

Experiences in recruiting volunteers through community based initiatives in Phase-1 vaccine trials in India

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Introduction

The recruitment of participants in sensitive clinical trials such as HIV vaccine trials poses significant challenges to researchers. Getting community support and ensuring community engagement is difficult due to HIV related stigma. Retention in clinical trials is another challenge as the study protocols and procedures are complicated and time intensive for the participants. Lower level of literacy, poverty, and lack of empowerment pose additional challenges,¹ in recruitment of volunteers in resource limited settings like India. Success of sensitive and complex clinical trials like HIV vaccine trials is dependent on effective partnerships between biomedical scientists, social scientists, and communities.

Recruitment of research participants within ethical framework is central to good research practice,² and asking potential participants to provide written informed consents is the gold standard in recruitment practice,³ community education is critically important in this context. A commissioned report to the US Bioethics Advisory Council,¹ commented that research projects may need to adopt a multistep consent process: to ensure that community and the potential participants are adequately educated.

Community education helps to build support for a trial, and assists in ensuring that participants are fully informed about the implications of participating in clinical trials.⁴ This may result in community ownership of the research being conducted. Cultural barriers can create

Success of HIV vaccine trials is dependent on infrastructural preparedness of the site, technical expertise of the trial team and strong Socio-political support of the local community. The processes followed and experiences gained while implementing various community based initiatives for recruitment of healthy volunteers during the three HIV vaccine trials in India are described. Major initiatives in community engagement implemented for the first time in India included establishment and involvement of Community Advisory Board and capacity building and engagement of lay community based volunteers called “peers” using “lay health promotion” model. Community education program designed for trial participants’ education, identification and enrollment was a three-tiered approach, moving from large community awareness meetings (first step) to facility-based small group meeting to provide trial specific information (second step); ending with one-to-one vaccine center based meeting with the volunteers to clear doubts, myths, and misconceptions about HIV/ AIDS, the experimental vaccine and HIV vaccine trials as well as to explain trial specific procedures (third step). It is important to focus on gender issues, locally relevant socio-cultural factors, informed consent, and post-trial care related matters during the conduct of sensitive clinical trials in socio-culturally diverse and resource limited setting like India.

Keywords: autonomy, Community Advisory Board, community engagement, gender issues, Phase 1 HIV vaccine trial, peer, recruitment, trial participation, volunteers

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difficulties for trial participants, especially for women whose decision making is controlled by their spouses.⁵ The need for being sensitive to cultural norms in implementing informed consent is very important where there could be conflict between ethos and ethics.⁶

All these issues are critically important in the Indian scenario. While preparing for the upcoming vaccine trial, the vaccine trial team of National AIDS Research Institute in Pune, India studied community willingness to participate in the clinical trials and the findings of the study were used in formulating appropriate awareness and recruitment strategies.⁷

Traditionally the first information-sharing step is the announcement of the potential clinical trial by the researchers, policy makers or program managers because of their knowledge and authority. However, this may be perceived as paternalistic attitude.⁶ To prevent this, National AIDS Research Institute (NARI

(Indian Council of Medical Research) and its trial partners in India took several steps to inform and engage different faces of the community during the conduct of the three HIV vaccine trials in India. The institutional committees of the respective sites approved all the three HIV vaccine trials. Written informed consents were obtained from the study participants who were screened and/ or enrolled.

Following the first HIV vaccine trial in Pune trial using AAV based HIV vaccine, another trial was conducted in Chennai using Modified Vaccinia Ankara (MVA) based HIV vaccine and the third trial was conducted at both sites using prime-boost strategy using DNA-MVA candidates. The safety data of all the three trials conducted in Pune and Chennai have already been published.⁸⁻¹⁰ The processes followed and experiences gained while implementing various community based initiatives for recruitment of healthy volunteers during the three HIV vaccine trials in India are described.

Taking a Socio-Culturally Appropriate Approach

The investigators of the first phase 1 HIV vaccine trial in India developed a recruitment model based on multi-level participatory approach employing expanded informed consent principle,¹¹ and employed a two-phased enrollment process using lay health promotion techniques (Fig. 1).

