Is male circumcision as good as the HIV vaccine we’ve been waiting for?

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‘In December 2006 officials from the US NIH did announce the discovery of an intervention at least as effective, for heterosexual transmission, as the long hoped for AIDS vaccine’

What would the reaction of the international public health community have been if a year ago scientists had announced the discovery of a vaccine or chemical gel that, in three separate clinical trials, had reduced the risk of heterosexual HIV infection in men by at least 60%? Considering that even with increasing access to antiretroviral therapy AIDS continues to be a huge killer – every day over 2,000 men become infected with HIV in sub-Saharan Africa alone [1] , which eventually also results in millions of new cases in their partners and children – would not such an announcement have surely sparked a massive surge of excitement and renewed investment in HIV prevention?

In fact, in December 2006 officials from the US NIH did announce the discovery of an intervention at least as effective, for heterosexual transmission, as the long hoped for AIDS vaccine. However, unlike many previous breakthroughs in medicine, this time the intervention was not discovered by a team of scientists toiling in academic or government laboratories. Rather, some two decades ago anthropologists, demographers and epidemiologists initially noticed, and then eventually proved beyond a reasonable doubt, that male circumcision (MC) very significantly reduces the risk of heterosexual HIV infection in men [2–5]. All three randomized controlled trials recently conducted in Africa to determine the effect of MC on HIV transmission were stopped early by their ethical review boards as a result of overwhelming evidence of significantly lower HIV incidence in men who underwent circumcision (MC) very significantly reduces the risk of heterosexual HIV infection in men [2–5].

All three randomized controlled trials recently conducted in Africa to determine the effect of MC on HIV transmission were stopped early by their ethical review boards as a result of overwhelming evidence of significantly lower HIV incidence in men who underwent circumcision as compared with those who remained uncircumcised [6–8]. The results were comparable to optimistic hopes for a highly effective vaccine [9], and were consistent with dozens of studies over the prior 20 years [10–12], in addition to a wealth of ecological data consistently showing much higher rates of HIV infection in those regions of Africa (and southeast Asia) where most men are not circumcised [2–5,12–14]. While the main, directly protective effect of MC is for men, in places where many men are circumcised large numbers of women will also end up benefiting as they will be less likely to have sex with an infected male.

The biological basis for the protective effect of MC is that the foreskin contains a large number of target cells, such as Langerhans’ cells, that are uniquely vulnerable to HIV infection [15,16]. In addition, uncircumcised men are more likely to acquire certain sexually transmitted infections, particularly ulcerative ones such as syphilis and chancroid, which probably facilitate HIV infection [17]. Most importantly, keratin – the protective coating covering most exposed skin – is largely absent from the inner foreskin and thus renders those target cells much more accessible to HIV [15,16]. In the absence of a foreskin, men are therefore significantly – and permanently – less likely to get infected with HIV through heterosexual intercourse. Moreover, MC is a one-time, relatively simple procedure that is readily acceptable throughout most of sub-Saharan Africa, and would ultimately be highly cost-effective, especially in high HIV prevalence areas.

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Currently, MC is the only modality for preventing sexual HIV transmission that has been proven to work by the highest standards of scientific evidence; specifically, findings from multiple randomized controlled trials [18]. In fact, it appears that the actual protective effect of MC is probably somewhat higher than the official 60% estimate cited by WHO and UNAIDS, especially among higher-risk men. In part, this is because some men who were randomly assigned to the circumcision arm in each trial did not show up for their appointment and, more importantly, a larger number of men who were randomly assigned to noncircumcision decided to get circumcised on
their own during the trial period. Hence, the ‘as-treated’ protective effect, taking into account the actual MC status of participants, was a 76% HIV reduction in the trial in South Africa (where HIV prevalence was highest) [19]; and averaging across the three trials it was 65% [12].

In addition, the trial participants included men at both low and high risk of exposure to HIV infection, so the findings may have tended to further underestimate the actual biological effect of MC (e.g., a number of men reported no sexual activity during the studies, so circumcision would have had no effect on their risk of infection). In the Ugandan trial, there was an approximately 70% protective effect when the analysis was restricted to men more likely to be exposed to HIV, such as those reporting multiple or nonmarried partners [8]. Analysis of the two other trials may even find a somewhat higher level of protection for high-risk men, since the lowest overall efficacy was found in the Ugandan trial (~50%). Such a higher level of protection is fully consistent with the most rigorous observational studies, such as cohort studies examining HIV incidence in circumcised versus noncircumcised men over time, most of which have found a protective effect of approximately 75% or even greater [5,10,12,20–22].

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Certainly, the potential for ‘risk compensation,’ or a potential increase in risky behavior subsequent to adopting a preventive measure such as MC (or a future vaccine), is an important concern to be closely monitored and addressed [23]. However, circumcision appears akin to a ‘strong immunization’, whose benefits would probably be extremely difficult to offset through such behavioral disinhibition (and a recent community-based study from rural Kenya suggests that within the context of adequate counseling, disinhibition from MC may be unlikely [24]). That said, clearly it will be vital to counter the possibility of risk compensation through effective counseling, education and communication programs that emphasize the continuing need for less risky sexual behavior, for example avoiding multiple concurrent partnerships and practicing correct and consistent condom use (Figure 1).

