Ethics

From Belmont Report

A Little History

• It is important to look at history
  – We learn from our mistakes
  – History can repeat itself!
• The Nuremberg Doctors Trial of 1946
• The ‘Milgram Study’
• Thalidomide Tragedy
• Untreated Syphilis Study
• Human Radiation Experiments

The Nuremberg Doctors Trial of 1946

• Due to medical experiments many people died
  – The German Air Force
    • high altitude experiment
      – 40% of the 200 participants died
    • parachuting into cold water experiment
      – 300 prisoner-subjects suffered a mortality rate of 30%
  • wound, burns, amputation, chemical and biological agent exposure experiment
    – many died or were ruined for life
• Many experiments went on throughout the WWII
  – A mortality rate of 25% was typical
The Nuremberg Code

- 15 of the 23 defendants were found guilty
- A Code was developed
  - Informed consent of volunteers must be obtained without coercion of any kind
  - Human experiments should be based upon prior animal experimentation
  - Anticipated scientific results should justify the experiment
  - Only qualified scientists should conduct medical research
  - Physical and mental suffering and injury should be avoided
  - There should be no expectation of death or disabling injury from the experiment

More Attention Needed

While the Nuremberg Code and subsequent ethical guidelines represented the most enlightened thinking of the time, many well-intentioned researchers did not know about them or did not apply this guidance to their research activities.

The ‘Milgram Study’

- Obedience to Authority

- This study involved administering electric shocks up to extreme levels
- Deception was used causing some psychological stress
- Informed consent was not obtained
- Federal guidelines now instruct IRBs and investigators to:
  - consider not only physical harms, but also psychological, social, legal, and economic
Thalidomide Tragedy

- Thalidomide used in Europe as a sedative, not approved in US
- Manufacturers supplied samples to US doctors who were paid to study its safety by giving the experimental drugs to patients
- They found that administering the drug was extremely damaging to the fetus if taken during the first trimester resulting in interference with normal development of arms and legs

Impact on the Hearings

- It was found that those taking the drug were not informed that they were being given an experimental substance, nor had they been asked to give their consent
- This led to:
  - The passage of the Drug Amendments of 1962 to the Food, Drug, and Cosmetic Act
  - The FDA issued regulations with a consent requirement for documenting consent in writing and informing subjects that they might receive a placebo
Untreated Syphilis Study

- Known as the Tuskegee Study
- The control group was denied the penicillin treatment even though it was widely available
- As a result:
  - Congress passed the National Research Act
    - this Act created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
  - The National Commission established the Belmont Report

The Belmont Report

- The cornerstone statement of ethical principles upon which the federal regulations for the protection of subjects are based
- The Basic Principles:
  - Respect for Persons
    - individuals should be treated as autonomous agents
    - persons with diminished autonomy are entitled to increased protection
  - Beneficence
    - persons are treated in an ethical manner by respecting their decisions and protecting them from harm
  - Justice
    - fairness in distribution

Respect for Persons

- This principle is captured in the consent process
- We must consider different types of participants
  - Vulnerable subjects
  - Prisoners
  - Children
  - Subordinate individuals
  - Decisionally impaired
Beneficence

- Obligations of beneficence affect both individuals and society
  - We must weigh the risks and the benefits
    - Risk refers to a possibility that harm may occur
    - Benefit refers to something of positive value
    - Determining the balance constitutes an ethical dilemma in research
  - Even if the benefit to science and society is great, never should we forgo subject protection

Justice

- The principle of justice is captured in the selection process
- Justice requires exclusion of those groups unlikely to be among beneficiaries of subsequent applications of the research
- Justice requires inclusion of diverse populations so that they may benefit from the research findings

Human Radiation Experiments

- Under government sponsorship
  - Researchers injected plutonium into unknowing subjects
  - Nuclear facilities had intentionally released radiation into the environment
- President Clinton created:
  - Advisory Committee on Human Radiation Experiments (ACHRE)
    - To determine what the ethical and scientific standards were for evaluating these events
  - National Bioethics Advisory Commission (NBAC)
Federal Regulations

- Directly derived from the ethical principles in the Belmont Report
- The common set of regulations is known as the “Common Rule”
  - Review of research by an IRB
  - Informed consent of subjects
  - Institutional assurances of compliance

Institutional Review Board (IRB)

- **Purpose:**
  - review research and determine if the rights and welfare of human participants involved in research are adequately protected
- The IRB has authority to approve, require modification, or disapprove all research activities

IRB Review

- All studies undergo continuing review to ensure that:
  - the risk-benefit relationship of the research remains acceptable
  - the informed consent process and documents are still appropriate
  - the enrollment of subjects has been equitable
- Any changes in the study must also receive IRB approval before being instituted
Considerations in IRB Review of a Study

