CHILDRENS’ AND PARENTS’/GUARDIANS’ UNDERSTANDINGS OF RIGHTS, RISKS AND BENEFITS ASSOCIATED WITH RESEARCH INVOLVING MINORS.

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Children’s’ and parents’/guardians’ understandings of rights, risks and benefits associated with research involving minors.

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Keywords

Rights.
Risks.
Benefits.
Informed consent/assent.
Confidentiality.
Research involving minors.
ABSTRACT

Researchers in the medical and social science fields have an ethical responsibility to make sure that they protect the rights of their research participants. They do so in part by minimising the risk for harm and maximising the potential for benefit to participants. In recent decades, advances in medical research have helped save or lengthen the lives of children around the world. With improved therapies, child and adolescent mortality and morbidity rates have decreased significantly in the past 25 years. Despite these advances, medical researchers and others argue that children have not shared equally with adults in medical advances and research ethics. Even though a majority of researchers want children to benefit from dramatic and accelerating rate of progress in health care that has been fuelled by scientific research, researchers do not want to place children at risk of being harmed by participating in medical and non-medical studies. Ethical conduct of health research involving children considers the necessities and challenges of health research and reviews the ethical and legal standards for conducting it. It also considers problems with interpretation and applications of these standards and conduct, concluding that while children should not be excluded from potential beneficial medical studies, some research that is ethically permissible for adults is not acceptable for children, who usually do not have legal capacity or maturity to make informed decisions about research participation. The ability to assess accurately the risks and benefits of a study are important to ensure that participants can make an informed decision regarding his or her own or his or her surrogate's participation. This study evaluated children's and parents' understandings of rights, risks and benefits associated with research involving minors. The study population consisted of 205 parents/guardians and 205 children aged 7 to 17 years who had been approached in one of the several ongoing health studies in 5 centres in mainland Tanzania. The Modified Newman Reactions to Research Participation for children and parents were used to collect information regarding perceptions of risks, benefits, rights associated with research involving minors and factors that
had influenced them to participate in various researches. In analysing reasons for research participation, the majority of participants expressed positive reasons. Only 97.7% of the children interviewed thought that participating in the research might improve their access to health care, 79% participated to help themselves and 78.1% did so for the sake of helping others. Most of the positive attributes of voluntariness were seen from responses since almost more than 70% responded positively to criteria used in analysing decision making in research participation. The study showed a positive correlation between the age of minors and financial benefits. A significant number of children (19.5%) aged 11-17 (mean age 14) reported that their main reason for participation in research was for financial gain. This suggests that the older the age of the child, the greater the chance that she/he can be induced by money. In analysis of reasons for participation and comprehension of information provided before and during participation, children aged 5-12 years old said they felt good about helping other people. Among the responders, 82% were aged 7-9 years old. This suggests that participants in lower age groups, when given adequate information, can freely volunteer and make proper decisions. Positive attributes were also observed when analysing factors for fair selection of study population, respect for recruited participants and study communities, scientific validity, social value, favourable risk benefit ratio and research rights. Identification of factors that influence participants’ perceptions of the risks, rights and benefits of research studies is important as a means to optimise the manner in which we protect them from uninformed risks involved in research participation. By creating age appropriate modules of information, children as young as seven years can understand potentially difficult and complex concepts such as risks and benefits associated with research participation.
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<th>Full Form</th>
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<tr>
<td>AAP</td>
<td>American Academy of Pediatrics.</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome.</td>
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<td>AZT</td>
<td>Azidothymidine.</td>
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<tr>
<td>CIOMS</td>
<td>Council for International Organizations of Medical Sciences.</td>
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<td>COHRED</td>
<td>Council on Health Research Development.</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus.</td>
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<tr>
<td>ICH-GCP</td>
<td>International Conference on Harmonization: Guidelines for Good Clinical Practice.</td>
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<td>IL</td>
<td>Illinois.</td>
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<td>IMR</td>
<td>Infant Mortality Rate.</td>
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<td>MARC</td>
<td>Mapping African Ethical Review Committees.</td>
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<td>MMR</td>
<td>Maternal Mortality Rate.</td>
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<tr>
<td>NBAC</td>
<td>National Bioethics Advisory Committee.</td>
</tr>
<tr>
<td>NIH</td>
<td>National Institutes of Health (United States).</td>
</tr>
<tr>
<td>NIMR</td>
<td>National Institute for Medical Research (Tanzania).</td>
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<tr>
<td>REC</td>
<td>Research Ethics Committee.</td>
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<td>RRPQ-P</td>
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</tr>
<tr>
<td>SD</td>
<td>Standard Deviation.</td>
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<tr>
<td>SPSS</td>
<td>Statistical Package for Social Sciences.</td>
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<td>UN</td>
<td>United Nations.</td>
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<td>UNAIDS</td>
<td>United Nations programme on HIV/ Acquired Immune Deficiency Syndrome.</td>
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<td>US</td>
<td>United States.</td>
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<tr>
<td>WHO</td>
<td>World Health Organization.</td>
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DECLARATION

I declare that this work is my own work, that it has not been submitted before for any degree or examination in any other university, and that all sources I have used or quoted have been indicated and acknowledged by complete references.

Lumuli Mbonile DATE

Signed:.....................
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1. INTRODUCTION AND LITERATURE REVIEW

1.1 History of Research Ethics

The world has a long history of human abuse especially in exploitation of research participants. The worst abuse dates back to the Second World War (WWII) when Nazi-German scientists used prisoners (young and old) in brutal medical experiments without the slightest regard for their dignity, rights and protection.¹

Due to reports of cases of medical experimentation in human beings done by Nazi scientists, the allied forces (WWII) held a trial in Nuremberg for scientists involved in both war crimes and human experimentation. The counsel proposed six principles which defined legitimate medical research practice. The six principles adopted by the council were later modified and six principles were added and it was later simply known as the Nuremberg Code. The ten principles outlined in The Nuremberg Code can be summarised as follows, essential voluntary consent, balance of risk and benefit ratio, reasonable social and scientific justification of research on human beings, protection of research participants and rights to research participation.²³ The Nuremberg Code is said to be the cornerstone of all medical research guidance, it was adopted by World Medical Association (WMA) and other national and international research ethics regulatory bodies all over the world.¹²³

Even though some argue that some current scientific advances resulted from exploitative experiments, still there is a need to condemn all practices that encourage exploitation of research participants regardless of their age, sex, race or social economic status.⁴

An equally infamous chapter in history occurred during a research project conducted by the U.S. Public Health Service between 1932 and 1979 in Tuskegee, Alabama. Six hundred low-income African-American males, 400 of
whom were infected with syphilis, were monitored for 40 years. Free medical examinations were given. However, participants were not told about their disease. Even though a proven cure (penicillin) became available in the 1950s, the study continued until 1972 with participants being denied treatment. In some cases, when participants were diagnosed as having syphilis by other physicians, researchers intervened to prevent treatment. Many participants died of syphilis during the study. The study was stopped in 1973 by the U.S. Department of Health, Education, and Welfare only after its existence was publicised and it became a political embarrassment which prompted the U.S. congress to create a commission for protection of human participants (National Commission for the Protection of Human Participants). The Commission’s primary task was to identify and develop ethical principles for the protection of research participants. In April 1997 the Commission released its first report on the protection of human research participants (Ethical Principles and guidelines for the protection of Human participants). The report was later called the Belmont Report (the conference where the document was drafted). To date the Belmont Report and the Declaration of Helsinki (which was developed after WWII) serve as cornerstones for ethical principles and regulations for protection of research participants.

1.2 History of Research Ethics in Developing Countries

Many developing countries were colonised by the developed world. Apart from being a major economic and labour source to the developed world, the citizens of these countries were also exploited as research participants. Many studies in the 18th–19th centuries on tropical diseases e.g. Malaria, Trypanosomiasis, Tuberculosis were conducted by many western world scientists without proper ethical review. As documented by Nazi scientists, experiments of military relevance were done in developing countries. Experiments on racial differences, altitude simulation, malaria, pathogenesis, endemic jaundice, typhus pathogenesis and treatment were mostly conducted in South America and Africa. Nazi Germany being the pioneer of much research on racial
differences in developing countries, their role in research misconduct and human right violations left a negative attitude among research participants in the developing world.

After the Second World War, Western European countries abandoned the developing world. Many colonies received their independence around 1940–1970, becoming new countries with new systems. Their main focus was to develop their own governments hence keeping less emphasis on research and research regulatory bodies. Very few developing countries were signatories to human rights declarations and the World Medical Association declaration on human experimentation (Declaration of Helsinki). Until the 1980s, there were no research ethics regulatory bodies in many developing countries. Only a few with international research collaboration felt the importance of having research ethics infrastructures after receiving requirements from donor nations/organisations.

Apart from the Nuremberg Code, Declaration of Helsinki and Belmont Report, an important chapter on research ethics in developing countries was opened with introduction by Nuffield Council on Bioethics, *The Ethics of research related to healthcare in developing countries*. This report includes ten chapters addressing healthcare, economic, social and cultural issues, ethical guidance framework, consent, standards of care, ethical review of research and risk and benefits of doing research in developing countries. This guideline together with framework on research conduct and care of HIV/AIDS (produced after 1999 UNAIDS meeting) and *U.S. National Bioethics Advisory Commission (NBAC) Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries* are the most used documents by almost all established research ethics committees in the developing world.

Even though there has been much effort to build research ethics capacity in developing countries, recent evaluation shows that this effort has not even covered 50% of targeted goals. This makes Africa relatively weak regarding
research ethics infrastructure and other human rights protection bodies when compared to the rest of the world.\textsuperscript{5,13}

1.3 History of Research Ethics in Africa

Since the introduction of western civilisation, Africa has been perceived as the most backward continent with many illiterate and poor people. Low levels of education and economic status have exposed many Africans to research misconduct and inhuman treatments.

The first documented research misconduct was documented as far as the beginning of the 15\textsuperscript{th} century. The Arab slave trade of early 15\textsuperscript{th}–16\textsuperscript{th} centuries was directly linked with human experimentation. Cross breeding of physically strong ethnic groups in order to get a genetically strong (superslave) group was said to have been practised by early Portuguese and Arab slave traders. Majority of studies on anatomical structures and race were conducted in Africa by traders, explorers and missionaries before 18\textsuperscript{th} century.\textsuperscript{14}

By the end of 18\textsuperscript{th} century, Africa faced a dark research history. In 1870 King Leopold II of Belgium called a meeting for the establishment of research places for scientific and philanthropic studies in central Africa. This meeting granted permission to explorers and researchers in Europe to conduct human research in Congo and other countries in central Africa. Human exploitation was common among African colonies after this agreement.\textsuperscript{15,16,73,74}

The first and second world wars did not leave Africa untouched. Many military experiments were done in African countries. Weapons of mass destruction (e.g. biological weapons) were produced and experimented in South Africa, Namibia and some North African countries. Increased research interests on racial differences and evolution of species led many research misconducts and racial division (mostly seen in Sub Saharan Africa).\textsuperscript{16} This era was followed by
international condemnation of human experiments and the later establishment of the Nuremberg Code, Human rights and Helsinki Declaration.

In 1967 Christian Barnard of South Africa managed to perform the first human heart transplant. His techniques together with others conducted by South African Apartheid government among racially and other marginalised groups, including homosexuals remain controversial (in terms of lack of ethics review) to the present.\textsuperscript{16,75,76,77}

The oldest committees to be established in Africa were from South Africa (1967) and Zimbabwe (1974).\textsuperscript{10,15} In the early 1980s, Africa was the focus of many studies on HIV/AIDS and other infectious diseases (for example malaria, meningitis etc.). The booming research collaboration between the North and South renewed the need for the establishment of strong research ethics infrastructure. Despite the increased focus on the need for protecting participants from Africa, many cases of misconduct have been documented, for example 073 (AZT trial) and Trovan trial.\textsuperscript{10,15}

An estimate done in 2001 by WHO African region office revealed that 64% of countries in Africa had at least one Research Ethics Committee (REC).\textsuperscript{10,15,17} Even though many countries had at least acknowledged the importance of having RECs, more than an estimated 25% of health related studies were conducted in Africa without being reviewed by local or international RECs. Many guidelines emphasised simple protocols to prevent exploitation of research participants. However, at that time 36% of countries in Africa had no ethics and regulatory guidance for human research.\textsuperscript{10,16,17} This could be due to inactive research process or poor documentation. With increased research ethics training programs like South African Research Ethics Initiative (SARETI), International Research Ethics Network for Southern Africa (IRENSA) and others, the number of research ethics experts and trainees has increased for the past 5 years. As documented by COHRED - Mapping African Ethical
Review Committees (MARC), up to year 2012 there were 171 RECs in Africa (26 north, 53 south, 41 western, 41 eastern and 10 central).18

1.4 Principles of Ethics and Regulatory Guidance for Research with Humans

1.4.1 Principles
Research involving human participants is premised on two fundamental moral commitments: to improve human welfare by advancing scientific knowledge and understanding of disease; and to preserve and protect the dignity and health interests of the research participant.6,8 Research aims to benefit individual participants and communities through the identification and testing of improved hypotheses/knowledge and therapeutic treatments and to benefit society by making knowledge and treatments available. The potential risk of harm to participants has led to widespread agreement that sound ethical standards must be observed in all research, irrespective of the geographic and economic setting in which it is undertaken. This is derived from the rule of common morality (universal).5,6 As a social institution, morality encompasses many standards of conduct, including moral principles, rules, rights and virtues.5,6,32,52,69

Common morality is applicable to all persons in all places, and we rightly judge all human conduct by its standards. Norms in common morality include those which forbid killings, causing pain and suffering to others, doing evil or harm.

