Human Subjects Protection: Training for Research Teams

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This session is intended to help physicians, clinicians, physician assistants, nurse practitioners, and office staff understand the key elements of human subjects protection.

This session is *not intended* to replace more detailed instructions and certification required for Principal Investigators and other researchers.
Outline

- History and Ethical Principles
- Institutional Review Boards (IRB’s)
- Informed Consent
- Records-Based Research
  - Health Insurance Portability and Accountability Act (HIPAA)
Section 1. History and Ethical Principles

Goals:

Discuss

- the Tuskegee syphilis “experiment”
- the National Commission
- the Nuremberg Code 1947
- the Beecher article 1966
- the Belmont report
- the three basic principles of human subjects protection
U.S. Public Health Service syphilis “experiment”

- Macon County, Tuskegee, AL
- The U.S. Public Health Service (PHS) deliberately withheld treatment from poor rural African-American men diagnosed with syphilis
- “experiment” went on from 1932 until negative publicity forced the project to close in 1972
The National Commission, The National Research Act

- the Tuskegee “experiment”:
- Led to the creation of The National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research
- Congress passed National Research Act in 1974
  - Title 45 Code of Federal Regulations part 46, DHHS Protection of Human Subjects, and
  - Title 21 Code of Federal Regulations part 50, FDA Protection of Human Subjects
The Nuremberg Code 1947

- Voluntary, informed consent is essential
- Experiment benefits society, unprocurable by other means
- Animal testing should precede human experiments
- Avoid unnecessary physical & mental suffering & injury
- Experiments conducted by scientifically qualified persons
- Human subjects may withdraw consent at any time
- Terminate experiment if injury or death is likely
- Updated in the Declaration of Helsinki 1964

Reviewed 22 examples of questionable ethics in U.S. published research

heightened awareness of problems with unethical clinical research
Belmont Report


Lays out three basic ethical principles underlying all human subjects research:
- Respect for Persons
- Beneficence
- Justice

http://ohsr.od.nih.gov/guidelines/belmont.html#gob2
Respect for Persons

- Respect for persons incorporates at least two ethical principles:
  1. individuals should be treated as autonomous agents
  2. persons with diminished autonomy are entitled to additional protections (e.g., children, prisoners, adults with diminished capacity, etc.)

- The extent of protection afforded depends on the risk of harm and the likelihood of benefit

- In human subjects research, respect for persons demands that subjects enter into research voluntarily and with adequate information
Beneficence

- Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being.
- In the context of human subjects research, beneficence is understood as an obligation.
- Two general rules have been formulated as expressions of beneficence in this sense:
  - first, do no harm; and
  - maximize possible benefits and minimize possible harms.
Who ought to receive the benefits of research and bear its burdens?

This is a question of justice, in the sense of “fairness in distribution” or “what is deserved”

Injustice
- when some benefit to which a person is entitled is denied without good reason; or
- when some burden is imposed unduly

Another way of conceiving the principle of justice is that “equals ought to be treated equally”
Confidentiality Protection

- Pertains to treatment of information disclosed in a relationship of trust with expectation of not being divulged
- Breaches are usually disclosing or transferring information to third parties
Applying Research Ethics

- Rules to govern investigator-subject relationship
- Informed consent
  - Withdrawal at subject discretion
  - Investigator must be sensitive to positions of power
  - Investigator maintain moral fiduciary relationship
Section 2. Institutional Review Board

- Goals:
  - Define when a study needs human subjects protection
  - Describe researcher’s responsibilities
  - Issues of subject selection
  - IRB composition and role
  - Types of IRB Review
  - Continuing IRB Review
The Research Participant

- An individual from whom a researcher:
  - Obtains data through interaction or intervention
  - Obtains identifiable private information

- Who is considered a research subject?
  - Patients
  - Office staff
  - Clinicians
Why Do We Need Formal Protections?

- Promote safety of participants
- Maintain ethical standards
- Implement valid research
- Allay concerns of general public
Who Protects Patients?

