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ETHICAL CHALLENGES AND DILEMMAS OF RESEARCH IN THIRD WORLD COUNTRIES

By

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GLOBAL HEALTH: AN OVERVIEW

- **Medical knowledge has greatly grown and medicine has recorded remarkable achievements**
- **Evolution from culture-based art into a global science**
- **Victory over many formidable diseases**
- **Improvement in human health and longevity**
- **Enormous health resources exist in the world**
- **Thanks to the industrial and commercial revolutions**
- **Thanks to science & technology**

COUNTER-BALANCE TO MEDICAL PROGRESS

- **Medical malpractices**
- **Uneven global distribution of available medical resources**
- **Uneven inverse distribution of the global burden of disease**
- **The rise and spread of even deadlier diseases and epidemics than those previously conquered**
- **Negative role of monopoly commerce, big business and the profit motive**
- **Breakdown in traditional health systems**

GLOBAL BURDEN OF DISEASE

- Disease burden (DB) has become a privileged yardstick/indicator for health assessment, reform, policy development, planning, resource allocation, etc.
- Traditionally DB has been assessed using epidemiologic methods and statistics on morbidity and mortality
- Recently more accurate methods, such as DALY's (Disability Adjusted Life Years), have been used to quantify DB
- Quantifies the impact of premature death and disability
- Measures the outcome of specific health interventions
- Such methods allow a more objective assessment and appreciation of the DB of any given part of the globe

THE 10/90 GAP

- No matter the yardstick used, the global DB is heavily weighted against developing countries, particularly those of sub-Saharan Africa
- Here poverty and ill health form a vicious circle
- There is a glaring discrepancy between the availability of health research funding and the diseases responsible for the highest global DB
- This has been termed the “10/90 gap”: of an estimated US$ 73 billion invested (publicly and privately) in global health research annually, less than 10% goes to research into problems accounting for 90% of the global disease burden
- The Global Forum for Health Research has set itself the task of bridging this gap

AFRICA'S FORMIDABLE DISEASE BURDEN

- Communicable diseases, malnutrition, childhood diseases, maternal/perinatal problems, epidemics
- Despite significant improvement in child mortality, the rate is still 20x higher than in developed countries
- Despite significant reduction in maternal morbidity/mortality, 100x more African women die from pregnancy-related causes than in the developed world
- Despite improvement in life expectancy in the past two decades, it is still 10 years shorter than developing world average and 25 years shorter than developed world average
- Moreover, life expectancy is rapidly plummeting as a result of current epidemics, violence and other health/life threats

AFRICA: THE GLOBAL HQ OF THE HIV/AIDS PANDEMIC

- **Sub-Saharan Africa has about 10% of the world's population**
- **As of the end of 2003, about 53.7 million people living with HIV/AIDS world wide**
- **70% of these in sub-Saharan Africa alone**
- **Africa has the fastest rate of spread in the world**
- **Of the 4.8 million new cases of infection in 2003, 3 million were in sub-Saharan Africa**
- **Since outbreak of the epidemic, more than 17 million victims have died in Africa, 2.2 million in 2003 alone**

WHY SITUATION IS PARTICULARLY CRITICAL

- **High levels of generalized poverty**
- **Heavy burden of allied diseases: TB, Malaria, Typhoid, Meningitis, etc.**
- **Paucity of modern healthcare resources/facilities**
- **High levels of illiteracy and lack of awareness**
- **Difficulties in loco-motion and other forms of communication**
- **Lack of political will, political instability, conflicts, civil wars**
- **Resilient habits and practices harmful to health**
- **Hopelessness**

TRIPPLE VULNERABILITY OF DEVELOPING WORLD POPULATIONS

- **Vulnerability: "Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. …they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests. (Paragraph 1, Commentary on CIOMS 13)**
- **Vulnerability: Liability to be harmed, exploited, deceived or unfairly treated**

- **As members of economically disadvantaged groups (Helsinki #8, CIOMS 10 & 13)**
- **As members of medically disadvantaged groups – high burden of disease (Helsinki #8, CIOMS 13)**
- **As minors, increasingly used as research subjects (Helsinki #8, CIOMS 9 & 14)**
- **In Africa vulnerability equally applies to researchers, scientists, institutions, and even governments**

ETHICAL IMPERATIVES OF RESEARCH, ANYWHERE, ANY TIME

- **"…considerations related to the well-being of the human subject should take precedence over the interests of science and society (*Helsinki 5)***

- **No harm (*primum non nocere)***
- **No exploitation**
- **No deceit (Informed Consent)**
- **No cheating (justice and fairness)**

CHARACTERISTICS OF INDUSTRIALIZED WORLD MEDICAL RESEARCH

Market-oriented

Profit-driven

Susceptibility to morally blind economic forces

High degree of ad hoc rationalizations and ethical ‘justifications’

Examples:

Definition of death and personhood debate directly related to need for non-therapeutic abortion and harvest of human spare parts from the ‘dead’

Placebo-control studies debate (Helsinki/CIOMS) directly related to need for HIV/AIDS vaccine research

CHALLENGES OF DEVELOPED WORLD MEDICAL RESEARCH IN THE DEVELOPING WORLD

- Can commercial motives be combined with altruistic philanthropy?
- Can such research be non-exploitative?
- Can it avoid harming the vulnerable?
- Can it avoid applying double standards?
- Can it avoid undue-inducement?
- Can it apply the imperative of autonomy or respect for persons?
- Can it separate ethical imperatives from culture and ideology?
- Dilemma: to go or not to go?

