ETHICAL ISSUES IN MEDICAL RESEARCH

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11th MOH-AMM Scientific Meeting (Incorporating the 18th NIH Scientific and Annual National Ethics Seminar)
13th August 2015
• Research on Human Subjects
• Autonomy and Informed Consent
• Social Justice
• Vulnerability and Exploitation
• Responsible Conduct of Research
• Conflict of Interest and Disclosure
• World Health Organisation Call for Disclosure
• Codes and Guidelines on Ethical Conduct of Research
• Medical Research and Ethics Committee Malaysia
Ethical issues need to be addressed when research involving human subjects is conducted. Human subjects are “living individuals about whom an investigator conducting research obtains:

• data through intervention or interaction with the individual
• identifiable private information”

Ethics is based on laws and regulations and societal norms.
“Prior ethical review is required if research activity involves human beings through:
• taking part in surveys, interviews or focus groups;
• undergoing psychological, physiological or medical testing or treatment;
• being observed by researchers;
• researchers having access to their personal documents or other materials;
• the collection and use of their body organs, tissues or fluids (e.g. skin, blood, urine, saliva, hair, bones, tumour and other biopsy specimens) or their exhaled breath;
• accessing their information (in individually identifiable, re-identifiable or non-identifiable form) as part of an existing published or unpublished source or database.”

• Researchers must have respect for persons. Researchers must recognise that study subjects have the autonomy and right to decide on whether they wish to participate or not participate in the research. Autonomy ensured by requiring informed consent.

• Informed consent must be obtained from study subjects and recorded.

• Requirements for obtaining informed consent include the subject:
  – is competent to understand and make decisions.
  – is informed on the research including risks associated with participation in the research.
  – volunteers to participate in the study.
• Researchers must follow principles of social justice.
• Researchers have to be just and fair when requesting for resources in conducting research or allocating resources for research.
• Researchers must be sensitive to cultural differences.
• Researchers must prevent exploitation and protect vulnerable groups.
• Special ethical considerations need to be addressed when study subjects belong to vulnerable groups e.g. children, prisoners and students.
Vulnerable groups

• A person’s susceptibility to inducement or coercion, or to harm, loss or indignity makes him/her vulnerable. This could be because of undue inducement, undue profit, exploitation.

• Vulnerable groups may not really be coerced, but feel constrained by the situation, whether illness, lack of food or shelter.
  • “I felt I had no other choice.”

• …between 50-100% of research subjects who are healthy volunteers self-report that financial need or financial reward is their primary motive for volunteering. *Tishler & Bartholomae, (2002)*

• Research misconduct - behaviours at odds with the core principles of science.

• To be considered research misconduct, actions must represent a “significant departure from accepted practices,” must have been “committed intentionally, or knowingly, or recklessly,” and must be “proven by a preponderance of evidence.” “Research misconduct does not include differences of opinion.”

• Those who are engaged in research misconduct put their scientific career at risk and threaten the overall reputation of science and the health and welfare of the intended beneficiaries of research.

• Protection of human participants is one of the areas addressed in responsible conduct of research.
U.S. Office of Science and Technology Policy defines misconduct as “fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.”

• Fabrication is “making up data or results.”

• Falsification is “manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.”

• Plagiarism is “the appropriation of another person’s ideas, processes, results, or words without giving appropriate credit.”

• Other institutions include “abuse of confidentiality in peer review and failure to allocate credit appropriately in scientific publications”
• Researchers may have conflict of interest when conducting research.
• Disclosure of conflict of interest increasingly being requested.
• Presenters at medical conferences need to disclose a financial relationship with a commercial interest whose products or services are presented.
• Authors of scientific papers need to disclose a financial relationship with a commercial interest whose products or services are presented.
• Conflict of interest may occur when representatives of industry, government and other interested stakeholders are involved in research.
• Conflict of interest may occur when findings are inconsistent with their organization's policies.

• Publication of findings may be blocked from publication at the insistence of a co-author.

• Conflict of interest can be addressed by agreement among co-researchers on overall goals and vision of the research project, who will do what, authorship, credit and responsibility, contingencies, communication and team members revealing real or perceived conflicts of interest.

14 April 2015 : WHO has called for increased transparency in research. Public statement issued calling for the disclosure of results from clinical trials for medical products, whatever the result.