- Federal agencies
  - Office for Human Research Protections (OHRP)
  - U.S. Food and Drug Administration (FDA)
- Funding agencies
  - National Institutes of Health (NIH)
  - Agency for Healthcare Research & Quality (AHRQ)
- IRBs, Oversight groups,
  Data and Safety Monitoring Board (DSMB)
- The researcher
IRB review

- An IRB must review and approve or deem exempt all research involving human subjects
  - Primary role is protection of subjects
  - Ongoing review of continuing research
  - Assess adverse events
  - Assess protocol violations
  - Badly designed research is not worth any risks and will not be approved
An IRB can

- Approve, disapprove or terminate all research activities
- Require modifications in protocols
- Require specific information be given to subjects beyond that required by Federal regulations
- Require documentation of informed consent
IRB members

- At least 5 members
- Research expertise
- Peers of the Principal Investigator (PI): similar background & knowledge in subject area
- Public member
- Medical ethicist (good, but not required)
- Diversity similar to community in race, ethnicity, and culture
To satisfy the IRB, the Research Protocol must explain:

- the study in sufficient detail to allow IRB members to judge the scientific merit as well as the risks and benefits
- the study population (i.e., subjects)
- all study interventions (including placebos)
- protection of privacy and confidentiality
- data protection and handling
Types of IRB Review

- Exempt
  - minimal risk to subjects
  - e.g., non-identifiable data, publicly available data

- Expedited
  - non-sensitive topic, no patient contact
  - waiver of consent, previous consent
  - e.g., using non-identifiable records

- Full Board Review
  - sensitive topic, patient contact (never exempt)
  - clinical research, e.g., test of drug efficacy, etc.
Example of Exempt Research

- Sitting in a shopping mall watching the number of people who use cell phones
- Determining timing of physicians arriving at hospital---no identification or knowledge of who they are
Types of IRB Submissions

- Initial submission
- Modification
- Continuous review (usually annual)
Data and Safety Monitoring Board (DSMB)

- Required for all clinical trials
- 5 to 10 experts in research
- Reviews research data every 6 to 12 months to look for early warning signs of harm and can stop the study
- Independent of researcher or funding agency
Data and Safety Monitoring Board (DSMB) Should

- Ensure that risks to subjects are minimized
- Avoid exposure of subjects to excess risk
- Ensure data integrity
- DSMB can stop a study:
  - if safety concerns arise, or
  - when study objectives have been met
Appropriate Population

- Women and children must be included whenever appropriate to the research question
- Vulnerable populations must be identified and protected
  - Children
  - Prisoners
  - Pregnant women and fetuses
  - The terminally ill
  - Students/employees
  - Comatose patients
  - Those with diminished capacity to consent
Can Researchers Pay Subjects To Participate?

- Researchers can pay subjects for time & effort
- Must not be considered a coercive amount:
  - $5 to answer 15 questions
  - $15 to complete a 30-minute survey
  - $100 to complete a panel of questionnaires
  - $1000 to take a study medication
- High rates of compensation may be considered “coercive”, especially for indigent subjects
Continuing IRB Review

- Ongoing informed consent
- Adverse event reporting
- Continuing IRB review
Ongoing Informed Consent

- Inform patients about new options (e.g. new drug)
- Explain pros and cons of new drug and study drug
- Give patient option to continue study drug or use new drug
- It is the researcher’s responsibility to keep patients informed and up-to-date
Adverse Event Reporting

- The responsibility of the PI and the study team
- Reported to
  - funding agency
  - Data and Safety Monitoring Board
  - IRB
- May also need to be reported to study participants as directed by DSMB and funder
Continuing IRB Review

- Must review at least annually
  - IRB will inform the researcher if they require review more often

- Must report
  - any new forms
  - any major changes

- Only emergency changes can be implemented before IRB approval
Who is Responsible for Human Subjects Protection?

- More than just the responsibility of the IRB
- The responsibility of every person who is involved in the implementation of a study
- What you would want for your family member or yourself
Section 3.
Informed Consent

- Goals:
- What constitutes “informed consent”?
- Elements of Consent
- Special Concerns
  - Language, culture, literacy level
  - Children
  - Proxy consent
  - Waiver of consent
  - Exceptions
Informed consent is a process that involves conveying accurate and relevant information about the study and its purpose:

- Risks
- Benefits
- Alternatives
- Procedures
- Answering questions
- Enable an informed decision
Elements of Consent

- **Competent**
  - Is the patient competent to provide consent?

