MALE CIRCUMCISION FOR HIV PREVENTION

MODELS TO INFORM FAST TRACKING VOLUNTARY MEDICAL MALE CIRCUMCISION IN HIV COMBINATION PREVENTION

23-24 MARCH 2016





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ACRONYMS

ART antiretroviral treatment

ASM Age Structured Mathematical (model)

DMPPT Decision-Makers' Program Planning Tool

EIMC early infant male circumcision

HIA HIV infection averted

MC male circumcision

MTCT mother-to-child transmission

PEPFAR President's Emergency Plan for AIDS Relief

PrEP pre-exposure prophylaxis

SNU subnational unit

STI sexually transmitted infection

VMMC voluntary medical male circumcision

WHO World Health Organization

UNAIDS Joint United Nations Programme on HIV/AIDS

EXECUTIVE SUMMARY

Since the WHO/UNAIDS recommendation in 2007 that medical male circumcision be considered an additional method of HIV prevention and should be rapidly scaled up in countries with low prevalence of circumcision and high prevalence of HIV, there has been considerable investment in implementing voluntary medical male circumcision (VMMC) programmes for HIV prevention in eastern and southern Africa. By end 2015, 11.7 million adolescent and adult males had undergone circumcision through these programmes. Initial projections of cost and impact of VMMC interventions were developed before the programmes were implemented at scale and based on best assumptions about the course of the HIV epidemic valid at the time of development (2007–2010). These projections need to be revised as circumcision scale-up has not been uniform between and within countries, with greater uptake among adolescent and younger men than men over age 30 years. Similarly, the future impact on HIV incidence and prevalence in focus countries must be projected according to current HIV epidemic estimates and expected declines in HIV incidence resulting from scaling up antiretroviral treatment (ART) to reach the 90–90–90 by 2020 and 95–95–95 by 2030 HIV testing and treatment targets.

In preparation for a new phase of VMMC interventions over the period through 2021, WHO and UNAIDS convened a small consultation of modellers and policy-makers to review and discuss different models and projections, and develop key messages to inform strategic directions over the next five years. The key conclusions and recommendations from the meeting are listed below.

- HIV incidence reduction targets and impact:
- The 9.1 million VMMCs conducted in the period 2008– 2014 will avert approximately one quarter of a million HIV infections by 2025.
- The VMMC programmes in priority countries in eastern and southern Africa are necessary to reach the 2020 and 2030 Fast Track prevention targets (under 500 000 and 200 000 annual new HIV infections by 2020 and 2030, respectively). The HIV testing and ART scale-up targets (90–90–90 by 2020 and 95–95–95 by 2030) are not sufficient by themselves to reach these overall targets.
- VMMC programmes are cost-saving in almost all priority VMMC countries when HIV treatment costs averted are considered.

- The impact of expanding circumcision to at least 90% of men will be even greater if the 90–90–90 targets for treatment expansion are not reached.
- While circumcision reduces a man's individual lifetime HIV risk, the indirect effect of preventing further HIV transmissions to women, their babies (vertical transmission) and from women to other men has an even greater impact on the population incidence, particularly for circumcisions performed at younger ages (under age 25 years).
- Prioritizing by age, risk group and geography:
- The greatest impact on HIV incidence in the next five years will be obtained in most countries by expanding circumcision coverage in the 20–24- and 25–29-year age strata, which correspond to the ages of highest HIV risk.
- Focusing on men at high HIV risk, as determined for example by having multiple sexual partners, will result in greatest impact and efficiency.
- The results of models that considered prioritizing by geography were mixed. There was a strong rationale for prioritizing by geography in a few countries – notably Kenya, Malawi and Tanzania – but most countries lacked sufficiently robust data to prioritize provinces or districts according to impact and cost-effectiveness of circumcision. In countries with clear geographic differences, particular regions or districts and major urban areas should be saturated with VMMC services before moving to other areas.

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- Coverage or saturation targets are advised to be set by age strata (not uniformly for the entire 15–49-year age group) and established where possible at subnational levels. Progress towards coverage targets should also be monitored by age strata at the subnational level.
- Circumcision services should be provided to younger adolescents aged 10–14 years as the eventual impact of circumcision in this age stratum will be large. Experience with implementing VMMC programmes has shown that acceptability of circumcision varies by age and personal circumstances, and generating demand among older men is both difficult and costly.
- Sustaining high male circumcision coverage for long-term benefits:
- Ending AIDS as a public health threat by 2030 will reduce new HIV infections to near zero in most communities, but will not extinguish the epidemic entirely. Continued control strategies will be necessary to ensure that the HIV epidemic remains at low levels.
- At the height of the HIV epidemic, generalized and hyperendemic epidemics occurred only in countries and communities where circumcision prevalence was low. Maintaining a high prevalence of circumcision among sexually active men is a simple and affordable strategy to prevent any future resurgence of the HIV epidemic that might occur if treatment programmes cannot be sustained or drug-resistant HIV strains emerge. The benefits of such resilience will persist for many generations.
- Sustaining high circumcision coverage through adolescent and early infant male circumcision:
- As VMMC programmes reach higher coverage among men aged 15–29 years, coverage will need to be sustained by offering circumcision to annual cohorts of adolescent boys.
- Countries need to develop efficient and sustainable adolescent VMMC services that provide circumcision to boys who were too young to have been circumcised in the catch-up phase.
- Even in countries considering or preparing for the introduction of early infant male circumcision (EIMC) into programmes as their primary long-term circumcision strategy, an adolescent circumcision programme will be required until EIMC is sufficiently comprehensive that over 90% of infants are circumcised and boys circumcised as infants reach adolescence.

- There will be almost no impact of EIMC on the HIV epidemic until boys become sexually active and reach the age of highest HIV incidence 20–25 years later.
- Programme and research considerations:
- Rapid expansion of VMMC among males aged 1 5–29 years is necessary to achieve the 2020 HIV prevention target.
- Services should be provided to men aged 30 years and over who request circumcision, although generating demand in this age group is likely to continue to be difficult and costly.
- Efforts should be made to identify and circumcise men at high risk of heterosexual HIV infection irrespective of age, as these men have the greatest absolute reduction in risk following circumcision. Effective mechanisms must be established to refer high-risk, HIV-negative men identified through HIV testing services and programmes to circumcision services.
- The relative costs and efficiency in reaching VMMC coverage targets through different service delivery models (for example, outreach, mobile or fixed site) should be assessed and those models best suited to the local context prioritized.
- VMMC programmes are a unique opportunity and mechanism to link adolescent boys and young men to information and services related to sexual and reproductive health, sexuality education, preventing alcohol and drug misuse, and addressing gender norms that contribute to intimate partner violence and violence against women. More work is needed to improve training and information materials to deliver education and counselling in an age-appropriate and culturally sensitive manner.
- Funding is critically needed for the next few years to complete the catch-up phase in those countries where 80% coverage of the age group 15–49 years has not yet been achieved and to increase this to 90% coverage among those aged 10–29 years while countries transition to services that sustain high circumcision coverage for annual cohorts of adolescent boys.

BACKGROUND AND CONTEXT

Since the WHO/UNAIDS recommendation in 2007 that male circumcision be considered an additional method of HIV prevention and should be rapidly scaled up in countries with low prevalence of circumcision and high prevalence of HIV, there has been considerable investment in implementing VMMC programmes for HIV prevention in eastern and southern Africa.

By end 2015, 11.7 million adolescent and adult males had undergone circumcision through the newly created circumcision programmes.1 A modelling study conducted in 2011 estimated that 20.3 million circumcisions were required to reach 80% circumcision coverage of the age group 15–49 years by the end of 2015 in 14 priority countries in eastern and southern Africa. The estimated total cost to perform this number of circumcisions between 2011 and 2015 and maintain 80% coverage through 2025 was US\$ 2.02 billion. This was projected to avert an estimated 3.36 million new HIV infections and result in a net saving of US\$ 16.5 billion due to HIV treatment and care costs averted.2 Many of the assumptions on which this model was based have changed since 2011, most notably the slower than anticipated progress in scaling up circumcision, highly variable coverage between countries, heterogeneous proportions of men circumcised in different age groups, lower overall HIV incidence rates and lower annual costs for ART.

Uncertainties in projecting the evolution of HIV incidence are compounded by the concerted effort by the global health community to end the AIDS epidemic as a global health threat by 2030, with ambitious targets to accelerate expansion of HIV testing and treatment coverage by 2020 and 2030. The UNAIDS Fast Track strategy aims for 90% of people to know their HIV status, 90% of those infected to be on ART, and 90% of those under treatment to be virally suppressed (90–90–90) by 2020, with coverage of each element of the treatment cascade increasing to 95% by 2030 (95–95–95). Corresponding prevention targets are to reduce the global number of annual new HIV infections to fewer than 500 000 by 2020 and fewer than 200 000 by 2030.3 Additional uncertainty about the future course of the HIV epidemic follows from the recommendation by WHO in November 2015 that oral pre-exposure prophylaxis (PrEP) be offered to all men and women at substantial risk of HIV infection.4 There are also uncertainties whether treatment scale-up will have the anticipated impact on new HIV infections as a result, for example, of lower than anticipated adherence or emergence of drug resistance to first and second line treatment regimens. Similarly for PrEP, the practicality, acceptability and sustainability of PrEP programmes beyond pilot and demonstration projects have yet to be established.

