A New Way to Protect Against HIV?
Understanding the Results of Male Circumcision Studies for AIDS Prevention

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This brochure is designed to help prevention advocates understand the ramifications of findings from ongoing studies of male circumcision for AIDS prevention, and to anticipate the opportunities and challenges that would emerge, if additional clinical trials of male circumcision show a benefit for AIDS prevention. It is part of AVAC's "Anticipating Results" series, which provides timely analysis of trials of AIDS vaccines and other new prevention technologies. For other publications in this series, visit www.avac.org.

A pivotal moment in the search for a new way to protect against HIV

In December, 2006, new evidence from clinical trials confirmed male circumcision as the first new biomedical HIV prevention strategy since the female condom was approved for use 13 years ago.[1]

This announcement brings exciting opportunities as well as challenges. Based on data from three trials, it appears that male circumcision reduces men's risk of HIV infection during vaginal sex by roughly 50%. Even though the rates of protection may not be as high outside of the controlled environment of a clinical trial, this is still a striking finding.

Adding the offer of safe, sterile male circumcision to existing AIDS prevention programs could avert many infections and save many lives. These programs could also provide a new way to reach men and adolescent boys who are frequently under-represented in health clinics and AIDS prevention programs.

AIDS prevention advocates have a very important role to play in the roll out of male circumcision at a global, national and local level. Two specific priorities for this work are:

1) To ensure that male circumcision is made available in programs which are staffed by trained personnel with the necessary supplies for performing safe, sterile and confidential procedures.
2) To ensure that these programs must also offer male circumcision *in addition to*, and not as a substitute for, other tools for risk reduction including counseling, male and female condoms, clean needles and harm reduction information.

Swift and urgent action must be taken to secure these goals. Male circumcision is a surgical procedure. If it is done in unsterile conditions or by untrained personnel, there is a substantial risk of infection, complication and even death. Demand for the procedure could increase sharply

[1] Before the US FDA approval of the female condom in 1993, AZT was identified in 1987 as an effective means of preventing mother-to-child transmission of HIV. Male condoms, clean needles, blood bank screening, post-exposure prophylaxis and universal precautions for health care workers had been identified previously.

as news of the potential benefit spreads. Safe, sterile, free services must be scaled up swiftly so that a vacuum is not created for exploitation by unsafe practitioners.

Roll out of male circumcision therefore requires work in many quarters: human resources, commodities procurement, communications, training, and technical assistance for governments and health ministries.

WHO and UNAIDS have undertaken important work in this area and should be fully funded to provide necessary leadership and technical assistance. It is critical that these and other normative agencies continue the important work already underway to develop guidelines and technical assistance tools for countries considering introduction or expansion of male circumcision programs to reduce the risk of HIV infection.

As important as these steps are, they are not sufficient. WHO/UNAIDS are not implementing agencies and the world has already witnessed the failure of funders and implementing groups to meet the "3 by 5" target which these groups set for treatment access, which aimed for 3 million individuals on antiretroviral treatment worldwide by 2005.

Simply put, guidance alone is not enough. Operational research is needed, as is leadership from developing countries and funding for health programs to ensure that male circumcision introduction is introduced in addition to, and not instead of, other interventions.

AVAC is committed to working with partners to develop campaigns to resource these programs wherever possible, and to monitor implementation of WHO/UNAIDS guidelines when they are made available.

This brochure is designed as a tool for advocates, policy makers and other stakeholders interested in supporting the roll out of male circumcision as a tool for reducing the risk of HIV infection via vaginal sex among circumcised men.

Box 1: The Key Points

- Three clinical trials have shown a protective benefit of approximately 50% for circumcised, HIV-negative men engaging in vaginal sex in three clinical trials in sub-Saharan Africa.
- Based on this evidence, there is a strong rationale for swiftly rolling out male circumcision as a strategy to complement current effective interventions like condoms, clean needles and behavior modification. Male circumcision cannot replace any of methods.
- There are no clinical trial data on the benefits of male circumcision for men who have sex with men or on the benefits for the female partners of circumcised, HIV-infected men.

