CHAPTER 2

Ethics

CHAPTER OBJECTIVES

By the end of this chapter, students will be able to:

- Define the basic principles of medical ethics
- Summarize the ethical violations of the U.S. Public Health Service Syphilis Study in Tuskegee
- Examine ways to maintain confidentiality of medical records and research data
- Explain the function of an institutional review board

KEY TERMS

Beneficence
Institutional review board
Justice
Respect for persons

Introduction

This chapter provides an overview of ethics. After a description of the role of the federal government in research, two historical landmark cases are presented, followed by definitions of the basic principles of medical ethics. This is followed by a discussion of how these principles are applied to the role of the institutional review board (IRB), development of informed consent documents, and consideration of special populations.

Historical Background

In 1949, following the Nazi Nuremberg trial in Germany, the U.S. National Institutes of Health, Office of Human Subjects Research was founded on the principles of the Nuremberg Code, which contains directives for human experimentation. The following summarizes the Nuremberg Code:[1]

- Voluntary consent is required.
- Research must be of societal value.
- Previous studies justify the need for the research or evaluation.
- Research and evaluation must avoid physical and mental suffering and injury.
- No research may be conducted if prior knowledge suggests the occurrence of death or disability.
- Risks must not exceed humanitarian benefits.
- Program planning and research must protect subjects from injury, disability, or death.
- Research and evaluations may only be conducted by qualified researchers.
- Individuals participating in research or evaluation may withdraw at any time.
- Researchers or evaluators must end their studies if there is cause for concern of subjects regarding their safety.

Later, the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP) was created for the protection of the rights of individuals involved in research and to provide clarification, guidance, and advice; distribute educational information; and maintain regulatory oversight.[2] In 1979, the U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research wrote the Belmont Report to describe the ethical principles that apply to human subject research. In 1981, the U.S. Department of Health and Human Services and the Food and Drug Administration revised the Belmont Report to be compatible with current statutes.[3]

It is important to review U.S. historical landmark cases that involved unethical practices in medical research. The two cases discussed here are the U.S. Public Health Service Syphilis Study in Tuskegee and the case of Henrietta Lacks.

U.S. Public Health Service Syphilis Study in Tuskegee

Syphilis is a sexually transmitted infection of great importance to public health because it may not present symptoms for years, increasing chances of it being

spread among people before being treated. Syphilis causes many health problems including painful lesions and sores and, if left untreated, dementia in later life. Syphilis may also be passed from an infected mother to her newborn child. In 1932, the U.S. Public Health Service started a research study about the progression of syphilis in Macon County, Alabama, near Tuskegee. Of the 600 impoverished African American males in the study, 399 had syphilis and 201 did not have syphilis. The men were never told that they were involved in a research study, and they did not receive proper medical care to treat syphilis. For study participation, the men received free medical exams, meals, and burial insurance; however, they were never allowed to quit participating in the study. In 1936, the study's first clinical report was published. In 1947, penicillin was available to effectively treat syphilis, yet the men never received treatment. During World War II, 250 men in the study registered for military service, were diagnosed with syphilis, and obtained treatment for syphilis. After 40 years, in 1972, the assistant secretary for Health and Scientific Affairs announced the end of the Tuskegee Study, and an advisory panel declared the study was unethical. By the time the study ended, 74 men were alive. Of the original 399 men, 28 had died of syphilis, 100 had died of related complications, 40 wives had been infected, and 19 children had been born with congenital syphilis. In 1973, a class-action lawsuit was filed on behalf of the men and their families. In 1974, an out-of-court settlement was reached for $10 million, plus lifetime medical benefits and burial services to all living participants. In 1975, the benefits were extended to wives, widows, and children. The last study participant died in January 2004, and in 2009 the last widow receiving benefits died. As of this writing, there are 15 remaining children receiving medical and health benefits. The Tuskegee Study left a legacy of mistrust among the African American community toward the medical establishment and many public health efforts.[4] On May 16, 1997, after 65 years, President Clinton apologized for government's syphilis study in Tuskegee, Alabama.[5]

Henrietta Lacks

Henrietta Lacks was an African American who lived in Virginia and worked as a tobacco farmer. In 1951, at age 30, she was diagnosed with cervical cancer. A physician from Johns Hopkins Hospital in Baltimore used a piece of her cervical tumor to grow a cell line to be used for medical research. Neither Ms. Lacks nor her family had any knowledge that her cells were used for research. They never signed an informed consent document. The immortal cell line was named HeLa from the first two letters of her first and last names. This cell line was the first human cells to ever grow in a culture medium. Henrietta's cells were used to

develop the polio vaccine, cloning, gene mapping, and in vitro fertilization, among other scientific advancements. Her cells were used for 25 years after her death.[6] It remains unclear why her cells never died. The story was uncovered when writer Rebecca Skloot researched the history of HeLa cells. Ms. Skloot revealed that the Lacks family was unaware that researchers sold vials of their mother's cells, never receiving any money. Ms. Skloot wrote a book, titled *The Immortal Life of Henrietta Lacks*, about what she found. The Henrietta Lacks Foundation was started to provide financial assistance to needy individuals who have made important contributions to scientific research without their knowledge or consent.[7]

