

Research Involving Human Subjects

Ethical Principles
in Research
Institutional
Review Board



Historical Perspectives on Human Subject Research

- History is not static. Yesterday's events are today's history.
- The public's perception of research, its benefits and its risks are shaped by the way research is conducted.

Historical Perspectives on Human Subject Research

- Prior to 1945 clinical research was conducted with no morale or ethical standards in place to govern what went on in the experiments.
- The research was typically done on individuals who did not have a choice about participating in the research or those because of socio-economic factors thought they would benefit from the research.

Historical Perspective on Human Subject Research

- All of that changed immediately after WWII and for the next 40 years a consensus was established about what should be the key ethical principles underlying research.
- There were three events that have had a significant impact on federal regulations for the protection of human subjects.

Three Events

- In chronological order they are:
 - The 1946 Nuremberg Doctors Trial
 - The 1960s Thalidomide Tragedy
 - The 1972 Tuskegee Syphilis Study Expose

While other events plays a role, these three events had the most direct impact on federal regulations.

The Nuremberg War Crime Trial of 1946

- At the beginning of World War II, Germany was the most scientifically and technologically advanced country in the world and even had a notable code of research ethics.
- In the field of medicine the Nazi government supported nutrition programs, research into ecology, public health, human genetics, cancer, environmental risks, and a host of other similar issues.

The Nuremberg War Crime Trial

- Women were even denied tobacco ration coupons because of the concern about the effect of nicotine on the fetus.
- German physicians stressed the importance of preventive medicine as well as curative medicine.
- The Nazis, however, exploited people's trust in physicians to disguise discrimination and murder as public health and medical research.

Medical Experiments

- The German Air Force was concerned about the survival at extremely high altitudes and the determination to maximize safe altitudes for bailing out of damaged aircraft.
- In one series of experiments researchers placed victims in vacuum chambers that could duplicate the low air pressure and lack of oxygen at altitudes as high as 65,000 feet.

Medical Experiments

- About 200 internees of the Dachau prison camp were used in these experiments and about 40% of them died as a result.
- Another Nazi concern was survival time after parachuting into cold water in the North Atlantic.
- Some victims of this research were submerged for hours in tubs of ice water

Medical Experiments

- Others were feed nothing but salt water for days;
- Still others were penned outside, unclothed and unsheltered in sub-freezing temperatures for 12 to 14 hours.
- No attempts were made to relieve the tremendous pain and suffering caused by these experiments.

Medical Experiments

- Experiments involving battlefield medicine included treatment of gunshot wounds, burns, traumatic amputations and biological and chemical agent exposures.
- While these are all legitimate concerns for a country at war, the techniques that were used were inhumane.

Medical Experiments

- In these experiments wounds were first inflicted upon the victims and then treated by various techniques.
- For example in one experiment victims were shot and their legs slashed and the resulting wounds were stuffed with glass, dirt and various bacteria cultures and sewn shut.
- When these wounds became infected, they were then treated anti-infective agents.

The Nuremberg War Crimes

- There were also experiments where victims were burned and then the inflicted burns were treated.
- There were experiments involving amputation of upper and lower limbs and treatments with transplants bones and, muscles, and nerves. About 50% of these victims died.
- I could go on and on about these inhumane experiments but I think you have heard enough about the experiments to know why a trial was inevitable.

Nuremberg War Crime Trials

- The Nuremberg War Crime trials consisted of a series of prosecutions of prominent members of NAZI military, politicians, economic leaders, and physicians.
- There were 23 defendants (20 were physicians) that were charged with murder, torture, and other crimes committed in the name of medical science.

Nuremberg War Crimes Cont.

- When the trial concluded on August, 1947, 15 of the 23 defendants were found guilty, 7 were sentenced to death.
- This trial may have ended up being forgotten over time except for the fact that the judgment included a series of standards, an ethical yardstick, now known as the Nuremberg Code.

Nuremberg Code

- The Nuremberg Code stated that:
 - Informed consent of volunteers must be contained without any coercion
 - Human experiments must be based on prior animal experimentation (which thank goodness we also have standards to protect animals involved in research experiments).
 - The anticipated results of the experiment must justify the need for the experiment.

Nuremberg Code

- Only qualified scientists should conduct medical research
- Physical and mental suffering should be avoided.
- Last, there should be no expectation of death or disabling injury from the experiment.

The Thalidomide Tragedy

- Thalidomide was approved as a sedative in Europe in the 1950s.
- Although the U.S. Food and Drug Administration had not approved the drug, manufacturers supplied physicians with samples and the physicians were being paid to study the safety and efficacy of the drug.

The Thalidomide Tragedy

- This was a common practice at that time.
- Unfortunately the results of the study showed that the drug was not harmful to women (the mother) it was extremely damaging to a fetus if taken in the first trimester of pregnancy.
- The drug interfered with the development of blood vessels and particularly affected development of arms and legs.

