

How did circumcision prevent HIV in clinical trials in Africa... and what does it mean for the United States?

*Educational briefing paper for US AIDS communities
based on information available as of March 29, 2007*

Recent research shows that circumcision¹ could be an effective new HIV prevention tool, especially in areas of the world with high HIV prevalence and low rates of circumcision. This promising news is clearly significant for sub-Saharan Africa. It is still unclear what this data could mean for HIV prevention strategies in the United States, where the epidemic is severe within specific communities, but is different from the epidemic in hard-hit regions of Africa where AIDS is common among the general population.

There is a lot of new and important data on circumcision, and much of it raises more questions than answers when we consider what it may mean for the epidemic in the US. For example, the studies in Africa mostly focused on women-to-men HIV transmission during vaginal sex — these trials did not address whether circumcision protects men who have sex with each other, or if it is protective for men or women during anal sex. They also did not yet provide answers about the role of circumcision in protecting women during vaginal sex. But in the US, nearly half of all infections occur through male-to-male sexual activity, and the vast majority of heterosexual transmission in the US is from men to-women.

While new data on male circumcision as an HIV prevention tool are very promising for some settings, particularly in the developing world, it is still unclear how this data could — or should — impact HIV prevention strategies in the United States.

HOW IS CIRCUMCISION DONE IN ADULT MEN, AND HOW CAN IT REDUCE TRANSMISSION OF HIV FROM WOMEN TO MEN?

Circumcision is a one-time procedure that could help *decrease*, but not eliminate, a man’s risk of acquiring HIV during vaginal sex, possibly for the rest of his life. Because it does not eliminate the risk of HIV, *some* circumcised men in the African studies did become HIV-positive, and many HIV-positive men in the US *are* circumcised.

Adult circumcision requires surgically removing the foreskin of the penis (Infant circumcision is a simpler procedure, which does not involve stitches). The foreskin contains “target cells” that HIV infects during the initial stages of

¹ Researchers and advocates use the term “male circumcision” to refer to what is commonly known as “circumcision,” because they want to make sure this is not confused with female genital mutilation (FGM), which is sometimes called female circumcision. Unlike male circumcision, there is no data that suggests that FGM offers any health benefits or prevents HIV. In fact, it is a dangerous practice and can cause many harmful effects, including damaging women’s urinary and reproductive tracts, which can lead to problems during pregnancy. Many advocates regard FGM as a violation of the human rights of women. In this document, we use the term “circumcision” to refer to men, as it is commonly used in the United States.

exposure. After it is removed during circumcision, the remaining skin develops a different, protective surface, which is called keratinized skin. This skin has fewer target cells.

Keratinization is thought to be one of the reasons why circumcision reduces men's risk of acquiring HIV during vaginal sex. Another reason may be that circumcision appears to reduce rates of genital ulcer disease, a condition that can increase the risk of getting or transmitting HIV.

OVERVIEW OF CIRCUMCISION STUDIES

Observations of the potential protective effect of circumcision

Over the years, researchers have observed that rates of HIV were lower in African and Asian populations where circumcision was common, and that there were much higher rates of HIV in countries where fewer men were circumcised.

In the US, two different observational studies on gay men and other men who have sex with men (MSM) showed that uncircumcised men were twice as likely to be, or become, HIV-positive. Another study observed that uncircumcised heterosexual men in an urban STD clinic had a 3.5-fold higher risk of HIV infection, but the results were not statistically significant.

However, observational studies like these did not prove a connection between circumcision and reduced risk of HIV infection – there could be other explanations for the apparent connection. The next stage of research was to conduct large-scale, randomized trials to investigate this theory.

Circumcision as an HIV prevention intervention for men who have sex with women:

Three randomized clinical studies in sub-Saharan Africa have shown that circumcision of males aged 15-48 can reduce *their* risk of acquiring HIV from women through vaginal sex by 50-60%. All three studies—conducted in South Africa, urban Kenya and rural Uganda—ended randomization early, after each study showed strong findings of a protective benefit from circumcision. All men in the trials were also given screening and treatment for sexually transmitted infections, condoms, and risk reduction counseling.

