Ethics in Human Subjects Research

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Objectives

- Discuss ethics.
- Discuss the history of human subjects research.
- Define ethical principles as they pertain to human subjects research.
- Discuss protections of participants in human subjects research.

What are ethics?

Ethics

- The system or code of morals of a particular person, religion, group, profession, etc.

Ethics can be defined as:

- Well-founded standards of right and wrong that prescribe what humans *ought* to do
- Usually in terms of rights, obligations, benefits to society, fairness, or specific virtues.
- Include behaviors that enjoin honesty, compassion and loyalty.

Ethics, defined

- Ethical behavior = legal behavior ± "something else"
- Ethics and legality do not always coincide:

  Behavior that is legal is not always ethical, and behavior that is ethical is not always legal.

Is being ethical the same as being lawful?

- The law often incorporates ethical standards to which most citizens subscribe.
- But laws can deviate from what is ethical.
- Pre-Civil War slavery laws and the old apartheid laws of South Africa are examples of laws that deviate from what is ethical.

Are ethics the same as feelings?

- Many people tend to equate ethics with their feelings.
- But being ethical is clearly not a matter of following one's feelings.
- A person following his or her feelings may recoil from doing what is right. In fact, feelings frequently differ from what is accepted as ethical.

Are ethics similar to religion?

- Most religions advocate high ethical standards. Yet if ethics were confined to religion, then ethics would apply only to religious people.
- Religion can set high ethical standards and can provide intense motivations for ethical behavior.
- Ethics, however, cannot be confined to religion nor is it the same as religion.

Is being ethical the same as meeting societal standards?

- In any society, most people accept standards that are, in fact, ethical.
- But standards of behavior in society can deviate from what is ethical.
- An entire society can become ethically corrupt.
- Lack of social consensus on many issues makes it impossible to equate ethics with whatever society accepts.

General Ethical Dilemmas

Concession Stand

- Typically, refreshments at a movie theater cost more that the movie tickets themselves.
- Is it wrong to sneak your own refreshments into the theater?
- What if you follow a certain diet and no refreshments allowed are available at the concession stand?

Ticket Master

- A couple wait in line for four hours to purchase tickets to a show.
- Tickets were limited, so each person was allowed only two tickets.
- As the couple reach the front of the line, a man approaches and offers them $100 bonus to each buy an extra ticket.
- Is it ethical to accept his offer?

Window Shopping

- You want to buy a digital video camera.
- You go to a department store to talk about various models with the store clerk and try them out in the store, to see which one you like best.
- You then order the camera for $100 less from the Internet.
- Is this ethical?

Do your bidding

- At an annual charity quilt auction, bids are running lower than usual, so you increase the bid on a quilt that you really did not want, but that you can see another woman really wants.
- Eventually, the woman wins the quilt and the charity gets the money.
- Was it wrong to cause the bidder to spend more than she might have otherwise?

What are professional ethics?

Professional Ethics

- The Code of Ethics of the American Society for Clinical Laboratory Science (ASCLS) sets forth the principles and standards by which clinical laboratory professionals practice their profession.

ASCLS Code of Ethics

- **I. Duty to the Patient**
  - Maintaining quality and accuracy of laboratory services provided
  - Using sound judgment in establishing and evaluating lab testing
  - Maintaining strict confidentiality of patient information and results

ASCLS Code of Ethics

- **II. Duty to Colleagues and the Profession**
  - Uphold dignity of profession by maintaining honesty and integrity
  - Advance profession by improving knowledge, adopting scientific advances, maintaining high standards, and seeking fair working conditions.
  - Establish cooperative professional working relationships to ensure high standard of care.

ASCLS Code of Ethics

- **III. Duty to Society**
  - Use professional competence to contribute to the general well-being of the community.
  - Comply with laws and regulations pertaining to clinical laboratory science, seeking to change those which do not meet high standards of the profession.

Bad Results

- A specimen from your sister's husband tests positive for HIV.
- You know that your sister and her husband are trying to conceive a child and do not use any method of prophylaxis.
- What should you tell your sister?