The Thalidomide Tragedy

- The subcommittee of the U.S. Senate had been holding hearings about the business practices of pharmaceutical companies and as a result were presented with slides of the birth defects caused by the use of this drug.
- Unfortunately many of the people that were given this drug were not even informed that it was an experimental drug.
- As a result of this investigation, in February 1963, the FDA issued regulations with consent requirements (which was rewritten in 1966 with additional protective requirements).

The Study of Untreated Syphilis

- At the turn of the 20th century the treatment of syphilis was, at best, crude and involved the use of mercury and arsenic compounds.
- This treatment was highly toxic to humans and resulted in severe reactions, even death.
- Some evidence even suggested that treated patients lived shorter lives than untreated patients.

The Study of Untreated Syphilis

- The Center for Disease Control designed a study to demonstrate the need for establishing syphilis treatments programs by investigating the effects of the untreated disease.
- This evolved from a genuine concerns about minority health issues.

Tuskegee Syphilis Study

- So in 1932, the Public Health Services worked with the Tuskegee Institute to recruit participants which were to be 600 African American males aged 25 and older.
- At the time of the study, African Americans had almost no access to medical care. With free health examinations, food and transportation, it was not hard to find participants.

Tuskegee Syphilis Study Cont.

- Even though the participants received medical examinations they were never told if it was determined that they had syphilis.
- They were either not treated at all or treated at a level that was insufficient to cure the disease.

Tuskegee Cont.

- The project was supposed to have lasted only 6 months but continued on for an additional 40 years until it finally came to an end.
- In July 1972 an Associated Press story about the Tuskegee Study caused a public outcry that led to a review of the study.

Tuskegee Study

- The review revealed that while the individuals had agreed to participate in the study, they had not been informed about the real purpose of the study.
- It was determined that the study was ethical unjustified and it was stopped a month later
- In 1973 the Health, Education, and Welfare regulations for human subjects research were completely rewritten and \$1.8 billion class action suit was filed on behalf of the student participants.

Ethical Principles in Research

- As you can see from what resulted in these three studies, something definitely needed to be done to protect human subjects in research.
- Because of these and similar events, the U.S. Department of Health and Human Services decided that it was time to establish some new standards in addition to what had resulted from the Nuremberg Code.

Ethical Protections

- There are now two key phrases that define the system of ethical protections.
 - Voluntary participation – requires that people not be coerced into participation.

This is especially relevant to research that relies on captive audiences.

Ethical Protections

- The other key phrase is informed consent. What this means is that the participant must be informed of the research procedures and the risks involved and then give their consent to participate.

The Belmont Report

- New standards established by the U.S. Department of Health & Human Subjects resulted in three basic ethical principles that were defined in what is called the Belmont Report.
- 1. Respect for persons – Respect for persons incorporates at least two ethical convictions:

The Belmont Report

- First, that individuals should be treated as autonomous agents
- Second, that persons with diminished autonomy are entitled to protection.
- The principle for respect thus divides into two moral requirements: the requirement to acknowledge autonomy and the required to protect those of diminished autonomy.

The Belmont Report

- 2. Beneficence – An obligation to protect persons from harm. Maximize benefits, minimize risks.
- 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.

The Belmont Report

- 3. Justice – Who should receive the benefits or research and bear its burden?
- This is a question of justice in the sense of fairness in distribution and what is deserved.
- An injustice occurs when some benefit to which a person is entitled is denied.

The Belmont Report

- There are several widely accepted formulations to ways to distribute benefits and burdens.
- 1. to each person and equal share
- 2. to each person according to individual need
- 3. to each person according to individual effort

The Belmont Report

- 4. to each person according to societal contribution
- 5. to each person according to merit
- Basically what is meant by justice is that the selection of research subjects needs to be scrutinized in a order to determine whether some classes (welfare patients, racial and ethnic minorities, etc.) are being selected simply because of their easy availability

The Belmont Report

- their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied.

Even with these clearly defined standards and principles, there is no way you can no anticipate every ethical circumstance. So, it was determined that Institutional Review Boards were needed to review and approve research protocols.

Institutional Review Board

- The Institutional Review Board of UTC operates under the U.S. Dept. of Health & Human Subjects regulations for the Protection of Human Subjects.
- We operate under a federal wide assurance which is our certification of compliance with federal regulations.

Institutional Review Board (IRB)

- All faculty, staff and students conducting research using human subjects or identifiable, private information about human subjects are required to have IRB approval before the project can be initiated.

Composition of the Board

- The IRB must consist of at least five members of consistently diverse backgrounds, including consideration of race, sex, and cultural backgrounds.
- Members must be able to ascertain the acceptability of research applications in terms on institutional commitment, applicable law, and professional standards;
- At least two members whose primary concerns are in behavioral/social sciences

Composition of the Board

- At least one member whose primary concerns are in non-scientific areas;
- Members must represent more than one profession/discipline;
- One member must be non-affiliated with the university;
- And the Director of Research Integrity

Specific Criteria for IRB Approval

- The IRB will consider whether:
- Risks to subjects are minimized;
- Risks are reasonable in relation to anticipated benefits;
- Selection of subjects is equitable;
- Informed consent is sought from each subject; and
- Informed consent is appropriately documented.

