Ethical Requirements in Scientific Research

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Our agenda:

- Definitions of some key terms
- Goals of research
- Scientific misconduct
- Objectives of Research Ethics
- Brief history of Research Ethics
- What makes a clinical research ethical?
- Roles of these ethical requirements

Key Terms:

- ***'Research'*** is a systematic investigation designed to produce or contribute to generalizable knowledge.
- ***'Research ethics'*** refers to the moral principles guiding research, from its inception through to completion and publication of results and beyond – for example, the curation of data and physical samples after the research has been published.

Research Ethics Committee (REC) Institutional Reviewing Board (IRB)

- is defined as a multidisciplinary, independent, body charged with reviewing research involving human participants to ensure that their dignity, rights and welfare are protected.
- The independence of a REC is founded on its membership, on strict rules regarding conflict of interests, and on regular monitoring of and accountability for its decisions.

'Human participants' (or subjects):

are defined as including:

- living human beings
- human beings who have recently died (cadavers, human remains and body parts)
- embryos and foetuses
- human tissue and bodily fluids
- human data and records (such as, but not restricted to medical, genetic, financial, personnel, criminal or administrative records and test results including scholastic achievements).

Goals of Research

- **Describe.**
- **Explain.**
- **Predict.**
- **Control.**

Goals of Research

- **DESCRIPTION**

  The accurate portrayal of a situation or phenomenon.

- **EXPLANATION**

  The statement of the cause of some situation or phenomenon.

Goals of Research

- **PREDICTION** تنبؤ, تكهن

  The ability to anticipate the occurrence of some event.

- **CONTROL** مراقبة, سيطرة

  Manipulation of some condition(s) to produce a change in behavior.

Successful research will require:

- **Partnerships** مشاركة, شراكة
  - Field-specific researchers + social scientists/methodologists + ethicists
- **Funding** موارد مالية
- **Creativity**

- Researchers and REC members must be encouraged to find and use such data

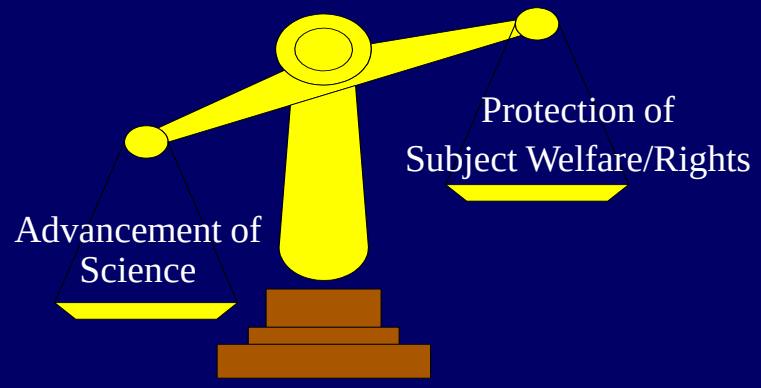
Scientific misconduct:

- **Piracy:** قرصنة، إنتحال مؤلفات ، سرقة أدبية، نهب، تزوير
  the deliberate exploitation of ideas from others without acknowledgement
- **Plagiarism:** إنتحال، سرقة أدبية، شيء منتحل
  the copying of ideas, data or text without permission or acknowledgement
- **Fraud:** خداع، تزوير، إحتيال
  deliberate deception, including the invention of data, and the omission from analysis and publication of inconvenient data

Objectives of Research Ethics

- To safeguard the rights, dignity and welfare of all human participants in research according to internationally accepted guidelines.
- To ensure that no vertebrate animals are subjected to unnecessary or excessive pain or discomfort as a result of research.

Balancing Twin Goals



History of Research Ethics

- ***Before 20th century***
  - Small scale, involving few individuals
  - Intent was therapeutic
- ***Beginning of 20th century***
  - Larger scale clinical trials
  - collect systematic data to improve health of society
  - groups of individuals
  - vulnerable groups → **•Prisoners •Orphans •Mentally ill**

No Formal Codes of Research Ethics

Background

WWII: Nazi War Crimes

- **Nuremberg Code 1947**

World Medical Association

- **Declaration of Helsinki**

1964, 2001, 2003

Tuskegee Syphilis Study

- **Belmont Report 1979**

Nazi Experiments

Hypothermia Experiments

A prisoner is submerged in a tank filled with cold water. The goal of this type of experiments was to determine how long German pilots would survive after parachuting into the cold north sea.

Nazi Doctors' Trial (1947)

Nazi doctors and scientists put on trial for the murder of concentration camp inmates who were used as research subjects

15 of 23 guilty, 7 hanged, 5 life sentences

The Nuremberg Code, 1947

First Codification of Research Guidelines
Human Rights + Welfare of Subjects

- Voluntary informed consent is absolutely essential
- Qualified researchers using appropriate research designs
- Favourable risk/benefit ratio
- Participant must be free to stop or withdraw at any time

The Declaration of Helsinki, 1964

- 'The well-being of the subject should take precedence over the interests of science and society'
- Consent should be in writing
- Use caution if participant is in dependent relationship with the researcher (e.g. doctor-patient; teacher-student)
- Limited use of placebo
- Greater access to benefits

Tuskegee Syphilis Study (1932 - 1972)

- Tuskegee, Alabama
  - High prevalence of syphilis
  - Although treatment existed, blacks in the rural southern town were not receiving treatment
  - Lack of funds/Lack of doctors
- Study natural course of syphilis
  - Enrolled 400 black males infected with syphilis to study the natural course of syphilis
  - Not an experiment but rather a "study in nature"

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Tuskegee Syphilis Study (1932 - 1972)

- Inadequate disclosure of information
- Subjects believed they were getting free treatment
- Told that spinal taps was therapy
- US Gov't actively prevented men from receiving penicillin
- 1972 press reports caused the U.S. Gov't to stop the study

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The Belmont Report, 1979

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

- Respect for persons
- Beneficence
- Justice

These are the fundamental principles of human research ethics and are considered universal, transcending geographical, cultural, economic, legal and political boundaries.