Donor Dilemma

- A screening test for the presence of a deadly blood borne pathogen is being performed on all blood units.
- If the test for this pathogen is added to the usual unit workup, approximately 5 infected donors (of 25 million total) will be identified each year and eliminated as donors.
- The cost to add the test is $60 million per year. Should the test be added to the usual unit testing?

Ethical Controversies in Medicine

- **Physician-assisted suicide**: Should doctors, traditionally committed to prolonging life, be involved in assisted suicide for patients with terminal conditions?
- **Abortion**: How much right does a woman have over her body, and how does that right balance with the rights of the fetus?

Ethical Controversies in Medicine

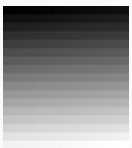
- **Conflicts of interest**: Should patients be made aware when a physician has relationships with drug companies?
- **Stem cell and genetic research**: Should human embryos be used in hopes of finding cures for devastating diseases? Can research be harmful to some in order to benefit many?

Moral and Ethical Absolutism

- An ethical view that there are absolute standards against which moral questions can be judged.
- Particular actions are absolutely right or wrong, regardless of the context of the act, with no gray area in between.
- Favored historically because it makes the creation of laws and upholding the judicial system much simpler.
- Example: Stealing would be viewed as always immoral, even if done for good (like stealing food to feed the starving).

Moral and Ethical Relativism

- Ethical view that actions are relative to social, cultural, historical or personal circumstances.
- Maintains that it is incorrect to assume that the same moral or ethical frameworks are applicable to all situations.
- Example: Stealing to feed a starving family would not be viewed as immoral or unethical.



RIGHT TO KNOW?

- A patient has a terminal illness, and the decision has been made not to tell the patient about his illness.
- If you believe you should always tell the truth (absolutism), you would tell him.
- If you believe in relativism, you might think it is better to not tell him or to only tell him certain details.
- Dilemma: there is no "right" answer

What are research ethics?

Research Ethics

- Continual analysis of motives for, process of, and social effects of biomedical research
- Historically, few efforts made to protect humans and animals in research
- Contemporary research ethics began with scandals of experimentation conducted by Nazis and Japanese soldiers during World War II.

Nazi research on humans, 1939-45

- Selected subjects from the imprisoned, the weak, and the abused—the "undesirables"
- Exposed subjects to extreme cold, pressure, diseases and unproven therapies
- Killed humans to obtain biological specimens

Nazi Experiments

- Many experiments designed to simulate situations that might arise during war
- Simulation of conditions in the North sea to study how long humans can survive in cold water
- Studies to rewarm the body to save lives
- Prisoners placed in vacuum chambers to test effects of high altitude on the body

Nazi Experiments, cont.

- Sewed contaminated glass, foreign objects or gauze into wounds
- Smashed the bones of prisoners with a hammer to simulate realistic war wounds
- Used radiation aimed at the ovaries of "objectionable" women to quickly sterilize them

Human research in imperial Japan, 1932-1945

- Chinese citizens – men, women and children – chosen at random to be subjects
- Vivisection
- Recreation of battlefield injuries
- Hypothermia
- Exposure to lethal infectious diseases

Japanese Experiments

- Decapitated prisoners to test sharpness of blades
- Amputated limbs to study shock due to hemorrhage
- Performed gastrectomies and tested reattachments of the esophagus to various parts of the intestinal tracts
- Tested various pathogens on prisoners to determine what inoculum was needed to cause disease

Tuskegee Syphilis study, 1932-72

- Medical uncertainty over different disease progression of syphilis depending on race
- Research study started in hopes of justifying treatment programs for African-Americans
- Carried out by U.S. Public Health Service, who enrolled 600 poor African-American men from Macon County, Alabama
- Researchers planned to study the men periodically until death, and then perform autopsies to gain data.

Tuskegee Experiments

- Participants were not informed of the true study goals
- Recruited by offering free medical examinations and blood tests
- Given free meals, free rides to the exams, treatment for minor ailments, and burial insurance
- Promotional letters and certificates of appreciation were sent to encourage participation.

