Social accountability in scientific research

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Agenda

- Why worry about social accountability in research?
- The pillars of research ethics
- What inhibits ethically responsible research?
- What is research misconduct?
- Warning signs of research misconduct
- Research in resource-poor contexts
- Social responsibility in research
- Case study discussion

Why worry about research ethics?

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a bit of history

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1932: Tuskegee syphilis study begins (ends 1972)
1939: Nazi WWII medical experiments begin (end 1945)
1944: US radiation experiments begin (end 1980s)
1947: Nuremberg Code is adopted

https://www.niehs.nih.gov/research/resources/bioethics/timeline/

The Nuremberg Code

1. The voluntary consent of the human subject is absolutely essential.
2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods, and not random and unnecessary in nature.
3. The experiment should be based on the results of animal experimentation and a knowledge of the disease or other problem under study, that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted, where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed the humanitarian importance of the problem to be solved.
7. Proper preparations should be made to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons.
9. During the course of the experiment, the human subject should be at liberty to bring the experiment to an end.
10. During the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

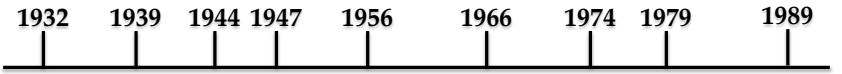
1932: Tuskegee syphilis study begins (ends 1972)

1939: Nazi WWII medical experiments begin (end 1945)

1944: US radiation experiments begin (end 1980s)

1947: Nuremberg Code is adopted

1956: Willowbrook experiments begin (end 1980)



1966: Henry Beecher describes 22 unethical medical experiments in NEJM

1974: US National Research Act is passed

1979: Belmont Report is released

1989: RCR training requirements begin

https://www.niehs.nih.gov/research/resources/bioethics/timeline/

The pillars of research ethics

principles of the Belmont report

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The Belmont Report

- Final product of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1974-1978), created by the 1974 National Research Act
- Identified the basic ethical principles that should underlie the conduct of human subjects research and developed guidelines for such research
- Published in 1979
- Forms the basis for the US Department of Health and Human Services (HHS) human subject protection regulations (45 CFR 46 subpart A), now known as the Common Rule

https://bioethics.georgetown.edu/library-materials/archives/belmont-report-anniversary-and-oral-history/

