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Online Ethics Course

Topic 8: Research governance and protocols for the protection of human subjects

Intended learning outcomes

After completing the topic, learners should be able to:

1. Understand basic principles of research governance, including ethical and legal requirements for studies that involve human subjects
2. Describe how best to protect participants' best interests in research involving human subjects

Biomedical research

- Biomedical research is the broad area of science that involves the investigation of biological processes and causes of disease through experimentation, observation, laboratory analysis and testing
- Clinical trials are conducted in order to find specific answers to specific questions using human subjects / volunteers

Types of clinical trials

- **Phase I** clinical trials are done to test a new biomedical intervention in a small group of people (e.g., 20-80) for the first time to try and evaluate safety (i.e., to determine safe dosage range and identify possible side-effects)

- **Phase II** clinical trials are done to study the biomedical or behavioural intervention in a larger group of people (several hundred) to determine efficacy and further evaluate safety

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- **Phase III** studies are done to study the efficacy of the biomedical or behavioural intervention in large groups of human subjects (several hundred to several thousand), comparing the intervention to other standard or experimental interventions as well as monitor adverse effects and collect information that will allow the intervention to be used safely

- **Phase IV** studies are done after the intervention has been marketed to monitor effectiveness of the approved intervention in the general population and collect information about any adverse effects associated with widespread use

Bioethics in medicine

- *Bioethics* is concerned with moral dimensions of the life sciences, including but not limited to medicine and health care; [Note, the term has not been widely used in this course because it is very broad and has no single definition; however, it is frequently applied in the context of biomedical research]
- *Medical Ethics* is the more precise term, usage dating back to the code of Hammurabi (Mesopotamia, 2030 BC); the Hippocratic Oath (Greece, 4th century BC), and the Susrut Samhita (ancient Sanskrit Ayurvedic)

Historical background

- Moses Maimonides (1135–1204), called upon doctors not to treat patients as a means to an end to learn new truths
- The scope was widened with development of Kantian Philosophy and the concept of categorical imperatives; Kantian Philosophy upholds the absolute right of humans to 'decide to be left alone'
- Means vs ends is at the root of much ethical debate around research – *who takes what risk (for what associated burden) and for whose benefit*

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- Introduction of rules and regulations governing research protocols mostly date from post-WW2
- The horrors of Nazi Germany, exposed during the Nuremberg trials of 1948, led the way to the development of internationally agreed standards (the *Nuremberg Code*)
- The first *Helsinki Declaration of the World Medical Association* followed in 1964 and has been regularly updated since; 2013 edition see: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

Helsinki Declaration

Recent changes to the document include:

1. *The distinction between therapeutic and non-therapeutic research being removed; Article 16 spells out the ethical principles that apply to healthy volunteers, with all others referred to as human subjects*
2. *The scope of ethical review by ethical committees was expanded to include human material and data*
3. *The concept of publication ethics was expanded to include the necessity of disclosing conflict of interest (Articles 14 and 30)*

Universal Declaration on Bioethics and Human Rights

Adopted by UNESCO in 2005, the declaration seeks to

1. *Provide a universal framework of principles and procedures to guide States in the formulation of their legislation, policies or other instruments in the field of bioethics*
2. *Promote respect for human dignity and protect human rights … consistent with international human rights law*
3. *Recognize the importance of freedom of scientific research*

https://unesdoc.unesco.org/ark:/48223/pf0000146180_eng

Cont.

Principles:

- *Respect for human dignity and human rights*
- *Maximization of benefit and minimization of harm*
- *Respect for autonomy and individual responsibility*
- *Necessity of carrying out medical intervention and scientific research only with the prior, free, and informed consent of the persons concerned; and respect for privacy and confidentiality*
- *Establishment of independent ethics committees*

Good Clinical Practice Guidelines

- The WHO published the *Handbook for Good Clinical Research Practice*, 2005 to promote international standards of conformity
- Guidelines such as the EU *Medicines for Human Use (Clinical Trials) Regulations,* 2004 seek to ensure harmonisation across the European Union
- *Indian Council of Medical Research* issued *Ethical Guidelines for Biomedical Research on Human Subjects* in 2001

Cont.

- The extent to which these protocols are followed is sometimes a matter of debate, especially in the developing world; (e.g., recent intervention by the Supreme Court of India about failures in compliance with international codes of practice)

  [URLs to various documents to be found under *Reading Suggestions*

National vs international

- Most governance frameworks are based on international guidelines and law; however, they have to be applied in context and interpreted according to the laws of the country to which they apply
- According to UNESCO, each country should have a national committee for bioethics with governance arrangements for conducting clinical trials
- Ethical guidelines protect human subjects, but they should not be a barrier to good research; in order to be effective, they need to be well-drafted, intelligently applied and upheld, including sanctions for unjustified breaches

Case example

In 2003, *Johnson & Johnson* began a placebo controlled trial to see if *Reperidone* was appropriate for acute mania

- Issues :
  - –Allegations that the informed consent obtained was not informed at all
  - –Recognized drugs were available for treatment of mania; placebo controlled trial was justified , and most patients were taken off their original drug before being inducted into the trial. However, no records were kept on why investigators felt that patients would be better in a trial with a placebo arm rather than staying on their original drug
- Lessons - Patient well-being must be respected when conducting clinical research

Reading suggestions

http://grants.nih.gov/grants/policy/hs/glossary.htm

http://unesdoc.unesco.org/images/0014/001461/146180e.pdf

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0068666

http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html

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