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PREVENTING HIV THROUGH SAFE
VOLUNTARY MEDICAL MALE CIRCUMCISION
FOR ADOLESCENT BOYS AND MEN IN
GENERALIZED HIV EPIDEMICS

WEB ANNEX 2.2

MALE CIRCUMCISION AND THE RISK OF HIV INFECTION IN WOMEN: SYSTEMATIC REVIEW AND META-ANALYSIS

Preventing HIV through safe voluntary medical male circumcision for adolescent boys and men in generalized HIV epidemics: recommendations and key considerations. Web Annex 2.2. Male circumcision and the risk of HIV infection in women: systematic review and meta-analysis

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WEB ANNEX 2.2 MALE CIRCUMCISION AND THE RISK OF HIV INFECTION WOMEN: SYSTEMATIC REVIEW AND META-ANALYSIS

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FRPEC216 - Male Circumcision and HIV Infection in Women - Systematic Review of Evidence

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Background: Women benefit indirectly from male circumcision because of reduced HIV acquisition and hence prevalence in men. Observational studies suggested HIV-negative women with HIV+ circumcised partner were less likely to acquire HIV than those with uncircumcised partner, but a randomized trial (RCT) of circumcision in HIV+ men suggested higher though not statistically significant risk of female HIV acquisition. To inform new WHO guidance on Voluntary Medical Male Circumcision (VMMC) for HIV prevention, we conducted a systematic review of impact of circumcision on HIV infection in women.

Methods: PubMed search for 'HIV infection' and 'male circumcision' identified 1 RCT and 6 observational cohort studies with data on HIV risk in women according to partner's circumcision status.

Results: HIV+ men in an RCT of immediate or delayed circumcision enrolled female partners to assess impact on women. HIV incidence was 11.5/100 py in partners of circumcised and 6.9/100 py of uncircumcised men (incidence ratio [IR] 1.6 [95% CI 0.6–3.7]). Excess risk was confined to couples who resumed sex before wound healing, consistent with a study of HIV+ men showing higher penile HIV shedding for 3 weeks following circumcision (Tobian PLoS Med 2015).

Two observational cohorts in serodiscordant couples showed lower incidence in partners of circumcised than uncircumcised HIV+ men (pooled adjusted IR 0.59 [0.35–0.99]). In 4 cohorts of women with undocumented or mixed partner HIV status pooled adjusted IR was 0.75 (0.56–1.00). See Fig. 1.

Conclusions: The discrepancy between the RCT and observational cohorts is likely explained by duration of exposure to the circumcised partner (several years in the observational studies, only recently in the RCT) and resumption of intercourse before wound healing. We believe there is biological plausibility for partners of circumcised men to be at lower long-term risk of HIV – less viral shedding after wound healing (Tobian PLoS Med 2015), fewer penile anaerobes following circumcision (Liu MBio 2013), lower incidence of bacterial vaginosis (BV) and severe BV in partners of circumcised men (Gray AJOG 2009) – but time until lower risk manifests is unknown. The short-term post-circumcision risk underlines the importance of HIV testing before VMMC, delaying VMMC for HIV+ men until stable on ART for their own health and preventing onward transmission, stressing sexual abstinence until wound healing, and the value of reaching adolescents prior to sexual debut.

Source: www.professional abstracts.com/icasa 2019/iplanner/#/presentation/2986

Fig. 1. Impact of circumcision on HIV incidence in women

	Infectio	ns/Pers-Yr						Incidence ratio
Author Year	Circ.	Not circ.						(95% CI)
RCT								
Wawer 2009	17/148	8/115				•		1.49 (0.62, 3.57)
Pooled	17/148	8/115						1.49 (0.62, 3.57)
Serodiscordant co	uples							
Gray 2000	3/58	46/349				-		0.41 (0.10, 1.14)
Baeten 2010	16/588	48/1096				<u> </u>		0.64 (0.36, 1.14)
Pooled	19/646	94/1445				!		0.59 (0.35, 0.99)
Other cohorts						 		
Kapiga 1998	44/1692	3/33	\leftarrow					0.29 (0.09, 0.97)
Turner 2007	34/1674	167/5636				•——		1.03 (0.69, 1.53)
Fatti 2017	1/393	7/304	←	*				0.22 (0.03, 1.86)
Borgdorff 2018	18/3653	134/15 705			*	-		0.58 (0.35, 0.94)
Pooled	97/7412	311/21 678				-		0.75 (0.56, 1.00)
All observational c	ohorts					! ! !		
Pooled	116/8058	405/23 123			\Leftrightarrow	 		0.71 (0.55, 0.91)
						<u> </u>		
			1/8	1/4	1/2	1 2	4	
			Incidence ratio (95% confidence interval)					

References

Baeten JM, Donnell D, Kapiga SH, Ronald A, John-Stewart G, Inambao M, et al. Male circumcision and risk of male-to-female HIV-1 transmission: a multinational prospective study in African HIV-1-serodiscordant couples. AIDS. 2010; 24(5): 737-44.

Borgdorff MW, Kwaro D, Obor D, Otieno G, Kamire V, Odongo F, et al. HIV incidence in western Kenya during scale-up of antiretroviral therapy and voluntary medical male circumcision: a population-based cohort analysis. Lancet HIV. 2018; 5(5): e241-e9.

Fatti G, Shaikh N, Jackson D, Goga A, Nachega JB, Eley B, et al. Low HIV incidence in pregnant and postpartum women receiving a community-based combination HIV prevention intervention in a high HIV incidence setting in South Africa. PLoS One. 2017; 12(7): e0181691.

Gray RH, Kigozi G, Serwadda D, Makumbi F, Nalugoda F, Watya S, et al. The effects of male circumcision on female partners' genital tract symptoms and vaginal infections in a randomized trial in Rakai, Uganda. AJOG. 2009; 200(42): e1-e7.

Gray RH, Kiwanuka N, Quinn TC, Sewankambo NK, Serwadda D, Mangen FW, et al. Male circumcision and HIV acquisition and transmission: cohort studies in Rakai, Uganda. AIDS. 2000; 14: 2371-81.

Kapiga SH, Lyamuya EF, Lwihula GK, Hunter DJ. The incidence of HIV infection among women using family planning methods in Dar es Salaam, Tanzania. AIDS. 1998; 12(1): 75-84.

Liu CM, Hungate BA, Tobian AAR, Serwadda D, Ravel J, Lester R, et al. Male circumcision significantly reduces prevalence and load of genital anaerobic bacteria. Mbio. 2013; 4(2): e00076-13.

Tobian AAR, Kigozi G, Manucci J, Grabowski MK, Serwadda D, Musoke R, et al. HIV shedding from male circumcision wounds in HIV-Infected men: A prospective cohort study. PLoS Med. 2015; 12(4): e1001820.

Turner AN, Morrison CS, Padian NS, Kaufman JS, Salata RA, Chipato T, et al. Men's circumcision status and women's risk of HIV acquisition in Zimbabwe and Uganda. AIDS. 2007; 21(13): 1779-89.

Wawer MJ, Makumbi F, Kigozi G, Serwadda D, Watya S, Nalugoda F, et al. Circumcision in HIV-infected men and its effect on HIV transmission to female partners in Rakai, Uganda: a randomised controlled trial. Lancet. 2009; 374(9685): 229-37.

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