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Quarterly Research Digest on Voluntary Medical Male Circumcision for HIV Prevention

Biological mechanisms

1. Kigozi, G., et al. **Foreskin surface area is not associated with sub-preputial microbiome composition or penile cytokines**. *PLoS One* 2020;15(6): e0234256.

   Online at: https://www.ncbi.nlm.nih.gov/pubmed/32574173.

   OBJECTIVE: Male circumcision (MC) reduces acquisition of HIV-1 in heterosexual men by at least 60%, but the biological mechanism for this protection is incompletely understood. Previous studies have shown that a larger foreskin size, increased abundance of anaerobic bacteria in the sub-preputial space, and higher levels of pro-inflammatory cytokines on the penis are all prospectively associated with risk of HIV-1 acquisition. Since coverage of the glans on the non-erect penis is dependent on foreskin size, a larger foreskin could result in a less aerobic environment that might preferentially support anaerobic bacterial growth and induce inflammation. We therefore assessed the relationship between foreskin size, penile microbiome composition and local inflammation.

   METHODS: This is a retrospective, cross-sectional analysis of 82 HIV-uninfected men who participated in a randomized trial of MC for HIV-1 prevention in Rakai, Uganda between 2003-2006. Sub-preputial swabs were collected prior to MC and assessed for cytokines (multiplexed immunosorbent assay) and bacterial load (qPCR) and taxon abundance (sequencing). Foreskin size was measured immediately after MC.

RESULTS: Foreskin surface area did not correlate with total bacterial load (rho = 0.05) nor the abundance of key taxa of bacteria previously associated with HIV-1 risk (rho = 0.04-0.25). Foreskin surface area also did not correlate with sub-preputial cytokine concentrations previously associated with HIV-1 risk (IL-8 rho = 0.05).

CONCLUSIONS: Larger foreskin size is not associated with either increased penile anaerobes or pro-inflammatory cytokines. These data suggest that foreskin size does not increase HIV-1 risk through changes in penile microbiome composition or penile inflammation.

2. Onywera, H., et al. **The penile microbiota of Black South African men: relationship with human papillomavirus and HIV infection**. *BMC Microbiol* 2020;20(1): 78.

   Online at: https://bmcmicrobiol.biomedcentral.com/articles/10.1186/s12866-020-01759-x.

   BACKGROUND: To date, the microbiota of the human penis has been studied mostly in connection with circumcision, HIV risk and female partner bacterial vaginosis (BV). These studies have shown that male circumcision reduces penile anaerobic bacteria, that greater abundance of penile anaerobic bacteria is correlated with increased cytokine levels and greater risk of HIV infection, and that the penile microbiota is an important harbour for BV-associated bacteria. While circumcision has been shown to significantly reduce the risk of acquiring human papillomavirus (HPV) infection, the relationship of the penile microbiota with HPV is still unknown. In this study, we examined the penile microbiota of HPV-infected men as well as the impact of HIV status.

   RESULTS: The penile skin microbiota of 238 men from Cape Town (South Africa) were profiled using Illumina sequencing of the V3-V4 hypervariable regions of the 16S rRNA gene. Corynebacterium and Prevotella were found to be the most abundant genera. Six distinct community state types (CSTs) were identified. CST-1, dominated by Corynebacterium, corresponded to less infections with high-risk HPV (HR-HPV) relative to CSTs 2-6. Men in CST-5 had greater relative abundances of Prevotella, Clostridiales, and Porphyromonas and a lower relative abundance of Corynebacterium. Moreover, they were significantly more likely to have HPV or HR-HPV infections than men in CST-1. Using a machine learning approach, we identified greater relative abundances of the anaerobic BV-associated bacteria (Prevotella, Peptinophilus, and Dialister) and lower relative abundance of Corynebacterium in HR-HPV-infected men compared to HR-HPV-uninfected men. No association was observed between HIV and CST, although the penile microbiota of HIV-infected men had greater relative abundances of Staphylococcus compared to HIV-uninfected men.

   CONCLUSIONS: We found significant differences in the penile microbiota composition of men with and without HPV and HIV infections. HIV and HR-HPV infections were strongly associated with greater relative abundances of Staphylococcus and BV-associated

bacterial taxa (notably Prevotella, Peptinophilus and Dialister), respectively. It is possible that these taxa could increase susceptibility to HIV and HR-HPV acquisition, in addition to creating conditions in which infections persist. Further longitudinal studies are required to establish causal relationships and to determine the extent of the effect.

Combination HIV prevention and HIV testing

1. Makoni, T. M., et al. **Linkage of voluntary medical male circumcision clients to adolescent sexual and reproductive health (ASRH) services through Smart-LyncAges project in Zimbabwe: a cohort study**. *BMJ Open* 2020;10(5): e033035.
Online at: https://www.ncbi.nlm.nih.gov/pubmed/32371506.

OBJECTIVES: WHO recommended strengthening the linkages between various HIV prevention programmes and adolescent sexual reproductive health (ASRH) services. The Smart-LyncAges project piloted in Bulawayo city and Mt Darwin district of Zimbabwe established a referral system to link the voluntary medical male circumcision (VMMC) clients to ASRH services provided at youth centres. Since its inception in 2016, there has been no assessment of the performance of the referral system. Thus, we aimed to assess the proportion of young (10-24 years) VMMC clients getting 'successfully linked' to ASRH services and factors associated with 'not being linked'.

