History and Ethics of Human Research

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Course Objectives

• Know the basic ethical principles of research involving human subjects
• Understand how these ethical principles developed and have evolved
• Understand the ethical basis of the Federal regulations
• Know the process to conduct an ethical review
Why Study History?

- History places ethics in perspective
- Ethics help explain what historical problems people were trying to solve
Why Study History?

- Those who fail to study history are condemned to repeat it.
- Those who fail to study this course are condemned to repeat it.

Ethics

History
Ethical Decision Making
Ethics and Morality

- **Ethics:**
  - The disciplined study of morality

- **Morality:**
  - What should one’s behavior and character be?
Why Study Ethics?

• Ethics is a process.
• The process provides a means to get a good answer.
• There is no “right answer.”
Types of Ethical Decisions

- Deductive - Principle based reasoning
- Inductive - Case based reasoning
Deductive Reasoning

Ethical Theory
- Principles
- Rules
- Particular judgments
- Judgment history

Ethical Theory
- Peace
- Violence solves nothing
- Refuse to join the army
- Judgment history
Case Based Reasoning

Ethical Theory
- Principles
- Rules
- Particular judgments
- Judgment history

Ethical Theory
- Family
- I must protect my children
- Join the army
- Previous History

I must protect my children

Join the army

Previous History
Ethical Conflict

Ethical Theory

Peace

Violence never solves anything

Refuse to join the army

Ethical Theory

Family

I must defend my children

Join the army
Managing conflict

• When the IRB is in conflict, step back and ask what are the ethical principles involved that are in conflict?

• Understand that this is expected.
  – Sometimes maximizing one ethical principle leads minimizes another.

• Have all members consider one principle at a time.
  – Put on the “beneficence” hat, then the “respect for persons” hat, and then the “justice” hat.

• Then balance the ethical principles.
  – Optimize each one knowing that they are in conflict.
Ethical Decision Making Process

• Develop rules based on ethical principles that balance the ethical principles.
• Gather the facts.
• Systematically consider each rule.
• Deliberate on whether the rules are met.
• The right process leads to the right decision.
• Reasonable people will disagree.
The Belmont Principles
The National Commission on Biomedical and Behavioral Research

- 1974: Identify the basic ethical principles that underlie the conduct of human research
- Develop guidelines to assure that human research is conducted in accordance with those principles

The Belmont Report (1979)
Belmont Principles

• Respect for Persons
• Beneficence
• Justice
Respect for Persons

- Treat individuals as autonomous agents
- Do not use people as a means to an end
- Allow people to choose for themselves
- Give extra protection to those with limited autonomy
Beneficence

• Acts of kindness or charity that go beyond duty

• Obligations derived from beneficence
  – Do no harm
  – Prevent harm
  – Prevent evil
  – Promote good
Justice

- Treat people fairly
- Fair sharing of burdens and benefits of research
- Distinguish procedural justice from distributive justice
Derived Rules: Beneficence

- Minimize risks to subjects by using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk
- Minimize risks to subjects by using procedures already being performed for diagnostic or treatment purposes
- Ensure risks to subjects are reasonable in relation to anticipated benefits to subjects and the importance of the knowledge expected to result
- Monitor the data collected to ensure the safety of subjects
Derived Rules: Respect for Persons

- Unless waiver is permissible, obtain legally effective consent
- Protect the privacy interest of subjects
- Maintain the confidentiality of data
- When some or all subjects are vulnerable coercion or undue influence, provide additional protections
Derived Rules: Justice

• Select subjects equitably
Basic History
Nuremberg Code

- Nazi Doctors’ Trial
- Supplement to Nuremberg Trials
- Written as part of the judgement
- Doctors convicted of murder, not for being unethical researchers
Effect of the Nuremberg Code

- No effect on research
- Medical profession thought it was:
  - Implicit to US researchers
  - Description of criminal research
  - Created after the fact to convict Nazis
  - Missed many aspects of research
Declaration of Helsinki

- 1964: World Medical Association
- Reinterpretation of Nuremberg
- Provoked a reaction by medical profession
- Journal editors required that research be performed in accordance with the Declaration
Public Health Service Policy

- 1966: All PHS supported research must undergo prior review to:
  - Protect rights and welfare of subjects
  - Assure appropriate informed consent
  - Determine acceptable risk/benefit balance

- Beginnings of the IRB
The Era of Standards

- Standards accepted by researchers
- Standards accepted by media

JUDGEMENT
Beecher Article


• 22 studies performed unethically
  – Major journals
  – Respected researchers
  – Questionable study design
  – No informed consent
Impact of Beecher Article

“Until this article we assumed that unethical research could only occur in a depraved regime like the Nazis”

Robert J. Levine, MD
Media Exposés

- Thalidomide
- Jewish Chronic Disease Study
- Willowbrook Hepatitis Study
- San Antonio Contraception Study
- Tea Room Trade
- Study of Untreated Syphilis in Black Males
Syphilis Study: History

- 1932: 300 black syphilitic males
- 1933: 300 controls added
- 1943: Penicillin for military
- 1949: Nuremberg Code
- 1951: Penicillin widely available
- 1966: Local ethics committee review
Syphilis Study Ad Hoc Panel

- Study be stopped immediately
- Inadequate oversight of human research
- Recommended Federal regulation of human research
Response to Research Abuses

- National Research Act
- May 1974 - 45 CFR 46
- June 1974 - National Commission
- April 1979 - Belmont Report
- 1981 - 45 CFR 46 revised
Applying Research Ethics
Ethical Decision Making Process

• Gather the facts
• Systematically consider each criterion
• Deliberate on whether the criteria for approval are met
• The right process leads to the right decision
• Reasonable people will disagree
Ascertain the Facts

• Does the protocol accurately reflect the issues with regard to ethical concerns?
  – Purpose
  – Importance
  – Risks/benefits

• This is not the job of the IRB committee!
  – Use experts on the committee
  – Obtain consultation

• Everyone on the committee must have the facts.
Systematically Consider the Criteria for Approval

- Protecting subjects is about asking the right questions.
- The answers are easy. It is the questions that are hard to remember.
Deliberate on Whether the Criteria for Approval are Met

- The criteria contain all the rules necessary for IRBs to protect subjects. Learn how to use them.
- The criteria are the responsibility of the IRB committee.
- None of the criteria require scientific expertise.
  - Minimized
  - Reasonable
  - Adequate
- Use a worksheet that follows the regulations.
- If as an IRB member you have not considered the all criteria: DON’T VOTE.
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