On December 13, 2006, the National Institutes of Health (NIH) announced the early termination of two randomised controlled trials of male circumcision—in Kenya and Uganda—on the basis of interim evidence that male circumcision provided a protective benefit against HIV infection of 53% among the 2784 Kenyan men and 51% among the 4996 Ugandan men enrolled in the respective studies. The Kenya and Uganda trials replicated the landmark findings of the South African Orange Farm study, the first randomised controlled trial to report a greater than 50% protective benefit of male circumcision. Before the availability of data from these three African randomised controlled trials, multiple observational studies correlated male circumcision with reduced risk of HIV infection. Systematic reviews and meta-analysis of observational studies provide further evidence of the association of male circumcision with reduced risk of HIV infection and a plausible explanation for the biological mechanism for reduced risk of infection has been suggested. Recently released longitudinal evidence of the range of health benefits that male circumcision provides, modelling based on the South African trials, and cost-effectiveness data in both North America and Africa provide further evidence to support the health benefits of male circumcision. Male circumcision is also associated with reduced risk of urinary tract infections, genital ulcer diseases, penile cancer, and a possible reduction in transmission of human papillomavirus (HPV) exists.

Yet enthusiasm generated from the three trials might not lead to accelerated scale-up. Regrettably, the global experience with access to antiretroviral drugs shows that strong science alone does not result in rapid, widespread rollout. Not until civil society, non-governmental organisations, and a chorus of advocacy groups successfully lobbied for universal access to antiretrovirals did widespread rollout in areas with a high burden of HIV areas begin in earnest. Rapid implementation of male circumcision will probably require a similar effort.

In areas where HIV-1 constitutes a generalised population epidemic, male circumcision could have dramatic life-saving effect at the population level. A recent article reported that 15-year-olds in South Africa leave school every year; 10 years ago, the chance was 29%. The article continues, “A third of women between the ages of 25 and 29 years are infected, while 19% of the country’s working-age population (age 20 to 64) is HIV positive.” In South Africa, which has an estimated adult prevalence of about 19%, and in areas with similarly high prevalence, one could expect male circumcision to have a similar effect to the herd immunity seen with intensive immunisation programmes. Recent modelling by Williams and colleagues, based on the protective rates achieved in the South African trial, showed that the greatest effect would be in southern Africa, where circumcision rates are low and HIV prevalence is high. Williams and colleagues projected that large-scale implementation of male circumcision has the potential to avert about 2 million new HIV infections and 300 000 deaths over the next 10 years. Over the subsequent 10 years, an additional 3.7 million HIV infections and 2.7 million deaths could be averted. Furthermore, they report that combining male circumcision with prevention strategies known to reduce transmission rates—eg, use of antiretrovirals—would further reduce new infections. In communities with high HIV prevalence, cost analysis is not just limited to preventing HIV infections and the associated cost of treatment (if available), but the economic benefits gained by entire countries by maintaining the health of the most productive age-groups of their populations.

In regions where HIV is not a generalised epidemic and access to antiretrovirals, condoms, and routine medical care is greater, male circumcision could have relevance for its other health benefits, and the associated risks should be considered in this context. For the general population, male circumcision might have population-level and cost benefits through decreasing urinary tract infections, HPV transmission (and thus cervical cancer), and incidence of genital ulcerative diseases. It could also have critical importance in specific segments of the population that are disproportionately burdened with sexually transmitted diseases, where circumcision rates are low, and HIV prevalence is high.