DESIGN: This was a cohort study using routinely collected secondary data.

SETTING: All three VMMC clinics of Mt Darwin district and Bulawayo province.

PRIMARY OUTCOME MEASURES: The proportion of 'successfully linked' was summarised as the percentage with a 95% CI. Adjusted relative risks (aRR) using a generalised linear model was calculated as a measure of association between client characteristics and 'not being linked'.

RESULTS: Of 1773 young people registered for VMMC services, 1478 (83%) were referred for ASRH services as they had not registered for ASRH previously. Of those referred for ASRH services, the mean (SD) age of study participants was 13.7 (4.3) years and 427 (28.9%) were out of school. Of the referred, 463 (31.3%, 95% CI: 30.0 to 33.8) were 'successfully linked' to ASRH services and the median (IQR) duration for linkage was 6 (0-56) days. On adjusted analysis, receiving referral from Bulawayo circumcision clinic (aRR: 1.5 (95% CI: 1.3 to 1.7)) and undergoing circumcision at outreach sites (aRR: 1.2 (95% CI: 1.1 to 1.3)) were associated with 'not being linked' to ASRH services.

CONCLUSION: Linkage to ASRH services from VMMC is feasible as one-third VMMC clients were successfully linked. However, there is need to explore reasons for not accessing ASRH services and take corrective actions to improve the linkages.

2. Wirth, K. E., et al. **Population uptake of HIV testing, treatment, viral suppression, and male circumcision following a community-based intervention in Botswana (Ya Tsie/BCPP): a cluster-randomised trial**. *Lancet HIV* 2020;7(6): e422-e433.

   Online at: https://www.ncbi.nlm.nih.gov/pubmed/32504575.

   BACKGROUND: In settings with high HIV prevalence and treatment coverage, such as Botswana, it is unknown whether uptake of HIV prevention and treatment interventions can be increased further. We sought to determine whether a community-based intervention to identify and rapidly treat people living with HIV, and support male circumcision could increase population levels of HIV diagnosis, treatment, viral suppression, and male circumcision in Botswana.

   METHODS: The Ya Tsie Botswana Combination Prevention Project study was a pair-matched cluster-randomised trial done in 30 communities across Botswana done from Oct 30, 2013, to June 30, 2018. 15 communities were randomly assigned to receive HIV prevention and treatment interventions, including enhanced HIV testing, earlier antiretroviral therapy (ART), and strengthened male circumcision services, and 15 received standard of care. The first primary endpoint of HIV incidence has already been reported. In this Article, we report findings for the second primary endpoint of population uptake of HIV prevention services, as measured by proportion of people known to be HIV-positive or tested HIV-negative in the preceding 12 months; proportion of people living with HIV diagnosed and on ART; proportion of people living with HIV on ART with viral suppression; and proportion of HIV-negative men circumcised. A longitudinal cohort of residents aged 16-64 years from a random, approximately 20% sample of households across the 15 communities was enrolled to assess baseline uptake of study outcomes; we also administered an end-of-study survey to all residents not previously enrolled in the longitudinal cohort to provide study end coverage estimates. Differences in intervention uptake over time by randomisation group were tested via paired Student's t test. The study has been completed and is registered with ClinicalTrials.gov (NCT01965470).

   FINDINGS: In the six communities participating in the end-of-study survey, 2625 residents (n=1304 from standard-of-care communities, n=1321 from intervention communities) were enrolled into the 20% longitudinal cohort at baseline from Oct 30, 2013, to Nov 24, 2015. In the same communities, 10 791 (86%) of 12 489 eligible enumerated residents not previously enrolled in the longitudinal cohort participated in the end-of-study survey from March 30, 2017, to Feb 25, 2018 (5896 in intervention and 4895 in standard-of-care communities). At study end, in intervention communities, 1228 people living with HIV (91% of 1353) were on ART; 1166 people living with HIV (88% of 1321 with available viral load) were virally suppressed, and 673 HIV-negative men (40%

of 1673) were circumcised in intervention communities. After accounting for baseline differences, at study end the proportion of people living with HIV who were diagnosed was significantly higher in intervention communities (absolute increase of 9% to 93%) compared with standard-of-care communities (absolute increase of 2% to 88%; prevalence ratio [PR] 1.08 [95% CI 1.02-1.14], p=0.032). Population levels of ART, viral suppression, and male circumcision increased from baseline in both groups, with greater increases in intervention communities (ART PR 1.12 [95% CI 1.07-1.17], p=0.018; viral suppression 1.13 [1.09-1.17], p=0.017; male circumcision 1.26 [1.17-1.35], p=0.029).

INTERPRETATION: It is possible to achieve very high population levels of HIV testing and treatment in a high-prevalence setting. Maintaining these coverage levels over the next decade could substantially reduce HIV transmission and potentially eliminate the epidemic in these areas.

FUNDING: US President's Emergency Plan for AIDS Relief through the Centers for Disease Control and Prevention.