In developing the strategic directions on VMMC for the period through 2021, a reassessment was necessary of experiences to date with scaling up VMMC programmes — successes, challenges and impact. Similarly, there was a need to project the future impact of VMMC programmes on HIV incidence and prevalence in focus countries according to different strategies for increasing circumcision prevalence in key age groups and sustaining high circumcision prevalence into the future.

In March 2016, WHO and UNAIDS convened a meeting of modelling experts and policy-makers to: review recent modelling work; identify the implications of different models, including common themes and messages from findings; recommend approaches for future strategic directions; and note key research and evaluation needs. Specifically, the objectives of the meeting were to:

- Review progress in the expansion of VMMC programmes through 2015, assess the impact of circumcisions performed to date and estimate future impact in the context of new HIV incidence data and projected expansions of treatment and other prevention programmes.
- 2. Share technical details of recently completed and ongoing modelling studies, including objectives, key questions and assumptions, parameters and their implications for interpreting model results and projections.
- 3. Discuss model results and key implications for global stakeholders on target-setting and prioritization by age, geography and/or risk group at country level.
- Identify key communication messages on progress and impact, uncertainties and strategic directions on VMMC through 2021.
- 5.Identify whether VMMC has a continued role in HIV prevention in focus countries in eastern and southern Africa given the projected scale-up of ART and oral PrEP.
- 6. Agree on evaluation priorities such as the impact of VMMC in the context of HIV combination prevention and Fast Track goals, identify data needs and approaches for this evaluation.

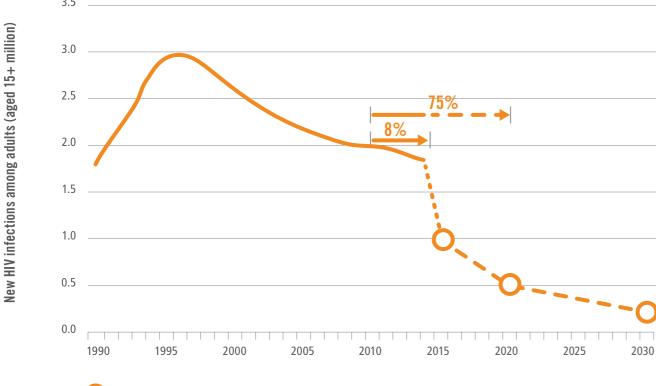
The meeting agenda (see Annex A) covered a review of global HIV treatment and prevention targets, progress with scaling up VMMC programmes, different models to estimate impact and costs of VMMC programmes, the impact of targeting by age, geography and/or risk profile, EIMC and other strategies to sustain high circumcision prevalence, and key advocacy and communication messages arising from the modelling review. The meeting was attended by representatives from different teams that had developed models of VMMC impact and costs, international organizations and consultants (see full list of participants in Annex B).

HIV PREVENTION IN 2016, PROJECTIONS AND BROADER CONTEXT

In contrast to the scale-up of HIV treatment, progress in reducing HIV incidence had been disappointing with an estimated 8% reduction in HIV incidence over the period 2010–2014 among adults aged 15 years and over (see Figure 1). This reduction was considerably short of the 2015 target (50% reduction from 2010 incidence) or the trajectory necessary to reach the UNAIDS Fast Track targets of fewer than 500 000 new HIV infections annually by 2020 (75% reduction) and fewer than 200 000 by 2030 (90% reduction). There was hope that rapid expansion of ART,

regular HIV testing, promptly starting all newly diagnosed HIV-positive persons on treatment, and use of oral PrEP among HIV-negative people at substantial risk of HIV infection would have a large impact on HIV incidence. In this context, it was necessary to assess the role and impact of VMMC programmes in the 14 focus countries in eastern and southern Africa to determine whether they were still relevant and necessary.

Figure 1 Estimated new annual HIV infections (UNAIDS, 2015)⁵

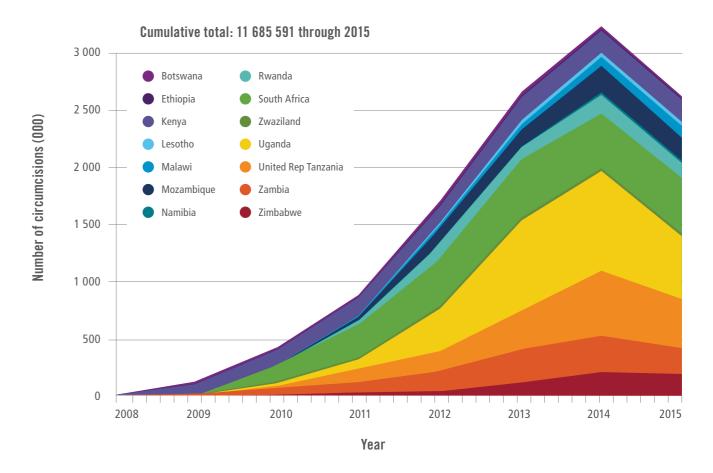


2015, 2020 and 2030 targets

VMMC programmes had been launched following strong evidence of efficacy and recommendations by WHO and UNAIDS in 2007 that countries with hyperendemic and generalized epidemics should scale up circumcision. Funding for VMMC programmes has been primarily from external sources -the Government of the United States of America President's Emergency Plan for AIDS Relief (PEPFAR), the Bill and Melinda Gates Foundation, and more recently the Global Fund to Fight AIDS, Tuberculosis and Malaria. Countries had contributed variable amounts of domestic resources to support VMMC expansion, mainly through deployment of healthcare workers to support the programmes. There had been rapid expansion in the 14 priority countries from 2009 (see Figure 2), with 2.66 million circumcisions performed in 2013 and 3.24 million in 2014; however, the number of new circumcisions in 2015 was only 2.62 million.1 While there remained substantial numbers of uncircumcised men in the age range 15-49 years, some countries had achieved at least

80% circumcision prevalence among adults and others were reaching this level in specific age groups. Attention was beginning to turn in some countries towards VMMC programmes that were less intensive than the catch-up or emergency phase to adopt a more sustainable model of offering circumcision to smaller annual cohorts of adolescent boys or young men who entered the eligible age range for circumcision. This has provided an opportunity to link VMMC with other educational and preventive services, such as male sexual and reproductive health, supporting women's sexual and reproductive health and rights, the education sector, youth groups and traditional leaders. To date little hard evidence of the benefits and impact of linking VMMC with other services exists, or of the wider impact of VMMC on health and development issues beyond the primary effect of reducing HIV incidence and prevalence in communities where VMMC programmes have been implemented.

Figure 2 VMMC programme expansion in 14 priority countries: number of annual circumcisions by country 2008–2015 (adapted from WHO Progress Brief)¹



MODELS OF VMMC IMPACT AND COSTS

Early models

Several mathematical models of the impact of scaling up VMMC programmes were developed and published in the period 2006–2008, soon after the results from three randomized controlled trials of circumcision and HIV prevention were completed.

These models, all set in the context of HIV epidemics in eastern or southern Africa with HIV incidence in the range 1.2–4.5 infections per 100 person-years, were reviewed by a small expert group convened by UNAIDS, WHO and the South African Centre for Epidemiological Modelling and Analysis.⁶ The models found that there were large benefits in providing male circumcision among heterosexual men in low male circumcision, high HIV prevalence settings with one HIV infection being averted for every five to 15 male circumcisions performed, and costs to avert one HIV infection ranging from US\$ 150 to US\$ 900 over a 10-year time period. In addition, the modelling projected little impact of potential behavioural risk compensation following circumcision on population-level HIV incidence and a substantial indirect benefit for women from a reduced HIV prevalence in circumcised male partners.

This review was used as the basis for developing a compartmental deterministic model in Microsoft Excel to estimate the epidemiologic impact (HIV infections averted), cost and net savings associated with different scenarios for scaling up VMMC, referred to as the Decision-Makers' Program Planning Tool (DMPPT).2 The model was populated with country-specific demographic and epidemiological data and used to explore different country-specific scale-up strategies. Under a common scale-up model of expanding circumcision prevalence to 80% among men aged 15-49 years within five years (2011–2015) and then maintaining this coverage rate for a further 10 years through 2025 in 13 of the priority countries or provinces, the model estimated that a total of 28.8 million circumcisions would need to be performed and these would avert 3.36 million HIV infections through 2025, approximately 8.6 circumcisions per HIV infection averted (HIA). Such a programme was estimated to cost US\$ 2 billion over the period 2011–2025 with an average cost of US\$ 809 per HIA. The discounted net savings due to ART and care costs averted were projected to be US\$ 16.5 billion over the same period. Results varied from country to country (for example, cost per HIA ranged from

US\$ 369 in Zimbabwe to US\$ 4096 in Rwanda) and were strongly determined by the country-specific HIV incidence. Detailed country-specific analyses were used to develop national circumcision scale-up plans, allocate financial resources and launch the VMMC programmes.

