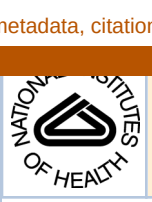

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ACCESS TO TREATMENT IN HIV PREVENTION TRIALS: PERSPECTIVES FROM A SOUTH AFRICAN COMMUNITY

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Abstract

Access to treatment, in HIV vaccine trials (HVTs), remains ethically controversial. In most prevention trials, including in South Africa, participants who seroconvert are referred to publicly funded programmes for treatment. This strategy is problematic when there is inadequate and uneven access to public sector antiretroviral therapy (ART) and support resources. The responsibilities, if any, of researchers, sponsors and public health authorities involved in HVTs has been hotly debated among academics, scholars, representatives of international organizations and sponsors. However, there is little published on community perceptions. Recent guidance asserts that communities should make inputs into treatment and care decisions. This qualitative study explored a South African community's perceptions of *who* should provide *what* to HVT participants as well as *how* and *why* this should be done. Twenty-nine adults working at or attending five primary health care clinics in two rural areas in KwaZulu-Natal participated in in-depth interviews. Respondents expressed that *researchers* should 'help participants to access' treatment and care 'because they are in a position to do so' and 'are in a relationship with' trial participants. Respondents suggested that researchers could help by 'facilitating referral' until such time that participants can access care and treatment on their own. We highlight a series of implications for researchers in HVTs, including their need to be aware of prospective participants' considerable trust in and respect for researchers, the responsibility that this places on them, and the need for clear communication with communities so as not to erode community trust.

Keywords

South Africa; HIV/AIDS; research ethics; HIV trials; community perspective

BACKGROUND

The AIDS pandemic continues to expand, especially in sub-Saharan Africa.[1] Initiatives to reduce HIV incidence are underway, such as prevention campaigns that promote abstinence, being faithful and using condoms (ABC), male circumcision and the testing of microbicides. However, the best hope to end the AIDS pandemic is the development and distribution of effective vaccines.[2] A number of HIV vaccine trials (HVTs) are currently underway in Africa, including in South Africa.[3] Ethical principles and human rights norms underpin

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[1]UNAIDS. 2008. Report on the Global AIDS Epidemic. Geneva: UNAIDS.

[2]A. Bernstein. 2005. *Promoting Innovation and Collaboration to Speed the Search for an HIV Vaccine*. Seattle, WA: Global HIV Vaccine Enterprise. Available at: http://www.hivvaccineenterprise.org/about/index.aspx [Accessed 27 Mar 2008]; B.R. Bloom. The Highest Attainable Standard: Ethical Is/sues in AIDS Vaccines. *Science* 2000; 279: 188; G. Lindegger, M. Quayle & M. Ndlovu. Local Knowledge and Experiences of Vaccination: Implications for HIV-Preventive Vaccine Trials in South Africa. *Health Educ Behav* 2007; 34: 108–123.

[3]AIDS Vaccine Advocacy Coalition (AVAC). 2008. *The Search Must Continue: AVAC Report 2008*. New York, NY: AVAC. Available at: http://www.avac.org/reports.htm#2008 [Accessed 28 Jul 2008].

questions about the obligations of researchers, sponsors and public health authorities involved in HVTs, including enabling treatment and care for participants. This is particularly significant in Africa, given inadequate and uneven access to antiretroviral therapy (ART) and support resources. Even with recent initiatives aimed at universal access to care and treatment, 70% of those in need in sub-Saharan Africa still remain untreated.[4]

The debate about *who* should provide *what* care and treatment to HVT participants continues. This debate is primarily taking place among academics, scholars and representatives of international organizations and sponsors[5]. Little research has been conducted with community members to elicit their perspectives on the provision of care and treatment to HIV prevention trial participants.[6] Communities can and should have a voice in how vaccine trials are conducted, including the issue of access to treatment.[7] This study explored a South African community's perceptions of *who* should provide *what* to HVT participants. It further explored respondents' perceptions of *how* and *why* this should be done.

The HIV epidemic in South Africa

The HIV/AIDS pandemic is a rapidly expanding global health disaster that is heavily concentrated in the developing world. As home to more than two thirds (68%) of all people living with HIV and more than three quarters (76%) of all AIDS deaths in the world, Sub-Saharan Africa constitutes the global epicentre of the pandemic.[8] South Africa is the country with the largest prevalence of HIV in the world. In 2006, the national HIV prevalence was 29%.[9] Heterosexual sex is the main mode of HIV transmission, and women between 20 and 40 years are the most affected,[10] with prevalence ranging between 28% and 36.4%.[11] There are large geographical variations in HIV prevalence across South Africa. The highest (36%) in 2006 was in the province of KwaZulu-Natal (KZN),[12] the site for this study.

