



Research Ethics Involving Human Subjects

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Objectives

- To give a historical perspective on the evolution of guidelines in research ethics
- To provide an overview of the international guidelines
- To discuss the universal ethical principles and elements of research ethics



ENGLAND 1796: Edward Jenner injects healthy James Phipps first with cowpox then three months later with smallpox and later discovered smallpox vaccine.



Reed, standing second from right, Volunteers, and others at Camp Lazear, 1901

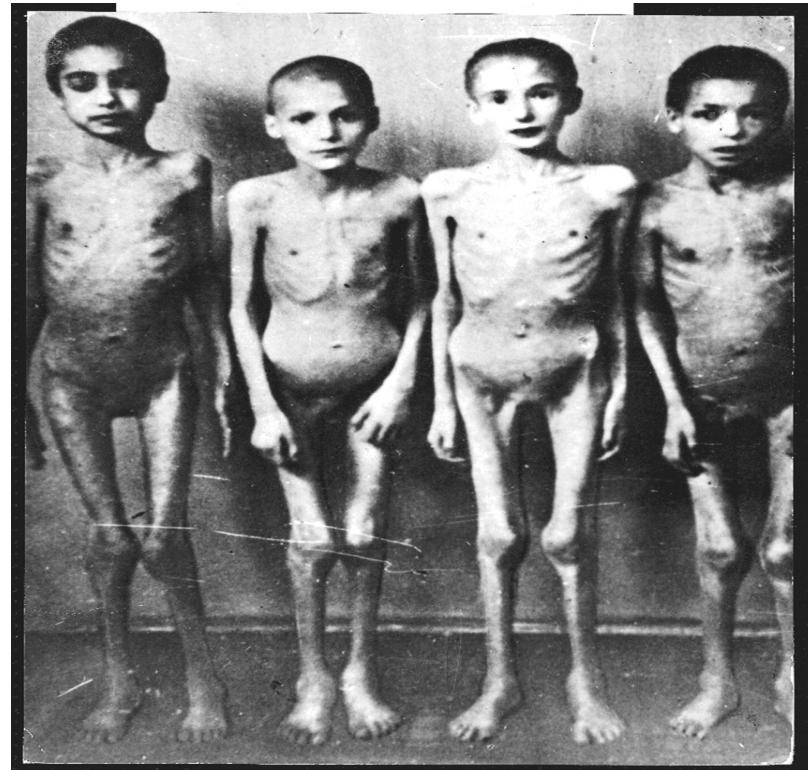
CUBA 1900s: Major Walter Reed (US Army) injects 22 Spanish immigrant workers in Cuba with the agent for yellow fever paying them \$100 if they survive, \$200 if they contract the disease

Auschwitz Nazi Camp: 1943

Dr. Josef Mengele

(known as the Angel of Death)

- Children – injected with chemical
- Prisoners with deformities – brutal surgeries, amputations
- Female prisoners – sterility and shock





THE NUREMBERG TRIALS

The Nuremberg Code is one of the most influential documents in the history of clinical research.



Nuremberg Code (1947)

- Voluntary consent
- Positive benefit-risk ratio
- Benefit to society
- Adequate facilities
- Pre-clinical phase
- Investigator qualification
- No unnecessary risk
- Freedom to withdraw
- Prevent disability / death
- End the study if unsafe

The Impact of the Nuremberg Code

- It is a basic human right not to be a subject of experimentation “against one’s will” or ‘without one’s free consent’ (UNHCR)
- The Nazi experiments were condemned (Declaration of Geneva)
- Protection against unwanted biological or medical experimentation.