Principles of participatory action research,¹² were adopted to ensure adequate education of the community and potential participants about HIV, its prevention and the research process. Active and systematic involvement of Community Advisory Board (CAB) and media helped in demystifying the process of vaccine trial and making it readily understood by the lay community. Study specific education material was developed to provide information on HIV/ AIDS, purpose of the clinical trials involving human volunteers, trial procedures, study sponsors

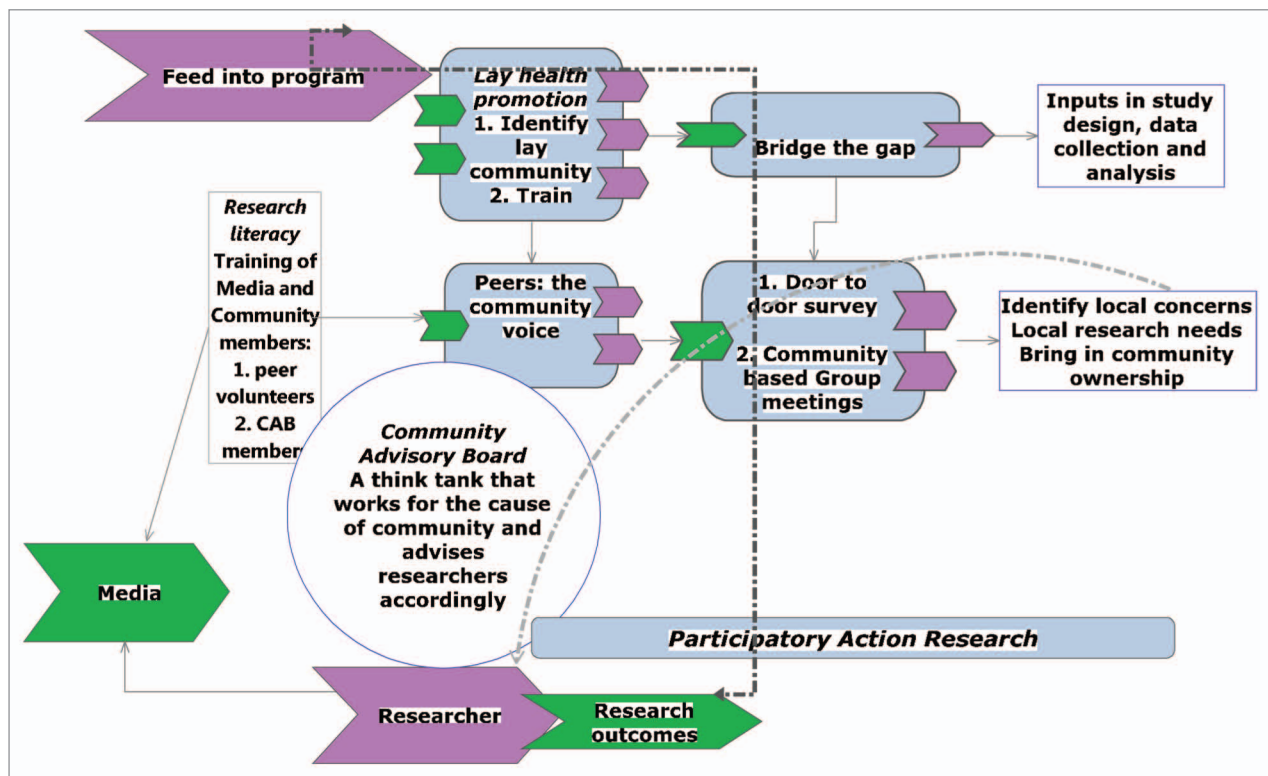


Figure 1. A conceptual framework of community involvement using lay health promotion model and using participatory approach to facilitate community based recruitment of healthy volunteers for phase 1 HIV vaccine trial in India. The structural components of recruitment plan were: (1) Community Advisory Board; (2) Community volunteers designated as peers. Peers and CAB were involved in evolving strategies of recruitment based on lessons learnt during interim assessments. Media was informed periodically.

and investigators. The education material was given to any individual on request irrespective of expressed interest in trial participation to ensure wider distribution of knowledge regarding HIV vaccines and trials. A community friendly electronic power point presentation was developed with the goal of making the community understand technical issues in a simplistic, visual, and non-technical manner during group and individual meetings. The following information was imparted to the community and potential volunteers:

1. Principles of immunization: How vaccines work in the body, what are antibodies and how vaccine induced antibodies are different than those following natural HIV infection.
2. The nature and structure of the vaccine candidate
3. Principles and procedure of conducting preventive Vaccine Trials
4. Side effects, stigma, and discrimination
5. Ethical principles including autonomy, rights and meaning of participation, and grievance redressal mechanism.¹³

Hearing the Voices of Community and Community Oriented Approach for Recruitment

Community based recruitment has been traditionally reported to be a challenge,¹⁴ but adequate and appropriate education and information sharing with the community are known to lead to improved enrollment in clinical trials.^{15,16}

As per the UNAIDS guidance on community involvement for HIV vaccine trial,¹⁷ community was engaged throughout the trial process in India. The structural components of the recruitment plan included: (1) Working closely with Community Advisory Board and (2) Involvement of community volunteers designated and trained as peers (Fig. 1).