Limitations of the DMPPT model were that the population was disaggregated into only four age/sex groups (females aged 15-24 and 25-49 years, males aged 15-24 and 25–49 years), circumcision prevalence was assumed to increase linearly and uniformly throughout the two male age groups towards the specified target, and the unit cost of circumcision was the same for all men. Experience with implementing VMMC programmes showed that the uptake of circumcision was much greater in younger than older men, motivating older men to attend the VMMC service was more complex and costly, and a large proportion of circumcisions were performed in adolescent boys aged 10-14 years when VMMC programme resources were not being fully utilized for the priority age range 15-49 years. In addition, the first generation models had projected a stable HIV incidence or a gradual decline over a 15-year time period based on recent historical trends in the absence of a circumcision intervention. The models did not account for the potential impact on HIV incidence of expanding ART to the UNAIDS 90-90-90 target for 2020 and 95-95-95 target for 2030, or for expansion of other HIV prevention interventions such as oral PrEP.

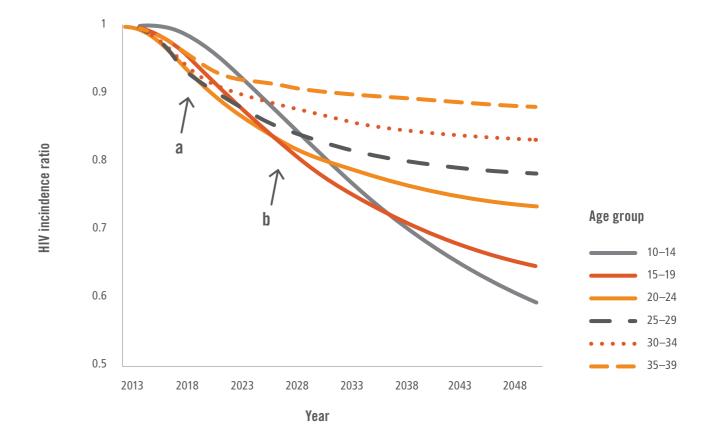
More recent models addressed these limitations by allowing for more age strata and greater flexibility in unit costs and circumcision coverage by age. Some, but not all, have incorporated sharp reductions in projected HIV incidence.

DMPPT model version 2

Katharine Kripke, Avenir Health, described the DMPPT 2 model that was built to address some of the earlier shortcomings. As before, estimates of country or provincial population structure (UN Population Division, World Population Prospects 2012), non-AIDS mortality and HIV incidence (from Spectrum/AIM or Spectrum/Goals models) by age and sex were imported from external sources and used to estimate HIV incidence among circumcised and uncircumcised men. The model was set up for each country based on the official national HIV prevalence and incidence estimates and projected the effect of changing circumcision prevalence in different age groups compared with the base scenario of maintaining circumcision prevalence at preprogramme levels. The main analyses assessed the impact of scaling up circumcision to 80% over five years

in specific age strata, maintaining that prevalence into the future and projecting future HIV infections in the whole population (men and women). The relative contributions of saturating different age strata were compared with a scenario of no scale-up of circumcision over baseline (that is, maintaining circumcision prevalence at preprogramme levels). The approach is illustrated in Figure 3 for South Africa – in this example, the greatest relative short-term impact (within five years) (see point a in Figure 3) is achieved by circumcising men in the 20–24-, 25–29- and 30–34-year age groups, while the greatest relative long-term impact (within 15 years) (see point b in Figure 3) is achieved by circumcising the 15–19- and 20–24-year age groups. The greatest impact after 25 years is achieved by circumcising the youngest (10–14 year) age group.

Figure 3 Reduction in HIV incidence through provision of VMMC to males, by age group, in the years 2014–2050 (example from DMPPT 2 model applied to South Africa)⁷



While the DMPPT 2 model could compare the relative impact of different age-specific scale-up strategies, it was considered less reliable for projecting the absolute number of HIAs due to uncertainties in HIV incidence projections (a limitation common to all VMMC models). The DMPPT 2 model could not simulate variations in sexual mixing patterns by age potentially correlated with HIV prevalence or infectiousness, nor could it reflect rapid or non-uniform scale-up of ART or new PrEP prevention interventions.

In common with most mathematical models, further limitations of the DMPPT 2 model are that projections, particularly long-term projections, are highly sensitive to HIV incidence estimates and lack of data limits the ability to carry out useful subnational estimates. Moreover, the model does not reflect important programmatic considerations and experiences, such as the challenges of demand creation, the availability of resources, and additional benefits of VMMC such as linkages to educational programmes, other HIV prevention services and treatment programmes.

The DMPPT 2 model was used to explore the relative impact of age prioritization in Kenya, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Uganda and the United Republic of Tanzania; subnational geographic prioritization in Kenya, Malawi, Mozambique, South Africa, Uganda and the United Republic of Tanzania; and district-level targets in Kenya, Lesotho, Malawi, Mozambique, Swaziland, Uganda, the United Republic of Tanzania and Zimbabwe. The model was further used to assess the impact of circumcisions conducted to end 2015 in all 14 priority countries. Key output metrics included number of HIAs, reduction in HIV incidence, circumcisions per HIA, total programme cost, cost per HIA, treatment costs averted, and net savings.

Goals model

John Stover, Avenir Health, outlined the structure of the Goals model, which was designed to estimate the cost and impact of general HIV interventions (treatment and prevention) and included a considerably more complex structure of risk groups, sexual mixing, HIV disease progression and infectiousness than the DMPPT models. It allowed for the impact of several different HIV prevention interventions (for example, oral PrEP, topical PrEP, male circumcision, condom use, HIV testing and counselling) and treatment interventions (such as, ART use according to different start criteria) to be estimated separately or in combination; for example, the impact of scaling up male circumcision in the presence or absence of treatment scaleup, and the impact of treatment scale-up in the presence or absence of male circumcision. As with other models, country or regional demographics were input from external sources and baseline HIV incidence estimated from historical national or regional data.

Incremental Analysis model

Nicole Fraser, World Bank, summarized the Incremental Analysis model developed to analyse the effect of circumcising one individual at a specific age and quantify outcomes in terms of current investments. The model was based on the Actuarial Society of South Africa's 2008 AIDS and Demographic model, which was a compartmental HIV disease progression and transmission model embedded in a demographic model. Compartments included sex, HIV risk group according to sexual activity (not sexually active, low level of risk, high risk [for example, a person with a sexually transmitted infection (STI)], intense risk [for example, a sex worker]) and age in one-year strata. For each risk group, individual sexual activity was characterized by assumptions on number of new partners per year, number of contacts per partner, and the distribution of partners by risk group. The model focused on heterosexual intercourse only and assumed that those below age 15 years or over 60 years were not at risk. Individuals aged 16-24 years could move in or out of higher sexual risk groups, but the risk group remained fixed for those aged 25 years or more. The model was adapted to include the impact of circumcision on HIV transmission dynamics and reflected existing circumcision prevalence. Instead of considering the impact of scaling up circumcision throughout the population, the model estimated the impact of a single circumcision performed at a specified age in 2013 and projected forward through 2058 (45 years), considering the benefit of lower HIV risk to the individual as well as benefits due to secondary or higher order transmissions averted. In addition to output metrics computed in other models, the Incremental Analysis approach also computed metrics such as amortization period and financial rate of return, which are more familiar to financial analysts and policy-makers. As with other models, there was no adaptation to evolving HIV incidence other than through the impact of the VMMC programme. The model was intended to compare the impact of circumcision at different ages and was, thus, not able to assess the impact of different HIV prevention interventions or combinations of interventions.

Age Structured Mathematical model

Maaya Sundaram, Bill and Melinda Gates Foundation, described the methodology of the Age Structured Mathematical (ASM) model developed in collaboration with Laith Abu-Raddad and Susan Awad, Weill Cornell Medical College Qatar, to compare the short- and longterm impact of preferentially scaling up circumcision in different age strata and/or subnational geographical areas, examining also the impact of EIMC. The primary measure used to compare different scenarios was the number of circumcisions per HIA. The ASM model is a population-level, deterministic, compartmental model of heterosexual HIV transmission consisting of coupled nonlinear differential equations that stratify the population into compartments according to sex, circumcision status, age (five-year strata: 0-4 years, 5-9 years, ... 95–99 years), sexual risk (six levels from lowest [general population] to highest [female sex workers and their male clients]), HIV status, and stage of infection (three levels: acute, chronic and advanced). The model was populated with demographic data and projections from the UN Population Division, and country-specific historical HIV prevalence data for 1990-2011 from UNAIDS. Behavioural and circumcision prevalence data from past demographic and health surveys were used to estimate HIV incidence. The model included the option of varying unit circumcision costs by age to reflect additional costs incurred to identify and motivate older men to volunteer for circumcision. The model included the impact of secondary and higher order transmissions prevented by circumcision, but did not provide the option to include a marked future change in HIV incidence. As with other models discussed, the model was primarily directed at comparing the relative costs, impact and efficiency of different scale-up scenarios, and was not designed to estimate absolute costs or impact with any great accuracy.

