Populations in research Requiring Additional Consideration and/or Protection

Vulnerability

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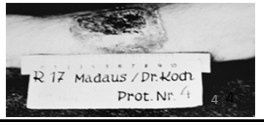
Outlines

- Definition
- Overview: research involving vulnerable subjects
- Informed consent
- Research involving
  - Adults incapable of giving informed consent
  - Terminally ill subjects
  - Children and adolescents
  - Students
  - Women and pregnant women
  - Prisoners and minorities

Why do we need to identify vulnerable subjects?

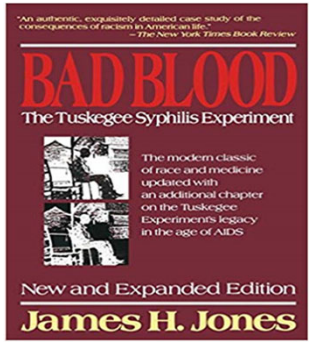
Nazi Human Experimentation

- Experiments on twins
- Bone, muscle, and nerve transplantation experiments
- Head injury experiments
- Sterilization and fertility experiments
- Malaria experiments
- Immunization experiments
- Epidemic jaundice
- Mustard gas experiments
- Sulfonamide experiments
- Sea water experiments
- Freezing experiments
- Experiments with poison
- Incendiary bomb experiments
- High altitude experiments
- Blood coagulation experiments

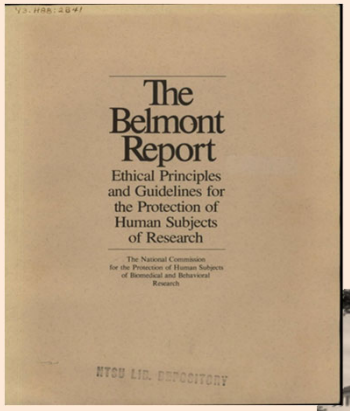


The Tuskegee Study of Untreated Syphilis

(1932-1972)



Three Principles



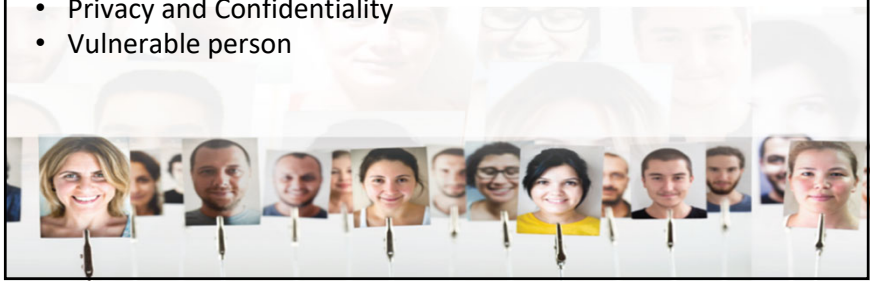
- ❑ Respect for person
- ❑ Beneficence
- ❑ Justice

(A.D. 1978)

Respect for Person

Respect for human dignity

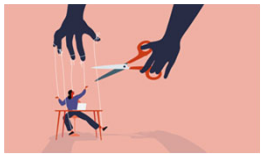
- Informed consent
- Voluntariness
- Privacy and Confidentiality
- Vulnerable person

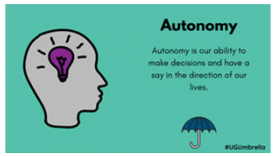


Belmont Report : Autonomy

Autonomy

- The right or condition of self-government
- Freedom from external control or influence; independence