The Pune study information model had 3 step approach: information sharing and announcing the trial by the researchers in the community (Level 1), receiving inputs from the representatives of the community regarding locally prevalent values, norms, and opinions (Level 2) and incorporating useful knowledge in the education and programs planned to provide the

Table 1. Number of volunteers and their referral sources contacted during community mobilization program for three phase1 HIV vaccine trials in India

Referral Source	Number of persons contacted	No. of persons enrollment
NGO	1562	50
Health care provider	2052	9
Academician	9841	2
Industry	1758	4
Community	17365	29
Total	32 578	94

information to the potential participants and the community (Level 3).¹⁸

Both the institutes that conducted the three HIV vaccine trials in India worked with locally constituted Community Advisory Boards (CAB).^{8,9} Contribution of Community Advisory Board members in discussions regarding the type of population to be targeted for enrollment, in creating “community literacy” among researchers and in development of informed consent forms as well as study information material in a non-technical and community language was crucially important. During CAB consultations to discuss trial recruitment strategies, investigators in Pune had proposed approaching blood donors as potential trial participants following the Thailand model.¹⁹ However the site CAB members in India strongly opposed the idea:

Blood donors are a rare commodity in the country. They would not be able to donate blood if they participated in the trial as they may test HIV antibody positive...at least for the trial period.

Eventually, despite being informed about the possibility of testing HIV positive and not being able to donate blood; one of the trial participants who participated in the vaccine trial expressed disappointment because he developed vaccine induced antibodies and was not able to donate blood on his birthdays, the practice he had followed for years.

The other group representing the community that helped in the vaccine trial recruitment process was that of “peers”. National AIDS Research Institute developed collaborative partnerships for community support, education, and field

based recruitment with seven non-governmental organizations (NGO) based in Pune.²⁰ Community coordinators of NARI identified 115 volunteers from the service area of 7 partner NGO who were imparted training and empowerment to work at the grass-root level in the community. They created awareness about the trials, identified potential volunteers, and guided them to meet key investigators from the trial team to participate in the trial recruitment process. The National Institute for Research on Tuberculosis (NIRT) collaborated with Y.R. Gaitonde Centre for AIDS Research and Education (YRG CARE), a local reputed NGO to identify volunteers for the second and third HIV vaccine trials conducted in Chennai.

The Profile of HIV Vaccine Trial Participants in India

Throughout the preparatory and actual vaccine trial phase, that is between December 2003 and January 2006, community awareness was created. In a span of 6 y, a total of 94 healthy volunteers were recruited in three phase I trials in India.^{8,10,18} At Pune site, 30 and 16 enrollments made were in the first (AAV) and third (DNA-MVA prime boost) HIV vaccine trials by reaching out to 8349 and 5881 individuals respectively. At the Chennai site, 32 and 16 volunteers were recruited in the second (MVA) and third (DNA-MVA prime boost) HIV vaccine trials by approaching 13 920 and 14 080 respectively.

Overall, 32 578 individuals were contacted from 5 different sources viz. people residing in the service area of partner NGO, health care providers, people working in the academia, industrial workers,

