Ethics in Research Involving Human Subjects

Wannee Deoisres, Rn, PhD
Associate Professor
Faculty of Nursing
Burapha University

fppt.com

What is “research”?

- A systematic investigation designed to develop or contribute to generalizable knowledge.

fppt.com

What is research involving human subjects?

- WHO defined research with human subjects as
  - 'any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new knowledge, in which human beings:

fppt.com

- are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment; or
- become individually identifiable through investigator's collection, preparation, or use of biological material or medical or other records.

(http://www.who.int/ethics/research/en/)

fppt.com

Clinical Care vs. Research

- Clinical care
  - provide direct benefit to the patient
- Research
  - Contribute to generalizable knowledge
  - Special attention to possible harm to the subject
  - Regulatory codes place the responsibility for the ethical conduct of research on the shoulders of the researchers
  - Researchers need to hold themselves to the highest standards of integrity and accountability

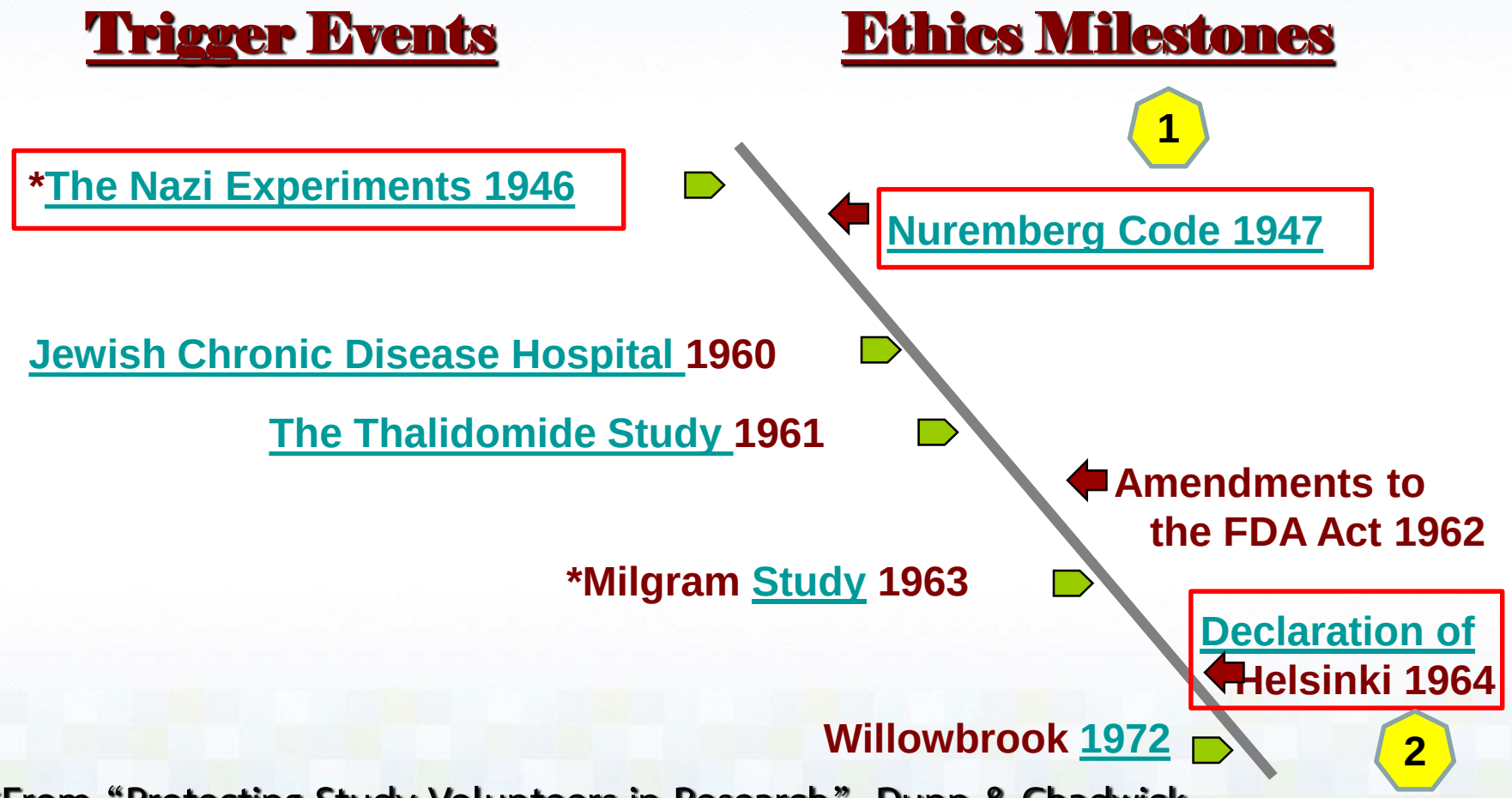
fppt.com

Ethical Codes, Standards and Regulations

- Developed in reaction to scandal and impropriety
- History of research ethics provides a bleak picture of the treatment of research subjects at the hands of researchers
- Only scandals reach the news