Availability of antiretroviral therapy (ART) in South Africa

The South African government's recent pursuit of treatment ideals is evidence of an advance in political commitment to fighting HIV. However, there is arguably a transitional 'waiting' period for many districts and municipalities before efficient treatment programmes are in place. Approximately 489,000 South Africans were enrolled in the public sector antiretroviral programme by the end of 2007. Of these, 370,000 have actually initiated treatment. Just over 520,000 people in need of treatment in 2008 are still not receiving it.[13] In KZN, mid-2006 indicators showed that among individuals 14 years and older 218,000 persons were in need of treatment, while only 51,000 (23%) were actually receiving ART.[14]

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[4]WHO/UNAIDS. 2008. *Towards Universal Access: Scaling up Priority HIV/AIDS Interventions in the Health Sector: Progress Report 2008*. Geneva: WHO. Available at: http://www.who.int/hiv/topics/treatment/en/index.html [Accessed 24 Sept 2008].
[5]UNAIDS/AVAC. 2007. *Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials*. Geneva: UNAIDS. Available at: http://www.avac.org/gpp.htm [Accessed 3 Apr 2008].
[6]C. Grady et al. Research Benefits for Hypothetical HIV Vaccine Trials: The Views of Ugandans in the Rakai District. *IRB* 2008; 30: 1–7; K. MacQueen et al. Community Perspectives on Care Options for HIV Prevention Trial Participants. *AIDS Care* 2007; 19: 554–560.
[7]AIDS Vaccine Advocacy Coalition (AVAC). 2005. Vaccine Trials: Leaving Communities Better Off. In *AIDS Vaccine Handbook: Global Perspectives*. P. Kahn, ed. New York, NY: AVAC: 137–144.
[8]UNAIDS. 2007. *AIDS Epidemic Update*. Geneva: UNAIDS. Available at: http://www.unaids.org/en/KnowledgeCentre/HIVData/EpiUpdate/EpiUpdArchive/2007/ [Accessed 4 Mar 2008].
[9]Department of Health, South Africa. 2007. *National HIV and Syphilis Prevalence Survey, South Africa 2006*. Pretoria: Ministry of Health. Available at: http://www.doh.gov.za [Accessed 10 Feb 2008].
[10]A.E. Pettifor et al. Highly Efficient HIV Transmission to Young Women in South Africa. *AIDS* 2007; 21: 861–865.
[11]Department of Health, South Africa. 2005. *National HIV and Syphilis Antenatal Sero-prevalence Survey in South Africa*. Pretoria: Ministry of Health. Available at: http://www.doh.gov.za/docs/index.html [Accessed 4 Sept 2007].
[12]Department of Health, South Africa, *op. cit.* note 9.
[13]Treatment Action Campaign (TAC). 2008. *Summary of HIV Statistics for South Africa*. Available at: http://www.tac.org.za/community/keystatistics [Accessed 07 Aug 2008].

Without therapy, AIDS is invariably fatal. In 2006 AIDS accounted for nearly 47% of all deaths in South Africa, the leading cause of death in the country. As of 1 July 2006, AIDS resulted in over 1.8 million deaths cumulatively in the country. More than a third of these deaths occurred in KZN.[15]

HIV vaccine trial status in South Africa

The scientific community continues to assert that preventive HIV vaccines and microbicides constitute the best hope for stemming the epidemic.[16] In 1999, the South African AIDS Vaccine Initiative (SAAVI),[17] along with other funders,[18] began investing in vaccine development and trials. HVTs involve a number of phases. Phase I and II trials enrol small numbers of healthy, HIV-uninfected volunteers at low risk of HIV infection to assess safety, tolerance and immune response, and to establish vaccination schedules and routes of vaccination. In Phase III, or efficacy trials, thousands of healthy volunteers at high risk of HIV infection are enrolled to assess the efficacy of vaccines in preventing HIV infection or in slowing disease progression. SAAVI is currently running a number of Phase I and II vaccine trials.

Access to treatment in HIV prevention trials

Volunteers for Phase III HVTs are at high risk of HIV infection. Trials are premised on the inevitability of infection for a proportion of participants, despite risk-reduction interventions. This means some participants will become HIV-infected while in trials. The controversial ethical question is: what treatment, if any, should be guaranteed to these participants? In most prevention trials, including in South Africa, participants are referred to publicly funded programmes for treatment.[19]

It makes sense to refer to local facilities for treatment, because this reflects shared responsibility, especially if researchers are building capacity in local facilities. However, this strategy is not without its problems. In some communities participants will have limited access to ART because government services are new and overburdened, or participants risk stigma and are subjected to long waiting times.[20] When treatment services are unreliable, the ethical obligations of researchers and sponsors arguably are as much in question as when treatment services do not exist.

Care and treatment for infected participants continues to be a contentious ethical debate.[21] Some have argued that sponsors are not responsible.[22] Others have argued that they are, based on different justifications. Some have argued for provision on the basis of ‘compensation for harm’, proposing that infected participants have been harmed by their trial participation.[23] Others have argued for provision in the name of *justice*, either as a

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[14]Department of Health, South Africa, *op. cit.* note 9.
[15]Ibid.
[16]Bernstein, *op. cit.* note 2.
[17]See http://www.saavi.org.za/index.htm
[18]International AIDS Vaccine Initiative (IAVI); US National Institutes of Health funded HIV Vaccine Trials Network (HVTN) and; FIT Biotech.
[19]These reference microbicide trials only, as there has been nothing similar published on HIV vaccine trials to date: Global Campaign for Microbicides (GCM). 2008. *Mapping the Standard of Care at Microbicide Clinical Trial Sites: Preliminary Findings and Summary Recommendations.* Washington, DC: Global Campaign for Microbicides. Available at: http://www.global-campaign.org/clientfiles/GCM_SOCreport_20080218.pdf [Accessed 16 Jul 2008]; K. MacQueen et al. 2006. *Partnering for Care in HIV Prevention Trials.* Bethesda: HIV Prevention Trials Network. Available at: http://www.hptn.org/ResearchEthics/PartneringForCare.htm [Accessed 7 Jul 2008]; C. Milford et al. 2006. Poster: Access to Care in HIV Prevention Trials: The MIRA Standard of Care Programme, Durban, South Africa. In *4th IAS Conference*. Sydney, Australia; Population Council. 2008. *Evaluating Services for Women who Test HIV-positive During the Phase 3 Trial*. New York: Population Council. Available at: http://www.popcouncil.org/projects/MIC_EvaluatingServices.html [Accessed 11 Jul 2008].
[20]GCM, *op. cit*. note 19, p.6.