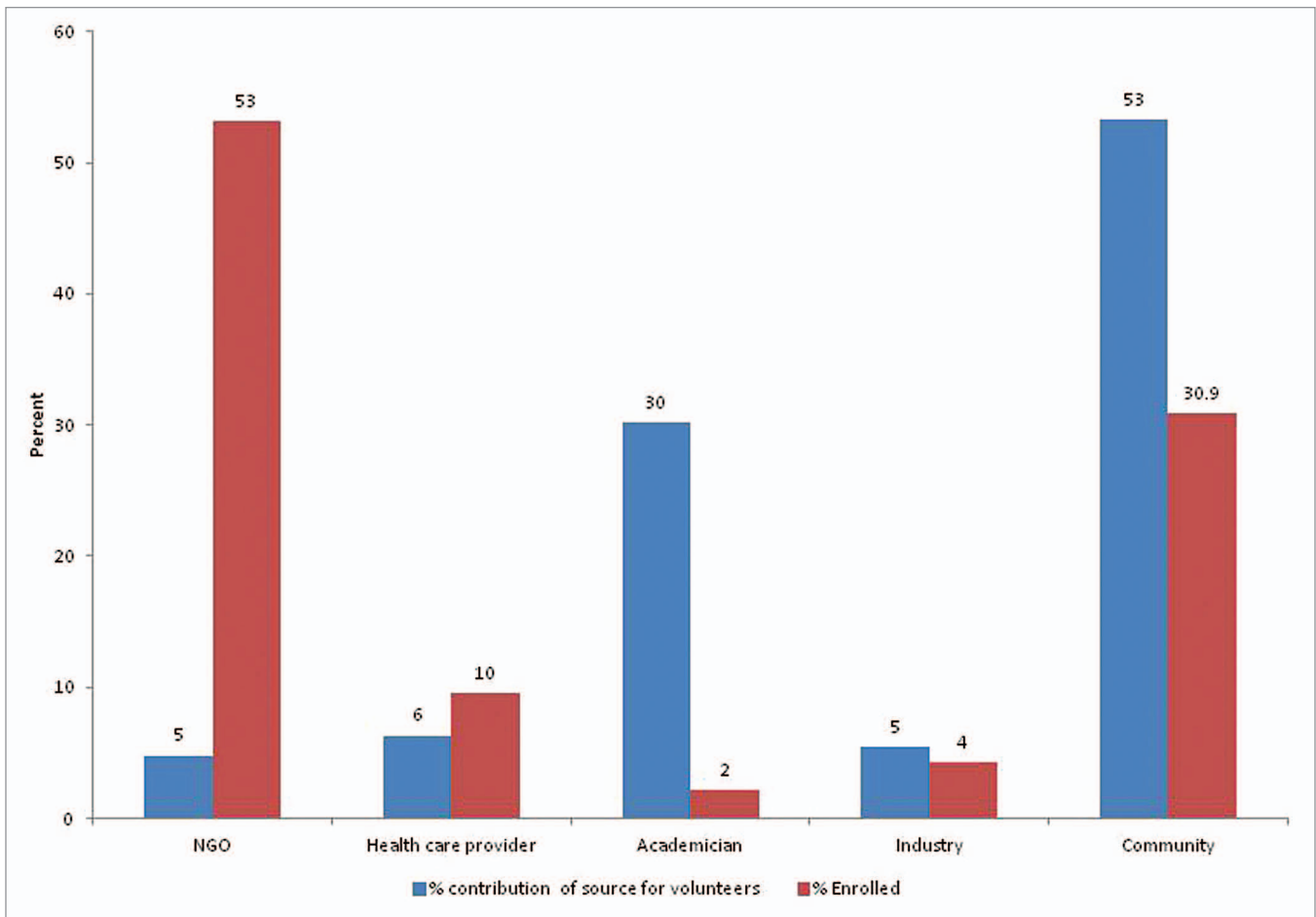


Figure 2. Proportion of volunteers enrolled from each referral source in 3 phase 1 vaccine trials conducted at Pune and Chennai in India.

and the general community in the three Indian HIV vaccine trials (Table 1).

Of the individuals reached in the first level meetings, 53% represented the general community including the civil society and 30% represented professional groups like academia. Nearly half of the enrollment was from NGO service areas (53%; 50/94) and nearly one third from the community and civil society (31%; 29/94) (Fig. 2). Nine (10%) health care providers participated in these trials in India. Academia and industries contributed very little to enrollment of volunteers (4.2%, 4/94).

It has been reported that individuals might participate in clinical studies for assured access to medical care or perceived personal benefits.^{21,22} It was anticipated that people from academia, industrial workers or health care professions with a better educational profile and better understanding of the technical process,

might be more enthusiastic about participating in HIV vaccine trials; however, this was not the case. Differential motivation to participate or not to participate in HIV vaccine trials among different sects of the Indian society with differences in educational status, awareness, and income is an area that needs exploration. The Indian trial experience supported the prevalent view that civil society organizations have significantly impacted health research and served a pivotal stakeholder role.²³

With the prevalent HIV related stigma,²⁴⁻²⁶ during that period, ensuring “research literacy” in the community and among the potential participants was essential. The site investigators ensured that each volunteer participated after acquiring adequate information and with full commitment. A two-step informed consent process for screening and enrollment was designed for HIV vaccine trials in India.