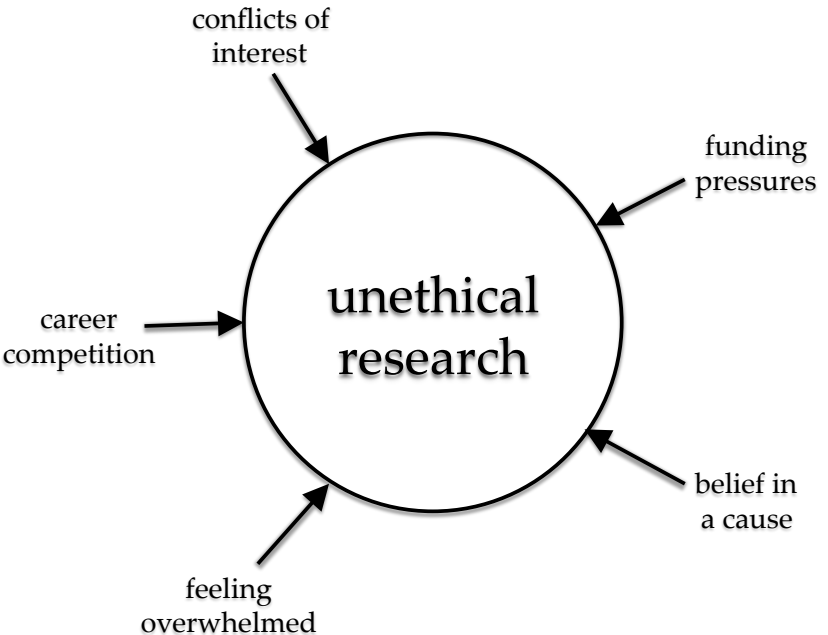
The Belmont Report

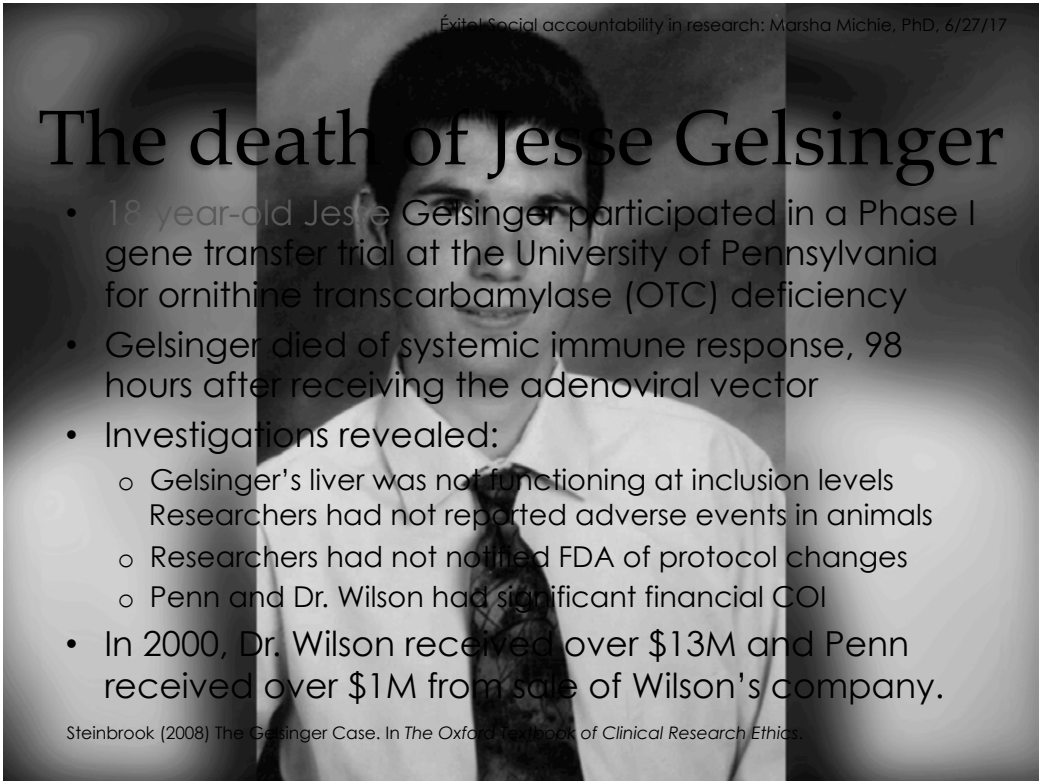
- The boundary between research and practice
- 3 principles:
    1. Respect for persons
    2. Beneficence
    3. Justice
- 3 applications:
    1. Informed consent
    2. Assessment of risks and benefits
    3. Selection of subjects

https://history.nih.gov/research/downloads/belmont.pdf

What inhibits ethical research?

structural and human factors


conflicts of interest
funding pressures
career competition
unethical research
belief in a cause
feeling overwhelmed



The death of Jesse Gelsinger

- 18 year-old Jesse Gelsinger participated in a Phase I gene transfer trial at the University of Pennsylvania for ornithine transcarbamylase (OTC) deficiency
- Gelsinger died of systemic immune response, 98 hours after receiving the adenoviral vector
- Investigations revealed:
  - Gelsinger's liver was not functioning at inclusion levels Researchers had not reported adverse events in animals
  - Researchers had not notified FDA of protocol changes
  - Penn and Dr. Wilson had significant financial COI
- In 2000, Dr. Wilson received over $13M and Penn received over $1M from sale of Wilson's company.

Steinbrook (2008) The Gelsinger Case. In *The Oxford Textbook of Clinical Research Ethics*.

ASU v. Havasupai Tribe

- Arizona State University researchers collected blood samples from the Havasupai tribe in 1989 for a genetic study on Type II diabetes.
- Samples were later used without the tribe's knowledge for research on schizophrenia, migration, and inbreeding.
- In 2004 the Havasupai sued ASU and the researchers for violation of civil rights and medical confidentiality, with other claims.
- ASU settled for $700K and returned all DNA samples.
- The case exacerbated Native Americans' mistrust of outside researchers, especially in genetics.

http://genetics.ncai.org/case-study/havasupai-Tribe.cfm

What is research misconduct?

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regulations and ethics

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Research misconduct

- Defined in Federal law and may warrant Federal investigation & sanctions
- Definition includes:
  - Fabrication
  - Falsification
  - Plagiarism
  - Must be intentional
- Definition excludes:
  - Unintentional errors
  - Laziness, sloppiness
  - Differences of opinion/interpretation

B Lo (2010) *Ethical issues in clinical research: A practical guide*.

Possible consequences

- Institutions are required to conduct an inquiry and, if warranted, a full investigation
- Federal agencies may conduct their own inquiry and investigation
- If misconduct is found, researcher(s) may face:
  - Suspension of federal grant
  - Debarment from future grants
  - Institutional penalties
  - Employment termination
  - Civil and criminal liability

B Lo (2010) *Ethical issues in clinical research: A practical guide*.

Other ethical problems

- Other ethical problems in research are not defined as research misconduct, but may be covered under other regulations.