Basic Principles of Medical Ethics

Medical ethics are a system of moral principles and values applied to medical, health, and biological science judgments and decision making. To understand ethics, it is important to learn basic terminology. The basic ethical principles are respect for persons, beneficence, and justice. After learning the definitions, it becomes apparent that each principle is understandable on its own. However, when several ethical principles are considered jointly, the overlap can lead to contradiction.

Respect for persons or autonomy is divided into two sections. First, each individual is treated with respect and is given adequate information to make an informed decision, including having no treatment or alternative treatments. Informed decisions should be made without excessive influence of others. Second, individuals with diminished decision-making capacity require extra protection, depending on the risk of harm and the likelihood of benefit. Throughout research involvement, autonomy should be reassessed to ensure that participating individuals maintain their self-determination and understand risks and benefits. All participants are shown respect, and no reasonable information is withheld. For example, when enrolling prisoners in a research study, they have a right to volunteer for research, but the prison living conditions should not lead to coercion or undue influence over the protocol.[3] Questions of respect for persons or autonomy include the following:

- Does each potential subject have the personal capacity to willfully choose to participate in the research or evaluation?
- Is anyone feeling internal or external pressure to participate?
- Are the subjects free to withdraw from the research?

Beneficence is aligned with the Hippocratic Oath principle of "do no harm," protecting individuals from harm by maximizing possible benefits and

minimizing possible risks. In medical research, experimental medical treatments are ethical when the chance of possible benefit outweighs the risk of possible harm. However, in medical research, because it is not known if the experimental treatment will benefit or harm the participant, it is necessary to recognize that benefits and risks may result while gaining knowledge. Beneficence assumes that risks are minimized as individuals and society benefit from participation in research. Beneficence is often ambiguous, especially when the research involves more than minimal risk with no definitive and measurable benefits. At this point, the participant's choice must be free of coercion, and he or she must be given all possible choices to make a completely informed decision. The researcher is required to stop the research at any time when it becomes clear that the participants are harmed.[8] Questions of beneficences include the following:

- Is the research providing benefits to the subjects?
- Is the research needed to move science forward?
- Is it possible that the researchers stand to gain more from the research than the subjects do, such as data collection for academic publications and future grant applications to promote their personal careers?
- Are the subjects protected from possible risks of harm, or are they being used as data points with limited regard for their well-being?

Justice requires a fair distribution of burden and benefits, so that every person with the same condition has an equal chance of being exposed and an equal chance of benefitting from the treatment.[8] There are two levels of justice: individual and social. Individual justice occurs when specific volunteers are recruited because they would potentially benefit from the research and other volunteers are specifically not recruited due to undesirable traits or medical conditions. Social justice requires the equal distribution of research benefit or burden across the target population rather than a select portion of the population.[3] When a researcher recruits volunteers, it is essential to justify the selection process. Volunteer research participants cannot be chosen simply because of their availability or their compromised position in society, but rather for reasons directly related to the research question. On the other hand, justice requires that when new medical technology is successfully developed, every individual with the medical condition should have equal access to the benefits of the new technology, regardless of ability to pay. Questions of justice include the following:

- Is there a fair distribution of burden and benefits?
- Does every person in the target audience have the same chance of being selected for the research?

- Are the patients with the same illness seeking care at the local county health department being recruited at the same rate as patients seeking care at a private physician's office?
- Because of lack of random assignment, is one group of patients serving as the nontreatment group while another group of similar patients is benefitting from the treatment?

Although respect for persons, beneficence, and justice are the main ethical principles, there are additional ethical principles—nonmaleficence, paternalism, and utilitarianism—often noted in medical research.[3]

Nonmaleficence is defined as refraining from causing harm or acting with malice toward a person. Questions of nonmaleficence include the following:

- Even if the research or evaluation is not causing harm, is it possible that it is not refraining from malice?
- What does a subject gain by being asked to disclose his sexual or criminal activity for the purpose of research or evaluation?
- Even if the subject signed the informed consent paperwork, does answering personal questions cause the subject to experience anxiety?
- If a person is involved in a longitudinal study for several years, do the constant reminders to remain involved feel like an invasion of privacy over time regardless of the research topic?

