

Standard of care: treatment trials

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Standard of care

- Basic issue: What care should be provided to clinical trial participants if not state of the art care is/can be provided?
- Should there be one standard of care irrespective of location of trial, or can care vary depending on local circumstances?

Standard of care issues

- 1. Traditional standard of care discussion.
Choice of trial design interventions
- 2. Ancillary care issues
- 3. Post-trial benefits

1. Trial design interventions

- What interventions should be provided as part of the design of the study
 - What should be provided in the control arm
 - What study intervention should be provided
- Problem arises when there is an effective intervention that cannot be provided to most people in host country for economic reasons

1. Trial design issues

- Presumption: provide at least as good interventions as those that are provided to those who receive state of the art care
 - Independent of place of trials
- Some argue that this should be only rule
- Many will allow exceptions. Two conditions:
 - Scientifically necessary
 - In order to obtain results useful for country where trial takes place

1. Examples

- Test a simplified diagnostic method to monitor effect of HIV treatment to take the place of viral load measurements
- Test interventions that will prevent HIV infection during breastfeeding, without bottle feeding
- Examples such as these show that exceptions are necessary

2. Ancillary care examples

- Treatment that is provided for study participants that is NOT necessary for the design of the study
 - Identification of conditions that need treatment during screening and study visits
 - HIV treatment in a malaria vaccine trial
 - HIV treatment in a study of malaria pathogenesis in children
 - Malaria treatment in a study of malaria pathogenesis

2. Guidance

- CIOMS: Although sponsors are, in general, not obliged to provide health care services beyond that which is necessary to conduct research, it is morally praiseworthy to do so

2. Ancillary care: current status

- No obligation to provide ancillary care during trial
- Many researchers do provide some amount of ancillary care
- Under-explored topic
- Belsky & Richardson have attempted to derive a limited obligation based on an entrustment model, rather than a “Good Samaritan” type obligation

3. Post-trial access to study intervention

- At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic, and therapeutic methods identified by that study
 - Helsinki-2000
- Only an obligation to provide study interventions, not ancillary care interventions, after trial is completed

3. Acute versus chronic conditions

- Post-trial access to study intervention is usually not a problem for acute conditions
- Not a problem to provide effective vaccine to control group
- Problem arises for
 - Continued treatment for chronic conditions when there is a potential for long term financial and logistical commitment

3. Lack of detailed guidance

- Almost no guidance regarding long term post trial obligations
- Even if there is provision for referral to national system of treatment, the system will probably provide a lesser standard of care than that which was available in the trial
- Question therefore also is whether there is an obligation to ensure state of the art care

Two separate issues

- Do we have an obligation to do what we can, both in concrete trials, and with regard to policy, to increase access to clinical trial interventions: yes
- Should ERCs require as a matter of policy that there are guarantees of access to clinical trial interventions before they approve a particular clinical trial? no

One position

- One has a strong obligation to guarantee access to clinical trial participants
 - To study drug
 - To treatments for the condition under study
 - Antiretroviral treatment to participants in hiv vaccine trials who seroconvert
- Problem: Disregards the fact that both study participants and health system may have other health care priorities

3. NIH ARV Guidance

- For antiretroviral treatment trials conducted in developing countries, the NIH expects investigators/contractors to address the provision of antiretroviral treatment to trial participants after their completion of the trial. The NIH recommends investigators/contractors work with host countries' authorities and other stakeholders to identify available sources of antiretroviral treatment
- Applicants are expected to provide NIH Program Staff for evaluating their plans that identify available sources, if any, for provision of antiretroviral treatment to research participants
- Priority may be given to sites where sources are identified for provision of ARV treatment

3. My position

- At a minimum researchers should address the issue of post trial access to care and treatment
- ERCs should NOT require guaranteed access (legally binding agreement, money in the bank)
- Need to work out examples of successful strategies
 - Streamlined referral processes
 - Specific conditions covered by specific sponsors of trials

Common theme

- Need to balance
 - research on diseases of poverty
 - provide state of the art care to everyone
- Sometimes trade-offs are necessary
- It is not obvious to me that concerns for the participants in the trial should always take precedence to the needs of the community from which they are recruited
- If they are not denied care that they ordinarily would receive