fppt.com

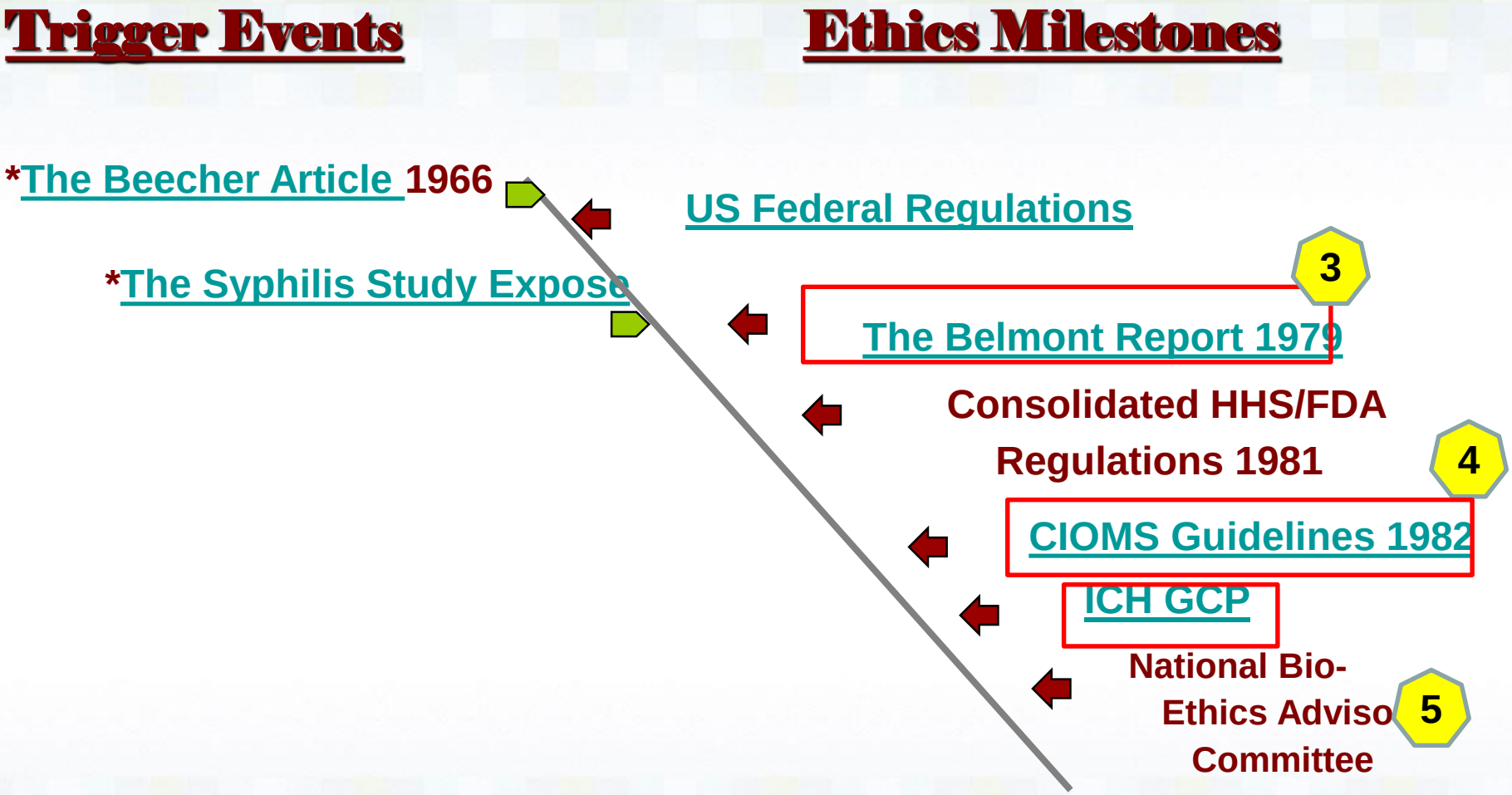
Research Ethics Milestones



*From "Protecting Study Volunteers in Research" Dunn & Chadwick

fppt.com

Research Ethics Milestones



fppt.com

Research Code of Ethics

- The Nuremberg Code (1947)
- The World Medical Association's Declaration of Helsinki (1964) (is the basis for Good Clinical Practices used today).
- The Belmont Report (1979)
- International Ethical Guidelines for Biomedical Research Involving Human Subjects) (CIOMS) (1982)

fppt.com

Thailand

- Forum for Ethical Review Committee in Thailand (FERCIT)
- Related laws, codes of ethics

fppt.com

History of Research Ethics

fppt.com

World War II-The Nuremburg Trial

- 20 doctors were charged with War Crimes and Crimes against humanity
- Joseph Mengele fled and was not tried.
- Lead to Nuremburg Code of 10 Principles

fppt.com

Experiments on twins

- Experiments on twin children in concentration camps were created to show the similarities and differences in the genetics of twins, as well as to see if the human body can be unnaturally manipulated.
- The central leader of the experiments was Josef Mengele, who from 1943 to 1944 performed experiments on nearly 1,500 sets of imprisoned twins at Auschwitz. About 200 people survived these studies.
- The twins were arranged by age and sex and kept in barracks between experiments, which ranged from injection of different dyes into the eyes of twins to see whether it would change their color to sewing twins together in attempts to create conjoined twins.

fppt.com

Freezing experiments

- intent of discovering means to prevent and treat hypothermia
- There were 360 to 400 experiments and 280 to 300 victims indicating some victims suffered more than one experiment.
- placed prisoners naked in the open air for several hours with temperatures as low as −6 °C (21 °F).
- assessed different methods of rewarming survivors
- people were dressed in fighter Pilot uniforms and submerged in freezing water
- some victims were thrown into boiling water for rewarming.

fppt.com

fppt.com

Bone, muscle, and nerve transplantation experiments

- to study bone, muscle, and nerve regeneration, and bone transplantation from one person to another.