*Most HIV vaccine trials aim for a 50% protection rate. The results of the circumcision trials showing 50-60% reduction in HIV risk for men are very significant — and comparable to our current expectations of an HIV vaccine. **We still need a vaccine that can protect women, men and babies, but circumcision is available today while an effective HIV vaccine is still at least ten years away.***

Circumcision as an HIV prevention intervention for women who have sex with HIV-positive male partners:

A related study in Rakai, Uganda was designed to evaluate whether HIV-positive men with T cell counts over 350 who undergo circumcision are less likely to transmit HIV to their female sexual partners. Unfortunately, the trial could not move forward because of difficulty recruiting enough participants, and could not effectively answer the trial question: *are HIV-positive men who become circumcised less likely to transmit HIV to their female sexual partners?*

It is important to note that we do not yet have enough data to conclude whether having a male partner who is circumcised has any direct protective benefit for women. Nonetheless, reducing the number of new infections among men would probably mean that fewer women would be exposed to HIV over time.

Early analysis from this study suggested, but did not prove, that the female sexual partners of newly circumcised men could be at increased risk of HIV if they had sex before the wound completely healed. However, this data was not statistically significant and results could change with further research and analysis.

Still, these early data stress the importance of clearly communicating the risks and benefits of adult circumcision, including the need to abstain from sex for at least one month following the procedure to allow the wound to fully heal. Researchers are continuing to monitor the HIV-positive men who had already enrolled in the trial and been circumcised, as well as their female partners, to determine if circumcision could provide a long-term protective benefit to women.

SUMMARY OF DATA ON CIRCUMCISION AND HIV		
Adult Circumcision and HIV Prevention	What We Know	What We Don't Know / Why It Matters
<p>Are HIV-negative circumcised men protected from getting HIV during vaginal sex?</p> <p>What other prevention services did men in the trial receive, and how did it impact the level of protection?</p>	<p>Three randomized studies in Africa have shown that men who are circumcised are 50-60% less likely to get HIV during vaginal sex than men who are not circumcised.</p> <p>All trial participants had at least three study visits, where they received risk-reduction counseling, HIV testing, STI treatment and free condoms.</p>	<p>We don't know if these benefits will be the same in the US because there is much less female-to-male sexual transmission here. Male-to-male sexual activity is the predominant mode of HIV transmission in the US.</p> <p>We don't know if circumcision will be as protective in real-world settings—where men may not receive a comprehensive prevention package as they did in the trials.</p>
<p>Are HIV-positive men who are circumcised less likely to transmit HIV to women than HIV-positive men who are uncircumcised?</p>	<p>Observational studies have indicated that HIV-positive men who are circumcised may be less likely to pass on HIV to their female partners. However, the men in those studies had been circumcised as infants or as youth, so their wounds were healed before they became sexually active.</p> <p>In the Rakai study, early data suggests that women <i>may</i> be at higher risk for HIV if their newly circumcised male partner has sex with them before his wound completely heals.</p>	<p>Data from the Rakai trial are very preliminary and the trial was too small to be “statistically significant.” The trial will continue to monitor those who had already been enrolled.</p> <p>Ongoing monitoring will also help determine if there are long-term protective benefits for women, which we do not currently know.</p> <p>Whether circumcision has a directly protective benefit for women could be an important question for the US, where most women are infected through heterosexual sex.</p>

SUMMARY OF DATA ON CIRCUMCISION AND HIV (CONTINUED)