https://www.charliehr.com/
https://www.ugdsb.ca/blog/ugumbrella

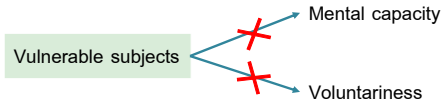
Belmont Report : Autonomy

Mental capacity

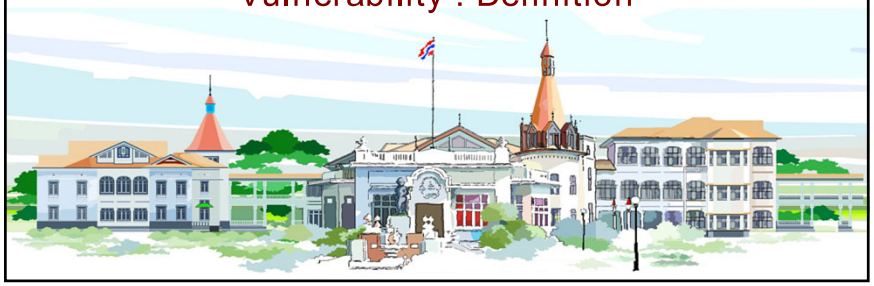
- To understand and process information

Voluntariness

- Freedom from the control or influence of others



Vulnerability : Definition



CIOMS Guideline 15 (2016)

Vulnerable subjects : Definition

- Persons who are incapable of protecting their own interests
- This may occur when persons have impairments in decisional capacity, education, resources, strength, or other attributes needed
- Impaired decision capacity will cause
  - Incapable to consent
  - Limiting capacity to consent

CIOMS Guideline 15 (2016)

Vulnerable subjects

- Individuals with limited capacity to consent
  - Adults incapable of giving informed consent
  - Children and adolescent
- Individuals in hierarchical relationships
- Institutionalized persons
- Women and pregnant women
- Other potentially vulnerable individuals (patients with incurable diseases, persons in disasters, disease outbreaks unemployed or impoverished persons, ethnic minority groups, homeless persons, nomads, refugees)

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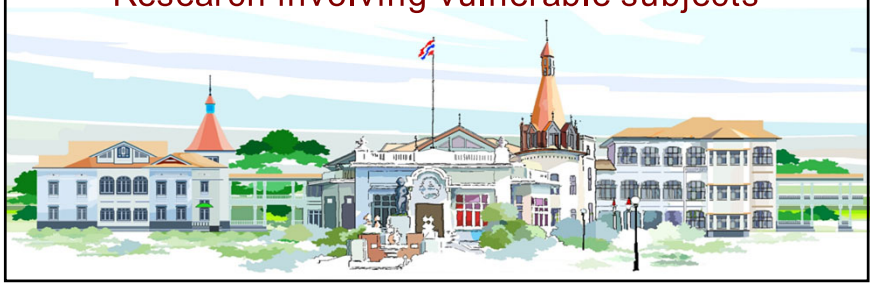
Research involving vulnerable subjects



CIOMS Guideline 15 (2016)

When vulnerable individuals and groups are considered for recruitment in research, researchers and research ethics committees must ensure that specific protections are in place to safeguard the rights and welfare of these individuals and groups in the conduct of the research.

CIOMS Guideline 15 (2016)

Special protections

- Allowing no more than minimal risk for procedure that offer no potential individual benefits
- Participants agree by permission of family members, legal guardians, or other appropriate representatives
- Research carries out only when it is targeted at conditions that affect these groups
- Safeguards can be designed to promote voluntary decision-making
- To limit the potential for confidentiality breaches

Informed consent

WMA Declaration of Helsinki 2013

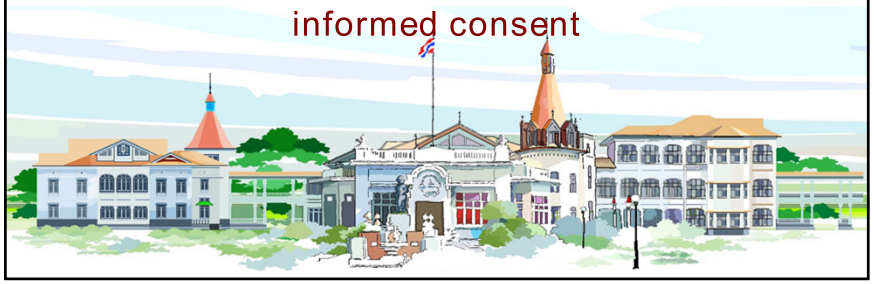
Informed consent

(26) In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study.

