Male circumcision is not the HIV ‘vaccine’ we have been waiting for!

‘Thousands of African men now line up to get circumcised in the mistaken belief that it will save them from HIV...’

Over the past several months, some researchers and health organizations [101] have proclaimed circumcision to be a compelling and important new HIV tool. A recent commentary claims that circumcision is “at least as good as the HIV vaccine we have been waiting for, praying for and hoping to see in our lifetimes” [1]. Thousands of African men now line up to get circumcised in the mistaken belief that it will save them from HIV, as some developing nations – lacking even rudimentary medical care and clean drinking water – rush to implement mass circumcision programs with encouragement and millions of pledged dollars from the US government [2,102,103]. In addition, there are calls for implementing mass neonatal circumcision [104].

The push to institute mass circumcision in Africa, following the three randomized clinical trials (RCTs) conducted in Africa [3–5], is based on an incomplete evaluation of real-world preventive effects over the long-term – effects that may be quite different outside the research setting and circumstances, with their access to resources, sanitary standards and intensive counseling. Moreover, proposals for mass circumcision lack a thorough and objective consideration of costs in relation to hoped-for benefits. For the health community to rush to recommend a program based on incomplete evidence is both premature and ill-advised. It misleads the public by promoting false hope from uncertain conclusions and might ultimately aggravate the problem by altering people’s behavioral patterns and exposing them and their partners to new or expanded risks [8]. Given these problems, circumcision of adults, and especially of children, by coercion or by false hope, raises human rights concerns.

Insufficient data for a real-world setting

The three African RCTs reported a 50–60% reduction in female-to-male transmission of HIV over follow-up periods of 21–24 months. It is beyond the scope of this paper to analyze these studies in depth. However, the world health community must examine the methodology and results of these studies much more carefully than it has done so far. Given that these studies are now being used to promote circumcision of millions of males, it is worth examining several other factors that might have influenced and skewed the results:

- All three of the studies were halted early
- The durations of the experiments were short
- No long-term follow-up has been or can be done
- A large number of participants were lost to follow-up
- Many infections appear to be from nonsexual sources [9]
- Other important confounding factors exist

Early termination

The early termination of the RCTs raises methodological problems that may have biased the results and the conclusions drawn from them. A systematic review of RCTs stopped early based on interim results found that treatment effects are often overestimated [10]. AIDS experts have expressed concern that the overall cases in the Auvert study were low enough to render the results at “serious risk of overestimation” [11].

There is no way to know if the short-term results of the trials would have continued. In the Kenya trial, the protective effect of circumcision seemed to disappear after 18 months. In the 18–24-month follow-up period, eight circumcised
and nine uncircumcised males contracted HIV, an insignificant difference. The question of whether the interventive effect would have continued to be insignificant past 18 months can never be answered. Furthermore, since the control group participants were all offered circumcision at the termination of the RCTs, all possibility for long-term follow-up was eliminated. Lead time bias, in which circumcised men likely have fewer seroconversions in the first weeks owing to their inability to have sex in the post-operative period, is exaggerated in early termination studies.

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Participant loss
The number of participants lost to follow-up is potentially problematic. Typically, attrition of a small portion of participants is not a cause for concern, but in these trials, the number lost was far greater than the number who contracted HIV. A total of 10,908 males were initially enrolled in the three clinical trials, 5497 in the control (uncircumcised) groups and 5411 in the intervention (circumcised) groups. By the end of the RCTs, a total of 64 circumcised and 141 uncircumcised males had contracted HIV. During the trials, a total of 703 participants, including similar numbers of circumcised and uncircumcised men, were lost to follow-up, their HIV status unknown. Depending on the HIV status of the males lost to follow-up, the statistical significance of the trial results could vary greatly [3–5].

Nonsexual transmission
Another problem in the RCTs is the large proportion of HIV infections that study participants contracted from nonsexual risks. According to the reported sexual behavior of the males in the Orange Farm trial, 23 of the 69 infections occurred in men who reported no unprotected sex during the observation interval. Similarly, in the Uganda trial, 16 of the 67 infections occurred in men who reported either no sex partners or 100% condom use. The trial in Kenya did not provide data on sexual exposures as related to HIV incidence. The proportion of nonsexual transmission in participants suggests that circumcision may not have the impact on the HIV crisis that is being promoted [9], and, indeed, could be contributing to the infections.