Enhancing uptake of VMMC

1. Rudrum, S. **Promoting male circumcision as HIV prevention in sub-Saharan Africa: An evaluation of the ethical and pragmatic considerations of adopting a demand creation approach**. *Glob Public Health* 2020 May 12: 1-15. [Epub ahead of print[]

   Male circumcision for HIV prevention is being promoted in 14 sub-Saharan African countries. Campaigns take a demand creation approach, a strategy based on generating awareness of and demand for an intervention. This article analyzes campaign materials, making the case that a focus on demand per se, at the expense of quality public health information, constitutes an ethical and pragmatic campaign flaw. Clinical trials have demonstrated that circumcision can reduce transmission of HIV from women to men by 53-60%. Since circumcision does not approach 100% prevention efficacy for men and does not directly protect women, behavioural and structural interventions remain necessary, leading international health bodies to position circumcision as an add-on to behavioural interventions. However, in practice, circumcision promotion often lacks information about behavioural prevention. At times, campaigns omit any HIV prevention message. Instead, campaigns variously favour representing circumcision as a route to normative masculinity, to sexual prowess, or to good citizenship, among others. Alongside their targeted outcomes, public health campaigns also contribute to public discourses around sexuality and non-HIV aspects of health, in this case potentially leading to confusion and mistrust. The current public health promotion strategy for circumcision threatens to undermine the social processes needed to support HIV prevention.

2. Vigliotti, V., et al. **Religion, faith, and spirituality influences on HIV prevention activities: A scoping review**." *PLoS One* 2020;15(6): e0234720.

   Online at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0234720.

   INTRODUCTION: Strategies to increase uptake of next-generation biomedical prevention technologies (e.g., long-acting injectable pre-exposure prophylaxis (PrEP)) can benefit from understanding associations between religion, faith, and spirituality (RFS) and current primary HIV prevention activities (e.g., condoms and oral PrEP) along with the mechanisms which underlie these associations.

   METHODS: We searched PubMed, Embase, Academic Search Premier, Web of Science, and Sociological Abstracts for empirical articles that investigated and quantified relationships between RFS and primary HIV prevention activities outlined by the United States (U.S.) Department of Health and Human Services: condom use, HIV and STI testing, number of sexual partners, injection drug use treatment, medical male circumcision, and PrEP. We included articles in English language published between 2000 and 2020. We coded and analyzed studies based on a conceptual model. We then developed summary tables to describe the relation between RFS variables and the HIV prevention activities and any underlying mechanisms. We used CiteNetExplorer to analyze citation patterns.

   RESULTS: We identified 2881 unique manuscripts and reviewed 29. The earliest eligible study was published in 2001, 41% were from Africa and 48% were from the U.S. RFS measures included attendance at religious services or interventions in religious settings; religious and/or spirituality scales, and measures that represent the influence of religion on behaviors. Twelve studies included multiple RFS measures. Twenty-one studies examined RFS in association with condom use, ten with HIV testing, nine with number of sexual partners, and one with PrEP. Fourteen (48%) documented a positive or protective association between all RFS factors examined and one or more HIV prevention activities. Among studies reporting a positive association, beliefs and values related to sexuality was the most frequently observed mechanism. Among studies reporting negative associations, behavioral norms, social influence, and beliefs and values related to sexuality were observed equally. Studies infrequently cited each other.

   CONCLUSION: More than half of the studies in this review reported a positive/ protective association between RFS and HIV prevention activities, with condom use being the most frequently studied, and all having some protective association with HIV testing behaviors. Beliefs and values related to sexuality are possible mechanisms that could underpin RFS-related HIV prevention interventions. More studies are needed on PrEP and spirituality/subjective religiosity.

Epidemiological studies

1. Kabapy, A. F., et al. **Attributes of HIV infection over decades (1982-2018): A systematic review and meta-analysis**. *Transbound Emerg Dis* 2020 May 12. [Epub ahead of print]

   Understanding the risk factors for HIV infection is the foundation of successful preventive strategies, which must bundle sociocultural, behavioural and biomedical interventions to halt disease transmission. We aimed in this study to provide a pooled estimation of HIV risk factors and trace changes across decades in order to drive consensus and accurate assessment of disease transmission risk. We comprehensively searched PubMed, ISI Web of Knowledge, Medline, EMBASE, ScienceDirect, Ovid, EBSCO, Google Scholar and the Egyptian Universities Library Consortium from October to December 2018. Two independent reviewers extracted data from eligible studies. Funnel plots were inspected to identify publication bias. Heterogeneity across studies was checked using the Q and I(2) statistics. The results were reported based on the pooled odds ratio (pOR) with 95% CI using a random-effects model. Meta-analysis of HIV risk factors revealed a superior role for risky sexual practices (unprotected vaginal/anal sex), injecting drug use (IDU), sharing needles, sexually transmitted infections (STIs), child sexual abuse and vertical transmissions. Trends across decades (1982-1999 and 2000-2018, respectively) showed rising evidence for prostitution [pOR (95% CI)= 2.3 (1.12-4.68) versus 2.69 (1.67-4.32)] and men who have sex with men (MSM) [pOR (95% CI)= 2.28 (1.64-3.17) versus 3.67 (1.88-7.17)], while transmission through IDU [pOR (95% CI)= 3.42 (2.28-5.12) versus 2.16 (1.74-2.70)], alcoholism [pOR (95% CI)= 2.35 (0.73-7.59) versus 1.71(1.08-2.72)], and sharing syringes [pOR (95% CI)= 6.10 (2.57-14.5) versus 2.70 (2.01-6.35)] showed notable decline. Harm reduction programs and condom use have been recognized as chief HIV prevention strategies, while male circumcision contributed a partial role. Collectively, sexual risk factors continue to be a key driver of the global HIV epidemic. Persistent and emerging risk factors identified in our analysis should constitute the forefront targets of HIV prevention programmes to accelerate efforts towards HIV elimination.

