

**Quarterly Research Digest**  
**On Voluntary Medical Male Circumcision for HIV Prevention**

1. Grabowski, M.K., et al. **Trends and determinants of human papillomavirus concordance among HIV-positive and HIV-negative heterosexual couples in Rakai, Uganda.** *J Infect Dis* 2016 Dec 23. pii: jiw631. [Epub ahead of print]

**BACKGROUND:** Limited data are available on human papillomavirus (HPV) infection among HIV-negative or HIV-positive couples followed longitudinally.

**METHODS:** Genital HPV was assessed in 725 concordant HIV-negative couples and 209 HIV-positive couples enrolled in a male circumcision trial in Rakai, Uganda using the Roche Linear Array assay which detects 37 HPV genotypes. HPV prevalence and determinants of genotype-specific concordance were assessed at annual visits. Cumulative detection of HPV genotypes over two years was also assessed.

**RESULTS:** At enrollment, HPV infection was detected in 54% of HIV-negative women, 56% of HIV-negative men, and 93% of HIV-positive men and women. For HIV-negative couples, genotypic concordance was 30% at baseline (n=219/725) and declined significantly with age (adjPRR=0.53, 95%CI=0.28-0.93 comparing women >40 to 15-19 years) and male circumcision (adjPRR=0.60, 95%CI=0.47-0.77), and increased among couples with recent intercourse (adjPRR=1.26, 95%CI=1.04-1.53). These associations were not seen in HIV-positive couples. Among couples with HPV results at all visits, one or more of the same genotypes were detected in both partners in 60% of HIV-negative couples and 96% of HIV-positive couples over two years.

**CONCLUSION:** HPV genotype-specific concordance is more common in HIV-positive couples, and irrespective of HIV status, the majority of couples exhibit HPV concordance over two years.

2. Patel, E.U., et al. **Penile immune activation and risk of HIV shedding: a prospective cohort study.** *Clin Infect Dis* 2016 Dec 22. pii: ciw847. [Epub ahead of print]

**BACKGROUND:** Genital immune activation is suspected to modulate local HIV RNA levels and the risk of sexual HIV transmission.

**METHODS:** A prospective, observational cohort study of 221 HIV-infected men undergoing male circumcision (MC) was conducted in Rakai, Uganda. Penile lavage samples collected from the coronal sulcus at baseline and 4 weekly visits after MC were assayed for pro-inflammatory cytokines and HIV-1 RNA. The main analysis was limited to 175 men with detectable HIV plasma viral load (VL>400

copies/mL; n=808 visits). The primary exposures of interest were individual and total cytokine detection at the previous visit. Adjusted prevalence risk ratios (adjPRR) of detectable HIV shedding (VL>40 copies/mL) were estimated by Poisson regression models with generalized estimating equations and robust variance estimators, and included adjustment for plasma HIV VL.

**FINDINGS:** Among men with a detectable plasma VL, penile HIV shedding was detected in 136 visits (16.8%). Detectable IL-1beta (adjPRR=2.14;95%CI=1.02-4.48), IL-6 (adjPRR=2.24;95%CI=1.28-3.90), IL-8 (adjPRR=2.42; 95%CI=1.15-5.08), IL-10 (adjPRR=2.51;95%CI=1.67-3.80), and IL-13 (adjPRR=1.87; 95%CI=1.15-3.03) were associated with penile HIV shedding at the subsequent visit. Men with 2-4 (adjPRR=2.36;95%CI=1.08-5.14) and 5-7 (adjPRR=3.00; 95%CI=1.28-7.01) detectable cytokines had a greater likelihood of detectable penile HIV shedding at the follow-up visit, compared to men with  $\leq 1$  detectable cytokine. The total number of detectable cytokines was associated with a higher penile log<sub>10</sub> HIV VL at the subsequent visit among HIV shedders.

**INTERPRETATION:** Pro-inflammatory cytokine production had a dose-dependent and temporal association with penile HIV shedding, suggesting that genital immune activation may increase the risk of sexual HIV transmission by driving local HIV replication.

3. Gyan, T., et al. **Determinants of morbidity associated with infant male circumcision: community-level population-based study in rural Ghana.** *Trop Med Int Health* 2016 Dec 19. [Epub ahead of print]

**OBJECTIVE:** Male circumcision services have expanded throughout Africa as part of a long-term HIV prevention strategy. We assessed the effect of type of service provider (formal and informal) and hygiene practices on circumcision-related morbidities in rural Ghana.

**METHODS:** Population-based, cross-sectional study conducted between May and December 2012 involving 2850 circumcised infant males aged under 12 weeks. Multivariable logistic regression models were adjusted for maternal age, maternal education, income, birth weight and site of circumcision.

**RESULTS:** 2850 (90.7%) infant males were circumcised. Overall, the risk of experiencing a morbidity (defined as complications occurring during or after the circumcision procedure as reported by the primary caregiver) was 8.1% (230). Risk was not significantly increased if the circumcision was performed by informal providers (121, 7.2%) vs. formal health service providers (109, 9.8%) (adjusted odds ratio [aOR] 1.11, 95% CI 0.80-1.47, p=0.456). Poor hygiene practices were associated with significantly increased risk of morbidity: no hand washing (148 [11.7%]) (aOR 1.78, 95% CI 1.27-2.52, p=0.001); not cleaning circumcision instruments (174 [10.6%]) (aOR 1.80, 95% CI 1.27- 2.54, p=0.001);

and uncleaned penile area (190 [10.0%]) (aOR 1.84, 95% CI 1.25-2.70, p=0.002).

