The Concept of Exploitation in Medical and Health Related Research Ethics:

Literature Analysis

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Abstract

Increased International collaborative research activities in poor and low-income countries have several unique claims on our attention. First, the idea of involving human beings in research, putting forward participants openly to trials presents a novel experiment in which various academic disciplines can play in order to enhance fair studies. Second, apart from the need to conduct research in medical and health related areas, there have been many ethical challenges including the necessity to prevent harm among research participants and to ensure that they receive a fair share of benefits from research results.

Despite existence of ethical guidelines and declarations, potential research participants from poor and low-income countries in particular, still risk exploitation due to limited health care access, and little awareness of research on human beings. It is, therefore, necessary for us to examine the main features of this system, which provides the framework within which research activities are done; in order to find out if and how research ethics can be used to enhance fair studies.

This thesis has attempted to provide a careful assessment of current debates on exploitation in medical and health related research ethics, with special emphasis on the different revisions of the declaration of Helsinki - and other relevant international declarations and ethical guidelines through literature analysis; to investigate the concept of exploitation among vulnerable groups in poor and low income populations. Empirical case studies including informal discussions with existing research ethics committee members were sought from Tanzania.

Analysed literature findings reveal that the concept of exploitation has been expressed in various ways. New forms of exploitation in medical and health related research ethics include the use of placebo and the modification of the concept of benefit to include forms of benefit not directly related to trials under consideration. There are strong urges to abandon the current revision of declaration of Helsinki and adopt the Universal Declaration on Bioethics and Human Rights (UDBHR), as the viable guideline in medical and health related research ethical requirements. The need to establish a coalition between member states regional wise is proposed as a desirable option in order to see to it that the UDBHR is implemented.

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Acronyms and Abbreviations

ART	Anti-Retroviral Treatment
ARV	Anti-Retro Viral
CAB's	Community Advisory Boards
CDC	Centre for Disease Control
CIOMS	Council of International Organization of Medical Sciences
COSTECH	Commission for Science and Technology
CPIH	Commission on Intellectual Property Rights, Innovation and Public Health
DMF	Dimethylformamide
DRC	Democratic Republic of Congo
FBI	Federal Bureau of Investigation
FedEx	Federal Express
GBD	Global Burden of Disease
GFHR	Global Forum for Health Research
HeLa	Henrietta Lacks
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
IRB's	Institutional Review Boards
KACA	Kilimanjaro Aids Control Centre
MACE	Mutually Advantageous and Consensual Exploitation
NCoB	Nuffield Council on Bioethics
NGO's	Non-Government Organizations
NIH	National Institutes of Health
NIMR	National Institute of Medical Research

REC's	Research Ethics Committees
TACAIDS	Tanzania Commission for AIDS
TFDA	Tanzania Food and Drugs Authority
TREDO	Tanzania Rural Education and Development Organization
UDBHR	Universal Declaration of Bioethics and Human Rights
UNESCO	United Nations Educational Scientific and Cultural Organization
URT	United Republic of Tanzania
USA	United States of America
WHO	World Health Organization
WMA	World Medical Association

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The Concept of Exploitation in Medical and Health Related Research Ethics: Literature Analysis

Background / Summary

Increased international collaborative research activities in poor and low-income countries have several unique claims on our attention. First, the idea of involving human beings in research, putting forward participants openly to trials presents a novel experiment in which various academic disciplines can play a role in order to enhance fair studies. Second, apart from the need to conduct research in medical and health related areas, there are many ethical challenges including the necessity to prevent harm among research participants and to ensure that they receive a fair share of benefits from research results. Despite the existence of ethical guidelines and declarations, potential research participants from poor and low-income countries in particular, still risk exploitation due to limited access to health care and little awareness of research on human beings. It is, therefore, necessary for us to examine the main features of this system, which provides the framework within which research activities are done; in order to find out if and how research ethics can be used to enhance fair studies.

This study aims at providing a careful analysis and assessment of current debates on exploitation in medical and health related research ethics, with special emphasis on the different revisions of the declaration of Helsinki - and other relevant international declarations and ethical guidelines. In particular I aim at investigating how the latest revisions of international declarations and guidelines in medical and health related research may have diluted the ethical requirements in terms of opening up a "loop hole" for exploitation of vulnerable groups in poor and low income countries.

Controversial issues include: The revision of the use of placebo and the modification of the concept of benefit to include forms of benefit not directly related to the trial under consideration.

Specific Issues:

- The concept of benefit in the literature on medical and health related research ethics

- The modification of the concept of benefit in revised declarations

- The concept of exploitation in the literature on medical and health related research ethics

Analysis:

1. Analysis of current theoretical conceptions of benefit and exploitation employed in the literature on international clinical research ethics.

2. Analysis of empirical studies addressing the issue of globalization of clinical research and the issue of exploitation[1].

Summary of Chapters:

Chapter 1: Ethical theories on Exploitation

This chapter provides an analysis of ethical theories on exploitation with particular emphasis on the following issues:

a) Different conceptions of exploitation in the literature on medical and health related research ethics.

b) Current forms of consensus regarding the concept of exploitation - what do different scholars agree and disagree on.

c) Forms of exploitation prevalent in medical and health related research, and

[1] Petryna, A. 2007. Clinical trials offshored: On private sector science and public health. *BioSocieties* 2: 21-40.
Glickman SW, McHutchison J, etal. Ethical and Scientific Implications of the Globalization of Clinical Research. New Eng J Med 2009, 360, 8:816-823.
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Ballantyne A (2010) How to Do Research Fairly in an Unjust World. American Journal of Bioethics; 10(6):26-35Volnei Garrafa, Jan Helge Solbakk, Susana Vidal , Claudio Lorenzo Between the needy and the greedy: The quest for a just and fair ethics of clinical research. Journal of Medical Ethics 2010; 36:500-504, doi:10.1136/jme.2009.032656.

d) Based on the analysis of different conceptions and forms of exploitation, to assess the possibility of suggesting more sustainable concepts.

Chapter 2: Development of the Concept of Benefit in Research Ethics

A critical analysis of the concept of benefit and its development with special emphasis on:

a) What is benefit?
b) How did the concept develop? Milestones/timeline of development of the concept in the scholarly literature in medical and health related ethics.
c) The current conception of benefit in transnational research ethics and,
d) Shift of benefit in terms of autonomy and decision making in medical research involving human beings eg. Bodies for sale? Docile bodies? etc.

Chapter 3: Empirical Indications of Exploitation: Some Case Stories

The core purpose of this chapter is to substantiate and demonstrate empirical indications of exploitation in medical and health related research activities in poor and low-income countries:

a) Investigating the situation in Tanzania
b) Tracing literature that inform about exploitation in Tanzania
c) Discussion with members of functioning research ethics committees to find out:
    - their personal understanding of the concept of exploitation in a Tanzanian context,
    - if they can provide examples of studies that indicate different forms of exploitation, link of reported forms of exploitation in other documented case stories.

Chapter 4: Analysis of the concept of Benefit in Current Declarations

a) Declaration of Helsinki - How the concept of benefit has been modified during the different phases of revision.
b) How the concept of benefit is expressed in other relevant declarations and guidelines (such as in CIOMS International Ethical Guidelines for Biomedical Research (2002) and the Universal Declaration on Bioethics and Human Rights (2005)).
c) The position of benefit for research in poor and low-income countries
d) Health needs and the "10/90" gap, a conception which refers to the mismatch in global spending on health research between affluent and poor and low-income countries.

e) How does benefit merge fairly? Or unfairly?

f) How ethics scholars have tackled the concept of benefit and benefit sharing in research

g) The use of placebo and the future role of the Declaration of Helsinki

Rationale:

This study has both theoretical and practical relevance. At the theoretical level, the study will contribute to the understanding of the concept of exploitation in medical and health related research ethics. At the practical level, the study will provide knowledge about current trends in transnational medical and health related research and a better understanding of current perceptions of benefit among researchers involved in such research. Furthermore, the hope is that it will contribute to a better understanding of the concept of exploitation, in particular during research undertaking.

Dissemination of results

Publications in international journals. Summarised version of some concepts and relevant chapters in a simple and understandable way to both researchers and research participants in poor and low income countries; presentations at local and international conferences just to mention a few means in which this work will be shared.

CHAPTER ONE

ETHICAL THEORIES ON EXPLOITATION

Introduction

This chapter seeks to provide a thorough analysis of ethical theories about exploitation with particular emphasis on and discussion of different conceptions of exploitation especially in the literature on medical and health related research ethics. It also aims at discussing forms and statements regarding the concept of exploitation by examining debates in medical and health related research endeavours. Finally, the chapter will try to assess the possibility of suggesting a more suitable conceptual framework addressing the issue of exploitation, based on a critical analysis of current conceptions and forms of exploitation.

Understanding exploitation as a concept

Exploitation is not a new term; neither does it denote unfamiliar situations despite raising a lot of controversies and concerns within our time. A number of ancient literary sources have simply described exploitation as a way in which one group oppresses the other by not giving what it is supposed to receive after the agreed duty. Religious literature describes such a tendency as an open welcome of anger from a supernatural power.

