Research with Minors

IRB FORUM

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GWU OFFICE OF HUMAN RESEARCH

Overview

- Belmont Report- Vulnerable Populations
- History of Research with Children
- Federal Regulations
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  - FDA
- Assent

Belmont Report

RESPECT FOR PERSONS

VULNERABLE POPULATIONS

Belmont Report

- Published by National Commission, 1979, the Belmont Report was written with the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

- The Belmont Report established three basic ethical principles that are the cornerstone for regulations involving human subjects:

* Respect for Persons

* Beneficence

* Justice

Respect for Persons

- Research must be voluntary (avoid coercion and undue influence) and informed (comprehended)
- Treat individuals as autonomous agents
- Best measures taken to protect privacy/confidentiality
- Monitor the welfare of subjects throughout the research
- Give extra protection to those with limited autonomy

Vulnerable Populations

- Vulnerable populations are so-named because:
- They are vulnerable to undue influence or coercion
  - Undue Influence = "…an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance"
  - Coercion = "…an overt threat of harm is intentionally presented by one person to another in order to obtain compliance."
- They have limited comprehension and understanding (i.e., children)
- The following groups are defined as vulnerable in the federal regulations:
  - Pregnant women, fetuses, and neonates
  - Prisoners
  - **Children**

History of Research with Children

HESS AND FISH

BABY ALBERT

WILLOWBROOK

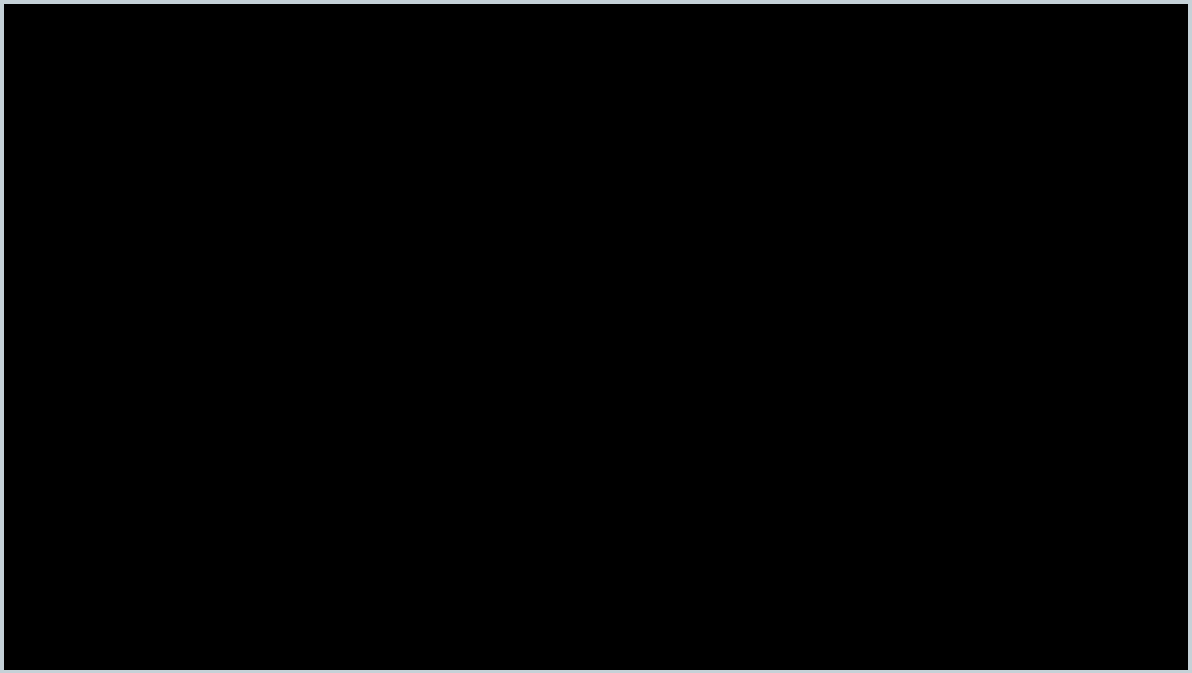
Hess and Fish- Scurvy Experiment

- Between 1914 and 1920, Alfred Hess and Mildred Fish conducted studies on etiology of scurvy;
- Withheld orange juice from institutionalized infants until they developed hemorrhages associated with scurvy;
- Similar studies performed to determine etiology of rickets;
- When the details of these studies became public, journalist and social reformer Konrad Bercovici wrote "no devotion to science, no thought of greater good to the greater number, can for an instant justify the experimenting on helpless infants, children pathetically abandoned by fate and entrusted to the community for their safeguarding."

Baby Albert

- Researchers Watson and Rayner wanted to study if fear was learned by attempting to induce a learned fearful response in an infant in 1920;
- Researchers made loud noises whenever the infant, Baby Albert, was presented with a rat to induce a fearful response;
- After a period of time, Baby Albert would spontaneously show a fearful response when presented with the rat;
- Response not localized to rat, but to all furry things including a fur coat and a rabbit;
- Researchers did not attempt to reverse the conditioned learning;

Baby Albert



Willowbrook

- Dr. Krugman conducted hepatitis vaccine trials with mentally incapacitated children at Willowbrook State School from the 1940s to early 1970s;
- Hepatitis infection was rampant between the children at the school so Dr. Krugman was searching for a cure or preventative measure;
- Researchers deliberately fed the children hepatitis in an attempt to induce infection, then fed part of the group antibodies and virus to confer immunity;
- Lead to distinction between Hepatitis A and B as some immune children would experience a second attack after inoculation;
- Study was approved by an ethics board and parental consent was sought;
- The consent form indicated the children would receive a treatment but did not indicate this was for research purposes.

