Research Ethics

Professor Ernest Hung Yu NG
Department of Obstetrics & Gynaecology
The University of Hong Kong
Definition of research ethics

- A set of principles or guidelines that will assist the researcher in making difficult research decisions and in deciding which goals are most important in reconciling conflicting values.
Clinical trials

- Studies involves humans
- Provides advances in patient care
  - Diagnosis
  - Treatment: drugs, devices, care processes
  - Prognosis
Agenda

1. History of research ethics
2. International guidelines on research ethics
3. Research ethics in the process of a study
History of research ethics

- No regulations not too long ago
- Twentieth century: many medicines and vaccines developed
- Many studies were conducted on marginal groups such as prisoners and children.
- Subjects not informed of trial details and risks.
Dark medicine

- 1847: J. Marion Sims, “the father of gynecology” performed experimental surgeries on enslaved African women without anesthesia. Many lost their lives to infection.
- 1896: Dr. Arthur Wentworth performed spinal taps on 29 children at Boston to determine if the procedure was harmful.
- 1897: Italian bacteriologist Sanarelli injected five subjects with bacillus searching for a causative agent for yellow fever.
- 1900: Walter Reed injected 22 Spanish immigrant workers in Cuba with the agent for yellow fever paying them $100 if they survived and $200 if they contracted the disease.
- 1906: Dr. Richard Strong, a professor of tropical medicine at Harvard, experimented with cholera on prisoners in the Philippines killing thirteen.
Dark medicine

- 1940’s: Nazi concentration camps and Japanese unit 731
- 1950’s: Thalidomide tragedy
- 1960’s: Human radiation experiments; New York City’s Jewish Chronic Disease Hospital; Willowbrook Studies; Milgram Study
- 1970’s: Tuskegee Syphilis; Stanford Prison Experiment
The Nuremberg Code

1. Voluntary consent of the subject
2. Experiment should yield fruitful results
3. Animal experimentation to justify the study
4. Avoid all unnecessary physical/mental suffering/injury
5. No experiment so death or disabling injury will occur
The Nuremberg Code

6. Risk never exceeds the benefit
7. Preparations to protect against injury, disability, or death
8. Only by scientifically qualified persons
9. Human subject should be at liberty to stop the experiment
10. The scientist must terminate the experiment if it is likely to result in injury, disability, or death
Declaration of Helsinki

1. Research with humans should be based on the results from laboratory and animal experimentation
2. Research protocols should be reviewed by an independent committee prior to initiation
3. Informed consent from research participants is necessary
4. Research should be conducted by medically/scientifically qualified individuals
5. Risks should not exceed benefits
Belmont Report

- Charged with defining ethical principles to guide the conduct of research
- Establish IRB responsibilities
- Ethical principles
  - Respect, Beneficence, Justice
Respect for Persons

- Individuals should be treated as autonomous agents
- Persons with diminished autonomy are entitled to protection (‘special populations’)
  - Children, mental disabilities and prisoners
**Beneficence**

- Do no harm
- Maximize benefits and minimize risks
- Applied at both an individual level for research participants and a societal level for the effect of the knowledge gained from the research
- Implication on pregnancy/children for infertility trials
Justice

- Fair distribution of burdens and benefits of research
- Selection of research participants should involve those groups who will benefit from research, not ‘convenience’ populations that are more likely to be disadvantaged
Good Clinical Practice (GCPs) for PIs

- PIs will be held accountable for the ethical conduct and integrity of the study
- Qualified PI and staff
- Appropriate delegation of responsibilities
- Adequate staffing, resources, & facilities
- Study drug accountability
- Appropriate communication with IRB
GCPs for study investigators

Comply with protocol & complete the study
- Enroll appropriate subjects; meet enrollment targets
- Follow randomization and blinding procedures
- Treatment administration per protocol
- Measurement of study outcomes
- Maintain audit trail (paper/electronic)
- Complete/process/file all study reports
- Appropriate post-study follow-up for participants
- Participate in dissemination of results
GCPs for study investigators

PIs must provide adequate medical care for study subjects

- Monitor, treat, & report adverse events (AEs)
- Inform participant & primary care MD when care is needed for intercurrent illness(es)
- PIs may refer subject to primary caregiver when appropriate
Ethical principles of research

- Integrity
- Competence
- Non-maleficence
- Dignity
- Justice
- Beneficence
- Autonomy
- Privacy
- Confidentiality
- Responsibility
- Honesty

Researchers

Participants
Research problem

Is it a significant problem that will benefit others? Does it worth public money?