Challenges and opportunities

We identify here 13 issues—challenges and opportunities—pertaining to male circumcision as a prevention strategy; the list will probably expand as new data become available. We wish to encourage discussion and to ensure that these issues are considered when new medical findings are released and implementation plans are developed. Furthermore, our hope is that these challenges will enrich the discussions as to how male circumcision could be used as an HIV prevention intervention, and what steps need to be taken to ensure it is implemented in an ethical and effective manner. In highlighting challenges, we intend to engage those involved in research, policy, and implementation of male circumcision to consider all the available evidence and to encourage dynamic, malleable, and contextual understanding of male circumcision and its potential applications.
Determining acceptability
Westercamp and colleagues reviewed 13 acceptability studies done in sub-Saharan Africa among non-circumcising communities. The median acceptability was 65% among men, whereas 69% of women favoured their partners being circumcised, and 81% of both men and women were willing to circumcise their male children. Price, pain, and lack of complications were universal concerns and need to be addressed in rollout of male circumcision. Implementation efforts can address these concerns by ensuring that the procedure is affordable to those who need it, that pain is minimised through proper anaesthesia, and that complications are limited by proper training, procedure, and oversight. Additionally, the opportunity now exists to further investigate and expand our current understanding of acceptability so that it includes issues related to male sexuality and bodily rights and integrity issues specific to men.

Communicating the benefits of male circumcision
The benefit from male circumcision is relative, not absolute, and the challenge will be to devise communication strategies to reinforce this point clearly. The recent developments in male circumcision present an opportunity to develop new and innovative prevention messaging, and especially to reinforce the need for combination prevention that encourages people to use all of the prevention tools available to them. Furthermore, we now have an opportunity to re-engage with policymakers and programme planners about the new opportunities that male circumcision presents for widespread invigoration of prevention.

Defining risk, benefit, and harm reduction
Risk and risk aversion have different meanings to different groups of people. The perception of risk is socially constructed and culturally imbedded within groups, and individual risk perception is perceived through this lens. Policy statements pertaining to routine male circumcision are no exception. The social and economic factors that inform risk perception by the American Academy of Pediatrics (AAP), the British Medical Society, or the professional bodies of any other developed country might not be congruent with those of societies within developing countries, in which the risk of morbidity or mortality resulting from HIV infection (or a host of other opportunistic infections) is considerably higher. For example, the AAP might focus on the immediate health of a neonate because the adult risk of HIV is not high in the USA and access to antiretrovirals is widespread. In developing countries where there is a high risk of HIV infection and access to life-saving drugs is less, local risk perception might dramatically differ from that in countries not experiencing generalised epidemics. Recent developments present the opportunity to re-examine the risk–benefit profile of interventions targeted to high prevalence areas and emphasise that harm reduction should be understood in terms of regionally specific health risks.

A framework for a combination prevention strategy
Too often, HIV prevention pits one strategy against another—eg, condoms versus partner reduction, treatment for sexually transmitted diseases versus antiretrovirals to reduce HIV viral load. Male circumcision provides the opportunity to move beyond dichotomous thinking and develop a discussion of HIV prevention that encompasses all evidence-based strategies. Concrete programmes can be developed that promote consistent availability of simultaneous prevention strategies. These programmes should be developed using the evidence base in response to regional specificities for optimum uptake and include measurable standards. Any rollout must take into account the fact that male circumcision will be introduced into a complicated prevention environment. Less than one in five of people at highest risk for HIV infection have access to effective prevention interventions. Within this context, it is entirely possible that male circumcision will be hailed as the great new intervention, compensating for the substantial failures of previous strategies, when in fact those strategies were never fully implemented.

Funding for social and behavioural research and fighting gender inequality
Although vaccines might change behavioural distribution, they will not solve gender inequality. The potential ethical implications of over-reliance on biomedical solutions at the expense of equity, social justice, and human rights missions cannot be dismissed. That male circumcision has been shown to be protective against HIV infection presents us with the opportunity to re-invigorate the discussion about gender, socioeconomic inequality, access to care, and stigma, and to develop concrete strategies for addressing these important background factors as implementation of biomedical strategies for HIV prevention progresses.