means to reducing inequalities in health care between collaborating nations,[24] as a fair balance of research-related risks (e.g. of acquiring HIV) and benefits (e.g. of gaining access to treatment)[25] or as reciprocity.[26] A further argument is that sponsors should ensure access to care and treatment on grounds of beneficence.[27] This argument supports sponsors' provision of more than is minimally required to conduct the research and rests on the notion that if sponsors of vaccine trials can do something beneficial, for example ensuring access to treatment, without sacrificing anything of comparable significance, they should do it. This has also been referred to as the 'Good Samaritan' argument.[28] Recent work has identified duties researchers have, if any, to provide ancillary care.[29] Richardson and Belsky (2004)[30] have proposed that researchers owe their subjects more than merely what the research protocol may stipulate. They argue that participants implicitly entrust certain aspects of their health to researchers when they give researchers permission to access their confidential medical information, to take samples and to perform certain procedures. It is based on this partial entrustment that researchers owe participants more than is required for the scientific conduct of the trial. The scope of this entrustment will vary, but since a participant typically gives permission for a disease under study to be monitored, care for that disease (in this case HIV) typically falls into that scope. Whether there is a responsibility to provide ancillary care then 'depends on the strength of the underlying, relationship based duty of care' [31] which rests on the depth of the researcher-participant relationship, and the participants' vulnerability, dependence and uncompensated risks or burdens.[32]

Engaging communities in research

Recent guidance emphasizes formative research with participating communities as an essential activity, in order to understand local perceptions, norms and practices. It asserts that participating communities should make inputs into treatment and care decisions, including *how* treatment services are accessed and how services might be monitored.[33]

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[21]B. Lo & N. Padian. The Obligation to Provide ART in HIV Prevention Trials. *AIDS* 2007; 21: 1229–1231; U. Schuklenk & R. Ashcroft. HIV Vaccine Trials: Reconsidering the Therapeutic Misconception and the Question of What Constitutes Trial Related Injury. *Dev World Bioeth* 2008; 7: ii-iv; U. Schuklenk & R. Ashcroft. Protecting the Vulnerable: Testing Times for Clinical Research Ethics. *Soc Sci Med* 2000; 51: 969–977; T. Tucker & C. Slack. Not If, but How? Caring for HIV-1 Vaccine Trial Participants in South Africa. *Lancet* 2003; 362: 955; UNAIDS. Treating People with Inter-current Infection in HIV Prevention Trials. *AIDS* 2003; 18: W1–12; Nuffield Council on Bioethics (NCOB). 2002. *The Ethics of Research related to Healthcare in Developing Countries*. London, UK: NCOB. Available at: http://www.nuffieldbioethics.org/go/ourwork/developingcountries/publication_309.html [Accessed 18 Apr 2008]; R. Macklin. Standard of Care: An Evolution in Ethical Thinking. *Lancet* 2008; 372: 284–285; C. Weijer & G. LeBlanc. The Balm of Gilead: Is the Provision of Treatment to those who Seroconvert in HIV Prevention Trials a Matter of Moral Obligation or Moral Negotiation? *J Law Med Ethics* 2006; 34: 793–808; R. Macklin. Changing the Presumption: Providing ART to Vaccine Research Participants. *Am J Bioeth* 2006; 6: W1.

[22]Bloom, *op. cit.* note 2; M. Specter. 2003. The Vaccine: Has the Race to Save Africa from AIDS put Western Science at Odds with Western Ethics? *The New Yorker* 3 February: 54–65; Weijer & LeBlanc, *op. cit.* note 21.

[23]Schuklenk & Ashcroft, *op. cit.* note 21.

[24]K. Shapiro & S. Benatar. 2005. HIV Prevention Research and Global Inequality: Steps towards Improved Standards of Care. *J Med Ethics* 31: 39–47.

[25]C. Slack et al. Provision of HIV Treatment in HIV Preventive Vaccine Trials: A Developing Country Perspective. *Soc Sci Med* 2005; 60: 1197–1208.

[26]Macklin, *op. cit.* note 21.

[27]Slack et al., *op. cit.* note 25.

[28]J. Hawkins. Justice and Placebo Controls. *Soc Theory Pract* 2006; 32: 31.

[29]Ancillary care is that which is not required to make a study scientifically valid, to ensure a trial's safety, or to redress research injuries. This definition is taken from: L. Belsky & H. Richardson. Medical Researchers' Ancillary Clinical Care Responsibilities. *BMJ* 2004; 328: 1494–1496. See also: R. Brownsword. The Ancillary-Care Responsibilities of Researchers: Reasonable but Not Great Expectations. *J Law Med Ethics* 2007; Winter Symposium: 679–691; H. Richardson. Gradations of Researchers' Obligation to Provide Ancillary Care for HIV/AIDS in Developing Countries. *Am J Public Health* 2007; 97: 1956–1961; H. Richardson & L. Belsky. The Ancillary-care Responsibilities of Medical Researchers: An Ethical Framework for Thinking about the Clinical Care that Researchers Owe their Subjects. *Hastings Cent Rep* 2004; 34: 25–33.