- Urgent, coordinated, well-funded action will be needed to translate these results into the real world, where shortages of human resources and medical commodities present significant challenges.

- Male circumcision represents an exciting opportunity to reach adolescent boys and young men with one of several critical interventions. These benefits will be offset if the intervention is not provided in safe, sterile, confidential settings as part of a comprehensive package of services and information related to HIV/AIDS and health.

What needs to be done?

To be effective, roll-out of male circumcision programs should achieve the following five over-arching goals. AIDS prevention advocates working on this issue can help the implementation process by maintaining focus on these objectives:

- Male circumcision must be offered in addition to, not instead of, the full array of proven HIV prevention strategies

- Male circumcision must be offered in programs which clearly explain the benefits and limitations of the procedure

- Male circumcision must be offered in appropriately staffed programs: a well-trained medical aide can perform the procedure as well as a surgeon provided she has adequate supplies of essential commodities

- Male circumcision must be offered in programs that contain clear, cultural- and context-specific messages which counteract changes in risk behavior which might follow the procedure

- Male circumcision must be offered in programs that are sensitive to the different meanings of the procedure, delineating its use as a strategy for HIV risk reduction, separate from its uses as marker of religious or tribal affiliation, *and* from the dangerous and wholly un-related practice of female circumcision

There are significant barriers to achieving these goals. To overcome them, funders, health ministers, program managers, advocates and other stakeholders will need to:

Anticipate and address human resources and infrastructure needs
The slow progress of roll out of antiretroviral therapy, prevention of mother-to-child transmission services, and abysmal shortages of male and female condoms worldwide are all stark reminders of how the world has failed to make good on proven interventions in the past.

As with the services listed above, male circumcision will be affected by gaps in funding and staffing of health care systems in the developing world. Without trained staffed and supplies, the procedure will not be safe and its efficacy will be severely compromised.

Developing countries must take the lead on this issue. Ministries of health should develop roll out plans which allocate new resources to male circumcision, and which make provisions for cadres of trained service providers, including medical officers and aides, given the extreme shortage of surgeons in virtually all developing countries.

In many instances these plans will require financial and technical assistance to become a reality. Donors and normative agencies like WHO and UNAIDS have begun to play this role, and should continue, with expanded financial support and recognition of this issue as a top priority for 2007 and beyond.

Create and execute an operational research agenda

An efficacy finding from a clinical trial (or even three clinical trials!) does not mean that all the questions about a procedure have been answered. The trials that have shown efficacy of male circumcision in reducing men's risk of HIV infection through vaginal sex are only the beginning.

Operational research is needed to learn more about best practices for male circumcision, even as it is being rolled out. Operational research answers questions about how to design effective programs in different settings. When it comes to male circumcision, there are many, many questions to answer. These include:

- **Best practices for integrating male circumcision services with existing AIDS prevention programs and messages**
  - From the community and individual perspective: How can male circumcision be positioned as an *additional* strategy rather than a replacement for male and female condoms and other risk-reduction techniques?
  - From the provider/program perspective: What resources are needed to add male circumcision to clinic services? For HIV counseling centers and other points of service that may provide information about male circumcision, what are the best approaches to communicating with staff who are performing the counseling, surgery, and follow-up for adverse events? Who should perform male circumcision and how should they be trained and monitored?
  - From the policymaker perspective: How do countries evaluate whether or not to add male circumcision to their preventive offerings? What are optimal strategies for phased rollout in different settings?

- **Changes in risk perception or behavior in circumcised men and their partners**
  The benefits of male circumcision could be offset by changes in risk-taking behavior if circumcised men and/or their partners assume that male circumcision provides full protection against HIV. Introduction of male circumcision therefore has to take place in the context of campaigns that reinforce the limitations (as well as the benefits) of male circumcision as an AIDS prevention tool and the need to use other forms of protection.

