Gender in AIDS vaccine trials

Addressing challenges in developing countries

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Today nearly half of all HIV infections worldwide occur among women, and in certain countries with generalized epidemics, HIV prevalence among women has surpassed that of men. In sub-Saharan Africa, 57% of adults infected are women. In South and Southeast Asia, the epidemic is rapidly spreading from key populations—such as sex workers and injecting drug users—to the general population, with women and girls increasingly affected. At the end of 2003, women accounted for 28% of infections in Asia. In Eastern Europe and Central Asia, evidence suggests that rates of infection among women are increasing compared to that of men—with women accounting for 33% of people living with HIV/AIDS in the region (UNAIDS, 2004). In the US, according to the Centers for Disease Control and Prevention, the proportion of all AIDS cases reported among adolescent and adult women has more than tripled since 1986. This paper focuses on the reality and needs of women in developing countries.

Both biology and gender account for the differential experiences of women and men affected by HIV. It is believed that HIV is more easily transmitted from men to women than vice versa. Several anatomical and physiological characteristics of women and girls play a role in the transmission and acquisition of HIV infection. Since the female genital tract has a greater exposed surface area than the male genital tract, women may be prone to greater per-exposure risk of infection. Coercive or forced sex can lead to microlesions (very small tears) in the vagina that facilitate entry of the virus. Young women, in particular, who have less mature tissue, are more susceptible to infection, as well as are more vulnerable to coercive sex. Women also often have sexually transmitted infections (STIs) that are left untreated, which increases vulnerability to HIV.

Social, cultural, economic and legal factors coalesce to create an unequal balance of power between men and women, compounding the risks women and men face. On the one hand, social norms restrict women’s ability to negotiate safer sex, demand fidelity in a relationship or seek relevant information about protection, treatment or health care. Social pressures to bear children, or the desire to have children, often affect women’s choices concerning the relative importance of pregnancy versus protection from infection.

Poverty, and women’s reliance on men for economic support, and more broadly, restrictions on women’s access to productive resources often force women to engage in unsafe sex, or may force them to exchange sex for money or material favors as a means of

![Estimate of percent of adults (15-49) living with HIV/AIDS who were female in 2001 and 2003](source: UNAIDS/WHO estimates 2004)
survival or to support their children. Young women are particularly vulnerable to infection for both biological and socio-cultural reasons. In many societies, young women have little knowledge about their bodies, their risks or HIV/AIDS; have few entry points to the existing health care system; and often are more susceptible to coerced transactional and intergenerational sex.

Men, on the other hand, are socially vulnerable due to cultural concepts of masculinity that increase men’s sexual freedom or may pressure them to have multiple partners or be sexually adventurous. It may also prevent them from seeking information regarding sexual health and protection since men are expected to be self-reliant. Gender norms conspire to fuel the epidemic throughout the world.

What do we mean by “gender”?

1. The terms “gender” and “sex” are often used interchangeably, but have very distinct meanings. “Sex” refers to biological characteristics— anatomical, physiological and genetic—that define a person as male or female. “Gender” is a term used to reflect the socially constructed nature of men’s and women’s identities, i.e., what society defines as “male” and “female” or “masculine” and “feminine.” We often collapse the two terms and simply use “gender.” We do so acknowledging that society and biology both play a role in men’s and women’s vulnerability to HIV and potential to benefit from an AIDS vaccine.

2. Gender roles are the socially and culturally determined attitudes, behaviors, responsibilities and expectations for males and females. Gender roles vary within and between cultures, but by and large they are based on the level of power that women and men have in relation to each other. Gender inequality—in the family, in communities and in society at large—heightens the impact of HIV/AIDS on women, limits women’s access to health care and services and increases the discrimination they face.

3. A gender analysis can be done in many ways. When examining “gender concerns” in AIDS vaccine trials in this paper, we focus more specifically on “women’s vulnerability” to HIV/AIDS and to the gender norms and inequalities that increase the impact of HIV/AIDS on women’s lives. This does not deny male vulnerability. It simply says that the issues defined by gender point to a much higher vulnerability for one gender than for the other. The task therefore is to understand how and why women are relatively more at risk, and ways in which gender norms limit women’s ability to make decisions or seek health care for themselves. An appreciation of these factors will help to understand the complexities of involving women in AIDS vaccine trials, and of ensuring that women benefit equally from the vaccine when it is available.