Moral principles which govern research conduct can be categorised into four clusters:6 (1) respect for autonomy – a norm for respecting and supporting autonomous decisions, (2) nonmaleficence – a norm of avoiding the causation of harm, (3) beneficence – a group of norms pertaining to relieving, lessening or preventing harm and providing benefits and balancing benefits against risks
and costs, and (4) justice – a group of norms for fair distribution of benefits, risks and costs.\textsuperscript{6,10,15,16}

Those moral principles together with moral characteristics, traits or virtues (honesty, integrity etc.), provide the framework of research norms and practice which are the building blocks of research ethics.\textsuperscript{6,10}

\textbf{1.4.2 Guidelines}

The chapter in the history of research guidance with human participants was first opened in Nuremberg in 1946, when an American military tribunal opened criminal proceedings against 23 leading German physicians and administrators for their willing participation in war crimes and crimes against humanity.\textsuperscript{2,3,4} Among the charges were that German physicians conducted medical experiments on thousands of concentration camp prisoners without their consent. Most of the participants of these experiments died or were permanently crippled as a result.\textsuperscript{2,3,4,5,6}

As a direct result of the trial, the Nuremberg Code was established in 1948, stating that,\textsuperscript{2,3,6,8} "The voluntary consent of the human subject is absolutely essential", making it clear that participants should give consent and that the benefits of research must outweigh the risks.\textsuperscript{2,3,4}

Although it did not carry the force of law, the Nuremberg Code was the first international document which advocated voluntary participation and informed consent.\textsuperscript{4}

In 1964, the World Medical Association established recommendations guiding medical doctors in biomedical research involving human participants. The Declaration governs international research ethics and defines rules for research, both therapeutic and non-therapeutic research. Some of the issues addressed in the Declaration of Helsinki include:\textsuperscript{2,3,4,5,6}
(a) Risk and benefits of research involvements (risks should not exceed benefits), protecting life, health, privacy and dignity of research participants.
(b) Informed consent.
(c) Independent review (research protocols should be reviewed by an independent committee prior to initiation).
(d) Good Research Conduct (research should be conducted by medically/scientifically qualified individuals).
(e) Scientific validity (research with humans should be based on the results from laboratory and animal experimentation).
(f) Research conduct in vulnerable populations.
(g) Researcher duties and obligations.

The Declaration of Helsinki was revised in 1975, 1983, 1989, 1996 and 2008 and is considered as the basis for Good Clinical Practices.\textsuperscript{2,3,4,16,25,47}

The United States National Commission for the Protection of Human Participants of Biomedical and Behavioral Research prepared the Belmont Report in 1979.\textsuperscript{2,3,4,5,6} The Belmont Report attempts to summarise the basic ethical principles identified by the Commission in the course of its deliberations. The report contains basic ethical principles and guidelines to be used by researchers and regulatory bodies in resolving the ethical problems that surround the conduct of research with human participants. The guideline outlines three basic ethical principles: respect for persons, beneficence and justice.\textsuperscript{2,3,4,5,6,15,16}

In 1982, the Council for International Organizations of Medical Research (CIOMS) released the first international guideline (\textit{International Ethics Guidelines for Biomedical Research Involving Human Participants}),\textsuperscript{7} which was developed after many concerns about the application of the Declaration of Helsinki in developing countries (taking into consideration differences in
biomedical research needs between the developed and developing nations). The guideline basically emphasises the following:7,9,19

- Ethical justifications and scientific validity of biomedical research involving human participants.
- Ethical review (committee-institutional, national and independent).
- Informed consent (individual, community).
- Obligations of sponsors and researchers.
- Benefits and risk of study participations (compensations-inducements, coercion etc).
- Principles and guidance of research conducted with vulnerable persons/populations.


The International Conference on Harmonization: Guidelines for good clinical practice (ICH-GCP Guidelines) were first introduced in 1996 by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (United States, Japan, and Europe).7,27 The ICH-GCP Guideline delineates standards for review committees, investigators and sponsors. It was mainly intended to guide research on drugs and devices even though it is rooted in the Declaration of Helsinki and other local regulations.5,7,8 The guidelines elaborate seven principles of conduct for research involving human participants:

- Consistency with Declaration of Helsinki and other ethical guidelines (in all clinical trials).
- Balance of Risk and Benefits.
- Protection of rights, safety, and well-being of research participants.
- Scientific validity.
- Review (institutional and independent).
- Responsibilities and obligations (physician/investigators and sponsors).
- Handling of investigational products, participants records, reports and interpretations.

The guidelines were adopted by UN Member states after several amendments.\textsuperscript{2,3,5}

Apart from the above, several guidelines were developed, each fitting a specific additional purpose or goal depending on different institutional or organisational interest.\textsuperscript{7,15,17,28} For example, the 1991 CIOMS/WHO International Guidelines for Ethical Review of Epidemiological Studies,\textsuperscript{19,28} the 1995 WHO Guidelines for Good Clinical Practice for trials on pharmaceutical products and other organisational-based guidelines (the U.S. Federal Drug Authority developed a guideline regulating pharmaceutical trials), there is also the Nuffield Council on Bioethics guideline on ethics of clinical research in developing countries.\textsuperscript{1,7,9,19,39,40}

\section*{1.5 Ethical Issues in Research}

Despite what the major guidelines indicate, many researchers may believe that informed consent makes clinical and non-clinical research ethical. However, informed consent is neither necessary nor sufficient for ethical clinical research. Instead of using informed consent only, Emanuel et al. proposed 8 requirements:\textsuperscript{20,78} (1) social value, (2) scientific validity, (3) fair subject selection, (4) favourable risk-benefit ratio, (5) independent review, (6) informed consent, (7) collaborative partnership and (8) respect for the enrolled participants.

\subsection*{1.5.1 Social value}

Ethical research must have positive social value through generation of knowledge for health. Without social value, research participants will be exposed to unnecessary risks. A study is said to be valuable only if it changes the social welfare of the target community and the world at large.
Implementation of research findings and ideas challenges many developed and
developing countries. Many communities have different health priorities so
determination of social value is always uncertain and problematic (describing
how useful the research will be to the target community is a challenge for many
researchers).

1.5.2 Scientific validity
Science and ethics always go together. Valid science is an ethical requirement.
All research must create reliable and valid data. In order to avoid exposing
participants to unnecessary risks, a study must have the following:

- Useful results: a research study must be designed so that the results
  are useful in the context of the health problem.
- Fair standard of care: the study design must realise the research
  objectives while neither denying health care service that participants are
  either entitled to nor requiring services that are not feasible to deliver in
  the context of the country’s health care system.
- Feasible: a study must be feasible, given the social, political and cultural
  environment in which the study is to be conducted.

1.5.3 Fair subject selection
Many participants in developing countries are at risk of research exploitation
because of poverty and low literacy. To avoid this phenomenon, conductors of
research in developing countries must ensure that the target population
selection is fair and justifiable. The selection must always aim at minimising the
risk and discouraging all methods that involve coercion, social marginalisation,
political powerlessness and economic deprivation.

1.5.4 Favourable risk-benefit ratio
All research should aim at offering a favourable risk-benefit ratio, or if risk
outweighs benefits, the social value must justify the risk outlined. In conducting
research in vulnerable groups (e.g. children), the risk to benefit ratio must
always be favourable to the group. In collaborative research, the target community should be given all powers to determine if the risks of participating are justifiable and acceptable.

1.5.5 Independent review

To minimise over-exploitation of research participants by researchers and to ensure public accountability, independent ethics review of all research protocols is necessary. Transparency through reviews by local community councils, non-governmental organisations, international organisations and ministry of health is to be encouraged in all research. Review must be independent and competent. Review bodies may have conflict of interest due to relationships with researchers or sponsors. To avoid such scenarios, the REC must be well trained and well equipped to identify and resolve ethical dilemmas in research.

1.5.6 Respect for enrolled participants

Research ethics is a continual process. Research institutions, organisations, promoters and donors have obligations to participants, former participants and host communities. Researchers are obliged to:

- Develop and implement procedures to maintain the confidentiality of information collected.
- Informing participants their rights (e.g. right to withdraw whenever they wish).
- Informing participants of newly discovered risks and information which arises during the course of research.
- Offer proper intervention programs whenever required.
- Offering best, affordable and sustainable health care program (in case of clinical research).
1.5.7 Informed consent
Informed consent has been recognised as a principle of ethical research for more than a century. Even though many communities differ in language, social traditions and practices, elements of informed consent are believed to be universal. Key elements of informed consent can be elaborated as follows:

1.6 Elements of Consent
Consent is the cornerstone of ethical conduct and regulation of research.\textsuperscript{5,6,29,30,31,32} It expresses the governing relationship between science and society hence it should not be compromised.\textsuperscript{6,38,59,61,63,56,67,68}

The philosophy of informed consent is rooted in beneficence and principle of autonomy especially respect for the autonomy of a person.\textsuperscript{8,10,30,31,32,38}

As defined by Mortimer,\textsuperscript{33} autonomy is the right to personal inviolability in control of one’s personal life, and the exercise of free will in taking risks. Being the building block of all ethical research conduct, informed consent is an important element of many research practices, and for it to be valid the following conditions (elements) should always be reflected: \textsuperscript{8,10,30,31,32}

1.6.1 Information (should be appropriate and comprehensive)
If consent is to be valid, information must not only be accurate, but provided in a culturally appropriate and understandable manner.\textsuperscript{6,9,15,31,38,59} Any scientific or technical vocabulary should be translated and explained to participants in clear and understandable language, delivered by trained personnel.\textsuperscript{6,9,15,31,32,33,38}

Being a process, informed consent procedures should continue during the study with evaluation of the level of understanding of information delivered. Reasons for participation should be clear and easily digested by each participant.\textsuperscript{6,9,34,36}
1.6.2 Understandable
The second condition for consent to be valid is that all participants should adequately understand essential aspects of the research.\textsuperscript{6,9,20,38} As elaborated by Lindegger and Bull,\textsuperscript{35} “provision of comprehensive information is not, in itself, considered sufficient grounds for assuming that the person fully understands that information. Consent procedures, therefore, may require some form of test of understanding, most commonly short yes/no or multiple-choice tests of factual information”.\textsuperscript{6,9,20,31,35}

1.6.3 Voluntary
Consent must be freely given or truly voluntary.\textsuperscript{1,6,9,20,31,35} If consent is obtained by means of deception and coercion, it is considered invalid in justification for involvement in research.\textsuperscript{9,36} Every participant should be evaluated to determine if they are psychologically capable to give legitimate consent before participation, especially if the research involves more than minimal risks.\textsuperscript{6,9,31,35,36}

1.6.4 Informed and formal
The fourth element of a valid consent is that it must be sufficiently informed.\textsuperscript{1,5,9,31,36} Provision of information to research participants and understanding are two different things. Hence, to ensure genuine consent, research participants must have sufficient information about the proposed research in order to make a reasonable decision on the basis of their own values and preferences.\textsuperscript{9} In any research, if necessary, the following information should be disclosed to participants: (1) the purpose of the study, (2) risks and benefits of participation, (3) various alternatives to participation (choices), (4) assurance of protection of privacy, (5) availability of compensation (if any), and (5) assurance of power over a decision to continue or discontinue with the study at any time.\textsuperscript{5,6,9,70}
1.7 Ethics in Health Research in Developing Countries

Inequality in infrastructure, access to care and research capability is apparently increasing globally.\textsuperscript{17,31} A rise in the inequality of health indicators (mortality-infant mortality rate (IMR), maternal mortality rate (MMR), quality of life and disease) persists in spite of a general increase in global wealth.\textsuperscript{1,9,10,29} The global burden of diseases is disproportionately large in developing countries; this is due to economic disparities, unequal distribution of health resources, poor infrastructure and other environmental factors (such as catastrophes, disease-prone climates etc.).\textsuperscript{15,29,31,40} Despite this, only a very small proportion of studies are focused on the problems primarily affecting the world’s poorest.\textsuperscript{8,29,41} This inequality is not only contributed to by economic gaps and other factors mentioned above, but is linked to problems arising from different research and health care levels in the global health hierarchy (global, national and institutional).\textsuperscript{9,29,32,34,41}

Globally, the standard of ethics review of research has increased within the past 50 years (after the Nuremberg trials).\textsuperscript{1,6,7,29,34} Despite this, developing countries have been slower in establishing research ethics infrastructure not only due to poor economies but also weak collaboration between developing countries and those with well-established research ethics review and regulatory bodies.\textsuperscript{9,17,31,39}

The current trend of transferring research from developed to developing countries (where cost and constraints of regulations may be lower) increases likelihood of participants’ exploitation especially if there is a huge gap in economy and education. Many international organisations are implicated in research misconduct in many developing countries. The majority of research misconduct is probably a result of poor regional and national monitoring.\textsuperscript{1,9,41}

Many elements comprise a strong global research ethics framework. The majority of developing countries do not have adequate research ethics
infrastructure. This can be due to inactive research activities or overdependence on external research expertise.\textsuperscript{42}

A study conducted by Kass et al. in 2007 revealed that the majority of countries in the developing world rely on U.S. regulations and guidelines, which to some extent decrease their efficiency.\textsuperscript{43}

Apart from research ethics infrastructure, many developed and developing countries resisted signing or ratifying international and regional human rights conventions which are the main pillars in the protection of every citizen (including research participants).\textsuperscript{9,9,15,31} Human rights violations are common to many developing countries.\textsuperscript{1,7,44,45} In such circumstances, it is very difficult to establish a functional and well-respected research ethics infrastructure.\textsuperscript{1,31,44}

Poor collaboration between developed and developing countries widens the gap since many poor and underdeveloped countries are unable to establish high standard research review and regulatory frameworks due to political instability, poor economy and prioritisation.\textsuperscript{45,58}

As explained above, many developing countries do not have well-established research ethic infrastructure.\textsuperscript{30,31,46} A survey conducted by Hyder et al. in 2002 among researchers in Africa, Asia and South America revealed that almost half of researchers in developing countries conduct research without review (ethical, scientific or technical).\textsuperscript{41,47,48} This has been the normal practice in all levels (national and institutional). And after a thorough review, all these directly linked to lack of knowledge of fundamentals of research ethics, poor regulatory mechanisms and review bodies, brain drain (where the best in research are recruited by well-off nations), political instability, poor resources and intellectual isolation (researchers).\textsuperscript{39,59}
Poor collaboration between regional members hinders the transfer of research ethics expertise from countries with well-established review frameworks.\textsuperscript{16}

Many developing countries are in internal conflicts and economic challenges to the extent of focusing on major burdens rather than pulling few resources for establishment or promotion of research conducts and review frameworks.\textsuperscript{16,31}

There is no common ground on establishing a new research ethics framework or in facilitating the existing framework but the majority of developing countries opt to adopt guidelines and monitoring tools from sponsor organisations and donor states which promote paternalism and double standards.\textsuperscript{39} Even existing RECs in developing countries are not up to the required standard, as examined by Milford et al. (2006) (in HIV vaccine trials). Almost all (97\%) African RECs have inadequate training in ethics (health research ethics, vaccine trials etc.).\textsuperscript{31,33,41} Many rely on review from donor countries and they may have minimal control over projects running in their communities. The current effort in optimising the research ethics framework in developing countries is done by international organisations such as Fogarty International Center, WHO, European Developing Countries Clinical Trials Partnership (EDCTP), UNAIDS and other regional and national non-governmental organisations.\textsuperscript{18,21}

Even though protection of research participants (in multicentre research) has been advocated by many international research organisations, the progress seen to date is slow and inadequate.\textsuperscript{50}

Ideally cultural diversities and disparities in health needs between developing and developed countries should be solved first to achieve a global standard on protection of research participants.\textsuperscript{1,5,9,31}
1.7.1 National and institutional levels

Although most developing counties adhere to international or national ethics codes, some research sponsors and regulatory agencies ignore these codes to pursue their interests. Many sponsors and donor nations take advantage of lack of local regulations and statutes as seen in the Trovafoxacin case in Nigeria. Rights of individuals participating in research have not been reflected in many developing countries’ constitutions and statutes (very few countries consider protection of research participants as a national priority). A majority of them don’t have functional RECs or regulatory bodies (it is estimated that more than 25% of health related studies in these countries don’t go for review). Reported reasons for poor research ethics conduct by many researchers and ethicists in developing countries include, ineffective guidelines, bureaucracies in the existing research ethics bodies, cultural conflicts (developing and developed), political instability, increased tendency of overdependence on international funds and lack of training.

