Policy Brief

The Journey Toward an AIDS Vaccine: Perspectives on Conducting Trials in Developing Countries

"We shouldn't see the experience thus far as a failure, even if the vaccine candidate failed; much of the path forward has now been developed, so we haven't failed at all. Being able to say yes or no, the vaccine worked or not, that is a success in research terms."

Assessing the Journey

The journey toward an AIDS vaccine has been long and at times discouraging. More than 20 years after the discovery of HIV as the cause of AIDS, a vaccine is still proving elusive. During this time, over 75 vaccine candidates have entered clinical trials, but only three have reached the stage of large-scale efficacy trials, and to date none has proven efficacious. The recent decision to halt the trials using the Merck Adenovirus vaccine (known as STEP in the U.S. and Latin America and Phambili in South Africa) is a new disappointment.

While it is frustrating that a safe and effective vaccine has not yet been discovered, it would be short-sighted to conclude that efforts to date have failed. Criticisms which focus exclusively on a successful final product as the outcome of interest for the AIDS vaccine field overlook important knowledge and other tangible benefits that the trials have yielded. While our ultimate goal is an AIDS vaccine, we should recognize the value of what we have accomplished as part of that journey.

This brief provides an overview of the intermediate achievements and possible areas for improvement in the process of developing an effective AIDS vaccine, as told through the voices of those most closely involved in AIDS vaccine trials, including volunteers, researchers, and other community members.

Reviewing the Impact of Research Efforts

The basic research and clinical trials undertaken to date have led to significant advances in scientific knowledge, even when individual vaccine candidates have not been successful. As important as these scientific advances, but sometimes ignored, are other social, economic, psychological, and educational benefits from conducting AIDS vaccine research. These impacts may be at the level of the individual, affecting volunteers participating in trials or research team members. They may be at the community level, influencing those not directly participating in trials, but touched by them. And they may be at the national or global level, strengthening institutions, processes, and systems. Identifying these impacts can provide a more comprehensive picture of the results of AIDS vaccine research efforts.

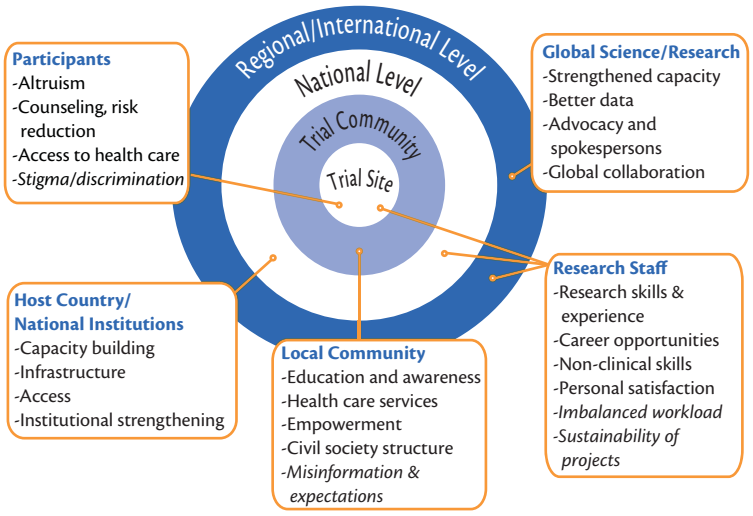
Gathering Perspectives

The International AIDS Vaccine Initiative (IAVI) interviewed nearly 100 individuals involved in AIDS vaccine studies in ten developing countries: Brazil, Haiti, India, Kenya, Peru, Rwanda, South Africa, Thailand, Uganda, and Zambia. These respondents and their experiences reflect the range of vaccine studies to date (from preparatory studies to Phase III efficacy trials), and the spectrum of stakeholder categories: research staff (local and expatriate), clinic staff, participants, community members, government officials, donors, and advocates for the field.

IAVI focused this analysis on developing countries for several reasons. It is important to conduct AIDS vaccine research, particularly large-scale trials, in countries hit hardest by the epidemic, and these are predominantly in the South. Given the genetic diversity of HIV, vaccine candidates must be tested where targeted subtypes (clades) are present, and this requires testing in Africa, Asia, and Latin America. Some have suggested that it is not feasible to conduct trials in resource-poor settings, because these countries have limited prior clinical trials experience, infrastructure and skilled personnel. The past decade has demonstrated, however, that it is possible to conduct AIDS vaccine research in developing countries to the highest ethical and technical standards.