Tuskegee Syphilis Experiment

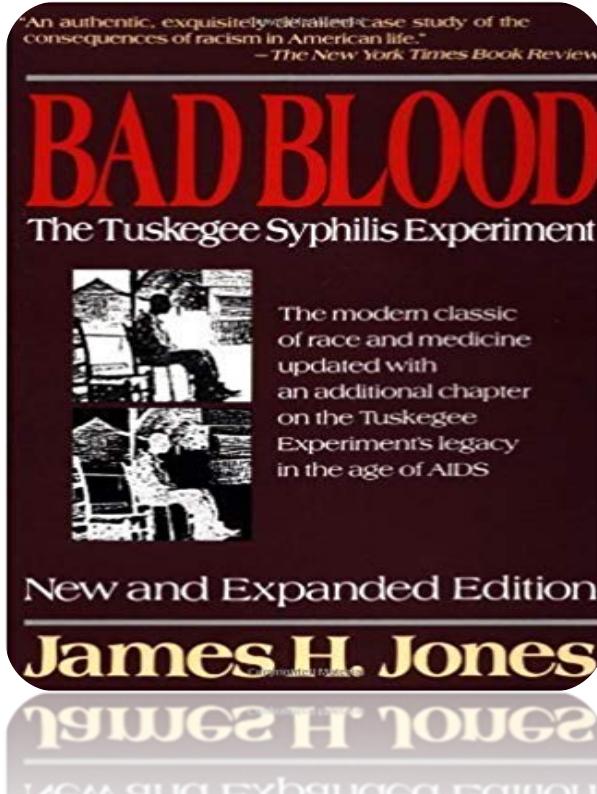
1932-1972: Alabama, USA

- US Public Health Service study on untreated syphilis; how syphilis kills and spreads; how syphilis affects black people compared to whites
- 399 illiterate black men were told they had ‘bad blood’ & could receive free treatment, transportation, meals, burial
- Researchers planned to get data from autopsies



The men's status did not warrant ethical debate. They were subjects, not patients; clinical material, not sick people (John Heller, PHS Head)

Tuskegee Syphilis Experiment 1932-1972: Alabama, USA



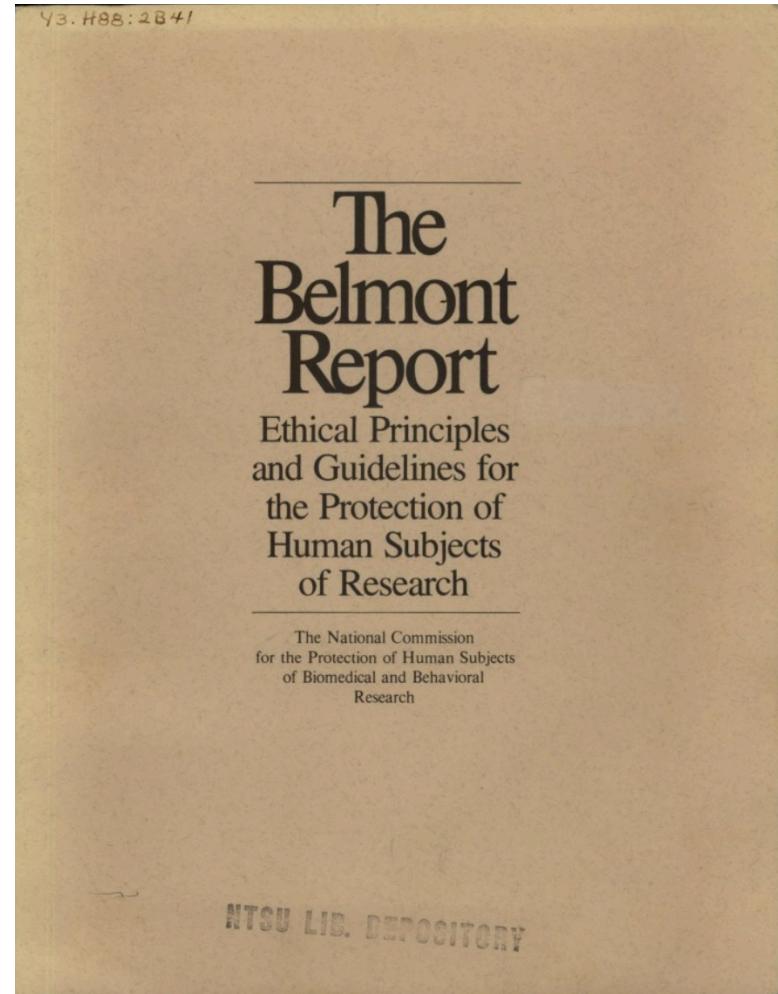
- By 1947, Penicillin became standard of treatment but the participants were not given treatment and they were prevented from getting information
- 1972, this was exposed by medial and this was followed by a Congressional investigation
- President Clinton in 1997 issued a public apology

