Vulnerability: Concepts and Applications

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Fat, bald and incontinent. Life seems to have dealt us a glancing blow.”
Vulnerability Beyond the Regulations

- **Vulnerability Defined**
  - Capable of being physically or emotionally wounded
  - Open to attack or damage

- **Audience Question:**
  - Are you vulnerable?
  - In what situations would you do something that you wouldn’t normally do?
  - Who do you blindly trust?

**Trust:** Firm belief in the reliability, truth, ability, or strength of someone or something.
The concept of ‘vulnerability’ in research ethics...

- Pregnant women, human fetuses and neonates; prisoners; & children
- Ethnocultural groups; economically disadvantaged; homeless persons; institutionalized persons
- Subordinate members of hierarchies or relationships (e.g. patient, student, employee)
- Individuals with cognitive impairment or severe/chronic illness
- Elderly adults

Audience: Are there others?
University of Virginia:
Eight (8) Categories of Vulnerability

- Cognitive or communicative (e.g. mental or language barrier)
- Institutional (e.g. student/professor; employee/employer)
- Deferential vulnerability (e.g. doctor/patient; family members)
- Medical vulnerability (e.g. medical need/desire)
- Economic vulnerability (e.g. prospect of ‘free’ care or payment)
- Social vulnerability (e.g. real or perceived discrimination)
- Legal vulnerability (e.g. consent is a risk)
- Study vulnerability (e.g. deception)
Power Taxonomy

- Reward ($$)
- Coercive (penalty)
- Legitimate (position)
- Expert (knowledge)
- Referent (respect)
- Plus three
  - Information
  - Charismatic
  - Moral

Is Inclusion Necessary?

- Competing ethical imperatives
  - Respect for persons → protect those with limited autonomy
  - Beneficence, Justice → do good (provide benefits of research); distribute benefits of research fairly
Is Inclusion Necessary?

- Are there less vulnerable populations which could answer the same scientific questions?
  - Phase II study of investigational drug for depression. Target population is inhabitants of a homeless shelter who have moderate to severe depression.
  - Survey of underage drinking among college freshman. Target population is students enrolled in the researcher's required "Introduction to Psychology" class.
  - Phase II study of an investigational antibiotic for hospital acquired pneumonia. Target population includes children, adolescents and adults.
Is Inclusion Necessary?

- “The argument in favor of conducting research involving children rests on ... the consequences of not conducting research involving children in those instances. Such consequences might include the perpetuation of harmful practices, the introduction of untested practices, and the failure to develop new treatments ...”

Is Inclusion Necessary?

- Benzyl alcohol poisoning (Gasping syndrome 1982)
  - decreased mortality rate (81% vs 46%) in infants <1000 g after removing benzyl alcohol (Pediatrics 77:500, 1986)
INFECTIOUS HEPATITIS*

Studies of Its Natural History and Prevention

ROBERT WARD, M.D.,† SAUL KRUGMAN, M.D.,‡ JOAN P. GILES, M.D.,§
A. MILTON JACOBS, M.D.,‖ AND OSCAR BODANSKY, M.D.,‖

NEW YORK CITY
Are Protections Adequate?

- Do prospective subjects have difficulty providing voluntary, informed consent?
  - Are there decisional issues?
  - Are there communication issues?
  - Are there social conditions which limit the subject's options?
  - Might the subject's hope for medical benefit influence judgment?
  - Can the subject consent for himself?
  - Would subject benefit from additional protection of an advocate?
Are Protections Adequate?

- Are conditions for informed consent satisfied?
  - Is information presented in an **understandable** manner?
  - Do subjects **comprehend** the details of the research and their rights as research subjects?
  - Is the process of consent conducive to true voluntariness?
Are Protections Adequate?

- Remember the "definition" of vulnerability:
  - "Persons are vulnerable in research either because they have difficulty providing voluntary, informed consent arising from limitations in decision-making capacity ... or situational circumstances ..., or because they are especially at risk for exploitation." (NBAC)
  - "Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence" (Declaration of Helsinki)

- Informed consent does not necessarily eliminate vulnerability
Are Protections Adequate?

- Are prospective subjects at risk for exploitation?
  - Is there a power differential?
  - Is the recruitment process acceptable?
  - Are there economic issues which might place subject at risk for undue inducement?
  - Are payment arrangements acceptable?
  - Would subject benefit from additional protection of an advocate?
Are Protections Adequate?

- Does the IRB have sufficient expertise?
  - “If an IRB regularly reviews research that involves a vulnerable category of subjects ... consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects” [45 CFR 46.107(a)]
Are Protections Adequate?

- “... the more reliable safeguard is provided by the presence of an intelligent, informed, conscientious, compassionate, responsible investigator.”