- **Maintaining safety and efficacy in non-clinical settings**
  The trials evaluating male circumcision for AIDS prevention have had the surgical procedure performed by highly-trained health care workers in controlled, sterile

settings. If male circumcision is shown to have a benefit, there will be increased demand for male circumcision and it is highly likely that private sector and informal points of service will emerge, which may compromise the safety and therefore the efficacy of the intervention. Scale-up will therefore have to include sufficient resources to meet demand in safe settings, and accurate, up-to-date information about safe points of service for the procedure.

- **Relationship of male circumcision for AIDS prevention to other contexts in which male circumcision is performed**

  For many communities around the world, male circumcision is a traditional practice with specific, deeply-rooted cultural significance. These traditional practices may sometimes involve non-medical professionals and non-sterile surgical procedures; they may also remove less of the foreskin than is removed during the procedure when performed for AIDS prevention. Rollout of safe, sterile male circumcision for AIDS prevention must be context-specific, address these concerns, and consider the roles of traditional male circumcision practitioners as conveying critical messages and potentially adapting the practice to ensure safety and efficacy for AIDS prevention.

- **How to respond to potential negative responses to male circumcision**

  Male circumcision is a procedure with great meaning and significance. There are constituencies that argue against it for a variety of reasons and will likely continue to do so regardless of the final data on AIDS prevention benefits. Evidence-based reporting on the attitudes, impact and community knowledge of male circumcision as an AIDS prevention tool will be among the most effective responses to these concerns. This research should also explore optimal strategies for distinguishing between male circumcision, with its potential health benefits, and female circumcision, which is a painful and dangerous procedure with no health benefits or preventive effect for AIDS, sexually transmitted infections or other conditions.

These open questions should not delay implementation. In fact, introduction of carefully-planned programs is the only way this information can be gathered and shared.

Box 2: Urgent Action Required

The following action items must be accomplished immediately to support access to male circumcision as a strategy for AIDS prevention:

1. Developing countries, particularly those in sub-Saharan Africa, should develop communications campaigns with accurate, context-specific information about male circumcision as an AIDS prevention strategy. They should also develop local plans for assessing need and planning for implementation. NGOs, CBOs, professional associations, and ministries of health will be instrumental in developing and disseminating these messages.

2. Developing countries, particularly those in sub-Saharan Africa, should use best available data to estimate the need for infrastructure and the financial and human resources required for

introduction of male circumcision in varying contexts; these should be integrated into international efforts to improve developing world health systems.

3. A stakeholder meeting should be used as the foundation for developing a coordinated, funded operational research agenda to address additional questions about male circumcision.

4. Treatment and prevention advocates should develop a network for holding key stakeholders accountable for these and other action items, including ensuring that funding for male circumcision rollout, should it be warranted, does not divert resources from other interventions or from additional research on new prevention technologies.

Box 3: History and Rationale of Male Circumcision for HIV Prevention

Male circumcision is one of the most common surgical procedures in the world, with 25-30 percent of men worldwide undergoing the procedure at some point in their lives. Male circumcision is practiced for many reasons: hygiene, religion, tradition or a combination of these.

In the last decade, male circumcision has become a focus of attention in international HIV prevention research. In the late 1980s, scientists observed that in some places in the developing world, levels of HIV infection were lower in places with high rates of male circumcision. There are always multiple explanations for observed correlations such as this one. Experimental trials were designed to test the hypothesis that providing circumcision to men would reduce their risk of acquiring or transmitting HIV.

The exact reason why male circumcision provides a protective benefit against HIV infection during vaginal sex is unknown. The male foreskin contains a concentration of HIV target cells, including Langerhans cells, which are immune cells that are targeted by HIV during the earliest stages of infection.

In particular, the inner side of the foreskin of the penis is highly susceptible to HIV infection; the skin that remains after circumcision is thought to be less so. In one laboratory study, scientists found that the tissue samples of the inner foreskin absorbed HIV up to nine times more easily than samples of cervical mucosal tissue from women. It is possible that circumcision helps protect men from HIV infection by removing these targets for HIV.