Subnational Units model

Stephanie Davis, Centers for Disease Control and Prevention, Atlanta, presented the Subnational Units (SNU) model designed to explore the impact of VMMC scale-up in the context of non-uniform ART expansion in Tanzania and Zimbabwe. This model was motivated by PEPFAR's plans to prioritize high HIV burden SNUs and/or populations in order to reach the 90–90–90 testing, treatment and viral suppression targets and 80% circumcision coverage. It was not clear if the priority SNUs for rapid ART scale-up (those with highest HIV prevalence) were also optimal for prioritizing VMMC scale-up (those with highest HIV incidence in men), nor whether VMMC impact might be lower in SNUs that had high treatment coverage. The model provided a framework for exploring the marginal impact of VMMC in situations where there was slower than planned ART scale-up and, conversely, the marginal impact of ART scale-up where VMMC scale-up was slower than planned.

Discussion

All models presented adopted a similar approach to estimating the impact of VMMC programmes on the HIV epidemic. The DMPPT 2, Incremental Analysis and ASM models projected either that HIV incidence remained at current levels notwithstanding the impact of circumcision, or assumed that recent historical trends continued. The Goals and SNU models made explicit assumptions about ART scale-up and were designed to explore the separate and joint impact of scaling up several HIV prevention interventions simultaneously.

All models necessarily involved simplifications of the complex dynamics and structural drivers of the HIV epidemic, but nevertheless were able to provide insights into how best to allocate resources and implement HIV policies that were simultaneously feasible and cost-effective, without necessarily being optimal. While further refinements to the models were easy to propose, many model enhancements were limited by the availability of sufficiently detailed data, such as HIV incidence by sexual risk groups, the sizes of different risk groups or the level of partner mixing.

RESULTS FROM MODEL FITTING

There was not time during the meeting to explore the full results of each analysis, but sufficient details were presented to extract key points and synthesize their implications. Several analyses presented were unpublished works in progress.

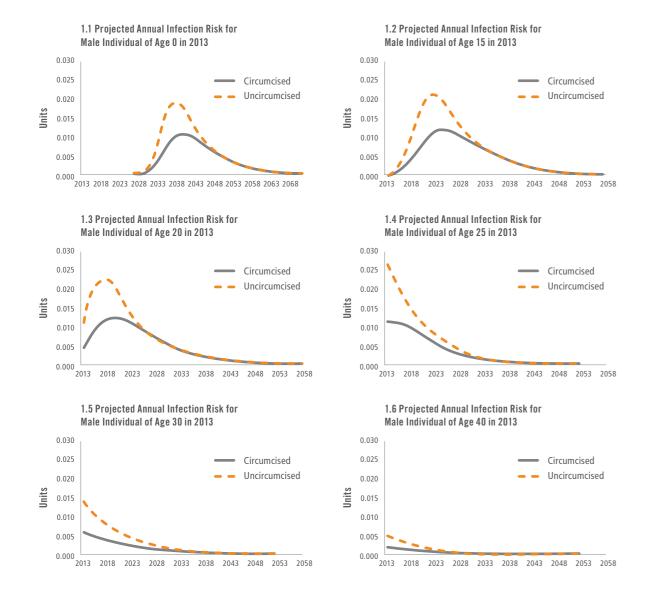
Different prioritization strategies

Age group

Nicole Fraser presented the Incremental Analysis model applied to South Africa, which considered the impact and cost of circumcision performed at different ages.⁸ The model projected annual HIV incidence over the period 2013–2058 (45 years) for an uncircumcised and circumcised male aged 0, 15, 20, ..., 40 years in 2013 (see Figure 4). The area under the curves corresponds to the total lifetime HIV risk for a circumcised and uncircumcised man and

the difference between the two areas corresponds to the overall reduction in risk. The greatest reduction in annual HIV risk occurred for circumcisions performed about age 25 years, which corresponded to the age of highest HIV incidence. Circumcisions performed at ages 0 or 15 years resulted in the greatest reduction in lifetime risk, though the effect was delayed by 15 years for circumcisions performed in infants. Circumcisions performed at older ages showed an immediate reduction in risk, though the difference in lifetime risk was less.

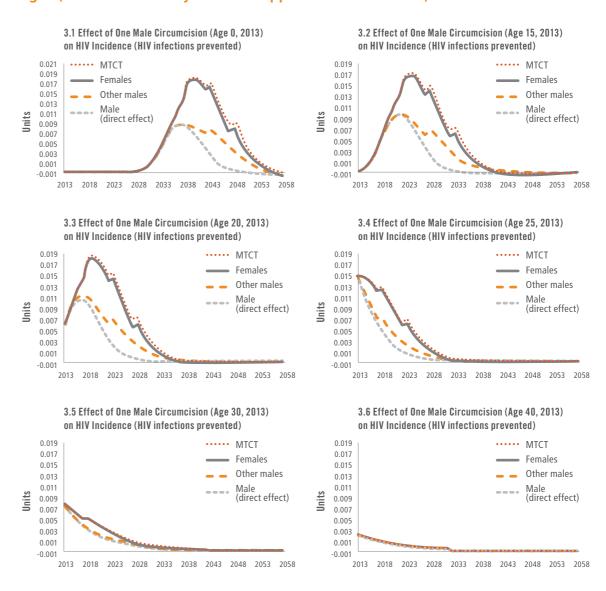
Figure 4 Projected annual risk of HIV infection for an uncircumcised and circumcised man according to age in 2013 (Incremental Analysis model applied to South Africa)⁸



The reduction in annual HIV risk for a circumcised man (direct effect) is shown in Figure 5 for circumcisions performed at different ages, together with reductions in risk from secondary and higher order transmissions avoided. These include reductions in risk among female partners, mother-to-child transmission (MTCT) and further indirect effects on other men. As before, the greatest reduction in direct lifetime HIV risk is seen among young men, although the impact is delayed by 15 years for circumcision performed at age 0. The indirect effects of secondary and higher order transmissions avoided reached

their zenith several years after the peak in the direct effect on the circumcised man, but in younger men the cumulative impact of secondary and higher order transmissions avoided exceeded the cumulative direct impact. The indirect effects were proportionately less for circumcisions performed at older ages compared with those performed at younger ages.

Figure 5 Direct and indirect effects of one circumcision performed at different ages (Incremental Analysis model applied to South Africa)⁸



Other key issues that emerged from the Incremental Analysis model included:

- While the lowest cost per HIA was for circumcision performed at age 0 when no discount was applied, the longer time to realize impact means that cost per HIA was lower when a 5% discount rate was applied. At this discount rate, circumcision performed at age 20 years resulted in the highest net saving.
- Between four and five circumcisions were required to prevent one HIV infection for procedures performed at ages 0, 10, 15 and 20 years; however, the number rose steeply for older age groups, for example 12.6 circumcisions were required per HIA at age 30 years and 46.2 circumcisions at age 40 years. This was due to the falling HIV incidence in older men and the lack of time for the benefit of prevented secondary and higher order transmissions to be realized.
- Compared with circumcisions performed at other ages, those performed at 15, 20 or 25 years were near optimal with respect to the number of circumcisions required to prevent one HIV infection, the discounted cost per HIA, net saving, amortization period and financial rate of return.
- The financial savings due to circumcision accrued over very long time periods and could help contain the cost of the HIV response. The one-off cost per HIA of circumcision performed at younger ages was similar to the annual cost of antiretroviral medication for HIV treatment.
- Since people living with HIV infection have a near normal life expectancy while under treatment, the cost savings from circumcision can be many times higher than the costs of the circumcision procedure.