NEED FOR CLEAR DISTINCTIONS AND EXPLANATIONS

- **Treatment or research? Or treatment combined with research?**
- **Scientific knowledge or art of treatment and healing?**
- **Business/commerce or altruistic philanthropy? Or business/commerce combined with philanthropy?**

HELSINKI 5, 29 & 30

- Intractable controversy has continued because of the difficulty in accepting the full implications of the above articles of Helsinki
- Other regulatory documents have tried to handle the controversial issues in various ways
- The CIOMS guidelines purport to interpret Helsinki and to indicate how its principles can be effectively applied in developing countries

CIOMS 11: Choice of control in clinical trials

- **As a general rule, research subjects in the control group of a trial of a diagnostic, therapeutic, or preventive intervention should receive an established effective intervention. In some circumstances it may be ethically acceptable to use an alternative comparator, such as a placebo or “no treatment”**
- **Placebo may be used:**
- **- when there is no established effective intervention;**
- **- when withholding an established effective intervention would expose subjects to, at most, temporary discomfort or delay in relief of symptoms;**
- **- when use of an established effective intervention as a comparator would not yield scientifically reliable results and use of placebo would not add any risk of serious or irreversible harm to the subjects.**

DECLARATION OF HELSINKI #5

- **In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.**

- **“Science and society invented by humans for humans, not vice versa”**

DECLARATION OF HELSINKI #29

- The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists

Note of Clarification Art. 29

- **Under pressure from powerful lobbyists, WMA published a highly ambiguous “ note of clarification”**
- **The note appears to allow use of placebo in certain cases outside of the “no other treatment available” arena**
- **It would seem to permit placebo so long as permanent damage is avoided and no more than transient discomfort is permitted**

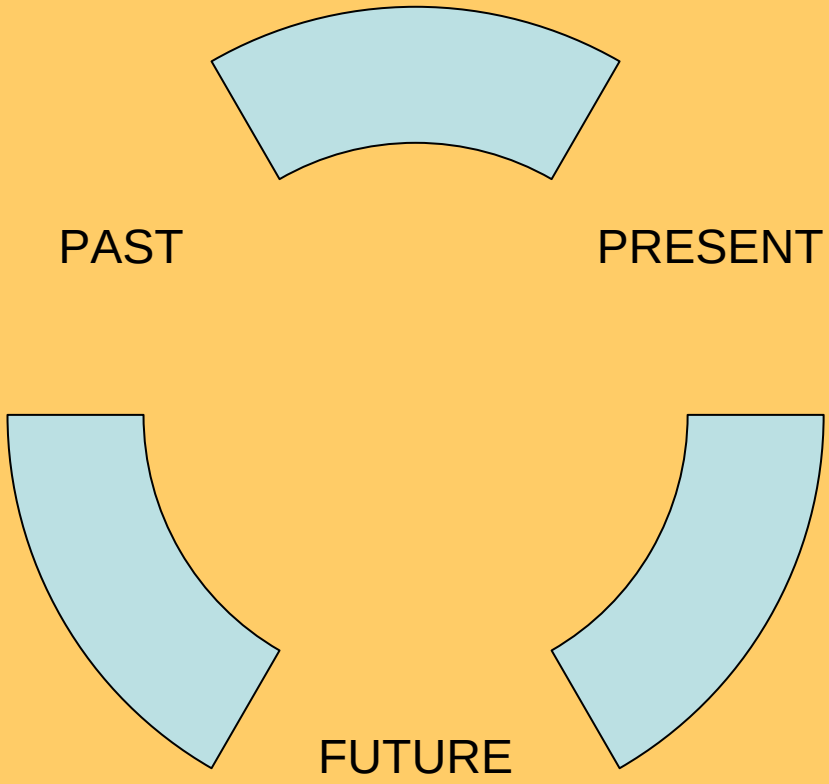
CIOMS 11 (Commentary): Exceptional use of comparator other than an established effective intervention

- **An exception to the general rule is applicable in some studies designed to develop a therapeutic, preventive or diagnostic intervention for use in a country or community in which an established effective intervention is not available and unlikely in the foreseeable future to become available, usually for economic or logistic reasons. …**

- **“Ethical reasons are the strongest that can be advanced for doing or refraining from doing anything and should not be set aside on the basis of economic, logistic, legal, political or pragmatic considerations”**

AN ANALOGY

- Can (should) a priest pronounce absolution for a sin before it is committed?



