this commentary.

#### Authors' contributions

BJM drafted the manuscript; JDK reviewed the draft and made changes before both authors agreed on the final text. Both authors read and approved the final manuscript.

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#### References

- World Health Organization and UNAIDS. (2007) New data on male circumcision and HIV prevention: policy and programme implications. 2007:http://who.int/hiv/mediacentre/MCrecommendations\_en.pdf.
- Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, et al. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 Trial. PLoS Med. 2005;2(e298):1112–22.
- Bailey RC, Moses S, Parker CB, Agot K, Maclean I, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet. 2007;369:643–56.
- Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 2007;369:657–66.
- Siegfried N, Muller M, Deeks JJ, Volmink J. Male circumcision for prevention of heterosexual acquisition of HIV in men. Cochrane Database Syst Rev. 2009;2(CD003362):38 pages.
- Weiss HA, Halperin D, Bailey RC, Hayes RJ, Schmid G, et al. Male circumcision for HIV prevention: from evidence to action? (Review). AIDS. 2008;22:567–74.
- Gebremedhin S. Assessment of the protective effect of male circumcision from HIV infection and sexually transmitted diseases: evidence from 18 demographic and health surveys in sub-Saharan Africa. Afr J Reprod Health. 2010;14:105–13.
- 8. Van Howe RS. Circumcision as a primary HIV preventive: Extrapolating from the available data. Glob Public Health. 2015;10:607–25.
- Auvert B, Taljaard D, Rech D, Lissouba P, Singh B, et al. Association of the ANRS-12126 male circumcision project with HIV levels among men in a South African township: Evaluation of effectiveness using cross-sectional surveys. PLoS Med. 2013;10(article e1001509):1–12.
- Bailey RC, Moses S, Parker CB, Agot K, MacLean I, *et al.* The protective effect of adult male circumcision against HIV acquisition is sustained for at least 54 months: results from the Kisumu, Kenya trial. XVIII International AIDS Conference, Jul 18–23, 2010. Vienna; 2010. Abstract#FRLBC1

- Gray R, Kigozi G, Kong X, Ssempiija V, Makumbi F, et al. The effectiveness of male circumcision for HIV prevention and effects on risk behaviors in a post-trial follow up study in Rakai, Uganda. AIDS. 2012;26:609–15.
- Lei JH, Liu LR, Wei Q, Yan SB, Yang L, et al. Circumcision status and risk of HIV acquisition during heterosexual intercourse for both males and females: A meta-analysis. PLoS ONE. 2015;10:e0125436.
- 13. Morris BJ, Wamai RG. Biological basis for the protective effect conferred by male circumcision against HIV infection. Int J STD AIDS. 2012;23:153–9.
- Chemtob D, Op de Coul E, Van Sighem A, Mor Z, Cazein F, et al. Impact of male circumcision among heterosexual HIV cases: comparison between three low prevalence countries. Israel J Health Policy. 2015;4:36.
- Potts M, Prata N, Walsh J, Grossman A. Parachute approach to evidence based medicine. Brit Med J. 2006;333:701–3.
- Warner L, Ghanem KG, Newman DR, Macaluso M, Sullivan PS, et al. Male circumcision and risk of HIV infection among heterosexual African American men attending Baltimore sexually transmitted disease clinics. J Infect Dis. 2009;199:59–65.
- Centers for Disease Control and Prevention. HIV infection among heterosexuals at increased risk – United States, 2010. http:// www.cdc.gov/mmwr/preview/mmwrhtml/mm6210a2.htm (accessed July 1, 2015) 2013.
- Kirby Institute. HIV, viralhepatitis and sexually transmitted infections in Australia Annual Surveillance Report 2014 HIV Supplement. http:// kirby.unsw.edu.au/sites/default/files/hiv/resources/ HIVASRsuppl2014\_online.pdf, 2014.
- National Centre for HIV Epidemiology and Clinical Research. HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report. https://kirby.unsw.edu.au/sites/default/files/hiv/ resources/2011AnnualSurvReport\_0.pdf 2011.
- European Centre for Disease Prevention and Control/WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2012. Stockholm: European Centre for Disease Prevention and Control; 2013. http://www.euro.who.int/ \_\_data/assets/pdf\_file/0018/235440/e96953.pdf, 2013.
- UNAIDS report on the global AIDS epidemic 2013. http://www.unaids.org/ en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/ UNAIDS\_Global\_Report\_2013\_en.pdf (accessed Oct 2, 2014). 2013
- 22. Centers for Diseases Control and Prevention. HIV Surveillance Report: Diagnoses of HIV Infection in the United States and Dependent Areas, 2011. Volume 23. http://www.cdc.gov/hiv/pdf/ statistics\_2011\_HIV\_Surveillance\_Report\_vol\_23.pdf, 2011.
- Sansom SL, Prabhu VS, Hutchinson AB, An Q, Hall HI, et al. Costeffectiveness of newborn circumcision in reducing lifetime HIV risk among U.S. males. PLoS One. 2010;5:e8723.
- 24. Centers for Disease Control and Prevention. Recommendations for Providers Counseling Male Patients and Parents Regarding Male Circumcision and the Prevention of HIV Infection, STIs, and Other Health Outcomes. Docket No. CDC-2014-0012. http://www.gpo.gov/fdsys/pkg/FR-2014-12-02/pdf/ 2014-27814.pdf (Accessed 27 Dec 2014) 2014.
- 25. American Academy of Pediatrics. Circumcision policy statement. Task Force on Circumcision. Pediatrics. 2012;130:e756–e85.
- Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, et al. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. Lancet Infect Dis. 2015;15(7):810–8.
- Morris BJ, Waskett JH, Banerjee J, Wamai RG, Tobian AAR, et al. A 'snip' in time: what is the best age to circumcise? BMC Pediatr. 2012;12(article20):1–15.
- Morris BJ, Bailis SA, Wiswell TE. Circumcision rates in the United States: Rising or falling? What effect might the new affirmative pediatric policy statement have? Mayo Clin Proc. 2014;89:677–86.
- El Bcheraoui C, Zhang X, Cooper CS, Rose CE, Kilmarx PH, et al. Rates of adverse events associated with male circumcision in US medical settings, 2001 to 2010. JAMA Pediatr. 2014;168:625–34.
- Weller S, Davis-Beaty K. Condom effectiveness in reducing heterosexual HIV transmission. Cochrane Database: Syst Rev; 2002;1:CD003255.
- Hearst N, Chen S. Condom promotion for AIDS prevention in the developing world: is it working? Stud Fam Plann. 2004;35:39–47.
- Lopez LM, Otterness C, Chen M, Steiner M, Gallo MF. Behavioral interventions for improving condom use for dual protection. Cochrane Database Syst Rev. 2013;10:CD010662.

