HEALTH RESEARCH ETHICS

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WHAT IS ETHICS?

- Ethics is a derivative or subset of morality, which is one of the main branches of philosophy
- Other subsets of morality are political philosophy, jurisprudence or philosophy of law, civics, ethos, etc.

WHAT IS MORAL PHILOSOPHY?

- Critical reflection on what is right/wrong, good/bad, in human conduct, actions, behaviour etc
- Ethics and politics are important derivatives/ subsets of morality; along with law they are the highly discursive aspects of morality, aimed at laying down principles, guidelines, regulations and rules of action/conduct
- Biomedical research ethics strives to lay down principles and guidelines for morally acceptable research involving humans

FUNDAMENTAL PRINCIPLES OF ETHICS

- Four fundamental principles of ethics have usually been recognized and widely discussed in moral literature.
- These principles are: autonomy, beneficence, non-maleficence and justice
- These principles have to do with respect for all other humans as moral equals, making sure that our actions are well-intended/motivated and calculated to achieve good ends or results, avoiding the infliction of harm, and treating others with fairness and equity

AUTONOMY (Self Rule/governance)

- Autonomy implies an individual who is master of himself/herself and can act, make free choices and take decisions without the constraint of another
- The necessary pre-conditions of autonomy are competence (the capacity to be a moral agent) and liberty or freedom
- Individual autonomy may be diminished or completely absent, as in the case of minor children, mentally handicapped or incapacitated persons, prisoners, etc.
- Autonomy is based on the moral imperative of respect for other human persons as moral equals

JUSTICE (I)

- Justice is *fairness* or *entitlement;* it implies giving to each his/her due
- Justice requires that "equals be treated equally and un-equals unequally"
- What this means is that human beings as moral equals should be treated equally unless there is a reasonable justification for treating them differently.
- The general moral idea underlying the principle of justice is that which states: *"Do unto others as you would have them do unto you if you were in their place and they in yours"*

JUSTICE (II)

- In medical research the principle of justice demands fairness in the treatment of individuals and communities and the equitable distribution of the burdens and benefits of research.
- This has important implications for such issues as choice of study population, recruitment into study, during and post-study benefits, etc.

BENEFICENCE AND NON-MALEFICENCE

- In medical research ethics, the principles of beneficence and non-maleficence translate into the duties to **maximize benefits** while **minimizing harms**, especially for the research participants.
- That medicine aims at achieving good/benefits (beneficence) goes without saying but non-maleficence has been further emphasized and enshrined in the medical slogan "*primum non nocere*" (above all/first do no harm!)

BENEFICENCE AND NON-MALEFICENCE…

- Generally, research, like other human activities, to be ethical, must aim at achieving good while avoiding harm.
- Non-maleficence is considered to be the most basic of all the cardinal principles of ethics; it lays down the least minimum condition for ethical correctness, as if to say: "even if you would not do good, at least do no harm"

WHY HEALTH RESEARCH ETHICS?

- Mankind is plagued with a heavy disease burden which is widely geographically distributed.
- Research is fundamental in providing information or evidence that will be used in reducing the disease burden.
- However, there is need to regulate the conduct of these studies in order to protect all stakeholders: **Researcher, study participants and sponsors or funding agency**.

CLASSICAL EXAMPLES OF ABUSES OF HUMAN RIGHTS IN HEALTH RESEARCH EXIST IN HISTORY

Abscesses (boils) caused by cowpox on a milkmaid's hand

- Jenner Innoculated cowpox virus to protect against smallpox
- Cowpox virus protective against smallpox virus
- Vaccination: '*vaca*' Latin word for 'cow'
- Today can we try something in humans like Jenner did?

•http://www.countway.harvard.edu/rarebooks/exhibits/waterhouse/index.html

PROBLEM WITH HUMAN SUBJECT EXPERIMENTATION (1):
1900 Prussian Directive

- Dr. Neisser studied immunization of health persons against syphilis by inoculating them with serum from syphilitic patients.
- 3 prostitutes inoculated; all contracted syphilis.
- No consent obtained.

PROBLEMS WITH HUMAN SUBJECT EXPERIMENTATION (2):
Nazi Germany (1)

- Dr. Mengele's Experiments:
- Infected one twin with a "germ". When he died, the other twin was killed and their organs compared at autopsy.
- Sewed twins together to create a Siamese twin.
- Studied subjects with genetic traits so as to better "purify the Aryan super race".
- Performed cross transfusions to "make boys into girls and girls into boys".