4. Men are also adversely affected by the social construction of gender identities, which can encourage them to engage in risk-taking behavior. In conducting AIDS vaccine trials, programs and guidelines have to be designed to address the needs of both women and men and to involve them as equal partners in protecting themselves.

5. This paper acknowledges that there are more than two “genders,” and that consideration of separate identities becomes particularly relevant when discussing HIV/AIDS. Considering the high vulnerability of transgendered people to HIV, issues related to transgender identities become critical in countries where the epidemic is prevalent in these populations, but we have kept the scope of this paper limited at present.
Reduction of women’s vulnerability to HIV—the potential of a vaccine

Prevention efforts of the last two decades have slowed the spread of HIV, but not curtailed it. Behavioral approaches are particularly difficult for women. For many women, it is not their behavior, but the behavior of their partners that makes them vulnerable to infection. That it is not as simple as “ABC”—abstain, be faithful, use condoms—has become accepted knowledge among prevention advocates. Abstaining from sex is not a feasible option for women who very often are either not in a position to choose or are in situations of forced or coerced sex. Being faithful can work only if adopted by both partners; the reality is that partners and husbands are increasingly infecting women who are themselves monogamous. Use of condoms is largely the choice of men. Married couples very often do not use condoms if they want to have children or if the use of condoms is perceived as lack of trust.

It is critical that we expand the range of prevention options available to women, men and adolescents—options that are accessible, affordable and appropriate to their needs and situations. Women and young girls need prevention options that they can initiate and control. If we look for parallels in the use of family planning methods, we have seen that women often prefer methods that can be used without the knowledge of the partner. Another lesson from family planning is that having a broader array of options to meet different needs of individuals increases overall use.

There is a clear recognition today that the comprehensive prevention, care and treatment continuum must include the technologies and approaches currently in use, expanded access to treatment and the urgent development of a vaccine and microbicides. Both technologies are still in the research and development stage, but could one day offer increased choices to women and men, and could give women greater control over their prevention decisions.

While we must strive to put control in the hands of women, we have to be careful not to place undue burden and responsibility for protection on women alone. Neither can we place undue expectations on the technologies since technologies alone cannot address inequity, disempowerment and behavior change. Advocates for a vaccine and microbicides must use the opportunity to talk about health and gender equity, and issues of unequal power and social dynamics that increase women’s vulnerability to HIV. The ability of women and girls to know about their risks and protect themselves must be enhanced. Men and boys must be educated to take responsibility for their sexual health and that of their partners.

In the end, technology is useful only if it is safe, accessible, affordable and available in a sustained manner to all who need it. The very inequity that makes women more vulnerable to HIV/AIDS may negatively affect their ability to access and use technology. Enforceable international and national policy and legal mechanisms must ensure ethical and gender-sensitive testing and delivery of an AIDS vaccine.

The International AIDS Vaccine Initiative (IAVI) is a global not-for-
IAVI is engaged in identifying and addressing issues in women’s and men’s participation in AIDS vaccine trials.

profit organization working to speed the search for a vaccine to prevent HIV infection and AIDS. Founded in 1996 and operational in 23 countries, IAVI and its network of partners research and develop vaccine candidates for use throughout the world. IAVI works with scientists in Africa and Asia to study how a vaccine can be effective in populations where most new HIV infections are occurring, and where different subtypes of the virus are circulating. IAVI is committed to supporting the development and implementation of strategies to increase understanding of the clinical trial process at the community level. As the world moves closer to finding a vaccine, IAVI focuses on identifying, mobilizing and supporting communities to participate in clinical trials.

Aware that gender plays a role in AIDS vaccine trials and in subsequent access to the benefits of new technologies, IAVI is engaged in developing a framework to identify and address critical issues related to women’s and men’s participation in AIDS vaccine trials. A series of consultative meetings in India and Kenya—held with women’s and reproductive rights advocates, people infected and affected by HIV, NGOs, scientists and trial administrators—has provided useful guidance on understanding the barriers to women’s enrollment and retention and on developing strategies to conduct gender-sensitive AIDS vaccine trials.

3 / Why is sex-equitable enrollment important in trials?

There are compelling biological, scientific, ethical and social arguments for inclusion of equitable numbers of women and men in trials.