Conflicting results
Prior to the three RCTs, observational studies of HIV in relation to circumcision status showed conflicting results. This should caution the world health community to question the RCTs’ unanimous conclusions. Recent survey data of circumcised versus uncircumcised males in several African countries show considerable variation in HIV rates. In some African populations, HIV infection rates are lower for circumcised males, while other studies and reports have shown opposite results [8,12,105]. For example, the 2005 survey data for Rwanda show an HIV-infection rate of 3.8% in circumcised men and only 2.7% in uncircumcised men [106]. Data for Malawi in 2004 show a 13% HIV-infection rate in circumcised males, but a lower 9.5% infection rate in uncircumcised males [9,107]. Clearly, circumcision status is not the only or determining factor in HIV prevalence patterns.

Sex workers
Accounting for the number of HIV-infected commercial sex workers in a region, circumcision status appears to become an irrelevant factor [13]. African regions with prominent Muslim populations tend to have high rates of circumcision and low rates of prostitution. The latter may account for lower HIV-infection rates previously attributed to circumcision. The role of commercial sex workers and concurrent sexual networks, a much more plausible infection vector than the possession of a foreskin, has not been adequately taken into consideration in plans to stop the epidemic [13–15].

Lack of risk calculation
Another concern about the three RCTs is the failure of the study teams to report the results in a way that compared HIV incidence per sexual exposure between the circumcised and uncircumcised populations. Per-incident risk calculation is necessary in order for men to weigh potential expected benefits from the surgery, based on anticipated sexual behaviour, against the risks and costs of circumcision. Without this information, men cannot be said to have given fully informed consent [9].

Other unconsidered factors
Other factors and conditions were present in the three RCTs that are not representative of the real world, potentially influencing the study results. These include the following:
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Circumcision could lead to increased HIV transmission
A recent study showed that female partners of newly circumcised HIV-positive males had a significantly increased risk of contracting HIV [16]. In Uganda, health officials do not have the resources to test for HIV in the men they plan to circumcise [108]. Mass circumcision of adults without HIV testing could increase the risk of HIV transmission to females.

Circumcision itself is known to spread HIV in Africa via contaminated medical instruments. One study estimates that circumcision increases the chance of infection by 300% [17]. Mass circumcision campaigns are not likely to have the same level of operator training or sanitary conditions as the clinical trials. For countries with limited economic resources to provide circumcision in a medical setting, these campaigns will encourage the inevitable ‘bush’ circumcision market. Regardless of the ratio between clinic and ‘bush’ situations, both could ultimately increase HIV transmission.

If the men in the three RCTs accurately reported their sexual behavior, many infections must have come from blood exposures, not sexual contact. Instituting mass surgery could further exacerbate the transmission of HIV through blood exposures in the clinics and hospitals where circumcisions will occur. Rather than promoting circumcisions, an alternate strategy to cut HIV incidence may be to improve infection control in hospitals and clinics [9].

Furthermore, promotion of circumcision as a method to prevent or reduce HIV transmission may already be leading circumcised men, and their sexual partners, into a false sense of security about being protected or immune from HIV. This, in turn, could undermine the current and effective ‘abstinence, be faithful and condom use’ (ABC) campaigns [18,19]. The RCTs reported no evidence of risk compensation behaviors during the study period. However, the study participants were receiving intensive counseling, free condoms and continuous monitoring during this period, circumstances that will most likely not exist in mass circumcision campaigns. Despite agreement that safe-sex messages must be built into circumcision campaigns, reports are already appearing that African males are indeed absorbing the message that circumcision means protection and other measures to prevent HIV are unnecessary [109]. Such potential risk-compensation behavior after circumcision has been inadequately studied in real-life settings over the long term. The likely result of promoting circumcision for HIV-risk reduction is that it will not complement condom use, as proponents hope, but, in reality, it will compete with condom use. It could not only negate any hoped-for protection from circumcision, but message confusion among Africans could lead to a dangerous erosion of behavioral gains already made in safe-sex campaigns.