2. Gottert A., et al. **Creating HIV risk profiles for men in South Africa: a latent class approach using cross-sectional survey data**. *J Int AIDS Soc* 2020;(Suppl 2): e25518.

   Online at: https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25518.

   INTRODUCTION: Engaging at-risk men in HIV prevention programs and services is a current priority, yet there are few effective ways to identify which men are at highest risk or how to best reach them. In this study we generated multi-factor profiles of HIV acquisition/transmission risk for men in Durban, South Africa, to help inform targeted programming and service delivery.

METHODS: Data come from surveys with 947 men ages 20 to 40 conducted in two informal settlements from May to September 2017. Using latent class analysis (LCA), which detects a small set of underlying groups based on multiple dimensions, we identified classes based on nine HIV risk factors and socio-demographic characteristics. We then compared HIV service use between the classes.

RESULTS: We identified four latent classes, with good model fit statistics. The older high-risk class (20% of the sample; mean age 36) were more likely married/cohabiting and employed, with multiple sexual partners, substantial age-disparity with partners (eight years younger on-average), transactional relationships (including more resource-intensive forms like paying for partner's rent), and hazardous drinking. The younger high-risk class (24%; mean age 27) were likely unmarried and employed, with the highest probability of multiple partners in the last year (including 42% with 5+ partners), transactional relationships (less resource-intensive, e.g., clothes/transportation), hazardous drinking, and inequitable gender views. The younger moderate-risk class (36%; mean age 23) were most likely unmarried, unemployed technical college/university students/graduates. They had a relatively high probability of multiple partners and transactional relationships (less resource-intensive), and moderate hazardous drinking. Finally, the older low-risk class (20%; mean age 29) were more likely married/cohabiting, employed, and highly gender-equitable, with few partners and limited transactional relationships. Circumcision (status) was higher among the younger moderate-risk class than either high-risk class ($p < 0.001$). HIV testing and treatment literacy score were suboptimal and did not differ across classes.

CONCLUSIONS: Distinct HIV risk profiles among men were identified. Interventions should focus on reaching the highest-risk profiles who, despite their elevated risk, were less or no more likely than the lower-risk to use HIV services. By enabling a more synergistic understanding of subgroups, LCA has potential to enable more strategic, data-driven programming and evaluation.

3. Kufa, T., et al. **Medical male circumcision and associations among sexually transmitted infections service attendees**. *AIDS Behav* 2020;24(5): 1422-1431.

   Medical male circumcision (MMC) is a proven intervention for preventing HIV acquisition among males. We describe the circumcision status, eligibility for MMC referral and associations with HIV positivity among symptomatic males attending sexually transmitted infections (STI) services. This study was a secondary analysis of cross-sectional data collected during sentinel surveillance for STI aetiologies. In the sentinel surveillance conducted at primary care facilities located in six South African provinces, an anonymous questionnaire was administered followed by collection of appropriate genital and blood specimens for laboratory testing including HIV, rapid plasma reagin (RPR) and HSV-2 serological testing. During analysis, multivariable logistic

regression was used to determine association between prevalent HIV infection and male circumcision among males who were HSV-2 AND/OR RPR serology positive and among those who were negative. A total of 847 males were included the analysis, among whom the median age was 28 years (IQR 24-32 years) with 26.3% aged < 25 years. Of these, 166 (19.6%) were medically circumcised, 350 (41.4%) traditionally circumcised while 324 (39%) were not circumcised. The yield of assessment for MMC referral was 27.7%. Overall HIV positivity was 23.1%. Compared to no circumcision, MMC had a statistically insignificant 62% lower odds of being HIV positive -among males who were HSV-2 and RPR negative- adjusted odds ratio [aOR] 0.38 [95% confidence interval (CI) 0.12-1.18], p = 0.094. Among those HSV-2 AND/OR RPR positive, MMC had a statistically insignificant 26% lower odds of being HIV positive- aOR 0.74 (95% CI 0.41-1.36), p = 0.334. In both groups HIV positivity increased with age but was positively associated with condom use at last sexual encounter [aOR 3.41 (95% CI 1.43-8.15)] and previous treatment for an STI syndrome [aOR 3.81 (95% CI 1.60-9.05)] among those HSV-2 and RPR negative. High HIV positivity and high yield of eligibility for VMMC referral among males attending STI services points to the need for better integration of HIV prevention and treatment with STI care.

4. Magadi, M., et al. **Understanding ethnic variations in HIV prevalence in Kenya: the role of cultural practices**. *Cult Health Sex* 2020 May 14: 1-18. [Epub ahead of print]

   Patterns of HIV prevalence in Kenya suggest that areas where various cultural practices are prevalent bear a disproportionate burden of HIV. This paper examines (i) the contextual effects of cultural practices (polygyny, male circumcision) and related sexual behaviour factors on HIV prevalence and (ii) the extent to which specific cultural practices in a community/county might explain existing ethnic variations in HIV prevalence in Kenya. The analysis applies multilevel logistic regression to data from the 2012/13 Kenya AIDS Indicator Survey. The results reveal striking ethnic variations in HIV prevalence in Kenya. The prevalence of polygyny in a community is positively associated with HIV prevalence, while a higher level of male circumcision in a county is protective for both men and women. The effects of these factors are stronger for men than women at both individual and contextual (community/county) levels. These cultural practices and associated risk factors partly explain existing ethnic differences in HIV prevalence in Kenya, but there remain significant ethnic variations that are not explained by these cultural practices or related sexual behaviour factors. These call for stronger empirical evidence to offer stronger theoretical explanations and inform effective policy and practice to address HIV epidemic in adversely affected communities in Kenya and similar settings in sub-Saharan Africa.

