



International Vaccine Research



Standard of care, standard of
prevention

Standard of Care

- Used in the following contexts
 - What should be provided to the control group in randomized, controlled vaccine clinical trials
 - Placebo or established preventive method
 - What should be provided to participants who become ill with a disease other than that being studied
 - TB or malaria in an HIV vaccine study
 - What should be provided to participants in prevention studies who acquire the “target disease” during the trial
 - ARVs in HIV prevention trials

Care and treatment

- What should be the “standard of care” in preventive vaccine trials?
 - What trial participants would receive in their community or the country if not in the vaccine trial?
 - What participants in a preventive vaccine trial would get in North America or Europe?

Promising ART

- Some argue that promising ART to potential participants in preventive HIV vaccine trials is an “undue inducement” to enroll
 - Trial participants are healthy and do not currently need treatment
 - If promise of possible treatment would be an undue inducement, then why not the vaccine, with its hoped-for efficacy?

Declaration of Helsinki

- No specific mention of vaccine trials
- No specific obligations regarding provision of medical treatment during research
- General statement of obligation (paragraph 10)
 - “It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject”
 - Open to strong and weak interpretations

Strong and weak interpretations

- “It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject”
 - Researchers must minimize risks in research, take steps to prevent known potential harms, and provide treatment for adverse events that result from the research (weak)
 - Researchers must make arrangements to provide medical care and treatment for other diseases vaccine trial participants may acquire during the research that threaten their life or health (strong)

CIOMS International Ethical Guidelines

- Guideline 21: Ethical obligation of external sponsors to provide health-care services
 - Health-care services that are essential to the safe conduct of the research
 - “Although sponsors are, in general, not obliged to provide health-care services beyond that which is necessary for the conduct of the research, it is morally praiseworthy to do so”
 - “It might be agreed to treat cases of an infectious disease contracted during a trial of a vaccine designed to provide immunity to that disease”
 - Decision rests on an *agreement*, not an *obligation*
 - NOTE: This guideline addresses only the obligation of external sponsors—not other parties

What the opponents argue

- Research is not therapy
 - Obligations of researchers are not those of physicians treating patients
- Treatment would not be financially affordable
 - “Double standards” are ethically acceptable based on economic considerations
 - Poorer countries may have a lower standard of care ⁸

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- New UNAIDS/WHO guidance document

- Ethical Considerations in Biomedical HIV Prevention Trials
 - Updated from 2000 vaccine Guidance Document and expanded to include other biomedical HIV prevention trials

2007 Revision

- Need arose to revise 2000 guidance document
 - Broadened scope of ethical guidance from vaccines only to other biomedical HIV prevention trials
 - Changed circumstances regarding availability of care and treatment in many developing countries
 - Evolution of thinking about what is owed to participants who acquire HIV infection while enrolled in a prevention trial

What's new?

- ◎ New GP 15 on Control Groups strengthens old GP 11 on Control Groups
 - “The use of a placebo control arm is ethically acceptable in a biomedical HIV prevention trial only when there is no HIV prevention modality of the type being studied that has been shown to be effective in comparable populations”
 - This requires interpretation on a case by case basis
 - How to interpret ‘the type being studied’?
 - What are criteria for comparability among populations?

What's new?

- New Care and treatment (GP 14) significantly strengthens old Care and treatment (GP 16)
 - Participants who acquire HIV infection during the conduct of a biomedical HIV prevention trial should be provided access to treatment regimens from among those internationally recognised as optimal. Prior to initiation of a trial, all research stakeholders should come to agreement through participatory processes on mechanisms to provide and sustain such HIV-related care and treatment.

What's new?

- ◎ Standard of prevention (GP 13) replaces Risk-reduction interventions (old GP 14) by providing access to all state of the art risk reduction methods
- ◎ Researchers, research staff, and trial sponsors should ensure, as an integral component of the research protocol, that appropriate counseling and access to all state of the art HIV risk reduction methods are provided to participants throughout the duration of the biomedical HIV prevention trial. 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.

Challenge

- “Do you really mean *all* state of the art prevention methods?
 - Does that include male circumcision?
 - Would it include a partially effective vaccine or microbicide when such methods become available?”
- “If so, it would make it impossible—or at least, unfeasible—to design future vaccine or microbicide trials and obtain a result”
- How to respond to this challenge, from a scientific and methodological point of view?

GP 13 commentary

- Negotiations [among all research stakeholders, including the community] should take into consideration feasibility, expected impact, and *the ability to isolate the efficacy of the biomedical HIV modality being tested, as other prevention activities improve.*

Unanswered questions

- Assuming the UNAIDS/WHO guideline for standard of prevention is accepted in practice
 - What should happen if the “state of the art” prevention package will not be readily available or sustainable in the community following completion of a vaccine trial?

Unanswered questions

- The UNAIDS/WHO guidance calls for consultations with the community before, during and after initiation of a trial. What should be done if the community determines that it would be unfair to provide preventive methods to the trial participants if those methods are not also provided to family members?

Unanswered questions

- What steps would be appropriate for inclusion of male circumcision in the prevention package for a vaccine trial?
 - Referral, including payment for the procedure for participants?
 - Referral without providing payment?
 - Having providers at the trial site?