IRB

- There are five research review categories that we will discuss briefly.
- Some research projects are clear cut and it is easy to decide under which category they fit. However, some projects are more difficult. So, what you need to remember is that if your project involves human subject participants and you are not sure what to do, you can contact the

IRB

- the Compliance Division at 425-4431 for assistance.

IRB Categories for Review

- The five review categories are:
 - Exempt
 - Expedited
 - Full Board Review
 - Continuing or Annual Review
 - Classroom Exemption

Exempt Research

- First we will talk about exempt research.
- Certain types of research are exempt from federal regulations. Those include:
- Research conducted in an established educational setting involving normal education practices, such as research on regular and special educational instructional strategies, or research comparing instructional techniques, curricula, or classroom management methods.

Exempt Research

- Educational test (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior unless information is recorded in a manner where the participant can be identified.

Exempt Research Categories

- There are let certain vulnerable populations that do not qualify for exemption even though the research itself may be of minimal risk. These populations include:
 - Children
 - Cognitively impaired individuals
 - Incarcerated people
 - Pregnant women

Exempt Classification Examples

- You are observing the number of people that utilize the River Walk
- You are conducting an anonymous survey on adult sleeping patterns
- You are providing samples of new fruit juices (pomegranate blueberry, guava orange) and asking folks what tastes the best

Exempt

- So, as a general rule for research to be exempt it must not have any information that can be linked back to an individual and pose no more than minimal risk.
- At UTC an application for exemption is submitted and reviewed and approved by the IRB Chair.

Expedited Research

- There are types of research that pose no more than minimal risk to the participants but because they contain identifying information or certain medical procedures, they do not qualify for exempt review.
- Most social and behavioral science research contain no more than minimal risk and will qualify for expedited review (surveys, interviews, oral histories, etc.)

Expedited Review

- Certain medical procedures such as gathering blood samples or non-invasive specimen collections contain no more than minimal risk and qualify for expedited review.
- Clinical studies that do not include the investigation of new drugs or medical devices qualify for expedited review.

Expedited Review Samples

- Some examples of expedited research include:
 - A survey to determine the effect that one student can have on the rest of the class
 - A case study of medical records relating to a rare congenital brain anomaly
 - A clinical study to determine the effectiveness of Tylenol for arthritis pain

Expedited Review Process

- At UTC an expedited review is conducted by two IRB members and generally takes 7-10 days for approval.

Full Board Review

- Any research that involves more than minimal risk to participants requires full board review.
- There are many types of risk that must be considered, not just physical risk. These include:
emotional/psychological risks, risks that could jeopardize employment or financial status, risks that could result in civil or criminal liability; insurability, or anything that would put the participant in jeopardy.

Full Board Review

- At UTC if full board review is required, the application is submitted to all IRB board members for an initial review.
- A full board meeting is convened and two IRB members are responsible for presenting the research information to the board.
- The board members discuss the program and make a decision to approve the project, disapproved the project or defer the decision until additional information is obtained.

Annual or Continuation Review

- IRB approval is only valid for one year so if the research project will exceed one year a continuation application must be submitted and approved by the IRB. The IRB Chair approves all continuation application and this process typically takes only a few days.

Classroom Assignment Exemption

- If you are conducting a research assignment where the purpose of your work is to learn about the process of engaging in research; there will be no publications, formal reports, or presentations at professional conferences, then the project is exempt from IRB review.

Classroom Assignment Exemption

- For classroom assignments the Professor teaching the course is responsible for ensuring that the work of the students in the course is in compliance with the IRB.
- The student submits the IRB application directly to the Professor.
- The Professor sends a classroom assignment form describing the content of the course to the IRB for review and approval.

Classroom Assignment

- Classroom assignment exemption is not applicable to independent studies, honors projects, theses, or dissertations.

Informed Consent

- Along with the IRB application you are required to submit either an informed consent form or a cover letter.
- The informed consent form is the written authorization of the participant to be a part of the research project.
- The consent form contains all of the details about the research (including risks/benefits) and explains that participation is voluntary and that a subject can withdraw from the project at any time.

Cover Letter

- If a survey is being conducted that contains no identifying information then the participant's signature is not required. The Researcher provides a cover letter along with the survey to the participant detailing the content of the research.
- And of course, participation is totally voluntary.

Health Insurance Portability and Accountability Act (HIPAA) – the Privacy Rule

- If you are conducting research that contains protected health information (any information that will lead to the identity of the participant) you most circumstances you will need written authorization, under a few limited situations individual authorization is not required.
- HIPAA is rather complex and not something that I think any of you will need to be concerned with at this point so we will not go into any further detail.

IRB Processes

- At UTC we have developed application forms for all of the research categories that are available on line at the IRB web page.
- We have also developed sample consent forms and cover letters.
- There is also a wealth of additional information contained on the web page that might be of interest to you.

Contact Information

- All of this information can be found at:
- www.utc.edu/Administration/InstitutionalReviewBoard
- Should you have any additional questions you can call the compliance division at 425-4443.