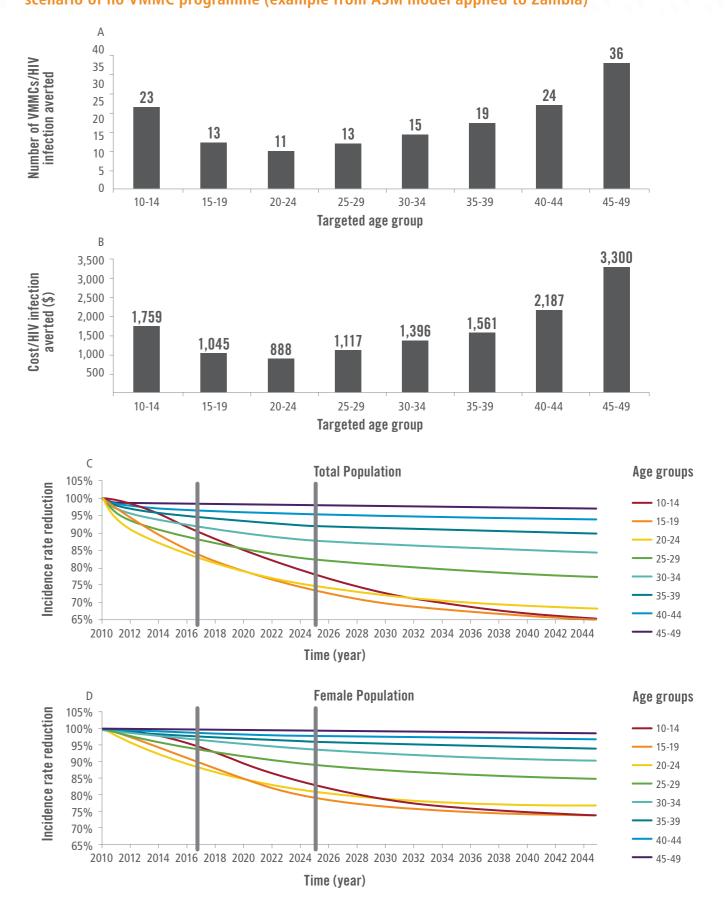
Katharine Kripke summarized the results of analysing the impact of scaling up circumcision in five-year age groups using the DMPPT 2 model in Malawi, South Africa, Swaziland, Uganda and the United Republic of Tanzania. For each country a scenario in which circumcision was scaled up from the preintervention prevalence to 80% over the period 2014–2018 in separate five-year age strata was run and the impact and costs projected forward over a 15-year period. Broadly similar results were obtained in each of the five countries, in particular:

 The lowest estimated numbers of circumcisions per HIA over 15 years were in the 20–24-, 25–29- and 30–34-year age strata, with minor differences between these three strata.

- The numbers of circumcisions per HIA in other age strata were considerably greater, particularly at the extremes of the age ranges (10–14 and 45–49 years). In the oldest age strata, the men were exposed to the risk of HIV infection for less time than younger men and there was less time for the benefit of secondary transmissions to accrue. By contrast in the younger age strata there was a delay before the adolescent boys became exposed to HIV and entered the period of highest HIV incidence.
- While the 10–14-year age stratum contributed little to the total number of HIAs over the 15-year time frame, a greater impact would be realized over the longer term. There had been high acceptability of circumcision and good uptake of the VMMC programme in this age group in all five countries. This contrasted with the low uptake and considerable costs expended to attract older men to the VMMC programmes.

A very similar conclusion was reached by use of the ASM model applied to the populations of Zambia¹³ and Zimbabwe¹⁴, which considered scale-up scenarios starting in 2010 to reach 80% coverage in specified five-year age groups by 2017 and then projected impact forward through 2025 (see Figure 6). In both countries, the most immediate impact was derived from circumcision in older age strata, but over the 15-year time frame considered circumcising younger men (under age 30 years) had greater absolute impact on the number of HIAs and resulted in fewer circumcisions per infection averted and lower costs per infection averted. Impact was estimated to increase further beyond 2025.

Figure 6 Impact of scaling up to 80% circumcision coverage in specific five-year age strata over seven years (2011–2017) and maintained through 2050 compared with baseline scenario of no VMMC programme (example from ASM model applied to Zambia)¹³



VMMC: Voluntary medical male circumcision

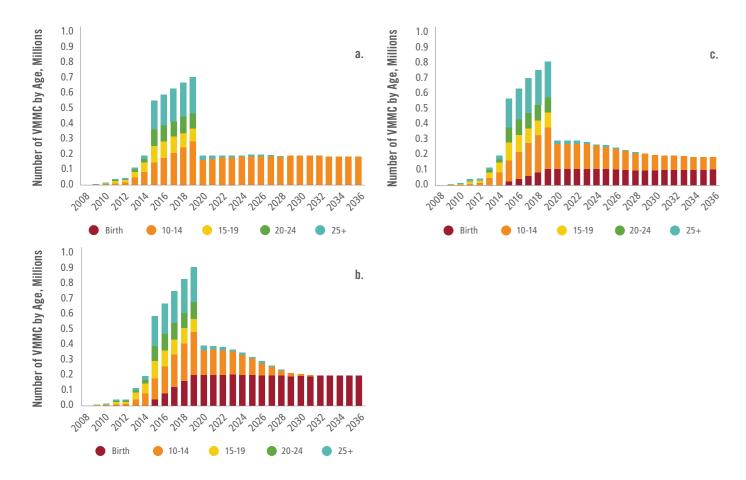
A) Number of VMMCs needed to avert one HIV infection (effectiveness) by 2025; B) Cost per HIV infection averted (cost effectiveness) by 2025; C) Proportion of incidence rate reduction in the total adult population throughout the years up to 2045; D) Proportion of incidence rate reduction in the female adult population throughout the years up to 2045.

Early infant male circumcision

The DMPPT 2 model was used to investigate the impact and cost of adding an EIMC component to the Zimbabwe VMMC programme, specifically considering the timing of introduction and pace of expansion. The annual number of circumcisions by age group required to reach 80% prevalence during the catch-up phase 2015–2020 in Zimbabwe in the absence of an EIMC programme is modelled in Figure 7a. In order to maintain 80% circumcision prevalence beyond 2020, approximately

180 000 circumcisions among adolescents (ages 10–14 years) are required annually as younger age cohorts become eligible for circumcision. If EIMC is scaled up to 80% over 2015–2020 (see Figure 7b) the adolescent programme needs to be maintained beyond the catch-up phase but is not required after 2032. However, a steady-state EIMC prevalence of 40% (see Figure 7c) requires the adolescent programme to be maintained indefinitely, although at a lower level than required without an EIMC programme.

Figure 7 Number of annual circumcisions required by age strata to achieve and maintain 80% circumcision prevalence in three scenarios (example from DMPPT 2 model applied to Zimbabwe)¹⁵



 $VMMC\ scaled\ up\ to\ 80\%\ coverage\ among\ age\ 10-34\ years:\ a.\ without\ EIMC;\ b.\ plus\ 80\%\ EIMC;\ c.\ plus\ 40\%\ EIMC.$

To compare overall impact and costs, the models were projected forward 35 years through 2051 with HIV incidence declining until 2020 based on recent historical trends and then held constant. As noted previously, the projected reduction in HIV incidence within 15 years was greatest for circumcisions performed in the 25–29- and 20-24-year age strata, and least for EIMC and the 10-14year age stratum. After 30 years the greatest reduction in HIV incidence was in the 10–14-year age stratum and least for EIMC and the 35-39-year age stratum. Adding EIMC to a VMMC programme focused on the 10-34-year stratum required an estimated additional 2 million circumcisions and would result in an extra 2000 HIAs (marginal gain 1000 circumcisions per HIA) over the period 2015–2051. The total cost of such a programme would be lower than a 10-34-year age stratum only programme over the period 2015–2051 if the unit cost of EIMC was at most 50% the unit cost of an adolescent or adult circumcision. It was concluded that the marginal gain in HIAs was small over the period 2015–2051 but a long-term programme to maintain high circumcision prevalence could be substantially less expensive if based on early infant rather than adolescent circumcision. The timing and speed of introducing the EIMC programme made little difference to its eventual impact or cost. Results from the model were very dependent on the assumed discount rate and very sensitive to assumptions regarding the future course of the HIV epidemic.

Geography and sexual risk groups

The country-specific models additionally considered whether there were large differences in impact, cost and efficiency when different provinces or regions of the country were considered separately.^{7,9,11–14} The variation in impact was largely driven by differences in overall HIV incidence in each region or province with about a 10-fold greater efficiency in Malawi in the highest incidence region (western Malawi, 18 circumcisions per HIA) than the lowest (central eastern Malawi, 207 circumcisions per HIA). Similarly, there was large heterogeneity in Tanzania¹² and Uganda¹¹ (five-fold and four-fold gains in efficiency between the highest and lowest incidence regions, respectively), but much less so in South Africa,⁷ Zambia¹³ or Zimbabwe¹⁴. In Malawi there was a three-fold difference in efficiency when considering urban or rural areas.9 However, in all countries, except Malawi, the uncertainty in the estimates was greater than the variation in estimates between subnational regions due to limitations in HIV incidence estimates at that level. In addition, scaling up VMMC was cost-saving across all subnational regions, so excluding certain regions based on relative cost-effectiveness was not well justified in these analyses.

The ASM models in Zambia and Zimbabwe included mechanisms to model the impact of different sexual mixing patterns and sexual risk groups. The model structures were informed by empirical data on the number of sexual partners, their risk group, and rates of partner exchange from sub-Saharan African countries. The impact of focusing the VMMC programme on individual or sets of sexual risk groups was estimated in a similar way to that for age, that is by modelling expansion to 80% circumcision coverage only in the relevant stratum. The models predicted that only one circumcision was required to prevent one HIV infection in the highest sexual risk groups in both Zambia and Zimbabwe compared with 80 and 60 circumcisions, respectively, in the lowest sexual risk groups. 13,14 While the feasibility of focusing VMMC programmes on selected sexual risk groups has not been explored, these models highlight the importance of identifying men at highest risk of HIV acquisition due to their sexual behaviour and encouraging them to undergo circumcision. The ASM models may have exaggerated the impact of sexual risk groups by assuming that men and women remain in the same sexual risk group throughout their sexually active lifespan, while a more realistic model would consider a gradual transition toward lower sexual risk as a man's marital status changes and he becomes older.