Defining the effect of male circumcision on women
Mathematical modelling suggests that lowering the overall incidence of female-to-male transmission will lower prevalence rates for both men and women, resulting in reduced male-to-female transmission. Other studies suggest that controlling viral load in HIV-positive men could reduce transmission to their female partners. Male circumcision combined with viral load suppression could dramatically reduce incidence rates for men and women. Nonetheless, the degree to which male circumcision will benefit women as a prevention intervention, or potentially increase their risk of infection as a result of behavioural disinhibition, is uncertain and is a growing concern among public-health officials, social scientists, and policymakers. Tracking the effect of male circumcision on women is urgent.
circumcision on both men and women can also offer the opportunity for health systems to engage couples in conversations about risk, protection, and sexuality, rather than relying on female-centred or male-centred approaches to protection.

Religious and cultural practices
Male circumcision offers the opportunity to re-engage with religious and ethnic groups in HIV prevention. Because such practices carry major religious, social, and cultural meaning for many of these groups, some who have not always been comfortable with HIV prevention, male circumcision as an HIV prevention strategy could provide new avenues for dialogue. Many groups with diverse social histories that practice male circumcision for religious and ethnic reasons exist worldwide. In mapping the context of existing practices and strategies for potential interventions, local religious institutions and leaders should be consulted and should occupy central roles in advocating for HIV prevention. Although the three trials that show protective benefit against HIV infection were done in Africa, the potential application of male circumcision in areas of rapidly emerging epidemics where the main means of transmission is heterosexual, will require careful and immediate examination of local religious or cultural acceptability. The need for engagement is especially critical in regions where male circumcision might have no religious or cultural significance.

When to circumcise
The results of the clinical trials present the opportunity to re-examine national and professional policies on infant circumcision. Neonatal circumcision is considerably safer and substantially less expensive than adolescent or adult circumcisions.11,13–18 If male circumcision proves effective and is only rolled out to neonates, it would take at least a generation before a population-level effect occurs. An adult intervention raises important questions regarding the capabilities of existing health systems, increased complexity of the procedure, higher complication rates, and greater expense. Managing complications and the associated costs in resource-poor settings also raises concerns. At the same time, there is a need to address the ethics of compromising a child’s bodily integrity for an issue that might not affect him for many years to come.

Male circumcision versus female genital mutilation
The demand for male circumcision might lead to the increased practice of female genital mutilation (female circumcision), especially in places where both practices are done, potentially reversing decades of work fighting the harm that such procedures cause women and girls. Other than an unfortunate similarity in the naming of the procedures, male circumcision and female circumcision have no common health benefits. Female genital mutilation has no medical benefits and, in fact, could promote disease transmission and acquisition. Several possible components could be added to male circumcision interventions to ensure that participants do not believe similar benefits are gained from female genital mutilation. One possibility is to introduce joint counselling services for men and their female partners during the consent process. Additionally, male circumcision could be integrated as part of reproductive health services that provide both the circumcision procedure and family planning that distinguishes the two practices.

Safety and complications
Although circumcision seems to provide numerous lifetime medical benefits, it is not without risk. The assessment of personal and public-health benefit versus relative risk could differ dramatically due to regionally specific confounding factors. In regions where high HIV prevalence exposes the population to risks that have a devastating effect on entire societies, the risks associated with male circumcision could be outweighed by the potential lives saved. Complications associated with male circumcision depend on a host of factors including age at which the procedure is done, training of personnel doing the procedure, availability of instruments, and the level of sterility under which the surgery is done. In the South African trial, in which circumcisions were done by trained personnel under closely monitored conditions, 3.8% of the men reported complications immediately after surgery, and at the 18 months follow-up this proportion had fallen to less than 1%. Unacceptably high numbers of complications arising from traditional circumcisions in parts of sub-Saharan Africa are well documented.19–21 Complications are not limited to traditional circumcisions; poorly trained medical personnel are also responsible for many.20–22 Even in countries with developed health systems, to accurately report complication rates is difficult because they vary widely depending on the type of study, setting, person doing the surgery, and most importantly, how complications are defined. This problem is compounded in resource-limited settings where multiple confounding factors could be present and basic sentinel surveillance is often limited. Nevertheless, evidence is emerging that shows that safe procedures using accessible resources could be established in such settings.20 The WHO/UNAIDS UN Work Plan on Male Circumcision is attempting to improve the safety and surveillance of current male circumcision practices by assisting countries in obtaining the necessary data for informed policy development.20

