Subject Selection and Recruitment

Dave Wendler
Department of Clinical Bioethics
NIH, USA

Goals

Selection and Recruitment should:

1. Distribute burdens and benefits fairly
2. Ensure social value of research
3. Enhance scientific validity
4. Minimize risks to subjects
5. Maximize benefits to subjects
6. Protect the vulnerable

Potential Conflicts

- In some cases, these different goals may conflict.
- For instance, minimizing risks to subjects may decrease the social value of the research.

Tradeoffs

In cases of conflict, investigators, ethics review committees, and sponsors must “balance” the competing goals.

Subject Selection

- Subject selection involves determining which subjects may enroll in the research.
- Subject selection is determined by inclusion/exclusion criteria.

Research as a Benefit

- Exclusion without a good reason may be unfair or discriminatory.
- People are clamoring for access to clinical trials...demanding they, and others like them, are owed such as a matter of justice. (Levine, 1994)

Fairness

- To ensure fairness, begin by assuming everyone is eligible.
- Exclude individuals from this pool only when there is a good reason.

Priority of Science

- The scientific goals of the study should be the *primary* consideration in determining who can enroll.
- This involves ensuring the value of the study and enhancing its validity.

Ensuring Value

- Exclude individuals not suitable for answering the scientific question.
- For instance, individuals with conditions that make it impossible to assess the drug being tested (e.g. brain tumors).

Enhancing Validity

- Exclude individuals who cannot satisfy the protocol requirements.
- For instance, subjects who cannot (or do not) make the required clinic visits.

Minimize Physical Risks

- Exclude individuals who would face significantly higher risks.
- For instance, individuals with poor kidney function in a phase II study of a drug with renal clearance.

Maximize Benefits

- Select subjects who are more likely to benefit from participation.
- For instance, a study of a new anti-HIV drug may focus on individuals with low CD4 counts.

Protecting the Vulnerable

- There is an order of preference in selecting subjects, for instance, adults before children. (Belmont Report)
- Exclude vulnerable subjects unless their participation is needed for scientific reasons. (CIOMS 2002 draft)

Subjects Who Can't Consent

- Exclude individuals unable to consent, unless their participation is necessary to answer the scientific question posed.
- For instance, exclude individuals with severe Alzheimer's Disease from early phase malaria studies.

Scope of “Necessity” Requirement

Should subjects who face significantly higher risks, and subjects who cannot consent be excluded from trials that offer important potential medical benefit?

The Justification?

- In some cases, enrollment may be in 'riskier' subjects' best interests.
- Thus, excluding these subjects cannot be justified on the grounds it protects them.

Research vs. Clinical Care

- It is important to distinguish research from clinical care.
- Excluding ‘riskier’ subjects minimizes the aggregate risks of research.
- Applies to physical and moral risks.

Additional Safeguards

- Informed consent is a primary research safeguard.
- Hence, when enrollment of subjects unable to consent is necessary, the study should include additional safeguards.

Sufficient Evidence

- Adults unable to consent should be enrolled only with sufficient evidence that it is consistent with their remaining preferences and interests.
- Some commentators require that this evidence be documented in a formal advance directive.

Surrogates

- Subjects unable to consent should be enrolled only with the permission of an appropriate surrogate.
- Are health care surrogates sufficient for research purposes?

Subject Recruitment

Subject recruitment involves active attempts to enroll specific individuals or groups within the pool of eligible subjects.

Finding the Right Community

- In many cases, the choice of communities from which to recruit is determined by institution location.

Selecting a Community

- In some cases, investigators have a choice of possible communities.
- In these cases, the principles of subject recruitment apply in deciding which community to select.

Goals of Selection and Recruitment

1. Distribute burdens and benefits fairly
2. Ensure social value
3. Enhance scientific validity
4. Minimize harm
5. Maximize benefit
6. Protect the vulnerable

Declaration of Helsinki -2000

Medical research is only justified if there is a reasonable likelihood the populations in which the research is carried out stand to benefit from the results of the research.

Social Value/Community Benefit

- To what extent must communities benefit from research involvement?
- To what extent must the community benefit from the research results?

Community vs. Individual Benefit

Should the requirement of benefit be added to the conditions on selection of individual subjects?

Recruitment

- Targeted recruitment
- Inviting referrals from colleagues
- Advertising
- Inviting own patients

Recruitment for good reasons

- Do not focus recruitment on individuals who are (or appear to be?) vulnerable
- Ensure subjects are recruited for reasons of science, not compromised position (Belmont Report).

Incentives to Enroll Subjects

- Investigators are under considerable pressure to recruit subjects, sometimes receiving financial incentives. (US Inspector General 2000)
- Physicians receive payments for referring their patients to trials.

Concerns about Incentives

- To what extent do incentives to refer patients pose a conflict of interest?
- To what extent might use of incentives encourage investigators to enroll riskier/inappropriate subjects?

Advertising

- What effect does advertising have on recruitment?
- Does advertising affect consent?
- May benefits be advertised?
- Must risks be advertised?

Payment

- What role should payment play in recruiting research subjects?
- Is it acceptable to advertise payment?