

Conducting Research with Vulnerable Populations

Responsible Conduct of Research Workshop

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Objectives

By the end of this presentation, you will be able to:

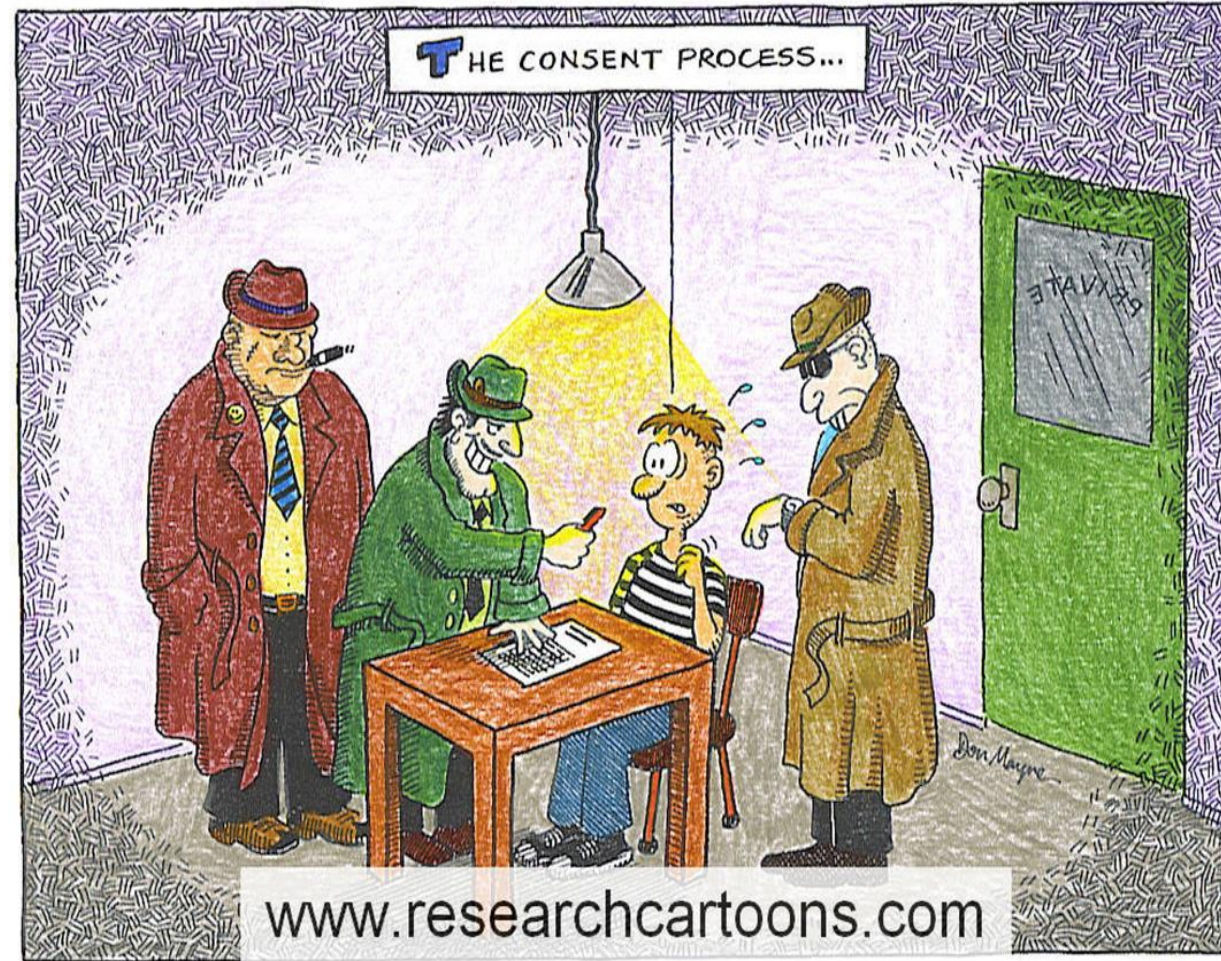
- Define vulnerability in terms of human subjects research.
- Discuss the ethical principles involved in human subjects research with vulnerable populations.
- Identify where to find the GVSU HRRC policies and procedures that apply to research with vulnerable populations.
- Describe measures to reduce risks in research projects with vulnerable populations.