**CONCLUSION:** The risk of morbidity after infant male circumcision in rural Ghana is high, chiefly due to poor hygiene practices. Governmental and nongovernmental organisations need to improve training of circumcision providers in hygiene practices in sub-Saharan Africa. This article is protected by copyright. All rights reserved.

4. Baggaley, R., et al. **Beyond the 90-90-90: refocusing HIV prevention as part of the global HIV response.** *J Int AIDS Soc* 2016;19(1):21348. Online at: <http://www.jiasociety.org/index.php/jias/article/view/21348>

**INTRODUCTION:** The remarkable expansion in availability of antiretroviral therapy (ART) over the past two decades has transformed HIV infection into a manageable chronic condition. People with HIV infection now live long and healthy lives on treatment that is simpler, safer and cheaper. According to UNAIDS estimates, the global coverage of ART reached 46% in 2015, resulting in a 26% decrease in annual HIV-related deaths since 2010. Such success has positioned treatment access at the centre of the global HIV response as a way to prevent mortality, morbidity and HIV transmission through a "Treat All" approach. Continuing expansion of treatment is needed to further reduce HIV-related mortality. This progress with treatment, however, masks a stagnation in the estimated annual number of new HIV infections. Continuing levels of HIV incidence despite treatment scale-up stem from several factors, which should be addressed in order to prevent new infections and decrease the numbers of people requiring treatment in the future.

**DISCUSSION:** ART can only reach those already diagnosed, and although it is unclear what proportion of new infections occur during acute and early infection prior to treatment initiation, phylogenetic studies suggest that it might be substantial. Thus, better testing approaches to reach the 40% of people with undiagnosed HIV infection as early as possible are critical. New approaches to reach men, young people and key populations, where HIV risk is highest and HIV prevention, testing and treatment coverage is lowest, are also needed. Overall coverage of effective prevention interventions remains low, enabling HIV transmission to occur, or time is required to show population-level effects. For example, the full impact of the medical male circumcision intervention will be seen once a larger proportion of men in age cohorts with high incidence are circumcised. Finally, strategically focused pre-exposure prophylaxis interventions have the potential to prevent HIV acquisition among populations at substantial risk, averting treatment costs in coming years.

**CONCLUSIONS:** The United Nations (UN) targets to end AIDS include the "90-90-90" targets for HIV diagnosis, treatment and viral suppression. While 90-90-90 has been widely emphasized and adopted by countries and international funders,

the focus thus far has largely been on increasing access to ART - the second "90." A similar emphasis on achieving UN HIV prevention targets and adequate funding for meeting these is essential, alongside treatment, in order to reduce population-level incidence and change the trajectory of the HIV epidemic over the long term.

5. Carrasco, M.A., et al. **Low uptake of voluntary medical male circumcision among high risk men in Malawi.** *AIDS Behav* 2016 Dec 9. [Epub ahead of print]

Malawi is one of 14 priority countries for voluntary medical male circumcision (VMMC) initiatives with the lowest VMMC uptake. Using data from a study of 269 men accessing VMMC in southern Malawi and latent class analysis, men were classified based on four risk factors: ever tested for HIV, condom use at last sex, having casual/concurrent sexual partners, and using alcohol before sex. Two distinct classes were identified: 8% of men were classified as high risk, while 92% were classified as low/medium risk. Poisson regression modeling indicated that men who had lower education (risk ratio [RR] 1.07,  $p < 0.05$ ) and were ages 19-26 (RR 1.07,  $p < 0.05$ ) were more likely to be in the high risk group. The low numbers of men in the high risk category seeking services suggests the need to implement targeted strategies to increase VMMC uptake among such high risk men.

6. George, G., et al. **Early resumption of sex following voluntary medical male circumcision amongst school-going males.** *PLoS One* 2016;11(12):e0168091.  
Online at:  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0168091>

Voluntary medical male circumcision is an integral part of the South African government's response to the HIV and AIDS epidemic. Following circumcision, it is recommended that patients abstain from sexual activity for six weeks, as sex may increase the risk of female-to-male HIV transmission and prolong the healing period. This paper investigates the resumption of sexual activity during the healing period among a cohort of school-going males in the KwaZulu-Natal province of South Africa. The analysis for this paper compares two groups of sexually active school-going males: the first group reported having sex during the healing period ( $n = 40$ ) and the second group ( $n = 98$ ) reported no sex during the healing period (mean age: 17.7, SD: 1.7). The results show that 29% ( $n = 40$ ) of young males (mean age: 17.9, SD: 1.8) who were previously sexually active, resumed sexual activity during the healing period, had on average two partners and used condoms inconsistently. In addition, those males that engage in sexual activity during the healing period were less inclined to practice safe sex in the future (AOR = 0.055,  $p = 0.002$ ) than the group of males who reported no sex during the healing period. These findings suggest that a significant proportion of young males may currently and in the future, subject themselves to high levels of

risk for contracting HIV post circumcision. Education, as part of a VMMC campaign, must emphasize the high risk of HIV transmission for both the males their partners during the healing period.

7. Sousa, J.D., et al. **Male circumcision and the epidemic emergence of HIV-2 in West Africa.** *PLoS One* 2016;11(12):e0166805.

