

# Gender and HIV Vaccine trials: Ethics and social science issues

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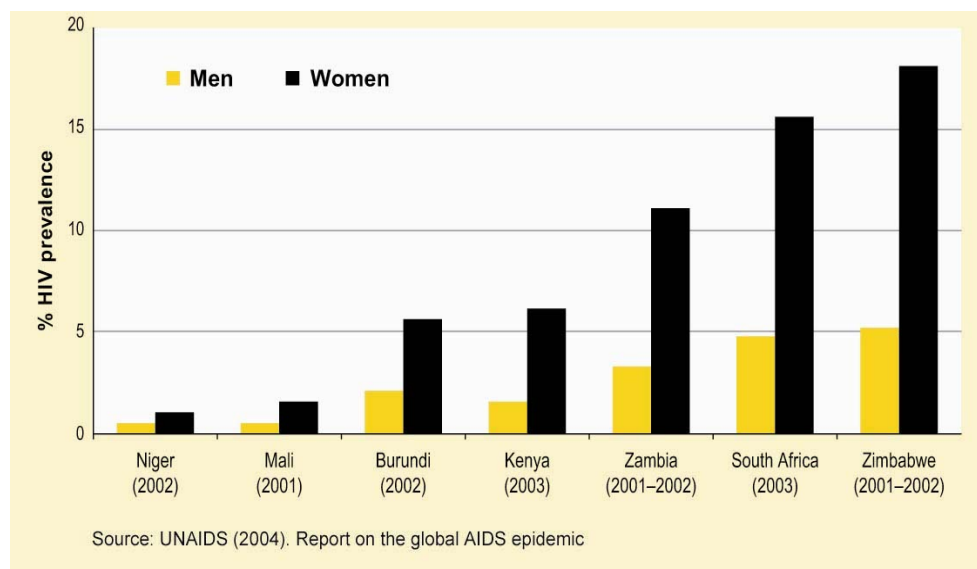
There are several HIV vaccine efforts underway globally. Women in developing countries, especially in southern Africa, carry a disproportionately large burden of HIV infection and thus stand to benefit most from a successful HIV vaccine. They are also required to play a significant role in trials to test vaccines. Participation in HIV vaccine trials, however, requires participants to understand the complex nature of the procedures and presumes that they have autonomous decisional capacity. This paper outlines some of the problems underlying these assumptions, and makes recommendations that could improve autonomous and capacitated ethical decision-making by this at-risk and vulnerable population.

“Vaccine science has rarely paused to consider gender differences, and has rarely had to.”<sup>1</sup>

Successful vaccines for polio, tetanus and other infectious diseases were developed without considering sex hormones or the male and female genital mucosa. HIV is a sexually transmitted virus and although it progresses similarly in men and women, there are some differences in how the virus interacts with men’s and women’s bodies. Also significant are the marked differences in the vulnerability of women and men at the societal level. For these reasons, HIV vaccine trials are embedded in a broader scientific and social perspective deter-

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**Figure 1: HIV Prevalence among 15-24-year-olds in selected sub-Saharan African countries, 2001-2003**

mined by gender.

In general, women's active informed participation in clinical trials and prevention efforts is vital, especially when women are among the most vulnerable populations. In particular, women's distinct vulnerability to HIV means that vaccine trials must include women because vaccines have to be tested in high-risk groups. Additionally, women must be included in vaccine research with special consideration to ethical issues because of their infective and social vulnerability.

## Women's Unique Vulnerability to HIV

Looking more closely at the position of women in Southern Africa, it can be asserted that women are the axle around which HIV infection turns. Statistics show

that in sub-Saharan Africa, 58% of adults infected are women, 75% of young people infected are female and women are 30% more likely to be HIV positive than men.<sup>2</sup> <sup>3</sup> Because women are hardest hit by this epidemic, it is imperative that women benefit from a vaccine.

In addition to these striking statistics, the need for a focus on gender is evident from research demonstrating that gender impacts on the transmissibility and acquisition of HIV. One example is a study of sero-discordant couples (in which one partner tests HIV positive while the other tests negative) in Zambia, which suggests gender differences in how viral load relates to transmissibility. Women with viral loads above 100,000 were nearly six times more likely to pass on the virus than women with less than 10,000 copies, while for men the difference was less than two.<sup>4</sup> A second example is that of the HEPS (Highly Ex-

posed Persistently Sero-negative) study in Kenya which found that, among a cohort of female sex workers, a small minority demonstrated immunological resistance to HIV despite repeated exposure to HIV from multiple partners.<sup>5</sup>

Given these and other studies pointing to gender-specific outcomes, it seems likely that a vaccine will generate gender-specific effects. Results from the experimental vaccine against HSV-2, as well as from the VaxGen study suggest that vaccines may not always be gender blind.<sup>6,7</sup>

Women's vulnerability to HIV can be identified in the biological, social, economic and legal domains.