NAZI GERMANY MILITARY EXPERIMENTS(1)

Involved 200 Jews, 50 gypsies, 500 Poles, and 1,000 Russians: war prisoners or concentration camp inmates:

- High-altitude (low-pressure) experiments: put prisoners in low-pressure tanks, how long could survive with little oxygen, autopsies followed;
- Freezing exp.: force prisoners to remain outdoors, naked, freezing, 9-14 hrs; or put in freezing water 3hrs; try re-warming bodies;
- Malaria exp.: infect prisoners, give drugs, many died;
- Typhus exp. Inject prisoners with antityphus "vaccine". Then infect with typhus; controls infect with typhus no treatment;

NAZI GERMAN MIL. EXPT(2)

- Mustard Gas Expt: inhale mg; try various treatments;
- Sulfanilamide expt: inflict wounds, apply bacteria,etc to wound; control group: wound then infect, no sulfanilamide;
- Poison expt: feed patients various poisons, many died; kill survivors for autopsy;
- Sterilization experiment: use chemicals or x-rays instead of surgery.
- ETC. ETC.

POST WAR RESPONSE (1)
"The Case Against the Nazi Physicians"

***Nuremberg Doctors' Trial – 1946 –47**

23 defendants; 3 non-physicians

15 found guilty

7 were hanged (4 physicians)

5 sentenced to life in prison

4 sentenced to 10-20 years in prison

7 were acquitted and freed.

***Separate Trial:**

31 "underlings" were also found guilty; 22 of them were hanged.

POST WAR RESPONSE (2)

Nuremberg Code of Medical Ethics (1948)

- **Adopted by the World Medical Association '64**
- **True voluntary consent; freely given; prior to experimental procedures**
- **Truly necessary, well thought out experiments in which the expected benefits justify the risks and there is no unnecessary psychical or mental suffering or injury.**

INTERNATIONAL ACCEPTANCE OF THE NUREMBERG CODE *WMA:

- **Helsinki Declaration (1964)**
  - Praised the code
  - Rejected it for widespread use
  - Modified the code
- **Further modifications (1975,1983, 1989, 1996, 2002)**
- **Clarification Para 29, 2002.**

Tuskegee Study

- **Study participants poor and illiterate; most had never seen a doctor before**
- **Free physical examination**
- **Free transport to the clinic**
- **Hot meals on exam days**
- **Free treatment for minor ailments**
- **Burial stipend**
- **Nurse Rivers – tracked participants/patients**
- **Press later labeled it "racial medicine";**
- **Late 1970s US Gov compensation authorized;1997 Pres. Clinton apologized.**

LEADING ETHICS GUIDELINES:

- Belmont Report (1979)
- Declaration of Helsinki, 2000 (www.wma.net)
- CIOMS (2002) Interational Ethical Guidelines for Biomedical Research Involving Human Subjects (www.codex.uu.se/texts/international.html)
- CIOMS (2008) Internatinal Ethical Guidelines for Epidemiological Studies. Provisional Text <http:www.cioms.ch/080221Feb 2008.pdf>
- ICH GCP Guidelines 1996 (www.ifpma.org)

OTHER SOURCES

- National Bioethics Advisory Commission (www.bioethics.georgetown.edu/nbac/human/overvol1/html).
- Nuffield Council on Bioethics (www.nuffieldbioethics.org/filelibrary/pdf/errhdc-fullreport.pdf).
- WHO/TDR Operational Guidelines for Ethics Committees that Review Biomedical Research (2000).
- What African codes/guidelines? AfroGuide

ABUSE OF HUMAN RESEARCH PARTICIPANTS IN AFRICA (1)... SOUTH AFRICA CABINET, 1985: PW BOTHA

"...I wish to announce a number of new strategies that should be put to use to destroy this Black bug. We should now make use of the chemical weapon. **Priority number one**, we should not by all means allow any more increases of the Black population lest we be choked very soon. I have exciting news that our scientists have come with an efficient stuff. I am sending out more researchers to the field to identify as many venues as possible where the **chemical weapons could be employed to combat any further population increases**. The hospital is a very strategic opening, for example and should be fully utilized. The food supply channel should be used. We have developed excellent **slow killing poisons and fertility destroyers**..."

TROVAN TRIAL IN NIGERIA

- Pfizer tested a new drug Trovan on 200 children in Kano, Nigeria in the middle of a meningitis epidemic;
- Govt approval/clearance not obtained;
- Informed consent from parents not obtained, not told could withdraw;
- 11 children died, many others injured;
- Control group received low doses of an effective drug, some in control group died.

OTHER RECENT ABUSES IN AFRICA

- Tenefovir Trial in Cameroon
- HIV vaccine trial U. Nairobi/Oxford U./community sex workers

ARE ABUSES IN AFRICA LIMITED TO TRIALS?

