

# 4

## Chapter 4: Seven Steps to Improving HIV-Related Care





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Early planning forms the basis of any effective health care system for participants in an HIV/AIDS clinical trial. For example, *Ethical Considerations in Biomedical HIV Prevention Trials* from UNAIDS/WHO states, “The provision of antiretroviral treatment to trial participants who acquire HIV infection during the trial requires planning for logistics and implementation.” In fact, planning makes up the foundation of all levels of health care offered to clinical trial participants. Nonetheless, it is not easy to meet those health care needs without jeopardizing the conduct of trials or detracting from the goal of identifying critically needed new HIV-prevention technologies. In an effort to help trial planners manage these issues, we used results from the Partnering for Care project and others to identify seven steps to developing a system of care.

As planners review these steps, they will see a variety of obstacles that can emerge. Developing an effective and lasting system of care requires an assessment of many factors, from medical and scientific to cultural and demographic. Indeed, by expecting challenges, planners stand a much better chance of success. Only then can they create a health care program that meets as many needs of the participants as possible.

Our seven-step plan follows.

## **Step 1:**

### **Build a public health attitude among research leaders and staff**

The success of a trial-related system of health care revolves around the attitudes of the people running the trial. Developing a public health attitude depends on several factors:

- Recognizing that HIV-prevention research is conducted in a larger context of health care delivery and public health policy
- Knowing that the research team might need to go beyond the minimum level of care necessary to meet scientific goals
- Understanding the limits of what the research team can accomplish in terms of providing health care while still meeting research goals
- Expecting to build partnerships to extend care
- Embracing the value of empowering community members to more effectively access health information and local resources for care
- Appreciating that a key component to sustainable improvements in the health of host-community members is strengthening the capacity of the local health system

In combination, these factors can fuel a better health care program, because they help the research team solve problems that may arise. Often, a “can-do” attitude grows from a stated sense of moral responsibility for the well-being of research participants that, in turn, creates a willingness to invest personally in building relationships, identifying resources, and creating solutions.

For instance, the research team at the MU–JHU project in Kampala, Uganda, wrote grants that sought funding to serve the needs of their participants. The staff also contributed personal time and money and arranged for community volunteers who helped study participants. Such altruism clearly goes beyond what is required of researchers.

## **Step 2:** **Assess the local community's values, attitudes, and priorities**

Developing a trial-related system of health care must fit with local cultural norms. According to *Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials* from UNAIDS/AVAC, “Respect for communities includes respect for communal values; protecting and empowering social institutions; and, where applicable, abiding by the decisions of legitimate communal authority.” Consequently, a health care program for participants in a clinical trial must consider several factors:

- What are the key public health goals of the study population or local community?
- Is the local community open to working with outside groups?
- How does the local community view HIV/AIDS? For example, are infected people shunned?
- How does the local community view health care in general, and is it open to public health education?
- Are there any forms of treatment that go against local values? For example, is condom use stigmatized because it is associated with HIV or certain sexual behaviors?
- Is the local community involved in other issues — such as economic or political challenges — that could affect health care?
- What belief systems are present in the community, and how do people view the relationship between health and faith, prayer, and spirituality?

These factors can interact in ways that benefit or block trial-related health care. For example, HIV hit Brazil in the early 1980s, when the country also faced political unrest — battling a dictatorship. Still, those people fighting the dictatorship teamed up with nongovernmental organizations and medical professionals to actively battle this disease. As a result, HIV-prevention research in Rio de Janeiro works alongside the communities. As noted in *Partnering for*

*Care in the HIV Prevention Trials Network. Part I: Overall Findings*, Brazilian AIDS activist Herbert de Souza said, “AIDS has to be viewed as a social issue and not an individual problem.” Planners of health care in clinical trials for HIV/AIDS can create even more thorough and effective programs by mirroring that philosophy.

To determine how local community values, attitudes, and priorities might impact health care in a clinical trial, see Appendix 4: Checklist — Local Obstacles and Issues.