Paternalism involves a relationship of uneven power between a healthcare provider and a patient. For example, it is paternalistic for a healthcare provider to insist on a treatment without informing and educating the patient about all available options. In this case, without the patient's consent, the healthcare provider takes the role of a parent and places the adult patient in the role of a child. Questions of paternalism include the following:

- Did the healthcare provider treat the adult patient as a child?
- Was medical information withheld from the adult patient because the healthcare provider did not think the person should be told about the medical diagnosis?
- Was the adult patient given information about alternative medical treatments, or was the patient only given information on the treatment the healthcare provider thought was best?

Utilitarianism is the decision, behavior, or action that achieves the greatest good for the greatest number of people.[8] For example, some healthcare providers might think it is ok to recruit cancer patients to determine the dosage of a new

medication. The research is not designed to help these current cancer patients, but rather to determine the correct dosage for future patients. This type of research design involves questionable ethics. Questions of utilitarianism include the following:

- Is the research design aimed at current or future patients?
- Is only one specific group, such as Medicaid patients, recruited for a research study, but all patients with the same medical condition will benefit from the research?

Ethical Links Between Research and Evaluation

Building on the historical background and basic ethical principles already discussed, let's explore the ethical links between research and evaluations. Keep in mind that the purpose of research is to create new knowledge, whereas the purpose of evaluation is to improve programs. Any type of research that involves collecting any type of data (interviews, tissue samples, survey completion, etc.) from human subjects must involve an ethical review to ensure the physical, psychological, and social safety of the human subjects. Now let's discuss evaluations. Even though evaluations are not creating new knowledge like research, most evaluations do involve collecting data from human subjects. Although there are differences between the purpose of research and purpose of evaluation, the need to protect human subjects remains the same. That being said, there can sometimes be some blurring between research and evaluation on certain projects. It is possible for one project to involve both research and evaluation. For example, a funded project conducts research to develop an innovative teen pregnancy prevention curriculum for after-school programs, and the same team implements the innovative curriculum and conducts the evaluation to determine if teen pregnancy rates have dropped over the five-year longitudinal evaluation. Because the team involved is conducting both the research and the evaluation (often at the same time), it would be wise to hold both activities to the same research standards.

Confidentiality of Medical Information and Research Data

Confidentiality of medical information and research data is an essential component of health care as well and research and evaluation studies. After obtaining informed consent from an individual, healthcare providers and investigators are responsible for protecting every aspect of their personal information including

contact information, survey responses, medical data, test results, and interview responses. They are responsible for maintaining this protection for the duration of the research and until seven years after the completion of the research. It cannot be emphasized enough that all data must be stored in locked cabinets or in password-protected databases. More elaborate procedures are necessary when the collected data involves sensitive information such as criminal activities or sexual behaviors. When studies involve assigning codes for identifiers, the investigators must separate the actual names from the assigned codes to maintain confidentiality. Investigators are responsible for ensuring that their staff receives the required training on federal guidelines related to data confidentiality. For example, hospital administrators must ensure confidentiality of patient medical records just as investigators must protect data collected from study participants.

The most common training for patient and data confidentiality is related to the Health Insurance Portability and Accountability Act (HIPAA), which passed in 1996 under President Bill Clinton. Title I of HIPAA protects health insurance coverage for workers and their families if they change or lose their jobs. Title II of HIPAA is known as *administrative simplification* and establishes the national standards for electronic healthcare transactions and national identifiers for providers, health insurance plans, and employers.[9] For the consumer, HIPAA provides individuals the right to determine who may read or receive a copy of their medical records, add corrections to their medical records, give permission for sharing health information, and file a complaint with the healthcare provider, health insurer, or the federal government. If anyone feels that their medical records have been handled inappropriately, they may file a complaint at the U.S. Department of Health and Human Services website, www.hhs.gov/ocr/hipaa/. The type of medical information that is protected includes information added to the individual's medical record, conversations shared between healthcare providers about an individual's care, personal medical information in computer system databases, and billing information.[10]

Whether in health care or research, hospital administrators, principal investigators, and head researchers are responsible for ensuring that each person providing health care or working on research is familiar with the details of HIPAA and knows how to protect the privacy of patient data, records, conversations, surveys, and any other information that is collected. There are several websites that offer training for HIPAA and research certification, including the following:

http://www.unc.edu/hipaa/training.htm
http://privacy.health.ufl.edu/training/visitors/instructions.shtml
http://www.hhs.gov/ocr/privacy/hipaa/understanding/training/index.html

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Table 2-1 Professional Codes of Ethics

Health Education	http://www.nchec.org/credentialing/ethics/
Nursing	http://www.nursingworld.org/codeofethics
Medicine	http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics.page
Pharmacy	http://www.pharmacist.com/code-ethics
Physical Therapy	http://www.apta.org/EthicsProfessionalism/
Public Health	http://www.apha.org/NR/rdonlyres/1CED3CEA-287E-4185-9CBD-BD405FC60856/0/ethicsbrochure.pdf
Public Health Leadership Society	http://www.phls.org/home/section/3-26/
American Evaluation Association	http://comm.eval.org/codeofconduct/

