Assessment of Risks and Benefits

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Framework for Ethical Analysis

- Beneficence
  - Moral requirements
    - Do no harm
    - Maximize benefits/minimize harms
  - Practical applications
    - Study design
    - Assessment of risks and benefits
Topics to be Covered

- Principle of beneficence
- Study design
  - What is research?
- Assessment of risks and benefits
  - Risks
  - Benefits
  - Balancing
Section A

Principle of Beneficence
Definition/ Theory

- Central to health professions
- Different views of beneficence
  - Frankena
  - Beauchamp and Childress
Definition/ Theory

- Beauchamp and Childress formulation
Definition/ Theory

- Principle of utility
  - Beneficence at core
  - Maximizing principle
- Ethic of care
  - Relationships
Principle of Beneficence

- Applied to research ethics
  - Study design
Section B

What is Research?
What is Research?

“Research—a systematic investigation including research development, testing, and evaluation designed to contribute to generalizable knowledge.”

Source: 45 CFR § 46.102 (e)
What is Research?

- “Human subject—a living individual about whom an investigator conducting research obtains . . .
  - (1) data through intervention or interaction with the individual, or
  - (2) identifiable private information.”

Source: 45 CFR § 46.102 (f)
What is Research?

- Distinguishing research from practice
Research vs. Practice

1. What is the goal of the investigator?
   - Local or generalizable

2. Is there intent to publish the results?
   - Journal requirements
Research vs. Practice

3. How did the investigator come to know/interact with the patient/client?
   - Stranger?

4. Will usual care be changed or manipulated?
Research vs. Practice

5. How novel is the care or intervention?
   – Does it deviate from standard practice?

6. Will there be systematic data collection?
Research vs. Quality Assurance

Criteria 1

- “Initiative should be regulated by research regulations if the majority of patients are not expected to benefit directly from the knowledge to be gained.”

Source: Casarett, Karlawish, Sugarman. JAMA, 2000, 283 (17): 2275-80
Research vs. Quality Assurance

Criteria 2

- “If the majority of patients are likely to benefit from knowledge to be gained, initiative should be reviewed and regulated as research if participants would be subjected to additional risks or burdens beyond the usual clinical practice to make its results generalizable.”

## Research vs. Quality Assurance

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Criteria 1</th>
<th>Criteria 2</th>
<th>Research?</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU Chart Review</td>
<td>No Benefit</td>
<td>N/A</td>
<td>Yes</td>
</tr>
<tr>
<td>Satisfaction Survey</td>
<td>Benefit</td>
<td>No Burden</td>
<td>No</td>
</tr>
<tr>
<td>CCU Catheter Comparison</td>
<td>Benefit</td>
<td>Burden</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Source: Casarett, Karlawish, Sugarman. JAMA 2000 283 (17): 2275-80*
Research?

- If activity is determined to be research:
  - Federal guidelines apply
  - Must be reviewed by an IRB
Section C

Assessment of Risks and Benefits
IRB Responsibility

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to the anticipated benefits, if any, to subjects, and the importance of the knowledge that may be reasonably be expected to result

Source: 45 CFR § 46.111
Risk Concepts

- Risk—probability and magnitude of some future occurrence of harm
- Harm—injury, setback to interests
- Risk assessment
## Risk Concepts

### RISK ASSESSMENT

<table>
<thead>
<tr>
<th>Probability</th>
<th>Major</th>
<th>Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Low</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
Risk Concepts

- Uncertainty—lack of predictability
- Risk perception—perceptions based on personal experience/attitudes/psychology
- Relative risk
Risk Concepts

- Minimal risk—“Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research is not greater in and of itself than those encountered during daily life or during the performance of routine physical and psychological examinations or tests.”

Source: 45 CFR 46.102(I)
Risk Concepts

Minimal Risk

- Implications for . . .
  - Consent
  - Enrollment of vulnerable populations
Risk Concepts

Minimal Risk

- Therapeutic vs. non-therapeutic
Individual Risk

- Physical
  - Bodily injury
  - Healthy volunteer vs. patient
  - Early testing
  - Delay
  - Related to RCT
Individual Risk

- Psychological
  - Stress, discomfort
  - Disclosure of medical information
  - Deception
Used with permission of New Life Community Church of Stafford: http://www.new-life.net/milgram.htm
Milgram Experiment

“I observed a mature and initially poised businessman enter the laboratory smiling and confident. Within 20 minutes he was reduced to a twitching, stuttering wreck, who was rapidly approaching a point of nervous collapse.”

Individual Risk

- Inconvenience
- Wrongs to personhood
Individual Risk

Individual Risk—Social Risks

- Risks to reputation/stigma
  - Breaches of confidentiality
- Economic
Community Risk

♦ Readings
♦ “Community”
  – Ethnic/tribal
  – Immigrants
  – Marginalized group
  – Minority group
  – Extended family
  – Religious group
Community Risk

Community Risk—Social Risks

- Stigma
- Economic
- Exploitation
Section D

Benefits
Benefits

- Concept
  - Something of value related to health/welfare
Possible Benefits

Individual Benefit

- Physical
  - Medical
  - “Inclusion” Benefit
    - Lantos
    - Peppercorn, et al.
Individual Benefit

- Psychological
  - Hope
  - Altruism
- Kinship
- Social
Individual Benefit

- Economic
  - Access to medical care
  - Monetary
Possible Benefits

Financial Compensation

- Concerns

Possible Benefits

Financial Compensation

- Models
  - Market
  - Wage-payment
  - Reimbursement

Benefits

- Community Benefit
  - Medical
  - Material
Balancing Risks and Benefits

- Goals
  - Minimize risk
  - Maximize benefit
Section E

Case Example: Research in the Emergency Room
Research in ER

- Will patients with severe head trauma benefit from anti-oxidant therapy?
- Investigators wish to study whether the drug polyethylyene glycol-superoxide dismutase (PEG-SOD) will limit the degree of brain injury suffered by head trauma patients.
- To date, data from animal models and limited human trials demonstrate a possible benefit.

Research in ER

- The study design will randomize patients to receive either one of two possible doses of PEG-SOD or placebo.
- Given the circumstances of the patients’ injuries, they are typically unable to give informed consent.

Research in ER

Furthermore, if the patients are to benefit from PEG-SOD, the investigators must administer the drug expeditiously, within two hours of presentation to hospital.

Research in ER

- Consider risks and benefits
  - Individual
  - Group
Research in ER

- Consider alternative methods of consent
  - Surrogate
  - Deferred
  - Waiver
Research in ER

- Consider alternative methods of consent
  - 1996 waiver
    - Life threatening situation
    - Available treatment unproven
    - Valid scientific data necessary
Research in ER

- Consider alternative methods of consent
  - 1996 waiver
    - Obtaining consent not feasible
    - Participation holds out potential for direct benefit
    - Research could not be carried out without waiver
Research in ER

- Consider alternative methods of consent
  - 1996 waiver
    - Investigator will try and reach decision-maker
    - IRB approved
    - Protections
    - Subject notified ASAP