Circumcision of HIV-infected men

Susan Awad and colleagues considered the impact of relaxing the recommendation to encourage HIV testing prior to circumcision. 16 They argued that HIV testing might deter HIV-uninfected men at high risk of infection from presenting to circumcision services due to fear of learning their status; so removing the emphasis on HIV testing might result in more high-risk men being circumcised. But any increased VMMC coverage among high-risk negative men would be offset by circumcising some men already infected with HIV. This would be a waste of resources as there is no reduction in the risk of acquiring HIV infection in an already infected person; however, there would be a benefit if there was a demonstrated reduction in the risk of transmission from men to women resulting from circumcision. The evidence on this point is mixed – observational data show a reduction in this risk, although this was not confirmed in the only randomized trial that addressed this specific question. Using Zambia as an example and projecting forward 15 years, it was concluded that expanding VMMC programmes regardless of HIV status increased their effectiveness (in terms of circumcisions per HIA) by about 10% if there was a 20% increase in VMMC uptake among higher-risk males. In addition, if there was a 20% or 40% reduction in the risk of male-to-female transmission due to circumcision there would be an 18% or 35% increase in programme effectiveness, respectively. In these circumstances, VMMC programmes could reduce the HIV incidence rate in men by nearly as much as expected by some ART programmes and, additionally, women would benefit from the intervention almost as much as men.

Circumcision in the context of treatment scale-up

Impact of circumcisions performed to date

An updated analysis using the DMPPT 2 model was conducted to estimate the impact of circumcisions performed to end 2014 over the 14 priority countries.17 This model estimated impact and costs of circumcisions performed in five-year age strata based on programme data and compared with estimated impact and cost under the assumption that 80% circumcision prevalence had been achieved throughout the 15–49-year age range. Cost and impact were projected forward through 2025 under a model of no further circumcisions and, thus, estimated the impact of circumcisions performed to date. Future ART scale-up to 90–90–90 targets was modelled by modifying the base Spectrum/Goals files for each country to include a linear expansion from 2014 treatment levels to 81%

(90% tested x 90% treated) by 2020 and 90% (95% tested x 95% treated) by 2030 plus a progressive reduction in infectiousness of patients on ART to reflect the expected increase from 90% to 95% virally suppressed over the same period.

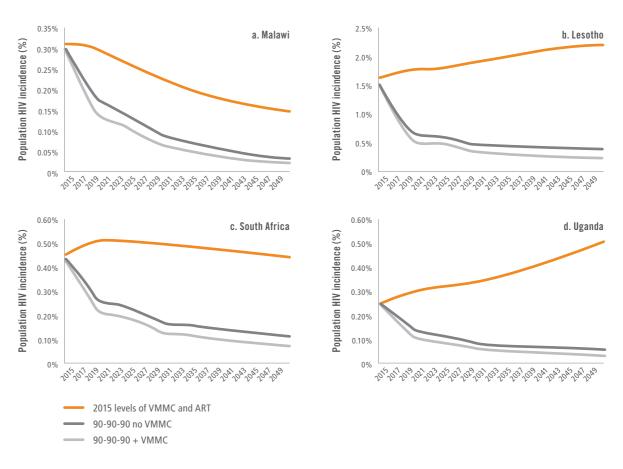
In all 14 priority countries, circumcision uptake had been proportionately higher in younger compared with older men. Only three countries (Ethiopia, Kenya and Tanzania) had performed more than the originally planned total number of circumcisions required to reach 80% coverage among the age group 15-49 years. The 9.1 million total circumcisions performed in the 14 countries represented about 40% of the previously projected 20.3 million needed to reach 80% coverage among males aged 15-49 years. The impact of circumcisions performed by end 2014 was less than previously modelled due to the smaller total number of circumcisions, proportionally more younger men circumcised, and a faster than previously projected reduction in HIV incidence. The circumcisions performed by end 2014 were projected to avert 240 000 new HIV infections by 2025 compared with 1.1 million by 2025 if coverage had reached 80% by 2015 and was maintained through 2025. The age stratum 10–19 years represented 66% of circumcisions performed by 2014 and was projected to contribute 52% of the total number of HIAs by 2025. The estimated median cost per HIA of US\$ 4400, calculated in the specific context of ART scale-up, compared favourably with the costs of other prevention interventions (treatment as prevention, prevention of MTCT of HIV) that had been estimated without taking account of the new UNAIDS treatment scale-up goals.

Limitations of this analysis were that the ages of VMMC clients were only available in broad age categories and uncertainties about the success and pace of ART scale-up to the 90–90–90 targets by 2020 and the 95–95–95 targets by 2030 were not modelled.

Goals/Spectrum specifically balancing male circumcision and other interventions

Katharine Kripke and colleagues had examined the impact of VMMC programmes in four countries (Lesotho, Malawi, South Africa and Uganda) in the context of expanding ART to the 90–90–90 treatment coverage goal by 2020, as well as several scenarios under which the goal was not reached. This model used HIV incidence projections from the Goals/Spectrum models. Across all four countries, scaling up VMMC was projected to reduce HIV incidence, adding to the reductions attributable to expanding treatment to the 90–90–90 targets (see Figure 8). While this required additional short-term costs, total annual costs were projected to be lower from 2020.

Figure 8 Projected annual HIV incidence in Lesotho, Malawi, South Africa and Uganda with and without ART and VMMC scale-up (Goals/Spectrum models)¹⁸

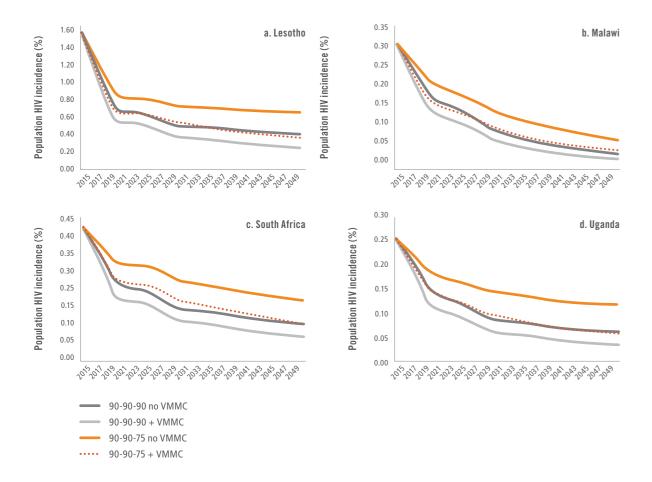


Projected total annual HIV incidence under models of: no VMMC or treatment expansion beyond 2015 levels; scaling up to 90–90–90 treatment target by 2020 with no further VMMC expansion; or scaling up treatment to 90–90–90 target and VMMC to 90% by 2020.

In a situation where the 90–90–90 treatment target was not met (for example, achieving only 75% viral suppression) (see Figure 9) the scaled-up VMMC programme would result in similar impact to that projected if the 90–90–90 treatment target was achieved and there was no further expansion of the VMMC programme. A similar result was shown if 90% viral suppression was achieved in women only and not men.

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Figure 9 Projected annual population HIV incidence in Lesotho, Malawi, South Africa and Uganda with optimal and suboptimal ART scale-up, with and without VMMC scale-up by 2020¹⁸



Projected total annual HIV incidence under models of ART expansion to 90-90-90 target or 90-90-75 by 2020 with and without VMMC expansion to 90% by 2020.

Kenya and Zimbabwe modelling consensus

John Stover presented a summary of a modelling workshop held in Kenya in March 2016 during which results from three models applied to the country's HIV epidemic were reviewed and discussed. The models were from Avenir Health, Imperial College London and the Institute for Disease Modeling. The consensus conclusions from the review of the consolidated results were that the Kenyan VMMC programme had already had impact and its benefits would grow significantly in the future. The programme was very efficient with as few as five to 15 circumcisions necessary to prevent one new HIV infection. There would be substantial savings in the future due to treatment costs averted, and VMMC was seen as an important component in ending AIDS as a public health threat by 2030. For example, in the Homa Bay region expanding ART to the 95-95-95 goals for 2030 was projected to reduce the annual number of new HIV infections to 2100 without the VMMC programme, but to 1100 if combined with the continued expansion and maintenance of VMMC.