Basic Ethical Principles

- **Respect for persons**
 - Right to make one's own decisions without coercion
- **Beneficence/Nonmaleficence**
 - Do no harm
 - Benefits must outweigh harms
 - Harm is minimized
- **Justice**
 - Distribution of risks and rewards is equal and distributed among groups without respect to individual or group characteristics

Respect for Persons

- Freedom, power & authority to make choices that are important to oneself.
- **Autonomy is respected and supported via process of Informed Consent**
 - Informed consent is a process.
 - Policies for children and other vulnerable populations



Beneficence/Nonmaleficence

- There must be an acceptable benefit/harm ratio
- Potential harms must be reduced as much as possible
 - Screening for inclusion
 - Methods that reduce unnecessary harms
 - *Appropriate involvement of vulnerable populations*
 - Risk of harm must be justified
- Benefits must be maximized as much as possible
 - Good study design
 - Experienced or supervised by experienced researchers



Justice

- Fair procedures in the selection of subjects
 - Non English speaking
 - Minorities
 - Other
- Vulnerable populations not chosen just because of their availability
- Equal treatment of subjects



Vulnerability

- Increased risk of being harmed
- Unable to fully protect their own interests
- Harm can be physical, social, legal, economic, mental



Presidential Commission for the Study of Bioethical Issues (2016).

Types of Vulnerability

- Categorical Approach
 - Certain groups of society have common characteristics that may make them vulnerable
 - US Code of Federal Regulations 45 CFR 46.111(b)
 - Children
 - Prisoners
 - Pregnant Women
 - Mentally disabled persons
 - Economically or disadvantaged persons

45 CFR 46.111(b)

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Problems with Categorical Approach

- May miss certain people that are vulnerable
- May be stereotypical
- People may belong to more than one group
- Group membership may change over time

Contextual Vulnerability

Vulnerability is sensitive to context

1. Cognitive or communicative vulnerability
2. Institutional vulnerability
3. Differential vulnerability
4. Medical Vulnerability
5. Economic Vulnerability
6. Social Vulnerability

National Bioethics Advisory Commission (2001).

Who is Vulnerable?

- Pregnant women, fetuses and neonates (additional protections in 45 CFR 46 subpart B)
- Prisoners (additional protections in 45 CFR 46 subpart C)
- Minors (additional protections in 45 CFR 46 subpart D)
- Persons who are significantly disadvantaged due to social, economic or educational circumstances including the sensory and mobility challenged, the poor, and the illiterate
- Persons with diminished decision making capacity (e.g. developmentally delayed or cognitively impaired)
- Racial minorities
- The very ill
- Institutionalized persons
- Persons in independently unequal authority relationships to the researcher, e.g. students in research conducted by their course instructors, athletes in research conducted or supported by their coaches, and employees in research conducted or supported by their employer.

Vulnerable Populations: Children

- Reasons for vulnerability
 - Unable to ethically and legally consent
 - Lack of ability to make autonomous decisions
 - Adults have power and authority over them.
- Additional Protections
 - Ensure they are protected from unnecessary risks
 - Parental permission, child assent/dissent, risk minimization

Human Radiation Experiments

- 1927 – 10 African American children were told by healthcare professionals that a new treatment for ringworm was found. Parents gave permission for the treatment.
- The children were given high doses of radiation to their scalps.
- Parents were not told that this was a research study.
- Significant damage to the children's scalps occurred.
- Vertis Hardiman (pictured) was 5 when he received the "treatments."
- He lived a full life despite his health issues.



<http://www.holeinthehead.com/vertus-hardiman-biography/>

Protection of Children in Research

- Regulations 45 CFR 46, Subparts A and D
- OHRP - Special protections for children as research subjects
- IRB must consider the risks and benefits of the study, the age of the subjects, health status, etc.

Children and Consent/Assent

- Children cannot give written consent
- Parental permission must be obtained prior to enrollment.
- If the child is of age to understand, must obtain:
 - Assent to participate (after parental consent)
 - 45 CFR 46.402(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.”
 - GVSU HRRC guidance – policy 820 – children 7 years and older (assent)

Prisoners

- Vulnerable because of:
 - Isolation
 - Lack of autonomy
 - Authority relationships
 - May be willing to take extra risks to gain a benefit

Protections for Prisoners

45 CFR 46 Subpart C

- IRB must have prison representative
- No coercion must take place
- Must not have greater risk than benefit (when compared to prison life)
- Fair selection of participants
- Must be related to prison environment/prisoners
- Information must be understandable to population
- Parole boards cannot look at research as behavior
- Follow up care is provided if needed

Research in Individuals who do not have consent capacity

- Cognitively impaired due to disease (i.e. Alzheimer's)
- Developmentally disabilities
- Individuals with mental illnesses
- Persons who are under the effect of certain medications
- Trauma