According to the Bible and the Quran for instance, God created human beings in his own image who should not be subjected to any form of exploitation, and punishment for exploitation is clearly expressed:

"…I shall not turn it back on account of their selling someone righteous for mere silver, and someone poor for the price of a pair of sandals" (Amos 2:6 b)[2].

"Woe onto defrauders, those who when they take the measure from mankind, demand it in full but if they measure unto them, or weigh for them, they cause them less…" (Quran 83:1-6)[3].

Both Christian and Muslim theology insist on honesty in dealing with other humans avoiding exploitation by paying them what they ought to receive in accordance with what they have

[2] New World Translation of the Holy Scriptures (1984)Watch Tower Bible and Tract Society of Pennsylvania New York

[3] As provided by Engineer A. from Islamic Economics: A progressive Perspective Occasional Papers No 8 Vol 7 August 1991; Institute of Islamic Studies Bombay http://www.indiarightsonline.com/Sabrang/relipolcom81-90.nsf/5e7647d942f529c9e5256c3100376e2e/f688802cf9475993e5256d760035252c/$FILE/ced01277.pdf accessed 01 October 2010

done, and not less. I could have gone further to explain other religious notions on exploitation such as e.g. in Buddhism where indiscriminate exploitation of both animals and human beings are one among the worst form of sins against God and no one can achieve re-birth after death without being weird against exploitation[4] This, however, I consider beyond the scope of this discussion.

From times immemorial, exploitation has been looked at with a slant eye. The advent of colonialism and subsequent establishment of empires in various parts of the world for example, have been linked with exploitation whereby the often spoken "master-slave relationship" has prevailed for centuries; to denote a predisposition of unfair treatments among one group of individuals in producing goods and services. Lots of spectacular and magnificent buildings and towers, huge ships, railways, heavy industries and the like, though aesthetically beautiful and/or useful, have been a result of many activities that require exploitation of both human and natural resources (Morris 1998).

In a general sense, to exploit something means to take advantage of it and not to destroy or waste it (Wilkinson 2003). One can see this as a positive explanation for things like natural resources being obtained and used for beneficial purposes to human beings. On the other hand, the same term can be used in an evaluative or normative manner to indicate negative connotations when assessing the extent or burden of activities that are done by human beings when facilitating lucrative gains for a certain segment of a population or society. Exploitation in a moral sense means actions that make others suffer in a number of ways where in most cases the gains are hidden from the one who has been involved in producing them. In this manner, it can be argued, the one exploited is sometimes made unaware of exploitative intentions, plans or actions against him or her.

Exploitation is an ambiguous and complex concept which it has proved difficult to come to terms with. Because of this ambiguity and complexity, it has raised many debates in various disciplines. Some examples of exploitation are focusing on personal intention of obtaining desired results such as "A weight lifter exploits his muscles to lift weights" or, "A carpenter exploits his tools to build beautiful chairs" (Hawkins and Emanuel 2008). These two examples, it can be argued, might fit in the materialistic point of view where commodities and valuable items are believed to determine all means to achieve the ends. Here for instance, a weight lifter is using his or her own muscles (and not the physical power of someone else)

[4] In Buddhism Core Belief at: http://www.religioustolerance.org/buddhism1.htm Accessed 30 September 2010

willingly and knowingly to achieve the ends of greater advantages and perhaps wealthier gains to him / herself. The carpenter does not chop off his own hand to make a beautiful chair. But if school children are employed in the factory and offered biscuits as a token, many would deem it unacceptable despite of the production of beautiful chairs.

Kantian vs utilitarian theories on exploitation

Two types of ethical reasoning originating from a philosophical understanding of the concept of exploitation are embedded within the theoretical frameworks of utilitarianism and deontological arguments. Systematic reflection on these theories is needed so as to have a comprehensive clarification in dealing with practical ethical problems we encounter (Tanner, Medin et al. 2008). According to utilitarian theories, the moral character of an action can be assessed with a view to the consequences (in terms of harms or benefits) it brings. In this premise, good intentions are always assisted by the right actions to produce the best outcomes (consequences), and bad consequences are a result of bad intentions preceded by bad actions (Alexander and Moore 2007). Therefore in this analysis, conclusions about what is wrong or right are based on the consequences as illustrated in the following diagram:

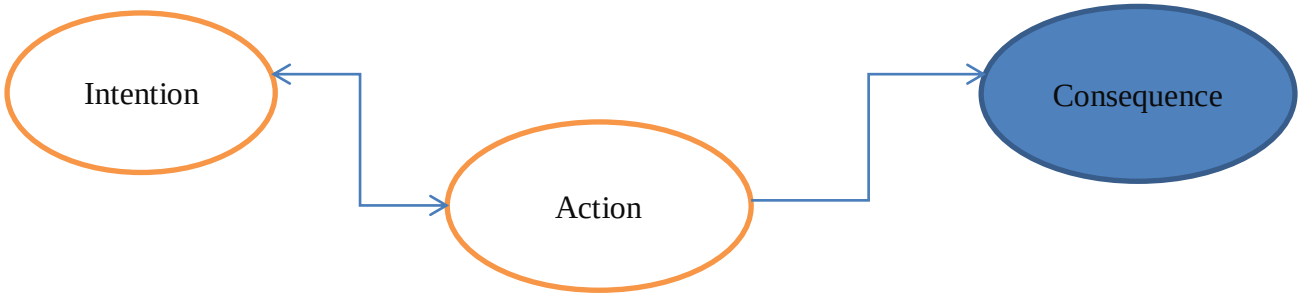

Fig 1: Interlink between intentions, actions and consequences (as conceptualized by the author).

As arrows in the above diagram indicate, assessment of exploitation can be done by looking at a combination of intentions and the subsequent actions which are inter-linked to cause consequences.

The concept of exploitation may be expressed within this framework with the meaning that we must have intentions in order to act in a way that will result in exploitative consequences. Among the easy and prevalent views especially in medical and health related research, have been those looking at exploitation by judging the consequences in terms of actions or vice versa; without looking at intentions. For instance, let's say a research participant has encountered adverse effects of a drug on trial. Critical assessment of exploitation in this case

would be the answer to the question: Did researchers intend to inflict harm to participants? Or rather, what was the intention behind this study? I believe that any obtained answer if correctly placed within this framework can lead us to give the true judgement of exploitation.

Most utilitarian view supporters propose producing the greatest amount of good for the majority of the population. Therefore, the so called "*negative utilitarianism*" stance is applied in order to minimize the amount of harm for the greatest amount of the population. It is further argued that this is the most effective ethical practice because there are more ways in which harm is inflicted to individuals than good; and the greatest harms are considered more consequential than goods. There are many different forms of utilitarianism, but the two most well-known are act-utilitarianism and rule-utilitarianism. *Act utilitarianism* on one hand, focus the attention on each individual act, and chooses that individual act which will generate most happiness. *Rule utilitarianism*, on the other hand, focuses the attention on potential rules of action. Therefore, in order to determine whether the rule should be followed, or not, it is important to identify which rule would give rise to most happiness if it was adhered to by everybody. This suggests an obligation of strictly acting according to the given rules that aims at bringing about the most happiness.

The moral status of medical and health related research relies upon the ends rather than the means under utilitarian theories. For instance, according to utilitarianism a study that would promote social goods for many can be justified, even if those who are involved in research are generally weak and those who enjoy the end product of research would be typically well off.

In deontological ethics (also known as duty based or right– based ethics), the understanding of what is right or wrong is built upon considering the values, rights and duties (or principles). Thus, deontological ethics holds that some actions would be condemned due to their nature and that if an action is not corresponding to anticipated rights, then it is morally not permitted. Most advocates of deontological ethics argue that an action might be considered wrong regardless of its likelihood of bringing good to the majority. Such a consideration is taken if the action seems to violate the right or duty based ethics and established rules that can serve as the basis for making moral decisions for specific situations (Teson 1992; Payne 2006; Pellegrino 2009; Williams 2009).

Those who look at the concept of exploitation from the vantage point of a deontological theoretical framework argue that it must be considered morally wrong to involve vulnerable populations in medical and health related research due to the nature and complexity of their

life situations. For example, the often criticized are situations where children or sick individuals are involved without their awareness. For deontologists, the conformity to moral norms is the most important no matter good the act would bring.