Online at:

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0166805>

**BACKGROUND:** Epidemic HIV-2 (groups A and B) emerged in humans circa 1930-40. Its closest ancestors are SIVsmm infecting sooty mangabeys from southwestern Cote d'Ivoire. The earliest large-scale serological surveys of HIV-2 in West Africa (1985-91) show a patchy spread. Cote d'Ivoire and Guinea-Bissau had the highest prevalence rates by then, and phylogeographical analysis suggests they were the earliest epicenters. Wars and parenteral transmission have been hypothesized to have promoted HIV-2 spread. Male circumcision (MC) is known to correlate negatively with HIV-1 prevalence in Africa, but studies examining this issue for HIV-2 are lacking.

**METHODS:** We reviewed published HIV-2 serosurveys for 30 cities of all West African countries and obtained credible estimates of real prevalence through Bayesian estimation. We estimated past MC rates of 218 West African ethnic groups, based on ethnographic literature and fieldwork. We collected demographic tables specifying the ethnic partition in cities. Uncertainty was incorporated by defining plausible ranges of parameters (e.g. timing of introduction, proportion circumcised). We generated 1,000 sets of past MC rates per city using Latin Hypercube Sampling with different parameter combinations, and explored the correlation between HIV-2 prevalence and estimated MC rate (both logit-transformed) in the 1,000 replicates.

**RESULTS AND CONCLUSIONS:** Our survey reveals that, in the early 20th century, MC was far less common and geographically more variable than nowadays. HIV-2 prevalence in 1985-91 and MC rates in 1950 were negatively correlated (Spearman rho = -0.546, IQR: -0.553--0.546,  $p \leq 0.0021$ ). Guinea-Bissau and Cote d'Ivoire cities had markedly lower MC rates. In addition, MC was uncommon in rural southwestern Cote d'Ivoire in 1930. The differential HIV-2 spread in West Africa correlates with different historical MC rates. We suggest HIV-2 only formed early substantial foci in cities with substantial uncircumcised populations. Lack of MC in rural areas exposed to bushmeat may have had a role in successful HIV-2 emergence.

8. Strode, A.E., et al. **Addressing legal and policy barriers to male circumcision for adolescent boys in South Africa.** *PLoS One* 2016;106(12):1173-1176.

Online at: <http://www.samj.org.za/index.php/samj/article/view/11597/7745>

With millions of adolescents becoming infected with HIV globally, it is essential that barriers to much-needed interventions are reduced for at-risk adolescents. In this article we review the legal and policy framework in South Africa for adolescent access to male circumcision. We are of the view that the framework does confer protection for adolescent boys while enabling access to male circumcision; however, we identify ambiguities and tensions that exist between the Children's Act, regulations and national guidelines. We recommend reform to further enable access by this vulnerable group to this prevention modality.

9. Prodger, J.L., et al. **Chemokine levels in the penile coronal sulcus correlate with HIV-1 Acquisition and are reduced by male circumcision in Rakai, Uganda.** *PLoS Pathog* 2016;12(11):e1006025.  
Online at:  
<http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006025>

Individual susceptibility to HIV is heterogeneous, but the biological mechanisms explaining differences are incompletely understood. We hypothesized that penile inflammation may increase HIV susceptibility in men by recruiting permissive CD4 T cells, and that male circumcision may decrease HIV susceptibility in part by reducing genital inflammation. We used multi-array technology to measure levels of seven cytokines in coronal sulcus (penile) swabs collected longitudinally from initially uncircumcised men enrolled in a randomized trial of circumcision in Rakai, Uganda. Coronal sulcus cytokine levels were compared between men who acquired HIV and controls who remained seronegative. Cytokines were also compared within men before and after circumcision, and correlated with CD4 T cells subsets in foreskin tissue. HIV acquisition was associated with detectable coronal sulcus Interleukin-8 (IL-8 aOR 2.26, 95%CI 1.04-6.40) and Monokine Induced by gamma-interferon (MIG aOR 2.72, 95%CI 1.15-8.06) at the visit prior to seroconversion, and the odds of seroconversion increased with detection of multiple cytokines. Coronal sulcus chemokine levels were not correlated with those in the vagina of a man's female sex partner. The detection of IL-8 in swabs was significantly reduced 6 months after circumcision (PRR 0.59, 95%CI 0.44-0.87), and continued to decline for at least two years (PRR 0.29, 95%CI 0.16-0.54). Finally, prepuce IL-8 correlated with increased HIV target cell density in foreskin tissues, including highly susceptible CD4 T cells subsets, as well as with tissue neutrophil density. Together, these data suggest that penile inflammation increases HIV susceptibility and is reduced by circumcision.

10. Thornton, R., et al. **Medical male circumcision: How does price affect the risk-profile of take-up?** *Prev Med* 2016;92:68-73.

**OBJECTIVE:** The benefit of male circumcision is greatest among men who are most at risk of HIV infection. Encouraging this population of men to get circumcised maximizes the benefit that can be achieved through the scale-up of circumcision programs. This paper examines how the price of circumcision affects the risk profile of men who receive a voluntary medical circumcision.

**METHODS:** In 2010, 1649 uncircumcised adult men in urban Malawi were interviewed and provided a voucher for a subsidized voluntary medical male circumcision, at randomly assigned prices. Clinical data were collected indicating whether the men in the study received a circumcision.

**RESULTS:** Men who took-up circumcision with a zero-priced voucher were 25 percentage points less likely than those who took-up with a positive-price voucher, to be from a tribe that traditionally circumcises ( $p=0.101$ ). Zero-priced vouchers also brought in men with more sexual partners in the past year ( $p=0.075$ ) and past month ( $p=0.003$ ). None of the men who were most at risk of HIV at baseline (those with multiple partners and who did not use a condom the last time they had sex) received a circumcision if they were offered a positive-priced voucher. Lowering the price to zero increased circumcision take-up to 25% for men of this risk group. The effect of price on take-up was largest among those at highest risk ( $p=0.096$ ).