Gender Issues

Women have traditionally been under-represented in clinical trials of any phase.²⁷⁻²⁹ Various strategies have been used to include women in clinical research which could benefit them, for example, cervical cancer screening,^{20,30} but barriers have still remained. Considering women’s greater vulnerability to HIV due to a complex mix of biological, economic, and social variables unique to India, the vaccine trial teams in India took special efforts to inform women, ensured adequate enrollment of women and addressed some of the gender issues. Advanced gender training was conducted for the HIV vaccine trial teams in Pune and Chennai. It was realized that time needs to be invested in educating potential women volunteers as well as their spouses and families because women are unable to exercise autonomy in India. The existing gender norms in

Box 1. Gender training is critical for the research team to understand gender relevant issues in the trials

Need for gender training-a case at Pune site

Mrs. Surbhi*, a middle-aged social worker showed keen interest in contributing to the social cause by participating in the vaccine trial. The issue of family involvement and support was repeatedly discussed with her, but she kept ignoring the matter. She insisted that it was perfectly within her rights to decide about participating in the vaccine trial. Mrs. Surbhi was screened and found to be medically eligible to participate in the vaccine trial. She visited the clinic with her spouse, prior to the enrollment visit. Mrs. Surbhi reiterated that she was looking forward to participate in the trial, but suggested that the trial team should talk with her spouse. Mr. Sam*, her spouse, mentioned that he was very enthusiastic and supportive of her participation in the vaccine trial. On enquiry he talked about his casual affairs and it appeared that he had a hope that the trial vaccine might protect his spouse from AIDS. In a separate discussion, Mrs. Surbhi shared her suspicions about her spouse's fidelity and she explained that she wanted to win her husband back by complying with his wish to participate in the trial. A case of "coercion" by the spouse was noticed and Mrs. Surbhi's participation was forestalled. The woman was informed about "false sense of security" following the use of experimental vaccine. (*Names are fictitious)

Box 2. Need for assessment of preparedness of potential volunteers

Participant: "I am becoming weaker. My wife also feels that. You talk with her."

Wife: "I feel he is becoming weaker...you take this out of his mind that he is ...[/sick/]"

And one day, the same volunteer came and informed: "My wife has left".

Even now, nearly 7 years after HIV vaccine trial participation, the volunteer contacts the trial team: "I have got myself tested. Please see my reports. Am I Ok?"

The participant has a feeling that he has become weak due to trial participation and getting HIV infected. He does not get re-assured despite counseling and serological evidence of absence of HIV infection. The fact that his wife left him must also have made a strong impact on him. It is unclear if the reason for this is related to vaccine trial participation because both of them had jointly taken the decision to participate in the HIV vaccine trial

the country could render women vulnerable to coercion or they were likely to be misled into participation. A case has been described below an important gender issue (Box 1).

Other challenges to successful recruitment of women into vaccine research also emerged. A crucial requirement for childcare emerged as the study specific procedures were time-consuming. Insistence of women participants to hasten and complete study related procedures during the visit (who used to be worried about their young children) put pressure on the trial team. Such child care needs have been reported in other trials also.³¹ A nurse and a counselor offered childcare help to the women clinical trial participants who brought their children along with them. Hence, provision of childcare for optimal and hassle-free participation of women in vaccine trials is recommended. Confidentiality remained an important and critical issue for women participants who were worried about harmful consequences including violence resulting from possible disclosure of their vaccine trial participation. Some women participants also found it difficult to comply with protocol specific contraceptive usage or procedural requirement of urine pregnancy test (UPT) as some of them were widows or had utilized permanent method of family planning. CAB objected to the need for UPT among widowed and unmarried

women. The community education material was further modified to include the reasons for UPT and contraception in the trials. Gender training was found to be an important component for the researchers involved in HIV vaccine trials.

A number of potential women participants withdrew after qualifying in the screening eligibility tests. Reasons for non-participation of "medically eligible" women from HIV vaccine trials even after initial commitment need to be investigated.³²

Psychological Fitness to Participate in Difficult Clinical Trials and Personality Types

Ethics committees in India raised concerns about ability of potential participants to bear the "stress of HIV vaccine trial participation." A recent mental model study to understand perceptions about vaccine induced antibodies among men having sex with men in India has reported the mental fear of HIV related stigma resulting from vaccine trial participation.³³ A case in the third trial at one of the two HIV vaccine trial sites is described (Box 2).

