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"What makes research ethical?"

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"WHAT MAKES RESEARCH ETHICAL?"

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Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? JAMA. 2000 May 24-31;283(20):2701-11.

Introduction

- What makes research involving human subjects ethical?
  - Informed consent is necessary (in most cases) but not sufficient
  - Other issues: clinical research in developing countries, use of placebos, phase 1 research, protection for communities, involvement of children
- A systematic framework is proposed to evaluate clinical studies

The 7 Ethical Requirements

1. Social or Scientific Value
2. Scientific Validity
3. Fair Subject Selection
4. Favorable Risk-Benefit Ratio
5. Independent Review
6. Informed Consent
7. Respect for Potential and Enrolled Subjects

Value

- To be valuable, research should
  - evaluate an intervention that could lead to improvements in health or well-being
  - be a preliminary study to such research
  - Lead to general knowledge about structure/function of human biological systems
- Why?
  - Responsible use of finite resources
  - Avoidance of exploitation
- Consider comparing the relative value of different clinical research studies

Scientific Validity

- "Scientifically unsound research on human subjects is ipso facto unethical in that it may expose subjects to risks or inconvenience to no purpose."
  - International Ethical Guidelines for Biomedical Research involving Human Subjects – CIOMS, 1993.
- Research should have a clear scientific objective, be designed using accepted principles, methods and reliable practices, have sufficient power, offer plausible data analysis plan
- Must have honest null hypothesis, "clinical equipoise"
- Why?
  - Responsible use of finite resources
  - Avoidance of exploitation

Fair Subject Selection

- Scientific goals of the study should be primary basis for determining who will be enrolled
  - Groups should not be excluded without good reason
- Recognize that subject selection can affect the risks and benefits of the study
- Groups/individuals who bear the risks of research should be able to enjoy its benefits
- Why?
  - Equals should be treated similarly, benefits/burdens should be distributed evenly

Favorable Risk–Benefit Ratio

- Assessment of potential risks
  - Risks to individual subjects are identified and minimized
    - Procedures which are consistent with sound research design
    - Using procedures already being performed on the subjects for diagnostic/treatment purposes
  - Potential benefits to individual subjects are enhanced
    - Should be consistent with the scientific objectives, tests and interventions
    - Extraneous benefits (e.g. payment, more unrelated health services) should not be weighed against the risks
  - Risks and benefits to individual subjects are compared
    - The more likely/serious the potential risks are, the greater the prospective benefits should be

Favorable Risk–Benefit Ratio

- What if no clinical benefit to subjects (e.g. Phase I trial)?
  - "risk-knowledge calculus"*: when do benefits to society outweigh risks to individuals
  - No stable framework
  - Utilitarian approach controversial
    - *Weijer C. Thinking clearly about research risk: implications of the work of Benjamin Freedman. IRB. 1999 Nov-Dec;21(6):1-5.
- Why?
  - Beneficence
    - Need to enhance benefits
    - Need to avoid the exploitation of subjects
  - Nonmaleficence
    - Need to reasonably reduce the risks

Independent Review

- Minimize the potential impacts of conflicts of interest (e.g. to conduct high-quality research, complete the research expeditiously, protect research subjects, obtain funding, advance career)
- Social accountability
- Who?
  - Granting agencies
  - Local IRBs
  - Data and safety monitoring board

Informed Consent

- Purpose:
  - To ensure that individuals control whether or not they participate
  - To ensure that individuals participate only when research is consistent with values/interests/preferences.
- To provide informed consent:
  - Must be accurately informed of details
  - Understand this information and how it relates to their situation
  - Make a voluntary and uncoerced decision about whether to participate
- Non-autonomous persons should be respected
  - Substituted judgement
  - Best interests

Respect for Potential and Enrolled Subjects

- Respect privacy by managing information in accordance with confidentiality rules
- Subjects should be permitted to change their mind and withdraw without penalty
- Enrolled subjects should be provided with new information regarding the intervention should it become available
- Welfare of subjects should be monitored.
- Study subjects should be informed about what was learned from the research

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