Healthcare Providers: Medical Care Versus Medical Research

Medical research poses ethical concerns because healthcare providers have the ethical obligation to "do no harm" and protect individuals by maximizing possible benefits and minimizing possible risks. However, the role of healthcare providers changes when they conduct medical research. In research, healthcare providers are conducting experiments to gain new knowledge and answer research questions, rather than to treat an individual's illness. To answer research questions, individuals are recruited to voluntarily participate in medical research. In the research planning phase, it is the researcher's responsibility to review basic ethical principles and confirm that any possible violations are minimized as much as possible. For example, during the informed consent process, it is not possible for a healthcare provider to be certain that the research will protect individuals from harm. The research may involve comparing Drug A and Drug B against the currently available standard of care, Drug C. Medical research never intends to harm volunteers, but individuals may experience a negative reaction to the experimental drug. On the other hand, research may show that Drug A is superior over Drug B and Drug C, so the researcher needs to switch all participating volunteers to Drug A to maximize benefits and reduce risks. Let's revisit the ethical principles by examining the following questions:

- Does the proposed research involve a special population, such as pregnant women, individuals with mental or physical disabilities, elderly individuals, or prisoners?
- What training does the research staff need prior to recruiting subjects?

- If the subjects are involved in the research for several years, how often are the subjects reeducated on the research and asked to sign a new informed consent form?
- If the subjects benefit from participation, is there a fair distribution of the anticipated benefits?
- If the research involves observing subjects in public locations, would a reasonable person be offended by the invasion of their privacy?
- How has the researcher planned for maintaining the confidentiality of the data?

Before moving on, let's apply the ethical principles to a few case studies.

Physical Therapy Example

A 76-year-old patient had heart surgery. After surgery, he moved into the hospital-owned inpatient rehabilitation center for eight weeks of physical therapy. He started to improve during the first few weeks, but lately he has been skipping appointments and stays in his room. The patient told the physical therapist that he wants to go home. His physician thinks the gentleman needs to stay for the full eight weeks. The patient needs his physician's signature to check out of the clinic. From notes in the patient's chart, his physician knows the gentleman wants to go home. The physician is intentionally not responding to the patient's telephone calls, because he knows that the gentleman is not strong enough to go home and care for himself. Is the physician making an ethical decision for this patient?

Nursing Example

It is common for nurses to work in various medical specialties within a hospital. One day the nurse may be asked to move from a medical floor to a postsurgical floor because of a shortage of nurses. For this type of move, the nurse is using approximately the same skills for both types of patients. When a nurse is asked to cover a nursing shortage in a pediatric critical care unit, the nurse is presented with an ethical dilemma. Because the nursing code of ethics focuses on patient safety, should the nurse oblige her employer and work her shift in the unfamiliar critical care unit or adhere to patient safety and refuse to work in the critical care unit?

Medical Example

A second-year resident is asked by her attending physician to obtain patient consent for a surgical procedure to reduce the patient's shoulder pain following a sports injury. After reviewing the patient's chart, the resident realizes that the

scheduled procedure is not required to eliminate the shoulder pain. At a recent conference, the resident learned that a simple injection of cortical steroid has been proven to be just as effective for this type of shoulder pain. The resident is not comfortable obtaining the patient's signature on the surgical consent form, because she knows that the procedure is not necessary, is expensive, and requires several hospital days for postoperative recovery. What ethical principles are being violated in this situation?

Hospital Administration Example

Healthcare providers in a hospital setting observe situations where they cannot help but think about the cost associated with caring for a terminally ill patient who would be better served in the hospital hospice unit. Caring for terminally ill patients on a medical floor involves spending valuable healthcare dollars that some would argue might better serve other patients with a higher chance of survival. What ethic principle includes this type of argument?

Hospital Ethics Committee Example

A 36-year-old quadriplegic patient of sound mind requests to be removed from life-support systems during his current hospitalization. He has been a quadriplegic for 18 years and does not wish to continue to live in this medical condition. He obtained a do-not-resuscitate (DNR) order a few years ago. His healthcare practitioners refuse to remove his life-support devices. The patient and the healthcare practitioners refer the case to the hospital ethics committee for resolution. What ethical principles does the committee need to discuss?