Following the first HIV vaccine trial in India, the specially constituted National Advisory Board (NAB) for HIV vaccine trials in India had advised that potential participants be assessed for their psychological fitness for participation in such sensitive trials. Following recommendations of

NAB and NARI Ethics Committee, during the third HIV vaccine trial in India, a voluntary psychological and personality assessment test of the potential volunteers was introduced. Among those who opted for the assessment, it was observed that those with lower scores never returned for participation despite early expression of motivation to participate. Assessment of personality has some ethical angles. There can be a possible controversy about the appropriateness of the selected instrument to assess personality and the assumption that the personalities so detected with some deficiencies would face problems in bearing the trial related stress. World over, the ethicists and the researchers need to build some consensus to address the issue of psychological vulnerability of potential trial volunteers.

Reasons for Vaccine Trial Participation

There was almost equal participation of men and women representing various socio-economic strata. Altruism has been reported to be the main motivator for participation in HIV vaccine trials both in the OECD (Organizations for Economic Cooperation and Development) and the non-OECD countries the world over.^{7,34,35} Altruism was one of the major reasons for participation in Indian HIV vaccine trials as well,⁷ and no regional differences were

**Box 3. Family involvement in Indian vaccine trials
Chennai site**

Volunteers D0012636 & 37: A couple decided to participate together primarily for doing good for the society.

Volunteers D0012654 & 55: A pair of brothers-in-laws participated. They were accompanied by their families to know more about the trial and it was jointly decided that men in the families would participate.

Volunteers D0012639 & 40: A pair of sisters who learnt about the trial came in with their grown up children and spouses to participate in the trial.

noted among participants for volunteering in clinical trials. Knowing a person with HIV infection was another motivator both at Pune and Chennai sites.

Some examples from the trial sites are quoted below:

When I took care of a neighbor who had AIDS, I understood the agony and pain associated with this killer disease. When she passed away I was looking forward to getting involved in fight against this disease, and what better opportunity than to volunteer for this preventive vaccine trial? [A volunteer from Chennai site]

She wants to do something for preventing HIV/AIDS as some of her relatives (brother, his son, and sister's son) died of HIV/AIDS. [A peer sharing what a volunteer had told her ...from Pune]

Participation of social workers, especially community level peers in the vaccine trial is an example of true ownership of the trial signifying successful participatory research model.

I am a peer, I want to set example for the community ...If I participate, I can set an example for others. [Peer who had volunteered for trial participation at Pune site]

I read in the newspaper some time back the gesture of Bill Gates, who had donated a huge sum for AIDS research. I thought to myself that even if I take 10 more births I would not be able to donate even a fraction of the same. But when I read about this trial in the paper I was thrilled of the prospect of involving myself in a worthy noble cause like this [A volunteer from Chennai site]

I am a very ordinary person and I did not have the opportunity for higher education. But my dream was to contribute to research and development and I have fulfilled my dream by volunteering in this International Phase I Vaccine Trial [A volunteer from Chennai site]

Shared Decision making is cultural norm: A debate about autonomy and non maleficence

The stepwise recruitment approach helped in carefully guided and shared decision making in HIV vaccine trials in India. Family involvement; especially that of the spouse, was observed to be useful at both sites in all the three trials. We experienced more instances of failure of enrollment following lack of family involvement in the decision making process. At Chennai site, examples of family involvement and support for this noble cause were noted (Box 3).

Despite major emphasis on autonomy in medical decision making in the 20th century, the medical community and the public have been increasingly embracing shared decision making in the United States and elsewhere in the 21st century.^{4,36,37,38,39} On one hand autonomy signifies capacity to make decisions,⁴⁰ on the other hand it has been criticized for promoting a pernicious model of human individuality that overlooks the importance of social relationships and dependency.⁴¹ In Indian trials, we pursued both; with majority preferring the shared decision making approach.

Key Messages and Lessons Learned from the HIV Vaccine Trials in India

The trials demonstrated that community engagement and ownership is possible even in resource-limited settings. Recruitment process was participatory and culturally relevant. Coordinated

efforts of the medical, social science, and field teams helped to resolve participant problems and issues. Participants are a representative mix of both genders, different educational backgrounds as well as socio-economic strata. The gap between intention to participate and actual participation exists and to bridge that the reasons for stepping back need to be explored. Although the community based recruitment approach is labor intensive, it is rewarding and capable of providing committed volunteers.

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