‘Campaigns to promote safe-sex behaviors have been shown to accomplish a high rate of infection reduction, without the surgical risks and complications of circumcision, and at a much lower cost.’

Finally, shifting attention and resources to circumcision messages takes resources away from proven behavioral prevention methods and efforts to upgrade Africa’s health infrastructure. By focusing on short-sighted surgical solutions, valuable time and resources are diverted from addressing the root problems of HIV transmission.

The French Conseil National du SIDA (National AIDS Council) recently issued a statement that sums up most of the above concerns: “Implementation of male circumcision as part of a raft of preventive measures could destabilize healthcare delivery and at the same time confuse existing prevention messages. The addition of a new ‘tool’ could actually cause a result opposite to that which was originally intended” [20].

Circumcision costs & harms outweigh potential benefits
Very little attention is being given to the surgical complications associated with circumcision or the cost of treating these complications. Even if mass circumcision campaigns produce complication rates similar to the extraordinarily low
complication rates in the RCTs, which is unlikely, tens of thousands of African males will still suffer from them. A more realistic complication rate of 20.2% was documented in a study of Nigerian neonates circumcised by medical practitioners [21]. A true cost–benefit analysis cannot be carried out without accurate complication rates. Estimates of the cost of complications are likely to mushroom with the inclusion of infection rates in unsanitary conditions, need for repeat surgeries for poorly performed circumcisions and treatment of inflammation of the urinary meatus leading to stenosis (occurring in up to 10% of circumcised males) [110].

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While it is not possible to make a direct comparison of the cost of condoms versus the cost of circumcision, it is worthwhile to consider the significant cost discrepancies between these two strategies. In the RCTs, circumcisions were performed at a cost of approximately US$69 each [22]. Condoms cost three cents each [111]. African males require an average of 84 condoms per year [23]. For the cost of one circumcision, which, according to the RCTs, might be 50% effective, a man could receive a 32-year supply of condoms and protect himself and his partner(s) 87–100% of the time [24].

The millions of dollars that would be directed toward circumcision could have a far greater impact on health outcomes in Africa if used toward promoting safe-sex campaigns, HIV testing, provision of antiretrovirals and other core public health needs.

Unethical medical practice
 Furthermore, the results of studies performed on consenting adult African males should not be extrapolated to a health policy for newborns. It is unprecedented and unethical for an inadequately evaluated prophylactic surgery to be offered as a 'health benefit' to parents of newborns to reduce risks of an adult-acquired disease for which alternative preventative measures, in addition to condoms, are likely to be available before today's infants reach sexual maturity [25].

Newborns are not sexually active and, therefore, not at risk for sexually contracted diseases. Ethically and according to human rights law, circumcising an unconsenting child is in many ways similar to forcing circumcision upon an unwilling adult. Children deserve special protection from practices that put them at unnecessary risk and abrogate their rights to self-determination in the future.

More effective prevention strategies available
 If all African adult males were immediately circumcised (and its effectiveness were the same as reported in the RCTs), over the next 10-year period, it would reduce the number of HIV cases in sub-Saharan Africa by only 8%, with a 1% reduction of deaths [26]. There are better, more cost effective and less risky strategies available.

Education, safe-sex practices and consistent condom use are proven, effective measures for curbing HIV transmission [27]. Uganda, Senegal and Thailand have successfully lowered their HIV-infection rates without resorting to surgery. For example, HIV prevalence declined in Uganda by 47% following increased safe-sex education and condom promotion [7]. This 'social vaccine' is available and effective now and does not entail the complications of surgery. Uganda was successful in part because of leadership; leadership in other quarters can extend this success elsewhere. Thailand's success was with the highest risk group (prostitutes), and the strategy only needs extension to other segments of the population. These models emphasize the importance of tackling the behaviors that lead to HIV infection. Continuing to put time and money into effective programs, just as these countries did, is what will be most effective in the long-term, not the promotion of circumcision [112,113].

