



Subject Selection and Recruitment

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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
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Potential Conflicts


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

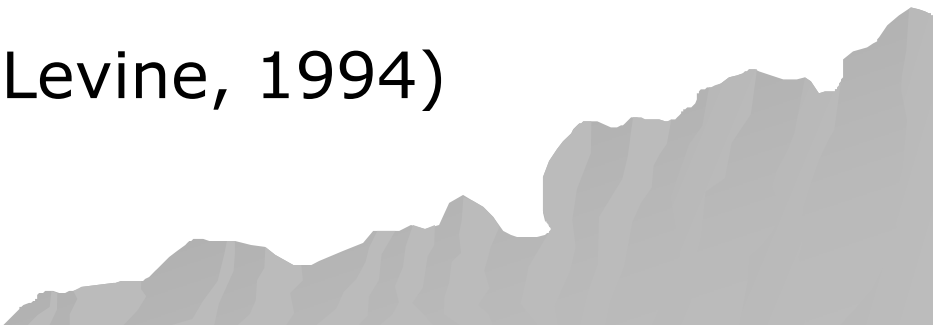
In cases of conflict, investigators, ethics review committees, and sponsors must “balance” the competing goals.



Subject Selection

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

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

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


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



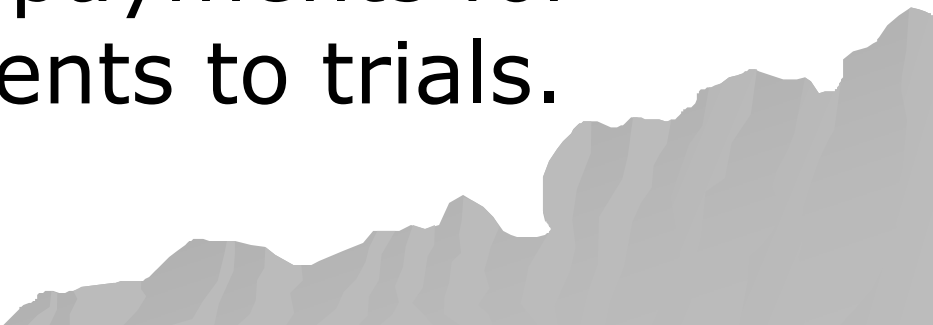
Recruitment

- Targeted recruitment
 - Inviting referrals from colleagues
 - Advertising
 - Inviting own patients
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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).
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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.
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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?
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Advertising

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

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