Photo Credit: Vanessa Vick

Summary of Impact of AIDS Vaccine Studies



Note: *Italicized items* refer to challenges or concerns cited by respondents

Impact at the Individual Level

Study Participants

The health and well-being of AIDS vaccine study volunteers have improved as a result of their participation. Greater self-esteem has been the most significant personal impact, along with increased access to health information and services. Yet volunteers have also faced challenges from potential stigma and discrimination.

Altruism

- In Thailand, some injecting drug users saw their involvement in the first efficacy trial as an "honorable" contribution, particularly important given the value placed on altruism in Thai Buddhist culture.

Counseling/Risk Reduction

- Two Ugandan volunteers said that what they learned about HIV and prevention from the trial helped them to lower their level of risk behavior. In fact, they found their trial experience so fulfilling that they volunteered as peer leaders once the trial ended, and began providing support and information to people living with HIV and AIDS.

Access to Health Care

- Trial participants have gained access to health care services, including monitoring and treatment (or referrals) in settings where these services are hard to obtain and are thus especially valuable. In addition, many trials have provided antiretroviral therapy (ART) for participants who become HIV-infected. In Thailand, a trust fund was established to supplement government provision of ART, and in India, a national consultation was held to define appropriate guidelines, resulting in commitments to provide five years of ART for participants who contracted HIV during a vaccine trial.

> "Many of our participants needed outside health care—to see specialists or to have surgery. We were able to see them here and refer them—this wasn't a formal program, but rather something we were able to do because of our informal network of colleagues who were health workers."

Stigma/Discrimination

- In an extreme case of stigma associated with trial participation, a Kenyan medical student lost her job and encountered difficulties with the medical board. In such cases, the principal investigators (PIs) have intervened directly on behalf of volunteers, and promoted education and awareness within the community to dispel myths and misinformation about the trials. Research teams now proactively work with volunteers to discuss how best to explain their participation in both private and public situations.

Research Staff

Research staff cited professional development as the primary benefit of working on AIDS vaccine studies. The skills and experience gained, career enhancement, and greater exposure to social science and non-clinical fields were seen as overwhelmingly positive. However, research staff have also faced challenges from heavy workloads, high emotional tolls, and uncertain funding.

Research Skills & Experience

- Many research personnel have acquired new skills that can be transferred to other scientific efforts. In Thailand, data management staff responsible for the AIDS vaccine efficacy trials are now applying their expertise to malaria vaccine trials, and their institution competes with contract research organizations for work in clinical trials. Other AIDS vaccine units have expanded into microbicide research and drug trials.

Career Opportunities & Non-Clinical Skills

- A Brazilian researcher noted that by working with colleagues from social science backgrounds, clinical staff became more sensitive to participants' concerns and were more open to new ideas, thus building beyond their technical capabilities.

- Involvement in vaccine studies has enhanced career opportunities for research team members, providing them with greater technical skills, strengthened academic credentials through publications and presentations, and participation in professional networks. While beneficial to individuals, the downside for the research field is that junior staff are "employable" elsewhere and may be more likely to leave after a few years.

> "Many people on our trial team, because of their experience, training, and exposure, got good opportunities and moved on. But we consider this a benefit because we have been able to spread them to other places where they can do important work."

Impact at the Community Level

Communities have benefited from AIDS vaccine studies through enhanced health education and health care services. Conducting vaccine studies has empowered community organizations and structures, including community advisory boards and civil society groups. But a recurring challenge for vaccine studies has been the need to address misinformation and unrealistic expectations about trials within communities.

Education & Awareness

- In Kenya, South Africa, and Uganda, AIDS vaccine trials sponsored community events in which HIV-prevention messages were conveyed, sometimes through storytelling and drama. In Cape Town, for instance, "The Future Fighters," a group of adolescent trial participants, used song and dance to conduct training and vaccine advocacy throughout their township, especially targeting other young people.

Health Care Services

- Community members not participating in AIDS vaccine trials have also benefited from improved access to healthcare services. Potential volunteers who did not qualify for the studies nevertheless received medical diagnoses and referrals for treatment. As part of general outreach, staff from the Kenya AIDS Vaccine Initiative (KAVI) held medical camps where they provided treatment and information on HIV prevention and vaccines to the community at large.

Misinformation & Unrealistic Expectations

- Prior to launch of a vaccine trial in Haiti, a *New York Times* article questioned the ethics of ongoing HIV research work. Research teams have learned to work with the media, community groups, and government officials to respond to the media, including instances of misinformation and to better explain the nature of vaccine trials.

- Respondents in Kenya, Peru, and Thailand felt that the failure of vaccine candidates was a blow to the morale of volunteers, government officials, and the general public, who had assumed that the vaccines would work. Interviewees suggested that better communication strategies must be developed, including educating constituencies not only before and during trials, but again when results become available.