Henry Beecher 1966
Case Example #1

- Researcher has interest in creating a phagocytic cell to target viruses
- Research team reads a paper that cervical fluid could be a more stable growth medium
- The availability of cervical fluid is limited and costly
- The researcher decides that members of the team will be a good source for the new growth medium
- Members of the team were asked to collect samples at home, return to the lab, and then grow the medium for use
Case Example #1 (cont.)

- Are there human subjects?
- If yes, are they vulnerable?
- What is the risk?
- What protections are typical?
- What questions would you ask?
- How would you protect the participants?
Case Example #2

- Researchers were interested in marketing their bariatric surgical technique as a “cure” for Type II diabetes
- The procedure was called “Ileal Interposition”
- Researchers were interested because they saw a reduction in diabetes cases from their patients after the weight loss surgery
- They intended to recruit patients who were not clinically obese
- They hoped to find effective results and have insurance pay for the “cure”
Case Example #2 (cont.)

- Are there human subjects?
- If yes, are they vulnerable?
- What is the risk?
- What protections are typical?
- What questions would you ask?
- How would you protect the participants?
Case Example #3

- Phase I study of investigational drug XYZ123 in children with advanced relapsed cancer
  - Preclinical studies show broad antitumor activity
  - MTD determined in adults
    - Dose level 1 is 0.8 of adult MTD
  - Standard phase I design
Case Example #3

- Are subjects vulnerable?
  - Why?
- Is inclusion necessary?
- Are protections adequate?
Case Example #3 (cont.)

- Are phase I studies in patients with life-threatening illness ever truly voluntary?
  - “Incapacitated and hospitalized because of illness, frightened by strange and impersonal routines, and fearful for his health and perhaps life, he [the patient-subject] is far from exercising a free power of choice when the person to whom he anchors all his hopes asks, ‘Say, you wouldn’t mind, would you, if you joined some of the other patients on this floor and helped us to carry out some very important research we are doing?’”

“There is an experimental treatment using mice that looks very promising. Unfortunately, you’re a hamster.”
Case Example #4

- Researchers were interested in predicting the reoffending behavior of sex offenders based on confiscated police videos of their crime.
- The perpetrator and victim images will be seen by researchers after criminal prosecution.
- The police department agreed to release the videos to help with their criminal profiling.
- The university had a policy about viewing pornography on state property/campus.
- The researcher intended to use a GRA for the assessments.
Case Example #4 (cont.)

- Are there human subjects?
- If yes, are they vulnerable?
- What is the risk?
- What protections are typical?
- What questions would you ask?
- How would you protect the participants?
Case Example #5

- Researchers were interested in creating signage on highways that capture the attention of drunk drivers.
- The vehicle had two steering wheels and brake pedals for passenger intervention.
- A closed driving course was identified.
- Carve outs of animals and paid staff to play construction workers were hired.
- Individuals would be given the alcohol of their choice and allowed to consume until they reach the legal limit of intoxication.
- Team members will drive inebriated participants home afterwards.
Case Example #5 (cont.)

- Are there human subjects?
- If yes, are they vulnerable?
- What is the risk?
- What protections are typical?
- What questions would you ask?
- How would you protect the participants?
Researchers were interested in increasing engagement and reducing high risk activity related to pregnancy and STD/STI.

Research plan included 2-3 graduate students going to nightclubs and setting up an informational table.

Patrons offered health information, condoms, and rapid HIV test.

Pre-test counseling, testing, and post-test counseling offered in a separate room if interest is provided.

The work shift would end around 3 o’clock a.m.
Case Example #6 (cont.)

- Are there human subjects?
- If yes, are they vulnerable?
- What is the risk?
- What protections are typical?
- What questions would you ask?
- How would you protect the participants?
Case Example #7

- Researchers were interested in risk factors for STDs among Somali immigrants.
- PI and graduate student will review records of persons diagnosed with STD at two inner city free clinics; those of Somali descent will be sent letters inviting participation.
- Student will conduct phone interviews to determine patterns of sexual activity correlating with STDs.
- Identifiers will be maintained and clinic records will be prospectively monitored to determine incidence of repeat infection.
Case Example #7 (cont.)

- Are there human subjects?
- If yes, are they vulnerable?
- What is the risk?
- What protections are typical?
- What questions would you ask?
- How would you protect the participants?
Sorry, your highness, but you’re really not the dictator of Ithuvania, a small European republic. In fact, there is no Ithuvania. The hordes of admirers, the military parades, this office -- we faked it all as an experiment in human psychology. In fact, your highness, your real name is Edward Belcher, you’re from Long Island, New York, and it’s time to go home, Eddie.
Thank you and Questions

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