Evaluation Example

An evaluation team from the state university was hired by the state health office to provide a recommendation on whether the clinic should remain open. The university and the state senator were both from the city where the clinic was located. The evaluation team was aware of these political challenges, but they decided they would accept the project. During the first month, the clinic administrator arranges personal interviews with a few select clinic board members as a way to assist the evaluation team with making connections. A few weeks later, the clinic financial officer offered to supply billing data. During the second month, the evaluation team was told by several employees that the number of patients seen at the clinic was lower than what was recorded in the electronic medical records and that the submission of fraudulent insurance claims was a

common practice. However, these staff members also stated their fear of being unemployed if the clinic closed. The evaluation project was getting complex and teeming with a variety of ethical issues. Although it is not the job of evaluators to become investigative detectives, they do need to be aware of underlying legal and politics issues. What ethical principles apply to this situation? How should the evaluation team proceed?

Institutional Review Board

An institutional review board (IRB) is a committee that serves to formally approve, monitor, and review every type of biomedical and behavioral research that involves human subjects. The purpose of the IRB is to protect the rights and welfare of the research subjects. At the national level, the U.S. Food and Drug Administration (FDA) and the U.S. Department of Health and Human Services (DHHS) oversee the IRB regulations including approval, required modifications of research, and disapproval of research.[11] Keep in mind that each agency or division under the FDA and DHHS has its own rules and regulations for biomedical and behavioral research and evaluation. At the local level, institutions have their own IRB committees, such as universities, hospitals, clinics, health departments, and school districts. Every IRB committee performs oversight functions of all research conducted on human subjects within their institutions. In some situations, researchers must obtain IRB approval from more than one committee. For example, if a university researcher receives state funding to conduct an evaluation at a local health department clinic, the investigator must receive IRB approval from the university IRB as well as the local health department IRB committee.[3]

To accomplish the purpose of the IRB, the committee members review research protocols, informed consent documents, recruitment brochures, surveys, interview and focus group question guides, and all other materials related to the research. The IRB also reviews procedures involving previously collected patient data or secondary data, such as patient charts, lab and medical test results, prescription drug data, satisfaction surveys, financial information, and any other type of outcome data. The protocol is to assess the research ethics and methods, and to ensure that participation is informed and voluntary and that all subjects are capable of making personal decisions. The IRB committee approves research and evaluations that provide informed consent for subjects, shows that the risks to the subjects are balanced with potential societal benefits, and proves that subject selection is fair with equal distribution of risks and benefits to eligible

participants.[12] Each IRB committee requires a written application with the following required components:[3]

- Research protocols and amendments
- Written informed consent forms
- Participant recruitment procedures and advertisements
- Written information provided to participants
- Research or evaluation plan
- Information about availability of compensation and schedule of payments
- Safety information to accommodate any adverse conditions resulting from the research, including name and contact information of lead researcher, evidence of the researcher's qualifications, and names of all personnel involved with any aspect of research

Depending on the type of research, IRB committees request additional information and multiple document revisions prior to making a final approval decision. Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and selection of individuals for research.

Informed Consent

Informed consent is the hallmark of human subject research because it reflects the individual's right to respect and autonomy. Informed consent is not a one-time encounter to obtain an individual's signature, but rather an ongoing process to ensure that human subjects continue to understand that their involvement is voluntary. According to the DHHS,[12] informed consent must include the following components: full disclosure, comprehension, adequate compensation, and voluntary choice.

Full disclosure: Full disclosure involves revealing the purpose and expected duration of the subject's participation, procedures involved, description of potential risks and benefits, appropriate alternative procedures or treatments, confidentiality of records, and a statement affirming that participation is voluntary and that refusal or withdrawal will not result in a penalty or loss of entitled benefits. All informed consents must be written using laypeople's words with simple sentence structure and presented in the preferred language of each potential human subject for maximum comprehension. Here are a few examples of how to simplify medical terminology: bruise instead of hematoma, arms instead of upper extremities, pills instead of medications. In addition, informed consent documents include information on the researcher's name and how to contact

them to answer questions, as well as information about the ability to withdraw at any time from the research without penalty. It is important that participants know that their participation is not required for their care and understand the range of risks and benefits involved. The written informed consent document is given to the person and orally discussed by the researcher each time, and in some situations there must be a third party present to witness the process as well as the person's and researcher's signatures.[12]

Informed consent problems arise when certain aspects of the research are likely to change a patient's response or behavior; for example, if the research involves healthcare provider interactions with patients. If healthcare providers are told that their patient interactions will be videotaped, it is likely that the healthcare provider will act differently. In this case, it is sufficient to invite healthcare providers to participate in a quality improvement study and inform them that the exact purpose will be revealed when the research is concluded. Whenever research involves incomplete disclosure, it is required that incomplete disclosure is essential to complete the research, undisclosed risks are no more than minimal, and debriefing sessions are planned along with dissemination of results. Full disclosure may never be withheld to increase recruitment or cooperation.[3]