> "There is a growing sense of impatience in some communities – they feel like they have been talking about AIDS vaccines for 10 years, and now they're being told that it will take another 10 years."

Impact at the National Level

At the national level, AIDS vaccine studies have built scientific capacity, strengthened institutions, enhanced physical infrastructure, and laid the groundwork for future access to vaccines. It will be challenging, however, to maintain and further develop this capacity.

Capacity Building

- Vaccine studies have provided employment for national researchers, helping to counteract the "brain drain" that often negatively affects low- and middle-income countries. Researchers have remained at home, or returned from abroad, in order to implement the studies. At the same time, they have provided role models for the next generation of scientists in developing countries.

Infrastructure

- Equipment and facilities from AIDS vaccine studies remain after research projects end, supporting other research and health care activities. An additional upper floor was built and equipped at Kenyatta National Hospital in Nairobi expressly for vaccine study work. At the Tuberculosis Research Centre in Chennai, India, an entire floor was converted into a vaccine trial site and was modified and equipped for AIDS vaccine trials.

Institutional Strengthening

- In Uganda, securing regulatory approval for the first vaccine trial took almost two years, involving six different committees and reaching the Cabinet level. The government has since streamlined the process, with only one regulatory committee required for approval, thus strengthening institutional capacity and improving regulatory processes. As part of AIDS vaccine efforts, Brazil, Kenya, and Thailand have developed national AIDS vaccine plans, establishing a clear road map for future research and investment needs.

> "HIV vaccines, which have been such a high-profile new technology, have really forced developing country regulators to prepare in a way we hadn't done for anything else."

Impact at the Global Level

At the global level, AIDS vaccine research has contributed significantly to knowledge on how to better conduct future studies, especially in developing country settings. These studies have spawned new champions for AIDS vaccines, and have served as a positive and inspiring examples of how the global community can come together to address common problems.

Strengthened Capacity

- A decade ago, AIDS vaccine trials had been conducted in just six countries worldwide, and only two of them – Cuba and Thailand – were developing countries. At the end of 2007, a total of 19 low- and middle-income countries had hosted AIDS vaccine research efforts, reflecting dramatic growth in experience and capabilities.

Better Data

- Recent studies found that many healthy African volunteers were being excluded from AIDS vaccine trials based on medical criteria developed for Western populations. This has led to research to define 'normal' values for local populations, helping to recalibrate the criteria for volunteer participation. Such efforts have improved safety and streamlined the recruitment process throughout Africa, with effects beyond AIDS vaccine trials.

Advocacy & Spokespersons

- Ugandan President Museveni, whose country undertook the first AIDS vaccine trial in Africa, has advocated for increased funding for vaccine research with G8 leaders. The heads of state of India, Brazil, and South Africa have used their tripartite political coalition to advocate jointly for AIDS vaccines, largely because of the role each country has played in research and development.

> "The fact that you are doing it globally helps increase the momentum, and the sense that this might really work...The momentum must be kept going, because in some ways it is our last hope in controlling the epidemic."

Lessons Learned

The issues and lessons identified in this study underscore two important themes. First, there is a *critical need for better communication about vaccine studies*. Virtually all respondents mentioned the need to ensure more, better, earlier, and continued communication as part of vaccine studies. This should be done with the broadest range of stakeholders possible, and err on the side of too much rather than too little communication.

Second, although AIDS vaccine studies have led to major advances in capacity building with significant benefits, *additional resources are required to maintain those benefits*. Many of the study sites are at risk of retrenchment, and research personnel could be laid off, if there is a gap in project-specific grant funding. Sustainable domestic and international financing is needed to preserve the capacity that has been developed. In addition, the expansion of clinical studies has led to growing demands on regulatory agencies. While regulatory capacity has generally improved, in many instances it remains insufficient to meet current and future requirements. There is need for additional investment from external sponsors and donors as well as from national governments.

Conclusions

This review provides some initial insights into how those involved in AIDS vaccine research perceive the impact of those studies. Overall, the intermediate benefits of conducting such research appear to have been substantial at individual, community, national, and global levels. Going forward, it will be useful to undertake additional quantitative research to further document these results.

As we strive to develop an AIDS vaccine, no matter how long that search may be, we should remember that the journey itself is significant—and that along the way we can also make important contributions to better public health and to social and economic development.

> "No matter whether the vaccine works or not – at least we have started to move forward. It's like riding a bicycle; you start to push the pedals – once, twice, then a million times, that's how you make progress."

This summary is drawn from IAVI Policy Research Working Paper #16, The Journey Toward an AIDS Vaccine: Perspectives on Conducting Trials in Developing Countries. This and other IAVI policy research publications are accessible online at www.iavi.org.

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