- The risks to the participants
- The anticipated benefits to the participants and others
- The importance of the knowledge that may reasonably result
- The informed consent process to be employed

Informed Consent

- What does this entail?
  - **Information:**
    - Informed consent is a process of information exchange that takes place between the prospective participant and the investigator, before, during, and sometimes after the study
  - **Comprehension:**
    - Investigators are responsible for ascertaining that the participant has comprehended the information
  - **Voluntariness:**
    - An agreement to participate in the research constitutes a valid consent only if voluntarily given

Protocol

- Protocol is a formal document that establishes the conditions under which research is to be conducted
- The investigator should include:
  - the specific scientific objectives
  - budget, personnel and facility considerations
  - research methods and procedures
  - the analytical methods
  - description of data monitoring
  - security measures to protect the data
  - human subject issues
Human Subject Issues

- Inclusion criteria
- Exclusion criteria
- Justification for any inclusion of vulnerable subjects
- The intended gender distribution of the subjects (*women of childbearing potential may not be routinely excluded from participating in research)
- The age range of subjects
- The intended racial and ethnic distributions of the subjects
- Any potential benefits
- Alternatives that are available should the subject select not to participate in the study
- The recruitment methods

Human Subjects Issues cont.

- Who will obtain consent and how the process of informed consent will be structured
- If all subjects will not be capable of giving consent, describe additional protections
- Assessment of understanding of the information presented
- Justification of any non-disclosure and description of post-study debriefing
- Justification of any costs that the subjects will incur
- Description of any reimbursements or incentives such as cash payments

Vulnerable Participants

- Additional protections may be necessary when conducting research with vulnerable participants
- The vulnerable population includes:
  - Children
  - Mentally disabled
  - Individuals with cognitive disorders
  - Prisoners
  - Pregnant women
Protocol Deviation

• The investigator may only deviate from the protocol to eliminate an immediate hazard to participants without prior IRB approval
• The deviation is considered an amendment
• The IRB must be notified as soon as possible

Amendment in a Study

• It must be approved by the IRB before implementing the change
• Changes in a consent form may require reconsent of those currently participating

Multiple Project Assurance

• Multiple Project Assurance (MPA) is required for federally sponsored research
• A fundamental condition of an Assurance is that the institution must establish and maintain an IRB that oversees the conduct of the research
Violation of MPA

- If obligations set forth in an Assurance have been violated, the Office for Protection from Research Risk (OPPR) has the authority to:
  - terminate or suspend the Institution’s Assurance
  - suspend or restrict any ongoing studies
  - departmental restrictions
  - individual restrictions

Violations of FDA Regulations

- Disqualification/debarment of individuals from clinical research
- Disqualification of institutions and/or IRBs from conducting or approving clinical research
- Other sanctions including seizures, injunctions, criminal charges, and monetary penalties
Drug or Device Accountability Records (DARs)

- DARs are used to provide evidence that all materials are accounted for and that their final disposition is controlled.
- DARs are forms that are customized documents tailored to the individual protocol.
- Not only is the investigator’s signature required, but also any persons who dispenses the drug(s) or device(s) to ensure accountability.

Form FDA 1572

- A list of commitments in which the investigator is making to the FDA for conduct of the study can be found on the back of this form.
- This form is also referred to as the “hanging paper” - why?
  - It is a criminal offense to sign this document if
    - it contains false information
    - if commitments made within the signed document are ignored.

Form FDA 1572

- Who signs this form?
  - This form requires the names of the principal investigator, the co-principal investigators, and any sub-investigators.
- What does this form mean?
  - Signing this form is an agreement to conduct the investigation according to the provisions listed on the Form.
Adverse Events

• If any adverse events take place, the investigator must report them to:
  – the sponsor
  – the reviewing IRB

Source Documentation

• Source documentation is where the information is first recorded - original documents
• The investigator is required to prepare as well as maintain adequate and accurate records of all observations and other data pertinent to the study for every participant

Source Documentation - list

• The documents should include things like:
  – demographic information
  – evidence for supporting the condition for which the participant is being studied
  – general information/medical history
  – physical findings
  – documentation that informed consent was obtained for each participant prior to participation in the study
Judgement

- Professional judgement should be used throughout a study
  - to maintain the integrity of the research process
  - to keep the participant informed of his/her role in the process relationship with the investigator(s)

Investigator’s Responsibility

- Investigators bear the ultimate ethical responsibility for their work with human participants
- Other responsibilities include:
  - compliance with federal/state laws and regulations
  - assuming fiscal management
  - supervising and training of students, post docs, and residents
  - complying with the terms and conditions of the sponsor’s award
  - submission of all technical, progress, invention, and financial reports on a timely basis

Investigator’s Responsibility cont.