DECLARATION OF HELSINKI #30

- At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study

PROPOSED NOTE OF CLARIFICATION

- “This paragraph reflects the ethical principle that patients who take on the potential risks of a medical research study should, wherever possible, receive the benefits that result from the study. The WMA realises that certain conditions need to be fulfilled before the requirements in this paragraph can be fully realised, for example:

- i. *the study has identified a prophylactic, diagnostic or therapeutic method that is superior to other methods;*
- ii. *the results of the study are consistent with those of other studies of the same method;*

PROPOSED NOTE OF CLARIFICATION (CONTINUED)

- iii. *the method has been approved and authorized for use by the appropriate authorities;*
- *iv. the physician has determined that the method is appropriate for the patient.*

- *Before undertaking a study, the physician should make every effort to ensure that all patients entered into the study will have access to any available prophylactic, diagnostic or therapeutic method that the study proves to be the most effective and appropriate for such patient, once it has been authorized by the appropriate authorities. Any such arrangements, or the reasons for their absence, should be described in the study protocol (paragraph 13) that is submitted to the ethical review committee"*

PROPOSED AMENDED VERSION OF PARAGRAPH 30

- *“Before undertaking a study, the physician should make every effort to ensure that all patients entered into the study will have access to any available prophylactic, diagnostic or therapeutic method that the study proves to be the most effective and appropriate for such patients, once it has been approved by the appropriate authorities. When informing the patient about the study the physician will explain the treatment options after the study and how they relate to the patient’s condition and will state explicitly if it is foreseeable or likely that the sponsors will not be able to provide effective and appropriate treatment to the patient after he or she leaves the study. Any arrangements for the continuation of treatment beyond the study, or the reasons for their absence, should be described in the study protocol (paragraph 13) that is submitted to the ethical review committee”*

DOING WITHOUT HELSINKI?

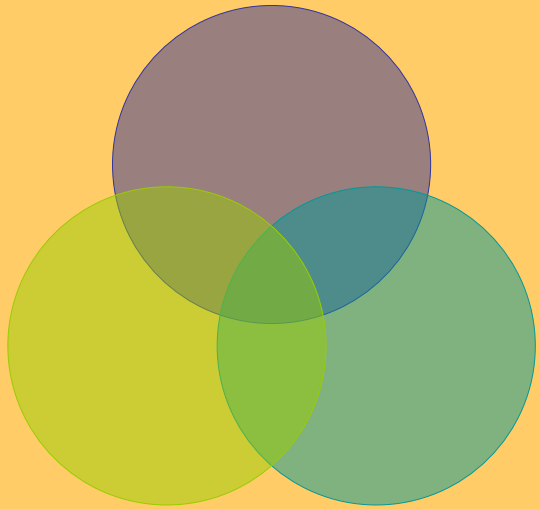
- Helsinki is the most internationally acknowledged and respected regulatory document
- Heretofore FDA regulations required compliance to the DoH and GCP for all studies under its jurisdiction
- Currently there is a proposal to remove mention of the DoH and make do with the GCP guidelines of the International Conference on Harmonization (ICH)
- Visit: http://www.citizen.org/publications/release.cfm?ID=7330

THE INDISPENSABLE NECESSARY PRECONDITIONS OF MEDICAL RESEARCH

- **Good science/scientific design**
- **Adequate resources/funding**
- **Well-informed, free and willing subjects**
- **The role of the third person of the above trinity has been generally undermined and undervalued**

Distributive Justice?

- **What about a well-informed contract between:**
- **Sponsor**
- **Investigator**
- **Subject**
- **???**



A SAFE ASSUMPTION

- **Until there is more convincing evidence to the contrary, it is safest to assume that many of the industrialized world researchers, sponsors of research and pharmaceutical companies presently rushing to the non-industrialized world to conduct sundry medical researches are doing so for the purpose of taking advantage of the prevailing 'favourable' situation, for their own benefit, and that the result, at the end of the action, will be greater and not less inequalities in global health.**

KISUMU DECLARATION?

- **MORAL INTERGRITY AND NOBLE INTENT DECLARATION**

- **We, the investigators, sponsors and funders of this study/research, hereby solemnly declare, on our honour, that our intentions in carrying out this research are noble and primarily motivated by the desire to acquire knowledge that could help in alleviating suffering and improving the lot of human beings, without any distinction or discrimination; that we have no overt or covert intention or any hidden agenda to harm, deceive, exploit or unfairly to treat, now or in the future, any human being or group of human beings. We solemnly pledge that, in carrying out this research, we will maintain the utmost respect for all participants and experimental subjects and objects, including any plants and animals. We will do everything within our powers to prevent knowledge gained through this research from being abused or used in ways contrary to the above solemnly declared aims and intentions.**