### **Step 3:**

#### **Assess assets and constraints of the public-health system**

Any trial-related system operates within a larger system of public health, and that must be assessed and considered in developing a trial-related program of health care. In particular, clinical trial planners must remember that a study takes place under a range of assets and constraints: local community issues, as well as larger economic, political, and social situations. This range of assets and constraints must be considered. For example, if a trial takes place in an area that often lacks crucial pharmaceuticals, simply referring participants for care for common ailments such as malaria will be inadequate. Guidelines for assessing assets and constraints are outlined in the box titled “Assessing Assets and Constraints from the Public Health System”; to apply these guidelines to the planning of health care for participants in a clinical trial, see Appendix 5: Checklist — Public Health System Constraints.

## Assessing Assets and Constraints from the Public Health System

The following are guidelines that planners can use, adapted from the results of the Partnering for Care project:

- Consider the common medical needs in the area, such as other infectious diseases. How are these needs likely to affect trial participants? How are they likely to affect trial implementation?
- Examine the available local care, such as clinics and pharmaceutical availability and cost. How can these be used to provide health care to trial participants? Will the trial staff need to provide additional time and materials to offset insufficient local resources? Is the cost of key pharmaceuticals prohibitive for the public sector?
- Consider the implications of marshaling local resources for participant care or of injecting new resources into the host community. Will doing so create or exacerbate inequalities between trial participants and nonparticipants?
- Do the local services limit the types of care offered at specific locations? Will this require trial participants to visit multiple locations for health care?
- Consider treatments that are likely to be needed by a participant's family members, including a spouse or children. Which conditions will the trial address, and how? How will providing these added treatments affect the trial financially and logistically?

- **Consider economic constraints, such as lack of health insurance, even in developed countries. Will this prevent trial participants from receiving some forms of health care? Are free services available when needed?**
- **Study any ongoing changes in government programs related to care that might affect participants. Could these changes affect the ways participants seek health care? Will these changes affect the local resources that provide health care?**
- **Note other funding opportunities that could improve care. Could such opportunities reduce the financial responsibilities of the clinical trial? Could other financial resources improve the quality of health care for trial participants? Are there funds that researchers can access to improve care both within the trial and the larger community?**

## Step 4: Engage the community

Many of the steps listed here involve local communities in some way. Consequently, effective health care related to an HIV/AIDS clinical trial must involve the local community (see Appendix 6: Checklist — Engaging the Community). Engaging the community can produce community support of the trial which, in turn, helps to provide participants with more effective health care both during and after the trial. As well, a solid, long-term relationship with the community is important for ongoing programs of care and future trials.

*As Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials notes, “Effective community engagement during the entire life-cycle of a biomedical HIV prevention trial, and beyond, through genuine, transparent, meaningful participatory processes enhances both the quality and outcome of research.”* However, to make that engagement as strong as possible, the planners should involve communities before the trial begins.

Clinical trial planners and leaders can engage communities in a variety of ways: the following points are adapted from information in *Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials*.

- Budget community involvement and education into a trial’s plan
- Begin involving communities early in the protocol development process
- Share goals of a study with communities through written plans or public meetings
- Make someone on the research team responsible for community interactions
- Develop a CAB or other formal means of collaboration, with regularly scheduled meetings and a range of members, such as:
  - Government representatives
  - Community members of various ages and sexes, particularly people who share the characteristics of the study population
  - People living with AIDS

- o Local religious leaders
  - o Traditional healers
  - o Members of the local media
  - o NGO/CBO representatives
  - o Health officials
- Regularly review the researcher–community relationship through meetings between trial leaders and staff and the communities where the trial takes place

In the Partnering for Care project, researchers documented several examples of interactions that improved relations between community members and clinical trial planners and staff. In Philadelphia, for instance, a CAB made educational videos about research on an HIV vaccine. Such information, education, and communication strategies can be developed to foster not only dissemination and sensitization about research, but to ensure that researchers are informed about and engaged with communities in a substantive way.

For example, the NARI project in Pune, India, focuses considerable energy and resources on involving the local community. There, the HPTN principal investigator and community program supervisor give 30 percent of their time to activities related to community involvement. Moreover, the clinical staff contribute about 20 percent of their time to community activities. This project includes 15 full-time staff members who run a community outreach office that was designed specifically to build and nurture the project's interaction with the local community.