1.8 Ethical Issues in Research with Children

1.8.1 Data on ethics in health research with children

Research advances have, each year, helped to save or lengthen the lives of tens of thousands of children around the world by preventing, and/or reducing illness or disabilities and improving the quality of life of children and their families and countless others. Since the 1950s, for example, researchers have created vaccines against polio, measles, mumps, and a number of other childhood infections that have dramatically reduced deaths, disability, and discomfort from these diseases. Children and their families have also benefited from research demonstrating the harm or ineffectiveness of what were once standard therapies, for instance, high-dose oxygen for premature infants.
Despite these advances, ethicists and others have argued that infants, children, and adolescents have not shared equally with adults in advances from research (especially in biomedicine). In particular, many drugs with potential uses have not been tested in studies that include children. These drugs are prescribed to children on the basis of data from animals and adults even though their physiology is different. The reason for that extrapolation started in the early 1940s and 50s after the Thalidomide and Tuskegee cases. These and other cases alerted all major research organisations to review researchers’ practice involving pregnant women and children so as to prevent extra harm to these two groups.

Currently the number of children participating in clinical research has increased dramatically. In Europe, after evaluation of involvement of children in clinical trials, it was discovered that more than half of pharmaceutical trials didn’t involve children even though the product targeted all age groups. This prompted the European Forum for Good Clinical Practice to develop special registration to promote research in children. In 2004 the UK government allocated 100 million pounds to new research involving children.

In 1977, the US Commission for the Protection of Human Participants of Biomedical and Research released a report to encourage research with children. In their report they highlighted importance of assent, the reasonability of parents and guardians on their children’s participation, responsibilities of research ethics committees in protection of rights and dignity of research participants.

In June 1996, the National Institute of Child Health and Human Development and the American Academy of Pediatrics (AAP) convened a workshop to address the inclusion of children as participants in research. After reviewing reports, background papers, a study of a sample of NIH-sponsored clinical research abstracts suggested that 10–20% inappropriately excluded...
The conveners concluded that there is a need to enhance the inclusion of children in clinical research.\textsuperscript{23,31,32,53}

The conclusion was based upon scientific information, demonstrated human need, and considerations of justice for children in receiving adequately evaluated treatments.\textsuperscript{1,6,23,16} The need reaches across a broad spectrum of health research, including studies on pharmaceutical and therapeutic agents, behavioural, developmental and life cycle issues including childhood antecedents of adult disease, prevention and health services research.\textsuperscript{62,63}

The AAP reported that only a small fraction of all drugs and biological products marketed in the U.S. have had clinical trials performed in paediatric patients and a majority of marketed drugs are not labelled for use in paediatric patients.\textsuperscript{63} The scenario is not very different from that seen in Europe, Australia and Japan since all major research industries operate with similar standard operating procedures (after harmonisation).\textsuperscript{62} The academy also reported that many drugs used in the treatment of both common childhood illnesses and more serious conditions carry little information in the labels about use in paediatric patients. In addressing these inadequacies, the Food and Drug Administration (FDA) has published a proposed regulation calling for changes in the testing of prescription drugs to ensure that manufacturers specifically examine the drugs’ effects on children if the medications are to have clinically significant use in children.\textsuperscript{55}

In January 1997 the NIH announced (NIH Guide for Grants and Contracts, volume 26, Number 3, January 31, 1997) plans to develop a policy for the inclusion of children in NIH-supported human subject research.\textsuperscript{64}

The World Health Organisation (WHO) reported that globally 1 000 children under age of five die every hour,\textsuperscript{65} many of these cases are preventable with proper interventions (e.g. making the products of research available to studied
communities). As explained in the 10/90 gap, almost all research done in children in developing countries ends up benefiting the few in the developed world. A good example: many studies on diarrhoeal diseases (which cause 17% of death among under-fives) are conducted in developing countries (Vibrio Cholera, Rotavirus, Salmonella vaccines and management) but they end up on the market in the developed world. With this increase in trend of unequal distribution of research benefits, WHO and other research organisations decided to develop policies and guidelines in ensuring good ethical practice especially to research involving vulnerable populations.

There are very few countries in Africa with comprehensive ethical-legal frameworks regulating research with children, even though the majority of HIV, Malaria and HPV vaccine trials are conducted on this continent. Even though the exact number of children involved in research in Africa and other developing countries is unknown, it is estimated that approximately half of under 18s are involved in some sort of research (ethical and unethical). For example, in South Africa, 12 000 young people between the age of 9–24 have received the HPV vaccine by 2007, most of them being females and males between the ages 9–15 (20%).

Because adolescents are severely affected by the HIV epidemic, the focus of HIV vaccine trials is on them. Before the failure of STEP trials, many adolescents were recruited in Phase II vaccine trials, but this was possible after a long debate on whether to involve them or not. Africa being deeply rooted in communitarian ethics, there are several cultural barriers that prevent children being involved in research, requiring a well-organised and culture-sensitive ethical legal framework.

1.8.2 Ethical principles for the conduct of research with children

The historical origin of current ethical principles for conducting research with children arises from the Nuremberg Trials (Nuremberg Code) and the Declaration of Helsinki.
The principles for conducting research contained in the Declaration of Helsinki and other guidelines apply to all human participants, adults and children. For example, the following elements of informed consent can be seen in all guidelines: adequate information must be provided to the research participants, participation in the research must be freely volunteered, with the understanding that the participant can withdraw at any time, and in addition, informed consent should be obtained, preferably in writing.

In the Declaration of Helsinki there is one section which refers specifically to research with children which states: “when the subject is a minor, permission from the responsible relative replaces that of the participant in accordance with national legislation. Whenever the minor child is in fact able to give consent, the minor’s consent must be obtained in addition to the consent of the minor’s legal guardian.” The guidelines are clear that the consent of the child should be sought in addition to that of the responsible adult, and by evaluating the risk and benefits of participation.

Most national and international guidelines allow children to be enrolled in research only when their parents or legal guardians give their permission. Many guidelines, including the Council for International Organizations of Medical Science (CIOMS) guidelines, including guidelines from South Africa and the U.S., also require assent.

The Tanzanian and Ugandan guidelines allow children to be enrolled in research that does not offer prospect of direct benefit only when: “adequate provisions have been made for the solicitation of the children’s assent.” Similarly, the Indian Council on Medical Research guidelines state that: “the assent of the child should be obtained to the extent of the child’s capabilities.” Other guidelines mandate that researchers must respect the dissent of research participants. According to the Guidelines for the Ethical
Conduct of Biomedical Research Involving Human Participants in Kenya, when the “child refuses to participate in the research, that refusal must be respected unless there’s no other medical alternative from which the child could benefit”. The assent requirement is one of the principal requirements for research involving minors, and often the only requirement to specify when children should have a say in whether they participate in clinical research. Failure to require children’s assent when appropriate represents a failure to respect children as research participants, while failure to waive the assent requirement when appropriate may block parents’ decisions to enrol their children in potentially beneficial research.

1.9 Ethical Issues in Research with Children in Africa

As outlined in many guidelines, many citizens of developing countries are potentially vulnerable because of the lack of political power, education, unfamiliarity with medical interventions, extreme poverty or dire need for health care and nutrition.

Children being the weakest in society are highly vulnerable to all kinds of exploitation. Bearing this in mind the international research ethics community decided to group them under a special category – “Vulnerable groups”. Many guidelines have recognised the position of developing countries in research, e.g. in 2002 CIOMS added a special guideline for so-called underdeveloped communities. This initiative was also copied by Nuffield and many other international and national guidelines.

This concern is especially warranted in research involving children because of their unique vulnerability in research settings. Children, especially in developing countries, are vulnerable because of their more limited cognitive competencies and poor exposure, which may constrain their capacity to understand and defend their rights as research participants and to make reasoned decisions concerning research participation. They are also vulnerable because of
their limited social power which impairs their ability to exercise independent
decision-making concerning research participation when parents and
caretakers (e.g. school personnel) and researchers support their involvement
(in proxy consent). Children are also vulnerable because of their ambiguous
standing in the law which undermines their control not only over participation in
research (with parents exercising proxy consent)\textsuperscript{6,8,9,23} but also over the
disposition of research material (e.g. blood samples etc.), their withdrawal from
research participation, and other decisions that normally accompany research
involvement.\textsuperscript{23,50,40,64} For these reasons, research involving children requires an
even more sensitive appraisal of risk because children have limited capacity to
resist intrusions into their rights as research participants.\textsuperscript{61}

Many developing countries have a long history of cultural norms and traditions
which if not clearly understood might impair some key research ethics
elements;\textsuperscript{1,71} e.g. any decision about participation in research is usually
obtained predominately by males (father, male guardian, chiefs, sub chiefs and
elders, representatives of communities etc.).\textsuperscript{1,26,31,40,47} Under these
circumstances involvement of children in research may be determined by that
group of society. Children, being seen as communal belongings, cannot decide
for themselves in any matter that involves their bodies or psyche.\textsuperscript{40,47} A study
conducted by Molyneux et al. in rural Kenya revealed that the majority of
participants accepted the decision-making mandate to be under jurisdiction of
fathers and other males and elders.\textsuperscript{47} Mothers will have such mandates only
when given permission by the above group. This culture varies depending on
the type of household (rural, urban, nuclear or extended), mother’s age,
education, income-earning role, specific relationship the mother has with
husband, what was requested, who is available or could be available within the
time given.\textsuperscript{1,38,40,44,47}

Making independent decisions is a problem among communities in many
developing countries. Many parents have very little formal education. As
reported in Kenya by Molyneux et al, in 2001, local paediatric wards recorded that over 90% of parents of children had less than four years of formal education.\(^7\)

Research principles and techniques are always confused by many researchers. Many elements of research ethics require a minimal understanding but research varies from techniques and level of risks involved. Poor understanding of techniques used and increased illiteracy have exposed many communities to unethical research. This together with poor ethical-regal frameworks expose not only children but also other age groups to exploitation and injustices.\(^1,26,31,32,40\)

In understanding ethical issues of research in developing countries, an important additional safeguard is needed to avoid the exploitation of potentially vulnerable populations in developing countries.\(^31,32,57\) Clinical trials sponsored or regulated by foreign sources should be limited to those that are responsive to the host country’s health needs. If the intervention being tested is not likely to be affordable in the host country or if the health care infrastructure cannot support its proper distribution and use, it is unethical to ask persons in that country to participate in the research, since they will not enjoy any of its potential benefits.\(^1,9,17\) Research participants in developing countries are less likely to have continued access to the intervention being evaluated than are participants in developed countries. This raises the ethical question of whether any health care benefits will ever reach the citizens of the host country.\(^9,34,67\) In addition, there is always a concern that the developed country may be exploiting a country that is poorer, less powerful, and therefore more vulnerable.\(^9,17,31\) Although it has long been recognised that collaboration between peoples of different nations has great potential to generate substantial benefits for both sides, there is often controversy over the nature of the collaboration and whether the distribution of any benefits will be equitable.\(^9\)
Given these issues, researchers, sponsors, and RECs in developed countries must take great care to ensure that the justification for conducting a trial or any health research in a developing country is adequately articulated.\textsuperscript{9,26,71} This is especially important if the trial is to be conducted in a country or region where the population may be vulnerable to exploitation because of pervasive poverty and disease or lack of understanding of the scientific issues surrounding the health problem and the role of research in the search for a solution.\textsuperscript{1,6,38,71}

Research in a developing country might be justified in a number of ways.\textsuperscript{9,16} The research might address an important health problem in that country, or it might represent a joint effort by the country sponsoring or conducting the study and the host country to address an important health problem in both countries.\textsuperscript{16} However, conducting research in a developing country because it is more convenient, efficient or less troublesome to do so is never a sufficient justification.\textsuperscript{9,16,17,71}

Initiatives to reduce the burden of disease in developing countries are urgently needed.\textsuperscript{16,29} Research that is responsive to the health care needs of these countries constitutes one such initiative.

More information is needed for research involving children and other vulnerable groups in developing countries.\textsuperscript{7,71} This study hopes to contribute by trying to explore perceived applicability of principles of research ethics to vulnerable populations, especially children, in developing countries.
2. AIMS AND OBJECTIVES OF THE STUDY

The overall objective of the proposed study was to assess children’s and their parent’s/guardian’s understanding of core ethical aspects in research involving children (rights, risks and benefits).