- Removal of eyes from cadavers in Malawi
- HIV infections in Libya
- Unnecessary delays in implementing research results
- Research on orphans, Nairobi,
- ETC, ETC

NEED TO DOCUMENT AND PREVENT ABUSES IN AFRICA

Ethical Considerations in the Design of Health Research Projects

- For research to be ethically acceptable, it should meet some basic minimum standards which is a basis for its evaluation.
- The research should be scientifically and ethically sound (hypothesis driven with clear objectives, powered sample size, data analysis plan etc.)

Ethical issues

During design of a research project, many ethical questions do arise and these include:

- A rigorous research protocol (SOPs)
- Value of the research to the scientific and research community.
- Risk/benefit analysis of the project
- Selection of research participants
- Informed consent
- Ethical review

Favorable risk-benefit ratio…

For a research project to be ethically acceptable, it should have a favorable risk/benefit ratio to the individual research participant and to society generally in terms of the knowledge that will be gained from the research project.

IRCs should undertake a systematic analysis of the risks and benefits of a research project to individual research participants and society; and ascertain that the anticipated benefits justify the risks

…..RISK/BENEFIT RATIO

- Risks may include psychological, mental, social, physical, economic harms etc.
- Benefits may include such aspects as medical care and free treatment. Is giving food items or money benefit or an inducement?
- In balancing these elements, the risks and benefits to the individual research participant will normally carry special weight

What do some ethical codes say about risks and benefits?

- Declaration of Helsinki point 17: research to be done only if **"….the risks involved have been adequately assessed and can be satisfactorily managed."**
- **"…cease any investigation if the risks are found to outweigh the potential benefits…."**

What do some ethical codes say about risks and benefits? (2)

- CIOMS guideline 8 (2002) stipulates that ".. the investigator must ensure that potential benefits and risks are reasonably balanced and risks are minimized"
- Guideline 9: emphasises extra caution when dealing with vulnerable people

Some specific factors to consider

POTENTIAL RISKS	POTENTIAL BENEFITS
A. To individual participants	
➢ Psychological trauma ➢ Stigmatization ➢ Side effects from treatment ➢ Undue Inducement ➢ Inconvenience ➢ Possibility of deviations from approved protocol ➢ Physical pain ➢ Wrong diagnosis	➢ Treatment ➢ Health care ➢ Information and education ➢ Monetary benefits ➢ Personal satisfaction

Some specific factors to consider 2

POTENTIAL RISKS	POTENTIAL BENEFITS
B. To community/population	
➢ Exploitation ➢ Stigmatization ➢ Over-researching ➢ Economic loss ➢ Negative change in value systems	➢ Health care ➢ Access to interventions ➢ Upgrading of infrastructure ➢ Community development ➢ Economic boost ➢ Positive change in value system

Some Specific Factors to Consider 3

POTENTIAL RISKS	POTENTIAL BENEFITS
C. To the Researchers/Institution	
➢ Credibility could be damaged ➢ Unsuccessful projects may affect reputation ➢ Hostile environment due to unethical research conducted by other researchers previously.	➢ Career development ➢ Monetary gain ➢ Personal satisfaction ➢ Institutional development

Health Research is Dynamic

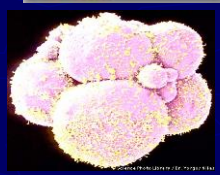
- Health research is always changing due to:
  - technological developments
  - socioeconomic factors
  - new diseases
- Consequently, ethical issues in health research in general and risks/benefits in particular are also dynamic and needs o be reviewed regularly

Dynamics of Health Research

NEW DISEASES AND TECHNOLOGY

Genetic Engineering
Vaccine Development
In-vitro Fertilization
Prenatal Diagnosis
Pre-implantation diagnosis
Cloning and embryo research
Stem cell Research
Genetically Modified Crops
Traditional Medicines

NEW RISKS AND BENEFITS



Committees in Health Research and Health care

1. Policy making and/ or advisory committee
2. Health professional association committee
3. Health care/hospital ethics committee
4. Research ethics committee

RESEARCH ETHICS COMMITTEE (IRB, EC, ERC)

Is a committee whose primary responsibility is to protect the rights and welfare of research participants and to function as a kind of regulatory committee focusing on what is right or wrong and what is desirable or undesirable?

It systematically and continually addresses ethical dimensions of health sciences, the life sciences, innovative health policies.

Who is on the IRB?

