Human Subjects Protection: Training for Research Teams

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Intended Audience

- 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

Beecher article 1966

- Beecher HK. Ethics and clinical research. N Engl J Med 1966; 274(24): 1354-1360.
- Reviewed 22 examples of questionable ethics in U.S. published research
- heightened awareness of problems with unethical clinical research

Belmont Report

- The National Commission published this report in 1979
- 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

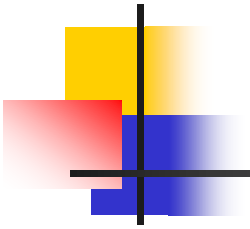
- Respect for persons incorporates at least two ethical principles:
  - 1. individuals should be treated as autonomous agents
  - 2. persons with diminished autonomy are entitled to additional protections (e.g., children, prisoners, adults with diminished capacity, etc.)
- The extent of protection afforded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

Justice

- 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

The Research Protocol

- 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

What Constitutes Informed Consent?

- 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 and equal or better chance of survival

Section 4. Medical Records Research, HIPAA Issues

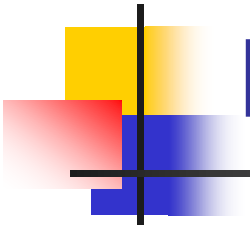
- Goals:
- Issues of access for medical records research
- Protect confidentiality of subjects
- Obtain all required approvals before initiation of study

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
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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)

Summary: Medical Records Research, HIPAA issues

- 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
  - http://phrp.nihtraining.com/users/login.php