Biology

It is possible that a vaccine will work differently for men than for women due to the biological differences in terms of risk of infection. Research has also indicated that differences might exist in men and women’s viral loads (the amount of virus in the blood) following HIV infection. In order to know that a vaccine is effective for women and men, it is important to enroll significant numbers of both women and men in clinical trials. A single trial may not be able to determine whether the vaccine works differently for men than for women, but it can detect trends in the effect of a vaccine. Past clinical trials did not always include enough women participants and were unable to distinguish such trends.

Science

In order to ensure that an AIDS vaccine submitted for licensure has been tested in the populations in which it will be used, it is necessary to include women. Unless a vaccine is tested in women, it will not be clear whether it is efficacious or harmful for them. Regulatory authorities will require that the vaccine be tested in the populations in which it will be used.

Ethics

The principles of health equity require that women be involved in all appropriate clinical research. Evidence shows that vaccine research programs usually benefit all participants—those receiving the test vaccine and those receiving a placebo—because the education, counseling and care components of these trials reduce participants’ risk of contracting HIV. Excluding women from trials deprives them of these benefits.

Social factors

Women comprise more than half of all people living with HIV/AIDS. In spite of the epidemiological reality, women have had minimal involvement in trials, as compared to men. The challenge is to identify obstacles to women’s enrollment. Scientists, health providers, community stakeholders and women and men themselves have to work collaboratively to ensure that the AIDS vaccine is tested in all populations.
Considerable effort and planning are required, particularly in developing countries, to ensure women participate in trials and stay through the entire duration of the trial. Commitment is needed on the part of trial sponsors and trial teams to navigate the conflicting interests between public health imperatives to bring a vaccine to clinical trials as quickly as possible and ensuring that men and women are enrolled in significant numbers.

Enrollment and retention of trial volunteers

Despite the many cultural and practical barriers to enrolling women in AIDS vaccine trials, IAVI is committed to an equitable selection of trial participants when conducting trials. Since data from past clinical trials have not given conclusive evidence of what constitutes the optimum number of any particular group that should be enrolled, IAVI’s goal is to enroll women in significant numbers to allow identification of trends and gender-specific issues.

The challenge lies in investing the time and effort needed to explain the process and trial requirements to women, communities and families. Trial staff need to be aware of gender-related factors that hinder women’s participation: (a) many women lack the autonomy to make independent decisions about HIV testing or trial enrollment; (b) women often shoulder additional responsibilities of child care, care of the elderly and housework and may not be as readily available as men to attend information sessions or frequent clinic visits; and (c) in cultures where a woman’s perceived worth is often tied to her fertility, trial requirements that she avoid pregnancy during the course of the trial may place constraints on her participation.

Informed consent

Many of the standard procedures regarding informed consent are based on the assumption that the decision to participate in a research study is a completely rational one, made by the individual alone, but the reality reported by many researchers in the field is that complex social and cultural dynamics can prevent a full communication of the nuances of informed consent procedures, particularly to members of vulnerable groups, including women.

Prevalent gender norms can leave women vulnerable to influence and even coercion from husbands, family and community members, as well as health care providers, thus negating the true spirit of informed consent. Informed consent protocols, and staff taking consent from volunteers, must recognize these power dynamics and respect and support each potential volunteer’s right to decide whether or not to participate without coercion or constraint.

Information has to be presented in language that is easily comprehended and in a manner that prepares volunteers to fully understand their rights, risks and benefits. Volunteers must be tested to assess that they fully understand the information provided before consent is taken. Individuals with gender expertise should be involved in developing the consent process and monitoring the incorporation of gender concerns on an ongoing basis.

Confidentiality, stigma and discrimination

Confidentiality should be absolute for men and women. But for a woman, confidentiality is a critical issue since disclosure of participation in trials itself may lead to stigma and discrimination. She may be subjected to violence or may even be abandoned by her husband or family on the basis of her presumed risk-taking behavior or on the assumption that the woman is protecting herself from the risk-taking behavior of her sexual partner.

All trial personnel—those who are recruiting, testing and conducting trials—should be trained to handle issues of confidentiality in a gender-sensitive manner. Any breach of confidentiality can lead to greater risks for women in terms of blame, violence and loss of economic support. All diagnostic test results should be shared with participants only, and support should be provided in case a participant wishes to keep her
results private or share them with family. If possible, the research study site or clinic could be masked under a neutral, non-threatening name since visits to an HIV/AIDS or STI clinic may themselves be stigmatising.

