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What are the ethics?

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What governs clinical trials?

- Ethical codes
  - Nuremberg Code
  - Declaration of Helsinki (October 2000)
  - Belmont Report

Nuremberg Code

- 10 Guiding Principles
  - Voluntary consent of the human subject is absolutely essential
  - Experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature

Nuremberg Code

- Experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment

Nuremberg Code

- Experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury

- 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

Nuremberg Code

- Degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment

- Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death
  - GMP, GCP

Nuremberg Code

- Experiment should be conducted only by scientifically **qualified persons**. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment

- During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible

  - Participant may withdraw at any time

Nuremberg Code

- Course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probably cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject
  - PI may withdraw the participant

Declaration of Helsinki

- Most current ethical code
- Developed as a result of the Tuskegee Syphilis trials
- “Provides guidance to physicians and other participants in medical research involving human subjects.” - DoH 2002

Declaration of Helsinki

- “The health of my patient will be my first consideration.”
- “…considerations related to the well-being of the human subject should take precedence over the interests of science and society.”
- “Some research populations are vulnerable and need special protection.”

Basic Principles

- Design and performance be clearly formulated and conform to generally accepted scientific principles
  - protocol: background, objectives, inclusion/exclusion criteria, treatment plan, follow-up procedures
  - informed consent document
- A statement of ethical considerations should be included
  - purpose section of informed consent document
  - protocol

Basic Principles

- Only scientifically qualified persons should conduct the research
  - Human Studies Training Module
- Risk/Benefit analysis should be conducted
  - protocol and informed consent document
- Informed consent of study volunteers
  - 8 elements of informed consent
  - no finder's fees
  - waivers and modifications of consent

Basic Principles

- Special considerations for consenting minors and cognitively impaired
  - assent 7 and older
  - legal authorized representative

- Ability to withdraw or refuse
- Preserve result accuracy
- Maintaining confidentiality

Additional Principles

- “When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects”
- Comparison with current methods should take place
- Patients should have access to methods once study is complete.

Additional Principles

- Patient should be told which treatments are related to research.
- If no proven treatments, drugs, therapies exist, unproven measures may be used with patient consent.

DEBATES

- Placebo vs. existing treatment
  - availability of products
  - research questions differ among populations
- Narrow focus
  - public health, epidemiological, social, behavioral research not encompassed by DoH
- “Best method” determination
  - takes more than one clinical trial
- Limited representation of patients, persons from developing countries, women

Belmont Report

- 3 Guiding Principles
  - Respect for Persons
    - Informed Consent
    - Vulnerable Populations
  - Beneficence
    - Risk/Benefit Ratio
  - Justice
    - Equitable Subject Selection

Additional Considerations

- Respect for Persons
  - Vulnerable population: Could research be carried out without population? Safeguards? Coercion?

- Risk/Benefit analysis
  - physical, psychological, physiological
  - how risks minimized
  - benefit to the participant
  - Research vs. standard of care

Additional Considerations

- Justice
  - Are populations being targeted because they are easy to obtain?
  - Why are populations being excluded?
  - Why is there a disparity in recruitment?