2.1 Specific Objectives

1. To evaluate children’s understanding of key ethical issues involved in research.
2. To assess children’s understanding of assent in deciding to participate in research.
3. To see if children can distinguish risky from non risky research†.
4. To evaluate parents’ (of minors involved in research) understanding of key ethical issues (informed consent, risk, rights, and benefits) in research with children.
5. To compare understanding of key ethical issues between children who have participated in research with those who have not.

†. Classification of risk is according to Brunel University (Appendix X) and NBAC.
3. METHODS

3.1 Study population and setting
This study involved children between ages of 7 and 17 and their parents/guardians who participated in research conducted by National Institute of Medical Research (NIMR) and those receiving clinical care in secondary and tertiary health care units around Tanzania.

Inclusion criteria
1. Children between the ages of 7 and 17 years.*

Exclusion criteria
1. Children below 7 years and above 18 years.**
2. Adults with no legal relationship with escorted children.
3. Children unable to assent and parents unable to consent.

Notes:
* Tanzanian constitution defines a child as a person below 18 years.72
** Tanzanian primary school starting age is 6 years (Tanzania Ministry of Education and Vocational Training).

3.2 Study design, size and sampling
This was an exploratory study. Participants were approached from National Institute of Medical Research (NIMR) centres, secondary and tertiary health care units where they were recruited in different research projects. Permission was obtained from NIMR investigators and detailed information of the purpose of the study was presented to parents, guardians and their escorting children. Assent and consent was obtained from participants followed by assessment of understanding of key information on the research they entered (parents and children).
A modified Newman’s reactions to research participation questionnaire (RRPQ) for both children and adults was used to capture data on positive and negative appraisal for research participation, assessment of informed consent, trust in research team and understanding of rights and benefits of participation in research (Appendix II, III, IV). The tool is a questionnaire with 60 questions (to both children and adults) with 3-5-response scale (strongly agree, neutral, strongly disagree, agree and disagree). Participants were given an option of completing the questionnaire or having the interviewer administering it verbally.

The sample size in this study was estimated by the following calculations

\[ x = Z(\frac{c}{100})^2 r(100-r) \]  \hspace{2cm} (1)

\[ n = \frac{N x}{[(N-1)E^2 + x]} \]  \hspace{2cm} (2)

\[ E = \sqrt{\frac{(N-n)x}{n(N-1)}} \]  \hspace{2cm} (3)

Taking \( n \) as a sample size, \( N \) as the population size, \( r \) is the fraction of responses and \( Z(\frac{c}{100}) \) as the critical value for the confidence level \( c \). Then the sample size can be deducted from;

\[ n = \frac{N x}{[(N-1)E^2 + x]} \]

Using 5% as a margin of error the confidence level \( c \) will be 0.95 and the critical value \( Zc/100 \) will be 1.96. From statistical estimates of the study population, if chosen random randomly from a study population of 400(\( N \)) the response distribution(\( r \)) has to be 50% to avoid skewing of data.

\[ n = \frac{400*960x}{[(400-1)4.979^2 + 960]} \]

\[ n = 197 \]
The sample population of 197 is the minimum recommended sample size. In this study 294 participants were approached – within statistically recommended range. A pilot test was also used to estimate the population standard deviation and with power adjustment the estimated the sample size was approximately 205 (nQuery Advisor®, version 7.0). Only 48 participants were recruited for evaluation of sample size and sample power adjustment (actual and planned power tests) according to nQuery Advisor®, version 7.0. Other data obtained from this pilot group was not used analysed further.

Control group: to determine the possible correlation in level of understanding a control group was used. This group was recruited from the same study population. Approximately 205 families were classified as controls and recruited for the study (the criteria used to select the control group are summarised in Table 11). The control group data was only used in comparing the level of understanding of children involved in research to those not involved in research (specific objective number 5).
4. DATA MANAGEMENT AND ANALYSIS

Each element in the assessment tool (modified Newman’s reactions to research participation questionnaire-RRPQ) was given a score range (such as consent, benefit and risk). Participants were scored according to the level of understanding of key research elements elaborated prior/during recruitment. Since participants were recruited from different research centres (NIMR and Health care facilities) analysis was only based on key items designed on RRPQ. Statistical analysis was done using SPSS 10.0 (SPSS, Inc., Chicago IL, USA), in which key variables were subjected to statistical tests.

The analysis of the previous questionnaire was done in two phases: first, a frequency analysis of socio-demographic data (Part I of the questionnaire) and correlational analysis of reactions to research participation together with social demographic data and data evaluated from the control group were computed (Parts II and III of the questionnaire). No specific tool was used to capture and analyse qualitative comments and suggestions (qualitative data – Part IV of the questionnaire) but the data obtained was summarised and used as part of the results and discussion sections to support the qualitative analysis. Since most of the data contained more than two categorical ordinal variables which and not normally distributed, Spearman’s correlation coefficient ($r$) was used to analyse correlations. The Pearson’s correlation and other correlational analyses were used only for confirmation when variables were positively significant or when they were normally distributed.

Interpretation of $r$ value.
Each item in the Modified Newman questionnaire was tallied with other items for estimation of correlation. The value obtained was interpreted between -1 and 1. A value of 0 means no linear correlation and values near 1 show a strong correlation. Negative values mean that the two variables are inversely related, that is, as one variable increases the other variable decreases. In
analysing each section of the questionnaire the following guideline was used; correlation coefficient value of at least 0.8 was considered a very strong correlation, 0.6–0.8 moderately strong, 0.3–0.5 fair and less than 0.3 a poor correlation. Pairing and analysis were used together with $p$ values and Coefficient of determination ($r^2$) to determine negative or positive correlation of the grouped variables (e.g. consent, risks, benefits, right etc. – ethical constructs and definitions – Table 2). Each study objective was measured based on the contents of ethical constructs. A positive correlation of the items in a specified objective was regarded as linear and hence shows a positive relationship (Chapter 1.3).
5. ETHICAL AND LEGAL CONSIDERATIONS

Ethical clearance and permission to do the study was obtained from University of Pretoria Faculty of Health Sciences Research Ethics Committee and Tanzania’s National Institute of Medical Research – National Health Research Ethics Review Sub-Committee (Appendix III, IV and IV).

Research centres and hospitals (secondary and tertiary) were informed prior to this research. The study commenced after receiving permission from their committees or research boards (letters available on request).

Participants were approached during their routine visit or recruitment at NIMR research centres and hospitals (tertiary and secondary).

5.1 Assent (Children)

Assent was obtained from participants aged 7–17 years. Information on different meanings of research, aim of the research, methods to be used, risks, benefits and purpose of his/her participation into research were explained in detail using easily understandable language and examples tailored to different age groups and level of education. Participants were given a chance to ask questions at every step and option of participating or not to participate in the research.

If he/she agreed to participate in the research, the participant signed (thumb print) the assent forms before two witnesses and researcher (who also signed the form).

Information obtained was anonymous (no identifiers) and participants had a free choice of either continuing or stopping at any time during the interview.
Their participation status (not participating, participating) did not interfere with procedures (research centres) or care they were given at the centres/hospitals at which the research was conducted.

5.2 Informed Consent (Parents and Guardians)
Signed informed consent was obtained from parents and guardians participating in the research after receiving in-depth information on the aim of the study, methodology, risk and benefits. Participants' information was anonymous (no identifiers).

5.3 Confidentiality
All the information obtained was anonymous i.e. no identifiers were used, though each questionnaire/assessment tool was assigned a specific identification number (not linked to participants' identifications) for data analysis. To the extent permitted by the applicable laws and/or regulations, the records were not to be made publicly available. If the results of this study will be published, participants, centres and hospital identity will remain confidential.

5.4 Benefits (Indirect)
There were no direct benefits to participants.

Benefit to society of the study will hopefully be:
- Gaining new ethical and scientific knowledge on research that involves minors, knowledge that might be used in creating and amending guidelines for protecting minors as research participants.
- Policies: Children’s rights and protection while participating in research and other activities.
5.5 Risks

The study was exploratory, all participants volunteered freely and most of them appeared interested in knowing more about research ethics.
6. RESULTS

6.1 Introduction
In this chapter the results of the study will be presented. The results include the data obtained from questionnaires on the following categories: (i) socio-demographic data, (ii) reasons for participation, (iii) reaction to participation, (iv) comments from participants. Qualitative comments from participants will also be discussed and included as part of research recommendation.

6.2 Socio-demographic data
A total of 294 families were approached. Only 261 met the inclusion criteria and consented. By the end only 205 completed the interview as required by interviewer (Figure 1). A total of 56 families who consented did not finish interview for various reasons (Table 1).
Although the children’s and parents’ availability varied, all 205 families completed the interview and 89 declined or failed to finish the interview for various reasons. Of 89 participants who declined or failed to finish the interview, 32 (36%) were not included because their age was below 7 and above 18 years old, 26 (29%) was due to parental disapproval, 2 (2.3%) due to sickness, 13 (14.6%) due to unexplainable situations and 3 (3.4%) due to interference with routine clinical procedures (Table 1).

The reasons for exclusion at both stage one and two of this research are summarised in Table 1.
Table 1: Reasons for exclusion ($n=89$)

<table>
<thead>
<tr>
<th>Researcher</th>
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<tbody>
<tr>
<td>1. Sick child, parent or guardian ($2$)</td>
<td></td>
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<tr>
<td>2. Age below 7 years and above 18 ($32$)</td>
<td></td>
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<tr>
<td>3. Interviews interfering with routine clinical or research procedures ($3$)</td>
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<table>
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<th>Parents/guardians</th>
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<tbody>
<tr>
<td>1. Time taken to participate in the research (parents complain) ($8$)</td>
<td></td>
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<tr>
<td>2. Unexplainable uncomfortable situations ($13$)</td>
<td></td>
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<tr>
<td>3. Interview interfering with work schedule ($1$)</td>
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<table>
<thead>
<tr>
<th>Children</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Parent/guardian disapproval ($26$)</td>
<td></td>
</tr>
<tr>
<td>2. Unexplainable uncomfortable situations ($4$)</td>
<td></td>
</tr>
</tbody>
</table>

---

6.2.1 Distribution by recruitment site, geography and type of research

Families were recruited from different centres in mainland Tanzania (Figure 2). 45 (22%) of the families were in therapeutic trials and (160) 78% in non-therapeutic studies.
According to national population distribution, Muhimbili National Hospital (MNH), Tanga and Mbeya are classified as urban, Bagamoyo, Ifakara and Tukuyu as peri-urban centres. There were 120 (59%) participants from urban centres and 85 (41%) from rural centres (Figure 2).

6.2.2 Age and sex distribution
The 205 children in the study were aged between 7–17 years, (mean age=10.1, Standard deviation=3.1). The distribution by age intervals was as follows; 58 (28.3%) were 7–9 years old, 66 (32.2%) were 10–12 years old, 50 (24.4%) were 13–15 years old and 31 (17.1%) were 16–17 years old. Sixty-nine per cent of the children were females and 31% were males.
6.2.3 Level of education and religion

All participating children reported to belong to the same religion as the escorting parent/guardian. Of the children interviewed, 55 (27%) had secondary education, 104 (51%) had primary education; of this group 64 (61.5%) had primary education level 6–7 and 40 (38.5%) had primary education level 1–5, 32 had (16%) dropped out from either primary school or secondary school and 12 (6%) had no formal education (only attended Islamic classes – madrassa or never entered any formal education).

Figure 3: Children’s education level (n=205).
6.2.4 Parents'/guardians' occupation, marital status and relationship with escorting child

One hundred and twenty-seven of the participating parents were mothers (61%), 21 (10%) fathers and 57 (29%) were other legal guardians (aunt/uncle, sister or grandmother). 148 (72.2%) were married or in a formal relationship (as per Tanzanian constitution, if a couple live together in the same household for more than 6 months), 72 (46 (22.4%) single parents/guardians, widows and 11 (5.4%) did not indicate their marital/relationship status.

Parental education level varied according to centres. Of 205 parents/guardians interviewed, 82 (40%) had primary education, 39 (19%) secondary education, 8 (3.9%) tertiary education (university, technicon, institutes and colleges), 29 (14.1%) had no formal education or went to other religious teachings and 47 (23%) were school drop-outs (majority from primary schools).

Source of income/employment varied according to centre (urban or peri-urban). Of the 205 parents/guardians 47 (22.9%) reported being housewives, 17 (8.3%) had no formal job or were retrenched, 10 (4.9%) retired, 31 (15.1%) had formal jobs in a formal work sector, 8 (3.9%) businessmen/women and 92 (44.9%) reported having small businesses. Relationship with escorting child is summarised in Figure 4 below.
6.3 Reaction to Participation Analysis

The Reactions to Research Participation Questionnaire (RRPQ) consists of 60 items rated on a 5-point scale ranging from *strongly agree* to *strongly disagree* (Appendices I and II). The questionnaire was constructed by Newman and Kaloupek in 1996. It is based on key items/words constructed from the social science literature. From a review, Newman and Kaloupek came up with ethical constructs (Table 2, Appendices I–III). Item content was reviewed for representativeness, wording and applicability to different research protocols. Sixty items were generated, and negatively worded items are reverse scored so that for each item higher scores represent more favourable reactions to the research experience. In analysing data, items are divided in two main categories, confirmatory and exploratory.
Table 2: RRPQ Ethical constructs and definitions.

<table>
<thead>
<tr>
<th>Ethical term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost/ risk</td>
<td>Experience negative consequences (e.g. intrusion, physical damage, privacy invasion, low wages from work, or inconvenience).</td>
</tr>
<tr>
<td>Benefit</td>
<td>Experience positive reactions (e.g. emotions, response to treatment, kinship).</td>
</tr>
<tr>
<td>Cost benefit ratios</td>
<td>Analysis of the benefits relative to costs experienced.</td>
</tr>
<tr>
<td>Adequacy of consent</td>
<td>Accurate information is provided in an understandable and clear manner a priori regarding procedures, potential adverse consequences, and positive consequences.</td>
</tr>
<tr>
<td>Adequacy of consent</td>
<td>(1) Lack of concern regarding how participants was identified and approached (including suspicion, fear, and so forth); and (2) Perception of choice or absence of actual or perceived coercion with respect to recruitment.</td>
</tr>
<tr>
<td>Faith in confidentiality</td>
<td>Confidence that information provided by the respondent will not be shared with non-research staff not presented in a way to identify the individual.</td>
</tr>
<tr>
<td>Perception of the study</td>
<td>Concern that the study is safe and that others are not harmed by participation.</td>
</tr>
<tr>
<td></td>
<td>(1) Research team is competent and</td>
</tr>
</tbody>
</table>
Perception of science professional, and (2) the team and project appears well designed and controlled.