**CONCLUSIONS:** Reducing the price of circumcision surgery to zero can increase take-up among those who are most at risk of HIV infection.

11. Kripke, K., et al. **Impact and cost of scaling up voluntary medical male circumcision for HIV prevention in the context of the new 90-90-90 HIV treatment targets.** *PLoS One* 2016;11(10):e0155734.  
Online at:  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0155734>

**BACKGROUND:** The report of the Joint United Nations Programme on HIV/AIDS (UNAIDS) for World AIDS Day 2014 highlighted a Fast-Track Strategy that sets ambitious treatment and prevention targets to reduce global HIV incidence to manageable levels by 2020 and end the AIDS epidemic by 2030. The 90-90-90 treatment targets for 2020 call for 90% of people living with HIV to know their HIV status, 90% of people who know their status to receive treatment, and 90% of people on HIV treatment to be virally suppressed. This paper examines how scale-up of voluntary medical male circumcision (VMMC) services in four priority countries in sub-Saharan Africa could contribute to ending the AIDS epidemic by 2030 in the context of concerted efforts to close the treatment gap, and what the impact of VMMC scale-up would be if the 90-90-90 treatment targets were not completely met.

**METHODS:** Using the Goals module of the Spectrum suite of models, this analysis modified ART (antiretroviral treatment) scale-up coverage from base scenarios to reflect the 90-90-90 treatment targets in four countries (Lesotho, Malawi, South Africa, and Uganda). In addition, a second scenario was created to reflect viral suppression levels of 75% instead of 90%, and a third scenario was created in which the 90-90-90 treatment targets are reached in women, with men reaching more moderate coverage levels. Regarding male circumcision



(MC) coverage, the analysis examined both a scenario in which VMMC were assumed to stop after 2015, and one in which MC coverage was scaled up to 90% by 2020 and maintained at 90% thereafter.

**RESULTS:** Across all four countries, scaling up VMMC is projected to provide further HIV incidence reductions in addition to those achieved by reaching the 90-90-90 treatment targets. If viral suppression levels only reach 75%, scaling up VMMC leads to HIV incidence reduction to nearly the same levels as those achieved with 90-90-90 without VMMC scale-up. If only women reach the 90-90-90 targets, scaling up VMMC brings HIV incidence down to near the levels projected with 90-90-90 without VMMC scale-up. Regarding cost, scaling up VMMC increases the annual costs during the scale-up phase, but leads to lower annual costs after the MC coverage target is achieved.

**CONCLUSIONS:** The scenarios modeled in this paper show that the highly durable and effective male circumcision intervention increases epidemic impact levels over those of treatment-only strategies, including the case if universal levels of viral suppression in men and women are not achieved by 2020. In the context of 90-90-90, prioritizing continued successful scale-up of VMMC increases the possibility that future generations will be free not only of AIDS but also of HIV.

12. Kripke, K., et al. **Modeling impact and cost-effectiveness of increased efforts to attract voluntary medical male circumcision clients ages 20-29 in Zimbabwe.** *PLoS One* 2016;11(10):e0164144.

Online at:

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0164144>

**BACKGROUND:** Zimbabwe aims to increase circumcision coverage to 80% among 13- to 29-year-olds. However, implementation data suggest that high coverage among men ages 20 and older may not be achievable without efforts specifically targeted to these men, incurring additional costs per circumcision. Scale-up scenarios were created based on trends in implementation data in Zimbabwe, and the cost-effectiveness of increasing efforts to recruit clients ages 20-29 was examined.

**METHODS:** Zimbabwe voluntary medical male circumcision (VMMC) program data were used to project trends in male circumcision coverage by age into the future. The projection informed a base scenario in which, by 2018, the country achieves 80% circumcision coverage among males ages 10-19 and lower levels of coverage among men above age 20. The Zimbabwe DMPPT 2.0 model was used to project costs and impacts, assuming a US\$109 VMMC unit cost in the base scenario and a 3% discount rate. Two other scenarios assumed that the program could increase coverage among clients ages 20-29 with a corresponding increase in unit cost for these age groups.



**RESULTS:** When circumcision coverage among men ages 20-29 is increased compared with a base scenario reflecting current implementation trends, fewer VMMCs are required to avert one infection. If more than 50% additional effort (reflected as multiplying the unit cost by >1.5) is required to double the increase in coverage among this age group compared with the base scenario, the cost per HIV infection averted is higher than in the base scenario.

**CONCLUSIONS:** Although increased investment in recruiting VMMC clients ages 20-29 may lead to greater overall impact if recruitment efforts are successful, it may also lead to lower cost-effectiveness, depending on the cost of increasing recruitment. Programs should measure the relationship between increased effort and increased ability to attract this age group.