A similar consensus meeting had been held in Zimbabwe in December 2015 involving the same three modelling groups as well as the team from Weill Cornell Medical College that had applied the ASM model to the country's HIV epidemic. In Zimbabwe, the circumcisions already performed were projected to avert as many as 75 000 new HIV infections by 2030, representing 10% of all new infections. Continued expansion of the VMMC programme would increase that number to 240 000–310 000 infections averted, or 30% of projected total new infections. While achieving the 95–95–95 ART goals by 2030 was projected to reduce the total national annual number of HIV infections from 40 000 in 2015 to 9000 by 2030, this would be further reduced to 4000 if the VMMC programme was expanded as projected.

SNU model

Stephanie Davis presented preliminary results of applying the SNU model in Tanzania and Zimbabwe. The work was still ongoing and required further analysis and discussion with the relevant country teams. Key points from the work already completed showed that the ultimate impact of VMMC would be substantially less than originally projected if rapid treatment scale-up in ART priority areas proceeded as planned, although VMMC would remain highly effective in many SNUs. Several SNUs where VMMC had the highest potential impact were not included in the priority ART scale-up areas and would, thus, be areas where support for continued VMMC expansion should be focused. In some areas where HIV incidence was high and the total population size was large consideration should be given to providing services through periodic circumcision campaigns in preference to maintaining routine services throughout the year as a mechanism to contain costs and deliver circumcision efficiently.

CONCLUSIONS AND RECOMMENDATIONS

On the basis of the review of the different models, their methodological strengths and limitations, and the consistency of the results the group developed a set of key recommendations to inform development of the new VMMC strategic directions through 2021 and updated implementation plans in priority countries in eastern and southern Africa.

Advocacy and communication

- VMMC programmes in priority countries in eastern and southern Africa are necessary in order to reach the 2020 and 2030 Fast Track prevention goals (under 500 000 and 200 000 new HIV infections annually by 2020 and 2030, respectively). The treatment scale-up targets (90–90–90 by 2020 and 95–95–95 by 2030) are not sufficient by themselves to reach these goals.
- Funding is critically needed for the next few years to complete the remainder of the catch-up phase before VMMC programmes transition to the sustained phase of offering circumcision to specific age cohorts each year. The annual cost of sustaining high circumcision coverage is considerably less than the annual costs of the catalytic catch-up phase of the VMMC programmes.
- VMMC programmes are cost-saving in almost all priority countries. The total cost of one circumcision is similar to the cost of one year of antiretroviral medication and about half the cost of delivering one year of HIV treatment. In 10 of the 14 priority countries the estimated cost per HIA is under US\$ 7000, with a median cost of US\$ 4400, within the context of scaling up to reach the 90–90–90 by 2020 and 95–95–95 by 2030 treatment targets.
- While circumcision reduces a man's individual lifetime HIV risk, the indirect effect of preventing further HIV transmissions to women, their babies (vertical transmission) and from women to other men has an even greater impact on the population incidence, particularly for circumcisions performed at younger ages (under age 25 years). The impact of secondary and higher order transmissions averted is less for circumcisions performed at older ages, although it remains substantial.
- The impact of expanding circumcision to at least 90% of sexually active men is substantially greater if the 90–90– 90 treatment expansion targets are not reached.

Importance of sustaining high circumcision coverage

- Ending AIDS as a public health threat by 2030 will reduce new HIV infections to near zero in most communities, but will not extinguish the epidemic entirely. The epidemic will continue to spread in key populations, in particular among sex workers and their clients, men who have sex with men, and injecting drug users. Future control strategies will need to ensure that the HIV epidemic remains confined to these high-risk groups and does not spread into the general population by people 'bridging' between different risk groups. Circumcision is a cost-effective and robust containment strategy.
- At the height of the HIV epidemic, generalized (HIV prevalence greater than 5% in the general population) and hyperendemic (over 15% HIV prevalence in the general population) epidemics only occurred in countries and communities where circumcision prevalence was low. Maintaining a high prevalence of circumcision among sexually active men is a simple and affordable strategy to prevent any future resurgence of the HIV epidemic that might occur if treatment programmes cannot be sustained or untreatable drug-resistant HIV strains emerge. The benefits of such resilience will persist for many generations.

Sustaining high circumcision coverage through adolescent and early infant circumcision programmes

- Once the VMMC programmes have reached all men aged 15–49 years who wish to be circumcised, high circumcision coverage can be sustained by offering circumcision to a smaller number of adolescent boys each year. In most countries, this is likely to be the 10–14-year age group, a high proportion of which presented for circumcision services during the catch-up phase despite being outside the priority 15–49-year age range.
- Countries need to develop efficient and sustainable adolescent VMMC services and provide these to boys who were too young to have been circumcised in the catch-up phase. The total number of circumcisions to be performed each year will be substantially less than during the catch-up phase.

- Even in countries considering or preparing for the introduction of EIMC programmes as their primary long-term circumcision strategy, an adolescent circumcision programme will be required until the EIMC programme is sufficiently comprehensive that over 90% of infants are circumcised and boys circumcised as infants reach adolescence. Even if EIMC programmes are scaled up very quickly, adolescent programmes will be required for at least 15 years and possibly many more. It will be important for countries to maintain circumcision services for boys and young men migrating from low circumcision areas who wish to become circumcised.
- There will be almost no impact of EIMC on the HIV epidemic until boys become sexually active and reach the age of highest HIV incidence 20–25 years later.
- The sustained circumcision services need to be welcoming and attractive to adolescent boys ('adolescent-friendly') and take the opportunity to provide additional information and counselling. Depending on context and country priorities, such additional information should cover – in an age-appropriate and culturally sensitive manner – sexual and reproductive health, contraception, sexuality education, preventing abuse of alcohol and other recreational drugs, and prevention of intimate partner violence and violence against women.
- Universal health coverage schemes (health insurance) should be explored as a way of ensuring sustainable financing of circumcision programmes. Male circumcision is cost-saving in almost all priority VMMC countries, and circumcision has long-term benefits not only by reducing the risk of HIV infection but also reducing the risk of human papilloma virus infection and subsequent genital cancers in men and women.
- Modelling studies are currently not able to demonstrate
 whether EIMC programmes are more or less cost-effective
 than a sustained VMMC programme based on adolescent
 circumcision. The unit cost of providing circumcision is
 expected to be lower for early infant compared with
 adolescent circumcision, but more experience with EIMC
 programmes and accurate costing data are necessary
 before a full comparison can be made.
- The time horizon is very important in understanding the cost and impact of all VMMC programmes. This particularly applies to EIMC programmes as the HIV prevention benefits do not start to accrue until the boys become sexually active. Thus, projected cost and impact of EIMC programmes must be interpreted more cautiously than for adult and adolescent circumcision programmes, which require shorter-term projections.

 Large investments have already been made to introduce adult and adolescent VMMC programmes, in particular by training providers, managing logistics, and understanding ways of ensuring the provision of high quality, safe and efficient services. These skills and knowledge can be further used to sustain adolescent VMMC programmes. By contrast, new investments are required to build and sustain skills and services for EIMC programmes.

Setting targets and priorities for VMMC programmes

The majority of the focus countries have established programmes to offer circumcision to all men in the age range 15–49 years and have set ambitious targets to reach 80% of these men within five years. Experience has shown that circumcision is highly acceptable among younger men and adolescent boys, who have come forward for circumcision in large numbers, but older men have been quite reluctant. Coverage rates among men over the age of 30 years have been low and attempts to generate more demand in this age group have been both difficult and costly.

The VMMC models presented at the meeting were used to assess the costs and impact of expanding circumcision coverage in five-year age bands and according to geographic location or risk profile. They provided insights into how to optimize the second phase of the VMMC programmes in the light of recent experience. Accordingly, the experts recommended that VMMC programme managers consider the following:

- Acceptability of circumcision varies by age and personal circumstances, and the costs of generating demand among older men are high.
- Coverage or saturation targets should be set by age strata and not uniformly for the entire 15–49-year age group.
- The greatest impact on HIV incidence in the next five years will be obtained by expanding circumcision coverage in the 20–24- and 25–29-year age strata as this is the age range at which men are at highest risk of HIV infection.
- Rapid expansion in the 20–24- and 25–29-year age strata is essential if the 2020 HIV prevention target is to be reached.
- Services should be provided to men aged 30 years and over who request circumcision, but generating demand in this age group is likely to continue to be difficult and costly.

- Circumcision services should be provided to younger men in the 10–19-year age stratum as the eventual benefit of circumcision in this age stratum will be large, even if the greatest impact in terms of high HIV incidence reduction in the population will take some years to be realized.
- Efforts should be made to identify and circumcise men at particularly high risk of HIV infection irrespective of age, as these men will benefit from the greatest absolute reduction in HIV risk following circumcision. Examples include men attending STI clinic services (private and public sector), HIV-uninfected men in serodiscordant couples (including those identified during routine testing in antenatal care), and men in certain occupational groups with historically high infection rates, such as migrant workers and those living in isolated communities.
- As ART programmes expand men in high-risk groups will be the focus of HIV testing in order to initiate ART rapidly if found to be infected. Strong mechanisms need to be developed for referring men from high-risk groups who test HIV-negative to circumcision services.
- Countries should first expand circumcision services in geographic areas with high HIV incidence, such as particular regions or districts and major urban areas.