Have you done a thorough literature review to see if other studies exist?

Is it ethical to repeat the study if it has been done before?

- Confirm
- Extend
- Refute

Responsibility

Competence

Non-maleficence

Beneficence
Research question

- Clearly identify the purpose of the study
- Does it expose participants to unacceptable risks or invasion of privacy?
- Any risk to husband and pregnancy/children?
Research design

- Is your choice of the study design an ethical choice?
  - Observational versus Interventional
  - Benefits / Risks ratio

- Is it methodologically sound?

- Do you have the expertise to do it?  Pilot?
Types of possible harm

- Physical
- Psychological
- Social
- Economic
- Legal

Beneficence

Non-maleficence
Vulnerable populations

- Minors
- Minority groups
- Mentally incompetent
- Prisoners
- Your students/staff
Informed consent

- About you & the research:
  - Who are the researchers & their contact information?
  - Who is sponsoring?
  - What is the purpose of the research?
Informed consent

About the participants:

• How were they selected?
• Assure: participation is voluntary and withdrawal possible at any time
• What are the benefits & risks?
• What is the level and type of their involvement?
• How will confidentiality be protected?
Data collection

- Respect participants
- Respect privacy & confidentiality
- MONITOR
Data analysis

- How will you protect the anonymity of participants?
- How will you analyze the data? Do you have the experience?
- How long will you keep the data once analyzed?
  - Where & how will you keep it?
Confidentiality

- All information collected in a research project should remain confidential
  - Participants should be assigned a code
  - Data should be locked away in a secure setting
  - Electronic databases should also be protected
Research dissemination

- Authorship:
  - Who will do what & when?
  - Authorship order
  - Conflicts of interests: financial
Authorship

The International Committee of Medical Journal Editors (ICMJE) recommends authorship decision based on:

1. substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data
2. drafting the article or revising it critically for important intellectual content
3. final approval of the version to be published
Authorship

- All who qualified should be listed.
- Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship.
- All contributors who do not meet the criteria for authorship should be listed in an acknowledgments section.
Investigator conflicts of interest

- Professional gain: publications/promotion
- Financial gain
  - Patient finder’s fee to collaborators
  - Recruitment bonuses
  - Affiliation with/funding from sponsor for future studies, consultant relationships
- Other incentives (e.g., travel, presentations)
- Per patient payment system presents conflicts of interest inherent in capitalist society
Consequences of investigator conflicts of interest

Attempting to ↑study enrollment
- Coercing subjects to enroll and discouraging withdrawal, treatment alternatives
- Enrolling fictitious or ineligible patients

Bias trial toward positive results
- Failure to report adverse events
- Failure to comply with protocol regimens
- Alteration of outcome data
- Data fabrication
Safeguards against financial conflicts of interest

- Full disclosure (institution, collaborators, journal editors, FDA)
  - Disclosure not meant to prevent investigators from participating in research
  - Disclosure statements also apply to study staff, spouses, and dependent children
- Regulatory/legal action for failure to comply
Sponsor conflicts of interests

Pressure investigator to withhold negative results or to “spin” positive results

- Unreasonable control of data analyses
- Discrediting investigator’s research (through word-of-mouth, publications, presentations)
- Threat of loss of contractual work
- Threat of legal action
Conclusion

- All investigators should be familiar with the three international Guidelines for the prevention of unethical clinical research.
Thank you for attention