13. Tchuente, M., et al. **Estimating client out-of-pocket costs for accessing voluntary medical male circumcision in South Africa.** *PLoS One* 2016;11(10):e0164147.  
Online at:  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0164147>

In 2010, South Africa launched a countrywide effort to scale up its voluntary medical male circumcision (VMMC) program on the basis of compelling evidence that circumcision reduces men's risk of acquiring HIV through heterosexual intercourse. Even though VMMC is free there, clients can incur indirect out-of-pocket costs (for example transportation cost or foregone income). Because these costs can be barriers to increasing the uptake of VMMC services, we assessed them from a client perspective, to inform VMMC demand creation policies. Costs (calculated using a bottom-up approach) and demographic data were systematically collected through 190 interviews conducted in 2015 with VMMC clients or (for minors) their caregivers at 25 VMMC facilities supported by the government and the President's Emergency Plan for AIDS Relief in eight of South Africa's nine provinces. The average age of VMMC clients was 22 years and nearly 92% were under 35 years of age. The largest reported out-of-pocket expenditure was transportation, at an average of US\$9.20 (R 100). Only eight clients (4%) reported lost days of work. Indirect expenditures were childcare costs (one client) and miscellaneous items such as food or medicine (20 clients). Given competing household expense priorities, spending US\$9.20 (R100) per person on transportation to access VMMC services could be a significant burden on clients and households, and a barrier to South Africa's efforts to create demand for VMMC. Thus, we recommend a more focused analysis of clients' transportation costs to access VMMC services.

14. Hankins, C., et al. **Voluntary medical male circumcision for HIV prevention: new mathematical models for strategic demand creation prioritizing subpopulations by age and geography.** *PLoS One* 2016;11(10):e0160699.  
Online at:  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0160699>

Over 11 million voluntary medical male circumcisions (VMMC) have been performed of the projected 20.3 million needed to reach 80% adult male circumcision prevalence in priority sub-Saharan African countries. Striking numbers of adolescent males, outside the 15-49-year-old age target, have been accessing VMMC services. What are the implications of overall progress in scale-up to date? Can mathematical modeling provide further insights on how to efficiently reach the male circumcision coverage levels needed to create and sustain further reductions in HIV incidence to make AIDS no longer a public health threat by 2030? Considering ease of implementation and cultural acceptability, decision makers may also value the estimates that mathematical models can generate of immediacy of impact, cost-effectiveness, and magnitude of impact resulting from different policy choices. This supplement presents the results of mathematical modeling using the Decision Makers' Program Planning Tool Version 2.0 (DMPPT 2.0), the Actuarial Society of South Africa (ASSA2008) model, and the age structured mathematical (ASM) model. These models are helping countries examine the potential effects on program impact and cost-effectiveness of prioritizing specific subpopulations for VMMC services, for example, by client age, HIV-positive status, risk group, and geographical location. The modeling also examines long-term sustainability strategies, such as adolescent and/or early infant male circumcision, to preserve VMMC coverage gains achieved during rapid scale-up. The 2016-2021 UNAIDS strategy target for VMMC is an additional 27 million VMMC in high HIV-prevalence settings by 2020, as part of access to integrated sexual and reproductive health services for men. To achieve further scale-up, a combination of evidence, analysis, and impact estimates can usefully guide strategic planning and funding of VMMC services and related demand-creation strategies in priority countries. Mid-course corrections now can improve cost-effectiveness and scale to achieve the impact needed to help turn the HIV pandemic on its head within 15 years.

15. Tchenche, M., et al. **The cost of voluntary medical male circumcision in South Africa.** *PLoS One* 2016;11(10):e0160207.  
Online at:  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0160207>

Given compelling evidence associating voluntary medical male circumcision (VMMC) with men's reduced HIV acquisition through heterosexual intercourse, South Africa in 2010 began scaling up VMMC. To project the resources needed to complete 4.3 million circumcisions between 2010 and 2016, we (1) estimated the unit cost to provide VMMC; (2) assessed cost drivers and cost variances across eight provinces and VMMC service delivery modes; and (3) evaluated the costs associated with mobilize and motivate men and boys to access VMMC services. Cost data were systematically collected and analyzed using a provider's perspective from 33 Government and PEPFAR-supported (U.S. President's Emergency Plan for AIDS Relief) urban, rural, and peri-urban VMMC facilities. The cost per circumcision performed in 2014 was US\$132 (R1,431): higher in public hospitals (US\$158 [R1,710]) than in health centers and clinics (US\$121

[R1,309]). There was no substantial difference between the cost at fixed circumcision sites and fixed sites that also offer outreach services. Direct labor costs could be reduced by 17% with task shifting from doctors to professional nurses; this could have saved as much as \$15 million (R163.20 million) in 2015, when the goal was 1.6 million circumcisions. About \$14.2 million (R154 million) was spent on medical male circumcision demand creation in South Africa in 2014-primarily on personnel, including community mobilizers (36%), and on small and mass media promotions (35%). Calculating the unit cost of VMMC demand creation was daunting, because data on the denominator (number of people reached with demand creation messages or number of people seeking VMMC as a result of demand creation) were not available. Because there are no "dose-response" data on demand creation (\$X in demand creation will result in an additional Z% increase in VMMC clients), research is needed to determine the appropriate amount and allocation of demand creation resources.

16. McGillen, J.B., et al. **PrEP as a feature in the optimal landscape of combination HIV prevention in sub-Saharan Africa.** *J Int AIDS Soc* 2016;19(Suppl 6):21104.  
Online at: <http://www.jiasociety.org/index.php/jias/article/view/21104>

**INTRODUCTION:** The new WHO guidelines recommend offering pre-exposure prophylaxis (PrEP) to people who are at substantial risk of HIV infection. However, where PrEP should be prioritised, and for which population groups, remains an open question. The HIV landscape in sub-Saharan Africa features limited prevention resources, multiple options for achieving cost saving, and epidemic heterogeneity. This paper examines what role PrEP should play in optimal prevention in this complex and dynamic landscape.