The ultimate population-level impact of MC would be further amplified by a ‘herd immunity’ phenomenon if a sufficiently large proportion of men were to become circumcised in the population. Many vaccines which are considerably less than 100% effective at the individual level (e.g., the childhood measles vaccine), have proven quite effective at the population level, if coverage rates are high [25]. This herd-immunity effect is clearly suggested by historical ecological data; for example, MC is universal in most of west/central Africa, which continues to have much lower HIV rates than in the rest of the continent, even though the pandemic began there over 80 years ago [1–5,11–14,26]. Modeling suggests that widespread circumcision in the rest of sub-Saharan Africa could avert up to 2 million new HIV cases and 300,000 deaths over the next 10 years, and 3.7 million infections and 2.7 million deaths in the following 10 years, many of those among women [27]. This would not only save millions of lives, but would also abate the need for large future expenditures of AIDS medications, hence, studies have demonstrated that MC would be a highly cost-effective intervention in the longer term [28].

A dozen acceptability studies conducted in different parts of Africa where MC is no longer traditionally practiced have found that the majority of uncircumcised men want the procedure performed, and generally an even higher proportion of women in those regions would prefer to have a circumcised partner [29]. The main reasons for wanting MC, as reported in these surveys as well as in some qualitative studies conducted in Africa [11,30], are related to common perceptions of improved hygiene, lower risk of sexually transmitted or other infections, ‘better sex’ (for both partners) and easier condom use. Of note, most men and women surveyed do not believe that MC actually reduces HIV risk – although this could change as the results from the randomized controlled trials are more widely disseminated.

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In a 2006 household survey of Swazi men in both urban and rural areas, 87% said they would want the procedure if it helped reduce the risk of HIV infection [29]. In January of that year, the media reported on a ‘circumcision riot’ when over a hundred men in the capital city were turned away because not enough physicians were available at a ‘free circumcision Saturday’ event [34].

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Unlike a possible future AIDS vaccine or many other prevention interventions, MC has also been shown to eliminate or significantly reduce the risk of acquiring or spreading a number of other diseases and medical problems, including various sexually transmitted infections such as syphilis and chancroid [17], and conditions such as balanitis (severely infected foreskin) and phimosis (intractable foreskin, which makes sex uncomfortable or difficult) [35]. Of considerable public health importance, MC has been shown to significantly reduce rates of human papillomavirus infection in men, and thus greatly reduces the risk of penile cancer, as well as cervical cancer in their female partners [36]. While penile cancer is rare in developed countries, it is still a significant killer in some developing regions where access to clean water is problematic, and in many developing countries cervical cancer kills more women each year than AIDS [37].

In early March of 2007, more than 100 world experts convened in Switzerland to consider the data. On March 28 the WHO and UNAIDS declared that the evidence supporting the benefits of MC was “compelling”, and affirmed that male circumcision should now be made an additional element of comprehensive prevention efforts to stem the heterosexual spread of infection in high HIV prevalence parts of Africa [38].

Unfortunately, they may have missed the urgency of the moment and failed to fully recognize the need to raise MC to the center of prevention and male reproductive health programs – along with efforts to reduce the level of multiple sexual partnerships – as the key elements of HIV prevention needed in the hardest-hit parts of Africa [39,40].

Figure 1. Poster from the Family Life Association of Swaziland.
So the question must be asked: why the continuing delays in the implementation of male circumcision? Why do some prominent officials, nongovernmental organizations, Ministries of Health and international organizations vacillate as thousands become infected every day, preferring to debate over cultural imperialism, the ‘rights’ of the foreskin, the ‘real world’ validity of randomized trials and so on? They neglect to realize that, for example, HIV has been circulating in West Africa for over 80 years and yet there is still no country there, or elsewhere, where nearly all men are circumcised and adult HIV prevalence is above 6% [12,41]. This long-running ‘natural experiment’ provides a kind of real-world demonstration of the potential long-term impact of MC. So why – given that AIDS in Africa is one of the worst humanitarian crises in centuries – do some decision-makers continue to debate and delay and counsel patience?

We can speculate, though not excuse. We understand the very real operational challenges, implementation logistics, safety concerns and the enormous task of scaling up a surgical procedure so that it is readily available for millions of impoverished people. This is not the time for patience and delay, however, but for concerted action. The professional, governmental and advocacy communities’ ongoing tolerance for the glacially slow introduction of MC, especially in southern Africa, must be confronted. International and national leaders as well as donor agencies must be held accountable. They must be asked every day, not whether or why, but when? When will those who can speak out for the thousands who are now needlessly infected every day, work to ensure access to widely available, voluntary MC services, especially for those millions of poor men who simply cannot afford to pay for a safe procedure? This is an equity issue: as the waiting lists for public medical circumcision in countries such as Swaziland, Zambia and Kenya grow … people are being denied access to a potentially life-saving service.