Biologically, the susceptibility of the vaginal tract makes women seven times more likely than men to become infected during any given sexual encounter.<sup>8</sup> Additionally, asymptomatic STDs in women are more likely, and the presence of untreated STDs increases the risk of HIV infection.<sup>9</sup>

Women's social inequality and their vulnerability to HIV are interdependent. We submit that rural women in developing countries should potentially be regarded as vulnerable populations as their social position is compatible with the criteria outlined by UNAIDS' guidance (Point 3) defining vulnerability in the context of HIV vaccine trials.<sup>10</sup> Some acquired vulnerabilities are generic to developing countries. These include poverty and landlessness, the post-colonial degradation of traditional protective factors, male migrancy for employment and the increased risk of women in informal trading environments.<sup>11</sup>

Violence against women in which women are victims of rape, coercive sex or partner violence constitutes a serious social risk increasing the vulnerability of women

to HIV. In South Africa, it is estimated that between 19 and 28% of women are subjected to violence, either by a current or ex-partner. A study conducted in Soweto demonstrated that women with violent or controlling male partners are at increased risk for HIV infection.<sup>12</sup>

Women's lower socio-economic status in African society and uneven power dynamics within relationships may perpetuate and increase women's risk for HIV infection by limiting women's power to negotiate condom use or other forms of protection.<sup>13-15</sup> Furthermore, preventive programs do not provide women with comprehensive information necessary to protect their sexual and reproductive health. For example, in attempting to prevent unwanted pregnancy, some women resort to anal intercourse without knowing that this practice increases their risk of HIV infection.<sup>16</sup>

In addition to lack of information, socio-cultural factors influence aspects of partner choice and sexual practices in ways that increase the vulnerability of women to HIV infection. For example, some African men prefer dry sex and young female sex partners, which leads to increased tearing of vaginal tissues and increased risk of infection.<sup>17-19</sup> In addition, women are more likely to act as caregivers to orphans and ill family members, and this burden adds to women's vulnerability.<sup>20, 21</sup>

Furthermore, women's economic dependence on men increases the likelihood that they will engage in transactional sex and limits their access to and control of resources to protect their own reproductive and general health.<sup>22</sup>

Gender-insensitive laws also play a role in increasing women's vulnerability to HIV by perpetuating male-female sexual

power dynamics. For example, in Botswana, the South African AIDS law project found that tribal courts treat adultery as a female crime only. This suggests that men can have multiple partners, a practice that increases the risk of HIV infection for women.<sup>23</sup> Moreover, in Lesotho and Swaziland, women married in community of property (i.e., without a prenuptial agreement to the contrary) are considered legal minors and cannot sign contracts without the permission of their husbands.<sup>24</sup> A legal environment that encourages gender discrimination is a fertile ground for the spread of HIV.<sup>25</sup>

In addition to women's greater biological vulnerability, the economic, legal and social disadvantages faced by women and girls in most developing societies greatly increase their vulnerability to HIV. These vulnerabilities have implications for the conduct of HIV vaccine trials in rural African settings. In order to enroll sufficient numbers of people with a risk of infection in vaccine trials and to obtain gender-specific data, large numbers of women, especially rural women, will need to be recruited for participation.

## Ethics of HIV Vaccine Trials

In order for HIV vaccine trials to be implemented successfully, gender issues will need to be considered in terms of: 1) the ability of women to give adequately informed and voluntary consent to participation and 2) the ability of women to meet the ongoing and multiple requirements of trial participation (clinic visits, risk reduction behavior compliance and monitoring, blood draws, etc.). These two issues will

make different demands and have different impacts on women in stable partnerships, women with multiple partners and women engaged in commercial sex work.

Women's autonomous and informed participation in HIV vaccine research is essential to prevention efforts in general, especially to prevention efforts that could benefit women in particular. The account given above of the position of women in many parts of Africa, however, suggests that the experience of consent in such populations may be seriously compromised. This means that the enrolment and retention of women, in terms of their ability to meet vaccine trial requirements, may be compromised. The danger of low enrolment and retention rates is that women may not reap the benefits of a much-needed vaccine that has been tested for differential effects on men and women.