**METHODS:** We use a model that was previously developed to capture subnational HIV transmission in sub-Saharan Africa. With this model, we can consider how prevention funds could be distributed across and within countries throughout sub-Saharan Africa to enable optimal HIV prevention (that is, avert the greatest number of infections for the lowest cost). Here, we focus on PrEP to elucidate where, and to whom, it would optimally be offered in portfolios of interventions (alongside voluntary medical male circumcision, treatment as prevention, and behaviour change communication). Over a range of continental expenditure levels, we use our model to explore prevention patterns that incorporate PrEP, exclude PrEP, or implement PrEP according to a fixed incidence threshold.

**RESULTS:** At low-to-moderate levels of total prevention expenditure, we find that the optimal intervention portfolios would include PrEP in only a few regions and primarily for female sex workers (FSW). Prioritisation of PrEP would expand with increasing total expenditure, such that the optimal prevention portfolios would offer PrEP in more subnational regions and increasingly for men who have sex with men (MSM) and the lower incidence general population. The marginal

benefit of including PrEP among the available interventions increases with overall expenditure by up to 14% (relative to excluding PrEP). The minimum baseline incidence for the optimal offer of PrEP declines for all population groups as expenditure increases. We find that using a fixed incidence benchmark to guide PrEP decisions would incur considerable losses in impact (up to 7%) compared with an approach that uses PrEP more flexibly in light of prevailing budget conditions.

**CONCLUSIONS:** Our findings suggest that, for an optimal distribution of prevention resources, choices of whether to implement PrEP in subnational regions should depend on the scope for impact of other possible interventions, local incidence in population groups, and total resources available. If prevention funding were to become restricted in the future, it may be suboptimal to use PrEP according to a fixed incidence benchmark, and other prevention modalities may be more cost-effective. In contrast, expansions in funding could permit PrEP to be used to its full potential in epidemiologically driven prevention portfolios and thereby enable a more cost-effective HIV response across Africa.

17. Young, M.R., et al. **Factors associated with preference for early infant male circumcision among a representative sample of parents in Homa Bay County, Western Kenya.** *AIDS Behav* 2016;20(11):2545-2554.

Several countries scaling-up adult medical male circumcision (MMC) for HIV prevention intend to introduce early infant male circumcision (EIMC). To assess preference for EIMC in a community with a mature adult MMC program, we conducted a cross-sectional survey of a representative sample of mothers (n = 613) and fathers (n = 430) of baby boys ("index son") at 16 health facilities in western Kenya. Most (59 %) were for EIMC, generally. Just 29 % were for circumcising the index son. Pain and protection from HIV were the most frequently cited barrier and facilitator to EIMC, respectively. In multivariable logistic regression, ever talking with the partner about EIMC and positive serostatus were associated with preference for EIMC for the index son. Attitudes towards EIMC are favorable. Willingness to circumcise an infant son is modest. To facilitate EIMC uptake, education about EIMC pain management and encouraging discussion between parents about EIMC during pregnancy should be integrated into programs.

18. Crosby, R.A., et al. **Circumcision status is not associated with condom use and prevalence of sexually transmitted infections among young black MSM.** *AIDS Behav* 2016;20(11):2538-2542.

This study investigated whether intact young Black MSM differed from their circumcised counterparts regarding condom use behaviors and perceptions and HIV/Chlamydia/gonorrhea. Young Black MSM completed a self-interview, including a pictorial item assessing circumcision status and measures of condom use. Twenty-seven percent of 388 participants reported not being circumcised.

With one exception, no associations tested approached significance. The mean frequency of unprotected insertive anal sex for circumcised men was about twice as high compared to those intact ( $P = .04$ ). Intact young Black MSM did not differ from circumcised men relative to prevalence of STIs (including HIV) or condom use behaviors as reported only by insertive partners.

19. Golub, G., et al. **The relationship between distance and post-operative visit attendance following medical male circumcision in Nyanza Province, Kenya.** *AIDS Behav* 2016;20(11):2529-2537.

To date, there is no research on voluntary medical male circumcision (VMMC) catchment areas or the relationship between distance to a VMMC facility and attendance at a post-operative follow-up visit. We analyzed data from a randomly selected subset of males self-seeking circumcision at one of 16 participating facilities in Nyanza Province, Kenya between 2008 and 2010. Among 1437 participants, 46.7 % attended follow-up. The median distance from residence to utilized facility was 2.98 km (IQR 1.31-5.38). Nearly all participants (98.8 %) lived within 5 km from a facility, however, 26.3 % visited a facility more than 5 km away. Stratified results demonstrated that among those utilizing fixed facilities, greater distance was associated with higher odds of follow-up non-attendance (OR 5.01-10km vs. 0-1km = 1.71, 95 % CI 1.08, 2.70,  $p = 0.02$ ; OR >10km vs. 0-1 km = 2.80, 95 % CI 1.26, 6.21,  $p = 0.01$ ), adjusting for age and district of residence. We found 5 km marked the threshold distance beyond which follow-up attendance significantly dropped. These results demonstrate distance is an important predictor of attending follow-up, and this relationship appears to be modified by facility type.

20. Kangmennaang, J., et al. **Circumcision status and time to sexual debut among youth in Sub-Saharan Africa: evidence from six Demographic and Health Surveys.** *AIDS Behav* 2016;20(11):2514-2528.

This paper examines the relationship between circumcision status and timing of sexual debut among unmarried youth in Sub-Saharan Africa using Demographic and Health Surveys. Results from survival analysis indicate that the association between circumcision and timing of first sex is place and context specific. Compared to uncircumcised, circumcised men in Rwanda, Uganda and Namibia hasten sexual initiation, whilst circumcised youth in Ethiopia and Mali delayed sex initiation. In Togo however, we found parity in timing to sexual debut. Our multivariate results reveal that, knowledge of HIV/AIDS risk and educational level also feed into the association between circumcision and timing of sex initiation- implying that efforts to prevent new HIV infection through circumcision could benefit from a proper understanding of how diverse set of factors interact in specific contexts to shape youth's decisions to initiate early sex.