Comprehension: When researchers or evaluators are explaining the informed consent document, it is important that participants understand every aspect of the research. This understanding means that the document must be written in the preferred language of the individual and at an appropriate written and verbal literacy level. The time and location of obtaining consent are considered. Consents are obtained during normal business hours in a quiet location. Individuals may wish to have family members present to hear the explanation and ask questions, although the participating individual makes the final decision. For example, if research is explained quickly in a noisy hospital waiting room, chances are that the individual will not be allowed sufficient time to make an informed choice. Obtaining the informed consent is viewed as an educational process. It is the researcher's responsibility to ensure that individuals understand and comprehend the information. As potential risks increase, so does the obligation of complete understanding prior to giving consent. Sometimes an added safeguard is used, such as asking the individual to repeat the explanation of the research. IRB committees need to make every effort to enhance the subject's comprehension. Even with the best intentions, a researcher may communicate every aspect of the informed consent document, but the subject fails to fully understand his participation in the study. The reasons for lack of understanding may be, for example, mental capability being diminished by age or physical or mental disabilities;

being under the influence of medications, alcohol, or other substances; fear of reduced healthcare services; need for monetary compensation; or real or imaginary feelings of coercion. When research involves a specific medical condition, such as dementia, an individual's legal guardian is asked to sign the informed consent, make surrogate decisions, and protect him or her from harm.[12]

Adequate compensation: Adequate compensation for participation in research is not specifically stated in the federal regulations. The IRB committee determines the risk of possible coercion as well as reasonable compensation for each situation. Incentives must not be so attractive that potential participants are blinded to the risks or conceal accurate information for admission into the lucrative research. Compensation does not need to be a cash payment. Other types of compensation include bus tokens, travel reimbursement, babysitting services, movie tickets, or gift cards.[12]

Voluntary choice: Voluntary choice involves an agreement to participate in research after individuals understand every aspect of the study. In addition, they must be free of coercion and undue influence. Coercion occurs when a person in power threatens harm if individuals do not agree to participate in the research and sign the consent form. For example, a prisoner would experience coercion if the warden announces that all prisoners must participate in the study or else special privileges will be evoked. Undue influence happens when an excessive incentive is offered for participation; for example, if a pharmaceutical company expedites patient recruitment by offering $1,000 to every Medicaid patient with hypertension to take eight doses of a new experimental hypertension drug. Because Medicaid patients likely need $1,000, they could sign consent forms without asking questions in order to receive the excessive cash payment. Undue influence also occurs when a family member is persuaded to convince the patient to participate in the study, thus removing the patient's choice. Threatening to revoke healthcare services is also a threat of undue influence.[3]

Other considerations of informed consent involve observational research, active and passive consents, secondary data, and cultural and diversity concerns.

Observational research: When human behavior is observed, researchers request an informed consent waiver because subjects may act differently when observed. For example, researchers may wish to observe human behavior, so they stage a biker hitting a pedestrian at a crowded intersection. For this type of research, IRB committees apply common sense and consider the degree of risk for the subjects involved without their consent.

Active consent and passive consent: These terms are commonly used in a school setting when research involves noninvasive study with students under age

18 years. When a passive consent form is used, the researcher gives the students a document to take home to their parents or guardians. With passive consent, the parent or guardian may read about the noninvasive research. If the document is not returned to school, the student will participate in the research. If the parent or guardian does not wish the student to participate, the signed form must be returned to school. Because it is common that students do not give such forms to their parents, some parents are never made aware of the research. In this case, regardless of the reason the parent never responds, the student is allowed to participate in the research. To clarify, passive consent means the student participates by passive parental consent. For active consent, the researcher sends the document home with the students. In this case, however, the student is unable to participate unless the document is signed by the parent and returned by the student. Parents need to be "active" for their child to participate. In this case, the researchers offer incentives for students to return the signed form in a short period of time. For example, the class with the greatest number of returned signed forms by Friday receives a pizza party, or each student who returns a signed form receives a school t-shirt.

Secondary data: Common examples of secondary data include patient medical charts, birth and death certificates, traffic violations, motor vehicle records, medical billing records, school attendance records, and insurance company vehicular claims data. Most secondary data are obtained in the form of aggregate data, which is defined as records that do not contain any personal or identifying information that could be linked back to a specific individual. For example, hospital administrators use secondary data to determine if the rate of patient readmissions due to nosocomial or hospital-acquired infections has increased or decreased during a specified period of time. Secondary aggregate data provide specific information about patients who were readmitted to the hospital within 30 days of discharge. Data are deidentified and do not include patient names, addresses, or contact information. By linking the initial diagnosis with the readmission diagnosis, hospital administrators are able to pinpoint the possible cause of the infection by specific location within the hospital, type of procedure or treatment, type of infection, medical specialty, and so on. Biased data would result if patients are readmitted to another hospital with an infection.