5. Thior, I., et al. **"Urban-rural disparity in sociodemographic characteristics and sexual behaviors of HIV-positive adolescent girls and young women and their perspectives on their male sexual partners: A cross-sectional study in Zimbabwe**." *PLoS One* 2020 15(4): e0230823.

   Online at: https://www.ncbi.nlm.nih.gov/pubmed/32324764.

   We conducted a cross sectional survey in Zimbabwe to describe urban-rural disparity in socio-demographic characteristics and sexual behaviors of HIV-positive adolescent girls and young women (AGYW) and their male sexual partners. Between September and November 2016, we interviewed 360 sexually active HIV positive AGYW, aged 15--24 years attending ART and PMTCT clinics in urban and rural health facilities in Harare and Mazowe district respectively. HIV positive AGYW in rural areas as compared to those in urban areas were older, less educated, more frequently married or cohabiting, had lower number of male sexual partners in their lifetime and in the last 12 months preceding the survey. They were mostly heterosexually infected, more likely to disclose their status to a family member and to be more adherent to ART (OR = 2.5-95% CI = 1.1-5.5). Most recent male sexual partners of HIV positive AGYW in urban areas as compared to those from rural areas were mainly current or former boyfriends, single, more educated, less likely to have a child with them and to engage in couple voluntary counseling and testing (CVCT). They were more likely to patronize dancing and drinking venues and involved in transactional sex (OR = 2.2-95% CI: 1.2-4). They were also more likely to be circumcised (OR = 2.3-95% CI: 1.3-4.1) and to use condom more consistently in the last 12 months preceding the survey. Our study findings called for the strengthening of HIV prevention interventions in urban areas among HIV positive AGYW who had more than one partner in their lifetime or are patronizing dancing and drinking venues. In Zimbabwe, promotion of CVCT, index testing, male circumcision and condom use should be sustained to engage male sexual partners of both urban and rural HIV positive AGYW in HIV prevention.

Impact and coverage

1. Farley, T. M., et al. **Impact of male circumcision on risk of HIV infection in men in a changing epidemic context - systematic review and meta-analysis**. *J Int AIDS Soc* 2020;23(6): e25490.

   Online at: https://www.malecircumcision.org/resource/impact-male-circumcision-risk-hiv-infection-men-changing-epidemic-context-%E2%80%93-systematic.

   INTRODUCTION: WHO/UNAIDS recommended Voluntary Medical Male Circumcision in 2007 based on systematic review of observational studies prior to 1999 and three randomized controlled trials (RCTs). To inform updated WHO guidance, we conducted a systematic review and meta-analysis of impact of circumcision on the risk of HIV infection among heterosexual men.

METHODS: Studies in PubMed of HIV incidence and changes in prevalence in heterosexual men by circumcision status were identified. Pooled incidence rate ratios were computed using fixed- and random-effects meta-analysis and risk of bias was assessed using the ROBINS-I tool.

RESULTS AND DISCUSSION: In three RCTs, the pooled incidence ratio was 0.41 (95% CI 0.30 to 0.56), with risk difference 10 (8 to 12) fewer infections per 1000 person-years (py). Pooled incidence ratios were 0.34 (0.24 to 0.49) in two post-RCT follow-up studies, 0.29 (0.19 to 0.43) in men at high HIV risk (five cohorts), 0.48 (0.33 to 0.70) in four community-based cohorts before circumcision scale-up, and 0.56 (0.49 to 0.64) (7 [6 to 8] fewer per 1000 py) in six community-based cohorts during circumcision and antiretroviral treatment scale-up. Heterogeneity between studies was low except in men at high HIV risk. We estimated 520,000 (425,000 to 605,000) fewer infections occurred in men by end of 2018 from 22.7 million circumcisions performed since 2008 and increasing by 155,000 (125,000 to 180,000) annually if epidemic conditions remain similar. After exclusion of studies with high risk of bias and those conducted outside Africa, pooled incidence ratios were similar. There was no evidence of confounding nor changes in risk behaviour following circumcision. In post-hoc exploratory analyses we observed a trend of decreasing effectiveness of circumcision in cohorts with lower HIV incidence.

CONCLUSIONS: Efficacy of medical male circumcision on HIV incidence from randomized controlled trials was supported by effectiveness from observational studies in populations with diverse HIV risk and changing epidemic contexts. Voluntary Medical Male Circumcision remains an important evidence-based intervention for control of generalized HIV epidemics.

2. Hall, M. T., et al. **The past, present and future impact of HIV prevention and control on HPV and cervical disease in Tanzania: A modelling study**. *PLoS One* 2020;15(5): e0231388.

   Online at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0231388.

   BACKGROUND: Women with HIV have an elevated risk of HPV infection, and eventually, cervical cancer. Tanzania has a high burden of both HIV and cervical cancer, with an HIV prevalence of 5.5% in women in 2018, and a cervical cancer incidence rate among the highest globally, at 59.1 per 100,000 per year, and an estimated 9,772 cervical cancers diagnosed in 2018. We aimed to quantify the impact that interventions intended to control HIV have had and will have on cervical cancer in Tanzania over a period from 1995 to 2070.