21. Cook, R., et al. **Female partner acceptance as a predictor of men's readiness to undergo voluntary medical male circumcision in Zambia: The Spear and Shield Project.** *AIDS Behav* 2016;20(11):2503-2513.

Online at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4696907/>

The World Health Organization has recommended the scale-up of voluntary medical male circumcision (VMMC) for HIV prevention in sub-Saharan Africa; however, men are often uninterested in undergoing VMMC. The Spear & Shield project enrolled 668 men and female partners from ten Zambian community health centers into parallel interventions promoting VMMC for HIV prevention or time-matched control conditions. A mediation model was utilized to examine the relationships between changes in women's acceptance of VMMC and men's readiness to undergo the procedure. Results demonstrated that, at 12 months post-intervention, a 5.9 % increase in the likelihood of undergoing VMMC among men in the experimental condition could be attributed to increased women's acceptance. From a public health perspective, involving women in VMMC promotion interventions such as the Spear & Shield project could significantly impact the demand for VMMC in Zambia.

22. Wang, Z., et al. **Needs assessment and theory-based promotion of voluntary medical male circumcision (VMMC) among male sexually transmitted diseases patients (MSTDP) in China.** *AIDS Behav* 2016;20(11):2489-2502.

Voluntary medical male circumcision (VMMC) is an evidence-based biomedical HIV prevention method. It is under-utilized in countries outside Africa, including China. The present single-arm, non-blinded test-of-concept trial was designed to promote VMMC among 179 male sexually transmitted diseases patients (MSTDP) in Shenzhen, China. It was based on behavioral health theories and results of a formative survey. At month 4, 45.5 % of the MSTDP responded positively to the intervention (19.9 % had taken up VMMC and 25.6 % intended to do so in the next 6 months). Adjusted analysis showed that cognitive variables measured at baseline (perceived self-efficacy, subjective norm and behavioral intention) significantly predicted adoption of VMMC during the 4-month follow-up period. Process evaluation involving clinicians of the STD clinics was positive. At month 6, 36.0 % of the circumcised participants used condom less frequently with their regular sex partner. We recommend scaling up the intervention, taking prevention of risk compensation into account.

23. Irungu, E.M., et al. **Use of a risk scoring tool to identify higher-risk HIV-1 serodiscordant couples for an antiretroviral-based HIV-1 prevention intervention.** *BMC Infect Dis* 2016;16(1):571.

Online at: <https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-016-1899-y>

**BACKGROUND:** Antiretroviral therapy (ART) and pre-exposure prophylaxis (PrEP) reduce HIV-1 transmission within heterosexual HIV-1 serodiscordant



couples. Prioritizing couples at highest HIV-1 transmission risk for ART and PrEP would maximize impact and minimize costs.

**METHODS:** The Partners Demonstration Project is an open-label, delivery study of integrated PrEP and ART for HIV-1 prevention among high risk HIV-1 serodiscordant couples in Kenya and Uganda. We evaluated the feasibility of using a validated risk score that weighs a combination of easily measurable factors (age, children, marital status, male circumcision status, condom use, plasma HIV-1 levels) to identify couples at highest risk for HIV-1 transmission for enrollment. Couples scoring  $\geq 5$  met the risk score eligibility criteria.

**RESULTS:** We screened 1694 HIV-1 serodiscordant couples and enrolled 1013. Of the screened couples, 1331 (78.6 %) scored  $\geq 5$  (with an expected incidence  $> 3$  % per year) and 76 % of these entered the study. The median age of the HIV-1 uninfected partner was 29 years [IQR 26, 36] and 20 % were  $< 25$  years of age. The HIV-1 uninfected partner was male in 67 % of partnerships, 33 % of whom were uncircumcised, 57 % of couples had no children, and 65 % reported unprotected sex in the month prior to enrollment. Among HIV-1 infected partners, 41 % had plasma viral load  $> 50,000$  copies/ml.

**CONCLUSION:** A risk scoring tool identified HIV-1 serodiscordant couples for a demonstration project of PrEP and ART with high HIV-1 risk. The tool may be feasible for research and public health settings to maximize efficiency and minimize HIV-1 prevention costs.

24. Kroidl, I., et al. **Effect of *Wuchereria bancrofti* infection on HIV incidence in southwest Tanzania: a prospective cohort study.** *Lancet* 2016;388(10054): 1912-1920.  
Online at: [http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(16\)31252-1.pdf](http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)31252-1.pdf)