Cultural and diversity issues: IRB committees verify that the research staff has appropriate cultural and diversity sensitivity training so that participating individuals are treated with respect. If participating individuals feel comfortable, they are more likely to respond honestly to personal questions. For example, even though the researcher from one culture views the interview question as routine,

the responding person from another culture may view the identical question as intrusive. Topics that may be considered sensitive in various cultures include diverse marriage and parenting attitudes, sexual behaviors, employment loyalty, loyalty to healthcare practitioners, religious beliefs and practices, use of traditional medical treatments, and so on. Researchers and evaluators need to be comfortable with not only the topic but also the potential ethical issues that may arise when recruiting individuals from various cultural backgrounds.[12]

Risk/Benefit Assessment

The risks and benefits of research are carefully weighed by the IRB committee, researcher, and participating individual. Based on known data, risk is defined as the chance that harm may occur. Risk is usually viewed as high, moderate, or low. Risks may include psychological, physical, legal, social, or economic harm. A benefit is viewed as a positive health or welfare value. The risk–benefit ratio assessment is considered as the probability and extent of possible harm versus anticipated benefits. In the IRB application, it is essential to clearly state known risks according to the medical literature as well as available alternative choices. When risk–benefit ratios are unknown, the researcher is unable to disclose the information in the informed consent. This situation is called *equipoise* and is defined as the uncertainty of the therapeutic treatment effectiveness. This issue requires that the informed consent document state that the effectiveness of the experimental treatment is unknown.[13] Risk–benefit ratios are also a concern when the research participant is pregnant or becomes pregnant in the future. Again, the informed consent document must include a statement about the possibility of unforeseeable risks, including risks to the current or future embryo or fetus, the ability to become pregnant, and for males the ability to impregnate a partner in the future. Lastly, for researchers, the risk–benefit ratio must be fully disclosed in the informed consent document as well as in the research design. For the IRB committee, any potential risks must be justified and offset by benefits when feasible. Participating individuals must understand the risk–benefit ratio, have the opportunity to ask questions throughout the research, and know that they can withdraw from the study at any time.

Selection of Individuals and Special Populations

When IRB committees review an application, particular attention is paid to special populations that may be recruited for participation in the research or evaluations. Each category of special populations poses unique considerations related

to informed consent. Depending on the degree of risk and therapeutic component, some groups of individuals are more suitable for recruitment than others, unless the research is related to a specific medical condition, such as depression among institutionalized individuals. Also, individuals who are dependent on public healthcare services should not bear the burden of research when advantaged individuals are also recipients of benefits. Other special populations receive specific IRB regard. For example, children or individuals with mental health disabilities may not be able to understand the scope of the research. As for prisoners or institutionalized individuals, it is questionable if their consent is truly voluntary or perceived as mandatory. Hospitalized and very sick patients may have diminished comprehension because of medications, emergency treatment, or pain management. These patients may concede their rights to gain additional or faster medical benefits or enroll in research to please their healthcare practitioners. Such individuals need protection against research recruitment for reasons like convenience, medical diagnosis, or socioeconomic status.[12] In research studies or evaluation projects, recruiting pregnant women is an ethical slippery slope. On one hand, if the research involves enhancement of prenatal care, pregnant women need to be enrolled in research to move prenatal science forward, but on the other hand, there is a fundamental obligation to the health and well-being of the woman and the fetus. Lastly, the elderly constitute a special population, and their issues incorporate many of the previously stated concerns for all special populations. Overall, the investigators and the IRB committee must be aware of the unique ethical concerns when recruiting individuals from special populations. IRB committees must not overprotect special populations to the detriment of research, and one group of subjects should not bear more risks for the benefits of another group. Adequate representation of special populations is important, especially in research that may disproportionately affect that same population.[3]

Summary

This chapter provides a historical overview of medical ethics, including two landmark cases that violated federal laws and doctrine. This discussion was followed by a discussion of the basic principles of medical ethics with examples. The next section described the purpose of the institutional review board and how to design comprehensive informed consent documents, including the consideration of special populations.

Case Study: *Diaz vs. Hillsbourgh County Hospital Authority*

In 1987, Karen Perrin reported to the high-risk perinatal outpatient clinic at Tampa General Hospital with affiliation to the University of South Florida in Tampa. She was looking forward to a busy day and the change of pace. Karen had worked at Tampa General since January 1986. Her normal assignment was labor and delivery, but as a part-time nurse, it was not unusual for her to fill in elsewhere. For the next two weeks, Karen worked at the outpatient high-risk pregnancy clinic while Sue, the clinic's head nurse, took time off for her wedding. In total, Karen was assigned to work in the clinic for a total of four weeks. She worked in the clinic for two weeks, returned to her regular position for two weeks, and then was again temporarily assigned to the clinic for two additional weeks because Sue's daughter became ill.