Forms of exploitation in medical and health related research

There is no doubt that medical and health related research involving human beings has improved the treatment, care, and well-being of people in the world. This is because the end point of this kind of research activities is the knowledge that will be generated and which is expected to not only be beneficial among individuals involved in the research but also to the group of patients suffering from the same ailment as well as to the society as a whole. Despite development of medical and health related research and its positive outcomes, some concerns have been raised about two groups of researchers: First, those who are interested in doing research to advance knowledge while at the same time being observing the likely harms that might occur to research participants; and second, those who while they are engaged in developing knowledge, they purposely involve vulnerable research participants in studies without due consideration of the associated potential risks to them (Benatar 2004). Some moral and ethical principles have been proposed and eventually applied when conducting studies that involve human participants. Most of these principles insist on respect for human dignity and adherence to the social benefits that would lead to acceptable standard of life as a result of participating in the said study. Therefore, sometimes calling a study exploitative would require more consideration of the benefits accrued from it in relation to its ethical or unethical conduct (Resnik 2003). There are special cases, however, where some medical and health related research activities have been documented as scandalous to a large extent. The following table provides a detailed summary of some of these studies:

Accounts of selected documented unethical studies among vulnerable groups:

Study	Years	Details
Pfizer sponsored Meningitis epidemic study – Nigeria	1996	Study sought to curb a meningitis epidemic in Kano, Nigeria, using a trial antibiotic namely trovan which was yet approved to be used by children. "Eleven children who received that experimental drug died and 200 others became deaf, blind or lame"(Macklin 2004; Lysaught 2009).
The Tuskegee syphilis study among poor Black-Americans in Alabama, USA	1932-1972	The U.S. Public Health Service aimed at documenting the natural progression of syphilis among black-Americans despite the discovery of its cure. Participants were denied treatments and were not even told about their disease (Brandt 1978; Gamble 1997).
A series of human experiments among patients of Vipeholm Mental Hospital in Lund, Sweden	1945-1955	To determine the effects of carbohydrates in the formation of cavities. Participants were intentionally provided with excessive sugar to encourage tooth decay. Up to 1949 the teeth of about fifty of 660 participants were completely destroyed (Krasse 2001; Wikipedia 2010).
Willowbrook School Study New York State, USA	1963-1966	A study aimed at finding out the effectiveness of hepatitis vaccination by intentionally infecting mentally handicapped children with hepatitis virus either orally or by injection (Rothman 1982; Ethics 2010).
Jewish Chronic Disease Hospital Study in New York City, USA	1964	A study aimed to develop information on the nature of human transplantation rejection processes. Patients without cancer were injected with live cancer cells. Investigators didn't tell the patients to avoid scaring them, and also with a belief that the cells might be rejected (Standler 1997; Lerner 2004).

Table 1: Summary accounts of abusive studies in medical and health related research

In these, and more studies, not only were the rights of study participants violated, but also in some circumstances their health were compromised leading to research associated deaths (Emanuel EJ 2004). Although atrocities in research have been documented globally, historically those that happened in poor and low-income countries have rarely received the same attention (Macklin 2004). The most recent disclosure of unethical research relates to a 60 years old study involving U.S. medical researchers who in the period of 1946-1948 intentionally gave a group of Guatemalans gonorrhea and syphilis to study the diseases 'in vivo' (http://www.msnbc.msn.com/id/39463624/ns/health-health_care/):(Frieden and Collins

2010; Solbakk 2010). This, not only adds to many unethical studies that have been documented previously, but also rings an alarm bell perhaps necessitating a new look in order to strengthen the guidelines and regulations, which have been put in place to guide medical and health related research involving human beings all over the world.

Among important questions one can ask are if it is morally permissible for scientists to intentionally inflict harm in the name of science with confidence that one day the president or principle investigator will come out with a statement of apology. The other could be if compensation will be made enough to cover for the lost lives as a result of such kind of vicious experimentation. Critics of trends in medical and health related research activities conducted in impoverished communities argue that; they are "potentially exploitative because of poverty". Also "Lack of human and material resources, illiteracy and poor leadership styles in most of these countries make it an easy, cheap and convenient place to conduct human research" (Lavery 2007).

Competing conceptions of 'exploitation' in medical and health related research ethics

Two types or forms of exploitation have been debated for a long time. The first is called *"Harmful and Non-consensual Exploitation"* where potential harm is inflicted to individuals. As Standler puts it, "…non-consensual experiments are often performed on captive people in an institution, particularly people who society has regarded as less worthy" (Standler 1997). The harmful non-consensual exploitation can be seen in trials (like the famous 1940's Nazi and Tuskeege experiments) which were performed on participants without their consent while researchers either gave incorrect or no information. In general, such or similar experimentations are said to have no importance or benefit to the involved population.

The second form is called *"Mutually Advantageous and Consensual Exploitation"* (MACE) which involves agreement between the two parties with sharing of advantages between them (Wertheimer 2008). In this manner of sharing it doesn't matter whether one part gets more advantages than the other as long as there is an agreement between them. To illustrate this, Wilkinson gives an example of characters A and B where B is unemployed, has no food and is in danger of losing life if he doesn't get food soon. There are no other alternatives like charities or social welfare services around, and he cannot commit a crime because he lives near the police premises. A has a factory and offers B a job but he has to do 50% more work and also accept 70% less pay. B accepts the terms in order to survive (Wilkinson 2003). In

this example there is a mutually advantageous exploitation since A has taken advantages of B's situation. At the same time there is a consensual exploitation since B has willingly accepted to work under exploitative terms in order to survive. Similar to this example might be that of a poor person who accepts to sell one of his or her kidneys in order to better provide for the family. In this kind of exploitation, exploiters are said to take advantages of the exploited, but we are urged to believe that the exploited agreed and consented for the transaction because of a kind of benefit they feel they will get from it.

There exists a lot of differing and competing conceptions of exploitation put forward by a number of scholars in medical and health related research ethics though. Among them is the one criticizing the method used for clinical trials where available interventions are not provided to research participants during the process. In such trials, there is a tendency of comparing efficacy of active treatments to one group of participants and without treatment (placebo) to the other. In this view, medical and health related research is considered exploitative and unethical if researchers would withhold available treatment intentionally in order to measure effectiveness of a new intervention on test (Bayer 1998; Emanuel and Miller 2001).

Other exploitation claims include unavailability of the products resulted from interventions tested in poor and low income countries. It is argued that, any medical or health related research is deemed exploitative if the gained knowledge seems not to benefit the host country in which it was conducted. This is more evident when the developed drug is not available due to high prices or if that drug was not meant to help solving the existing burden of disease in the host country (Garrafa, Solbakk et al. 2010).

There are also questions about the level of knowledge and economic situations possessed by research participants. It is claimed that some researchers tend to take advantage of circumstances caused by poor health care access and little knowledge about research among participants in poor and low income countries (Macklin 2004; Voo, Chin et al.). In such a situation, exploitation seems to be obvious among research participants who miss the expected outcomes.

Another similar exploitative situation has been termed 'globalization of clinical research', which is said to be manifested in the increased number of clinical trials carried out or sponsored by the drug companies in poor and low-income countries. Such trials are

formulated within the framework that they can be accomplished quickly with less supervision and thereby produce drugs in question as soon as possible (Glickman, McHutchison et al. 2009). It is believed that research participants are manipulated due to existing disparities in terms of education, health care systems, income and the general social welfare.

Some other scholars have come up with what is known as the '*permitted exploitation principle'* which states in part that "it is wrong to interfere with or seek to prevent transactions that are beneficial to the parties involved even if the transaction itself is unfair, unjust, or exploitative" (Mayer 2007). This principle seems to put a barrier with regard to interfering in exploitative practices which undermine the other part. It can be argued that if medical and health related research work is exploitative it should not be permitted regardless of transactions. One can argue that there are no acceptable reasons for putting individuals into risks simply because they have accepted to join the study due to any condition (such as social, economic, political or cultural vulnerability).

Forms of exploitation in medical and health related research ethics: Current debates and consensus

a. The paradox of informed consent

The right of research participants to decide for themselves in a free and informed manner is considered a key principle in all guidelines regulating research that involve human beings. The original informed consent procedures originate from the post-world war II Nuremberg Medical Trial, which having gone through legal and ethical considerations, realized that almost all medical experiments conducted during that time were unethical and did not consider human participants as autonomous individuals. Most of these experiments led to death or permanent impairment to people who were forced to participate. The Doctor's trial resulted in the so called *"Nuremberg code"*, in which voluntary consent is deemed *absolutely essential*. In addition, the code emphasises the importance of protecting human research participants by providing clear information on aspects such as potential harms that could happen during research, considerations of individual understanding and autonomous decision making. (Weindling 2001).

Despite the Nuremberg code, and other subsequent guidelines and declarations pertaining to medical and health-related research involving humans, there have been a lot of misunderstandings over how valid could informed consent be, especially in cross–cultural

settings where individual consent is considered not enough. It is argued that, in all these settings informed consent is always being compromised by less autonomy making it sometimes difficult to obtain as required (Benatar 2002). If this is the case, it can be argued, that informed consent cannot be taken for granted, since the conditions under which research participants are recruited can vary a lot from place to place.

The so called "voluntary informed consent" has been exhaustively discussed over the years ranging from verbal, written (and signed either with an inked thumb or pen), communities / group consent up to the current electronic (e-consent) that can be achieved via established modals in specific settings such as hospitals and the like (O'Keefe, Greenfield et al. 2005). Greater concerns have been put on the type and amount of information that participants ought to receive and how long the informed consent document is supposed to be in order to provide clear and precise information. The other is the capacity for research participants to understand scientific terms such as "randomization", "double blind", "placebo"; and much more (Appelbaum, Roth et al. 1987). These are just a few among many channels in which exploitation might occur. It can be argued that no matter how one agrees with regard to participation in a study, there remains a controversy on how the study in question maintains the integrity of the participant in all stages.

b. The question of payment or compensation for research participants

The other often criticized trend is the question of compensation to research participants in which exploitation occurs due to interactions between researchers and participants. An interaction is deemed intimidating in the presence of less or no compensation, when participants volunteer to participate in research either due to their weaker economic position or due to attractive compensation that tend to 'blind' the forthcoming risks as a result of their participation (Lemmens and Elliott 1999). In their provocative article *"Guinea pigs on the payroll: The ethics of paying research subjects"*Lemmens and Elliot insist that healthy participants become vulnerable because of their financial needs while if patients agree to enroll in the study it might be because of their medical condition which they believe will best be taken care of. In this situation research is considered exploitative though apparently it might have been agreed upon and precisely documented.

c. Risk vs. Benefit ratio

In her tentative definition of exploitation Macklin (2004) says (though without applying it to specific research involving humans), "it occurs when wealthy or powerful individuals or

agencies take advantage of the poverty, powerlessness, or dependency of others by using the latter to serve their own ends …" This argument is also supported by the so called "unfair and uneven distribution of risks"(Emanuel, Wendler et al. 2004; De Castro 2007) whereby one group of population seems to bear all responsibilities and consequences of medical and health related research activities despite social, economic and political constraints and the other group receive the end results.