Voluntary counseling and testing

The process of enrolling volunteers in a trial begins with an HIV test to see whether they are infected or not. HIV testing should take place on a voluntary basis with appropriate pre-test and post-test counseling. Since those who participate in the trial are HIV-negative at the time of enrollment, they should be counseled regarding prevention and protection. A very clear message must be given that the vaccine, or participation in a trial itself, will not assure protection.

Given that women are most often at risk due to the behavior of their partners, counseling ought to assist women in perceiving their own risks of infection. Counseling should also seek to empower women and men to protect themselves from becoming infected, make decisions regarding pregnancy and prevent mother-to-child transmission of HIV. Men need to be counseled to understand their risks and prevention options for themselves and their partners. Voluntary couple counseling might facilitate couple communication and make it easier for couples to get tested together and share their test results. Studies have shown that a majority of women need to seek permission from their partners prior to testing. Couple counseling could therefore be one way to make this process easier for women. Counselors must be trained to be sensitive to the possibility of potential conflict when a woman takes the decision to test or disclose her status to her partner.

Social harm and benefits

Most of the risks of social harm in HIV trials are linked to voluntary or involuntary disclosure of information about participation in a trial or about the HIV status of a volunteer. For women, the fear of stigma attached to disclosure is compounded by fear of violence or threats of violence from their partners. These risks can be reduced through careful planning and conduct of the trials; proper voluntary counseling and testing; appropriate referral mechanisms; community education; and rigorous adherence to procedures of confidentiality.

Risks can manifest themselves in many ways—physical, social, psychological, economic, medical and legal. Social harm might include stigma and discrimination; violence; abandonment; deprivation of food, care and medical treatment; access to and loss of employment; and medical, life and travel insurance. Trial researchers must stay attuned to the social and economic context of the participants in order to assess social harm.

Benefits for trial volunteers are largely a result of the education, counseling and health care components of a well-designed trial. These benefits usually translate into reducing participants’ risk of becoming infected with HIV. But we have to bear in mind that despite counseling on safer sex, risk for women volunteers in a trial is often determined by the partner’s behavior and is influenced by the socio-cultural and economic context of a participant.
Preparing the site

Some basic requirements are necessary to make the physical environment of trial sites gender-sensitive. These include:

- Convenient location to enable women to attend;
- A reception area and space that would be non-intimidating, welcoming and volunteer-friendly;
- Privacy—both in terms of not being seen or heard—when interviews are conducted;
- A waiting area with general space for families and a specially designated area for women and children;
- Child care during medical examinations or counseling sessions;
- Clean toilets, a canteen, appropriate audio-visual material and educational literature are necessary for an overall quality environment.

Organizational aspects and staff structure necessary to ensure gender-sensitive trials include:

- Gender balance in terms of staff who have volunteer contact (e.g., doctors, laboratory assistants and technicians);
- Trained and gender-matched counselors where culturally appropriate;
- Setting up support groups, particularly for women volunteers, to enable them to communicate potential difficulties with an intermediary support group;
- Clinic hours and days to suit work schedules of women and men;
- Trial-related services placed within broader health care service so that participation in a trial is not apparent.

Participation of community groups and women’s organizations

Community groups and women’s organizations working in the area of HIV/AIDS and reproductive health can be strong allies in helping to sensitize and mobilize volunteers. They can provide a valuable link to those communities, help to assess and shape current attitudes and awareness about an AIDS vaccine, help people understand the role a vaccine might play in controlling HIV/AIDS and address apprehensions and fears.

It is equally important to work with community leaders, but since it is often men who are identified as community leaders, it is important to ensure that they are aware of gender sensitivities. Both community groups and leaders can help to address gender-specific issues by making communities aware that some women and men are disproportionately at risk for a variety of reasons and therefore have to be enrolled as trial participants in order to benefit from the research.

Community advisory boards (CABs) in several trial countries have played a significant role in educating the community on vaccine development and trials and in mobilizing volunteers. Ideally, CABs should have an equal representation of women and men.

The physical environment of trial sites should be gender-sensitive.
5 / Integrating gender in AIDS vaccine trials

Key concepts

Integrating a gender perspective in AIDS vaccine trials is a process of looking at barriers and implications of participation in a trial for women and men respectively. It involves using a gender lens to examine the differential impact that trials can have on women and men, particularly those who are in a disadvantageous position.