- Sections of bones, muscles, and nerves were removed from the subjects without use of anesthesia. As a result of these operations, many victims suffered intense agony, mutilation, and permanent disability

fppt.com

Other experiments

- Head injury experiments
- Malaria experiments
- Immunization experiments
- Mustard gas experiments
- Sulfonamide experiments
- Sea water experiments
- Sterilization and fertility experiments
- Experiments with poison
- High altitude experiments
- Blood coagulation experiments

fppt.com

Nature of German Experiments World War II

- Set in racist context in concentration camps
  - Jews
  - Women
  - Homosexuals
  - Twins
  - Mentally ill
- Killing for reason of race and disability well underway
- Military vs. other types of research

fppt.com

Ethical Justifications

- Sacrifice of few to benefit the many
- War allows waving of consent
- Experimentation on the terminally ill/doomed
- Experimentation on prisoners
- Subjects could benefit
- Not responsible for values or policy

fppt.com

Response - Nuremberg Code

- Informed consent is essential
- Benefit must outweigh risk to the subject
- Experimentation must be voluntary
- No coercion or force
- Focused on research involving prisoners
- No consideration for mentally ill

fppt.com

fppt.com

Declaration of Helsinki

- World Medical Association – 1964
- Codes existed for delivery of health care but not for research
- Identified research as that involving human subjects including research on identifiable human material or identifiable data
- Interest to the wellbeing of the subject far outweighs the benefit to society
- Special populations
  - Economically and medically disadvantaged
  - Those unable to give consent
  - Those who may be subject to giving consent under duress
  - Those who will not benefit from the research
  - Where research is combined with medical care

fppt.com

Declaration of Helsinki

- Therapeutic research
  - Offers some potential benefit to the subject
  - Consent can be procured from a legal guardian
    - Surrogate consent
    - Ensures that children, mentally ill can participate
- Nontherapeutic research
  - Purely investigational
  - Consent can never be waived
- Has been revised 4 times

