Global Variation in the Impact of Male Circumcision in Preventing HIV among MSM

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Background
The effectiveness of voluntary male medical circumcision (VMMC) as an HIV prevention measure among heterosexual men has been demonstrated in clinical trials (1). However, the efficacy and population-level effectiveness of VMMC among men who have sex with men (MSM) remains uncertain, and is likely to depend on the behavioral and demographic characteristics of specific MSM populations, such as:
- sexual role segregation
- current coverage of circumcision
- willingness to undergo VMMC
- condom use.

Observational studies have found differing results. A meta-analysis did not reveal sufficient evidence that male circumcision protects against HIV in MSM, but concluded that the measurable protective effect observed in studies conducted before the era of highly active antiretroviral therapy warranted further investigation (2). A systematic review concluded that while no statistically significant population-level effect has been measured, a measurable protective effect was observed among predominantly insertive MSM (3).

We used mathematical modelling to assess the potential impact of VMMC among MSM in different settings worldwide and to help determine the settings in which it could be an effective HIV prevention measure for MSM.

Methods
We developed a deterministic compartmental model of HIV transmission among MSM (Figure 1) and simulated the HIV epidemic in nine selected countries (see Table 1). The MSM were divided by: status, with HIV positive MSM split between three stages of HIV infection: acute, chronic and pre-AIDS; sexual role preference: either ‘Top’, defined as being the insertive partner in more than 50% of their relationships, or ‘Bottom’, defined conversely, as circumcision status.

The model incorporates infectivity by type of sex act (receptive/insertive), sexual mix by role preference, condom use, three stages of HIV with varying infectivity, and assumes a 40%-67% VMMC efficacy during insertive anal sex (0% efficacy for receptive sex).

Plan of Analysis:
We conducted two types of analysis, a worldwide and a country-specific analysis, as follows:

- First, we reviewed the literature to define plausible ranges of biological and sexual behavioural parameters, HIV prevalence among MSM and pre-intervention coverage of male circumcision across countries—i.e. the worldwide range used in the worldwide analysis. We then identified countries with data on sexual role segregation (i.e. % Top or % Bottom) and condom use – to conduct country-specific analyses (Table 1).

- Worldwide analysis consisted of a sensitivity analysis to identify the most influential parameters on VMMC HIV impact and the country-specific analysis. To do so, the parameters were sampled from their worldwide ranges [shown in Fig 2] 200,000 times using Latin Hypercube sampling. Here, we used wide ranges assuming that nothing is known about condom use (p) and role segregation (θ, ω) since this information is rarely available. The model was run to equilibrium and the 5,391 parameter sets that reproduced plausible mixing scenarios and with HIV prevalence falling within our plausible worldwide range (1.8% – 35%) were retained (4). These worldwide parameter sets were used to estimate VMMC impact.

- Country-specific analyses were done in 3 steps: i) the model was first calibrated (as described above) to available country-specific HIV prevalence among MSM and pre-intervention coverage of male circumcision, using the worldwide ranges for the remaining parameters values. Each of the country-specific fitting parameter sets were used to estimate VMMC impact in each country. ii) we stratified the impact estimates by level of role segregation, iii) we repeated the analysis in i) for countries where additional data on condom use and role segregation was available (Table 1). These steps of analyses allowed us to produce country-specific impact estimate and to evaluate the influence of missing information on key parameters.

Pre-intervention %

USA | Canada | Mexico | Peru | India | China | Australia
---|---|---|---|---|---|---
Female | 49 | 24 | 22 | 21 | 10 | 7 | 7
Male | 51 | 76 | 78 | 79 | 90 | 93 | 93

Table 1: Pre-intervention % of the 2000 male population aged 15 to 49 years (Column 1). Prevalence data are the mean of data from the last 10 years (Column 2). Data not available are marked (ND).

VMMC prevention scenarios:
We compared intervention strategies of VMMC scale-up where 25%, 50% and 100% of uncircumcised, uninfected Tops were circumcised over the course of 5 years. Impact was measured as the cumulative average of new HIV infections averted over 5, 10 and 25 years (i.e., 2015–2055).

Results

Worldwide sensitivity analysis:
Sensitivity analysis revealed that pre-intervention coverage of male circumcision, the proportion of Tops in the population and the level of role segregation were the most influential parameters (Fig 2). Even more so than the relative risk attributable to receptive over insertive intercourse, and the efficacy of VMMC. Greater impact was seen when MSM had a strong preference for either insertive (high ω) or receptive (low ω) intercourse (low Rijk) (Fig 2).

Conclusions
VMMC among MSM is likely to have the greatest impact in highly role-segregated settings with low circumcision coverage, such as Peru or India. However, the public health benefits among MSM would likely be modest and slow to accumulate. The intervention is unlikely to avert more than 10% of infections even in the most favorable settings under realistically achievable intervention coverage of 50%, given that not all men would be willing to undergo VMMC.

The level of uncertainty around role segregation in MSM populations worldwide, and the lack of information available for the countries we considered a major problem when assessing the impact of VMMC intervention, as can be seen by comparing the difference in results between Figures 4A and 4C. Further work to determine this information is necessary to inform conclusions.

References

Figure 1: Model showing how the relative risk attributable to receptive over insertive intercourse, and the efficacy of VMMC. Greater impact was seen when MSM had a strong preference for either insertive (high ω) or receptive (low ω) intercourse (low Rijk) (Fig 2).