Data from the recent trial in Uganda show that circumcision is associated with a lower prevalence of genital ulcer disease (GUD), which is a risk factor for acquiring HIV . Also, removal of the penile foreskin causes more rapid drying of the penis after sex, bathing or urination. This may reduce the likelihood of bacterial or other sexual infections which flourish in damp environments.

There are still no data on whether circumcision of HIV-positive men provides reduces the risk of transmission to female partners. All of the factors that apply to HIV-negative men also apply to HIV-positive circumcised men.

Male circumcision trials to date

As of late 2006, three trials have shown a protective benefit of male circumcision in reducing risk of HIV infection through vaginal sex. These trials took place in South Africa, Uganda and Kenya and are summarized in Table 1.

In all of these trials, male study volunteers agreed to be circumcised and to be randomized to one of two study arms: a group in which all men were offered male circumcision immediately after randomization and a control group in which they were offered circumcision at the end of the study follow-up period.

All three studies were closely monitored by a Data and Safety Monitoring Board. The role of a DSMB is to assess progress in clinical trials and make recommendations on whether to continue, change or terminate them. If interim data review by a DSMB shows that there is a significant benefit for individuals in the intervention arm, the DSMB can find that it is unethical to continue the randomized study. In this case, the board can recommend that all volunteers be given access to the intervention immediately.

In all three trials, the Data and Safety Monitoring Board conducted interim reviews and found a significant benefit in terms of risk reduction in the circumcised men versus the men in the control arm. In each trial, the Data and Safety Monitoring Board recommended that all of the volunteers be offered circumcision immediately. In other words, the evidence for a protective benefit of circumcision in the study population was strong enough that it was considered unethical to continue the study without offering circumcision to the control group.

The first trial to show efficacy was conducted in South African trial. These data were presented at a conference in July 2005; the data were published in November 2005.[2] The trials in Kenya and Uganda confirmed this finding. The Ugandan trial also included a broader age range (men aged 15-49).

The data were comparable across the three trials; in each case there was a protective benefit of greater than 50% among the men in the intervention arm. It is important to note that this reduction in risk was seen in clinical trial settings where men received treatment for sexually-transmitted infections, free condoms and circumcision performed in sterile conditions by trained personnel.

All three trials are described in Table 1. There are some key differences among the trials, particularly the age range, which is much wider in the Ugandan trial. Other differences are the

[2] B. Auvert, et al. Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial. *PLoS Medicine* Vol. 2, No. 11, e298 doi: 10.1371/journal.pmed.0020298

technique used for circumcision (both the sleeve method and the forceps-guided method are widely used worldwide) and the frequency of study visits.

A fourth, ongoing trial in Uganda has enrolled HIV-infected men. This study will gather data on whether male circumcision is safe in HIV-infected men, reduces selected STIs in these men, and on whether the procedure may reduce HIV and STI transmission to female partners. Data from this trial are anticipated in late 2007.

The two Ugandan trials have been conducted through the Rakai Health Sciences Project in southern Uganda and are closely coordinated. In addition to the data from the studies of HIV-positive men, HIV-negative men, and men who have asked not to know their status, this research project is also following community members who are not enrolled in the trials, to assess their attitudes and behaviors.

TABLE 1: Completed and Ongoing Prospective, Randomized Trials of Male Circumcision for HIV Prevention

Funded by / Conducted by	Study Population	Study Question/ Design / Method[3]	Key Findings / Timeline for Results
SOUTH AFRICA			
ANRS / ANRS, National Institute for Communicable Diseases (South Africa)	3,274 18-24 year old men in a semi-urban, informal settlement	Does circumcision reduce male risk of HIV infection by female partners? Study visits at months 3, 12, 21 post-randomization; circumcision performed using the forceps guided method	Male circumcision reduced the risk of HIV infection by 60-61%
UGANDA			
National Institutes of Health / Johns Hopkins University, Rakai Health Sciences Project	Approximately 5000 15-49 year old men in rural Uganda (Rakai District)	Does circumcision reduce male risk of HIV infection by female partners? Four visits over two years of follow-up; circumcision performed using the "sleeve" method	Male circumcision reduced the risk of HIV infection by 48%
Bill & Melinda Gates Foundation / Johns Hopkins	800 HIV-infected men and 1000 men who decline to know their status	Does circumcision reduce female risk of infection by HIV-positive, circumcised male partners?	Study ongoing; data expected in late 2007