Vaccine analogy is misleading
 Comparing male circumcision to a 'vaccine' is misleading, as it plays on the general perception that vaccines offer near-complete protection from an illness with few side-effects. This 'vaccine' claim gives a false sense of security because individuals who engage in high-risk behaviors will be at high risk for HIV infection, whether they are circumcised or not. If a pharmaceutical HIV vaccine was available and was only 50–60% effective and likely to decrease condom use and other safe-sex practices, it would not be acceptable because it could increase the HIV-infection rate by altering behavioral patterns [8].

The erroneous message of protection from circumcision given to African males is alarming and dangerous. Dr Robert Bailey, one of the
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RCT authors, was recently quoted as saying, “[Circumcision is] the most effective prevention method we know about for heterosexual guys, if it’s done properly” [114]. With statements like this in the news, it is easy to understand why some males may mistakenly conclude that if they are circumcised, they no longer need to use condoms.

Other countervailing data

A recent study in the USA, examining HIV rates in both heterosexual and homosexual populations, found no statistical difference in HIV rates among circumcised and uncircumcised males in either group [28]. Another recent US study evaluating HIV infections in high-risk populations also found no benefit from circumcision [29]. The USA, where the majority of adult males are circumcised, has a much higher HIV-infection rate than European nations, where circumcision is rarely practiced [115].

Recent evidence demonstrates that the Langerhans cells in the foreskin have a protective effect against pathogens, including HIV, by producing the protein langerin. The previous theory was that Langerhans cells are a key entrance point for HIV-1. Circumcision, it was argued, protected against HIV disease because removing the foreskin also removed the Langenhans cells. However, it has now been shown that langerin transports HIV-1 to locations within the Langerhans cell where the virus is destroyed. The authors of this study argue that “strategies to combat infection must enhance, preserve or, at the very least, not interfere with langerin expression and function” [30]. It is only when the Langerhans cells are overwhelmed by a high viral load that the virus can enter the body.

This immunological function of the foreskin may explain the results of recent vaccine trials in which uncircumcised men were more likely to get infected after receiving the vaccine. The authors of the vaccine study speculate “the vaccine was abrogating some immune mechanism that normally protected uncircumcised ‘tops’ (referring to men who have sex with men) from infection through the mucosa of the foreskin” [116].

Conclusion

Regardless of whether circumcision might offer some heterosexual males a partial degree of protection from HIV, numerous other issues need to be thoroughly considered before instituting mass circumcision campaigns.

In short, given the large number of unknowns, confounding factors and lack of long-term follow-up in the three RCTs, it is premature to recommend circumcision as an HIV-prevention strategy. Much more evidence must be gathered on real-world efficacy of male circumcision as a prevention tool before mass surgeries are implemented.

An objective scientific assessment must be conducted to determine if the three RCTs are applicable in real-world settings. And, to determine the true cost of a circumcision campaign, there must be a comprehensive resource analysis of the plan. These mass circumcision costs also must be compared with the opportunity costs of funding ABC campaigns.

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As part of these assessments, the very real risks of circumcision surgery, including directly increasing HIV transmission to men as well as indirectly increasing transmission to women, surgical risks such as hemorrhage, other infections, meatal stenosis, need for repeat surgery and even death, must be considered.

Finally, the value and function of the foreskin as an integral part of the male sexual organ [31] and the ethical issues surrounding such surgery, including informed consent, the possibility of coercion and the dangerous implications of conveying erroneous messages of HIV immunity, must also be carefully considered in any analysis.

ABC programs offer nearly full protection from HIV infection, yet even if circumcision’s effectiveness matches the 50–60% effectiveness the RCTs reported, it only partially protects men, does not protect women at all, and leaves women more vulnerable to unsafe sex practices being forced upon them.

Those promoting circumcision argue that circumcision is an additional tool that will ultimately reduce infections more than just relying on condoms, monogamy and abstinence. However, African males are already lining up to be circumcised, thinking they will no longer need to use condoms. Rather than complementing ABC programs, promoting circumcision will undermine the ABC approach by diverting funds and encouraging risk compensation behavior, ultimately leading to an increase in HIV infections.
The world community must cautiously review and carefully consider the long-term consequences of mass circumcision campaigns, from the risk of increasing deaths and infections to human rights violations. In the rush to save lives, many may instead be lost and human rights trampled in the stampede. Circumcision is not the panacea the world has been waiting for in the battle to stem the HIV crisis.

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