Tuskegee Experiments

- Study continued even after penicillin was shown to cure syphilis, in 1945
- Still no treatment was offered to study participants
- Names of participants were circulated among physicians to ensure no treatment would be given
- Ethical concerns raised in 1947
- First news articles condemn studies in 1972; study ends

Tuskegee Experiments

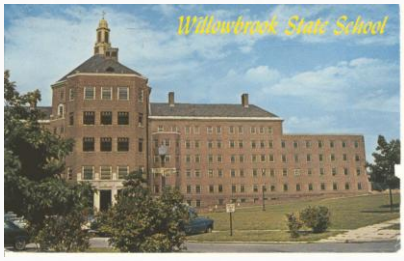
- By the end of the study:
  - 28 men had died directly of syphilis
  - 100 were dead of syphilis-related complications
  - 40 of their wives had been infected
  - 19 of their children had been born with congenital syphilis

Tuskegee Experiments

- 1973 – Congress held hearings; class-action lawsuit filed
- 1974 - $10 million out-of-court settlement was reached; U.S. government promised lifetime medical benefits and burial services to all living participants
- 1975 – Benefits also given to wives, widows and offspring.
- 1997 – President Clinton issued formal apology

Willowbrook Hepatitis Experiments

- 1955 – 1970: Willowbrook State School, Staten Island, NY
- Institution for mentally disabled children
- Due to overcrowding, hepatitis was a major problem for patients and staff
- Research study initiated to study whether injections of antibodies against hepatitis would provide protection against the virus



Willowbrook Hepatitis Experiments

- Two experiments
  - Children *already* residing at Willowbrook: some injected with antibodies vs. some not injected
  - *Newly admitted* residents given antibody injections: some deliberately given virus vs. some not given virus
- Researchers obtained consent from parents
- Children on waiting list to enter Willowbrook were granted immediate admission for consenting to participation

November 15, 1958 — **Willowbrook Study**
Staten Island, New York

Dear Mrs. _____:

We are studying the possibility of preventing epidemics of hepatitis on a new principle. Virus is introduced and gamma globulin given later to some, so that either no attack or only a mild attack of hepatitis is expected to follow. This may give the children immunity against this disease for life. We should like to give your child this new form of prevention with the hope that it will afford protection.

Permission form is enclosed for your consideration. If you wish to have your children given the benefit of this new preventive, will you so signify by signing the form.

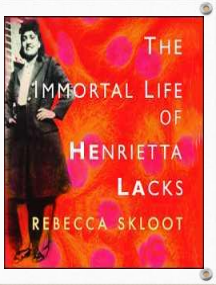
Willowbrook Hepatitis Experiments

- Hepatitis antibody injections showed strong protective effect in those who received them.
- Study also concluded that two strains of hepatitis existed, Hepatitis A and Hepatitis B.
- 1972 – TV story exposing overcrowded and inhumane living conditions; resulted in class-action lawsuit
- Civil Rights of Institutionalized Persons Act of 1980 passed
- Residents placed elsewhere over time but facility remained in operation until 1987

Henrietta Lacks

- Poor African-American tobacco farmer from Virginia
- 1951: Diagnosed with cervical cancer at Johns Hopkins Hospital - common place of treatment for the poor
- Tumor rapidly metastasized throughout her body
- Lacks died later that year

- Both normal and cancerous cells were taken from Lacks's cervix and given to a research lab at Johns Hopkins, without her knowledge or permission
- Previously, scientists spent much effort to grow cells in culture
- ***HeLa* cells** were found to grow exceptionally well in culture: *immortal cell line*
- Extremely useful in medical and biological research



HeLa cells

- First human cell line to grow successfully *in vitro*
- Cells were freely donated by the researcher to any scientist who requested them
- Used by Jonas Salk to test the first polio vaccine in the 1950s
- First human cells to be successfully cloned in 1955
- Allowed for numerous advances in research: cancer, AIDS, gene mapping, pathogenic infections, effects of radiation, toxins…

HeLa cells

- More than 60,000 scientific articles published
- Cells have gone to the moon to test effect of zero gravity.
- Cells commercialized in the 1980s; still being cultured, sold and used today
- Lacks family did not learn of cells until 1970s
- Questions raised about whether family should be compensated and about medical privacy

How are human subjects protected now?