Dr Marie-Paule Kieny: “Our intention is to promote the sharing of scientific knowledge in order to advance public health,” “It underpins the principal goal of medical research: to serve the betterment of humanity”. “Failure to publicly disclose trial results engenders misinformation, leading to skewed priorities for both R&D and public health interventions.” “It creates indirect costs for public and private entities, including patients themselves, who pay for suboptimal or harmful treatments.”

Unreported trials lead to misinformation

*Jasarevic T. and Bagozzi D. (2015)*
WHO’s call for disclosure includes older unreported clinical trials, the results of which may still have an important bearing on scientific research today.

WHO also reaffirms the need for all clinical trials to be registered on a WHO primary clinical trial registry so that they can be accessible through the International Clinical Trials Registry platform.

This will ensure transparency as to which clinical trials have occurred, and allow verification of compliance with public disclosure requirements.

WHO public statement expands a 2005 call for all clinical trials to be registered.

International Clinical Trials Registry Platform is expected to further transparency
Lisa A. Bero, Robert M. Krughoff, and George Loewenstein

• “Disclosure of financial relationships or conflicts of interest - would be greatly improved if they explicitly called for more extensive and standardized public disclosure by researchers, physicians, and senior officials of institutions”.

• Standardised public disclosure would require standardized content, formats, and procedures for disclosure to institutions and a secure national online database system.

• Standardised public disclosure would require any information on financial relationships or conflicts of interest that is institutions be made available to the public through the online system.
Convey: The Solution to a Fragmented and Burdensome Process


- Convey – new secure online system developed to address a recommendation from the 2009 Institute of Medicine report Conflict of Interest in Medical Research, Education, and Practice to develop a centralized repository for disclosing financial interests.
- Convey – designed to reduce the amount of time physicians, researchers, and scientists spend making required disclosures of financial interests.
- Convey expected to simplify the process of disclosing required information by providing a repository for individuals to enter and maintain records of their financial interests.
Codes and Guidelines on Ethical Conduct of Research

- Nuremberg Code (1947)
- Declaration of Helsinki (1964) - World Medical Association (latest version 2013)
- Belmont Report (1979)
- CIOMS/WHO International Ethical Guidelines for Biomedical Research Involving Human Subjects
- WHO Operational Guidelines for Ethics Committees that review Biomedical Research (200??)
- ICH/WHO Guidance on Good Clinical Practice
- Guidance on GCP for Trails on Pharmaceutical Products
Comparison of International Guidelines for Research Involving Humans


- “Independent review by IRB and/or Ethics Committee
- Favourable risk benefit ratio
- Scientific validity and social value
- Informed consent including special populations
- Justice and the fair selection of study participants, respect for recruited participants and study communities
- Data and safety monitoring
- Quality assurance and quality control
- Standard of care for control groups, provision of new product or best treatment upon conclusion of the study
- Requirements regarding trial registration, control group treatment, privacy and confidentiality of personal data”
The Declaration of Helsinki, first developed by the World Medical Association in 1964 and the latest version in 2013, is a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

“Main ethical principle in this declaration is that medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.”
• In Malaysia, the Medical and Research Ethics Committee (MREC) of the Ministry of Health is guided by the ethical principles expressed in the Declaration of Helsinki (2013).

• The MREC also makes reference to the National and International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS), and the Belmont Report.

• The MREC establishes its own standard operating procedures based on the Operational Guidelines for Ethics Committees that Review Biomedical Research (WHO), ICH as well as Malaysian Guidelines for Good Clinical Practice.
• MREC ensures research conducted in the Ministry of Health conforms to international scientific and ethical standards
• Ensures Ministry of Health policies are followed when research is conducted in MOH facilities and by MOH staff
• Membership of MREC: Clinicians, Public Health specialists, researchers, NIH Directors, representative of Academy of Medicine Malaysia, lay persons.
• Meets twice a month and Principle investigator presents research proposal
• Research registered in the National Medical Research Register
• Researchers need to be continuously reminded of ethical issues in medical research.

• Mechanisms to address ethical issues need to be in place and be given as much priority as is given to the research questions and projects.

• Responsible conduct of research is key for research to progress and contribute to scientific knowledge.