Towards a more sustainable conception of exploitation

It is often difficult to answer if conceptions can be sustainable because of changing ideas from time to time. It is sometimes difficult also to refute different conceptions as given by respected scholars without considering their social, political, economic, cultural and even linguistic inclination. Perhaps it is important to understand that most of these conceptions have been developed within the framework of an array of different understandings of the world which might not be universal. In the beginning of the years 2000 Benatar wrote an article *"Reflections and recommendations on research ethics in developing countries"*. In this article he gave a complex narrative of a pregnant mother from one of the poorest countries of the world who is asked by collaborative researchers to participate in HIV research despite inadequate health care facilities and her little understanding of the disease and research. Several unanswered questions are raised as the participant doesn't understand why she should be studied and if her spouse or community members will agree, and more importantly what will happen to her and her baby after the study is completed. She is not alone, for most of such questions are often not answered due to already established frameworks in which according to Benatar, "the privileged lives have been constructed and maintained through modern and sophisticated methods of exploitation of people across the globe" (Benatar 2002).

The fact that prominent researchers, sponsors or drug manufacturing companies may have much more gains than research participants in poor and low income countries, can be correctly considered as a platform for attention to design studies that should protect these participants. Unfortunately, this platform is being dimmed by power relations and it is always weak due to contorted theories and academic arguments to the extent that study participants in these countries are taken for granted. The promotion of human health should go hand in hand with proper protection of anticipated risks and clear focus on the kind of benefits to both study participants and the intended population. I would like to suggest some few

considerations when looking at the concept of exploitation with an eye of a person from a poor and low income country:

i) When the researcher employs "hidden risks" as a strategy to obtain consent for the participant to enter the study that he or she would have rejected if correctly informed.

ii) When vulnerability in terms of both economic and social welfare are used as a means to allure the research participants to join a study whose products would be unaffordable or else having no meaning to them at the end.

iii) When more risks than benefits are anticipated.

Key issues in this argument are risks, vulnerability and benefits and I suggest that a sustainable concept of exploitation in medical and health related research ethics should reflect these issues: Medical or health related research activities undertaken among a vulnerable population due to their social, cultural, political, and economic or any situation without their understanding of the risks or beneficial outcomes.

Summary and concluding remarks

This chapter does not have a great deal to say about religious conceptions of exploitation, rather some stand points have been used to explain how the concept has evolved among human beings since ancient times. On one side, the concept has been used to denote economical oppression in materialistic contexts whereby individuals are said to be exploited when working for the others and receive undue payments. On the other side, according to medical and health related research ethics, the concept developed on the historical background of atrocities and unethical controversies where individuals have been subjected into harm and even death during research without their knowledge. The proposed three key issues: Risks, vulnerability and benefits should be adhered to when trying to discuss issues pertaining to exploitation in the context of medical and health related research ethics.

CHAPTER TWO

DEVELOPMENT OF THE CONCEPT OF BENEFIT IN RESEARCH ETHICS

Introduction

A critical analysis of the concept of benefit and its development in medical and health related research ethics is undertaken in this chapter. Major focus is on the discussion of this concept in the literature. The current discussion on benefit sharing in medical and health related research between affluent and poor and low income countries is also discussed; and a shift of benefit in terms of autonomy and decision making process in medical and health related research involving human beings (e.g. bodies for sale, docile bodies?) is also addressed.

What is benefit in medical and health related research

The importance of medical and health related research lies on a premise that if we know why people get sick, then we can be able to understand how to alleviate their suffering and improve their health. For several reasons it might not be easy to note the direct benefit in this type of research. For example, if a researcher is studying a problem that does not exist among the research participants involved; and the benefit generated from this research leads to helping patients located in a community in another part of the world, it is not clear whether and eventually to what extent such forms of benefit can be said to comply with the requirements in medical and health related research ethics. Most of the expected benefits however, might include issues such as better curative or preventive measures of a certain disease, improvement of health services, or proven existence of a certain health problem so that actors can start looking for solutions etc. Sometimes health research undertakings might be risky to participants and as a general requirement researchers are supposed to explain all possible risks before undertaking a study. In some areas of research these requirements are not adequately observed, and there are allegations that researchers have tended either to cause so called "undue inducement" by providing a large offer of money or give "false hopes" or rather, "therapeutic misconception" to participants who take part in research studies (Appelbaum, Roth et al. 1987; Dickert and Grady 1999; Wertheimer and Miller 2008).

The issue of benefit and benefit sharing in medical and health related research ethics has been the subject of intense debate during the past decades.(Glantz, Annas et al. 1998; Glickman, McHutchison et al. 2009; Garrafa, Solbakk et al. 2010; Lorenzo, Garrafa et al. 2010). The trend of using participants from impoverished communities for studies without a due regard of their economic, political and social vulnerability, the often called globalization or

"transnational" clinical research and the shift of trial sites to these communities plus investments in drugs trials that do not target the burden of diseases in poor and low income countries are just to mention a few debatable topics.

Perhaps the most contradictory concerns are the ones involving how to determine involvements and distribution of benefits brought by individual research participants; and the question what kind of rights research participants have in relation to benefitting from research and which obligations researchers or sponsors have in this respect (Simm 2007; Johansen, Aagaard-Hansen et al. 2008). The literature is filled with accounts of cases where researchers have carried out studies among individuals or groups and reaped huge benefits while ignoring their participants. For instance, on the front flap of the book *"The Immortal Life of Henrietta Lacks"* Rebecca Skloot gives an account of a famous case from the1950's: "Doctors took (Henrietta's) cells without asking..." Such cells taken from Henrietta's body did not die like others during experiments. These famous cells namely "HeLa" according to the two initials of her name, have led to the scientific discovery of a polio vaccine, and has been used extensively to researching effects of contaminations from toxic substances and much more (Skloot 2010). Since it has later been revealed that, Henrietta's family has lived without even health insurance all these years, and their mother's cell line has been used almost all over the world for medical experiments and discoveries without their knowledge, there is a questionable bill to settle as far as benefit and benefit sharing is concerned.

Another astonishing account is that of St Martin Alexis whose gastric juice from the wound that caused permanent fistula on his stomach after a gunshot accident was used for studying the physiology of digestion (Markel 2009). It is documented that, despite the poor life condition, Alexis partially healed wound was left open and continued to be a source of obtaining gastric juice for experiments throughout the rest of his life. Such experiments brought out the praised outcomes of demonstrating the duration and the process of normal digestion and the influence of emotions and environment on the digestive actions; while at the same time treating Alexis as a "laboratory" or a "guinea pig"(Tanner 2000).

Possibly another interesting account is that of blood samples which were taken from some members of a small hunters community in the Papua New Guinea; with a teasing information that researchers wanted to see an insect from their blood - whose discovery came out with existence of antibodies which were used to produce immortal cell line as the basis for leukaemia therapy (Emerson, Singer et al. 2011). Similar to Henrietta and Alexis, these

community participants were not aware of the discovery and subsequent experiments carried out on their body fluids. No doubt they remained poor while contributing to scientific discoveries that made scientists both famous and rich as a result of their research findings.

Important moral questions that need to be asked are: What kind of right one has to claim unique characteristics of one's own body tissue or cells? Can such tissue and cells be sold or compensated? If so, is uniqueness in humans taken and valued because we are humans? (Davis 2001). In contrast, what right does one have to use any body parts of another person for whatever reason without informing what is going on? These are just a few among questions that have been raised when discussing the meaning of benefit in health research involving human beings.

Some researchers often refer human participants as 'subjects' or "cases" in many instances during medical and health related research and other scientific endeavours for that matter. Ironically, a subject in this sense is considered an object of inquiry. In my opinion, a subject doesn't have any benefit on its own. One can get benefits such as knowledge, promotion and the like from mastering the subject. If that is the case, then a human participant in medical and health related research would be considered more or less the same as any object of study such as Biology, Physics or Engineering; in which an individual concentrates to gain knowledge and discover new things so as to become famous and receive a raise from the current position etc.

Some scholars are arguing that determination of benefits to study participants should be considered on at least three levels: First being the target group - also called the "Who" - which includes study participants from the community or the host country where the study is conducted. The second level is the consideration of time or duration in which the study will take place, i.e. the "When". This also ranges from the actual period of the study and the estimated time of services that will be rendered after the study is over. And the third is the kind of benefit to be provided, i.e. the "What". Benefits to be considered in this endeavour would range from medical to non-medical related assistance during and after the study (Johansen, Aagaard-Hansen et al. 2008). Though simple as it seems to be, the suggested principle of benefit sharing is often not followed completely by researchers. Most studies tend to easily get the target group, consider the duration of the study and continue with the study

without considering what would be the benefit of that study to both the study participants and the community at large. The following section will discuss this tendency.