Adult Male Circumcision and HIV Prevention	What We Know	What We Don't Know / Why It Matters
<p>Is circumcision protective during anal sex?</p> <p>If so, is it just protective for the inserter (top) or can it also protect women and men who are penetrated (bottoms) if the top is circumcised?</p>	<p>Men in the African studies were asked about anal sex with women and men. One man in the Kenya trial and none in the Uganda trial said they had sex with a man. A few men in these trials said they had anal sex with women, but not enough to tell us whether circumcision is protective during anal sex. However, these data about rates of anal sex are based on self-reporting, which could be unreliable as it is a stigmatized behavior.</p> <p>In the US, two studies have observed that uncircumcised gay men and other MSM were twice as likely to be, or become, HIV-positive.</p>	<p>There have not been any randomized clinical trials to study the protective effect of circumcision during anal sex, either with men or women.</p> <p>Without clinical trials, we cannot confirm or disprove the observational findings, in order to determine the benefits of circumcision during anal sex. In addition, trials should evaluate risks and benefits for tops (insertive partners) as well as bottoms (receptive partners), to clarify issues for men who are both.</p> <p>Determining whether circumcision is protective during anal sex could be a key question for the US, since 47% of HIV transmissions occur through male-to-male sex. In addition, MSM around the world are at high risk of HIV, often having the highest prevalence and incidence in their countries.</p>
<p>Is circumcision safe to perform in HIV positive men?</p>	<p>Initial data from one of the studies found that HIV-negative and HIV-positive men had the same safety rate, but HIV-positive men took slightly longer for their wounds to heal.</p> <p>However, the trials had much higher safety rates than those reported in public health clinics—likely because the circumcision procedures were performed by highly trained medical staff in clean and sterile operating rooms.</p>	<p>We don't know how safe the procedure will be for HIV-negative and HIV-positive men when circumcision becomes more widely available.</p> <p>There is a need for hiring additional health care workers, adequate training and sterile equipment in developing countries in order to make circumcision more widely available.</p> <p>Circumcision of adult men in the US is extremely rare, and would require training for providers if it became more common.</p> <p>Generally, newborn males in the US are circumcised before their sero-status (if their mother is HIV-positive) or lifetime risk for HIV is determined.</p>

Circumcision in the US

Most males in the US are circumcised as newborns. However, the national rate of infant circumcision has been declining. The National Hospital Discharge Survey (NHDS) reported that newborn circumcision had dropped from 65% in 1999 to 57.4% in 2004.

There are also dramatic differences in circumcision rates between geographic regions. While almost 80% of male newborns in the Midwest were circumcised in 2004, only one-third of newborn males in the West were circumcised during that same year. Many factors play into these regional disparities, including immigration patterns, changing cultural norms, the religious and ethnic make-up of areas, and state differences in Medicaid coverage for circumcision.

Percent of newborn male circumcision, 2004	
Source: NHDS 2004	
Regions, as defined by US Census	% of male newborns circumcised in hospitals
West	31.7%
South	58.5%
Northeast	66.4%
Midwest	79.5%

Unfortunately, the only data available on male circumcision broken down by race and ethnicity is fifteen years old. In 1992, the National Health and Social Life Survey reported that 77% of men reported being circumcised, of whom 81% identified as white, 65% as African American, and 54% as Latino.²

In 1999, the American Academy of Pediatrics stopped recommending routine circumcision. Since then, sixteen states have dropped Medicaid coverage for circumcisions that are not considered medically necessary. Half of these states are in the West, where circumcision rates are the lowest.

States that do not provide Medicaid coverage of routine infant circumcision include: Arizona, California, Florida, Idaho, Louisiana, Maine, Minnesota, Mississippi, Missouri, Montana, Nevada, North Carolina, North Dakota, Oregon, Utah, and Washington.

HIV/AIDS and circumcision in the US

Right now, the only solid evidence we have on circumcision is that it reduced the risk of men in the sub-Saharan African trials getting HIV during vaginal sex. Female-to-male transmission is a much more common mode of transmission in Africa than in the US. In the US, nearly half (47%) of all new cases diagnosed in 2004 occurred in MSM. 33% of newly-diagnosed people were exposed through heterosexual contact³— most of whom were women. In the US, the vast majority of heterosexual HIV transmission is from men-to-women, not women-to-men. It is also believed that some men who report contracting HIV from women may do so because of the stigma around male-to-male sex.

The following table lists states with the highest rates of new AIDS cases and shows the percentages of new infections due to male-to-male and heterosexual contact. Data on the gender of individuals exposed during heterosexual sexual contact were not available.

² CDC HIV/AIDS Science Facts: Male Circumcision and Risk for HIV Transmission: Implications for the United States. March 2007.

³ CDC HIV/AIDS Science Facts: Male Circumcision and Risk for HIV Transmission: Implications for the United States. March 2007.