Other International Guidelines

- The U.S. Code of Federal Regulations (CFR), 1991
  (also called *The Common Rule*)
  -- prior approval; continuing review
- Council for International Organizations of Medical Sciences (CIOMS), 1993
  -- developing countries; role of ethics committees
- WHO & International Conference on Harmonisation (ICH); GCP Guidelines, 1995, 1996
- National Bioethics Advisory Commission (NBAC) – USA, 2000
- The Nuffield Council on Bioethics – UK

What makes clinical research ethical?

In the absence of a ***UNIVERSALLY*** applicable ethical frame-work for a research. There are (eight) requirements that provide a systematic and coherent frame-work for determining whether clinical research is ethical:

1- Social or scientific value	**القيم الاجتماعية والعلمية**
2- Scientific validity	**الصلاحية العلمية**
3- Fair subject selection	**العدل فى اختيار الأشخاص محل البحث**
4- favorable risk-benefit ratio	**تغليب المنافع على المخاطر**
5- Independent review	**المراجعة المستقلة**
6- Informed consent	**الموافقة المستنيرة**
7- Respect for enrolled subjects	**احترام الأشخاص محل البحث**
8- Community partnership or perspective	**منظور المجتمع**

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(1) Social Value

To be ethical clinical research must lead to improvements in health or advancement in generalizable knowledge

- Research without value includes:
  - Substantial overlap with prior studies
  - Intervention can never be implemented
  - Unimportant hypothesis

- Justification of social value as an ethical requirement
  - waste resources
  - exposing subjects to burdens or risks

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(2) Scientific Validity

Research must be conducted with an appropriate methodology to ensure that the results will answer the original research questions

- **Invalid research:**
  - underpowered studies
  - studies with inappropriate endpoints or statistical tests
  - studies that cannot enroll sufficient subjects

- Justification of validity as an ethical requirement
  - Waste resources
  - Cannot justify exposing subjects to burdens or risks

(3) Fair subject Selection (Equitable Selection of Subjects)

- Selection of subjects is equitable
- Convenient (vulnerable) groups should not be targeted.
- Higher risk is a reason to exclude certain groups.

- REC should take into account:
  - Purposes of the research
  - Setting of the research
  - Special problems of individuals vulnerable to coercion or undue influence

Equitable Selection

What issues are we looking for in protocols?

- Inclusion/exclusion criteria
- Recruitment methods

(4) Favorable Risk-Benefit Ratio

- Risks are identified
- Risks are minimized
- Potential benefits enhanced
- Risks are reasonable to potential benefits to subject and society

Favorable Risk-Benefit Analysis

RISK OF HARMS
Participants

POTENTIAL BENEFITS
Participants + Society

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Minimization of Risk
What are procedures to minimize risk?

- Substitute invasive procedures with less invasive
- Use qualified personnel
- Necessary infrastructure to handle emergencies
- Exclusion criteria to prevent enrolling subjects at higher risks
- Monitoring
- Avoid conflicts of interest

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(5) Independent Review

- Investigators have multiple legitimate interests
  - Promote research to advance health of society
  - Protect subjects' welfare
  - Potential conflicts of interests
- Independent review
  - Free from institutional, political, financial influences
  - Competent review
- Research ethics committees (RECs)

(6) Informed Consent

- Informed consent will be sought from each prospective subject or the subject's legally authorized representative

Informed Consent

- Informed consent ensures that individuals themselves decide:
  - whether to enroll in research and
  - whether research fits with their own values, interests, and goals.
- Research on individuals who cannot decide requires surrogate consent
  - children and mentally impaired

Informed Consent Requirements

- ***Disclosure of Information***
- ***Comprehension***
  - ***Decision Making Ability***
- ***Voluntariness***

(7) Respect for Enrolled Subjects

- The ethical requirements of research do not end with a signed consent document.

- Respecting enrolled subjects includes:
  - Permitting withdrawal
  - Protecting confidentiality
  - Monitoring welfare throughout the study

Privacy and Confidentiality

- When appropriate, there are adequate provisions to protect the *privacy of subjects* and to maintain the *confidentiality of data*.

(8) Community Partnership

To be ethical clinical research must involve the community in which it occurs.

- Community participation in planning, conducting and overseeing research and integrating results into the health system
- Knowing perspectives of individuals who will participate in research

Survey Research

Roles of these ethical requirements

- **These guidelines are meant to guide the ethical developmnt, implementation, and review of individual clinical protocols.**
- **They intended to elucidate the ethical standars specific for clinical research and assume general ethical obligations, such as intellectual honesty and responsibilty.**
- **These requirements are not limited to a specific tragedy or scandal or to the practices of researchers in 1 country; they are meant to be *universal* , although their application will require *adaptation to particular cultures, health conditions,* and *economic settings*.**

THANK YOU

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