Current trends of benefit sharing in medical and health related research

The dramatic shift of location of clinical trial sites led by big pharmaceutical companies and at least two reputable USA National agencies, the National Institutes of Health (NIH) and the Centres for Disease Control (CDC) (Angell 2005); to poor and low income countries over a period of more than 15 years has raised a lot of concerns among scholars in research ethics. At least five possible reasons have been suggested by Glickman et al. to be the major driving forces behind this trend: One is *cost saving*. It is anticipated that substantial saving may be achieved by moving phase 2 and phase 3 clinical trials to places where lower salaries are normally paid to study coordinators and the supporting staff. The second is *time saving.* Since time costs account for 50% of costs to develop new drugs, therefore it is imperative that globalization of clinical trials may shorten the timeline for clinical testing and thereby reduce the costs. The third is *easier access* to potential research participants that will help speed up the recruitment process which is often long in other places. The fourth reason is an opportunity for *fewer regulatory barriers* in poor and low-income countries which helps to facilitate the conduct of clinical trials for pharmaceutical and device companies. And the fifth is the *rise in regulatory barriers and concomitant costs* in wealthy countries which speed up the outsourcing of clinical trials in poor and low- income countries (Glickman, McHutchison et al. 2009). Although it is widely accepted that effective treatments have to be made available to trial participants, this is often ignored on the basis of political, social and economic structural issues within the host countries. The new manufactured drugs resulting from various trials have further been expensive, unaffordable and sometimes not meant for either curative or preventive measures in the countries where such trials were conducted (Lavery 2007; Voo, Chin et al. 2008; Garrafa, Solbakk et al. 2010). From the perspective of poor and low income countries, a study has no benefit if the population or at least the welfare of trial participants is not promoted.

To curb the situation, implementation of the so called "post-trial benefits" approach has been recommended to mean that beneficial outcomes of the study ought to be discussed by both researchers and participants in the host countries before the start of the study in question, and most acceptable studies would be those responsive to existing problems that need to be solved (Zong 2008; Schuklenk 2010). One of the critiques raised against this approach relates to

difficulties in calculating the value of research and making a fair decision on who will receive benefits depending on the operating health system of the host countries (Voo, Chin et al. 2008). Against such a critique, one can argue that the praiseworthy scientific and ethical studies would be those striving for finding solutions to both existing medical and health related problems among research participants; together with how weak systems can be improved for the welfare of present and future generations.

Another alternative approach suggested in the literature is called "cautionary approach" which addresses the question of acceptability for researchers in industrialized countries to use citizens from poor and low income countries as research participants. This approach recommends that a successful research activity that involve vulnerable populations must have a direct benefit to that population and that there should be a realistic plan that would ensure provision of the new intervention resulted from such research (Glantz, Annas et al. 1998). This approach however, has been criticized as "procedural", since it involves agreements between participants, researchers and sponsors who might have conflicting opinions in terms of fair distribution of benefits (London 2010). The procedural approach gives an account of agreements between sponsors, researchers, and participants on how research outcomes will be shared after a successful study. Ideally, this approach suggests a mutual creation of a distribution system that allows a fair share and equitable partnership between researchers and the involved communities.

Angela Ballantyne in the paper *"How to do research in an unjust world"* (2010) proposes the Maxmin principle which would determine fair distribution of basic goods in the context of international research. The said principle requires more advantage of benefits distribution to be focused on the vulnerable communities during transaction, because of the evident weak bargaining capacity and lack of basic goods and decent social life among them. Therefore, in order to implement this principle, a global research tax should be applied where research sponsors would be made to gain a minimal benefit in a way that the surplus is distributed more to the vulnerable research populations (Ballantyne 2010). Some of the criticism against the proposed global research tax is that if host countries would receive tax revenues for research, then this would attract poor and low income countries to participate in any research as much as they can even by force from their governments (MacDonald and Walton 2010). Doubtful feelings are that fraudulent researchers can easily use this approach in poor and low income countries to negotiate with the type of dishonest and insensitive leaders; who would accept their fellow citizens to be enrolled and hence involved into risky studies.

It has further been envisaged that sponsoring companies may not be ready to pay tax and if they do so, then they may even prepare false contracts so that the resultant products will be in favour of their legal and intellectual properties in order to determine the price they want (McMillan 2010). This imagination stems from the fact that, still at present, most research results and products are mostly not available or affordable in poor and low income countries where studies are done.

Further concerns that have been raised against the global tax for research are that big pharmaceutical companies would complain to the World Trade Organization using other companies like those of oil and household appliances, as a point of reference since they might not face the same stern global tax strategies, something which could jeopardize the current relationship between affluent and poor and low income countries (Resnik 2010). One can argue that the present or future relationship between nations should be strengthened and built upon a process which strives to find out how medical and health related research can be used to improve people's lives while minimizing risks among participating vulnerable individuals at any point of their existence.

According to the viewpoint of the "fair benefit approach" (Emanuel 2002; White 2007; Wertheimer 2008;) it has been suggested that research activities in poor and low income countries should be done within a framework that would fit into providing a guarantee of health care services that are not for the study in question among participants, plus improving the public health care services to reach even those who are not involved in the study. This may also include employment and other economic activities plus long term research collaboration A clear temptation for this kind of sacrifice comes from negotiated benefits which might not be responsive to the health needs per se. Suggested benefits such as employment or economic activities are just a few of such negotiations. Therefore, the approach cannot be really fair since it creates a dual manipulation in terms of interactional relationship between a) research group and community leaders and b) Community members and their leaders where the later means that community members would be incited to join in the studies following the former unfair negotiations between leaders and researchers and research sponsors. Although the perspective of fair benefit has been the mostly advocated, one can see it as a free way to mutually advantageous exploitation with the understanding that there might not be any difference between research participants and any individual who would agree mutually (hence fairly?) to accomplish any agreed activity despite its risk.

The alternative of applying the human rights based approach to international research using the so called Global Burden of Disease (GBD)-oriented research incentives has been a matter of discussion in recent years. In this approach agreement for rewarding the patent rights proportional to GBD together with mass production of the discovered drugs would not only make the new drug available but also affordable for the community members in order to curb the GBD (Pogge 2007). Among the challenges for implementing this approach is the Trade-Related Aspects of Intellectual Property Rights (TRIPS) where mass production of the discovered essential drugs has financial implications and therefore the patents are "restricted" by intellectual property rights for both innovative and financial reasons by drug manufacturers to the extent of being difficult to be distributed "freely". For that reason it is suggested that such essential medicines should not be considered as limited commodities inaccessible due to TRIPS but as free to be accessed by any drug manufacturer in the world to use for generic drug production which will enhance affordability and availability among impoverished communities. To retain income for the original drug producer and the associated innovation, alternative incentive for research must be established (Solbakk 2011). Ideally, it is anticipated that if patent holders and generic drug producers would agree with each other, their collaboration will result into making medicine available to the poor patients notably those with chronic diseases and also for preventive interventions. I think this is a promising approach though there are always resistances when it comes into money and rigorous cost, benefit and effectiveness analysis which might be a barrier. Moreover, most views on this and other approaches are only suggestions which require responses especially from the giant pharmaceutical companies which invest a lot of money in research and subsequent drug manufacturing and, of course, dictate on the prices and patent rights.

The question of autonomy, decision making and benefits in medical and health related research

Among other troubling issues in medical and health related research are how the process of individual decision making to take part - or not part - in research can be realized, both among researchers and participants. Some scholars argue that one should be left to make personal decision while others argue that participants must be led step by step in understanding the likely risks and benefits in an anticipated study. It might be surprising if one can be ready to join risky research without determining the outcomes, although for some moral reasons there are those who are ready to offer their body parts for the sake of saving their relatives or best friends and thus accept even to shorten their lives in this process.

Nevertheless, the most disturbing accounts are where human organs from living people are stolen in a number of ways for transplantation to others. It has been reported in many instances that people are killed and their body parts such as eyes, skin, kidneys livers and more are taken away to be traded (Becker 1999; Wilkinson 2003). Perhaps this tendency has something to do with legal actions because human body parts trade is not acceptable in many parts of the world and it doesn't even sound correct seeing someone selling say a human heart in the established market if any.

Another astounding account is the mistrust between researchers and citizens from poor and low income countries when human tissues and samples are sought for research purposes. This mistrust stems from a failure of researchers who collect samples from research participants without proper informed consent and leave without returning any meaningful benefit to the studied population (Emerson, Singer et al. 2011). As a solution, Emerson et al proposes the so called *"tissue trust"* arguing that "preventing exploitation and restoring trust while simultaneously promoting global health research calls for innovative approach…". In my opinion such a trust can be built upon answering basic questions that seeks justification as to why samples should be shipped outside the host countries and how should they be archived or disposed of after the study is over. Ignoring this fact will be considered like that tendency of researchers from affluent nations looking for "docile bodies" as illustrated by contemporary bioethicists (Lysaught 2009). This tendency can furthermore be illustrated in contrast to the African view of human person where one cannot just use another as an object of contempt and ridicule since each, apart from being interconnected, has spiritual elements that can be understood in a complex divine world view (Gbadegesin 1993; Metz 2010). I know that

communities have attachments not only to each other but also to their body parts including tissues, fluids etc. I won't be surprised if a researcher is asked to bring back blood samples after analysis, an agreement that is impractical in biomedicine! Therefore making a clear explanation that will not bring conflicts in terms of these endeavours is crucial.

