Comment on a paper by Eline Korenromp et al. "The impact of the program for medical male circumcision on HIV in South Africa: analysis using three epidemiological models"

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Comment

The paper by Korenromp and colleagues attempts to answer the difficult question of the impact of Voluntary Medical Male Circumcision (VMMC) in South Africa. For this, they use a demographic projection model, simulating the expected effect under a variety of assumptions, namely that VMMC reduces the probability of transmission from infected female to male by 60%. They use realistic values of the dynamics of the South African population, of HIV transmission, and detailed one-year age group. The projection model appears well calibrated, and fits the data well. They find only a minor expected impact: 77,000 HIV cases averted among men age 15-49, whereas 1.04 million were expected to occur in the 10 years between mid-2008 and mid-2017 (7.4% of total). This is a small impact for a huge undertaking, and probably the highest impact that one could expect. However, this type of mechanistic model does not make provision for behavioral factors, in particular for selection biases (men who undertake circumcision may be a selected group), and risk compensation (when men are circumcised they may take more risks). Did prevalence or incidence among men and women really decline by 7.4% in South Africa over the 2008-2017 period? Answers can be searched for in six demographic surveys with information on HIV prevalence conducted in South Africa in 2002, 2005, 2008, 2012, 2017 (SABSSM) and 2016 (DHS). In addition, sentinel sites of pregnant women provide additional information on HIV trends.

The impact of public health programs depends on both clinical efficacy and population coverage. When programs have high efficacy (> 95%) and high population coverage (> 90%), one usually finds a high demographic impact 10 years after the beginning. For instance, when measles vaccination was implemented in USA in 1962, measles incidence dropped by 93% in 10 years, and the disease was under control within 20 years. When the polio vaccination program was implemented in the world in 1987, polio incidence dropped by 87% in 10 years, and the disease was under control in 20 years. Many other examples could be found on disease control programs as well as in family planning programs. Is this the case for male circumcision and HIV in South Africa?

Following the Orange Farms clinical trial (2006), South Africa embarked on an ambitious program of circumcision in 2008. The program started slowly (18,000 circumcisions in 2008), took off in 2011 (300,000 circumcisions) and reached a steady state by 2013 circumcising about 500,000 men a year, with a cumulated total of 3,1 million men circumcised by mid-2017, about 20% of the population of men age 15-49. According to SABSSM surveys, the proportion of circumcised men age 15-49 was 36.8% in 2002, 39.8% in 2008 and 56.2% in 2017, which corresponds to the number of circumcised men during the VMMC campaigns, with minor differences being explained by circumcisions before age 15, and by the fact that traditional circumcisions continued to be performed. What was the demographic impact of the VMMC program 10 years later? Did the program change the course of the epidemic?

HIV prevalence was increasing in South Africa from 1990 to 2005, but trends changed after 2005 following the large Anti-Retroviral Therapy program (ART) which reached a large proportion of the population and changed the mortality and the transmission of the disease. In contrast, HIV seroprevalence hardly changed over the 2005-2017 period, and trends were basically the same before- and after- 2011, when the VMMC program could have had an additional impact. This was true among men age 15-49, among women age 15-49 (surveys), as well as among pregnant women (sentinel sites). Furthermore, according to survey data, the number of HIV infections among adults age 15-19 remained about the same (1.1 million) in 2005-2011 and in 2011-2017, although there were fewer men and more women (Table 1).

Table 1: Trends in prevalence of circumcision and HIV, adults age 15-49, South Africa

Adults 15-49	Before VMMC		After VMMC	Change
	2005	2011	2017	2011-2017
% men circumcised	38.3%	44.4%	57.4%	+13.0%
% men HIV+	12.5%	14.2%	14.4%	+0.2%
% women HIV+	19.6%	23.0%	28.0%	+5.0%
% pregnant women HIV+	29.3%	29.9%	30.4%	+0.5%

Source: Interpolated from survey data (SABSSM 2002, 2005, 2008, 2012, 2017, and DHS 2016); Antenatal clinics for pregnant women.

There were large differences in VMMC uptake by province: 3 provinces had low uptake (Eastern-Cape, Free-State, Limpopo), 3 provinces had medium uptake (Western-cape, Norther-Cape, KwaZulu-Natal), 3 provinces had high uptake (North-West, Gauteng, Mpumalanga). There was no significant correlation between the increase in male circumcision and change in HIV prevalence for men ($\rho = -0.167$) and for women ($\rho = -0.014$), and even a positive correlation with HIV among pregnant women ($\rho = +0.263$). The only province where the decline in HIV prevalence was at the same time significant (−5.7%, $P = 0.002$) and correlated with increasing male circumcision (+24.1%) was Kwazulu-Natal. But even there, this was associated with increasing prevalence among women (+0.8%), as well as among pregnant women (+2.8%), as if there were some risk compensation.

Table 2: Changes in prevalence of circumcision and HIV between 2008 and 2017 in nine provinces, adults age 15-49, South Africa

VMCC uptake (9 provinces)	Changes between 2008 and 2017			
	% Circumcised Men	% HIV+ Men	% HIV+ Women	% HIV+ Pregnant women
Low (<18%)	+13.5%	+0.2% (ns)	+4.2% (*)	+0.6% (*)
Medium (<26%)	+21.8%	−0.4% (ns)	+4.5% (*)	+1.9% (*)
High (>26%)	+29.0%	−0.6% (ns)	+3.9% (*)	+0.8% (*)

NB. Calculated from 2008 and 2017 SABSSM surveys; (*) P< 0.05; (ns) P> 0.05

Circumcision existed before 2008 in South Africa, and the increase in proportion circumcised was only moderate. In terms of population coverage, this program did not compare with mass vaccination programs. Likewise, its efficacy was low compared with high efficacy of vaccines or contraceptives: therefore, the program could only have a small demographic impact, if any.

The strategy of male circumcision to control HIV was criticized from the beginning, because of its low clinical efficacy and because population coverage could not be guaranteed: since circumcision is genital mutilation, it requires adult informed consent and should not be applied to children [Garenne 2006, 2007]. Furthermore demographic evidence showed that circumcised and intact ethnic groups in South Africa had the same levels of HIV prevalence and the same dynamics of disease spread. Cumulating all available surveys in South Africa gives an odds ratio of 1.13 (95% CI = 1.05-1.22) of HIV prevalence by circumcision status. The same was true all over Africa: countries traditionally circumcising men had the same levels of HIV prevalence in the early 2000' [Connolly et al. 2008; Garenne 2008; Rosenberg et al. 2018].

When behavior is implicated, and especially for sexual behavior, many interferences could be expected, biasing the expected results. In the case of VMMC, one could expect that when men felt somewhat protected they could take more risks, and therefore be more likely to acquire and transmit the disease. This was the case following the VMMC campaign in Zambia over the same period of time, and seems be the case as well in South Africa [Garenne & Matthews 2019].

The cost per circumcision was estimated at 132 USD, so the total program between 2008 and 2017 costed about 409 Million USD, a huge cost for hardly any effect. Was the VMMC program worth it? Could this amount of money be better invested in more efficient programs? The ethics of such a program was already questioned at the beginning [Garenne 2007; Connolly et al. 2008]. Is it time to reassess the whole program?

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