Perceptions of the research teams’ respect for the individual, including cultural sensitivity

Research team communicates respect for both the autonomy and vulnerability of individual, and is sensitive to issues of culture and ethnicity.

The Reactions to Research Participation Questionnaire for Children (RRPQ-C) and the Reactions to Research Participation Questionnaire for Parents (RRPQ-P) are 12-item measures designed to assess four content areas: the individual’s positive appraisals of research participation, negative appraisal of research participation, assessment of informed consent and trust in the research team and understanding of his/her rights as a research participant (Appendices I, II, III).

The measures are identical except for response scale: the child measure uses a three-point scale (“no, “maybe”, “yes”) to be appropriate for younger school aged children and the parents’ measures use a five-point scale (strongly agree to strongly disagree). The Reaction to Research Participation Questionnaire was designed to cover a range of related concepts rather than a single unitary construct. The RRPQ-C and RRPQ-P have shown acceptable internal consistency (RRPQ-C $\alpha = 0.62-0.69$; RRPQ-P $\alpha 0.78-0.80$) in prior studies and in this study sample RRPQ- C $\alpha$ was 0.65 and RRPQ-P $\alpha$ was 0.78. Exploratory factor analyses have provided evidence that the RRPQ-C and RRPQ-P each cover the four content areas described (since the kit was modified from the original Newman RRPQ, a consistency test should be done to prove that it covers the four contents highlighted by Newman).

In this study, summary scores were created for two broad aspects of research reactions, each of which combined two related content areas: positive appraisal
and trust / information. The positive appraisal score was created by summing items in two factors, positive appraisal items 2, 7, 9 and the reverse items 1, 4 and 6. The trust / information score is the sum of items from the remaining two factors, informed consent items 3, 5, 8 and participants’ rights items 10, 11 and 12 were also used (Appendices I and II).

6.3.1 Reasons for participation and reactions to participation
Reasons for participation were evaluated by eight key items. On the best top three items the participants ranked their reasons as most important, second most important and third most important.

In this study, 205 children responded to the best three reasons as to why they decided to participate in the research they were in at the time of interview. On interviewing children, 91.7% thought that participating in research might improve their access to health care, 79% did it to help themselves and 78.1% participated for the sake of helping others (altruism).

Only 10 (4.9%) children reported that they couldn’t say “no” when they were recruited while a majority (89.3%) reported that they could say “no”. Forty (19.5%) reported that their main reason for participation was money. Curiosity (“I was curious”) and “I don’t know” were least reported by children as a reason for participation, 12.7% and 19% were counted “I don’t know” and “I didn’t want to say no” as most important, respectively (Table 3).
Table 3: Reasons for research participation – children (n=205)

<table>
<thead>
<tr>
<th>Reason</th>
<th>Most</th>
<th>Second</th>
<th>Third</th>
</tr>
</thead>
<tbody>
<tr>
<td>I was curious</td>
<td>26 (12.7%)</td>
<td>22 (10.7%)</td>
<td>157 (76.6%)</td>
</tr>
<tr>
<td>I don't know</td>
<td>39 (19%)</td>
<td>43 (21%)</td>
<td>117 (57%)</td>
</tr>
<tr>
<td>Felt I had to</td>
<td>68 (33.2%)</td>
<td>69 (33.6%)</td>
<td>68 (33.2%)</td>
</tr>
<tr>
<td>To help others</td>
<td>160 (78.1%)</td>
<td>24 (11.7%)</td>
<td>21 (10.2%)</td>
</tr>
<tr>
<td>Thought it might improve my access to health care.</td>
<td>188 (91.7%)</td>
<td>10 (4.9%)</td>
<td>7 (3.4%)</td>
</tr>
<tr>
<td>For the money</td>
<td>40 (19.5%)</td>
<td>38 (18.5%)</td>
<td>127 (62%)</td>
</tr>
<tr>
<td>To help myself</td>
<td>162 (79%)</td>
<td>22 (10.7%)</td>
<td>21 (10.2%)</td>
</tr>
<tr>
<td>I didn't want to say no</td>
<td>10 (4.9%)</td>
<td>12 (5.9%)</td>
<td>183 (89.3%)</td>
</tr>
</tbody>
</table>

RRPQ-C/RRPQ-P choices: 1=Most/Yes, 3=Second/Maybe, 5=No/third.

On interviewing parents/guardians on the reasons for participation, 192 (93.7%) felt that their participation would improve access to health care and only 3 participants reported this factor in the top three reasons for their research participation. By the end of the interview, 122 (59.5%) felt they had to participate after being briefed on research risk and benefits (Table 4).

The third factor reported by many participants was “to help others” (71.2%). Of the 205 responders, 104 (50.7%) felt that their participation would help them or their escorting child (Item 7, Table 4) and only 6.3% identified money as the top reason for their research participation; the same percentage was analysed on the “I don't know item” (Table 4).
Among 205 parent and guardian responders, 183 (89.3%) reported the “I didn’t want to say no to a research” as the lowest factor (Table 4).

Table 4: Reasons for research participation – parents/guardians (n=205).

<table>
<thead>
<tr>
<th>Reason</th>
<th>Most</th>
<th>Second</th>
<th>Third</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I was curious.</td>
<td>80</td>
<td>79</td>
<td>46</td>
</tr>
<tr>
<td>2. I don’t know.</td>
<td>13</td>
<td>18</td>
<td>174</td>
</tr>
<tr>
<td>3. Felt I had to.</td>
<td>122</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>4. To help others.</td>
<td>146</td>
<td>45</td>
<td>14</td>
</tr>
<tr>
<td>5. Thought it might improve my access to health care.1</td>
<td>192</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>6. For the money.</td>
<td>13</td>
<td>24</td>
<td>168</td>
</tr>
<tr>
<td>7. To help myself/my child</td>
<td>104</td>
<td>58</td>
<td>43</td>
</tr>
<tr>
<td>8. I didn’t want to say no.</td>
<td>32</td>
<td>69</td>
<td>101</td>
</tr>
</tbody>
</table>

(1) Thought it might improve my child’s access to health care.

RRPQ-C/RRPQ-P choices: 1=Most/Yes, 3=Second/Maybe, 5=No/third.

The Reactions to Research Participation Questionnaire had 12 items, each item measuring a separate ethical construct (Table 2). Among 205 children interviewed, 163 (79.5%) reported “no” to the item “being in this study made me feel good about myself”, 178 (88.8) also said “no” to the item “being in this study was boring”. A total of 186 (90.7%) of the children interviewed reported “yes” to the item “I feel good about helping others” and 175 (85.4%) felt the same on the items “I knew I could stop at any time” and “I knew I could ask to take a break whenever I wanted”. Only 29 (14.1%) of the children felt there was no privacy on things said in research, and 25 (12.2%) expected not to be told the truth about the study before it started (Table 5).
Table 5: Reactions to research participation: Number and percentage of children endorsing each item (n=205).

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Maybe</th>
<th>Yes</th>
<th>Not answered</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Being in this study was boring.</td>
<td>178 (86.8%)</td>
<td>17 (8.3%)</td>
<td>10 (4.9%)</td>
</tr>
<tr>
<td>2.</td>
<td>I am glad that I was in this study.</td>
<td>2 (1.0%)</td>
<td>52 (25.4%)</td>
<td>150 (73.2%)</td>
</tr>
<tr>
<td>3.</td>
<td>It was my choice if I was in the study(^1)</td>
<td>14 (6.8%)</td>
<td>39 (19%)</td>
<td>152 (74.1%)</td>
</tr>
<tr>
<td>4.</td>
<td>Being in this study made me feel upset or sad.</td>
<td>176 (85.9%)</td>
<td>16 (7.8%)</td>
<td>10 (4.9%)</td>
</tr>
<tr>
<td>5.</td>
<td>The things I said will stay private(^2)</td>
<td>29 (14.1%)</td>
<td>36 (17.6%)</td>
<td>138 (67.3%)</td>
</tr>
<tr>
<td>6.</td>
<td>I am sorry I was in this study.</td>
<td>163 (79.5%)</td>
<td>20 (9.8%)</td>
<td>22 (10.7%)</td>
</tr>
<tr>
<td>7.</td>
<td>Being in this study made me feel good about myself.</td>
<td>2 (1%)</td>
<td>45 (22%)</td>
<td>154 (75%)</td>
</tr>
<tr>
<td>8.</td>
<td>I was told the truth about the study before it started.</td>
<td>25 (12.2%)</td>
<td>26 (12.7%)</td>
<td>152 (74.1%)</td>
</tr>
<tr>
<td>9.</td>
<td>I feel good about helping other people</td>
<td>0 (0%)</td>
<td>19 (9.3%)</td>
<td>186 (90.73%)</td>
</tr>
<tr>
<td>10.</td>
<td>I knew I could skip questions or parts of the study if I wanted to.</td>
<td>8 (3.9%)</td>
<td>25 (12.2%)</td>
<td>170 (82.9%)</td>
</tr>
<tr>
<td>11.</td>
<td>I knew I could stop at any time.</td>
<td>17 (8.3%)</td>
<td>13 (6.3%)</td>
<td>175 (85.4%)</td>
</tr>
<tr>
<td>12.</td>
<td>I knew I could ask to take a break whenever I wanted.</td>
<td>17 (8.3%)</td>
<td>13 (6.3%)</td>
<td>175 (85.4%)</td>
</tr>
</tbody>
</table>

Note (1) it was my choice if I was in the study (I could have said no even if other people wanted me to say yes)
(2) The things I said will stay private (no one else will know I said them)

Positive appraisals dominated the responses in parents’ reactions to participation questionnaire, 104 (50.7%) strongly agreed that it was their choice to be in the study and they could skip questions or part of the study if they wanted to or stop at any time (Item 3, 10 and 11). From the same cohort, 113 (55.1%) agreed that being in the study made them feel good and they were glad that they were participating (47.8%). Only 129 (62.9%) strongly disagreed.
that they were sorry that they were in the study and 126 (61.5%) strongly disagreed that being in the study made them feel upset or sad. Only 11 (5.4%) of the 205 parents interviewed strongly disagreed that things said in the study would stay private and 10 (4.9%) felt that they were not told the truth about the study before it started (Table 6).
Table 6: Reactions to research participation: Number (percentage) of parents endorsing each item ($n=205$).

<table>
<thead>
<tr>
<th></th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Not sure</th>
<th>Agree</th>
<th>Strongly agree</th>
<th>Not answered</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Being in this study was boring.</td>
<td>98 (47.8%)</td>
<td>97 (42.3%)</td>
<td>3 (1.5%)</td>
<td>1 (0.5%)</td>
<td>6 (2.9%)</td>
</tr>
<tr>
<td>2.</td>
<td>I am glad that I was in this study.</td>
<td>0 (0%)</td>
<td>1 (0.5%)</td>
<td>5 (2.4%)</td>
<td>98 (47.8%)</td>
<td>99 (48.3%)</td>
</tr>
<tr>
<td>3.</td>
<td>It was my choice if I was in the study</td>
<td>1 (0.5%)</td>
<td>1 (0.5%)</td>
<td>15 (7.31%)</td>
<td>84 (41%)</td>
<td>104 (50.7%)</td>
</tr>
<tr>
<td>4.</td>
<td>Being in this study made me feel upset or sad</td>
<td>126 (61.5%)</td>
<td>62 (30.2%)</td>
<td>6 (2.9%)</td>
<td>10 (5%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>5.</td>
<td>The things I said will stay private</td>
<td>11 (5.4%)</td>
<td>13 (6.3)</td>
<td>28 (13.7%)</td>
<td>8 (3.9%)</td>
<td>72 (35.1%)</td>
</tr>
<tr>
<td>6.</td>
<td>I am sorry I was in this study.</td>
<td>129 (62.9%)</td>
<td>61 (29.8%)</td>
<td>14 (6.8%)</td>
<td>1 (0.5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>7.</td>
<td>Being in this study made me feel good about myself.</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>56 (27.3%)</td>
<td>113 (55.1%)</td>
<td>36 (17.6%)</td>
</tr>
<tr>
<td>8.</td>
<td>I was told the truth about the study before it started</td>
<td>10 (4.9%)</td>
<td>0 (0%)</td>
<td>18 (8.8%)</td>
<td>82 (40%)</td>
<td>94 (46%)</td>
</tr>
<tr>
<td>9.</td>
<td>I feel good about helping other people by being in this study.</td>
<td>1 (0.5%)</td>
<td>0 (0%)</td>
<td>18 (8.8%)</td>
<td>82 (40%)</td>
<td>94 (46%)</td>
</tr>
<tr>
<td>10.</td>
<td>I knew I could skip questions or parts of the study if I wanted to.</td>
<td>2 (0.4%)</td>
<td>1 (0.5%)</td>
<td>14 (6.8%)</td>
<td>84 (41%)</td>
<td>104 (50.7%)</td>
</tr>
<tr>
<td>11.</td>
<td>I knew I could stop at any time.</td>
<td>2 (1%)</td>
<td>1 (0.5%)</td>
<td>14 (6.8%)</td>
<td>84 (41%)</td>
<td>104 (50.7%)</td>
</tr>
<tr>
<td>12.</td>
<td>I knew I could ask to take break whenever I wanted.</td>
<td>1 (0.5%)</td>
<td>1 (0.5%)</td>
<td>14 (6.8%)</td>
<td>84 (41%)</td>
<td>104 (50.7%)</td>
</tr>
</tbody>
</table>

Note (1) It was my choice if I was in the study (I could have said no even if other people wanted me to say yes)
(2) The things I said will stay private (no one else will know I said them)
6.4 Statistical Analysis

6.4.1 Sampling methods, analysis techniques and data correlation
Several parameters were analysed for possible correlations. This study evaluated each summary scale with other variables in both RRPQ-C and RRPQ-P. To avoid bias, items with very few variables were not compared. The summary scores observed were not normally distributed hence non parametric correlation (Spearman's) for associations with continuous variables and a Wilcoxon rank-sum test to compare scale scores between groups (sex, relation with escorting parents/child) were used. If a significant association was seen for any variable analysed together with the summary scale, further analyses to elucidate the relationship were conducted. This was done by examining variables’ association with each RRPQ-C or RRPQ-P item within the same scale. In each secondary analysis the alpha level for significant results was set at 0.008. This was done in order to correct for multiple comparisons (as done by other researcher in many previous studies). In evaluating the first part (socio-demographic) with reasons for participation and reactions to participation, the following emerged:

6.4.2 Correlation of age, sex, religion, education level and relationship to escorting adult with elements of consent/assent (voluntariness)
On the questionnaire the following items were established as the best in measuring consent to research participation (Table 7).
Table 7: Consent/assent constructs.

