Human Subjects Protection: Training for Research Teams

Brought to you by:

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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"

- Took place in 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
- This led directing to the creation of 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. Following this
- 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

After WWII Nazi war crimes were investigated and this resulted in the :

Key elements of The Nuremberg Code 1947 included:

- Experiments with humans must include Voluntary, informed consent is essential
- Experiments must benefit society, and the results must be unprocurable by other means
- Animal testing should precede human experiments
- At all times investigators should Avoid unnecessary physical & mental suffering & injury
- Experiments must be conducted by scientifically qualified persons
- Human subjects may withdraw consent at any time
- Researchers must terminate experiment if injury or death is likely
- An Updated version of this code is included in the Declaration of Helsinki 1964

Beecher article 1966

- Beecher HK. Ethics and clinical research. N Engl J Med 1966; 274(24): 1354-1360.
- This article brought to the attention of the medical community of the United States that unethical medical research was going on at that time.
- Reviewed 22 examples of questionable ethics in U.S. published research
- This article 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

https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

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 occurs
    - 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 of confidentiality are usually disclosing or transferring information to third parties

Applying Research Ethics

- Rules to govern investigator-subject relationship
- Informed consent
- Withdrawal of informed consent can be done at any time at subject discretion
- Investigator must be sensitive to positions of power, particularly when you recruit patients of your practice to research.
- Investigators must maintain a moral fiduciary relationship. You are duty bound to provide the best care for your patients and to protect them, even when they are involved in your research projects.

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
- Elements of Continuing IRB Review

The Research Participant

- An individual from whom a researcher:
- Obtains data through interaction or intervention or
- Obtains identifiable private information
- Who is considered a research subject?
- Patients
- Depending on the nature of the study other's may also be considered a research subject such as:
    - Office staff
    - Clinicians

Why Do We Need Formal Protections?

- To Promote safety of participants
- To Maintain ethical standards
- To Implement valid research
- To 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
- There is an ongoing review of continuing research
- These reviews are there to assess adverse events as well as
- 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
- It may Require modifications in protocols as submitted,
- It may Require specific information be given to subjects beyond that required by Federal regulations
- It may also require documentation of informed consent

IRB members

- Composed of at least 5 members who have research expertise
- They are considered to be peers of the Principal Investigator (PI): that is they have similar background & knowledge in subject area
- Also a member of the Public is the member of the IRB.
- May include a 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
  - It must describe the study population (i.e., subjects)
  - all study interventions (including placebos)
  - It must describe how investigators plan to protect privacy and confidentiality
  - And how they plan to handle data as well as data protection

Types of IRB Review

- Exempt
- Involves minimal risk to subjects
- e.g., non-identifiable data, publicly available data
- Expedited
- non-sensitive topic, no patient contact
- There is either a waiver of consent or previous consent
- e.g., reviewing non-identifiable records
- Full Board Review, where all the board members are convened to review research protocol. This would involve research that covers a 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 with no identification or knowledge of who they are

Types of IRB Submissions

- Initial submission
- Modification
- Continuous review of all research protocols which is usually annual.

Data and Safety Monitoring Board (DSMB)

- Required for all clinical trials
- Includes 5 to 10 experts in research
- Reviews research data every 6 to 12 months to look for early warning signs of harm and they can stop the study
- The DSMB is Independent of researcher or funding agency

Data and Safety Monitoring Board (DSMB) Should

- Ensure that risks to subjects are minimized and that the research
- Avoids exposure of subjects to excess risk
- Ensure data integrity
- The DSMB can stop a study:
    - if safety concerns arise, or
    - when study objectives have been met

What is an Appropriate Population?

- Women and children must be included whenever appropriate to the research question
- Vulnerable populations must be identified and protected

- Vulnerable populations include:
  - 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?

- Yes researchers can pay subjects for time & effort
- But the amount of compensation must not be considered a coercive amount. For example:
- $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

- You as a researcher must inform patients about new options (e.g. new drug or devices) as they become available.
- It is your duty to explain the pros and cons of new drugs or devices versus the study’s drugs and devices to research participants.
- You must give the patient the 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 is to report adverse events to the
- 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

- Research projects must be reviewed at least annually
  - IRB will inform the researcher if they require review more often
- As a researcher you must report any new forms or major changes
- Only emergency changes can be implemented before IRB approval but in
- almost all cases changes must be approved before they are implemented.

Who is Responsible for
Human Subjects Protection?

- More than just the responsibility of the IRB
- It is the responsibility of every person who is involved in the implementation of a study
- It is 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. Explaining:
- Risks
- Benefits
- Alternatives
- Procedures
- Answering questions from the patient

✓ Informed consent is a process; it is not about getting a piece of paper signed. It is about giving the patient enough information to enable them to make 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, with no negative consequences to themselves?

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
  - The consent form 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. Researchers must be aware of these problems.

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 the child's assent and the parent's consent 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

✓ All of these elements must be in place for an exception of informed consent to be allowed.

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 (The Health Insurance Portability and Accountability Act) includes a (Final Privacy Rule)

- This includes an authorization to view Protected Health Information (PHI) in medical records
- It is important as a researcher to understand that authorization for disclosure of PHI different from Consent for Research
- Authorization may be incorporated into Consent Form or researchers may use 2 separate forms (depending on IRB requirement)
- One for the research subject to consent to the study and the second for the research subject to give authorization for the researcher to view or access PHI.
- Waiver of authorization may be possible but only through the IRB.
- Compliance to the HIPPA rule is the key to protecting the Confidentiality and Privacy of your patients.

Risks of Medical Records based Research

- Placing the subject at risk of criminal or civil liability if their private information is revealed.
- It could damage the subject's financial standing, employability or reputation
- It could damage a company or other entity

Privacy Concerns

- Protecting the individual's privacy is an example for "Respect for Persons"
- There are 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
- You must 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

Institutional Review Boards

- 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.

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