[30]Ibid.

[31]Belsky & Richardson, *op. cit.* note 29, p.1495.

[32]Richardson & Belsky, *op. cit.* note 29.

[33]D. Tarantola et al. Meeting Report: Ethical Consderations Related to the Provision of Care and Treatment in Vaccine Trials. *Vaccine* 2007; 25: 4863–4874; UNAIDS/AVAC, *op. cit.* note 5.

These inputs can improve the quality and acceptability of the research as well as offset accusations of token community consultation.[34] A community voice can assist in establishing the most appropriate and least harmful course of action for access to care and treatment. The opinions and expectations of communities and potential trial participants are an important piece of the puzzle in formulating this ethical course of action. If the debate is motivated by what beneficence in research with humans requires, then community voice is important. Beneficence requires sensitive and intelligent *action*. To determine the most appropriate action, it is important to consult with the intended beneficiary and find out what, for them, would count as help.[35] Weijer & LeBlanc (2006)[36] term this 'moral negotiation' that 'allows communities the ability to identify benefits that are consistent with their own health-related priorities'.[37] The basis of this moral negotiation rests on the principle of respect for communities that is reasonably interpreted as bestowing on researchers 'an obligation to take seriously the values of the community'.[38]

Community perception studies

Several studies have elicited patients' views of medical research from developed countries.[39] There is limited empirical research on perspectives of medical research from developing countries,[40] and fewer data exist describing what communities from developing countries think about the issue of care and treatment in HIV prevention trials.[41]

In a survey exploring community perceptions of research benefits and harms in Uganda,[42] the majority of respondents indicated that researchers should provide some benefit to the wider community following a trial. More than half of the respondents specified that this benefit should be either general medical care or care for HIV-infected community members. Another study, at 10 microbicide trial sites in seven countries (including South Africa), assessed stakeholders' (including health service providers, HIV prevention research participants and community stakeholders), perceptions of fair care and treatment for participants in HIV prevention trials.[43] While many respondents perceived the direct provision of basic healthcare and the referral of participants to off-site healthcare service providers as a fair means of meeting the health needs of research participants, concerns were

[34]AIDS Vaccine Advocacy Coalition (AVAC), *op. cit.* note 7.
[35]P. Tindana et al. Grand Challenges in Global Health: Community Engagement in Research in Developing Countries. *PLoS Med* 2007; 4: e273.
[36]Weijer & LeBlanc, *op. cit.* note 21.
[37]Weijer & LeBlanc, *op. cit.* note 21, p.804.
[38]Weijer & LeBlanc, *op. cit.* note 21, p.805.
[39]A. Asai et al. Focus Group Interviews Examining Attitudes towards Medical Research among the Japanese: A Qualitative Study. *Bioethics* 2004; 18: 448–470; S. Edwards et al. Informed Consent for Clinical Trials: In Search of the "Best" Method. *Soc Sci Med* 1998; 47: 1825–1840; P. Ellis & P. Butow. Focus Group Interviews Examining Attitudes to Randomised Trials among Breast Cancer Patients and the General Community. *Aust N Z J Public Health* 1998; 22: 528–531; J. Sugarman et al. What Patients Say about Medical Research. *IRB* 1998; 20: 1–7; R. Strauss et al. Willingness to Volunteer in Future Preventive HIV Vaccine Trials: Issues and Perspectives from Three US Communities. *J Acquir Immune Defic Syndr* 2001; 26: 63–71; S. Madsen et al. Attitudes towards Clinical Research amongst Participants and Non-participants. *J Intern Med* 2002; 251: 156–168.
[40]N. Barsdorf & D. Wassenaar. Racial Differences in Public Perceptions of Voluntariness of Medical Research Participants in South Africa. *Soc Sci Med* 2005; 60: 1087–1098; N. Kass, S. Maman & J. Atkinson. Motivations, Understanding, and Voluntariness in International Randomised Trials. *IRB* 2005; 27: 1–8; D. Wendler et al. Research on Stored Biological Samples: The Views of Ugandans. *IRB* 2005; 27: 1–5; D. Shaffer et al. Equitable Treatment for HIV/AIDS Clinical Trial Participants: A Focus Group Study of Patients, Clinician Researchers, and Administrators in Western Kenya. *J Med Ethics* 2006; 32: 55–60; C. Thiessen et al. Personal and Community Benefits and Harms of Research: Views from Rakai, Uganda. *AIDS* 2007; 21: 2493–2501; J. Stadler, S. Delaney & M. Mntambo. Women's Perceptions and Experiences of HIV Prevention Trials in Soweto, South Africa. *Soc Sci Med* 2008; 66: 189–200; Tindana et al., *op. cit.* note 35; C.S. Molyneux, N. Peshu & K. Marsh. Trust and Informed Consent: Insights from Community Members on the Kenyan Coast. *Soc Sci Med* 2005; 61: 1463–1473; C.S. Molyneux et al. 'Even if they ask you to stand by a tree all day, you will have to do it (laughter)…!': Community Voices on the Notion and Practice of Informed Consent for Biomedical Research in Developing Countries. *Soc Sci Med* 2005; 61: 443–454; Nuffield Council on Bioethics, *op. cit.* note 21.
[41]Grady et al., *op. cit.* note 6; MacQueen et al., *op. cit.* note 6; Nuffield Council on Bioethics, *op. cit.* note 21; Shaffer et al., *op. cit.* note 40; Thiessen et al., *op. cit.* note 40.
[42]Grady et al., *op. cit.* note 6.
[43]MacQueen et al., *op. cit.* note 6.