Health systems
Implementation of male circumcision might immediately strain the resources of health systems in many countries, especially those that need it the most. Large-scale rollout of such an intervention would initially require substantial human and financial resources.
Although achieving high rates of circumcision might be beneficial, it should not be at the cost of other disease prevention strategies—eg, antenatal care, malaria control, or nutrition. Since an internationally agreed-upon public-health goal is for all women to give birth in health facilities, offering male circumcision to babies in clinics would at least not divert national resources from current efforts to build systems, and might be a strategy that has multiple benefits.

The need to ensure that there are sufficient qualified personnel available to do circumcisions is critical. Whether the procedure needs to be done by a physician, or whether nurses or others can do it, should be immediately addressed and these discussions should include local authorities and community members. Basic competency levels must be established together with mechanisms for certifying that personnel are able to meet these standards. This type of model is already happening in South Africa where traditional surgeons are certified to do male circumcision safely and, from anecdotal information, many more are eager to work with physicians and nurses.

In many African regions, the most circumcisions are done by traditional circumcisers. In Lesotho, for instance, traditional circumcisers perform about 8000 circumcisions a year, substantially outnumbering those done by the health-care system, which already has a shortage of physicians. Yet current WHO and UNAIDS guidelines emphasise male circumcision as a clinical practice within health delivery settings. We are now provided with the opportunity to re-assess this approach; this bias toward an already overwhelmed health system runs the risk of retarding scale-up of male circumcision and unnecessarily confining its benefits to those who have access to health care.

The broader context of sexual and reproductive health
The opportunity to intensify linkages between sexual and reproductive health and HIV/AIDS is not simply a service issue but is at the core a policy and programme issue as well. These linkages are complex and involve family planning, maternal and infant health, and management of sexually transmitted infections and of other sexual and reproductive health issues on the one hand, and HIV/AIDS prevention, treatment, and care on the other.

Addressing perceptions of inequitable power relations
The uneven power relations implied by the way in which developed countries are doing trials in developing countries for a practice that has been declared medically unnecessary for babies in the west could give rise to a perception of new forms of colonialism. We now have the opportunity to change the discussion framework by ensuring that countries that stand to benefit the most or will shoulder the burden of potential harm have central leadership in the development of research agendas, as well as the assessment, planning, and implementation of any intervention.

Steps forward
Immediate steps should be taken to engage stakeholders in assessing potential scale-up of male circumcision. Evidence to support the hypothesis that circumcising HIV-infected men reduces transmission to their partners is currently unknown.

Because all three trials presented similar and convincing data, the pressure will begin mounting for broad implementation of male circumcision, especially in high-prevalence areas where the principle mode of HIV transmission is vaginal-penile sexual contact. Questions will arise regarding the benefits of male circumcision for concentrated epidemics—eg, those occurring in India, China, many parts of Latin America, Europe, Australia, New Zealand, and the USA—and especially when these epidemics involve mainly men who have sex with men, where the highest transmission risk is not to the insertive partner (who could benefit from male circumcision), but to the receptive partner during anal intercourse. Questions will continue to arise about the benefits of infant versus adolescent or adult circumcision. Controversies will continue to rage as to whether male circumcision is mutilation, or whether it is justified for health, religious, and cultural reasons.