- Research without IRB approval
- Lack of informed consent
- Financial mismanagement
- Conflicts of interest
- Discrimination
- Poor mentoring

B Lo (2010) *Ethical issues in clinical research: A practical guide*.

Warning signs of research misconduct

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red flags to look for

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What to look for

- Some common signs of research misconduct: things are just too good to be true
- Progress at one site much greater than at other sites
- A researcher's productivity is phenomenal
- Data is very uniform with few/no outliers
- Data much better than at other sites or in other studies
- In publication record: copied passages or photos, changes in authors or order of authors, change in journal name, abstract listed as an article, or article doesn't exist

B Lo (2010) *Ethical issues in clinical research: A practical guide*.

Research in resource-poor contexts

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special ethical considerations

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Resource-poor contexts

- Respect for persons
  - Informed consent beyond a signature
  - Individual and community consent
- Beneficence
  - Individual and community benefits and risks
  - Which standards of care?
  - Duties of ancillary care
- Justice
  - Who does the research benefit?
  - Does the research address issues important to this community?
  - What happens after the research is over?

Social responsibility in research

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science as part of society

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Why social responsibility?

- Science is funded (directly or indirectly) by the public
- Research is carried out in the name of society as an expression and reflection of the society's needs, interests, and priorities
- Risks and burdens placed on research subjects—even if small—are only justifiable if research is valid and addresses an important need
- Researchers' special knowledge gives them an ability and responsibility to oppose misuse of their work, and to facilitate an informed citizenry to promote democracy.

https://www.aaas.org/news/social-responsibility-and-research-ethics-not-eitheror-both

Social responsibility

- Be a responsible citizen of the scientific community
  - Contribute to interdisciplinary conversations, peer review, and mentoring
  - Honor your values
- Even in basic research, consider downstream ethical implications, and potential uses or misuses
  - Draw on interdisciplinary peers and mentors
- Think carefully about how to communicate your science to the public
  - Talk with mentors, peers, and your institution's public relations office
  - Recognize and actively counter hasty conclusions
- Consider contributing to policy briefs, whitepapers, or advocacy efforts related to your science

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Case study

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thinking through research ethics

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Dr. Elena Salazar is a physician/researcher who has developed a relationship with the few remaining Kawésqar people—a village of about 200 on an island off the coast of Chile. Though their ancestors were decimated by European diseases and pushed from their native lands, the Kawésqar today enjoy generally good health, though they are very poor. Dr. Salazar has provided medical care during her visits, and also taken blood samples from healthy adults for study.

On analysis, Dr. Salazar has found that many of these samples contained leukemia-like cells, suggesting that the Kawésqar might have developed some natural immunity to leukemia. She returns to collect additional blood samples to facilitate genome-wide study of the Kawésqar. However, the council of elders refuses to allow this study. They believed that the samples she took before was solely for treating illness, and they do not want outsiders taking blood from their people for other reasons.

On a call back to her lab, Dr. Salazar's lab director suggests that she approach individual families directly, explaining that their blood could help her save many lives, and perhaps improve their own health as new gene therapies are developed. He tells Dr. Salazar that only the individual donor can give informed consent for research, and the council of elders should not be able to decide whether individuals freely consent to give samples. He also offers additional funds for Dr. Salazar to pay study participants, or to buy goods that could improve the everyday lives of the Kawésqar families who participate.

Questions:

1. Should Dr. Salazar approach individual families and explain her study to them in hopes of collecting blood samples?
    - What benefits and risks might there be for individual Kawésqar who choose to participate in the study?
    - What might be the consequences (good and bad) for Dr. Salazar and other scientists conducting this kind of research?
2. Does Dr. Salazar have implicit responsibilities to the Kawésqar village, the council of elders, or the Kawésqar families she is close to?
    - If so, how does her lab director's suggestion meet (or not meet) those responsibilities?
3. If Dr. Salazar decides not to take her lab director's suggestion, how else might she proceed to facilitate her research?
    - Who should she consult with?
    - Who might she collaborate with?
    - What steps could she take right away, and what goals might she work toward?

Resources

- Your institution offers guidance:
  - Office of Research Integrity/Ethics and Compliance
  - Ethics consultation service
  - Clinical and Translational Science center
  - Human subjects research: IRB
  - Animal research: IACUC
  - Stem cell research: SCRO
  - Conflicts of interest: COI committee
  - Whistleblowing/concerns: Ombuds


thank you
gracias
merci
danke
obrigado
dziękuję
go raibh maith agat
teşekkür ederim
ngiyabonga
謝謝
рахмат
Баярлалаа
спасибо
spas
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kia ora
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welalin
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faafetai lava
vinaka
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dhanyavad
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তোমাকে ধন্যবাদ
감사합니다