   METHODS: A deterministic transmission-dynamic compartment model of HIV and HPV infection and natural history was used to simulate the impact of voluntary medical male

circumcision (VMMC), anti-retroviral therapy (ART), and targeted pre-exposure prophylaxis (PrEP) on cervical cancer incidence and mortality from 1995-2070.

FINDINGS: We estimate that VMMC has prevented 2,843 cervical cancer cases and 1,039 cervical cancer deaths from 1995-2020; by 2070 we predict that VMMC will have lowered cervical cancer incidence and mortality rates by 28% (55.11 cases per 100,000 women in 2070 without VMMC, compared to 39.93 with VMMC only) and 26% (37.31 deaths per 100,000 women in 2070 without VMMC compared to 27.72 with VMMC), respectively. We predict that ART will temporarily increase cervical cancer diagnoses and deaths, due to the removal of HIV death as a competing risk, but will ultimately further lower cervical cancer incidence and mortality rates by 7% (to 37.31 cases per 100,000 women in 2070) and 5% (to 26.44 deaths per 100,000 women in 2070), respectively, relative to a scenario with VMMC but no ART. A combination of ART and targeted PrEP use is anticipated to lower cervical cancer incidence and mortality rates to 35.82 and 25.35 cases and deaths, respectively, per 100,000 women in 2070.

CONCLUSIONS: HIV treatment and control measures in Tanzania will result in long-term reductions in cervical cancer incidence and mortality. Although, in the near term, the life-extending capability of ART will result in a temporary increase in cervical cancer rates, continued efforts towards HIV prevention will reduce cervical cancer incidence and mortality over the longer term. These findings are critical background to understanding the longer-term impact of achieving cervical cancer elimination targets in Tanzania.

Male circumcision methods, including devices

1. Millard, P. S., et al. **Minimally invasive, sutureless, adolescent male circumcision with topical anesthetic: a field trial of Unicirc, a single-use surgical instrument**." *Transl Androl Urol* 2020;9(2): 516-522.

   Online at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7214996/.

   BACKGROUND: Circumcision has been shown to reduce the rate of HIV transmission in Africa. It is most cost effective if performed in younger men. Surgical assist devices can increase the efficiency and potentially reduce the cost of performing circumcisions.

   METHODS: We used the Unicirc disposable instrument to perform circumcisions in an outpatient primary care clinic. The trial was non-blinded. Circumcisions were performed under topical anaesthetic and the wound was sealed with cyanoacrylate tissue adhesive. The primary outcome was intraoperative duration; secondary outcomes were intraoperative and postoperative pain; adverse events (AEs); time to healing and patient satisfaction; and, cosmetic result.

RESULTS: A total of 82 adolescent boys (aged 10-15 years) were circumcised. The median intraoperative time was 10 minutes and the median blood loss was 1 mL. All wounds were healed by 4 weeks and cosmetic results were excellent. There were no AEs.

CONCLUSIONS: Adolescent circumcision with Unicirc under topical anesthetic and wound sealing with cyanoacrylate tissue adhesive is safe, rapid, and heals by primary intention with excellent cosmetic results. It is cost effective and can be used for large scale programs.

2. Al Hussein Alawamlh, O., et al. **No-flip ShangRing circumcision in 10-12 year old boys: Results from randomized clinical trials in Kenya**. *PLoS One* 2020;15(5): e0233150.

   Online at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7244118/.

   BACKGROUND: Attention has recently turned toward the use of device-assisted male circumcision to help scale up male circumcision services in sub-Saharan Africa, with increasing emphasis on younger age groups. We assessed the use of the ShangRing for circumcising the subset of boys aged 10 to 12 years who were enrolled in two randomized clinical trials in Kenya.

   METHODS: We performed a sub-analysis of outcomes in 197 boys aged 10 to 12 years; a subset who were enrolled in two randomized clinical trials to assess the use of the no-flip ShangRing circumcision technique in men and boys. One trial assessed spontaneous detachment vs. planned removal of the ShangRing 7 days post-circumcision. The second trial compared the use of topical vs. injectable anesthesia with ShangRing circumcision. Aside from baseline characteristics, data was collected and analyzed for each trial separately.

   RESULTS: All participants were successfully circumcised. Duration of circumcision, participants requiring a dorsal slit, rate of adverse events, time to complete wound healing, and participant satisfaction were similar between the two groups in each trial. Mean time required for spontaneous ShangRing detachment was 14.82+/-3.76 days. Topical anesthesia showed a significantly lower mean pain score at the time of application (0.64+/-1.71 vs. 1.55+/- 2.21, $p = 0.03$) as well as postoperatively (0.54+/-0.88 vs. 1.72+/-1.56, $p<0.0001$). Median dwell time of the topical anesthetic was 43 (IQR: 35.5-60) minutes, while the median time it took the injectable anesthetic to take effect was 2.04 (IQR: 1.72-3.09) minutes.

   CONCLUSION: No-flip ShangRing circumcision had a positive safety profile among young adolescent boys, specifically ages 10-12 years. The use of spontaneous device detachment and topical anesthesia with the procedure have shown promising outcomes in this age group. This may have the potential to further increase the acceptability of

ShangRing circumcision, and therefore accelerate the scale up of male circumcision services in sub-Saharan Africa.