<table>
<thead>
<tr>
<th>POSITIVE APPRAISAL</th>
<th>NEGATIVE APPRAISAL/TRUST/INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reasons why you decided to participate (part II).</strong></td>
<td><strong>Reasons why you decided to participate (part II).</strong></td>
</tr>
<tr>
<td>1. I felt I had to.</td>
<td>1. I don’t know.</td>
</tr>
<tr>
<td>2. I was curious.</td>
<td>2. For the money.</td>
</tr>
<tr>
<td>3. To help others.</td>
<td>3. I didn’t want to say no.</td>
</tr>
<tr>
<td>4. Thought it might improve access to health care.</td>
<td>5. For myself.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Reactions to participation (Part III).</strong></th>
<th><strong>Reactions to participation (Part III).</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Item 1,4,5,6,7,8,10,11,12,14,16,18,17,19,20,21</td>
<td>Item 2,3,13,15,17,21,27,28,32,34,39,41,46,48,50,51,53,54,57</td>
</tr>
<tr>
<td>23,24,25,26,29,30,31,33,35,36,37,38,40,41,44,45,47,48,49,52,55,56,57,58,59,60.</td>
<td></td>
</tr>
</tbody>
</table>

Appendices I and II contain item 1-60 (Reaction to participation).

In analysing each item category in the RRPQ-C, age showed a positive association with many items but item 9 showed a significant association with child’s age ($r=0.25$ and $p=0.001$). Further assessment of item 9 showed greater variation with age of the child ($X^2=12, df=3, p=0.08$). Almost all children between 5–12 years said they felt good about helping other people. Many younger children responded to the item “I feel good about helping other people”: 82% of 7–9 year olds, as did 79% of 10–12 years, 32% of 13–15 year olds, and 21% of 16–17 year olds. The same item was analysed on RRPQ-P and showed no significance. The same applied to sex, religion and level of education ($r=0.000$).
**Correlation note**: All correlated items in this study were arranged as follows:

- **RRPQ-C**: 1=no, 2=maybe (in the middle), 5=yes.
- **RRPQ-P**: 1= strongly disagree (no), 2=disagree, 3=neutral, 4=agree, 5=strongly agree (yes).

### 6.4.3 Correlation of age, sex, religion, level of education, marital status, occupation and relationship to escorting adult with elements of coercion

Elements of coercion were deduced from most of the items in voluntariness (Table 7). In analysing the seven socio-demographic items against items “for the money”, “I didn’t want to say no”, “I felt pressured to participate” (Item 17 of RRPQ-C and RRPQ-P), “I am concerned why I was selected in this study” (Item 21 of RRPQ-C and RRPQ-P), “I felt I couldn’t say no to participation” (Item 27), “I felt that I was being exploited for scientific purpose” (Item 39) reveals the following (Spearman’s rank coefficient correlation). With an $r$ value of or close to 0.000 the tested variables had no significant correlation. The Spearman’s test revealed the same for occupation, marital status and relationship with escorting adult child in RRPQ-P. Positive appraisal items on voluntariness were tested to check if there was a negative correlation with coercion criteria, item “being in this study is so boring” and parents’ level of education showed a negative correlation ($r=-0.62$ and $p=0.001$).

### 6.4.4 Correlation of age, sex, religion, level of education, marital status, occupation and relation to escorting adult with elements of confidentiality

In evaluating elements of confidentiality, three items in both RRPQ-C and RRPQ-C were used (Tables 8 and 9). In this category both Pearson’s and Spearman’s correlation tests were used. In analysing data at both level 0.01 and 0.05 all three items showed a positive correlation on the Pearson test only if the data were categorised. On Bonferroni adjustment all three items showed no correlation (all values were close to 0). The same applied to Spearman’s rank test (Tables 8 and 9).
Table 8: Children’s confidentiality correlation.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Sex</th>
<th>Religion</th>
<th>Education</th>
<th>Rel_escorting parent</th>
</tr>
</thead>
<tbody>
<tr>
<td>I trust that my replies will be kept private.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>I am not sure I trust the research staff.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>I trust the research staff.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Rel_escorting parent = relationship with escorting parent.

Table 9: Parents’ confidentiality correlation.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Sex</th>
<th>Religion</th>
<th>Education</th>
<th>Rel_esc Child</th>
<th>Mar-sts</th>
<th>Occup</th>
</tr>
</thead>
<tbody>
<tr>
<td>I trust that my replies will be kept private.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.0004</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>I am not sure I trust the research staff.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>I trust the research staff.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.0003</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Rel_esc C = relationship with escorting child; Mar-sts = marital status; occup = occupation.

6.4.5 Correlation of age, sex, religion, level of education, marital status, occupation and relationship to escorting adult with elements of risks

Items in Table 10 and other items in RRPQ-C and RRPQ-P were used to analyse participants’ understanding of risk endured while participating in
research. In analysis, and after pairing the items, most items tested in RRPQ-C showed no significant correlation. Spearman's rank correlation coefficient was around 0.000 which shows no correlation (Table 11). RRPQ-P also showed no significant correlation with seven socio-demographic measures. In total, 23 items in both RRPQ-C and RRPQ-P were used to evaluate research risk (Appendices I and II).

Table 10: Children’s risks correlation.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Sex</th>
<th>Religion</th>
<th>Education</th>
<th>Rel_escorting parent</th>
</tr>
</thead>
<tbody>
<tr>
<td>My condition worsens after participating.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>I felt that I was being exploited for scientific purposes.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>I am concerned this procedure could be risky to others.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.0001</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>When they told me possible bad effects if participating, I didn't take them seriously.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>I regret agreeing to participate</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.0001</td>
<td>0.000</td>
</tr>
<tr>
<td>I am concerned why I was selected in this study.</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

6.4.6 Correlation of age, sex, religion, level of education, marital status, occupation and relationship to escorting adult with elements of benefits

RRPQ-C and RRPQ-C contain 15 items that analyse understanding of research participation and benefits. In this study each of the 15 items was analysed for
possible correlation with each other and with socio-demographic measures. Analysis revealed no significant correlation for 11 of the 15 items tested ($r=0.000, p=0.001$) on both RRPQ-C and RRPQ-P.

### 6.4.7 Correlation of age, sex, religion, level of education, marital status, occupation and relationship to escorting adult with elements of consent (voluntariness), risks, benefits and confidentiality – A comparison between therapeutic and non-therapeutic studies

Of 205 families in the study, 160 (78%) were enrolled in research classified as non-therapeutic and 45 (22%) as therapeutic research. In analysing the two groups, the level of understanding of consent, assent, benefits, risks and confidentiality differed very slightly. Using both Pearson and Spearman’s tests to analyse differences of understanding between the two groups revealed no significant correlation; all the groups tested together or separately gave $r$ values close to 0.000 at the 0.01 and 0.05 levels.

### 6.4.8 Correlation of age, sex, religion, level of education, marital status, occupation and relationship to escorting adult with elements of consent (voluntariness), risk, benefits and confidentiality – A comparison between the research participants and those who have not participated

All 205 families were randomly selected from the areas where research participants originate. This group was classified as a control group in analysing potential differences on level of understanding of key ethical issues (risks, benefits, consent, assent and confidentiality). The criteria used for recruitment of the control group are summarised in Table 11.

<table>
<thead>
<tr>
<th>Table 11: Criteria used in selection of control group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Parents or legal guardian.</td>
</tr>
<tr>
<td>3. Not being recruited in current research.</td>
</tr>
</tbody>
</table>
4. Not involved in a research project for the past 6 or more months.
5. Dropped from any research.

Many of these families were selected from primary schools and hospitals in Tanga, Mbeya, Dar es Salaam, Bagamoyo, Ifakara and Tukuyu. The purpose of recruiting these groups was mainly for comparing the findings of other research studies showing that level of understanding of risk, benefits, consent, assent and confidentiality varied between the research-exposed group and groups not exposed to the research. In this group 67% reported they had not participated in any form of research or participated in short surveys that were considered as small studies.

Using Spearman’s rank test for the control group using each ethical construct, level 0.01 and 0.05 revealed no significant correlation \( r=0.000 \) and \( p=0.001 \) for all criteria correlated in the case group. Testing and retesting the items showed a positive correlation in the case group.

6.5 Participants’ comments
Part IV of the questionnaires captured participants’ comments whenever they felt like giving these to the researcher. The majority volunteered to comment and many comments were repeated themes or concepts or complaints. The researcher decided simply to group them into several categories (outlined below). No formal qualitative analytical system was used.

6.5.1 Report dissemination
The majority of participants reported concerns over the dissemination of research results. Many felt that the research results/reports would not be available to them, or if available it would be too technical to be understood by lay individuals. Participant 98 said, “It’s obvious that the report will not be
disseminated to all participants, instead data will be available to village committees, local government or hospital management.”

6.5.2 Concerns about international multicentre trials
Many research projects are from overseas i.e. funded and administered mostly by westerners or western nations. Knowing the source of funds and research expertise raised a concern as to whether the current research will be in the public interest or interest of foreign countries or organisations. On interview participant number 172 said, “Why all research work come from western nations? Why this initiative is not organised by our people and our government? The western involvement raises a doubt to me and many people may be the government wants to sell us, you never know.”

6.5.3 Benefits
No immediate were benefits were observed by participants recruited in the current research. Participants wanted immediate benefits e.g., free medications or medical services. Some felt the need to help others but insisted that their contribution should be acknowledged; they said researchers tend to praise themselves and their results, they forget about participants who have risked their lives for the good of the community. “You will hear several common phrases after end of research . . . we have discovered . . . and we are thinking of moving to next phase . . . no one think about us as participants” (participant number 172).

6.5.4 Risks
“Research risks are not commonly talked about at the time of recruitment, it’s only when we ask questions then they will start to open up and try to explain” (participant 91). Most of the participants, when invited to comment on research risks, responded that there must be openness in informing people before recruiting them into research.
6.5.5 Complaints after research
Participants speculated about poor care after research dissemination. They reported that the research studies they were attending did not have a clear framework for dealing with their problems or complaints after the end of research. They did not know where to go to after having problems after the end of the research. Participant number 64 said, “Today hospital services are good, we don’t know what will happen to us after the end of mradi (project).”

6.5.6 Sustainability of services (care after research)
“What will happen after research? Cease all services or continue sponsoring the new facility? If so, for how long?” (participant 34). Many raised concerns about availability of services that are fast tracked or routinely done to them during the research period. Their concern was whether these services would also be available at the same standard after the end of the research. Some participants attending therapeutic trials were offered free and fast medical services e.g. post-mortem done whenever there is concern over death of their children (whether death was related or was not related to research). This selective free service raised a concern about research outcomes among participants. Some felt that the free service was given to them because the research team was expecting their children to die (post-mortem to children at risk or death in exposure group).

6.5.7 Biased recruitment criteria
Recruitment criteria for some studies were believed to show some bias. Participants appeared to have been softly induced as some had been recruited to different studies. Most researchers believe that an experienced participant is a better participant, they opt to recruit more of them to avoid participant drop-out rates. Non therapeutic trials were reported to use the same participants over and over. This was either done via village committees which know every participant or by hospital attendants who are the key recruiters and know participants since they live together or share religious or social spheres.
Honoraria and prevention kits (things like treated bed nets and washing soaps) given to participants act as incentives (pushing participants to enrol in more than one study). “I am attending because at least here I receive treated bed nets when I am pregnant or when my son is sick I also get free washing soaps” (participant 123).

Many studies are based in hospital settings; participants said it’s difficult to refuse since it’s the only care setting available. Refusal sometimes resulted in being labelled as non-cooperative by health care workers who were also part of research teams. Fear of being rejected after refusing to participate was high. Most of these research communities are very small and it is easy to identify people hence fear of not being one of them is significant. Biased recruitment can also be seen in research conducted in primary and secondary schools. Most of these studies are reportedly enforced by school teachers or ministry of education together with ministry of health and social welfare. Parents are reportedly rarely informed about their children’s participation in most of the research conducted in schools.

Evaluation of risk is very important since many children don’t understand much about research and its associated risks. Children often obey their parents’ decisions regardless of risks involved. Evaluation of risks in research differs from one individual to the other. In evaluating risk parents also have their own predictors which are very different from children. This was reported by participant 46, “Sometimes we as parents are not involved in some of researches...only teachers decide when and who should participate in researches and other child health campaigns...well, it’s good sometimes am not involved since I would not allow my son or daughter to participate in research even though it is for the good cause...that is my understanding and my opinion, even the government cannot change it.”
6.5.8 Political influence
Political propaganda was reported to influence clinical research. Politicians reportedly use research participation as a tool. They give false hope to people by equating the research development and infrastructure to standard health care. Many participants flock to newly-built research centres after being told that its part of national or regional health development plans and research is just a routine procedure at the centre. False benefits and promises given to people by religious and political leaders were perceived as designed to attract them to participate in research. Participants reported that churches, village meetings and mosques were sometimes used as a platform to encourage people to participate in research without explaining risks involved. This was reported by participant 17, “Sometime we wonder why some research recruitment involves politicians and religious leaders, which raise doubt since some of them are not trustworthy.”