As another example, GCM's *Mapping the Standard of Care at Microbicide Clinical Trial Sites* found that STI care could improve through more work with local communities. The trials described in the GCM mapping study took place in areas with relatively high rates of STIs and limited public-sector services to diagnose and treat them, especially in women. Consequently, most of the trials provided STI testing and treatment for all women screened for trial participation, as well as treatment or referral for their sexual partners, as a service to the

community. Since STIs were secondary endpoints for all but one of the trials described, regular STI testing and treatment was done primarily for research purposes, but the decision to test and treat women at a first screening visit gave them free STI care, even when they proved ineligible to participate in the trial. The *Mapping* study concluded that trial staff could contribute in a sustainable way by training local providers in syndromic management of STIs and encouraging use of effective, single-dose treatments.

## **Step 5:**

### **Determine the extent of care to provide, and the balance between direct versus indirect care**

In *Ethical Considerations in Biomedical HIV Prevention Trials*, UNAIDS/WHO notes that a health care package for participants in HIV/AIDS clinical trials can involve many features:

- Counseling
- Preventive methods
- Treatment for other sexually transmitted infections
- Prevention of mother-to-child transmission
- Prevention and treatment of tuberculosis
- Prevention and treatment of opportunistic infections
- Nutrition
- Palliative care, including pain control and spiritual care
- Referral to social and community support
- Family planning
- Reproductive health care for pregnancy and childbirth
- Home-based care
- ART
- Legal assistance
- Services for orphans and vulnerable children (OVC)

A clinical trial team might not be able to provide this entire list. In fact, there is no consensus on the precise list of care that should be provided. For example, Henry Richardson writes in the *American Journal of Public Health* that when dealing with infected patients in a developing country, the “researchers might provide any of the following levels of care: 1) recommend treatment and provide a referral; 2) provide only palliative care for opportunistic infections;

3) provide palliative care and try to arrange funds to pay for ART; 4) provide palliative care and provide or pay for ART; or 5) provide palliative care, ART, and monitoring.” But for how long should researchers provide care? Planners of a clinical trial should decide ahead of time what services to provide for participants and for what period of time, such as to the end of the trial or longer. The potential for the emergence of drug-resistant HIV strains when ART is stopped — with implications for both individual and community well-being — underscores the importance of thinking about the long term.

To an extent, the offered treatment depends on the skills and resources of the clinical trial staff. So, during planning, the in-house capabilities must be considered to assess the potential for direct care. Each site must decide how far down the list of health care needs the research team can go without depleting the time, resources, and energy needed to do the research (see Appendix 7: Checklist — Care and Treatment Package).

In some cases, the nature of a trial will not include staff who can offer basic health care to participants. For example, at the HIV Prevention Research Unit at the University of Pennsylvania Center for Addiction Studies, the staff runs behavioral studies. Consequently, most health issues among trial participants get resolved through indirect care, or referrals. Because referrals are so important, considerable effort has gone into developing a comprehensive list of agencies and organizations that provide needed services. Personal contact between center staff and key service providers is also emphasized.

Direct and indirect care offer both pros and cons. Direct care, for example, provides many benefits: Participants can get health care without going to clinics with long wait times; it can reduce strain on local health care facilities; and it can build goodwill between leaders of a clinical trial and the local community. On the other hand, direct care also creates some trouble spots, such as taking away time and resources from the trial itself, as already mentioned. Moreover, there is also a risk that research sites that provide substantial health care directly to participants will draw staff away from already stressed health care facilities, thus inadvertently undermining local capacity. Finally, depending on the degree of direct care provided, it might create

perceptions of undue inducement for people to join a trial. As a result, it becomes especially important to clarify the difference between standard of care and the research intervention during the consent process, as therapeutic misconception is common in many resource-limited settings.

With indirect care, obstacles might be more apparent, such as requiring participants to arrange care at other facilities, find transportation, and so on. Nonetheless, indirect care can also provide advantages, such as building relationships between clinical trial teams and local professionals and leaders. This type of care can also enhance sustainability of care for participants after the research has ended.