Summary and concluding remarks

A critical analysis of the concept of benefit and its development in research ethics as provided in this chapter, is based on arguments which try to address the involvement and distribution of research outcomes between researchers, sponsors and people involved as participants in a given study. The current views on benefit sharing in medical and health related research between affluent and poor and low income countries are based on some proposed approaches from a number of scholars of medical and health research ethics. Three of these approaches are the global health research tax approach, the global burden of disease incentive and the fair benefit approach. As indicated in the chapter, there is a shift of benefit in terms of autonomy and decision making where sponsors of the "for profit making" type of research tend to ignore the welfare of vulnerable participants, thus using leaders from poor and low income countries to "allure" their citizens to enroll for studies that are non-responsive to medical or health related problems in their communities. Unfair benefits such as employment or financial gains have been discussed as unacceptable. The major conclusion of this chapter is a call for a new strategy that would make both parties responsible and accountable especially in providing clear explanation of the research process including proper informed consent in matter pertaining to samples, tissues and benefits in order to make medical and health related research acceptable and helpful to current and future generations.

CHAPTER THREE

EMPIRICAL INDICATION OF EXPLOITATION: SOME CASE STORIES

Introduction

The core purpose of this chapter is to substantiate and demonstrate empirical indications of exploitation in medical and health related research ethics in poor and low-income countries. Particularly, it aims at investigating and analyzing the situation in Tanzania by tracing literature that addresses the issue of exploitation. The chapter further aims at integrating ideas and opinions from some members of functioning research ethics committees on their personal understanding of the concept of exploitation in a Tanzanian context, as linked with the investigated indications of exploitation in documented case stories.

Tanzania: Location, background and political landmark.

Fig 1: Map of Tanzania Available at: http://www.mapsofworld.com/tanzania/tanzania-political-map.html.

'The United Republic of Tanzania' shortly Tanzania, is located along the Eastern part of Africa, bordering the Indian Ocean between Kenya and Mozambique. The country got its independence in 1961 from the British preceded by the Germans after the Second World War. English and Kiswahili are the official languages though there are over 130 local vernaculars. As indicated on fig 1, other neighboring countries are Uganda, Rwanda, Burundi, The Democratic Republic of Congo (DRC), Zambia and Malawi. Presently, Tanzania is a multiparty state led by the president of the union consisting of the mainland and the major island of Zanzibar with two isles, namely Pemba and Unguja, which remained to be the part of Arab sultanate of Oman since 1832 until independence (Jenkins, Mussa et al. 2011). The current Tanzania population counts 41,892,895[5]. The National Assembly with elected parliament members is the law-making body. Administratively, the country is subdivided into regions, districts, wards and villages where the central government and the local government

[5] As documented by CIA World Fact Book Available at: https://www.cia.gov/library/publications/the-world-factbook/geos/tz.html Accessed February 7, 2011.

are both legal and political entities. The legal system is governed by the Constitution of the United Republic of Tanzania (URT 1998).

There exists a rich literature that explains the SOCIO-political, economical, historical and geographical features of Tanzania as among the center of attraction for exploration in terms of trade, tourism and research. It is from this background that I will draw a foundation for discussing how medical and health related research activities are regulated before discussing the conceptual understanding of exploitation in a Tanzanian context. This I will do by focusing on a set of research case stories and reports indicating exploitation.

Brief account of the development of medical and health related research in Tanzania

Organized scientific research dates back to the colonial era prior to Tanzania's independence in 1961. The first establishment of a research institution in the country was a veterinary laboratory which was established in the central part of the country by the Germans in 1905; followed by the establishment of malaria, virology, and trypanosomiasis research centers by the British from 1919 (Mukama and Yongolo 2005). More such institutions were established after Tanzania won its independence, through the assistance of the United Nations, Educational Scientific and Cultural Organization (UNESCO). Several public health institutions serving as research centers were also built. Establishment of independent research institutions and universities also was a promising movement towards scientific research, as was collaboration with researchers and their institutions from abroad.

Like many other poor and low income countries, Tanzania has always been faced with institutional constraints in conducting medical and health related research. Furthermore, several state regulations have been dwindled by a shifting historical context of political and economic conditions (Songstad, Rekdal et al. 2011). Coupled with poor infrastructure, communicable and non-communicable diseases just the same as other poor and low income countries, Tanzania has in recent decades witnessed the influx of researchers sponsored by different organizations from foreign universities and drug manufacturing companies, working in collaboration with local universities and research institutions in medical and health related research activities.

Legal guidelines for medical and health related research in Tanzania

There are several legal guidelines made up by statutory bodies mandated by the United Republic of Tanzania, to approve and monitor research undertakings in all aspects. Here I will briefly present those dealing with medical and health related research.

The National Institute of Medical Research (NIMR)

The NIMR was established by the United Republic of Tanzania government Act no 23 of 1979, with responsibilities to control, coordinate, register, monitor, evaluate and promote medical and health research designed to alleviate diseases. The institute has a duty to grant ethical clearance for all medical and health related research to be conducted in the country (URT 1979). Together with the local research ethics committees, the institute reviews all proposed medical and health related research projects before issuing ethical clearance.

The Tanzania Commission for Science and Technology (COSTECH)

COSTECH was established by the government Act no 7 of 1986 and is responsible for research promotion and coordination. It offers research clearance permits for all foreign researchers, Tanzanians studying abroad and in need of doing research in the country, and all Tanzanians except employees and students from institutions of higher learning as well as employees of affiliated research institutions who are required to do research as part of their duties (URT 1986). Despite this provision, some foreign sponsored research activities do not follow this regulation after obtaining ethical clearance from NIMR. The act does not contain any provision to deal with those who do not comply with the requirements of COSTECH.

Tanzania Commission for AIDS (TACAIDS)

The TACAIDS was established under the Act no 22 of 2001. It is an independent institution related to the Prime Minister's office. Its major function is to formulate policy guidelines pertaining to the HIV/ AIDS epidemic and the management of its consequences in mainland Tanzania. In addition it is responsible for developing the strategic framework and planning of all HIV/AIDS control programmes and activities, including research (URT 2001).

The Tanzania Food and Drugs Authority (TFDA)

The Tanzania Food and Drugs Authority (TFDA) was established under the Tanzania Food, Drugs and Cosmetics Act No 1 of 2003. It has, among others functions, the function of regulating all matters relating to quality and safety control of food, drugs, herbal drugs, medical devices, poisons and cosmetics and to ensure that clinical trials on drugs, medical

devices and herbal drugs are being registered and conducted in compliance with accepted standards (URT 2003).

Policies and ethical guidelines for medical and health related research in Tanzania

There are lots of both national and international guidelines aimed at fostering the ethical conduct of medical and health related research. All documents of this nature have no legal binding; rather they function as walking sticks and they are subject to revisions from time-to time. At the moment there is no mechanism in place to deal with violation of ethical rules and regulations pertaining to medical and health related research, at least not at the national level.

The National Policy on HIV/AIDS

Established under the Prime Minister's office in 2001, the policy has outlined the following ethical guidelines regarding HIV testing and research:

For voluntary HIV testing, pre-and-post-test counselling shall be done to enable test results to be communicated to the person tested or, in the case of minors, to parents or guardians.

For unlinked HIV testing, no pre and post-test counselling shall be required. For blood donors who wish to know their test results, provision shall be made for follow up voluntary HIV testing with pre- and post-test counselling.

All HIV Testing shall be confidential. The public health legislation shall be made to authorize health care professionals to decide on the basis of each individual case and ethical considerations, to inform their patients or sexual partners of their HIV status. Such a decision shall only be made in accordance with the criteria such as proper counselling, informed consent, ethical clearance and professional conducts (URT 2001).

The National Health Research Ethics Review Sub-Committee

The National Health research Ethics Review Sub-Committee was established in 2001 as a sub-committee of the NIMR and issues Guidelines on Ethics for Health Research in Tanzania. The guidelines provides for the observance of the rights of research participants, need for researchers to strictly observe confidentiality and protection of research participants in both controlled and epidemiological studies (NIMR 2007).

Implications of this arrangement in terms of research conduct and. exploitation in a Tanzanian context

Despite elaborative guidelines there have been a kind of mixed understanding as far as professionalism, political positions and statutory regulations pertaining to medical and health related research conduct in Tanzania. Some of these are manifested in the duplication of responsibilities which are said to have been a source of the so called "inertia" and henceforth dumps the vulnerable population into risky research. As will be discussed in the subsequent sections, there is an apparent tendency of dishonest researchers to take advantage of a loop hole in this system; thus conducting unethical and exploitative studies among the poor and vulnerable participants who do not understand the process of research.