[3] Both the forceps-guided (or foreskin clamp) and sleeve method are performed under local anaesthesia. The forceps-guided technique uses a surgical instrument called a forceps to pull the foreskin forward prior to removal; the sleeve method uses surgical incisions to remove the foreskin. In the Ugandan trial of the forceps-guided method cauterization and stitches were used to minimize bleeding and close wounds; the Kenyan trial used the sleeve method with stitches to close the wound.

University, Rakai Health Sciences Project	5000 women partners of men enrolled in the Ugandan studies	Four visits over two years of follow up; circumcision performed using the "sleeve" method	
KENYA			
National Institutes of Health & Canadian Institute of Health Research / University of Nairobi, University of Manitoba	2784 18-24 year old HIV-negative men	Does circumcision reduce male risk of HIV infection by female partners? Six study visits (months 1,3,6,12,18,24) over two years; circumcision performed by forceps guided method; patients encouraged to receive all outpatient health care at study clinic	Male circumcision reduced the risk of HIV infection by 53%

What the current research does (and does not) tell us?

The most important questions that the research to date has answered are:

- When performed in sterile, clinical settings, is circumcision safe and does it help reduce the risk of HIV acquisition in circumcised, HIV-negative men?

- What are the rate and scope of side effects of male circumcision when performed aseptically by trained providers in clinical settings?

In addition, these studies have gathered information about whether male circumcision affects the rates at which men and their partners get other sexually transmitted infections. They have also looked at how sexual behavior is affected by male circumcision, if at all (e.g., after male circumcision, what are the changes in frequency of condom use or number of partners). Finally, the Ugandan trial is also gathering information on community attitudes from 3000 individuals from Rakai District who are not participating in the study.

These trials provide limited data available on rates of risk behavior among circumcised and uncircumcised men in these trials.

Such data are important, since the benefits of male circumcision could be off-set by an increase in high-risk acts like unprotected sex or an increase in the number of partners.

In the South African trial, men in the circumcision arm reported slightly higher rates of high risk acts than did men in the control arm. The procedure still reduced HIV risk in the intervention arm. The data for the Ugandan and Kenyan trials have not been fully analyzed to learn about patterns of behavior. Early data suggest that there were no major differences between the control and intervention arm. But we must wait for the full analysis, and remember that these data have

limited relevance to "real world" conditions, since volunteers received periodic risk-reduction counseling as part of their participation.

These trials do not provide any data about whether male circumcision provides protection during anal sex.

This is relevant to men who have sex with men and to heterosexual couples. A single prospective, observational study in California appeared to show a reduction in risk of acquisition to the insertive partner among circumcised men who have sex with men. But no randomized trials have been conducted to date.

This lack of information has the potential to lead to confusion and conflicting messages, particularly in communities of men who have sex with men in the developed world. It is important for organizations in the US and Europe to provide clear information about the strengths and limitations of the data which do exist; and to support informed dialogue among various communities.

Male circumcision performed by trained personnel in aseptic conditions has health benefits including reducing risk of HIV acquisition during vaginal sex; the data cannot be extrapolated to anal sex, but the procedure will not cause physical harm—and could potentially have a benefit—if performed under these conditions.

These trials do not answer the question of whether male circumcision provides a protective benefit to the female partners of circumcised, HIV-infected men.

This research is ongoing and should be considered a top priority. Determining whether there is "bidirectional" protection (from men to women and from women to men) for the procedure will have a significant impact on decision-making at the level of funders, program managers and governments.

Box 4: Circumcision, Culture and Tradition

Male circumcision is a marker for tribal and religious identity in many parts of the world. In many communities, it is a rite performed at a specific point in the male lifecycle.