raised about the sustainability of care beyond the life of the study as well as the adequacy of local healthcare facilities. Most respondents also disagreed with the provision of ART to sero-converters, if the treatment was limited to the duration of the trial only. In a Kenyan study, respondents (including clinical trial participants and researchers), agreed that it would be unfair to discontinue ART at the conclusion of a trial, and that researchers have a long term moral obligation to provide ART to participants beyond the conclusion of a trial.[44]

There is little published to date that voices the views of South African community members on the issue of access to treatment in HVTs.[45] The present study explored a South African community's perceptions of *who* is responsible for the provision of *what* care and treatment in HVTs. It further explored respondents' perceptions of *how* and *why* treatment should be provided.

METHODS

Sample

Our sample of 29 respondents was drawn from adult men and women working at or attending five primary health care clinics in two rural areas in KwaZulu-Natal where HVT preparation activities have been carried out. Demographic surveillance studies identify this area as high in HIV incidence; making it likely that future HIV prevention research will take place there. The perspectives of our respondents on access to care for trial participants are therefore relevant. For the purpose of clarity, throughout this paper the term 'respondent' refers to clinic staff, volunteers and clinic attendees who participated in interviews for our study. The term 'participant' refers to hypothetical HVT participants who are referred to by our respondents.

Data collection

Respondents were approached at the clinic and invited to participate after being informed of the aims of the study. Interviews were conducted in IsiZulu by local field workers and were recorded, with permission. We recruited consecutively until we reached saturation on key themes that emerged from the data. A first round of data collection happened between June and August 2005. Interviews were transcribed, translated and analysed and small revisions were made to the interview guide. A second round of data collection took place between February and April 2006 using the revised interview guide.

Instrument

The interview comprised the following domains: respondents' demographics, knowledge of HIV prevention trials, and perspectives on the issue of access to care and treatment in HIV prevention trials. The latter was elicited by the following open-ended questions:

1. When people decide that they are going to volunteer for a research study, they usually think about the benefits that they might obtain from being in the study, as well as the risks of being in the study. Can you tell me what things you would consider important to think about before entering a study?
2. Now let's think about the same considerations in terms of deciding to participate in a large research trial, such as an HIV vaccine trial. If someone asked you if you wanted to volunteer to be part of an HIV vaccine trial, what are the things that you would consider before making your decision?

[44]Shaffer et al., *op. cit.* note 40.
[45]MacQueen et al., *op. cit.* note 6.

The interview guide was developed by collaborators based at Johns Hopkins Bloomberg School of Public Health, the Johns Hopkins Berman Institute of Bioethics, and the HIV/AIDS Vaccines Ethics Group (HAVEG), University of KwaZulu-Natal, Pietermaritzburg. Inputs were obtained from representatives at a local research centre and community advisory board members. The interview guide was translated into isiZulu.

Data Analysis

Interviews were transcribed and translated into English. Data were managed and analysed using NVivo. Qualitative thematic content analyses identified prominent themes in participants' responses. Key themes were identified through a careful review of all transcripts. One researcher assigned codes to themes as they emerged from the data. Matrices and tables that categorize and display data were used to understand the dimensions by which the data are categorized and to facilitate comparisons. Matrices helped to display the full, yet condensed data set and describe the decision-making process that individuals go through in thinking about the issues at hand.

Ethics

Ethics approval was granted for data collection and/or analysis from the Nelson Mandela School of Medicine Research Ethics Committee at the University of KwaZulu-Natal (E037/04) and the Johns Hopkins Bloomberg School of Public Health Institutional Review Board (H.22.03.10.28.BX). The research was also reviewed by the scientific committee of the local research institution as well as approved by the local Community Advisory Board before the study commenced. Written informed consent was obtained for each interview. Respondents were compensated for time, inconvenience and transport costs, in accordance with the Nelson Mandela School of Medicine Research Ethics Committee instruction.

RESULTS

Respondents' demographics

A total of 29 respondents were interviewed. Respondents were either clinic employees/volunteers or clinic attendees. Fifteen respondents were employed at the clinics as nurses, cleaners or providing other assistance, seven were clinic volunteers, and seven were clinic attendees (see Table 1). Two were male and 27 were female, likely resulting from the fact that recruitment took place at clinics where females were more likely to be present. Respondents' ages ranged from 21 to 58 years. One respondent's age was unknown. Twenty-one respondents in this study had completed high school. Of the high school graduates, six had a certificate: four in counselling; one as a security guard; and one in computer literacy. Seven respondents had a diploma: four in nursing and three in public relations management. Three respondents had a degree in nursing.