But perhaps we need to have a clearer understanding of the concept of exploitation in a Tanzanian context at this juncture. Two Kiswahili terms are used locally to denote almost the same meaning: One is called *Unyanyasaji* derived from the verb *nyanyasa* which means a tendency of someone to take advantage of another due to weaknesses. In this, the weaker one is aware of what is going on but has no alternative and therefore just accepts the situation. The second is *Udhalimu* an adjective of the verb *dhulumu* which literally means taking more than agreed upon. It is closer to conning, theft, or deliberate taking more than what two parties have agreed on. The concept of exploitation in this context refers to two parties or sides where the one who oppresses the other must either be economically or politically stronger than the oppressed[6]. The following sections address medical and health related studies conducted in Tanzania which can illustrate the concept of exploitation in the said context:

[6] The explained conceptual understanding of exploitation is based on informal discussion with some members of existing research ethics committees in Northern Tanzania in 2010 and the University of Dar es salaam in 2011. There is a need to establish further if other community members in non-academic environment can have the same views since the words *nyanyasa* and *dhulumu* might carry different linguistic explanation and pronunciations depending on geographical location. Some extensions might not refer to medical or health related research.

Study No 1: Homeopathy for Health in Africa

This study is being conducted in Northern Tanzania by Jeremy Sherr[7]. According to Sherr, the study aims at carrying out trials investigating the effectiveness of homeopathy[8] in treating AIDS. He did a similar trial at the Nelson Mandela Hospital in South Africa some years ago. The study had three arms: 1) patients with homeopathy without Antiretroviral (ARV) treatments, 2) patients with homeopathy and ARV treatments, and 3) patients with ARV alone.

The initial year report of this study indicates that Sherr had not yet even received ethical clearance and that he was in the process of applying for such clearance[9]. According to Tanzanian law any clinical trial must be registered by the TFDA and also approved by the NIMR after having gone through the local research ethics committee. In addition, since Sherr is not a Tanzanian citizen his study must be approved by the COSTECH before start as well. Revelation that the researcher and his associates have been conducting the trial among the poor and sick communities without ethical and legal approval makes it questionable at this point.

The Traditional and Alternative Medicines Act no 23 of 2002 has a provision for promoting homeopathy treatment research (URT 2002), but this does not include studies that are denying participants from receiving already established therapies such as ARV. The fact that the researcher is documenting that he has added up nutritional projects and established a link with the local NGOs namely the Tanzania Rural Education and Development Organization (TREDO) and Kilimanjaro AIDS Control Centre (KACA) is plausible. But research participants without ARV might be deemed exploited if homeopathy treatment is regarded as placebo[10]. Within this context the concepts of *unyanyasaji and udhalimu* would imply that the

[7] In his personal website available at: http://semiskimmed.net/woo/jeremy_sherr_AIDS/two-meetings.html accessed on 9 February 2011, Jeremy Sherr explains his two meetings with Tanzanian health professionals and his detailed plan which is highly criticized by various leaders as unethical on the same page.

[8] According to the web dictionary available at: http://wordnetweb.princeton.edu/perl/webwn?s=homeopathy accessed 14 February 2011, Homeopathy is a method of treating diseases with small amounts of remedies that, in large amounts in healthy people, produce symptoms similar to those being treated.

[9] In this one year report, it is clearly stated that "We have written a research proposal and are applying for ethics approval from the government" Available at: http://www.homeopathyforhealthinafrica.org/project.php. Accessed 8 February 2011.

[10] Homeopathy treatment is equated to placebo in the Wikipedia Available at: http://en.wikipedia.org/wiki/Homeopathy Accessed 14 February 2011

sick participants have no alternative than finding any possible means thought to be of help. At the same time researchers take advantage to test their alternative conventional medicine strategies. To the other extreme we need further to establish why the study was started without ethical and research approval from relevant authorities for almost two years, despite an annual web-based published report.

Study No 2: Virodene PO5811

Towards the end of 2001 the Tanzanian government ordered a deportation of two South African researchers who were testing a harmful drug among AIDS patients. The drug, Virodene P058 was already banned in many countries like the UK and Germany after it had been discovered that it was a derivative of the industrial solvent dimethylformamide (DMF) which is a highly toxic substance, with the potential of activating the HIV virus. The researchers did not receive any approval from the NIMR until it was revealed that they had secretly started their trial in a military hospital called Lugalo and another private clinic owned by the former inspector general of the police in the country. The controversy involved powerful entities: the military, the pharmaceutical industry and politicians. In the midst of authorities, regulations and other strong powers there are patients who unknowingly have been given the highly toxic substance believing that they were receiving the right medications.

There are at least three concerns with regard to this study: One is whether deportation of researchers who purposely tested the toxic drug to sick patients represents enough punishment? Second, what are the ethical and legal mechanisms for dealing with unethical and dangerous studies that are conducted in restricted environments such as military premises? Third, what could be the welfare of those who were on the dose after the study was stopped? As a matter of fact, both ethical and legal regulations in the country are 'silent' with regard to these matters. It seems that researchers were aware of such loop holes and therefore got an ample chance of entering into agreement with the military authorities without involving the NIMR, TFDA or COSTECH as required. None of these regulatory authorities have any provision for sanctions when such situations occur, and the government action for deportation was just an alternative which has nothing to do with the unethical study done by the convicts.

[11] Available at http://www.essentialdrugs.org/edrug/archive/200109/msg00039.php Accessed 9 February 2011

The first two questions have to do with the legal mechanisms that are unclear. Perhaps that is why it was easy for researchers to conduct an unapproved study in the military hospital. The last question can be explained within the context of exploitation in the mentioned two meanings where patients had no alternative and therefore the toxic substances were offered to them *(nyanyasa),* and also where they believed to have been receiving the right medication, hence missing the right protection and correct treatment *(dhulumu).* (The Lugalo military hospital caters for in and outpatient services among army members and the civilians in the surrounding areas).

Study No 3: The Trials of Thomas Butler

Thomas Butler, an American microbiologist conducted a clinical trial in the Northern East of Tanzania to find out the efficacy of a new antibiotic - gentamicin - on the bubonic plague and later on to fight bioterrorism in case the germ is used for that purpose in the USA. In addition to taking samples from 42 patients who had not consented to participate in the study, the Federal Bureau of Investigation (FBI) in the USA accused Butler of possibly misplacing the samples thought to be dangerous for the citizens of the USA (Enserink and Malakoff 2003). The fact that the researcher administered 30% less of the antibiotic than is recommended represents a clear exposure of research participants to unnecessary risks lest they develop resistance to that deadly infection (Enserink 2003). And this actually fits both concepts of *unyanyasaji* and *udhalimu;* oppression, fraud, conning, or oppressing the vulnerable persons without alternative. One can imagine an already infected patient receiving a less recommended dose from a qualified and trusted doctor who has travelled all that far to bring "help". The following observations are worth noting in the presented case stories:

First, studies conducted among vulnerable participants are being assisted by qualified medical and health professional citizens acting as part-time entrepreneurs who consider potential risks to participants as more lightly (Lemmens 2004). In the first case Sherr had referred to a number of local professionals as collaborative partners. In the second case there is a link between researchers, military doctors and the Inspector General of the Tanzania police force who is mentioned as the owner of the second trial site, a private hospital in Dar es salaam. In the third presented case, the regional medical officer in the trial site is acting as the Principal Investigator, leaving Butler as an international consultant and then contorted to be the second

author in published results[12]. Powerful structures within the country such as the police, politicians and professionals are important in making sure that the welfare of research participants is observed as it is supposed to be. Their knowledge and positions are always a target for criticism if they take part in unethical studies.

Second, there is a suspected "hidden" agenda in exploitative and unethical studies. Like in the presented case stories, an on-going homeopathy treatment trial among an unspecified number of participants in the Northern Tanzania is unclear. The published first year report further indicates uncoordinated and ambitious mission where the researcher has listed a number of other projects such as poultry, education, nutrition, and partnership with local Non-Governmental Organizations (NGOs) probably extending beyond the trial site or objectives.

Moreover, now we know that the toxic derivative from industrial solvent cannot be acceptable for human treatments at any rate, but one can wonder what motivated the researchers to make a try while being aware that such trials would put patients in danger of losing their lives. Under close assessment one could say that the discovery of the plague bug in Tanzania and the interest to conduct research was not to save the Tanzanian population per se. The FBI and the Federal authorities in the USA had no interest in finding out what happened to the poor research participants who were under-dosed during the trials. In addition, they were not interested in knowing how the samples were handled through the FedEx courier when the researcher shipped them back to Tanzania (Enserink and Malakoff 2003). There is a need for relevant authorities in poor and low income countries to find out the proper safety for vulnerable citizens who are enrolled in questionable studies which might put them into risks.

Summary and concluding remarks

It is quite clear that progress in medical and health related research has resulted in the development of innovative curative and preventive measures which are important for the welfare of human beings in all parts of the world. Since at some points such research requires participation of human beings, there have been a number of both national and international regulations and guidelines which are responsible for establishing mechanisms for possible consideration of professional conduct that would protect the safety, so that they are not

[12] Mwengee is the first while Butler is the second author of these research results presented in the Oxford Journals in 2006. See *"Treatment of Plague with Gentamicin or Doxycycline in a Randomized Clinical Trial in Tanzania"* at http://cid.oxfordjournals.org/content/42/5/614.abstract

subjected to unnecessary harms. This chapter has highlighted and discussed the historical, economic and political situation that has shaped ethical and legal mechanisms of regulating medical and health related research in Tanzania. Some weaknesses and loopholes have been discussed through the analysis of case stories that indicate different forms of exploitation in a Tanzanian context.