Integration of gender is a strategy for including gender-specific interventions, which can target only women, men and women together, or only men, to enable them to participate in and benefit equally from trials. Since women are disproportionately affected by the epidemic, and since they are usually more vulnerable to infection and more vulnerable socially, their needs and situations require greater focus. For example, ongoing counseling and testing must take into consideration the imbalance of power that places women at greater risk and limits women’s ability to take preventive measures or make independent decisions to get tested for HIV. Depending on the specific socio-cultural context, counselors must help their clients either as couples or as individuals to perceive and prevent risks.

Conducting a gender-based analysis is the first step in influencing policy, program and decision-making processes. It is only when we ask, listen and observe that we can identify barriers to participation or ways in which to address them. Equally important are the monitoring and evaluation of the implementation procedures put in place. Commitment to integrating gender has to be instituted organizationwide, and gender advisory panels have to be empowered with requisite resources and structures to make them effective.

Key steps

The following recommendations have emerged from IAVI consultations with key stakeholders.

Set up a gender advisory board.

A gender advisory board, made up of independent experts on gender, health and HIV/AIDS, should be set up to provide advice and oversee incorporation of gender aspects throughout the trial process. The board’s role would be to support a gender review of protocols and

When planning for trials, some basic principles of integrating gender must be applied:

- Enroll sufficient numbers of men and women in trials to ensure trends in the effects of a vaccine can be identified within different subgroups;
- Identify issues and concerns across all phases and steps of a trial so that differences based on gender can be recognized;
- Speak to communities of women and men to better understand potential problems and solutions, and bring their perspectives into decision-making;
- Consult experts working in the field of HIV/AIDS, women’s health and gender and involve them as partners in designing, monitoring and evaluating gender-sensitive trials;
- Train all personnel involved in trials—clinicians, doctors, counselors and norm-setting bodies such as the ethics review committee—to conduct gender-sensitive trials;
- Mobilize political will at the highest levels and across the organizations involved and allocate resources for gender mainstreaming in order to translate concept into practice;
- Establish accountability mechanisms to track progress at all levels;
- Do not make any assumptions that biomedical technologies, in their application, can be gender-neutral—investigate the differential impact on men and women.
Develop gender-sensitive guidelines and protocols.

In developing protocols, guidelines, investigators’ brochures and questionnaires, a gender analysis framework has to be applied to the various components of the trial, including informed consent, inclusion and exclusion criteria, care and counseling, reimbursement, confidentiality and related issues of stigma and discrimination. This framework can be applied to identify issues and concerns across all phases and steps of a trial.

Train trial team to be gender-sensitive.

All individuals and organizations involved in conducting, or supporting, trials must be trained in understanding and integrating gender concerns in all aspects of the trial. These include protocol managers, researchers, trial administrators, counselors, doctors, the ethics review committees and community advisory boards.

Training has to be tailored for the respective individual or group depending on roles. For the group that will be in direct contact with the volunteers, a hands-on, skills-building training will be needed. For organizations that are primarily responsible for setting norms, training that focuses on building a gender perspective is required.

Establish accountability mechanisms.

A gender audit mechanism should be set up to review and monitor all aspects of the trial to ensure that the trials are gender-sensitive. Ideally, gender auditing should be incorporated as one of the functions of the ethics review committee. Gender training should be provided to this committee so that it can assume the responsibility of ensuring that the trials are both ethical and gender-sensitive.

Indicators including benchmark parameters, results and outcome indicators and process indicators must be developed to enable the ethics review committee to carry out the function of gender auditing.

The disproportionate impact of HIV on women and girls must be reversed.

In the same way that traditional gender norms can inhibit women’s participation in vaccine trials, these gender norms could ultimately prevent women from accessing a vaccine once it is available. Experience has shown that despite the health burden being greater on women, they also face greater constraints in accessing prevention and care. Factors that influence acceptability of and access to an AIDS vaccine must be well understood and incorporated in strategies for future access and use of a vaccine. The process of addressing gender concerns in trials may enhance understanding and help us develop systems to ensure equitable access of a vaccine. The disproportionate impact of HIV on women and girls must be reversed, and it is a matter of urgency that they have equitable access to prevention options, treatment and care.
Sources


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IAVI is a global not-for-profit organization whose mission is to ensure the development of a vaccine to prevent HIV infection and AIDS that is accessible worldwide. IAVI’s major financial supporters include the Bill & Melinda Gates Foundation; the Rockefeller, Sloan and Starr foundations; the World Bank; BD (Becton, Dickinson & Co.); the European Union; and the governments of Canada, Denmark, Ireland, the Netherlands, Norway, Sweden, the United Kingdom and the United States.

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