TRIAL REGISTRATION: ClinicalTrials.gov registration # NCT02390310.

Safety

1. Lucas, T. J., et al. **Case series of glans injuries during voluntary medical male circumcision for HIV prevention - eastern and southern Africa, 2015-2018**. *BMC Urol* 2020;20(1): 45.

   Online at: https://bmcurol.biomedcentral.com/articles/10.1186/s12894-020-00613-6.

   BACKGROUND: Male circumcision confers partial protection against heterosexual HIV acquisition among men. The President's Emergency Plan for AIDS Relief (PEPFAR) has supported > 18,900,000 voluntary medical male circumcisions (VMMC). Glans injuries (GIs) are rare but devastating adverse events (AEs) that can occur during circumcision. To address this issue, PEPFAR has supported multiple interventions in the areas of surveillance, policy, education, training, supply chain, and AE management.

   METHODS: Since 2015, PEPFAR has conducted surveillance of GIs including rapid investigation by the in-country PEPFAR team. This information is collected on standardized forms, which were reviewed for this analysis.

   RESULTS: Thirty-six GIs were reported from 2015 to 2018; all patients were < 15 years old (~ 0.7 per 100,000 VMMCs in this age group) with a decreasing annual rate (2015: 0.7 per 100,000 VMMCs; 2018: 0.4 per 100,000 VMMC; p = 0.02). Most (64%) GIs were partial or complete amputations. All amputations among 10-14 year-olds occurred using the forceps-guided (FG) method, as opposed to the dorsal-slit (DS) method, and three GIs among infants occurred using a Mogen clamp. Of 19 attempted amputation repairs, reattached tissue was viable in four (21%) in the short term. In some cases, inadequate DS method training and being overworked, were found.

   CONCLUSION: Following numerous interventions by PEPFAR and other stakeholders, GIs are decreasing; however, they have not been eliminated and remain a challenge for the VMMC program. Preventing further cases of complete and partial amputation will likely require additional interventions that prevent use of the FG method in young patients and the Mogen clamp in infants. Improving management of GIs is critical to optimizing outcomes.

2. Feldacker, C., et al. **Usability and acceptability of a two-way texting intervention for post-operative follow-up for voluntary medical male circumcision in Zimbabwe**. *PLoS One* 2020;15(6): e0233234.

   Online at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0233234.

BACKGROUND: Voluntary medical male circumcision (MC) is safe and effective. Nevertheless, MC programs require multiple post-operative visits. In Zimbabwe, a randomized control trial (RCT) found that post-operative two-way texting (2wT) between clients and MC providers instead of in-person reviews reduced provider workload and safeguarded patient safety. A critical component of the RCT assessed usability and acceptability of 2wT among providers and clients. These findings inform scale-up of the 2wT approach to post-operative follow-up.

METHODS: The RCT assigned 362 adult MC clients with cell phones into 2wT; these men responded to 13 automated daily texts supported by interactive texting or in-person follow-up, when needed. A subset of 100 texting clients filled a self-administered usability survey on day 14. 2wT acceptability was ascertained via 2wT response rates. Among 2wT providers, eight key informant interviews focused on 2wT acceptability and usability. Influences of wage and age on response rates and client-reported potential AEs were explored using linear and logistic regression models, respectively.

RESULTS: Clients felt confident, comfortable, satisfied, and well-supported with 2wT-based follow-up; few noted texting challenges or concerns about healing. Clients felt 2wT saved them time and money. Response rates (92%) suggested 2wT acceptability. Both clients and providers felt 2wT was highly usable. Providers noted 2wT saved them time, empowered clients to engage in their healing, and closed gaps in MC service quality. For scale, providers reinforced good post-operative counseling on AEs and texting instructions. Wage and age did not influence text response rates or potential AE texts.

CONCLUSION: Results strongly suggest that 2wT is highly usable and acceptable for providers and patients. Men with concerns solicited provider guidance and reassurance offered via text. Providers noted that men engaged proactively in their healing. 2wT between providers and patients should be expanded for MC and considered for other short-term care contexts. The trial is registered on ClinicalTrials.gov, trial NCT03119337, and was activated on April 18, 2017. https://clinicaltrials.gov/ct2/show/NCT03119337.

Social and behavioural research

1. Keetile, M. **An assessment of sexual risk behaviours among circumcised and uncircumcised men before and after the implementation of the safe male circumcision programme in Botswana**. *AIDS Care* 2020 May 23: 1-8. [Epub ahead of print]

HIV/AIDS prevalence is still high in Botswana. The main aim of this study was to assess and compare sexual risk behaviours of circumcised and uncircumcised men before and after the launch of the safe male circumcision programme. Data used for analyses were derived from the 2008 and 2013 Botswana AIDS Impact Surveys. Modified Poisson regression analysis was used to obtain prevalence ratios (PR) as measures of association

between circumcision status and multiple sexual partners, transactional sex, inconsistent condom use and intergenerational sex. The proportion of circumcised men increased two times between 2008 (12.5%) and 2013 (25.2%). Prevalence of multiple sexual partnerships was high among uncircumcised than circumcised (54.6% vs. 46.4%) men in 2008, but in 2013 after the introduction of the SMC programme it was slightly high among circumcised men than uncircumcised men (23.2 vs. 21.8%). In the adjusted analyses, being circumcised was significantly associated with having multiple sexual partners (2008=adjusted PR=1.31, CI=1.10-1.57; 2013= adjusted PR=1.12, CI=1.01-1.41) and transactional sex (2008=adjusted PR=1.98, CI=1.26-3.11; 2013=adjusted PR=1.60, CI=1.09-1.22) for both survey periods. These results indicate the need to continuously sensitise and encourage men to stop multiple sexual partnerships and transactional sex. Moreover, there is need to encourage all men to use condoms consistently.