The past decades have seen an ongoing controversial debate about whether the immune activation induced by helminths has an effect on the susceptibility of individuals to HIV. In view of this, we assessed the effect of lymphatic filariasis, a chronic helminth disease elicited by *Wuchereria bancrofti*, on HIV incidence in southwest Tanzania. In this population-based cohort study, we enrolled a geographically stratified randomly chosen sample of about 10% of the households in nine distinct sites in southwest Tanzania. All household members present were followed up and tested for HIV and circulating filarial antigen, an indicator of *W bancrofti* adult worm burden. Our main outcome of interest was HIV incidence in participants with or without lymphatic filariasis. Between May 29, 2006, and June 16, 2011, we enrolled 4283 households with roughly 18 000 participants. Of these, 2699 individuals from Kyela district participated in at least one round of the EMINI study. In the 1055 initially HIV-negative adolescents and adults with clearly defined lymphatic filariasis status, 32 new HIV infections were observed in 2626 person-years. HIV incidence in lymphatic filariasis-positive



participants (1.91 cases per 100 person-years) was significantly higher than the incidence in lymphatic filariasis-negative participants (0.80 cases per 100 person-years). The age-adjusted and sex-adjusted incidence rate ratio was 2.17 (95% CI 1.08-4.37,  $p=0.0300$ ). Lymphatic filariasis status remained an independent and significantly relevant risk factor for HIV infection when controlled for other known risk factors such as sexual behaviour and socioeconomic factors. To our knowledge, this is the first prospective study demonstrating a significantly increased risk of acquiring HIV for lymphatic filariasis-infected individuals. Immunological studies and interventional treatment studies that eliminate the adult worms and not only the microfilariae are needed to follow up on the results presented. European Union as part of EuropAid; German Federal Ministry of Education and Research; German Center for Infection Research.

25. Keetile, M., et al. **Factors associated with acceptability of child circumcision in Botswana -- a cross sectional survey.** *BMC Public Health* 2016;16(1):1053. Online at: <https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-016-3722-5>

**BACKGROUND:** Safe male child circumcision has been recently adopted as a potential strategy to prevent HIV/AIDS transmission in later life in Botswana.

**METHODS:** Data used was derived from a cross-sectional survey, the Botswana AIDS Impact Survey (BAIS) IV, conducted in 2013. A total sample of 7984 respondents in ages 15-64 years who had successfully completed the individual questionnaire during the survey were selected and included for analysis. Both descriptive and multivariable analyses were used to explore factors associated with acceptability of child circumcision. Data was analysed using SPSS version 22 program.

**RESULTS:** Results indicate that about 84 % of participants said they would circumcise their male children aged 18 years and below, while 93 % were aware of the safe male circumcision program. Bivariate analyses results show that acceptability of child circumcision was significantly associated with sex, age, education, religion, residence, HIV status of the parent, fathers circumcision status, father's intention to circumcise and parent's knowledge about the safe male circumcision program. Multivariable analyses results indicate positive association between respondent's HIV positive status (OR, 3.5), Men's circumcision status (OR, 3.7), men's intention to circumcise (OR, 9.3) and acceptability of child circumcision.

**CONCLUSION:** Results of this study indicate some relatively high acceptability levels for child circumcision. Some individual behavioural factors influencing acceptability of child circumcision were also identified. This study provides a proper understanding of factors associated with acceptability of child circumcision which will ultimately enhance the successful roll-out of the school going children circumcision program in Botswana.

26. Jenness, S.M., et al. **Effectiveness of combination packages for HIV-1 prevention in sub-Saharan Africa depends on partnership network structure: a mathematical modelling study.** *Sex Transm Infect* 2016;92(8):619-624.

**OBJECTIVES:** Combination packages for HIV prevention can leverage the effectiveness of biomedical and behavioural elements to lower disease incidence with realistic targets for individual and population risk reduction. We investigated how sexual network structures can maximise the effectiveness of a package targeting sexually active adults in sub-Saharan Africa (SSA) with intervention components for medical male circumcision (MMC) and sexual partnership concurrency (having >1 ongoing partner).

**METHODS:** Network-based mathematical models of HIV type 1 (HIV-1) transmission dynamics among heterosexual couples were used to explore how changes to MMC alone and in combination with changes to concurrency impacted endemic HIV-1 prevalence and incidence. Starting from a base model parameterised from empirical data from West Africa, we simulated the prevalence of circumcision from 10% to 90% and concurrency was modelled at four discrete levels corresponding to values observed across SSA.

**RESULTS:** MMC and concurrency could contribute to the empirical variation in HIV-1 disease prevalence across SSA. Small reductions in concurrency resulted in large declines in HIV-1 prevalence. Scaling up circumcision in low-concurrency settings yields a greater relative benefit, but the absolute number of infections averted depends on both the circumcision coverage and baseline incidence. Epidemic extinction with this package will require substantial scale-up of MMC in low-concurrency settings.

**CONCLUSIONS:** Dynamic sexual network structure should be considered in the design and targeting of MMC within combination HIV-1 prevention packages. Realistic levels of coverage for these packages within southern Africa could lead to a reduction of incidence to the low levels observed in western Africa, and possibly, epidemic extinction.

27. Wang, Z., et al. **Prevalence and associated factors of behavioral intention for risk compensation following voluntary medical male circumcision among male sexually transmitted diseases patients in China.** *AIDS Care* 2016;28(10):1332-7.

Risk compensation was an important concern of voluntary medical male circumcision (VMMC) promotion campaigns. No study investigated risk compensation following VMMC among male sexually transmitted diseases patients (MSTDP). A cross-sectional survey interviewed 308 uncircumcised MSTDP in Shenzhen, China. 26.9% of them intended to perform at least one of

the five types of risk compensation behaviors following VMMC. In the summary stepwise model, provision of incorrect response to HIV/sexually transmitted diseases knowledge items (multivariate odds ratios (ORM) = 2.30), genital herpes infection (ORM = 3.19), Risk Reduction Score for Unprotected Sex, and Negative Condom Attitudes Scale (ORM = 1.13) were significantly associated with behavioral intention to perform at least one type of risk compensation behavior following VMMC. The results provided a framework for developing related interventions. Prevention of risk compensation should be an essential component of VMMC promotion for all MSTDP, irrespective of their intention for VMMC.