- Hallett TB, Alsallaq RA, Baeten JM, Weiss H, Celum C, et al. Will circumcision provide even more protection from HIV to women and men? New estimates of the population impact of circumcision interventions. Sex Transm Infect. 2011;87:88–93.
- Tobian AA, Gray RH, Quinn TC. Male circumcision for the prevention of acquisition and transmission of sexually transmitted infections: the case for neonatal circumcision. Arch Pediatr Adolesc Med. 2010;164:78–84.
- Morris BJ, Gray RH, Castellsague X, Bosch FX, Halperin DT, et al. The strong protection afforded by circumcision against cancer of the penis. Adv Urol. 2011;2011:812368.
- Tobian AAR, Serwadda D, Quinn TC, Kigozi G, Gravitt PE, et al. Male circumcision for the prevention of HSV-2 and HPV infections and syphilis. N Engl J Med. 2009;360:1298–309.
- Gray RH, Kigozi G, Serwadda D, Makumbi F, Nalugoda F, et al. The effects of male circumcision on female partners' genital tract symptoms and vaginal infections in a randomized trial in Rakai, Uganda. Am J Obstet Gynecol. 2009;200(42):e1–7.
- Morris BJ. Castellsague X The role of circumcision in preventing STIs. In: Gross GE, Tyring SK, editors. Sexually Transmitted Infections and Sexually Transmitted Diseases. Berlin and Heidelberg: Springer; 2011. p. 715–39.
- Morris BJ, Cox G. Current medical evidence supports male circumcision. In: Bolnick DA, Koyle MA, Yosha A, editors. Surgical Guide to Circumcision. London: Springer; 2012. p. 201–213.
- Morris BJ, Hankins CA, Tobian AA, Krieger JN, Klausner JD. Does male circumcision protect against sexually transmitted infections? Arguments and meta-analyses to the contrary fail to withstand scrutiny. ISRN Urol. 2014;2014(article 684706):1–23.
- Serwadda D, Gray RH, Sewankambo NK, Wabwire-Mangen F, Chen MZ, et al. Human immunodeficiency virus acquisition associated with genital ulcer disease and herpes simplex virus type 2 infection: a nested case-control study in Rakai. Uganda J Infect Dis. 2003;188:1492–7.
- Corey L, Wald A, Celum CL, Quinn TC. The effects of herpes simplex virus-2 on HIV-1 acquisition and transmission: a review of two overlapping epidemics. J Acquir Immune Defic Syndr. 2004;35:435–45.
- 43. Moodley JR, Constant D, Hoffman M, Salimo A, Allan B, et al. Human papillomavirus prevalence, viral load and pre-cancerous lesions of the cervix in women initiating highly active antiretroviral therapy in South Africa: a cross-sectional study. BMC Cancer. 2009;9(article 275):1–8.
- Gottlieb SL, Low N, Newman LM, Bolan G, Kamb M, et al. Toward global prevention of sexually transmitted infections (STIs): the need for STI vaccines. Vaccine. 2014;32:1527–35.
- 45. Parker SW, Stewart AJ, Wren MN, Gollow MM, Straton JA. Circumcision and sexually transmissible diseases. Med J Aust. 1983;2:288–90.
- Bwayo J, Plummer F, Omari M, Mutere A, Moses S, et al. Human immunodeficiency virus infection in long-distance truck drivers in east Africa. Arch Intern Med. 1994;154:1391–6.
- Lavreys L, Rakwar JP, Thompson ML, Kackson DJ, Mandaliya K, et al. Effect of circumcision on incidence of human immunodeficiency virus type 1 and other sexually transmitted diseases: a prospective cohort study of trucking company employees in Kenya. J Inf Dis. 1999;180:330–6.
- Reynolds SJ, Shepherd ME, Risbud AR, Gangakhedkar RR, Brookmeyer RS, et al. Male circumcision and risk of HIV-1 and other sexually transmitted infections in India. Lancet. 2004;363:1039–40.
- 49. Vaz RG, Gloyd S, Folgosa E, Kreiss J. Syphilis and HIV infection among prisoners in Maputo, Mozambique. Int J STD AIDS. 1995;6:42–6.
- Tabet S, Sanchez J, Lama J, Goicochea P, Campos P, et al. HIV, syphilis and heterosexual bridging among Peruvian men who have sex with men. AIDS. 2002;16:1271–7.
- Newell J, Senkoro K, Mosha F, Grosskurth H, Nicoll A, et al. A populationbased study of syphilis and sexually transmitted disease syndromes in north-western Tanzania. 2. Risk factors and health seeking behaviour. Genitourin Med. 1993;69:421–6.
- Todd J, Munguti K, Grosskurth H, Mngara J, Changalucha J, et al. Risk factors for active syphilis and TPHA seroconversion in a rural African population. Sex Transm Infect. 2001;77:37–45.
- Urassa M, Todd J, Boerma JT, Hayes R, Islingo R. Male circumcision and susceptibility to HIV infection among men in Tanzania. AIDS. 1997;11:73–80.
- Gray R, Azire J, Serwadda D, Kiwanuka N, Kigozi G, et al. Male circumcision and the risk of sexually transmitted infections and HIV in Rakai, Uganda. AIDS. 2004;18:2428–30.