Ethical Concerns

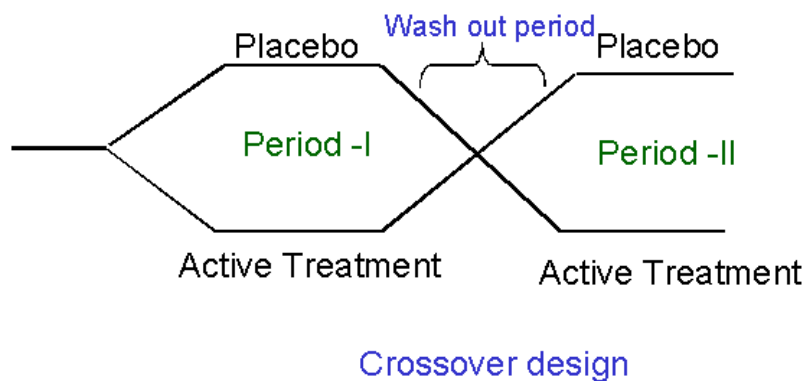
- Individuals with cognitive disorders may not be identified as being at risk
- Respect for persons
 - Persons with cognitive disabilities may not be able to understand, appreciate, and reason in regard to making a decision about a study.
- Easily coerced
- Consent capacity may fluctuate or change over time (important for longitudinal studies)

Cognitively Impaired: Minimizing Risks

- Have appropriate team members on study
- Assess for consent capacity
 - Use valid tools
 - Cognitive assessments do not equate to consent capacity
- Align consent process with subject's abilities
- Enhance consent process
- If no consent capacity, obtain consent from LAR and assent from subject.

Communicating about Risk

"It's a double-blind, placebo controlled, randomized, two-armed, crossover, clinical trial with a 72 hr. washout period. Here let me draw you a picture."



Does that answer your question?



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Who is the legally authorized representative?

- In Michigan, no law to define for research
- Most use health care proxy or closest relative.



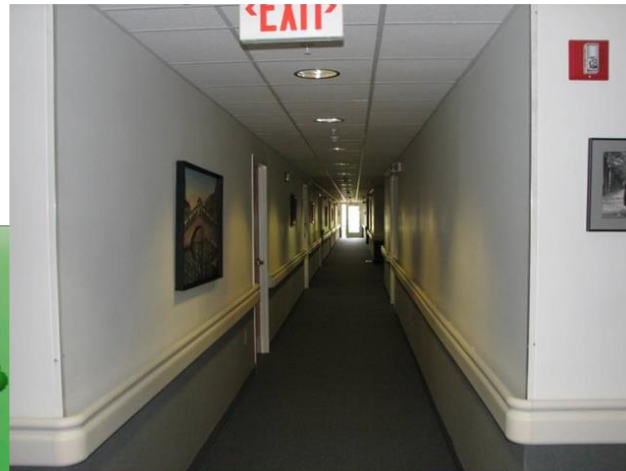
A word about assent...

- Assent is an agreement to participate
- Can be verbal
- May need to obtain multiple times
- Can be assessed for in severely cognitively impaired
- Dissent requires less cognitive ability than assent
- Must not conduct research in individuals that dissent
- Must have a plan for consent/assent/withdrawal in protocol

Example....Wayfinding study

The Problem....

Help! I'm LOST!
Everything looks the
same!



NIA:1R15AG037946-01A1

Subjects

- Individuals with early stage Alzheimer's disease
- Subjects may or may not have consent capacity
- Subjects may or may not have LAR

Methods

- Lots of cognitive tests
- Wayfinding assessment over 2 days in virtual reality environment
- Eye tracking glasses
- Risks: Simulation sickness (25%), frustration, embarrassment
- No benefit to participants



Risk Reduction

- Consent capacity assessment using a valid measure in the subject's home with decision maker present
- Simplified explanation of study
- Verbal assent for those who did not have consent capacity
- Consent from decision maker
- Assent on each day of the study
- Team included experts on dementia
- Data collectors were trained in a systematic way
- Protocol included when to withdraw a subject
- PI or other nurse researcher available at all times

Case Study

A researcher wishes to determine the effect of the DASH diet on growth and development of children age 5-10. She plans to obtain a sample of children from the local schools, and have parents have the children adhere to the DASH diet for two weeks. At the baseline and every two weeks for 6 months, subjects will have height, weight, and blood work assessed.

What are the considerations for enrolling children in this study?

Case Study

- A researcher wants to find out if mindfulness training helps persons with schizophrenia have less symptoms. She plans to recruit subjects from local psychiatrists' offices, support groups, and the community. She will enroll them in a year long study with 6 mindfulness sessions. She will employ the use of surveys that measure symptoms over this time.
- What are the considerations for the researcher for this study?
- How can risks be minimized?
- What are the biggest ethical issues?

Case Study

- A researcher wants to determine sexual patterns/behaviors in homeless individuals. She plans to recruit from local homeless shelters. She will meet with the subjects and interview them about sexual partners, prostitution, drug use, and the interplay of these factors. Subjects will receive a \$50 gift card for participation.
- What are the ethical issues with this study?
- What should be considered in this study?
- What category of vulnerability does this group belong to, and how might this influence study participation?

Final Advice

- Know the regulations.
- Know the laws.
- Know the policies at GVSU
 - (<https://www.gvsu.edu/hrrc/hrrc-policies-procedures-guidance-17.htm>)
- Address the risks
- Minimize the risks
- Adhere to the policies



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