- Must have at least 5 members (Scientist, epidemiologist, ethicist, community representative, clergy, legal adviser – preferably family law) – ensure gender balance of members.
- If studies include vulnerable populations, the IRB should have members who are familiar with these groups.
- Members may not vote on their own projects.
- Only actual IRB members may vote (consultant may be used but can not vote).

Informed Consent

- Voluntary participation in a study after a detailed sensitization on the risks and benefit of the study.
- Informed Consent is a process
- Requires information sheet detailing research objectives, protocol, risk(s)/ benefit(s) and other issues.
- Must be signed by participant/guardian or next of kin and a witness .
- May involve several stages e.g in pregnancy, comatose patients or vulnerable groups.

Informed Consent

- The process in which a patient learns key facts about a research study and then voluntarily agrees to take part or decides against it.
- Informed consent must be documented by the use of a written consent form approved by the IRB for all clinical studies.
- Consent forms must be signed by the subject or the subject's legally authorized representative.
- A copy must be given to the person signing the form.

Consent Form Requirements

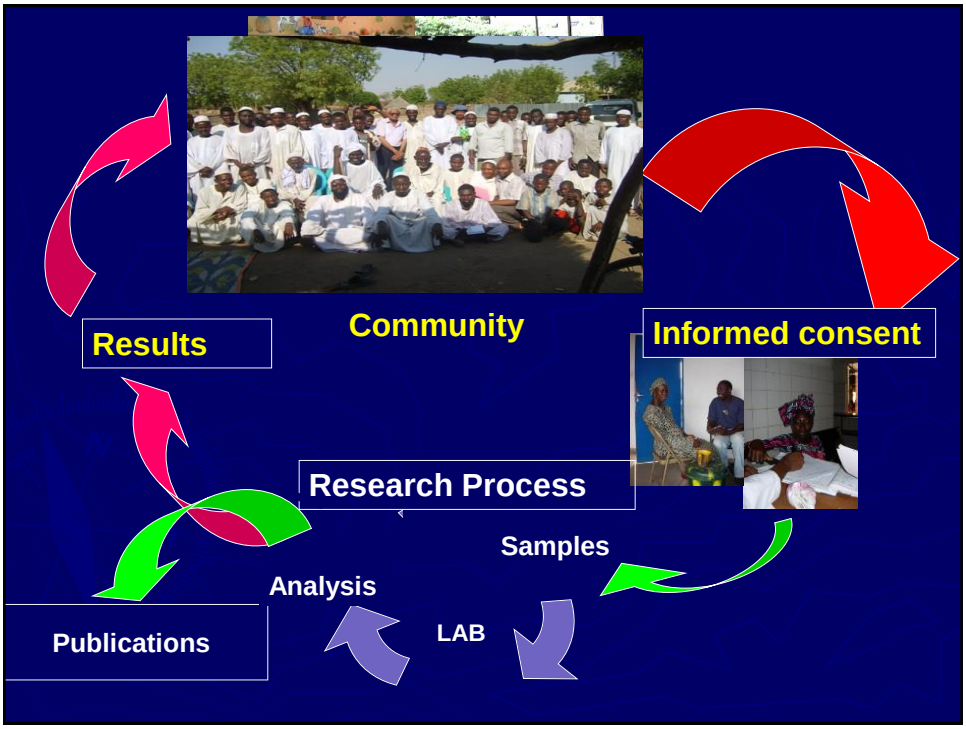
- The consent form MUST include the following information:
  - Statement that the study involves research
  - Explanation of the purposes
  - Expected duration of the subject's participation
  - Description of the procedures involved in the study
  - Identification of any procedures that are experimental
  - Risks or discomforts
  - Benefits
  - Alternatives to the research study
  - Statement of confidentiality
  - Statement about medical care and compensation should injury occur
  - Contact information for patients with concerns or questions
  - Statement that participation is voluntary and study withdrawal may take place at any time

Who obtains written informed consent?

- Principal Investigator

- Authorized Study Personnel
  - Registered nurse Aid (Enrolled Nurse)
  - Registered Nurse (SRN)
  - Research Coordinator / Designated Research Staff

- An IRB may waive the requirement for the investigator to obtain a signed consent form if…
  - The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context



What happens during and when the study is over?

- Ancillary care: provide or decline responsibility.
- Community benefit during the study
- When the study/trial is over who pays for example extended community benefit of intervention or product.
- How does the participant and community benefit from the research product/ deliverable?

Next Steps

- Need to keep reviewing/developing
  - Ethical guidelines
  - Legal frameworks
  - At national and international levels
- African countries should review/develop guidelines to reflect African perspectives and practicalities

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Thank You

Informed Consent ?