The process of informed consent rests on the assumption of autonomy and requires several additional factors: information, comprehension, voluntariness, capacity and explicit consent. Impairment of voluntariness due to oppressive psychosocial and economic conditions of women in rural areas in southern Africa calls into question the adequacy of standard (Western) informed consent procedures in such settings. We have very little empirical data on African women's experience of voluntariness and consent, but there is some data to suggest that in some settings, Africans do not perceive health research "volunteers" to be true volunteers.<sup>26</sup> Similarly, there is reason to believe that for many women in southern Africa, understanding and voluntariness are compromised, particularly for those at-risk women most likely to be candidates for Phase III HIV vaccine trials.<sup>27</sup>

Gender sensitive approaches are therefore key to designing consent procedures, recruitment and retention components and risk-reduction interventions in HIV preventive trials.

The need for gender-specific approaches to recruitment and enrolment is further evidenced by existing HIV vaccine trials with low female participation. For example, in the Kenyan trial, only two out of the 18 Phase I volunteers were women.<sup>28</sup> However, South Africa's Phase I trial at Chris Hani-Baragwanath Hospital shows promise. In 2003, a total of 3,024 clients, of whom 62% were women, were seen at the VCT clinic attached to the vaccine.<sup>29</sup> Much more data is needed on rates of enrolment and retention of women in HIV vaccine trials globally.

Trials may need to take account of the socio-economic position of female candidates for trials and offer support to potential trial participants, both during and after the trial. There is a need for a bridge between the standard Western conceptions of voluntariness, the standard practices of recruitment, retention, consent, and risk-reduction and the grounded position of African women in order to facilitate ethical and emancipatory health research practice. This bridge must be built on the voices of women and therefore requires informed and sensitive formative social science research prior to trial implementation.

Practically speaking, challenges will need to be addressed at multiple levels using multiple media, including research, advocacy, networking, capacity building and policy formulation. We have nine recommendations that could be implemented to address the challenges of participation of women in HIV vaccine trials:

1. Identify the enrolment practices and outcomes by gender for HIV vaccine trials in developing countries, generally, and in Southern Africa, specifically.
2. Conduct a systematic study of the sites with the best enrolment strategies to identify key factors associated with best enrolment and retention outcomes by gender.
3. Develop a "resource pack" of materials outlining key elements of best recruitment and enrollment practices to build capacity at other African sites
4. Build a global network and database of perhaps twenty key persons committed to improving the enrolment of women in African settings. They could assist in an advisory capacity with the meaningful and ethical inclusion of rural women in HIV vaccine trials. For example, the International AIDS Vaccines Initiative has a dedicated gender officer.
5. Study the preparedness of local communities for hosting HIV vaccine trials. The specific circumstances of rural women, their readiness to volunteer autonomously for a trial and the benefits that can accrue to local women through HIV vaccine trials must be considered.
6. Study the legal frameworks of targeted countries to identify laws that discriminate against women's health and engage in advocacy to promote an environment in which trials can be run ethically. Such studies are currently being undertaken by the Ethics, Law and Human Rights Working Group of the UNAIDS/WHO African AIDS Vaccines Programme.
7. Encourage closer cooperation and resource sharing between HIV vaccine and microbicide initiatives to promote best

practices.

8. Data from the above efforts could lead to the development of a global policy document, possibly from UNAIDS, specifying the minimum and optimal requirements for the ethical enrolment of women into HIV prevention studies.

9. Finally, the inequities requiring such a document should not be taken for granted and should be seen in the broader context of UN policies to reduce global poverty and discrimination, particularly for women in the developing world.

We believe that it is crucial to conduct intensive site-specific formative research into gender issues before proceeding with HIV vaccine trials. Such social science research would illuminate gender-specific nuances that may adversely impact on consent processes, recruitment, retention and risk-reduction interventions for women and would suggest how such problems need to be remedied. This process would ensure that the trial results and their ultimate hoped-for benefits are applicable to this disproportionately affected population.