In the studies that have taken place to date, education about the possibility that male circumcision could reduce the risk of HIV infection appears to have been well-received at the community level, regardless of cultural or traditional attitudes in the surrounding area. The trials have enrolled rapidly in both Kenya and Uganda.

It is important to remember that cultural and religious beliefs, rituals and attitudes towards circumcision will play a critical role in acceptability of male circumcision when introduced in the context of HIV prevention. This is true for communities that practice circumcision traditionally and for those that do not.

Internationally, there are also groups that are opposed to male circumcision altogether, and that have voiced opposition to introduction of male circumcision as an HIV-prevention strategy, thereby imperiling access to a procedure which could save many lives and avert thousands of HIV infections.

AIDS prevention advocates must work together to both acknowledge the importance of local context, attitudes, and to effectively anticipate and respond to potential sources of opposition.

Box 5: Selected Critical Points for Male Circumcision Public Health Messages

There are multiple messages related to male circumcision that will need to be communicated consistently, clearly and in context-specific formats to men considering the procedure and their sexual partners. Rollout of male circumcision as an AIDS prevention strategy should include funding for documentation and dissemination of effective messaging strategies in multiple contexts. Some of the core messages are:

- **Partial efficacy**: Male circumcision is not 100 percent protective and is not a substitute for other methods of HIV risk reduction. Its efficacy in protecting against transmission during anal sex has not been studied or proven.

- **A procedure with multiple "meanings":** Male circumcision is a strategy for AIDS prevention; it is also part of deeply-rooted cultural or religious traditions in many parts of the world. Introducing it as an AIDS prevention strategy will mean educating medical providers about the relevance of the surgery and reaching out to communities about the potential benefits of male circumcision for AIDS prevention, regardless of whether it is a cultural norm.

- **Context-specific programming and positioning:** There are opportunities for programs in which traditional and AIDS prevention functions are complementary; there is also a need for male circumcision programs that stress that the procedure does not stigmatize a specific identity or population as being at higher-risk for HIV exposure.

- **Male versus female circumcision:** Male circumcision, which has a positive health benefit, is in no way equivalent to female circumcision, which is dangerous to the health of girls and women and does not reduce the risk of AIDS or other diseases.

- **Scope of protection:** The nature of bi-directional protection (HIV-positive man / HIV-negative female partner versus HIV-negative man / HIV-positive female partner) is not fully known at this time. The data from future trials will provide insights and these will need to be translated into clear messages appropriately targeted at various groups including HIV-infected women, men who have sex with men. In addition, the studies to date have focused exclusively on transmission risk associated with penile-vaginal intercourse. There are no clinical trial data on protection for anal intercourse.

So what needs to happen now?

When a new biomedical intervention for HIV/AIDS is identified, countries, donors and other stakeholders look to "normative" agencies like the World Health Organization and UNAIDS to provide guidance on introduction and messaging.

In the case of male circumcision, the WHO, the UNAIDS secretariat and its partners are preparing specific policy recommendations for expanding and/or promoting male circumcision at the country level. These activities will build on work that WHO/UNAIDS began after the findings from the South African trial were announced in 2005.

The International AIDS Society has likewise urged the development of international guidelines that underscore the fact that male circumcision is a surgical procedure that must be performed safely, in a sterile, clinical environment, with opportunities for medical follow up.

All of these bodies have emphasized that male circumcision will not replace any existing strategy and that it does not eliminate the need for continued research on other new prevention options like AIDS vaccines and microbicides.

These moves at the international level are essential but they are not sufficient to ensuring successful roll out of male circumcision to protect against HIV infection.

Development of international guidance must be complemented by funding and technical assistance at the country level to help national governments and health ministries develop and implement policy around male circumcision for national AIDS programs.

Some of the focus countries for the US President's Emergency Plan for AIDS Relief (PEPFAR) have also committed resources to expanding access to male circumcision among its focus countries. Male circumcision should be considered for introduction in all PEPFAR-funded prevention programs as part of a comprehensive prevention program which includes male and female condoms and risk reduction counseling.