Avoiding branding of men as perpetrators of infection
Referring to discussion at the XVI International AIDS Conference of African men’s role in HIV transmission, Margaret Wente for The Toronto Globe and Mail wrote, “...changing the behaviour of African men is probably hopeless.” These kinds of stereotypes of African men serve to entrench both a negative perspective on African males’ sexuality, and intensify erroneous perceptions of moral depravity and common modes of thought about gender relations. African men are being portrayed as disease vectors, unconcerned about others, spreading disease and violence, and neglecting families.

Lurking just below the surface in many HIV discussions—especially of HIV in sub-Saharan Africa—is the perception that people in certain countries or regions are more promiscuous, more callous, less empathic, or less moral. Some imply that people living with HIV should abstain from or minimise sexual activity, including reproductive desires. The ensuing conversations about sexuality could become a justification for racism and inequitable judgments on populations from low-income or middle-income countries (or inner cities of high-income countries).

The data from the male circumcision trials provides an opportunity to address the need to improve gender equality, since it will go a long way toward resolving some of the most powerful dynamics of HIV transmission. To examine the disenfranchisement that both women and men face, and to develop programmes to fight structural inequities, will remain important. Vigilance will be required to avoid the trap of individualising problems or solutions that pit men and women against one another.
The male circumcision lobbying forces emerging from regions not experiencing generalised epidemics might not adequately represent the interests of populations in the areas most affected by HIV. To ensure comprehensive inclusion of all positions, especially voices from low-income and middle-income countries where these interventions will probably be implemented, is of paramount importance. Any intervention should be locally relevant and evidence based. Notably, these types of planning and development discussion with policymakers in sub-Saharan Africa have already begun.

The challenges are not intended to discourage the use of male circumcision for HIV prevention nor are they intended to slow the development of potential interventions. Rather, we present these issues to ensure that the discussion regarding the evolution and rollout of male circumcision reflects the full range of issues that should be considered for individuals and for populations.

So what next? Discussion of development of national strategic plans for male circumcision for countries with the highest HIV prevalence rates should be encouraged. These plans should include assessment of current capacity, the development of a single sentinel surveillance and reporting mechanism, clear guidelines on basic standards of care, plans for complication triage, measurable targets, cost analyses, and specific assessment of internal ethnic group practices. The development of such plans should include traditional practitioners and religious groups. Research on the ethnic and cultural dynamics of scale-up should be encouraged.

Additional modelling should be done. Modelling projections in areas of generalised population epidemics that estimate varying degrees of uptake, and additional factors such as combination prevention strategies, should be undertaken. Modelling should also be done with data from localised epidemics of heterosexually transmitted HIV infection in other regions of the world.

Plans at country and regional levels should be drawn up that estimate the number of male circumcisions needed to have an effect on the epidemic, and the human and financial resources necessary to achieve that effect. Such information is essential to ensure that the full benefit of male circumcision can be realised in areas of high prevalence and incidence. The WHO/UNAIDS UN Work Plan on Male Circumcision has taken steps to make this life-saving strategy affordable and safely available to relevant populations bearing the heaviest burden of HIV infection.

Specific focus needs to be given to ethical discussion, studies, and guidelines, since these issues are among the most difficult in the field of HIV prevention, especially regarding male circumcision in the context of research and in practice. We encourage a focus on stigma, since it is possible that male circumcision will present the opportunity to investigate and develop a more nuanced understanding of how stigma operates around HIV/AIDS.

The feasibility of comprehensive reproductive services targeting both men and women that include the provision of male circumcision and associated counselling and messaging, as well as family planning, counselling and treatment for sexually transmitted infections, the provision of condoms, contraceptive devices, and voluntary counselling and testing services should be assessed.

Conclusions
Male circumcision is the most compelling evidence-based prevention strategy to emerge since the results from mother-to-child transmission clinical trials. We encourage multilateral, bilateral, and government agencies, along with non-governmental organisations, to make this life-saving strategy affordable and safely available to relevant populations bearing the heaviest burden of HIV infection.

Conflict of interest statement
We declare that we have no conflict of interest.

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References