- Progress towards VMMC coverage targets should be monitored by age strata at subnational levels.
- The costs and efficiency in reaching VMMC coverage targets through different service delivery models (for example, outreach, mobile or fixed sites) should be assessed and the models best suited to the local context prioritized.
- VMMC programmes are a unique opportunity and mechanism to link adolescent boys and young men to information and services related to sexual and reproductive health, contraception, sexuality education, preventing abuse of alcohol and other recreational drugs, and prevention of intimate partner violence and violence against women. More work is needed to improve training and information materials to deliver education and counselling in an age-appropriate and culturally sensitive manner.

REFERENCES

- 1. World Health Organization. WHO Progress Brief: Voluntary medical male circumcision for HIV prevention in 14 priority countries in east and southern Africa. Geneva: World Health Organization; 2016, June. Report: WHO/ HIV/2016.14 (www.who.int/iris/bitstream/10665/246174/1/WHO-HIV-2016.14-eng.pdf.
- Njeuhmeli E, Forsythe S, Reed J, Opuni M, Bollinger L, Heard N et al. Voluntary medical male circumcision: Modeling the impact and cost of expanding male circumcision for HIV prevention in eastern and southern Africa. PLoS Med. 2011;8(11):e1001132.
- 3. UNAIDS. Fast Track: Ending the AIDS Epidemic by 2030. Geneva: Joint United Nations Programme on HIV/AIDS; 2014. Report: JC2686 (www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf.
- 4. World Health Organization. Policy brief: WHO expands recommendation on oral pre-exposure prophylaxis of HIV infection (PrEP). Geneva: World Health Organization; 2015, November. Report: WHO/HIV/2015.48 (http://apps.who.int/iris/bitstream/10665/197906/1/WHO_HIV_2015.48_eng.pdf.
- 5. UNAIDS. Invest in HIV Prevention: Quarter for HIV Prevention. Geneva: Joint United Nations Programme on HIV/AIDS; 2015. Report: JC2791 (http://www.unaids.org/en/resources/documents/2015/JC2791_invest-in-HIV-prevention,).
- 6. UNAIDS/WHO/SACEMA Expert Group on Modelling the Impact and Cost of Male Circumcision for HIV Prevention. Male circumcision for HIV prevention in high HIV prevalence settings: What can mathematical modelling contribute to informed decision making? PLoS Med. 2009;6:e1000109.
- 7. Kripke K, Chen PA, Vazzano A, Thambinayagam A, Pillay Y, Loykissoonlal D et al. Cost and impact of voluntary medical male circumcision in South Africa: Focusing the program on specific age groups and provinces. PLoS One. 2016:11(7):e0157071.
- 8. Haacker M, Fraser-Hurt N, Gorgens M. Effectiveness of and financial returns to voluntary medical male circumcision for HIV prevention in South Africa: An incremental cost-effectiveness analysis. PLoS Med. 2016;13(5):e1002012.
- Kripke K, Chimbwandira F, Mwandi Z, Matchere F, Schnure M, Reed J et al. Voluntary medical male circumcision for HIV prevention in Malawi: Modeling the impact and cost of focusing the program by client age and geography. PLoS One. 2016;11(7):e0156521.
- 10. Kripke K, Okello V, Maziya V, Benzerga W, Mirira M, Gold E et al. Voluntary medical male circumcision for HIV prevention in Swaziland: modelling the impact of age targeting. PLoS One. 2016;11(7):e0156776.
- 11. Kripke K, Vazanno A, Kirungi W, Musinguzi J, Opio A, Ssempebwa R et al. Modeling the impact of Uganda's safe male circumcision program: Implications for age and regional targeting. PLoS One. 2016;11(7):e0158693.
- 12. Kripke K, Perales N, Lija J, Fimbo B, Mlanga E, Mahler H et al. The economic and epidemiological impact of focusing voluntary medical male circumcision for HIV prevention on specific age groups and regions in Tanzania. PLoS One. 2016;11(7):e0153363.
- 13. Awad SF, Sgaier SK, Tambatamba BC, Mohamoud YA, Lau FK, Reed JB et al. Investigating voluntary medical male circumcision program efficiency gains through subpopulation prioritization: insights from application to Zambia. PLoS One. 2015;10(12):e0145729.
- 14. Awad SF, Sgaier SK, Ncube G, Xaba S, Mugurungi OM, Mhangara MM et al. A reevaluation of the voluntary medical male circumcision scale-up plan in Zimbabwe. PLoS One. 2015;10(11):e0140818.
- 15. Njeuhmeli E, Stegman P, Kripke K, Mugurungi O, Ncube G, Xaba S et al. Modeling costs and impacts of introducing early infant male circumcision for long-term sustainability of the voluntary medical male circumcision program. PLoS One. 2016;11(7):e0159167.
- 16. Awad SF, Sgaier SK, Lau FK, Mohamoud YA, Tambatamba BC, Kripke KE et al. P18.02 Circumcision of hiv positive males will not undermine the benefits of voluntary medical male circumcision programs in africa. Sexually Transmitted Infections. 2015;91(Suppl 2):A241.
- 17. Kripke K, Njeuhmeli E, Samuelson J, Schnure M, Ncube B, Dalal S et al. Assessing progress, impact, and next steps in rolling out voluntary medical male circumcision for HIV prevention in fourteen priority countries in eastern and southern Africa as of 2015. PLoS One. 2016;11(7):e0158767.
- Kripke K, Reed J, Hankins C, Smiley G, Laube C, Njeuhmeli E. 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.

ANNEX A — AGENDA

Fast Tracking VMMC in HIV Combination Prevention

World Health Organization, Geneva, Switzerland 23–24 March 2016

Time	Topic	Responsible
Wednesday 23	March 2016	
13:30 – 15:00	Welcome and introductions, meeting objectives	Peter Ghys
	Session 1: New global goals and progress in VMMC	-
	Fast tracking combination prevention by 2020	Karl Dehne
	New global goals insight into the modelling process and inputs	Jose Antonio Izazola
	VMMC progress through 2015	Julia Samuelson
	Session 2: Completed and ongoing VMMC modelling exercises	
	Overview of modelling studies and discussion to correct and identify gaps	Tim Farley
	Models used and key methodologies (DMPPTs and 2.1, Goals, SNU, ASSA, ASM)	W -1
	Discuss implications of various models and communication of similarities and differences	Katherine Kripke, John Stover, Nicole Fraser-Hu Maaya Sundaram
15:00 – 15:30	Coffee / tea break	
15:30 – 17:30	Session 2 (continued): Modelling studies on current VMMC impact and potential in context of new goals and 90–90–90	
	Progress and re-estimation of impact	Katherine Kripke
	Impact of programme achievements to date in Zimbabwe and Kenya: a consensus of multiple model applications	John Stover
	Effectiveness and financial returns of MC in South Africa	Nicole Fraser-Hurt Katherine Kripke
	Impact and cost of VMMC in 90–90–90 and gender differential	кашенне кнрке
	Early infant MC for long-term sustainability – costs and impact	Katherine Kripke
	Plenary discussion on VMMC in combination prevention and fast track goals including 90–90–90	
Thursday 24 Ma	arch 2016	
	Report back key messages Day 1 and clarifications	Tim Farley
	Continue review of modelling studies:	
	Circumcision and HIV-positive males	Susan Awad
	Prioritization and targeting by age and geography	
	- Zambia, Zimbabwe programme efficiency gains (Kenya?) (ASM model)	Susan Awad
	 Economic and epidemiological impact – implications of age and geographic targeting – South Africa, Swaziland, Tanzania, Uganda, Malawi, Lesotho and Mozambique. (DMPPT 2) 	Katherine Kripke
10:30 - 11:00	Coffee / tea break	
11:00 – 12:30	Continue review of modelling studies:	
	• 20–29-year-old analysis: Zimbabwe	Katherine Kripke
	Subnational unit analysis – VMMC and ART scale-up	Stephanie Davis
	Session 3: Towards target-setting and prioritization at country level	
	Synthesis of model limitations, uncertainties, key results	
	Implications for target-setting and prioritization at global and country level	
12:30 – 13:30	Lunch	

Time	Topic	Responsible
Thursday 24 M	arch 2016	
13:30 – 15:00	Session 3 (continued)	
	Group 1 Discussion	
	Key advocacy communication messages about use of models, progress and impact	
	Regional meeting on target setting and feasibility	
	Group 2 Discussion	
	• Key strategic actions needed to inform next five years and the new global VMMC framework 2017–2021	
	Report back	
15:00 – 15:30	Coffee / tea break	
15:30 – 17:30	Session 4. Prevention evaluation priorities	
	Considerations on evaluating the impact of VMMC within combination prevention approaches	Daniel Low-Beer
	List priorities and research and approaches for evaluation of prevention interventions	Peter Ghys
17:30	Next steps and close	

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