Nuremberg Code, 1947

- Voluntary consent of human subject is essential.
- Experiment should be beneficial to society and results unattainable by any other means.
- Research should be justified based on previous knowledge.
- Experiment should be conducted to avoid physical and/or mental suffering and injuries.

Nuremberg Code, 1947

- Risk of experiment should NOT exceed potential benefits.
- Subjects should be protected from experiments risks.
- Researchers must be fully trained and qualified.
- Human subject must be free to halt experiment at any point.
- Researchers must stop experiment at any point if continuation would be dangerous.

The Nuremberg Code, 1947

- Uneventful reception in the U.S.
- Treated as a state secret, kept classified and released only to key parties
- Not incorporated into German or American law

Declaration of Helsinki, 1964

- Set of ethical principles developed for the medical community by the World Medical Association
- Adopted in Helsinki, Finland in 1964
- Regarded as the cornerstone document on human research ethics
- First significant effort of the medical community to regulate research itself
- Based heavily on Nuremburg Code
- Has undergone seven revisions since adoption

Declaration of Helsinki, 1964

- "Concern for the interests of the subject must always prevail over the interests of science and society."
- Relaxation of conditions of consent: must be obtained "if at all possible from a responsible relative"
- Medical research involving a disadvantaged or vulnerable population is only justified if the research is responsive to the health needs and priorities of this population and if there is a reasonable likelihood that this population stands to benefit from the results of the research.

Belmont Report of 1979

- Recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- Identified basic ethical principles that should underlie all biomedical and behavioral research involving human subjects:
  - **Respect for persons**
  - **Beneficence**
  - **Justice**

Respect for Persons (Autonomy)

- Obligation of the researcher to treat all people with courtesy and respect and allowing them to make an informed decision regarding research participation.
- Must ensure that the participant has received a full disclosure of: Nature of the study, risks vs. benefits, alternatives, ample opportunity to ask questions
- Expressed in the informed consent document

Beneficence

- Obligation of the investigator to attempt to *maximize benefits* for the individual participant and/or society, while *minimizing risk* of harm to the individual

Justice

- Avoiding participant populations that may be unfairly coerced into participating
  - Prisoners
  - Institutionalized individuals
  - Children
- Requires equality in distribution of benefits and burdens among the population group(s) likely to benefit from the research
- An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly

Institutional Review Board for the Protection of Human Subjects (IRB)

- Reviews all research
- Determines if the principles are adhered to by the researcher
- Can terminate studies if adverse effects are greater than benefits
- For research to be published it must undergo IRB review
- Rigorous review process that may sometimes seem counterproductive

Components of an Ethically Valid Informed Consent Form for Research

- Full disclosure of:
  - Nature and purpose of research
  - Procedures
  - Benefits
  - Foreseeable risks
  - Alternatives
- How the confidentiality or anonymity of the participant will be ensured
- Compensation
- Medical treatment for injury due to study
- Who to contact with questions, complications and/or injuries

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Components of an Ethically Valid Informed Consent for Research

- **Understanding:**
  - Participant must understand what has been explained and must be given the opportunity to ask questions and have them answered by one of the investigators
  - Informed consent document must be written in lay language, avoiding any technical jargon.
- **Voluntariness:**
  - Participant's consent to participate in the research must be voluntary, free of any coercion or promises of benefits unlikely to result from participation.

Components of an Ethically Valid Informed Consent for Research

- **Competence:**
  - Participant must be competent to give consent
  - If not competent due to mental status, disease, or emergency, a designated surrogate may provide consent if it is in the participant's best interest to participate. In certain emergency cases, consent may be waived due to the lack of a competent participant and a surrogate
- **Consent:**
  - Authorize his/her participation in the research study
  - Preferably in writing, although at times an oral consent or assent may be more appropriate.

In conclusion…

- Ethical decisions are not always made easily.
- Ethics in human subjects research has evolved greatly in the past 60 years.
- Many protections are now in place for individuals who participate as subjects in human subjects research.
- It is important to maintain a balance between protecting participants while still allowing valuable research to proceed.