Ethical Frameworks and Standards of Prevention in HIV Prevention Trials

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Key Questions

• When must investigators make new HIV prevention tools available to all participants in on-going trials?

• When should new HIV prevention tools be included in the package of prevention services for future trials?

• When does it become obligatory to compare future methods to existing methods, rather than to placebos?
UNAIDS/WHO (2007) Ethical Considerations in Biomedical HIV Prevention Trials - Guidance

Point 13:

• Researchers, research staff, and trial sponsors should ensure … that appropriate counseling and access to all state of the art HIV risk reduction methods are provided to participants.

• New HIV risk-reduction methods should be added, based on consultation among all research stakeholders including the community, as they are scientifically validated or as they are approved by relevant authorities.
Consultation on Standards of Prevention

Adding new prevention tools should be done on case-by-case basis, using a local consultative process and guided by such general objective criteria as:

- Data from comparable populations and routes of exposure;
- The weight of evidence for estimates of effect;
- Feasibility; and
- Impact of the new tool on the ability to isolate the efficacy of other prevention methods being tested.
Core Bioethical Principles

• Respect for persons
  – Voluntary informed consent.
  – Protection of vulnerable persons.

• Beneficence
  – Maximize benefits and minimize harms.

• Justice
  – Non-exploitation.
  – Individuals and groups that participate in trials should benefit from participation.
When applied to HIV prevention trials, the three Belmont principles require that:

- Participants be informed of the risks and benefits of participation;

- Risks minimized and benefits maximized by providing an appropriate HIV prevention package and other services; and

- Trial participants and communities are not chosen solely for expedience or cost, and are not denied services to which they are normally entitled.
The principle of beneficence requires that trial participants be treated in an ethical manner, “not only by respecting their decisions and protecting them from harm, but also by making efforts to ensuring their well-being. Two general rules have been formulated as complementary expressions of beneficent actions: 1) do no harm, and 2) maximize possible benefits and minimize potential harms (1979, §B2).”
The Hippocratic Oath obligates a physician to do what is best for the patient, without consideration of other personal or social obligations.

If true, this therapeutic obligation poses a challenge for physicians engaged in clinical research.

Clinical trials violate a researcher’s therapeutic obligation unless there is equipoise:

“genuine uncertainty about the comparative therapeutic merits of each arm of a clinical trial.”
Clinical Equipoise

• Most often applied to debates about the use of placebos in therapeutic trials. Such trials would violate equipoise except:
  – When no treatment exists;
  – Standard treatment is unavailable or cannot be tolerated; or
  – Add-on studies where all participants also “receive all medications that would normally be prescribed.”

• There is debate about how clinically-derived principles like these apply to non-therapeutic research.

• There is debate about what consensus exists concerning the merits of different HIV prevention tools.
• Ethics (and international guidance) requires all trial participants to have information about and access to a range of proven and established HIV prevention services.

• It may not be obligatory, however, to always provide or ensure access to the full range of proven and established HIV prevention tools.

• The prevention package can vary in the type and the way services are provided so long as it: 1) is developed in consultation with the community; and 2) addresses the specific needs of the community.
Levels of Evidence

1. Good evidence
   - several large RCTs
   - clinical outcomes

2. Fair evidence
   - one or more smaller RCTs
   - observational studies
   - surrogate outcomes

3. Weak evidence
   - anecdotes
   - expert opinion

- W Cates, CROI 2007