## References

1. E. Bass, "Special Report: Women and AIDS Vaccines," IAVI Report 5, no. 8 (2001): 1.
2. World Health Organisation, *The World Health Report: Changing History* (Geneva: World Health Organisation, 2004), 8-9.
3. UNAIDS, *Report on the global HIV/AIDS epidemic* (Geneva: UNAIDS, 2004), 6-7.
4. A. d'Adesky, "Gender, HIV transmission and Vaccines: A Moving Target," IAVI Report 5, no. 8 (2001): 18-20.
5. R. Jefferys, "Closing in on the Immune Protection in the Women of Pumwani: Can a Cohort of Kenyan Sex Workers Help Guide us towards and AIDS vaccine?" IAVI Report 5, no. 8 (2001): 9-14.
6. T. Taha, S. Nour, N. Kumwenda, R. Broadhead, S. Fiscus, G. Kafulafula, C. Nkhoma, S. Chen and D. Hoover, "Gender differences in Perinatal HIV Acquisition among African Infants," *Pediatrics* 115, no. 2 (2005): 167-172.
7. A. d'Adesky, "Gender, HIV transmission and Vaccines: A Moving Target," IAVI Report 5, no. 8 (2001): 18-20.
8. Q. Abdool Karim, "Women and AIDS: Epidemiology and gender barriers to prevention in KwaZulu-Natal, South Africa," Paper presented at the XV International AIDS Conference, Bangkok, 11-16 July 2004.
9. D. Wilkinson, S. Abdool Karim, A. Harrison, M. Lurie, M. Colvin, C. Conolly and W. Sturm, "Unrecognized sexually transmitted infections in rural South Africa women: A hidden epidemic," *Bulletin of the World Health Organisation* 77, (1999): 22-28.
10. UNAIDS *Ethical Considerations in HIV preventive vaccine research*. (Geneva: UNAIDS, 2000).
11. S. Lee, "Women's vulnerability to HIV/AIDS in informal trading environments in Uganda and South Africa," *HEARD Quarterly Newsletter* no. 11 (July 2004), [http://www.ukzn.ac.za/heard/aboutheard/Newsletters/HEARD%20NL\\_Issue11.pdf](http://www.ukzn.ac.za/heard/aboutheard/Newsletters/HEARD%20NL_Issue11.pdf) (27 August 2004).
12. K.L. Dunkle, R.K. Jewkes, H.C. Brown, G.E. Gray, J.A. McIntyre and S.D. Harlow, "Gender-based violence, relationship power, and risk of HIV infection among women attending antenatal clinics in South Africa," *Lancet* 363 (1 May 2004): 1415-1421.
13. World Health Organisation, *The World Health Report: Changing History* (Geneva: World Health Organisation, 2004), 8-9.
14. V. Van Der Vliet, "Attacking AIDS in Uganda," *SAFIDS: South African AIDS Information Dissemination Service bulletin* 7, no. 7 (1999): 11.
15. S. Leclerc, "Science, AIDS and sexual culture in Africa," *Women's International Network News* 27, no. 1 (Winter 2001): 20-22.
16. UNAIDS, *Report on the global HIV/AIDS epidemic* (Geneva: UNAIDS, 2004), 6-7.
17. O. Shisana, "Gender and HIV/AIDS: Focus on Southern Africa," Paper presented at the Inaugural International Institute on Gender and HIV/AIDS, South Africa, 7 June 2004.
18. G.R. Gupta, "Editorial: How men's power over women fuels the HIV epidemic," *British Medical Journal* 324, (2001): 183-184.
19. E. Bass and R. Jefferys, "Women and HIV in Kenya: An interview with Dorothy Mbori-Ngacha," IAVI Report 5, no. 8 (2001): 7-8, 14.
20. Mail and Guardian, "AIDS 'carries the face of a woman'," *Mail and Guardian*, 20 March 2005.
21. World Health Organisation, *The World Health Report: Changing History* (Geneva: World Health Organisation, 2004), 8-9.
22. G.R. Gupta, "Editorial: How men's power over women fuels the HIV epidemic," *British Medical Journal*

- 324, (2001): 183-184.
23. N. Zungu-Dirwayi, O. Shisana, E. Udjo, T. Mosala and J. Seager, (Eds), *An audit of HIV/AIDS policies in Botswana, Lesotho, Mozambique, South Africa, Swaziland and Zimbabwe* (Cape Town: Human Sciences Research Council, 2004).
  24. T. Barnett and A. Whiteside, *AIDS in the twenty-first century: disease and globalization* (New York: Palgrave, 2002).
  25. O. Shisana, "Gender and HIV/AIDS: Focus on Southern Africa," Paper presented at the Inaugural International Institute on Gender and HIV/AIDS, South Africa, 7 June 2004.
  26. N.W. Barsdorf and D.R. Wassenaar, "Racial differences in public perceptions of voluntariness of medical research participants in South Africa," *Social Science and Medicine* 60 (2005): 1087-1098.
  27. C. Molyneux, D. Wassenaar, N. Peshu and K. Marsh, "Community voices on the notion and practice of informed consent for biomedical research," *Social Science & Medicine* (in press).
  28. E. Bass and R. Jefferys, "Women and HIV in Kenya: An interview with Dorothy Mbori-Ngacha," *IAVI Report* 5, no. 8 (2001): 7-8, 14.
  29. E. Vardas, "Progress at the Chris Hani-Baragwanath HIV vaccine trial site," Paper presented at WHO/UNAIDS African AIDS Vaccine Programme Conference, Addis Ababa, June 2003.