- Cook LS, Koutsky LA, Holmes KK. Circumcision and sexually transmitted diseases. Am J Publ Health. 1994;84:197–201.
- Diseker RA, Peterman TA, Kamb ML, Kent C, Zenilman JM, et al. Circumcision and STD in the United States: Cross sectional and cohort analysis. Sex Transm Infect. 2000;76:474–9.
- Buve A, Weiss HA, Laga M, Van Dyck E, Musonda R, et al. The epidemiology of gonorrhoea, chlamydial infection and syphilis in four African cities. AIDS. 2001;15 Suppl 4:S79–88.
- Weiss HA, Thomas SL, Munabi SK, Hayes RJ. Male circumcision and risk of syphilis, chancroid, and genital herpes: a systematic review and meta-analysis. Sex Transm Infect. 2006;82:101–9.
- Bärnighausen T, Bloom DE, Humair S. Economics of antiretroviral treatment vs. circumcision for HIV prevention. Proc Natl Acad Sci U S A. 2012;109:21271–6.
- Kacker S, Frick KD, Gaydos CA, Tobian AA. Costs and effectiveness of neonatal male circumcision. Arch Pediatr Adolesc Med. 2012;166:910–8.
- 61. Task Force on Circumcision. Cultural bias and circumcision: The AAP Task Force on Circumcision Responds. Pediatrics. 2013;131:801–4.

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