Among other clinic tasks, Karen cared for high-risk pregnant women who came to the clinic for amniocenteses. Amniocentesis is a procedure in which a needle is inserted through a women's abdomen to extract amniotic fluid for testing.[14] Karen entered each patient's name, hospital number, and Medicaid or insurance number into the "amnio" record log at the desk. She took the patient's weight and blood pressure, measured her belly, and checked her urine. She set up the tray of amniocentesis needles and test tubes and labels for the tubes. She explained the procedure to the patients, offered reassurance, and asked if they had any questions.[15]

During her clinic assignment, Karen noticed something unusual. The pregnant women did not ask questions about the procedure. "I kept seeing all these women having amnios. Over and over and over. I'd see them one week, I'd say, "Why are you back again?" I'm looking in their chart and I'm seeing that this is amnio #5, amnio #6. . . ."[15] When she talked with the pregnant women, it was clear that they did not understand why they were having so many amniocenteses. Their response was always the same: "The doctor told me, if I don't do them, my baby will die."[16]

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CASE STUDY *continued*

An Inquiry

In late 1987, Karen consulted her supervisor. A meeting was schedule with the vice president of nursing and director of the perinatal unit. They told her that the pregnant women were part of a medical study that had been approved by university and hospital institutional review boards. Therefore, they considered the matter closed. Her supervisor told her to drop the issue and not pursue additional investigation into the matter. Karen did not stop because she suspected that the women were unaware of a medical study. She continued to press for further investigation. In February 1988, a final meeting was held and the vice president of nursing made it clear that she had not taken any action and that she did not intend to investigate the matter further.

The Next Step

Karen shared her concerns with a friend who was a civil rights attorney, Stephen Hanlon. At the advice of Mr. Hanlon and the American Nursing Association, Karen was instructed to gather the evidence. She went to the high-risk clinic, took the amnio record log, made a copy, and returned the log to the clinic drawer. She returned a few days later to copy the last few pages, only to discover that "someone had taken a razor blade and cut all the pages out of the book. The pages were gone, and they were never found again. This was our only evidence."[15] She provided the copied amnio record log to Stephen Hanlon. She also found the contact information for 10 women in the log who had multiple amniocenteses. She contacted them by mail and stated that their rights may have been violated and invited them to contact her. Only one woman, Flora Diaz, age 16, responded.

The Lawsuit

In January 1990, Stephen Hanlon filed a federal class action lawsuit accusing the university, the hospital, and two physician researchers of ignoring DHHS regulations on informed consent. Although the lawsuit

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CASE STUDY *continued*

was initially filed in response to a fetal lung study[17] involving approximately 280 women, investigation revealed some 30 studies at Tampa General involving 5,000 pregnant women between November 1986 and January 1990. Because none of the women or their babies were harmed, this case is not about malpractice but rather a matter of dignity. The women were used as research subjects without their informed consent.

Doctors' Perspective

Walter Morales, MD, one of two physician researchers in the lawsuit, denied any wrongdoing. "I can assure you I would never do anything to a research subject that I wouldn't do to my own wife."[18] Furthermore, he noted that he wished the case had gone to trial instead of being settled because he did not believe that the facts would show the patients were coerced into signing the forms.[16] The results of the study were published in the *Journal of Obstetrics and Gynecology*, and as a result, the combined use of corticosteroids and thyrotropin-releasing hormone is now common practice in many hospitals.[19]

The Settlement

After almost 10 years of litigation, the case was settled out of court. Under the agreement, the university and the state of Florida paid $2.7 million and Tampa General Hospital paid $1.14 million.[20] In addition to the cash payment, the hospital and university agreed to revise record keeping so that information on study participants was easily accessible in a database. Tampa General Hospital and the University of South Florida also agreed to apply a standard readability test to their consent forms before submitting future projects to the IRB.

A Postscript

Karen Perrin, whistle-blower in this case, was removed from patient care and was laid off from the hospital in September 1990.[21] The hospital made attempts to revoke her nursing license, but she successfully

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CASE STUDY *continued*

defended her actions with the assistance of the American Nursing Association.[22] Karen completed her master's in public health in 1990 and her PhD in 1996 from the College of Public Health at the University of South Florida. Currently, she is an associate professor at the University of South Florida and lectures on medical ethics.[15] Dr. Perrin is the author of this text.

Case Study Discussion Questions

1. What other actions could the nurse have taken?
2. What is the role of the medical residents in this case?
3. What is the role of the nurse supervisor?

Student Activity

1. Write a 200-word case study describing a violation of an ethical principle related to an area of healthcare interest.
2. Obtain two examples of IRB applications from a local hospital, health clinic, school district, or university. Compare and contrast the information required on each document.
3. Obtain an advanced directive or living will from three different states. Compare and contrast the information required on each document.

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