- **Disclose**
  - Is enough information provided to allow an informed decision?

- **Comprehend**
  - Does the patient truly understand?

- **Agree**
  - Does the patient freely agree to participate?

- **Voluntary**
  - Is consent truly voluntary (i.e., free of coercion)?

- **Withdraw**
  - Does the patient understand that they can withdraw at any time?
Must Consent always be in Writing?

- Not when it might pose a confidentiality risk
- Not when there is minimal risk of harm and involves no procedures that usually require informed consent
Special Concerns

- Language
  - Must be language spoken most easily by the subject
  - Must be literacy appropriate

- Cultural issues
  - In some cultures it is considered rude to ask questions of an investigator or rude to decline what seems to be asked as a favor
Children

- It is appropriate to have children from age about 8 to 16 or 18 sign an assent
- This does not replace the parental consent
- Both should be obtained if the child is able to understand the study and to make an informed decision
Waiver of Consent

When is a waiver of consent appropriate?

- If the study involves no more than minimal risk
- If there are no adverse affects to a waiver of consent
- If the study could not reasonably be done without the waiver

An "information sheet" may be required for each participating subject

- Information may also be provided to participants at the completion of the study, if appropriate
FDA Regulations for Exceptions to Informed Consent

- Life-threatening conditions that meet all of the following:
  - Investigator and another physician believes the situation necessitates the use of a test article
  - Subject or representative cannot consent
  - Insufficient time to obtain consent
  - No alternative available that provides an equal or better chance of survival
Section 4. Medical Records Research, HIPAA Issues

- Goals:
- Issues of access for medical records research
- Protect confidentiality of subjects
- Obtain all required approvals before initiation of study
HIPAA (Final Privacy Rule)

- Authorization to view Protected Health Information (PHI) in medical records
- Authorization for disclosure of PHI different from Consent for Research
- Authorization may be incorporated into Consent Form or may be 2 separate forms (depending on IRB requirement)
- Waiver of authorization may be possible
- Key to protecting Confidentiality and Privacy
Risks of Medical Records based Research

- Place subject at risk of criminal or civil liability
- Damage the subject’s financial standing, employability or reputation
- Damage a company or other entity
Privacy Concerns

- Protecting the individual’s privacy is an example for “Respect for Persons”
  - Very strict rules about data collection and data management
  - Keep records secure (e.g., locked cabinet)
  - Remove identifying and linking information as soon as possible
  - Be aware of applicable state laws
Summary

History and Ethical Principles

- Tuskegee syphilis “experiment”
- National Commission
  - for the Protection of Human Subjects in Biomedical and Behavioral Research
- Belmont Report
  - Principles of Respect for Persons, Beneficence, and Justice
- Beecher article
  - awareness of unethical research
Summary

Institutional Review Boards

- **Exempt**
  - minimal risk to subjects
  - e.g., non-identifiable data, publicly available data

- **Expedited**
  - non-sensitive topic, no patient contact
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Summary

Informed Consent

- **Withdraw**: subjects may choose to withdraw at any time
- **Proxy consent**: may need proxy consent from authorized patient caregiver
- **Emergency exceptions**: another physician must agree that emergency consent conditions apply
- **Ongoing IRB review**: “Respect for Persons” requires subjects be informed if a new drug/device is available (i.e., a viable alternative to the study drug/device)
Consent to research project is not the same as consent to use or access Protected Health Information (PHI)

In the absence of patient authorization, a waiver of the HIPAA requirement must be obtained from IRB if medical records are reviewed for research purposes.
Additional Resources

- Office for Human Research Protections
  - http://www.hhs.gov/ohrp/education/

- Collaborative Institutional Training Initiative (CITI)
  - http://www.citiprogram.org/

- National Cancer Institute
  - Protecting Human Research Participants