6.5.9 Language barriers
Explanation of terms: Participants commented on use of complicated terms which were not easily translated into Swahili. Most of the terms used were not well known to participants and communities. The technical words used in research need thorough elaboration. Participants reported that most of the terms translated from other languages were not common e.g., participant 127 commented on the term “vinasaba’ (DNA) or “saratani’ (cancer) to be out of the community’s new vocabulary.

The use of foreign language: some participants reported that local researchers prefer to communicate in a foreign language in front of them when discussing a matter regarding either their illness or reason for participation. Participants felt that by doing so there was some hidden agenda, stigma or arrogance (researchers like to be seen as well educated or people who know everything).
6.6 Summary of Results

6.6.1 Socio-demographic data

In this study, 205 families were interviewed and their responses and comments were analysed to assess the level of understanding of key ethical issues in research involving minors in developing countries. Families were recruited from different centres in mainland Tanzania (Tanga, Mbeya, Muhimbili, Bagamoyo, Ifakara and Tukuyu). Families were grouped according to the centre they were from or type of research they were involved in. Of 205 participants involved in this study, 120 (59%) came from urban centres and 85 (41%) from rural centres; 160 (78%) were recruited in non-therapeutic studies and 45 (22%) in therapeutic studies.

Children involved were between the ages of 7–17 years (mean age 10.1 and standard deviation of 3.1). The distribution by age intervals was as follows; 58 (23.3%) were 7–9 years old, 66 (32.2%) were 10–12 years old, 50 (24.4%) were 13–15 years old and 31 (17.1%) were 16–17 years old. Sixty-nine percent were females and 31% males.

All participating children reported belonging to the same religion as the escorting parent/guardian. Of the children interviewed, 55 (27%) had secondary education, 104 (51%) had primary education; of this group 64 (61.5%) had primary education level 6–7 and 40 (38.5%) had primary education level 1–5, 32 (16%) dropped out from either primary school or secondary school and 12 (6%) had no formal education (only attended Islamic classes – madrassa or never entered any formal education).

One hundred and twenty-seven of the participating parents were mothers (61%), 21 (10%) fathers and 57 (29%) were other legal guardians (aunt/uncle, sister, or grandmother). Of 205 parents/guardians, 148 (72.2%) were married or in formal relationship (as per Tanzanian constitution, if a couple live together in
the same household for more than 6 months). 46 (22.4%) were single parents/guardians, widows and 11 (5.4%) did not indicate their marital/relationship status.

Parental education level varied according to centres. Of 205 parents/guardians interviewed, 82 (40%) had primary education, 39 (19%) secondary education, 8 (3.9%) tertiary education (university, technicon, institutes and colleges), 29 (14.1%) had no formal education or went to other religious teachings and 47 (23%) were school drop-outs (majority from primary schools).

Source of income/employment of parents involved in this study varied according to centre (urban or peri-urban). Of the 205 parents/guardians 47 (22.9%) reported to be housewives, 17 (8.3%) had no formal job or were retrenched, 10 (4.9%) retired, 31 (15.1%) had formal jobs in a formal work sector, 8 (3.9%) were businessmen/women and 92 (44.9%) reported having small businesses.

6.6.2 Reactions to participation analysis

Reason for participation and reactions to participation:

Reasons for participation were evaluated by eight key items. Participants ranked their reasons as most important, second most important and third most important. In this study, 205 children responded to the best three reasons as to why they decided to participate in the research they are in at the time of interview. From 205 interviewed children, 91.7% thought that participating in research might improve their access to health care, 79% did it to help themselves and 78.1% participated for the sake of helping others (altruism).

Only 10 (4.9%) children reported that they couldn’t say “no” when they were recruited while majority (89.3%) reported that they could say “no”. Forty
(19.5%) reported that their main reason for participation was money. Curiosity ("I was curious") and “I don’t know” were least reported by children as a reason for participation (12.7% and 19% respectively).

On interviewing parents/guardian on the reasons for participation, 192 (93.7%) felt that their participation will improve access to health care and only 3 participants reported the factor to be least on top three reasons for their research participation. Of 205 responses, 122 (59.5%) felt they had to participate after being briefed on research risks and benefits.

The third factor reported by many participants was “to help others” (71.2%). Of the 205 responders, 104 (50.7%) felt that their participation would help themselves or their escorted child (Item 7, Table 4) and only 6.3% identified money as the topmost reason for their research participation. The same percentage was analysed on the “I don’t know” item. Among 205 parent and guardian responders, 183 (89.3%) reported the “I didn’t want to say no to a research” as the least factor.

From 205 children interviewed, 163 (79.5%) reported “no” to the item “being in this study made me feel good about myself”, 178 (88.8%) also said “no” to the item being in this study was boring. Also from interview, 186 (90.7%) of the children reported “yes” to the item “I feel good about helping others” and 175 (85.4) felt the same on the items “I knew I could stop at any time” and “I knew I could ask to take a break whenever I wanted”. Only 29 (14.1%) children felt there was no privacy on things said in research, and 25 (12.2%) reported not being told the truth about the study before it started.

A positive appraisal dominated responses in parents’ reactions to the participation questionnaire. Of 205 participants, 104 (50.7%) strongly agreed that it was their choice to be in the study and they could skip questions or part of the study if they wanted to or stop at any time. From 205 parents interviewed,
113 (55.1%) agreed that being in the study made them feel good and they were glad that they participated (47.8%). Only 129 (62.9%) strongly disagreed that they were sorry that they were in the study and 126 (61.5%) also strongly disagreed that being in the study made them feel upset or sad. Only 11 (5.4%) of 205 parents strongly disagreed that things said in the study will stay private and 10 (4.9%) felt that they were not told the truth about the study before it started.

Correlation analysis of participants’ reactions to research:

In analysing age, sex, religion, level of education, marital status, occupation and relationship with escorting adults with elements of consent/assent revealed a significant positive correlation between age of children and item "I feel good about helping other people" ($r=0.25$ and $p=0.001$). Of the 205 children interviewed, almost all children between 5-12 years said they felt good about helping other people. Younger children responded more positively compared to older children.

Testing socio-demographic data with elements of coercion showed no positive correlation. All items tested with Spearman’s rank coefficient correlation test showed the $r$ value of 0.001 (not statistically significant). Positive appraisal items on voluntariness were also tested to evaluate if there were negative correlations with coercion. All items tested showed negative correlations with Spearman’s coefficient ($r$) ranging between -0.89 to -0.62 at $p$ value of 0.001.

Testing elements of confidentiality with socio-demographic data at level 0.01 and 0.05 revealed a positive Pearson correlation coefficient. On Bonferroni adjustment all items tested showed coefficient of 0.000 hence the correlation was not statistically significant. Testing the same categories using Spearman’s correlation test showed a coefficient rank value of 0.000 (not statistically significant).
Pearson correlation coefficient test and Spearman correlation coefficient test revealed no statistically significant correlations when tested on elements of research risks, benefits and in comparing the therapeutic and non-therapeutic groups, and research and control groups.

Participants’ comments on research participation:

Participants documented their experiences in research participation. On interviewing them several concerns emerged as problems in research participation in developing countries. Their concerns were mainly on research results dissemination, research benefits, research exploitation, risks, biased recruitment procedures, language barriers, political involvement in research studies, standard of care and access to quality hospital services after the end of research.
7. DISCUSSION

Many debates on research in developing countries centre on three main issues, standard of care, availability of interventions and informed consent.\textsuperscript{28,35,31} For many years researchers have tried to improve research participation by simply looking at these three criteria until Emanuel et al. proposed eight principles to be used as benchmarks to guide researchers and RECs in assessing ethical research conduct.\textsuperscript{78} The eight principles can be summarised as follows; (1) social value – enhancements of health or knowledge must be derived from the research; (2) scientific validity – the research must be methodologically rigorous; (3) fair selection of study population – scientific objectives, not vulnerability or privilege, and the potential for and distribution of risks and benefits, should determine communities selected as study sites and the inclusion criteria for participants; (4) favourable risk-benefit ratio – within the context of standard clinical practice and the research protocol, risks must be minimised, potential benefits enhanced, and the potential benefits to individuals and knowledge gained for society must outweigh the risks; (5) independent review – ensure public accountability through reviews mandated by laws and regulations; (6) informed consent – individuals should be informed about the research and provide their voluntary consent; (7) respect for recruited participants and study communities – participants should have their privacy protected, the opportunity to withdraw, and their well-being monitored, and (8) collaborative partnership – development of partnership with researchers, makers of health policies and the research community.\textsuperscript{78,79}

In this discussion the results will be discussed using the Emanuel et al framework. Since participants were grouped in non-therapeutic and therapeutic studies, each principle will be discussed based on type of study and the results obtained from the RRPQ-P and RRPQ.
Using the results from the previous chapter, the level of understanding of key ethical principles involved in research recruiting minors outlined by the study objectives are discussed briefly by following the main principles proposed by Emanuel et al.78

7.1 Informed Consent

In research ethics discussions, the literature in Africa is often represented in such a way that the process of obtaining individual informed consent is time consuming and difficult due to incompetence, difficulties in communication and comprehension arising from differences in language, religion, from non-scientific conceptions of health and illness or from poor education.80 Researchers have been urged to adapt the information ordinarily disclosed in the process of obtaining informed consent to local concepts of disease and health and some reportedly even lie in describing the nature of their study and ignore the process of obtaining informed consent because of problem of incompetency, time wasting and difficulties in obtaining informed consent in developing countries.78,80

Informed consent in research involving minors has been emphasised by many research ethics writers to counteract potential research exploitation in developing countries. The preposition of protecting child participation in research has been highlighted in detail by the “Proposed International Guideline for Biomedical Research Involving Human participants”, which states:5,78,79,84

Ideally, each potential research should possess the intellectual capacity and insight to provide valid informed consent, and enjoy the independence to exercise absolute freedom of choice over the extent of the collaboration without fear of discrimination. However, many investigators, and particularly those intended to sub serve the interest of underprivileged communities and vulnerable minorities including children
and mentally ill, would be barred if these preconditions were accepted as mandatory criteria for recruitment.\textsuperscript{5}

In obtaining individual informed consent, five benchmarks were proposed by Emanuel et al. Firstly, the local community should help to establish the recruitment procedures and incentives for participants that are consistent with cultural, political and social practices.\textsuperscript{78}

Secondly, disclosure of information should be sensitive to the local context. It should be done using the local language, culturally appropriate idioms, and analogies that the prospective participants can understand. Thirdly, "spheres of consent" ranging from village elders to extended family or heads of households may be required before researchers can invite individual participation. Fourthly, researchers should use consent procedures that are acceptable within the local community, while ensuring that an independent observer could verify voluntary participation by the individuals. Fifthly, special attention must be given to ensure that individuals are aware of their rights to refuse to participate or withdraw from research.\textsuperscript{5,6,42,78}

The ethical concept of "informed consent" contains three major elements: (1) comprehension (or understanding), (2) capacity and (3) voluntariness.\textsuperscript{5,78} All of these elements together constitute an important part of participants’ "self-determination" (the taking hold of their own life and action, determining the meaning and the possibility of what they undergo and do). The three elements presuppose a participant’s capacity to understand and to consent, a presupposition that will be examined later.

Comprehension of information implies that researchers must present participants with clear information. Researchers must ensure participants understand the information thoroughly. Participants must have adequate information about the procedures and their consequences in order to comprehend the information in detail.\textsuperscript{78}
Researchers are encouraged to use an educative approach by reviewing questions and answers with participants. Researchers may answer questions concerning the research risks and benefits, the services, the expectations of the researcher and the participants, and the research outcomes and result dissemination.

Capacity signifies that participants have the ability to make decisions, which are rational. If the participant doesn’t have the capacity to make a sound decision, a parent or guardian is usually responsible for authorising informed consent.82

Voluntariness signifies that the participant is given a decision-making opportunity. Voluntariness ensures the participant is making a decision based on her/his own accord – by his or her own free will or choice. Voluntariness also signifies that the participant is legally and psychologically able and competent to give consent. More importantly, voluntariness indicates the participant has complete power and is willing and choosing to enter into the research process.78

In this study, most of the factors mentioned above were evaluated to see if there was a pattern that deviates from the proposed elements and key criteria used in informed consent. Reasons for participation parts of the questionnaire captured positive and negative appraisal elements of informed consent. In analysing reasons for participation, the majority of participants expressed positive reasons. Only 97.7% of the children interviewed thought that participating in the research might improve their access to health care, 79% participated to help themselves and 78.1% did so for the sake of helping others. This can be explained by the fact that a majority of the children participating in research in these centres have either been assisted and counselled to make a fair and reasonable decision as to why they want to be involved in the research. Most of the positive attributes of voluntariness can be seen from the responses
since almost more than 70% responded positively to criteria used in analysing
decision-making in research participation.

Only 10 (4.9%) reported that they could not say “no” when they were recruited,
compared to 89.8% of the respondents who could say “no” or withdrew from the
research (the percentage was less significant when tested with other
correlates). The ability to accept or decline research participation shows that
participants were well informed and capable of making decisions.

Coercion in research cannot be overlooked since it directly gives room for
exploitation of minors. In this study there was a positive correlation between
age of minors and financial benefit. A significant number of children (19.5%)
aged 11–17 (mean age 14) reported that their main reason for participation in
research was for financial gain (money). This suggests that the older the age of
the child, the greater the chance that he/she can be coerced. The same
phenomenon was seen in their parents/guardians. However, the majority
responded positively to the two attributes of informed consent (voluntariness
and capacity).

Access to health care has been cited as a main factor for research participation
in many developing countries.⁸⁵ There is a tendency to confuse
necessary/standard hospital care with ancillary care provided by the research
centres.¹²,⁸⁵ Many research settings in Tanzania are based in hospitals and
health centres. With improvement of research infrastructure, many research
participants are attracted to participate thinking that their participation will
improve their access to health care facilities or procedures.⁴⁹ This was
supported by the results obtained by this study, in which 93% of children and
90.7% of parents and guardians involved in research reported that they were
participating in the research because they thought it might improve their access
to health care. Considering that research participants in developing countries
are typically separately poor and ill, the promise of good access to health care
might act as an inducement. When participants join a study, they implicitly give researchers permission to access confidential medical information, to perform procedures and treatments or to take samples. With this permission, researchers have discretionary power over how to use any collected medical information and potential diagnostic insights. Because researchers’ responses to these needs will greatly affect participants’ health and well-being, participants are vulnerable to researchers.68

Several factors were also analysed as attributes of informed consent. In this study significant positive appraisals were obtained: in items “it was my choice if I was in the study” (74% said yes), “being in this study made me feel good about myself” (75%), “I was told the truth about the study before it started” (74.1%), “I felt good about helping others” (90.7%), “I know I could stop at any time” (85.4%) and “I knew I could ask to take break whenever I wanted” (Table 5). Very few responded “Yes” to negative attributes, only 4.9% reported that being in the study was boring and 4.9% reported that being in the study made them feel upset or sad. The same pattern was found in the parents. These results suggest that the participants were well informed about research and also they made an informed decision to participate.