Different clinical trials might also encourage different forms of care. For example, GCM's report on *Mapping the Standard of Care at Microbicide Clinical Trial Sites* encourages cervical screening, in part because HIV-positive women run a higher risk of cervical cancer. There is also increasing support for providing women in microbicide trials with contraception to improve overall care, as well as to enhance research designs. Investigators in the GCM study also found that direct provision of contraception increased the time that participants spent on the study product. This increased the power of the study to show a difference between separate arms of the trial, because pregnant women could not use the product.

In some cases, trial leaders must consider health care for people who fail to qualify for a trial. For example, at the UZ–UCSF project in Harare, Zimbabwe, a clinical trial could not enroll HIV-positive people. Nonetheless, the local CAB wanted the trial leaders to provide care for people identified as HIV-positive during the screening process. As a result, the trial leaders developed a system of care for those people, which included both direct and indirect features. Those who screened ineligible for the study because they are HIV-infected received two additional counseling sessions at the research site and referral to services as needed, including general, opportunistic-infection, and social-welfare referrals. The partners of the potential participants who screened ineligible are also offered HIV testing.

## Step 6: Build relationships with nearby resources

The strength of interaction with local resources — clinics, hospitals, pharmacies, and so on — correlates with proximity. Trial sites with nearby resources tend to build better bonds that lead to better health care for the participants. For example, the Fiocruz site in Rio de Janeiro works with three government health care sites: two in the city and one in a very poor section outside the city. These three clinic locations provide patients with immediate access to some of the highest quality care in Rio. This collection of sites also gives participants a choice on where to seek health care.

Working with nearby partners provides several health care benefits:

- Improved ability to handle referral challenges
- Participants have easier access to further care, perhaps even within walking distance or near where they live or work
- Easier follow-up on referrals — for example, through meetings with referral staff

Working with nearby partners, though, can also create challenges:

- The proximity can make research staff feel compelled to escort participants to referral sites, which takes time and might violate a participant's privacy and confidentiality.
- Research staff can also be expected to provide more resources or staff time to referral sites than is possible.

In balance, however, nearby partners provide long-term benefits. For example, these relationships contribute to capacity building. “In the coming years, there will be increasing demands on clinical sites so that national governments, sponsors, and researchers should think about how to sustain site capacity and retain research staff expertise,” according to *Ethical Considerations in Biomedical HIV Prevention Trials*. “Given the long time frames of biomedical HIV prevention

research, special attention to communication and transparency is needed in order to build and maintain trust with participating communities, and to sustain site capacity even after the end of a trial.” Nearby partnerships can trigger such benefits, especially sustainability.

Likewise, GCM’s *Mapping the Standard of Care at Microbicide Clinical Trial Sites* examined how care continued after the study. It also found that study sites that set up stand-alone clinical facilities to provide care cannot continue it when the study is over. Even if those sites were utilized for new research, they only provide care related to screening or participation for that trial. However, sites that provided care for participants through partnering and capacity building of established public health facilities and were co-located with them (e.g., within or next door) enabled screened-out women, families, etc., to continue to access the same level of care as those participating in the trial. One site set up a parallel, mobile system of care for participants, but it is questionable whether this system will be sustainable when the trial is over.

In building partnerships, clinical trial planners and leaders must know what they can provide. This can include:

- Funding
- Infrastructure, such as clinic repairs or providing laboratory equipment
- Staff time — including medical screening done as part of the research protocol, which reduces strain on nearby staff
- Supplies
- Training

For example, the UNC project in Malawi mandates that all medical staff contribute one day a week in local clinics and hospitals. In addition, this project provided laboratory use, medical and office supplies, pharmaceuticals, and other resources for the Kamuzu Central Hospital.

On the other hand, clinical trial planners and leaders must know what they expect from partners. This can include:

- Additional medical treatment
- Further testing
- Psychological or social benefits for participants

The partnerships can also go beyond medical facilities. Local organizations can help with community interactions. For example, at the UNC Project in Malawi, the community-based group, National Association of People Living with HIV/AIDS in Malawi (NAPHAM), refers participants to the clinical trials. This group is active in the CAB and conducts educational dramas about specific research studies in marketplaces, in collaboration with community education staff. Such connections provide even broader capacity building.