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Advocacy organizations such as Medecins Sans Frontieres, Treatment Action Campaign and others who have made HIV treatment a reality must also now press for the widespread availability of safe MC services. The Family Life Association of Swaziland produced a poster to publicize MC. The media must also be engaged, and should report the continued delays and periodically tabulate the number of new HIV infections that have occurred due to the lack of available safe MC services. Since December 13, 2006 – the date of the NIH announcement on the overwhelming success of the randomized controlled trials – some 2,500,000 new HIV infections have occurred [1], representing thousands of new infections in men every day, eventually followed by a torrent of infections in their female partners and children.

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If this were an actual vaccine, packaged with a pharmaceutical company logo and shiny labeling, few people would be deliberating, constantly emphasizing a multitude of caveats and using bureaucratic-speak to stress the need for prevention ‘packages’ and comprehensive inclusive strategies in which the new vaccine would be ‘only one element among many other approaches’. There would instead be massive mobilization, press releases and corporate titans using their public relations organs to announce the bravado of their achievements. Unfortunately in these times of profit-driven healthcare, no single entity stands to earn large sums of money from MC. The procedure is not patented, owned nor trademarked. Can large-scale public health interventions be implemented without large corporate investment? Nearly all our current global initiatives – HIV treatment, malaria control and tuberculosis prevention – have a pot of gold at the end of the rainbow for their corporate sponsors. It is not obvious which corporate entity will stand to benefit from MC. Thus, while hundreds of millions of dollars are spent each year on advocacy, coordination, research and other activities by organizations focused on still hypothetical approaches such as a vaccine or a microbicide, a proposed International Male Circumcision Alliance, to be based in Africa and endorsed by many of the world’s leading HIV experts, has been unable to secure even a meager amount of seed funding to help get the effort launched.
The six of us have lived and worked in sub-Saharan Africa and other affected regions for decades. We have seen men as thin as shadows die in the hallways and on the grounds of hospitals. We have seen women widowed, children abandoned and entire families disappear. In the countryside there are hollow huts and empty villages; in the cities orphans roam the streets.

Two of us (Wamai and Agot) are from Kenya and have witnessed first-hand the devastation in the part of the country (Nyanza Province) where the virus has flourished due in large part, we now realize, because that is the one province where MC is not a cultural norm. Another (Bowa) is a Zambian urologist who has struggled to make safe MC available at the University Teaching Hospital in Lusaka; due to funding limitations, the demand for services has far outstripped supply and the waiting list has grown up to 8 months long. Another (Kagimba) was one of the original architects of the now famous ‘Zero Grazing’ behavior change (partner reduction) strategy in Uganda, and seeks to add MC to the ‘ABC’ prevention approach.

Now, 25 years after the pandemic was first identified, we have an important additional tool, the knowledge to help bring life back, to give people some hope. We need the rallying cry; above all, we need accountability. We need you – the reader, the media, the viewer, the voter, the caring man or woman on the street – to say not whether but when. When will there be widespread, safe and affordable MC services available in Africa? Every day we are counting and watching.

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Immediately, the front page of every major newspaper and other broadcast media around the world – certainly those in southern Africa – should report on the great impact that implementation of MC could bring. Country-specific data on the progress to implement safe services should be easily accessible and widely available for monitoring. If we can have sport scores reported around the clock, then we can also have tallies of how we are doing in reversing the HIV pandemic, such as estimates of the numbers of HIV infections averted and lives saved through this and other crucial prevention approaches.

Immediately, UNAIDS should announce the creation of an MC desk to promote and monitor safe MC and affordable male reproductive health services. Other global organizations can and must do the same. Responsibility, accountability, monitoring and evaluation need to be the buzzwords in the boardrooms of global health.

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Immediately, we can and must educate and share with the public the knowledge of the protective effect of MC. Together we can validate and value this as the lifesaving procedure that it is. We must also be fully transparent about the potential risks and limitations – inherent to virtually any public health measure – of MC, including the danger of unskilled and unsafe practitioners attempting to profit from the growing demand for the service. And unlike a potential HIV vaccine, MC would not have much impact on most epidemics outside of Africa, which are mainly driven by injection drug use and/or male-to-male anal intercourse. However, we must also work to correct the lingering misconceptions and false beliefs (mainly held outside of Africa) regarding the lack of benefits from safe circumcision. MC works: it is at least as good as the HIV vaccine we have been waiting for, praying for and hoping to see in our lifetimes.

Acknowledgements

We wish to thank Alan Brødy, Ward Cates, Kelly Curran, Helen Epstein, Steve Gesuale, Matt Hanley, Allison Herling, Doug Kirby, Willi McFarland, Daniel Mirel, Brian Morris, Robert Riviello, William Rodriguez, Jim Shelton and Dudu Simelane for their useful comments.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.
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