- Violations may result in loss of funding or debarment
- Investigators who also serve as sponsors must comply with the responsibilities of both the sponsor and the investigator
Institution’s Responsibility

- The institution has responsibility for educating researchers on issues of scientific integrity as well as the mandated responsibility to investigate cases of scientific misconduct

Scientific Misconduct

- A fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, and reporting research
- Does not include honest error of honest differences in interpretations or judgements of data

Allegations of Misconduct

- Individuals who in good faith have made an allegation of misconduct should not be the object of retaliation
- These individuals are known as “whistle-blowers”
- Retaliation against a “whistle-blower” who made the allegation of misconduct in good faith, may itself, be construed as an act of misconduct
Recruitment of Participants

- Direct advertising
  - flyers
  - posters
  - newspaper ads
  - press release
- Most be reviewed by the IRB
- Not state or imply benefits beyond that outlined in the protocol
- Not be coercive or use undue pressures
- Not be misleading to participants

Research Ethics: Part 2

From Textbook

What You Should Learn From Text and Lecture:

- Define research ethics
- What is the role of the IRB
- The what and how of submitting to IRB
- Know the APA ethical principles: Conduct of research with human participants
- What is the principle of informed consent
- Responsibility to participants during data collection
- Explain process of debriefing
- Ways confidentiality of data can be protected
Research Ethics: Part 2
Lecture Outline

• Define research ethics
• Society and science
• Professional issues
• In class proposal review
• Treatment of research participants

Definition

• Research ethics are a set of principles or guidelines that will assist the researcher in making difficult research decisions and in deciding which goals are most important in reconciling conflicting values.
Ethical Issues

• Science and society
  – Should society dictate what issues are investigated?
• Professional Issues
  – Fraudulent activities
  – Partial and duplicate publication

Ethical Principles: Human Participants

• A most fundamental issue confronted by scientists:
  – Treatment of research participants
• Ensure no physical and psychological harm
• Sample history
  – Radiation experiments
  – Syphilis experiments
  – Obedience to authority
  – Restroom study
  – Military, impact of stress

Institutional Review Board

• Psychology research creates special dilemmas
  – Maximally answer research question
  – May subject participant to stress, failure, pain, deception, and so on
• Must weigh gains of research against cost to participants
• Decision based on subjective judgement but Who’s decision is it?
Institutional Review Board

- IRB responsible for recommendation regarding cost-benefit
- IRB reviews research proposals and judges
  - protocols explained to participants
  - risks of harm reasonable relative to gain
- IRB must have sufficient information about the research protocol

Submitting to the IRB

For IRB to approve research need:
- The purpose and the rational of the research
- The research participants to be used in the study
- The location of the study
- Any agents (e.g., drugs) and procedures to be used
- The research design used to answer the research question
- The potential benefit to the research participant or general knowledge acquired from the study
- Any risks or hazards from participation in the study and precautions taken to reduce risk
- A description of how confidentiality will be assured
- A consent form for participation

Case Review

- Let’s stop and review the proposal that was listed as a hand out.
APA Ethical Principles: Conduct of Research with Human Participants

- **Principle A**: Investigator has responsibility to carefully evaluate ethical acceptability.
- **Principle B**: Considering if planned study creates “subject at risk” or “subject at minimal risk” is primary ethical concern of investigator
- **Principle C**: The investigator always retains responsibility.

APA Ethical Principles

- **Principle D**: Informed consent must be given. Must inform participant of obligations, responsibilities, risks, and procedures
- **Principle E**: Before conducting a study with deception
  - determine if deception is justified
  - determine if other techniques
  - give participants sufficient explanation ASAP

APA Ethical Principles

- **Principle F**: Participants have freedom to decline to participate or withdraw at any time
- **Principle G**: Protect participants from physical and mental discomfort. Inform participants of any such risks
- **Principle H**: After data are collected, provide participant
  - with information about nature of study
  - remove any misconceptions that may arise
APA Ethical Principles

- **Principle I:** Investigator has responsibility to detect and remove or correct any undesirable consequences, including long-term effects.
- **Principle J:** All information obtained is confidential unless advance agreement. When possible that others may obtain access, this possibility and plans for protecting confidentiality are explained as part of informed consent.

Ethical Consideration in Planning Research: Risk

- Categories of risk
- Evaluating risk
- Deprivation as risk
- Benefits of research

Voluntary Participation Must Be Assured

- Overt coercion
- Subtle coercion
- Excessive inducements
Informed Consent
• What is informed consent?
• Elements of informed consent
• Public behavior
• Competence to consent
• Readability of consent forms

Deception
• Forms of deception
• Why researchers use deception
• Alternatives to deception
• Consent to deception
• Minimizing harm in research involving deception

Ethical Considerations During Data Collection
• Avoidance of harm
• Withdrawal of consent
After Data Collection: Debriefing

• What is debriefing?

• What are the components of debriefing?

• What is effective debriefing?