The ethical and legal mechanisms to regulate research in Tanzania have been characterised by a mix and ambiguous, or rather a duplication of responsibilities that has caused inertia and thus created a loop hole for violating the rights of vulnerable research participants and subjecting them to ethically unjustifiable forms of harm and risks. The most probable reason for this could be that penalties for unethical and fraudulent researchers are currently unclear. In many instances unethical studies are conducted by foreign researchers who are being assisted by local professionals while operating in the same system, by side-lining the established authorities. There is a need to revisit existing mechanisms and strengthen them by having a strong regulatory authority with full mandate of providing adequate protection for vulnerable research participants.

CHAPTER FOUR

ANALYSIS OF THE CONCEPT OF BENEFIT IN CURRENT DECLARATIONS

Introduction

This chapter intends to give an analysis on how the concept of benefit in medical and health related research ethics is conceived of in different declarations and ethical guidelines. It aims specifically at describing how this concept has been expressed or modified in guidelines and declarations. Further discussion on the position of benefit for research in poor and low income countries in terms of health needs and the "10/90 gap" which refers to the mismatch in global spending on health care research between affluent and poor and low income countries, will be done to explain how benefit merge fairly or unfairly. The controversy of placebo use in research and how other scholars have discussed the concept of benefit will be considered in the light of looking at the future role of the Declaration of Helsinki.

Background to declarations

The World Medical Association (WMA) provided for the ethical principles in medical research involving human participants that was adopted by the 18th WMA general Assembly in Helsinki, Finland, (hence Declaration of Helsinki) June 1964. These principles have been amended and recorded several times in history since then. Further directives and international guidelines for research involving human beings have also been put in place from time to time. For instance the Council of International Organisations of Medical Sciences (CIOMS) in 2002 in collaboration with the World Health Organisation (WHO) developed 21 guidelines for biomedical research involving human participants with some emphasis on research in poor and low-income countries. The Nuffield Council on Bioethics (NCoB) has issued reports on human research and clinical trials in these countries mentioning the need for considering the socio-cultural variations in terms of informed consent and the role of Community Advisory Boards (CAB's) and in 2005 the United Nations Education Scientific and Cultural Organization (UNESCO) adopted the Universal Declaration of Bioethics and Human Rights (UDBHR) which among others, recognizes respect for human dignity and observance of human rights in ethical issues raised by advances in science and technology (UNESCO 2005). Some of the arising issues in these guidelines have been problems in adaptation and implementation of crucial elements that call for attention in medical and health related research mostly due to cultural contradictions and a quest for universal understanding of current practices as far as benefit and benefit sharing is concerned. Critics of these

international guidelines and declarations have stated that such issues have been addressed in general terms, and they can be interpreted in different ways. (Marshall 2003; Benatar 2005).

Changes of the concept of benefit in revised declaration of Helsinki

It is widely recognized that international research could bring benefit to the poor communities if deliberate efforts and plans are made in order to share the benefits accrued from research. To achieve this there is a need to have clear agreement between researchers, sponsors and the host country in which research participants are recruited. Among the controversial issues in terms of benefit and benefit sharing in medical and health related research, is the discussion of post-trial benefits which have been undergoing change in the latest revision of the Declaration of Helsinki and now indicates uncertainty with regard to the availability and affordability of successful experimental intervention for poor communities. The earlier version stated: "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" (Paragraph 30), while the latest version states (paragraph 33) that patients are entitled either "to be informed about the outcome of the study and also access …of other appropriate care or benefits", but in this revision such appropriate care or benefit are not clearly specified.

Furthermore, the additional principle 29 of the declaration of Helsinki to include the use of placebo or non-treatment in studies where proven preventive, diagnostic or treatment method exists is another element that has created a significant change in the concept of benefit in the current revision. Appropriate standard of care among research participants has been debated over a decade. Most of the arguments are put forward against applications of placebo or no treatment using available interventions when testing a new drug. Many documented studies have criticized the use of placebo in studies involving HIV / AIDS patients in areas where antiretroviral treatments (ART) are established interventions. Denying or withdrawing already existing intervention such as ART just as randomizing participants to two different trial drugs where one is inferior to the other, has always been seen as both inhuman and morally unacceptable (McIntyre, Bagenda et al. 1998; Forster, Emanuel et al. 2001; Macklin 2001; Kottow 2002; Solbakk 2004; Malmqvist 2011). Moreover, from a human rights perspective, proper treatment is a right all human beings possess and the opposite of it would be construed as a criminal offence against humanity.

Benefit in terms of global health research and healthcare needs

For more than a decade the Global Forum for Health Research (GFHR) has subsequently reported an estimate of only 10 per cent of the world's medical and health research resources being directed to health problems in poor and low income countries where the remaining 90 per cent has been located to other preventable health problems (GFHR 1999; GFHR 2000; GFHR 2002; GFHR 2004); and so on. The forms of collaborative transnational research to correct this, also known as 10/90 gap, has been a strategy throughout the years, leaving away complex ethical issues arising out of the interplay between such collaborations and most arguably, the global health inequalities in terms of standard of care, post-trial benefits and the challenge of acceptable mechanisms of strengthening both research and scientific capacity within the host countries which would require a new international moral commitment (Benatar and Singer 2000; Benatar and Singer 2010). Underpinning such a commitment, the missing hub has been a little observation on issues such as political, social and cultural background of the host countries, education needs to research ethics members, relevance of the proposed studies in the host countries, balance of benefits and evaluation of if and how the study findings will fit into the health care system within the host countries, among others.

Furthermore, International collaborative research activities have posed a number of ethical questions for Research Ethics Committees (REC's) – also known as Institutional Review Boards (IRB's), arising from issues such as data sharing and samples, imbalanced scientific development and capacity plus legal ownership and intellectual property rights. Developing a balanced mechanism for research collaboration has been seen as a strong barrier, more importantly in terms of trust between institutions in poor and low income countries from the south, and developed countries in the north. Yet, despite these challenges, research participants in poor and low income countries are witnessing and involved in an influx of transnational research activities, also called "Multi-country" studies having passed by a weak system of ethical reviews within their nations, or having approved by their fellow neighbouring countries. The question as to who should be responsible in balancing the on-going system in order to make a trusted scientific and non – scientific network that would clearly address benefits among the vulnerable participants has remained side-lined or rather, superficially answered.

Future perspective: A way forward

In order to ensure that international collaborative research meets the needs of participants and citizens in poor and low income countries, appropriate models for medical and health related research are crucial. Given the voluminous of international guidelines and regulations currently available, it is important to develop rigorous and clear procedures under which research activities will be done in acceptable ways; especially where some documents such as the Declaration of Helsinki and other guidelines seem to conflict with the reality of existing situations. It is from this background that Latin America has come up with the Declaration of Cordóba about ethics in research involving human beings, which proposes to abandon the Declaration of Helsinki and start using the UDBHR instead. Major explanations stem on four important issues: First, there are clear indications that the latest revision of Declaration of Helsinki will negatively affect the rights, well-being and safety of participants who join in studies. Second, acceptance of applying some forms of different standards of care because of either methods or other reasons is deemed unethical. Third, proposing the use of placebo where there are already established interventions is both unethical and against human rights. Fourth, the lack of strong obligations for post-trial benefits to study populations has much to do with disrespecting the host community that has accepted to participate in the study in question (Garrafa 2008; Garrafa, Solbakk et al. 2010). The need to establish a coalition between member states regional wise might be a desirable option in order to see to it that the UDBHR is implemented.

Though it is generally acceptable that independent research ethics review committees should take a lead in ensuring that appropriate and effective ethical standard are observed in research conducted in host countries, this has always been undermined due to limited capacity. In the first place, finding out who and how one should be responsible in building such a capacity, might be among the desirable ways towards building sustainable shared values and practices that are essential in solving medical and health problems of mankind. Having well written guidelines, signing declarations or mentioning their existence and putting trust in the actual practice are two different perspectives that need bridging.

Concluding remark

This chapter was not a replicate of the Declaration of Helsinki and its several revisions. Neither was it a replicate of other guidelines that govern medical and health related research. Attempts to give an analysis of the concept of benefit in these guidelines have been made by relying different arguments provided by different scholars. Most of arguable criticisms over the current revision of the Declaration of Helsinki stem in how the concept of benefit and benefit sharing has been expressed and modified or rather, ignored by researchers and sponsors plus the controversy of placebo use in research. Further discussion on the position of benefit for research in poor and low income countries in terms of health care needs and the "10/90 gap" has been discussed in terms of the emerging international research undertakings to correct it which have brought up further ethical complexities in terms of governance. The suggested way forward is based on the Latin American suggestions expressed in the Declaration of Cordóba about ethics in research involving human beings, to abandon the declaration of Helsinki and implement the UDBHR with a call to form a regional coalition between member states so as to honestly find out a solution of how and who should be responsible in building sustainable shared values and practices in order to bridge the gap between theory and the right practice towards solving medical and health related problems to human beings.

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