To build such partnerships, clinical trial leaders can use several approaches:

- Make contacts through acquaintances in the local community
- Connect with community members, perhaps through hiring a community liaison officer who can build strong local contacts and has effective networking skills, and who can visit referral sites on a regular basis
- Develop a formal partnering process, such as sending a member of the clinical trial staff to make a presentation to a potential partner identified by the community liaison officer
- Put agreements in writing, such as a “Memorandum of Understanding” or other locally relevant documents that outline what each will contribute to the partnership and how research participants will benefit

The sites studied by the Partnering for Care project used various partnership-building techniques. Projects in Durban and Hlabisa, for instance, used the community–liaison–officer approach. In Pune, a community programs supervisor works with the clinical trial’s principal investigator to build and sustain partnerships. The key, really, comes from developing a partnership-building plan and continuing to work at it.

## **Step 7:** **Develop a referral system**

Many of the steps above mention indirect care through referrals, often with partners. Nonetheless, simply building partnerships does not ensure effective indirect care (see box titled “Trials with Tenofovir”). Getting the most effective indirect care requires a referral system — a process that creates and follows a referral from start to finish, and documents the process (see Appendix 8: Checklist — Creating a Referral System). Such a system works best if it includes several features:

- A formal referral procedure, such as providing a participant with paperwork that outlines the intention of the referral
- Mechanisms that get participants to the referral site
- A follow-up procedure

At the UNC project in Malawi, staff members found that participants or their family often failed to obtain indirect care simply because they did not go to the referral site. The reasons for not going were often related to lack of transportation. Sometimes they also resulted from a decision to go home first, especially if the participant was concerned about a long wait at the referral clinic, with the result that efforts made to facilitate the referral were undone. To bypass that problem, a nurse on the clinical trial staff was available to escort the participant to the referral site, providing transportation if needed, and thus ensuring that the participant could receive needed care in an expedited way. Thus, this solution addressed the realities of the local health care system, as well as participant concerns about time away from family and household responsibilities.

However, to track the effectiveness of a referral, clinical trial staff must follow up on it. All 13 sites studied in the Partnering for Care project used some type of follow-up procedure. For instance, many sites performed this follow-up through discussions with the participant on the next visit in the clinical trial. Likewise, if a study placed staff members at a referral site for some exchange of

services, this also allowed referral follow-up. Even if a participant screened out of a trial, some studies tried to follow up on any related referrals, either by contacting the screened-out participant or the referral site to see if participants were accessing care. However, in many places, referral sites may not provide any information on their clients so as not to violate their privacy and confidentiality. Follow-up of screened-out participants can also require considerable staff time, especially in areas where 25 percent (or more) of participants might be screened ineligible due to HIV infection or other health reasons.

Referral follow-up also exposes potential problems:

- Costs to participants at the referral site
- Drug stock-outs at the referral site
- Incomplete referral treatment
- Long waits for care at referral sites
- Transportation issues
- Understaffing at the referral site

However, by discovering such obstacles to referral treatment, the clinical trial staff could implement solutions, such as:

- Provide funding to participants to cover referral costs. Typically, covering these costs has a minimal impact on site resources, but it removes a major obstacle for participants. Covering such costs can also be accomplished via a financial contract between the trial and a local provider or organization if direct reimbursement to participants is problematic.
- Stock needed pharmaceuticals at the study or referral site
- Provide medical documentation to reduce strain on the referral-site staff, improve participant treatment, and reduce wait times
- Provide transportation to the referral site
- If a referral site is understaffed, the clinical trial team might be able to provide some staff hours

Two sites employed referral slips as part of a follow-up system. A participant received a slip that documented the needed treatment, and then the trial staff could see if the slips ended up at the referral site, indicating that the participant completed the referral. Although this seems like a good system, it provided mixed results at best. In some cases, a referral slip helped trial participants move ahead in treatment lines, which was helpful. However, in terms of tracking the success of referrals, the slips occasionally got lost at the referral site. This highlights one of the issues for follow-up of referrals: They should not add an additional administrative burden to an already over-burdened referral site.