US/State**	Exposure category of infections (Percent)	
	Male-to-male sexual contact	Heterosexual contact (includes male-to-female – the majority of cases -- & female-to-male)
TOTAL in US	44.0%	13.4%
New York	28.6%	11.5%
Florida	40.3%	24.0%
California	67.6%	5.7%
Texas	55.1%	10.6%
Georgia	44.8%	14.0%
Illinois	49.8%	10.4%
Maryland	26.5%	18.3%
Pennsylvania	39.2%	16.9%
New Jersey	20.6%	15.5%
Louisiana	40.0%	11.7%
District of Columbia	44.5%	15.2%



A Closer Look at California

California has a roughly 30% circumcision rate among newborns, which is due in part to the high numbers of immigrants and Latino/as. The state does not provide Medicaid coverage of routine infant circumcision. In California, nearly 70% of HIV infections occur during male-to-male sexual contact. If circumcision is judged to be protective in the US context, there are complex policy issues to be tackled in this and other states.

Reported AIDS Cases Among Adults and Adolescents, by Transmission Category, Cumulative through 2005

**States listed are ranked top ten for new AIDS infections. DC not included in ranking.

To find statistics on your state: <http://www.statehealthfacts.org>

Nearly all circumcisions in the US are performed on infants. And we don't know which of them will be gay men, heterosexuals, or non-gay-identified MSM. We do know, however, that there are much higher rates of HIV in some communities in the US, most notably the African American community. Thus, it may be possible to advise parents about the impact of circumcision on their children's lifetime risk of HIV, using mathematical models that incorporate racial/ethnic data.

We also need further research to determine whether circumcision is protective against HIV during anal sex, including for both male and female partners. This research should explore whether insertive partners (tops) are less likely to get HIV if they are circumcised, as well as any possible protection for their receptive partners (bottoms).

The CDC is currently examining the potential role of circumcision as an HIV prevention intervention in the US, and plans to convene a stakeholder consultation in April or May 2007 in order to develop a research agenda and potential recommendations for circumcision in the US.

Summary: Explaining the Circumcision Data in the Context of the US Epidemic

Current data show that circumcision dramatically reduced the risk of HIV for men from vaginal sex in trials in three countries in Africa, but does not tell us about the protective benefits during anal sex. A majority of new infections in the US are due to male-to-male sex, and studies with gay and other MSM communities should be a top priority for the US research agenda. The second most common mode of transmission is from men to women, and we do not currently have enough information about the potential benefit for women if their male partners are circumcised.

The studies in Africa took place in areas with high prevalence and low circumcision rates. In the US, there are many disparities between communities in HIV risk and circumcision rates. We should begin to identify communities, such as African American and Latino communities, with high HIV risk and low circumcision rates, where implementing circumcision may have an impact. These communities could serve as future circumcision study sites in the US and could be prioritized for small pilot programs on circumcision as an HIV prevention tool.

However, given the differences between the US and African epidemics, it may indeed be that the projected impact of circumcision is negligible in the United States, or may be significant only in limited settings.

HIV/AIDS AND CIRCUMCISION IN AFRICA AND THE US		
Issue	Africa	US
HIV prevalence	High: generalized epidemic.**	Low: Risk is primarily limited to certain communities. High: Generalized epidemic in the African American community, and in gay men and other MSM of all races.
Primary mode of HIV transmission *	Heterosexual sex, with male-to-female transmission primary, but female-to-male transmission common.	Male-to-male sexual contact (47% of cumulative AIDS cases in the US, and half of new cases) is primary mode, but varies greatly by region and includes substantial rates of male-to-female and IDU transmission.
Circumcision rates	Overall very low, generally performed in adolescents. Very high in certain communities.	The CDC estimates that 75-80% of adult and adolescent males in the US were circumcised as infants, but recent statistics show that newborns are currently being circumcised at a much lower rate, about 50%.

* Within both Africa and the US, there are many diverse communities and varying epidemics.

** An epidemic is considered 'generalized' when more than 1% of the general population is HIV-positive. In the US, the overall prevalence in the general population is less than 0.5%, but it is significantly higher in the African American community and much higher among gay men and other MSM of all races/ethnicities.

THE BOTTOM LINES FOR COMMUNITY EDUCATION IN THE UNITED STATES

Can I get HIV if I am a circumcised man? Yes.

Can I transmit HIV if I am circumcised? Yes.

If I have sex with a man who is circumcised, am I less likely to get HIV? We do not have any evidence on this at the current time, either for men or women.