Respondents' perspectives on the issue of access to treatment and care in HIV prevention trials

Who and what: researchers should help participants to access treatment and care—The dominant narrative expressed by respondents was that *researchers* should give *some form of help* to participants who need treatment. There were no respondents in this study who attributed HIV infection to the actions of researchers or to the vaccine candidate. Over half of all respondents (with equal representation from workers and attendees) asserted that participants are responsible for acquiring HIV infection, from unsafe sex:

> It is not the researchers' fault they (participants) were careless because they were told to use protection. (*Female, 21 yrs, Clinic attendee*)

> I do not think anyone should be blamed because they inform you before you join. (*Female, 26 yrs, Clinic employee*)

> If you were told to use the condom I do not think is right to blame study researchers. It is your carelessness, people are getting sick, while at the clinic they are told to use the condom. The partner will say there is a condom when it is time to have sex, only to find out there is no condom. That is the mistake we make. You told them what to do; you cannot go house by house checking whether they use it or not, is up to them. (*Female, age unknown, Clinic volunteer*)

Nevertheless, very few respondents (3 nurses and 1 clinic attendee) indicated that participants were responsible for securing their own treatment. The vast majority of respondents (across workers and attendees) expressed that researchers should help in accessing treatment:

> They (researchers) should help if someone sero-converts. (*Female, age unknown, Clinic volunteer*)

> The research leader, all of you, you have to do something to help that person. You have to help the sick person. They should be given, so them to survive. (*Female, 42 yrs, Clinic employee*)

No respondents claimed that researchers should be forced to help, but most appealed to the idea that researchers are in a position where they *can* provide help to those infected:

> No they (researchers) are not forced, but they can help. (*Female, 26 yrs, Clinic attendee*)

Beyond stating that they *would like* researchers to help, or that they think researchers *should* help, a handful of respondents (from workers and clinic attendees) revealed an implicit assumption or expectation that researchers would help:

> Yes they need to be treated. Who can treat them then? They should be given from the study. (*Female, 21 yrs, Clinic attendee*)

Two of these respondents reacted negatively to the idea that researchers might not help:

> They should not turn their back on them. (*Female, 45 yrs, Clinic employee*)

Respondents' expectation of help appeared to come from, firstly: that workers had prior exposure to trials where research staff had given medical assistance to participants, and secondly: lack of confidence in local health care facilities, that is, no other good alternatives.

Why: researchers should help because they are in a relationship with participants—Respondents indicated that researchers should help because they are in a relationship with participants. An overriding theme in respondents' perceptions (across workers and attendees) was their way of understanding the nature of the researcher-participant relationship. Respondents appeared to view the participant-researcher relationship as supportive and caring:

> I think we need to assist each other. Clinics are too far, so the researcher should assist until I get ART. I think researchers need to assist the community, after finding the problem they must try and solve them. (*Female, 24 yrs, Clinic employee*)

> That one sero-converting shall have misbehaved. I presume he/she shall have been given advices but decide to engage in unsafe sex. All the same when a person becomes sick she is not left to die even if it is due to her carelessness. Instead she needs care. (*Male, 38 yrs, Clinic attendee*)

> For the study to go forward I think the researcher should assist. I think we should work together. If you find something that can help, you inform the participant. (*Female, 45 yrs, Clinic employee*)

Respondents presumed that trial participants would be able to trust researchers to make appropriate arrangements, take action in participants' best interests, and tell the truth:

> Interviewer: What if researchers are saying governments supply ART? Respondent: I can help myself then, if they are saying I can get them. (*Female, 26 yrs, Clinic attendee*)

Still within the notion of a supportive and caring relationship, some respondents thought researchers should help as a form of reciprocity for these participants' contribution to the research:

> I think the one who was giving you the vaccine need to assist all the way. They need to be there, to make sure that I am taking drugs accordingly. I think they should do something to help you, like sending you to the clinic, or do home visits. I think they need follow up visits. They do have their particulars. (*Female, 26 yrs, Clinic employee*)

> I think as human being they (researchers) can feel bad, thinking you made them join the study to put them at risk, forgetting that we are all at risk as human beings, you can use the condom for 5 years but one day without it you are at risk. I will not know how much because we are talking about the people's life. I think they need all your support. I think they need it. (*Female, 35 yrs Clinic volunteer*)

How: researchers can help by facilitating referral—Just over half of all respondents indicated that researchers' assistance in referral for accessing ART was essential. This view was expressed across all three groups. Respondents asserted that researchers should make appropriate referrals or 'arrangements' for participants to access treatment. Just over a handful thought referral was an appropriate form of help *if* it was 'assisted referral' to facilitate trouble-free and feasible access through the government sector:

> They (trial participants) can get treatment from the clinics, where they (researchers) would have made arrangements. (*Male, 37 yrs, Clinic attendee*)

> As they (researchers) are saying the ART rollout is coming to this area I think that researchers could just refer those to relevant sites. Like to mother and child study they are told once the study is finished that whatever they want they should go to the clinic. I do not see a problem. The researchers can refer them. (*Female, 45 yrs, Clinic employee*)

> There are lots of places like government places, but I know if I join the study it will be easy to be referred. (*Female, 28 yrs, Clinic volunteer*)

> I am saying they should refer that person because there is lots of training needed before getting ART. Researchers are not dealing with ART. Their duty is to find out if the vaccine works or not. My concern is that I want those people who seroconvert to know the right channels/methods. (*Female, age unknown, Clinic volunteer*)

Only two clinic employees felt that researchers should directly provide treatment, train clinic staff and leave ART with them when the study ends:

> We can still contact each other even if the study is gone. I think I would need to give them my contact details. Even if (the researchers) are gone, they do visit the clinic. I think they should train staff from the clinic and leave the ART with them,

> so they can give people and tell them how to take them and also tell them all the side effects. It won't stop because they are gone. For life, I should get it. (*Female, 45 yrs, Clinic employee*)

One third of respondents (mainly workers) argued that researchers *should* help with all health problems, not just HIV, even though this was not their responsibility alone. A few respondents thought that researchers should themselves treat everything:

> I think the researchers should be prepared to treat everything. (*Female, 45 yrs, Clinic employee*)

Two clinic employees also suggested that researchers should contribute to the existing local health infrastructure in the form of training caregivers, building clinics and coordinating with local government.