The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal.

Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

Research involving adults incapable of giving informed consent



Vulnerable Populations Questionable Capacity to Consent

- Research involving persons whose capacity to consent is questionable requires careful consideration to ensure such persons are provided additional safeguards for their safety and welfare.
- In some cases, individuals who are not able to give informed consent may receive permission to participate from a legally authorized representative and then give their own assent.

CIOMS Guideline 16 (2016)

- The assent of the subject has been obtained to the extent of that person's capacity,
  - After having been provided with adequate information about the research at the level of the subject's capacity for understanding this information.
- If participants become capable of giving informed consent during the research,
  - their consent to continued participation must be obtained.

WMA Declaration of Helsinki 2013

Waiver

(30) Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group.

In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.

Research involving terminally ill subjects

Vulnerable Populations : Terminally ill subjects

Protections

- ❑ Consent form states clearly the potential risks and benefits and characterizes the potential benefits appropriately
- ❑ Impartial third party perform IC and/or use patient advocate, consent monitor
- ❑ Potential subjects should not be approached: participation immediately after diagnosis or after they've learned a standard treatment has failed

Research involving children and adolescents

CIOMS Guideline 17 (2016)

- Research must always be conducted in adults first when exploring the possible toxicity of new drugs.
- Do not require that research first be conducted in adult if …
  - The research have a prospective for potential individual benefit for children and adolescent.
  - The prospect is justify the risks associated with interventions & procedures.
- Older children and adolescents who are capable of giving assent must be selected before younger children or infants unless there are sound scientific reasons for performing the research in younger children first.

CIOMS Guideline 17 (2016)

Before undertaking research involving children and adolescents, the researcher and the research ethics committee must ensure that:

- A parent or a legally authorized representative of the child or adolescent has given permission
- The agreement (assent) of the child or adolescent has been obtained in keeping with the child's or adolescent's capacity, after having been provided with adequate information about the research tailored to the child's or adolescent's level of maturity
- If children reach the level age of maturity during the research, their consent to continued participation should be obtained
- In general, the refusal of a child or adolescent to participate or continue in the research must be respected, unless, in exceptional circumstances, research participation is considered the best medical option for a child or adolescent.

45 CFR 46 subpart D : research involving children

- Research not involving greater than minimal risk
  - Consent parent and assent if appropriate
- Research involving greater than minimal risk but presenting the prospect of direct benefit to children can be done if
  - Risk is justified by the anticipated benefit to the subjects
  - Benefit/risk ratio as alternative method

45 CFR 46 subpart D : research involving children

- 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; IRB can approve if
  - The risk represents a minor increase over minimal risk
  - The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations
  - Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians

Women as research participants

CIOMS Guideline 18 (2016)

- Women have been excluded from much health-related research because of their child-bearing potential
- Mechanism to protect
  - Informed in advance of the possibility of risks to the fetus
  - sponsors and researchers must guarantee access to pregnancy tests, effective contraceptive methods before and during the research and to safe, legal abortion.

Pregnant women as research participants

Vulnerable Populations : Pregnant Women

- Pregnant women may only be involved in bio-medical research if the study regards the health needs of the mother and the fetus will be placed at risk only to the minimal extent to meet the health needs of the mother or risk to the fetus is minimal.
- The father's signature is required unless:
  - The purpose of the study is to meet the mother's health needs, or
  - The father is not reasonably available, or
  - The pregnancy was the result of sexual assault

CIOMS Guideline 19 (2016)