PEPFAR and other international initiatives cannot substitute for the work of national health ministries and AIDS control programs. Male circumcision may be perceived as costly relative to other prevention initiatives (see Box 6) and must be funded appropriately, with new resources. Every effort should be made to minimize the diversion of resources from other sectors of the AIDS response and/or sexual and reproductive health programs to male circumcision.

If safe, effective programs are not put into place quickly, there is a risk of private sector and informal practitioners filling the void and offering substandard services that carry the risk of wound infection, HIV and hepatitis B transmission (via nonsterile instruments), other serious, potentially fatal complications, and a missed opportunity for the counseling that needs to be provided as part of the service.

However, while there is a need for swift implementation, introducing and scaling up a new intervention *takes time*. This is true whether it is a commodity such as a condom, or a surgical procedure such as male circumcision. The best-prepared countries will likely adopt a phased-in

approach, which allows for operational research and the development of best practices that can be applied as the program expands.

Under these circumstances, timely communication to multiple audiences and through multiple channels is essential. Some of the critical messages to be considered are summarized in boxTK.

In the short-term, AVAC recommends that:

- *Countries undertake immediate outreach to medical professionals, community groups, opinion leaders and AIDS advocates and activists who will play a critical role in disseminating correct information about male circumcision. This step can happen even as a more formal process of developing formal country policy is being launched.*

- *Community groups initiate needs assessments and outreach campaigns to identify effective messages and communication channels for conveying them to multiple stakeholders.*

Looking ahead, AVAC anticipates the need to mobilize additional resources to ensure the sustainability of safe, effective male circumcision programs that place the procedure in the context of other AIDS prevention interventions (see Box 7). Advocacy will likely be needed to meet these goals.

In the mid-term, AVAC recommends that:

- *The Global Fund to Fight AIDS, Tuberculosis and Malaria, PEPFAR and other funding streams provide new resources for scale-up of male circumcision programs, including funds for training, monitoring and evaluation, and staffing.*

- *Funders, advocates and other stakeholders working on human resources challenges related to health systems in the developing world incorporate staffing needs for male circumcision programs into their plans and advocacy agendas*.

- *An operational research agenda is developed and funded to ensure that answers to important questions are gleaned as rollout unfolds.*

Finally, the next several years will bring data from studies of other new AIDS prevention approaches including cervical barriers, microbicides, vaccines, pre-exposure prophylaxis, and treatment of HSV-2 infection. An efficacy finding from any of these studies will raise many of the same challenges around messaging, funding, and implementation. Many of the solutions will also be the same. Steps should be taken to maximize the impact of male circumcision today and of additional interventions in the future.

Starting now, and continuing over the long term, AVAC recommends that:

- *Researchers, implementers and community groups working on AIDS prevention develop and share consistent messages and best practices concerning the introduction of new interventions into existing programs.*

- *Country-level programming take a comprehensive and forward-looking approach to AIDS prevention, with new interventions added to existing offerings in the context of clear messages about partial efficacy, the research pipeline, adolescent vulnerability and other related issues.*

- *Clinical trial sponsors and sites develop scenarios for the cost and size requirements of future prevention trials of new partially effective interventions (see Box 7), and use these estimates to secure adequate funding for the next generation of trials.*

Box 6: Program costs and requirements

Costs for implementation of male circumcision will vary. One estimate, based on experience in Kenya, puts the costs at approximately US$25 per procedure (using the forceps-guided method).[4] These costs include US$8 for medical commodities (sutures and needle, gauze, bandaging and analgesic), US$7 for surgical preparation (preparing the room, cleaning linens, sterilizing instruments), and US$10 in "overhead" (physician's fee, maintaining the room and equipment, and utilities). The investigators in the Ugandan studies estimate the cost per procedure at US$69.

There is a growing body of work on cost-effectiveness of male circumcision procedures. One study that used parameters similar to those in the Orange Farm community, where the first trial was held, found that in a population with an adult male HIV/AIDS prevalence of 25.6%, at full male circumcision coverage, every 1000 circumcisions would avert an estimated 308 infections over 20 years -- two-thirds in men and one-third in women. The estimated cost per HIV infection averted (HIA) is US$181, and net savings are estimated at US$2.4 million.[5] Here too, the Ugandan estimates are slightly higher, ranging from TK to TK.