Researcher's responsibilities are time-limited—Just over a handful of respondents (mostly clinic workers) insisted that researchers should facilitate lifelong provision of ART. However, respondents generally expressed that researchers' help should continue until participants can access treatment on their own:

> I think we need to assist each other; the researcher should assist until I get ART. (*Female, 24 yrs, Clinic employee*)

DISCUSSION

Understanding some of the intricacies of these perspectives provides concrete and helpful guidance for researchers and sponsors.

This research indicates that most respondents have strong expectations that researchers *should* help trial participants who get infected with HIV. This is one of the first times actual data document that South African communities have a clear expectation that vaccine researchers should 'manage' their HIV care and treatment needs. While there is still ongoing ethical debate about the degree to which specific ethical principles best ground prevention researchers' obligations to participants with HIV,[46] these data suggest that communities may be expecting facilitation of treatment access, so plans for facilitating treatment access on the grounds of community expectation are critical.[47] If plans are not made community trust may be eroded and research could be jeopardised.

This research indicates that the majority of respondents think an appropriate form of assistance would be for researchers to help participants to access treatment, where this service is feasible, until such time as they can do this on their own. This is similar to community voices from a larger, seven-country study (including South Africa) where participants supported the referral of participants to off-site healthcare service providers.[48] It also corresponds with the dominant mechanism for assisting participants, which is 'assisted referral' to local facilities.[49] It is worth noting that (while not the majority view) a few respondents do hold the view that researchers should directly provide treatment. It is also interesting to note that a handful of respondents said that participants should secure

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[46]Richardson, *op. cit.* note 29; Schuklenk & Ashcroft (2008), *op. cit.* note 21; C. Slack & M. Stobie. Response to 'HIV Vaccine Trials: Reconsidering the Therapeutic Misconception and the Question of what Constitutes Trial-related Injuries'. *Dev World Bioeth* 2008; 8:159–161; Weijer & LeBlanc, *op. cit.* note 21.

[47]Global Campaign for Microbicides (GCM). 2005. *Rethinking the Ethical Roadmap for Clinical Testing of Microbicides: Report on an International Consultation.* Washington, DC: GCM. Available at: http://www.global-campaign.org/researchethics.htm [Accessed 12 Apr 2008]; Global Campaign for Microbicides (GCM). 2004. *Mobilization for Community Involvement in Microbicide Trials.* Washington, DC: GCM. Available at: http://www.global-campaign.org/pubs.htm [Accessed 13 Apr 2008].

[48]MacQueen et al., *op. cit.* note 6.

[49]GCM, *op. cit.* note 19; MacQueen et al., *op. cit.* note 19; Milford et al., *op. cit.* note19; Population Council, *op. cit.* note 19.

treatment without the help of researchers. It is intriguing that three of the six nurses interviewed expressed this view. While the data does not allow us to comment on this in detail, this deserves additional attention in future research.

This research also indicates that the majority of respondents think that researchers should help because they are in a 'position to do so', and are in a 'relationship' with trial participants, and not because the research has harmed participants. This resonates with arguments based on beneficence,[50] rather than compensation for harm.[51] It endorses the 'Good Samaritan' argument present in ethics discourse.[52] This argument asserts that researchers, like everyone else, have some obligation to help simply by virtue of being moral agents. If one can do something beneficial to save a life without sacrificing anything of comparable significance, it ought to be done. Respondents in this study are arguing in line with the notion that since researchers can do something that will help those that are vulnerable or dying, they should. It also resonates with dimensions of an ethical model for working out researchers' obligations for providing health-care to trial participants. The model asserts that participants implicitly entrust certain aspects of their health to researchers when they sign up for a study. When participants give researchers permission for the disease under study to be monitored, they also entrust caring for that disease (in this case HIV) to researchers. Given this entrustment, researchers have special responsibilities to participants, sometimes beyond what is required for the sound scientific and safe conduct of the trial. The extent of these responsibilities is influenced bythe depth of the researcher-participant relationship, and the participants' vulnerability, dependence and uncompensated risks or burdens.[53] This finding also resonates with a recent Kenyan study where 11 focus groups identified the theme of researchers' moral obligations to participants and the community in clinical trials.[54]

Researchers may not be fully aware of prospective participants' considerable trust in and respect for researchers, and the responsibility that this attitude of respect and trust places upon them.[55] Respondents 'trust' researchers to ensure that access to treatment from these referral clinics is in fact realistic. This extends the responsibility of researchers from merely identifying potential treatment clinics for referral to ensuring that these clinics are realistically going to meet the HIV treatment needs of participants.

This study also reveals that some members of this community, a seemingly small minority, have expectations that may not be reasonable (e.g. the expectation that researchers will treat everything or will ensure that ART is provided long term). When preparing for HIV prevention trials, researchers should be clear about what components of treatment and care fall into the entrustment model,[56] educate communities and have clear consent processes so as not to erode community trust. For issues of high importance and potential expectation it may further be important to identify what communities' expectations are in order to make sure that information conveyed in the consent process was understood.