Federal Regulations

NATIONAL COMMISSION

OHRP

FDA

National Commission

- Among the charges of the commission was to "identify the requirements for informed consent to participation in biomedical or behavioral research by children."
- The Commission's report on Research Involving Children was published in 1977, and largely translated into regulations as 45 CFR 46 (Subpart D), "Additional Protections for Children as Research Subjects.“
- "Children" are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

Office for Human Research Protections (OHRP)

45CFR46.401-409, Subpart D

Definitions:

- (a) Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
- (b) Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
- (c) Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.
- (d) Parent means a child's biological or adoptive parent.
- (e) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

Food and Drug Administration (FDA)

21CFR50.50-56, Subpart D

Sec. 50.51 Clinical investigations not involving greater than minimal risk:

- Any clinical investigation within the scope described in 50.1 and 56.101 of this chapter in which no greater than minimal risk to children is presented may involve children as subjects only if the IRB finds that:
  - (a) No greater than minimal risk to children is presented; and
  - (b) Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in 50.55.

Food and Drug Administration (FDA)

21CFR50.50-56, Subpart D

Sec. 50.52 Clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects:

- Any clinical investigation within the scope described in 50.1 and 56.101 of this chapter in which more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, may involve children as subjects only if the IRB finds that:
  - (a) The risk is justified by the anticipated benefit to the subjects;
  - (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
  - (c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians as set forth in 50.55.

Assent

WHAT IS ASSENT?

WHO ASSENTS?

WHO CONSENTS?

Who is Considered a Minor?

- Regulations define children as individuals who have not reached the legal age of consent for procedures involved in research;
- Legal age of consent (or age of majority) is dependent on jurisdiction;
- Some minors may be considered emancipated minors, as such seeking parental permission would not be appropriate;
- In international research, age of majority may also be dependent on culture (whether or not individual is considered an adult in their community) and local laws;
- May also be dependent on marital status, military status, etc.

What is Assent?

- Before taking part in a research study, minors are asked for their assent. Assent means that they agree to take part. They may also dissent, which means they do not agree. *Mere absence of dissent does not imply assent.*
- To take part in the assent process, children must be mature enough to understand the study and what they are expected to do.
- As with the informed consent process, the assent process is meant to be an ongoing conversation between the child and research team.
- At GWU, it is generally required that children 7-17 be assented for research participation.

What is Assent?

- How much information should be included in the child assent? Depends on the age:
- Toddlers/Pre-K/Kindergarten: “Do you want to play blocks with me?”;
- Elementary school age: At least the basics: what is involved, for how long, voluntary, etc.;
- Middle school – High school: Varies, getting closer to adult consent form content;
- Clear statements that choice is up to them;
- “No one will be mad at you if you don’t want to”;
- “Even though Mom & Dad said okay, it’s up to you”;
- Be careful with words that may not be appropriate depending on age (even those common in research): e.g. “participation”, “voluntary”, “research”, “data”.

What is Assent?

An assent should contain the following:

- A statement that the child/individual is agreeing to be in the study that was described in the informed consent/permission document that his/her parent or legally authorized representative (LAR) signed.
- A statement that the child/individual has been told what it means to volunteer for a research study.
- A statement that the child/individual is making the decision on his/her own.
- A statement that the child/individual can decide to quit the study at any time, and no one will be angry with him/her.
- A statement that the child/individual has been told what will happen to him/her during the study.
- A statement that the child/individual can ask any questions at any time, and the doctor will answer them.
- A signature line for the child/individual to sign his/her name.
- As applicable:
  - A simple check box to let the child/individual check either that he/she agrees to be in the study or does not agree to be in the study.
  - A short statement that the parent/LAR believes that the assent document has been read by the child/individual, and that the child/individual seems to understand it.
  - A signature line for the signature of the parent/LAR.

Who Assents?

- The minor participating in the research must assent to the research;
- IRBs are charged with determining if population of children included in research is capable of providing assent;
- Take age and developmental level into account. Is assent developmentally appropriate?;
- Separate requirements may be made for different subgroups of children within the study
- Generally, it is recommended to use two assent forms
  - 7-12 years of age
  - 13-17 years of age

Who Gives Permission?

CATEGORY			
45CFR46.404 21CFR50.51 Research not involving greater than minimal risk.	45CFR46.405 21CFR50.52 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.	45CFR46.406 21CFR50.53 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.	45CFR46.407 21CFR50.54 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
PARENTAL PERMISSION			
At least one parent* The IRB may find that permission of one parent is sufficient.	At least one parent* The IRB may find that permission of one parent is sufficient.	Both Parents** Requires permission to be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.	Both Parents** Requires permission to be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

Questions??

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