Operational research will help refine estimates of program costs and identify strategies for lowering them, and further improve cost-effectiveness through techniques such as "task-shifting" of surgical procedures to nurses and medical officers and negotiation for affordable supplies.

In every setting, advocates should emphasize that successful implementation of male circumcision programs includes:

- Spaces for confidential counseling, surgery and, if necessary, post-operative recovery
- Sterile surgical equipment and supplies including gauze, gloves, steam for sterilizing instruments, bandages, and other commodities

[4] David Wilson and Joy de Beyer. *Male Circumcision: Evidence and Implications* World Bank Global HIV/AIDS Program (2006).
[5] http://www.aids2006.org/pag/Abstracts.aspx?AID=18449

- Trained staff including counselors, medical personnel to perform surgeries, and community educators to conduct outreach and follow-up and who are compensated for taking on these responsibilities

Funding for these elements must be sustainable.

In Zambia, a USAID-funded project helped strengthen male circumcision services in three public health facilities. When barriers such as cost to the patient and lack of trained staff were removed, the project saw a three- to four-fold increase in the number of surgical procedures performed. However, these services could not be sustained when donated consumable supplies ran out.[6]

Box 7: Implications for future trials of AIDS vaccines and other new prevention technologies

A positive finding for male circumcision in the current trials would be terrific news for the field of AIDS prevention. It would also bring new challenges for trial sponsors and sites that plan additional trials of AIDS vaccines and other new prevention technologies.

These trials would still be important and relevant. One reason is that the impact of male circumcision as an AIDS prevention strategy will be greatest in men. There is still a critical and unmet need for AIDS prevention methods that women can initiate and control. Another reason is that the best strategy for significantly slowing the rate of new AIDS infections is to identify a wide array of options, ideally including a safe and effective vaccine, that can meet the needs of men, women and children in different countries, communities and contexts. Choice is essential, as is accessibility.

Should male circumcision prove effective, future trials will have to address key questions:

- Should male circumcision be offered by the trial site to all male participants as well as to the partners of women enrolled in a trial?
- Will trials have to control for the effects of circumcision on enrolled participants?
- Would referral to an offsite facility be appropriate?
- Should access to the broader community be provided?

If the offer of male circumcision does become part of the standard prevention package provided to trial participants, then overall incidence (rates of new HIV infections) in trial communities will drop. While desirable, this also means that trials will have to be bigger or longer or both in order to generate statistically significant findings.

Increasing the size or length of a trial increases its costs. Some trial networks have already begun to develop estimates of how the introduction of a new, partially-effective intervention might affect future trials. This work is essential and should continue, with the end result that scenarios and budgets are available as advocacy tools to ensure appropriate funding for AIDS prevention research in the future.

[6] Reference TK – slide set shared by Zambia JHPIEGO staff

To learn more
www.avac.org/MC is an online clearinghouse of regularly-updated information on male circumcision including published data, UNAIDS/WHO statements, media releases and other resources

Why is a vaccine organization writing about male circumcision?

AVAC was founded in 1995 to advocate for the ethical development and global delivery of vaccines against AIDS. Over a decade later, we are still committed to that cause. We are also well aware that other new prevention technologies are likely to arrive sooner than a vaccine. And we think many of the issues we work on – accelerated research, community involvement and education, research ethics, global access, and policy analysis – are highly relevant to male circumcision. In the coming years, AVAC will continue to work in partnership with other advocates to advance ethical prevention research and ensure that the benefits are shared globally.

The AIDS Vaccine Advocacy Coalition (AVAC)

Founded in 1995, the AIDS Vaccine Advocacy Coalition (AVAC) is a non-profit, community- and consumer-based organization that uses public education, policy analysis, advocacy and community mobilization to accelerate the ethical development and global delivery of vaccines against HIV/AIDS.

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