- For research interventions or procedures that have no potential individual benefits for pregnant and breastfeeding women:
  - the risks must be minimized and no more than minimal; and
  - the purpose of the research must be to obtain knowledge relevant to the particular health needs of pregnant or breastfeeding women or their fetuses or infants
- Short-term and long-term follow-up of the fetus and the child may be required

Research involving students

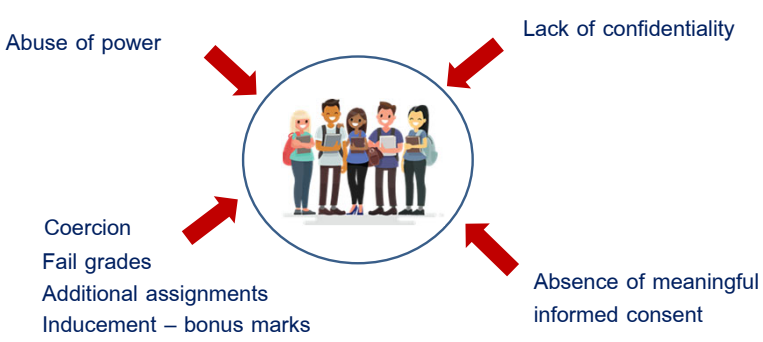
Why students?

- ✔ Healthy
- ✔ Mentally able
- ✔ Good understanding of the principles of autonomy and informed consent

Research involving students

- Research in students is seen as
  - Method of teaching researching techniques
  - A form of professional socialization
- Difficulty is increased when the researchers are also responsible for teaching the student they are researching

Ethical problems of research in students



Informed consent

Unequal power relationship between

Student vs. their lecturers

~~Voluntariness~~

Beneficence

Risk/Benefit Assessment

Two general rules:

(1) Balancing harms and benefits

(2) Maximize possible benefits and minimize possible harms

Risks

- ❑ Physical harm
- ❑ **Psychological harm**
- ❑ **Social and economic harms**
- ❑ Legal harm

Benefits

- ❑ Direct benefit to participant
- ❑ Scientific and social values

Anonymity and confidentiality

Ethical issues in anonymity are usually found in demographic information of CRF

- ❑ GPA
- ❑ Date of birth
- ❑ Hometown
- ❑ Hobbies

Justice

Fair treatment ?

Students should not be used because they are convenient, readily available and unlikely to refuse

"but only if the research questions relate directly to them"

Vulnerable Populations : Students

Various procedures may be used to reduce the possibility of unintentional coercion:

- Posting IRB approved advertisements throughout the campus to recruit from a broad base of students
- Recruitment procedures should not involve direct solicitation by superiors
- Informed consent state clearly that participation is voluntary, without authority figures present, protections in place to prevent retaliation
- Providing alternative and equal methods for meeting course requirements other than participating as a research subject.

Research involving prisoners

45 CFR 46 subpart C : research involving prisoners

- Study of the possible causes, effects, and processes of incarceration, and of criminal behavior or study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects
- Research on conditions particularly affecting prisoners as a class (e.g, vaccine trials) or research on practices which require the assignment of prisoners to placebo-control groups, the study may proceed only after the Secretary has consulted with appropriate experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of the intent to approve such research

Vulnerable Populations : Minorities

Protections

- Keep data strictly confidential
- Consider whether study design could incorporate participants from all segments of society
- Consult with community and include representatives of this group in study design and oversight to reduce potential for stereotyping and stigmatization
- Translated ICF, and translator present for IC process (not family member), & include provisions for continued communication

Conclusions

- Ethical research is guided by the principles of respect for persons, beneficence and justice
- Vulnerable subjects should be included but also deserve special protections
- Think carefully about the populations and take steps to ensure their rights and welfare are protected

Conclusions

When research involves vulnerable subjects, researcher should consider whether

- the research is specific to their conditions,
- exclusion of them will affect the research integrity or justice,
- the risk is minimized, and
- informed consent will be obtained by ethically acceptable means and from individual or appropriated representatives if needed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