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[50]Macklin, *op. cit.* note 21.
[51]Schuklenk & Ashcroft (2008), *op. cit.* note 21.
[52]Hawkins, *op. cit.* note 28.
[53]Belsky & Richardson, *op. cit.* note 29; Richardson & Belsky, *op. cit.* note 29; for further in-depth discussion on the trust invested in researchers by participants and the personal relationship between the two, see: National Bioethics Advisory Commission (NBAC). 2001. When Research is Concluded: Access to the Benefits of Research by Participants, Communities and Countries, in: Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries. Bethesda, MD: NBAC: 59. Available at: http://www.bioethics.gov/reports/past_commissions/index.html [Accessed 7 Jan 2009].
[54]Shaffer et al., *op. cit.* note 40.
[55]Nuffield Council on Bioethics, *op. cit.* note 21.
[56]Belsky & Richardson, *op. cit.* note 29.

However, the dominant voice of respondents reveals they are not expecting sponsors of vaccine trials to bear the sole burden of providing treatment. This removes the fear of unrealistic and inappropriate costs crippling research, an argument against obligations to ensure access that has been present in this debate.[57]

Notably, these data suggest that the voices and preferences of communities should be included when decisions are made about access to care and treatment in HIV prevention trials. This is not to suggest that these decisions be based entirely on what communities anticipate, as their expectations could be under or oversized and relatively uninformed. It does however suggest that when decisions are made about the appropriate type and level of care and treatment for minimizing potential exploitation of communities, the views of such communities should be seriously considered,[58] and used to expand the groundwork laid by ethical guidance. At the very least on a practical level, not appreciating what the community believes and expects could have unanticipated repercussions for researchers.[59]

LIMITATIONS AND FUTURE RESEARCH

The present study was conducted on a limited non-random sample in a rural region of KwaZulu-Natal in South Africa. This makes generalization of findings difficult, but statistical generalization was not the intention of the study. The small sample size was intentional and the qualitative methods enabled the research to explore the narratives of individuals in depth. The limitation that follows from this is that the sample does not allow for any disaggregation and analysis of the findings by strata such as educational level, gender, age or employment, all of which are likely to influence perceptions. This sample was heavily skewed with more women than men. This was not intentional but resulted from recruitment at rural clinics where women were more present. As such, the findings of this study should be compared to similar studies currently being carried out in different South African communities to assess the transferability of specific findings. Further quantitative research could also establish how broadly these views are held; and what demographics they correlate with, if any.

This sample included community members who were not currently participating in an HIV vaccine trial. The findings therefore reflect respondents' views of a hypothetical trial, which may not mimic those who actually are participating in clinical research.[60] Perceptions of actual HIV vaccine trial participants may differ and it might be informative to conduct the same research in this population. Nonetheless, our respondents' views on access to treatment in HIV prevention research make a valuable contribution to continued dialogue about this issue. Although alone not determinative, the expectations and preferences of potential research participants and communities should be carefully considered when debating access to treatment in HIV research. The results of this study highlight the essential role of meaningfully canvassing community expectations prior to the initiation of future HIV prevention trials. Given the devastating impact of HIV and AIDS, any related study attracts high levels of concern, expectations, and hopes. Understanding and integrating these expectations will increase community trust in the research process and is a fundamental part of moving toward meaningful community involvement.[61]

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[57]Bloom, *op. cit.* note 2; Specter, *op. cit.* note 22.
[58]Weijer & LeBlanc, *op. cit.* note 21.
[59]AVAC. 2005. *AIDS Vaccines at the Crossroads*. New York, NY: AVAC. Available at: http://www.avac.org/reports.htm [Accessed 7 Apr 2008]; J. Cohen. 2005. *Science Now 4 Feb 05 - Cameroon TDF PREP Study*. Paris: Actions Traitements. Available at: http://www.actions-traitements.org/spip.php?breve1402 [Accessed 12 Apr 2008].
[60]J. Flory & E. Emanuel. Interventions to Improve Research Participants' Understanding in Informed Consent for Research: A Systematic Review. *J Am Med Assoc* 2004; 292: 1593–1601.
[61]Weijer & LeBlanc, *op. cit.* note 21.

Biographies

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Table 1

Respondents' demographics

	Occupation	Education	Age	Sex
Clinic attendees (7)	Security guard	Grade 12	37	Male
	Cashier	Grade 12	26	Female
	Unemployed (4)	Grade 10	21	Female
		Grade 8	41	Female
		Grade 8	26	Female
		-	38	Male
	Research Assistant	-	54	Female
Clinic employees (15)	Nurses (6)	Degree: Nursing (3)	58	Female
			52	Female
			30	Female
		Diploma: Nursing (3)	48	Female
			42	Female
			24	Female
	General clinic assistants (6)	Diploma: Public Relations	32	Female
		Grade 12	42	Female
		Grade 10	45	Female
		Grade 9	45	Female
		Grade 8	39	Female
		-	45	Female
	Cleaners (3)	Grade 12	26	Female
		Grade 10	38	Female
		Grade 3	58	Female
Clinic volunteers (7)	Volunteer HIV counsellors (6)	Diploma: Public Relations (2)	36	Female
			35	Female
		Grade 12 (4)	35	Female
			33	Female
			28	Female
			-	Female
	General clinic volunteer	Grade 12	22	Female