2. Nxumalo, C. T., et al. **Circumcised men's perceptions, understanding and experiences of voluntary medical male circumcision in KwaZulu-Natal, South Africa**. *S Afr Fam Pract (2004)* 2020;62(1): e1-e8.
Online at: https://safpj.co.za/index.php/safpj/article/view/5083.

BACKGROUND: KwaZulu-Natal, South Africa, has rolled out voluntary medical male circumcision (VMMC) in response to recommendations that regions with a high human immunodeficiency virus (HIV) prevalence adopt VMMC as an additional HIV prevention strategy. There is a paucity of South African data on the motivators, barriers and experiences of adult male candidates regarding VMMC. This study was conducted to analyse circumcised men's perceptions, understanding and experiences of VMMC in KwaZulu-Natal, South Africa.

METHODS: A qualitative phenomenographic design was used. Ethical clearance was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE 627/18). Data were collected from 12 circumcised male candidates. Individual interviews were conducted and recorded by using an audiotape. Data were transcribed verbatim and analysed manually.

RESULTS: Participants' perceptions regarding VMMC are health related and appear to be the motivators for the uptake of medical circumcision. Circumcised men in this study appeared to misunderstand VMMC in terms of healing and performance time and the nature of the procedure. Negative experiences in terms of quality of care received were reported.

CONCLUSION: The study findings imply that practice interventions to promote demand generation for VMMC in KwaZulu-Natal, South Africa, should incorporate the perceptions and experiences of male candidates regarding the procedure. Tailored

messaging to address misunderstanding related to the nature of VMMC should also be provided. Regular in-service training on standardised VMMC implementation practices should be provided to ensure the delivery of optimum quality VMMC.

3. Wiginton, J. M., et al. **Masculine gender norms, male circumcision, and men's engagement with health care in the Dominican Republic**. *Glob Public Health* 2020;15(5): 654-665.
Online at: https://www.tandfonline.com/doi/full/10.1080/17441692.2019.1704817.

   Overall, adult men are less likely to seek and receive health care than women, but male circumcision for HIV prevention has been successful in engaging men in health services. The purpose of this paper is to examine the relationship between masculine norms and health care-seeking among men participating in a voluntary male medical circumcision (VMMC) programme in the Dominican Republic (DR). We employed a mixed methods approach integrating survey data collected 6-12 months post-circumcision (n = 293) and in-depth interviews with a sub-sample of these men (n = 30). In our qualitative analysis, we found that health care-seeking is connected to masculine norms among men in the DR, including the perceptions of medical facilities as feminine spaces. Participants' narratives demonstrate that male circumcision programmes may facilitate men overcoming masculinity-related barriers to health care engagement. In quantitative analysis, we found that being concerned about being perceived as masculine was associated with health care-seeking behaviour in the past five years, though this association was not retained in multivariable analyses. Findings indicate that male circumcision programmes can familiarise men with the healthcare system and masculinise health care-seeking and utilisation, easing associated discomfort.

4. Pintye, J. C., et al. **Sexual function after voluntary medical male circumcision for human immunodeficiency virus prevention: Results from a programmatic delivery setting in Botswana**. *South Afr J HIV Med* 2020;21(1): 1042.

   Online at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7203194/.

   BACKGROUND: Uptake of voluntary medical male circumcision (VMMC) remains modest in Botswana in spite of the government's commitment and service provision availability. Data on sexual function post-VMMC in programmatic settings could help guide messaging tailored to Botswana.

   OBJECTIVES: At 3-month post-VMMC, we evaluated changes in sexual function and satisfaction with the VMMC procedure amongst a cohort of HIV-negative, sexually active men aged 18-49 years who underwent VMMC in a public-sector clinic in Botswana. Methods: We assessed whether each of the following domains of sexual function had

improved, stayed the same or worsened since VMMC: sexual desire, ability to use condoms, ease of vaginal penetration, ease of ejaculation, ability to achieve and maintain an erection and hygiene or cleanliness.

RESULTS: Data on sexual function were available for 378 men at 3-month post-VMMC. Median age was 27 years - 54% had a higher than secondary education, 72% were employed and 27% were married. Nearly all (96%) the men reported improvement in at least one domain of sexual function, while 19% reported improvement in all six domains. One-fourth (91/378, 24%) of the men reported that at least one domain of sexual function worsened post-VMMC. The most frequently reported domain that worsened was sexual desire (11%); in all other domains, < 10% of the men reported worsening. Men who reported any worsening sexual function were 2.3-fold as likely to be less than 'very satisfied' with the VMMC procedure (risk ratio 2.36, 95% confidence interval [CI] 1.66-3.34, $p < 0.001$).

CONCLUSION: Emphasising improved sexual function experienced after VMMC in demand-creation efforts could potentially increase VMMC uptake in Botswana.