In the end, a referral follow-up system depends on energy from the trial staff. Someone from the trial staff must make regular visits to the referral site to observe the complete process. Only then can follow-up problems be identified and repaired.

For an overview of the resources that can be used with these seven steps, see Appendix 9: Checklist — Resources to Implement. This checklist provides suggestions of approaches and likely timeframes.

Through these seven steps, clinical trial planners, leaders, and staff can develop an effective health care system for participants in an HIV/AIDS study. The ensuing results will benefit the participants and create lasting relationships between trial staff, community leaders, and partners.

Between June 2004 and March 2006, FHI staff and others ran a Phase II clinical trial to determine whether tenofovir — an antiretroviral drug that has been used to treat HIV infection — could be used to prevent infection as well. The FHI trial was conducted in Cameroon, Ghana, and Nigeria, with funding from the Bill & Melinda Gates Foundation. As published in *PloS Clinical Trials*, too few HIV infections occurred during the trial to indicate whether tenofovir is protective, but this trial did show that short-term use of tenofovir is safe and acceptable for HIV-negative women at high risk of becoming infected. However, beyond the clinical results, this trial revealed some of the challenges in developing an effective referral system.

Before the trial started, FHI collaborated with host-country social scientists to conduct formative research at all sites. This research included assessments of the care and treatment available at each site for people living with HIV and AIDS. The clinical research teams at each site used this information to develop referral procedures for participants who tested HIV positive during screening, or during the trial itself. Here, we will focus on Cameroon, where the trial enrolled 400 women.

The Cameroon formative research team visited facilities and organizations that could potentially provide health care and services for the trial participants. In addition, researchers interviewed people living with HIV/AIDS and health care experts treating them to learn more about the resources available. Based on this information, the formative research team prepared a report, which was shared with the clinical research team. The latter then developed a referral system for women identified as seropositive. As planned, this system

would depend on a clinic that was implementing a new program for ART. Moreover, this clinic's chief medical officer was the main physician for the trial in Cameroon.

To facilitate referrals for all health care needs of trial participants, FHI added financial support for each trial site to hire a health counselor or referral manager. This position was designed to help trial participants obtain referral care, including women who tested HIV positive at screening and those who became HIV positive during this trial. The health counselor would also handle other obligations, including accompanying any seropositive woman to the referral service to help her register, developing relations with referral care providers, maintaining a database of referral options, and other administrative duties.

Despite these efforts, FHI staff found that Cameroon's referral system was having problems. About the same time, Act Up-Paris raised concerns about the ability of seroconverters to access HIV care and treatment, including ART. Ultimately, the difficulties with the referrals seemed to stem from poor communication and lack of an explicit agreement with the ART program at the local clinic prior to the beginning of the trial and referral of participants for care. As controversies about the trial mounted, tensions also increased with regard to referrals from the trial to the ART program.

In February 2005, Cameroon's Ministry of Public Health suspended this trial's ability to provide the study product (tenofovir or placebo) to participants. The Ministry's subsequent review of study procedures resulted in a number of recommendations, all of which were addressed. However, permission to restart the trial was never given, and FHI closed the Cameroon trial in September 2005.

Still, a meeting of various stakeholders spawned a plan for long-term care and treatment for the 10 women in Cameroon who seroconverted during the trial. This included funding for 10 years of pre-ART care and five years of ART care. The Ministry decided that a government hospital should provide this care and treatment. Consequently, FHI negotiated the 15-year contracts and deposited funds (provided by the Gates Foundation) to provide care for the women who became infected while enrolled in the tenofovir study in Douala, Cameroon.

Despite these efforts, it continues to prove extremely difficult to link the 10 women from the trial with the care and services that had been negotiated on their behalf. FHI staff have communicated repeatedly with contacts at the government hospital, but have not yet received any response. Efforts to work with a local community organization to facilitate the relationship between the seroconverting women and the hospital were initially successful, but then fell apart when a key person left the organization.

Based on this experience and other work, FHI now requires that referral procedures for seroconverters be formalized and standardized for the HIV prevention trials that it implements. Considerations when establishing such procedures should include: formal agreements with referral sites, designated funding to support the referrals, staff that manage referrals, and documentation that ensures that the procedures create the intended outcomes.