CASE STUDIES

CASE STUDY 1

BACKGROUND

A CLUSTER-RANDOMIZED TRIAL OF HOME-BASED VERSUS, HEALTH FACILITY-BASED CARE FOR HIV/AIDS:

In order to test the effectiveness of models of care for HIV/AIDS that rely less on the expertise of professional staff, that minimizes the burden to existing health services, and that do not require patients to travel long distances, a trial was conducted through a partnership involving The AIDS Support Organization (TASO), Uganda Ministry of Health (MOH), Medical Research Council (MRC) Unit on AIDS in Uganda, and the US Centers for Disease Control and Prevention (CDC). The trial compared facility-based care with home-based care.

The facility-based care arm was a model that is broadly similar to that being used in urban centers across Africa where patients are treated in hospital settings. In this arm, patients are asked to come to the TASO Clinic in Jinja (Uganda'a second largest town) to collect their drugs at 2 weeks after entry into the programme and every month thereafter. They are seen by a physician every three months, as well as monthly by a nurse who refers them to a doctor if necessary.

The home-based arm of the trial followed the mode used by TASO outside the Jinja clinic, with non-clinical field workers delivering drugs and monitoring patients in their homes at 2 weeks after ART-initiation and monthly thereafter. Patients are asked to come to the clinic for routine clinical review and counseling at 2 and 6 months and every 6 months thereafter.

Home-based care is popular with patients as it reduces the need to travel to clinics; it is also practical for the health services, which face a severe shortage of professional staff. However, its effectiveness was unproven; in particular, it was uncertain whether non-clinically qualified fieldworkers can monitor patients on anti-retroviral therapy (ART) adequately and make referral when needed. Also, regular home visits by fieldworkers may be unacceptable given the stigma associated with HIV, and may prove difficult to sustain when patients return to better health and are reluctant to stay at home to receive the visits.

It is against this background that this trial was designed to determine the effectiveness of home-based compared with facility-based ART delivery and HIV/AIDS care. Forty-four areas were defined geographically and grouped into strata according to estimated number of HIV+ patients and distance from the Jinja clinic. The clusters were randomized within each stratum to receive either home- or facility-based care. Patients in both arms were told to come to the clinic at any time they feel unwell. In exceptional cases, when a patient was bed-ridden and unable to travel, home-care would be provided by a TASO team including a physician, as resources allow. The trial was designed with 1000 patients, each followed for at least 3 years, a sufficient number to show approximate equivalence between the two modes of ART delivery. The primary endpoint was the time for plasma viral-load to exceed 500 copies/ml; secondary endpoints included adherence, clinical treatment failure, cost, and development of resistance to antiretroviral drugs.

Patients were able to refuse entry to the trial or withdrew at any time, for whatever reason. Patients who refused or withdrew received all subsequent care (including ART) from TASO according to the standard facility-based regime, which has been shown to be effective and is established as the standard of care in Africa, whereas the evidence on the effectiveness of home-based ART care for HIV/AIDS in Africa was lacking and inadequate.

QUESTIONS

1. Was TASO Obliged to offer patients who refused entry or withdrew from the trail a choice of either mode of care?

2. If a researcher feels that it is ethical to provide a choice of home or facility-based care to all patients, should the researcher try to force the health services to do so?

3. Is it ethical to give choice to participants in one arm and not the other? (That is, participants in the home-based care arm can drop out if they think they'd prefer facility-based care, whereas those in facility-based care can switch to home-based.)

4. Which mode of care should be provided to patients after the trial is over, if it turns out that treatment success rates are comparable with both modes? Would home-based care then qualify as one of the "best proven…methods identified in the study," as stated by the *Declaration of Helsinki*, paragraph 30?

5. Beyond obligations to the patients who participate in the trial, what to TASO, MOH, MRC and/or CDC owe to the "population or community" by way of ensuring that "any intervention or product developed, or knowledge generated, will be made reasonably available, as stated by CIOMS *International Guideline #10.*

DISCUSSION

(Thanks to Dr Arshi Farooqui and Dr. Zulfiqar A. Bhutta, Aga Khan University, for compiling this discussion of Case Study 1)

The discussion revolved around the issue of informed consent especially its process. It was suggested that for such researches investigators should follow a community participation approach right from the beginning i.e. right at the time of research proposal development. This approach is extremely important to control the issue of stigma and efforts should be made to discuss on these issues by involving community dialogue before approaching the individual research participant.

It was also discussed that for the research projects in which the designs are very difficult to implement and there are associated implicit or explicit stigma issues e.g. in HIV research, community information and the community consent or assent should be very carefully sought and deliberate attempts should be made to release only very necessary and limited information in order to avoid the risk of certain treatment arms being identified. In such research projects community information should be deliberately kept in very broad terms without project details. The relevant information in detail should then be provided at a household level or at an individual level this will decrease the risk of finger pointing at individuals because of some obvious characteristics. One group suggested that stigma could also be reduced by integration of research project into series of studies or with ongoing studies or with ongoing healthcare projects so that these become part of the routine follow-up. Another thought was that the developing countries have a cohesive culture and issues of stigmatization are always there in small communities and villages so much so that even going to hospital is stigmatizing to an extent sometime.

In the debate on preference of a particular study design over another, it was discussed that health systems research deals with groups not individual and in order to discuss preference of cluster randomized trial over other designs, researchers would feel easy for cluster randomized trial if the risk of intervention involved is low but if the risk of intervention is high then it’s difficult to select the cluster randomized trial. As far the participants are concerned, it would be easier to convince them that the whole area will be randomized rather than individuals. Cluster randomized trials are

powerful and stronger for intervention where issue of choice and different allocation are not problematic and there is general risk of contamination. However, the moment participants are offered choice in a particular cluster, there is immediate threat to cluster randomized trial design. Problem also arises when more and more participants request for changing the mode of treatment which will lead to selection bias. In situations where a researcher has to balance between an individual right in the cluster randomized setting there are constraint in terms of choices like issues related to traveling to health facility for the poor and the ill population and stigmatization issues.

Provision of post trial benefit was discussed and it was a unanimous voice that these benefits are now an established norm and especially for the trial participants it is now considered obligatory to make sure that at least some sort of post trial benefits are offered. It was also suggested that post-trial benefits should be negotiated with the research community at the time of pre-trial exploration.

Should autonomy of choice take precedence over issues of methodology or logistical issues in research design, this was debated at depth. Generally, one group had an opinion that given that the research is important for the participating community and there had been consultation with the communities regarding the risk involved (none to minimal risks only) methodological and logistical issues should take precedence over the autonomy as long as measures are taken to protect the participants. Another group argued that if the drop out rate from a trial is large or if it is too risky then there are serious issues with the study design and in such situations, autonomy should be given an edge over the holiness of methodology and logistical ease.

Pre-trial negotiations were also discussed and generally there was a consensus that the participating community should be involved in the discussion on the indigenous community health and research needs. Community should also be consulted on the scientifically sound and ethically justifiable research methodology that is acceptable to them. By doing so issues such as stigma could be reduced and community will be more enthusiastic to participate in this developmental process. These measures should be implemented by the researchers, research organizations, and research funding agencies.

SUGGESTED READING

Jaffar S, Govender T, Garrib A, et al. Antiretroviral treatment in resource-poor settings: public health research priorities. *Trop Med Int Health* 2005; 10(4):295-9

MRC Clinical Trials Series. Cluster randomised trials: methodological and ethical considerations. http://www.mrc.ac.uk/index/publications

Donner A and Klar N. Design and analysis of cluster randomisation trials in health research. Arnold, London, 2001.