- Provided the framework for the guidelines used by AMA, ASCI, AFCR,DOD and FDA today

fppt.com

Tuskegee Syphilis Study

- Conducted by the US Dept of Health Services (1932-1972)
- Undertaken with good motives but in the Context of racism
- Observational study 400 AA males in Alabama with latent syphilis - meaning that they had the infection but showed no obvious symptoms at that stage.

fppt.com

- For 40 years they were never told they had syphilis and were never treated for it, even when penicillin became a standard cure in 1947.
- They were simply told they had ‘bad blood’. Among the aims of the study was to see whether syphilis affected black men differently from white men.
- the men received free rides to and from the clinic at Tuskegee University, Alabama. There they were given hot meals and free medical treatment for minor ailments. Any treatments they thought they were also getting for their ‘bad blood’ were actually placebos, aspirin or mineral supplements
- Study ended in 1972 only 74 of the original participants were still alive. 28 died, and 100+ had complications, wives and chidren got infections.
- in 1997 US President Bill Clinton was moved to declare that ‘on behalf of the American people, what the United States government did was shameful’.

fppt.com

Response to Tuskegee

- Public and professional outrage led to
  - The Tuskegee Advisory Panel in 1973
  - Recommended termination of the study
  - Determined governments policies for reviewing scientific procedures and consent practices in federally funded research were inadequate
- A Federal Advisory Board (1974-78)
  - “National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research”
  - Result was the “Belmont Report of the National Commission” in 1979
  - 3 ethical principles central to the research enterprise

fppt.com

The Belmont Report

- Purpose of the report is to provide three principles (prescriptive judgments) that will ‘assist researchers, subjects, reviewers and interested citizens with an understanding of the ethical issues inherent in HSR’

- Statement consists of 3 parts
  - Distinction between research and medical practice
  - Establishment of 3 ethical principles
  - Remarks regarding application of the principles

fppt.com

The Belmont Report

- Practice
  - Interventions designed solely to enhance the wellbeing of the patient and that have a reasonable expectation of success

- Research
  - An activity designed to test an hypothesis, permit conclusions to be drawn, develop or contribute to generalizable knowledge

fppt.com

The Belmont Report
Three Ethical Principles

- Principle of respect for persons autonomy
- Principle of beneficence
- Principle of justice

fppt.com

I. Respect for human dignity

(persons autonomy)

fppt.com

- Respect for free and informed consent and Respect to autonomy of decision making
- Respect for privacy
- Respect for confidentiality
- Respect for vulnerable persons

fppt.com

Vulnerable Persons

- Mentally ill
- Persons with HIV/AIDS
- Comatose
- Handicapped
- Prisoner, students, soldiers
- Marginalized people such as immigrants, ethnic minority
- Homosexuality, socially vulnerable such as sex workers, drug addicts

fppt.com

II. Beneficence

fppt.com

- A risk benefit assessment be made: Balancing risks and benefits
- Minimizing harm
  - Physical harm
  - Psychological harm
  - Social and economic harms
  - Law such as being arrested

fppt.com

- Maximizing benefit
  - Physical benefits
  - Psychological benefits such as comfort from suffering, feeling of helping others in the future
  - Economic benefits such as financial benefits related to research participation
  - Benefit to science/society such as generalizable knowledge, effective interventions in the future, change in practice standards decreasing morbidity and mortality

fppt.com

III. Justice

fppt.com

- Fairness and equity
- Fairness in selection of subjects
  - Inclusion and exclusion criteria
  - No selection bias
- Benefit is denied or burden is imposed
  - Randomization

fppt.com

The Common Rule

- First time after more than 25 years in the making a comprehensive regulatory framework existed that formally governed all human subjects research conducted by the federal government or in facilitates receiving federal funds
- The common rule
  - Mandates role of the IRB
  - Defines requirements for informed consent
  - Codifies special requirements for vulnerable populations
    - Pregnant women, fetuses, IVF subpart A
    - Prisoners –subpart C
    - Children –sub part D
  - Requires institutional assurance of compliance

fppt.com

Ethics Committee
Institutional Review Board

fppt.com

Q & A

fppt.com