Belmont Report

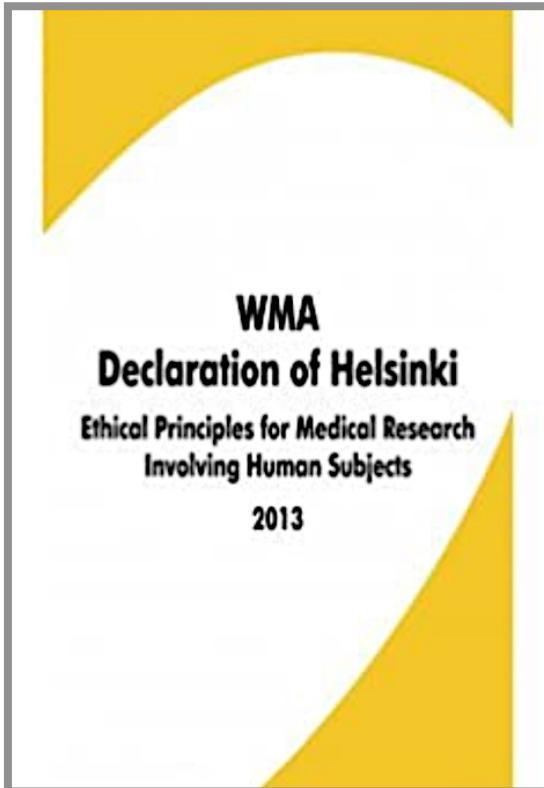
Ethical Principles and
Guidelines for the Protection
of Human Subjects of
Research

Basic Ethical Principles

1. Respect for Persons
2. Beneficence
3. Justice



Declaration of Helsinki



- It was developed by the World Medical Association, adopted in 1964 and has undergone amendments
- It seeks to guide doctors doing research on patients
- The Declaration used provisions of the Nuremberg Code
- Several national guidelines worldwide adopted it.

Declaration of Helsinki

World Medical Association (WMA)

1964 Helsinki

1975 Tokyo

1983 Venice

1989 Hongkong

1996 Somerset West

2000 Edinburgh (clarifications 2002 and 2004)

2008 Seoul

2013 Fortaleza

Declaration of Helsinki

1. The risks and burdens vs. benefits
2. Protection of vulnerable groups and persons
3. The need for sound scientific inquiry
4. Review of research protocols by research ethics committees
5. Privacy and confidentiality

Declaration of Helsinki

6. Obtaining informed consent
7. Use of placebo
8. Post-trial provisions
9. Research registration and publication of results
10. Use of the unproven intervention in clinical practice

Declaration of Helsinki

- Differentiate CLINICAL CARE and RESEARCH to the patient; refusal or withdraws must never adversely affect the patient-physician relationship.
- For use of identifiable human material or data, seek informed consent for its collection, storage and/or reuse; exceptions are only for impracticability upon approval of ERC