If I am circumcised, does it reduce the chance that I will get HIV? Maybe, but it is unclear if the data from the African heterosexual studies can be applied to gay, MSM, or heterosexual men in the United States.

If I am HIV-positive and circumcised, does it reduce the chance I can transmit HIV? We don't know yet.

I heard that HIV-positive men who were circumcised in one of the studies had higher rates of transmitting HIV. Are HIV-positive men here more likely to transmit to women if they are circumcised? In that study, initial data seemed to show that men who did not wait until their wound healed may have been more likely to transmit HIV. But the data were not statistically significant — meaning the observation is not a sure thing — and further analysis is being conducted. Regardless, the vast majority of circumcised men in the US were circumcised as newborns, meaning the wound is healed many years before they become sexually active.

If my newborn son is circumcised, will this reduce his lifetime chances of getting HIV? At this time, we don't know. It may be that it could make a difference in high prevalence communities, but it is also possible that it may make no difference given the distinctions between the US epidemic and the African context.

If I am a man who has anal sex with men, am I more at risk if I am not circumcised? Several studies observed that MSM were more likely to be, or become, HIV-positive if they were not circumcised. However, there has been no randomized study that enrolls uncircumcised men and then follows the outcomes of two groups: those who are randomly selected for circumcision and those who remain uncircumcised. That could potentially give us information of similar certainty to the studies that were done in heterosexuals in Africa. In short, we still don't have solid evidence that circumcision can protect against HIV during anal sex.

If I am a transgender woman who has had sex realignment surgery (bottom surgery), how does this research apply to me? If a woman is not circumcised at the time of her surgery, the foreskin may be utilized in the surgical reconstruction. There is no data at this time about how this impacts HIV risk.

POLICY ISSUES TO CONSIDER ON CIRCUMCISION, HIV AND THE UNITED STATES AIDS EPIDEMIC

Community education and access to information

- AIDS service organizations and community-based organizations must have access to regularly updated information and resources to provide accurate information explaining what we know and don't know about circumcision and what it could mean for US communities impacted by AIDS.
- This information should include accurate and current statistics on HIV transmission in their communities, including a breakdown of gender (men-to-women and women-to-men transmission) within heterosexual transmission rates.
- HIV/AIDS service-providers and advocates also need access to information on rates of circumcision in the communities they work—broken down at the state level and by race/ethnicity.

Research needs and data collection

- Clinical studies on the potential protective benefit of circumcision during anal sex are urgently needed and should be a top priority for the US research agenda. Research studies could be possible—and trial designs should be explored—in African American and Latino MSM communities, where HIV incidence is high and circumcision rates are relatively low.
- Hospitals, especially those in states that do not provide Medicaid coverage of circumcision, should track whether cost is a barrier for parents who do not have their children circumcised.
- State health departments and CDC should begin routinely collecting data on circumcision in newly reported HIV and AIDS cases in men, cross-referenced by mode of transmission, region and race.

Domestic policy

- The CDC is hosting a stakeholder consultation in the next several months to develop a US research agenda and discuss implementing a US policy on circumcision. We strongly support broad inclusion of community representatives at this meeting, including people living with HIV, gay men and other MSM, people from communities with high rates of HIV and low circumcision rates, and representatives from community-based and AIDS service organizations.
- Since 1999, the American Academy of Pediatrics has NOT recommended routine circumcision for newborn males. Communities should advocate for the American Academy of Pediatrics to revise this policy to reflect new data on the potential health benefit of circumcision and support re-instatement of Medicaid and other third-party payment coverage of circumcision.
- States should re-consider Medicaid payment for circumcision if they have eliminated coverage.

FOR FURTHER INFORMATION:

Male Circumcision and Risk for HIV Transmission: Implications for the United States (CDC)

<http://www.cdc.gov/hiv/resources/factsheets/circumcision.htm>

New Data on Male Circumcision: Policy and Programme Implications (World Health Organization)

<http://www.who.int/hiv/mediacentre/news68/en/index.html>

Advocacy Materials from the AIDS Vaccine Advocacy Coalition

<http://www.aidsvaccineclearinghouse.org/MC/#new>

or contact CHAMP at 212-937-7955 x 5

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