CIOMS 2016

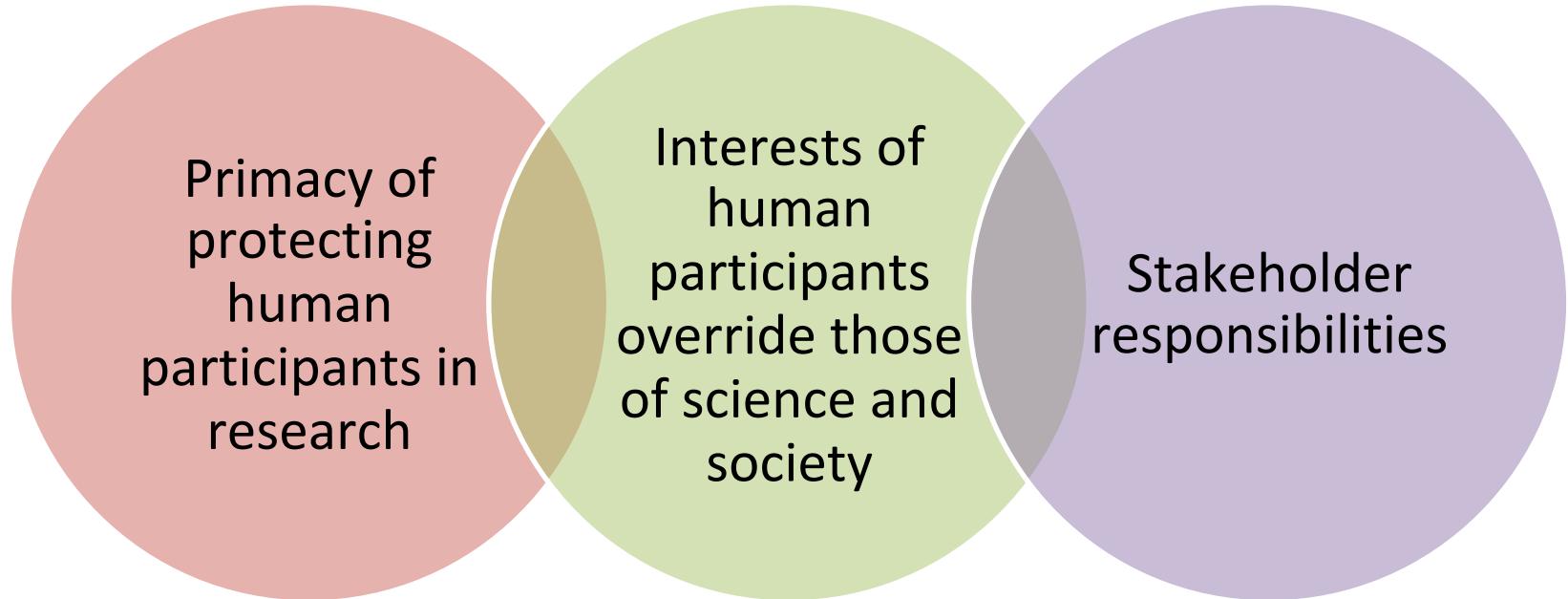
International Ethical Guidelines for Health-related Research Involving Humans

Prepared by the Council for International
Organizations of Medical Sciences (CIOMS)
in collaboration with the
World Health Organization (WHO)



Geneva 2016

Ethical Framework



Universal Ethical Principles

Respect for Persons

- Respect for autonomy
- Protection of persons with diminished autonomy

Beneficence

- Obligation to maximize benefits and minimize harm

Justice

- Equitable distribution of both the burdens and the benefits of participation in research

Ethical Elements



SOCIAL VALUE



INFORMED
CONSENT



VULNERABILITY



RISK BENEFIT
SAFETY



PRIVACY
CONFIDENTIALITY



JUSTICE



TRANSPARENCY

Elements of Research Ethics

Social Value

Study is relevant to a social or health problem

Scientifically sound

Dissemination plan for the beneficial outcomes of the study

Elements of Research Ethics

Informed Consent

Confirmation of willingness to participate (voluntary)

Complete information conveyed to respondent

In general, documented by signature and date

Elements of Research Ethics

Vulnerability

Incapacity to protect one's own interests (& to consent)

Increased likelihood of additional harm from research

Common vulnerabilities: cognitive, medical, social, economic, legal

Elements of Research Ethics

Risk, Benefit,
Safety

Risk: probability of harm

Benefit: favorable outcome

Target: Benefit > Risk

Elements of Research Ethics

Privacy & Confidentiality

Privacy is the right of persons not to share personal information

Confidentiality is the obligation to keep private information from being shared

Elements of Research Ethics

Justice

Research should not worsen social inequities

Access to research benefits or favorable outcomes must be guaranteed

Generally, distributive justice, or equitable distribution of risk, burden, benefit of research

Elements of Research Ethics

Transparency

Clear delineation of responsibilities of researchers and their institutions

Management of COI, protection of privacy & confidentiality of personal information

Use of harmonized and standardized procedures that can be audited, verified

Summary

- I. Historical perspective in the evolution of ethics guidelines for research
- II. International guidelines
- III. Universal ethical principles
- IV. Elements of research ethics