Comprehension: Additional issues in the informed consent process include the ability of potential participants to understand the scientific and technical aspects of research protocols (given the culture and belief systems within which they live and the influence and involvement of others in the consent process).83,85 In some cultures, the belief systems of potential research participants do not explain health and disease using the concepts and terms of modern medical science and technology. This is significant, because when people do not understand or accept scientific explanations of health and disease, the challenge of obtaining informed consent can be daunting.83,84,85 In this situation it is the duty of researchers to break down all necessary information to a level that is easily understandable. Researchers must devise creative measures to
overcome the potential understanding barrier. In this study many respondents commented on language. Participants reported use of foreign language and complicated terms at recruitment and during the course of the study. Most participants felt there was a need to break down all scientific terms and procedures to a level that can be easily understood by the local community instead of using complex and newly-coined Swahili words that are complex and have no meaning. Many reported that researchers tend to use foreign languages (especially English) while doing research procedures or during communication among themselves. The use of scientific terms and principles should be discouraged during recruitment unless well explained. Several participants reported that during recruitment researchers cited declarations that were not understood by the common people. In the study, participant number 48 reported, “They come and talk about declarations that we don’t know” (referring to Declaration of Helsinki that is commonly cited by researchers and research ethics communities, commonly written on the research questionnaires and information leaflets).

It is essential that the child has full information about the research in order to give their informed assent to take part, and that assent is freely volunteered. The child should also know that she/he can withdraw at any time. Many national and international guidelines contain these ethical principles but take them further in respect of research with minors. Careful thought needs to be given to translating the above principle into practice. Information presented to the child and parent should explain: what will happen when participating; what is being asked of the child; give option of either agreeing or disagreeing to take part in research without adverse consequences; may withdraw at any time; and be given in clear language at a level that the child can understand, using visual aids if necessary.

A further consideration is the possible impact of the research on children during and after research. This is particularly important where the participant has been
discussing painful difficult experiences. The researcher’s duties are to gather information on local sources of help and have them available to assist the participants as quickly and efficiently as possible.\textsuperscript{78,80,81,84,85}

Minors aged 14–17 with sufficient understanding are able to give their full consent to participate in research independently of their parents and guardians.\textsuperscript{84} Children under the age of 18 are able to give their full consent provided they have been counselled and do not wish to involve their parents and they have sufficient maturity to understand the nature, purpose and the likely research outcome.\textsuperscript{84} In this study, it was found that minors, when given information, can make an autonomous decision. In analysing the correlation of age, religion, sex, level of education with elements of consent; it showed a significant correlation of age with elements of informed consent. Children aged between 5–12 years old said they felt good about helping other people. Among the responders, 82\% were aged 7–9 years, 79\% were 10–12 years, 32\% were aged 13–15 and 21\% were 16–17 years old ($r=0.25$ at $p$ value of 0.001, $X^2=12$, $df=3$, $p=0.08$). This entails that participants of lower age groups, when given adequate information, can freely volunteer and make proper decisions. No significant correlation was observed when analysing age, sex, religion, level of education and relationship with escorting adults with elements of coercion and confidentiality (Spearman’s rank coefficient correlation was 0.000).

Parental consent is required where the minor is deemed incapable of understanding the implications of taking part in a study or where the child is regarded as incompetent to consent.\textsuperscript{1,5,6,9,78} Although the child’s assent is advised, the power to consent, in law, is with his/her parents or legal guardian.\textsuperscript{5} Those acting for a child are only acting legally if participation in the project is of benefit to the child. If not, the parent or guardian could be said to be acting illegally.\textsuperscript{78,84,85} One parent can give consent but it is preferable to have both. Where there is parental disagreement as to whether an incompetent child
should be volunteered for research, it is possible that one parent could apply to court to block the child’s participation.84

Many national and international guidelines have set a minimum education level for informed consent; this might be due to the fact that many developing countries have higher numbers of illiterate people hence the risk of undue influence is high.26,78 Tanzania, among many African countries with national research ethics guidelines, has not classified level of education as a requirement for informed consent. Only South Africa has set a minimum of Grade 7 as requirement for a good consent quality.26 Level of education is very important in assessing understanding of key ethical issues in research involving minors. Parents with a low level of education are very likely to be influenced and hence expose minor in research risks if they are not well informed.26,78,84 This study found a significant correlation between levels of education and elements of informed consent. Evaluation of coercion and voluntariness showed a negative correlation with item “being in this study is boring” and parents’ level of education \( (r=-0.62 \text{ at } p=0.001) \).

No significant correlation was observed between understanding of principles of informed consent between participants involved in therapeutic and non-therapeutic studies. This suggests that participants involved in this study were well prepared and they made decisions that are well informed. The same has been observed with the control group (study drop-outs). This can be explained by the fact that there is a likelihood that participants had been exposed to the research process before and since they are from a well-researched area, their understanding of key ethical issues was better than those from other communities.

7.2 Fair Selection of Study Population

Exploitation of poor populations has been documented in health research ethics since the Second World War.2,3 The poor, uneducated and powerless have
been used in high-risk research that benefit the privileged.\textsuperscript{78,85} To prevent unfair selection of participants Emanuel et al. proposed four elements.\textsuperscript{78} Firstly, study population selection should ensure valid science. Special criteria should be considered in selecting the study population; study population should be selected either based on high prevalence, incidence or transmission rate of infections, special drug resistance patterns or particular combinations. In this study it was very difficult to analyse the recruitment of participants in their respective studies because at the time of this research enrolment had already occurred and some participants had been in studies for more than six months. Many studies approved or conducted by NIMR are conducted in areas of high prevalence of Malaria, HIV and other Neglected Tropical Diseases (NTDs).\textsuperscript{85,86} All these diseases are said to be of public health importance and hence the Tanzanian government and other international organisations have considered the fight as a priority.\textsuperscript{85} All the studies associated with this research were categorised as high priority and of public health importance. Hence, selection of participants was only based on high prevalence of the disease, mortality and morbidity or disease burden to the community and economic development. 

Apart from the above, the questionnaire also assessed participant selection by analysing negative and positive items. Positive appraisal items like “I found participation to be interesting”, “volunteering made me feel good about myself”, “I was glad to be asked”, “information received before participating accurately described what I was required to do” and others were used to justify fair selection of participants. Negative appraisal items like “I am concerned why I was selected for this study”, “I felt that I was being exploited for scientific purposes”, “I felt pressured to participate” and others were also used to assess unfair participant selection. Analysis of two groups on a scale of 3 (no, maybe and yes) for children and scale of 5 (strongly agree, disagree, neutral, agree and strongly agree) for parents and guardians showed that 89% of participants responded positively to positive appraisal items. The value is very significant in suggesting that they saw their selection as fair. In analysing the positive
appraisal items for selection in correlation with therapeutic or non-therapeutic research groups, revealed no significant correlation. It suggests that all groups felt fairly selected.

Scientific considerations alone cannot be used to justify fair selection of participants. Other factors also should be considered in establishing whether the study population analysed in this study were fairly selected.\textsuperscript{1,2,3,83} Risk minimisation, social value, and strong collaborative partnership between the research team and the community should be analysed before confirming fair selection.\textsuperscript{78} All these factors were analysed and discussed separately in this study.

Familial coercion, social marginalisation, political powerlessness, and economic deprivation must be considered to determine the vulnerability of the community or groups within the community.\textsuperscript{85} It’s the duty of public health specialists and policy makers to set criteria used in selected areas considered to be of national interest when it comes to disease control.\textsuperscript{80} If a population is selected for a particular study, it should be clear that the population selected is scientifically appropriate and well protected.\textsuperscript{78,80} In this study participants were given a chance to comment on the scientific research in general. Many participants were concerned with health care systems and the role of the government in research and protection of research participants. Fear of the government was reported by many as an influence in recruitment. Participants reported that many research recruitments are sometimes mistaken as government orders due to the nature of research, area involved (mostly in government hospitals) or involvement of politicians and other government officials. Participant 178 commented as follows when asked about selection of research participants, “I didn’t not know that I can choose not to participate, I thought it is a government order since the research is in our National Hospital.” The fear of orders is deeply rooted from the former socialist government where communist slogans like “Kufata sera za serikali” (To obey government orders and policies) and
“zidumu fikra sahihi za mwenyekiti” (long live the chairman’s ideas) were used to force people to obey particular national programmes without question. Mass treatment, for example de-worming and Schistosomiasis, was done and continues to be done in primary schools around Tanzania without parental consent or child assent. Coordinated by primary school teachers, local government and researchers, stool and other samples were taken from primary school children without following all necessary ethical procedures. Several slogans have been used to force people to attend to these programmes and other research studies; the most reported by the participants is “hauwezi tishia serikali” (You cannot fight with the government).

Soft coercion: participants, like other citizens, are obliged to keep and obey laws, orders and national campaigns. Many research trials follow disease profiles of a particular country; it’s easy to recruit in the name of government through national campaigns. Participants reported that special favours have been given to research participants to the extent that the community felt it was better to participate in research to secure good access to health care and free gifts. They reported that most researchers do a routine visit to houses of participants involved in the research and also they give them priority when they are sick or during hospital visits. Free insecticide treated nets and others gifts are routinely given to research participants; this encourages people to participate even though they don’t know the risk involved. Participants enrol seeking favours or financial gains.

Research studies and national health campaigns are sometimes integrated as one; billboards that encourage research participation and those of national disease surveillance and preventions campaigns are common in national hospitals and streets. This may confuse many communities to think that research is part of national health campaigns, hence forcing them to participate as reported by participant number 17, “I cannot see the difference, when I see the poster or billboard encouraging me to participate then I just do that since it
Apart from the above, several criteria used in selection of participants have been criticised. Participants reported that some recruitment criteria were biased since they favour participants who have been in previous studies because they are well informed or simply because they cannot decline or withdraw from the research. The use of honoraria and hospital settings as recruitment areas has also been reported as factors to be looked at and rectified. Participants have reported that it is very difficult to decline research which is considered by many as part of routine hospital procedures. Participants also felt that they fail to decline when they are approached by recruiters who are hospital attendants since they share either social or religious sphere. The need to educate minors and their parents has been emphasised by all. Before research participation, participants should be evaluated if they are well informed and capable of making autonomous decisions.

7.3 Respect for Recruited Participants and Study Communities

The research process does not end with informed consent. Researchers have obligations to research participants, former participants and the host community. Maintenance of confidentiality is of the utmost importance during and after research. Confidentiality can be protected by confidential interviews (interviewing participants were they cannot be overheard), making sure that the data collected remains anonymous. Respect is also shown by informing participants of their right to withdraw, informing the community if there is newly-discovered risk, exacerbation of the disease being studied, adverse events and health problems. In this study several items were used to evaluate both positive and negative appraisal of confidentiality. Items used as positive appraisals are as follows, “I trust that my replies will be kept private”, “I trust research staff”, “I was treated with respect and dignity”, “I feel less suspicious of researchers now and participation made me feel like someone understands my
problems”. Negative appraisal items were; “I am not sure I trust the research staff”, “I found the questionnaire very offensive and I felt real out of control after participating”. The data showed that of 205 children interviewed, 138 (67.3%) reported “yes” things they said would stay private and 72 (35.1%) of the parents strongly agreed that things they said would stay private. Compared to negative appraisal scores, children were said to trust the researchers more than their parents/guardians. Only 1.2% of the children reported “yes” they don’t trust the research staff and that they were sorry that they were in the particular study. This suggests that children were informed of confidentiality, rights to withdraw from the research more than their parents/guardians. Correlations between the social and demographic data with elements of confidentiality in both children and parents showed no significance. This suggests that there were no differences in understanding key items used in evaluating confidentiality in both groups. The understanding of key items/elements of confidentiality was the same in all groups analysed (children, parents, therapeutic, non-therapeutic, active research group (the drop-outs).

Positive attitudes shown by researchers were reported to be one of the reasons why they participated in research. Participants reported that researchers in hospitals are very charming and welcoming compared to other health care workers who are not part of the research project, who were reported to be very harsh, aggressive and corrupt. This can be explained by the fact that most health care workers working research are well motivated by high salaries and other incentives hence less likely to be involved in unethical behaviour. In Tanzania there is always an underground battle between the research workers and other health care providers. Many workers who are not part of research projects are highly unmotivated by seeing their colleagues getting better salaries and incentives. This has created a gap between those employed by the government and those in research projects.
Researchers are encouraged to develop explicit strategies to inform participants and host communities of the results of the research. Being involved in research and assuming all risks involved, participants and their host community have a right to know what was found and its implications for public health and health care policies.\textsuperscript{78,83} This has not been done by many research projects in Tanzania.\textsuperscript{86} In this study participants reported concerns over results dissemination. Many participants felt that the research results would not be available after the end of research project; if available it would be too technical to be understandable by lay individuals in the community. They also reported that most researchers don’t report back or follow-up participants after the end of research. Empty promises given by researchers were exemplified in this report by participant number 89, “They normally use same phrases, they will say ohh! this will work to your child … you are helping your community and the government … government has used a lot of money to make sure that you have a better health, you can pay back this favour by signing and taking part in this research.”

7.4 Scientific Validity

One of the requirements of ethical research is valid scientific methodology. Research must be designed to yield reliable and useful data related to research questions it addresses with minimal risks to research participants.\textsuperscript{78} Thorough analysis of scientific validity and ethics would require a review of the complete research protocol but at the conceptual level the proposed study design must efficiently answer the primary study questions. This is necessary but not sufficient justification to determine unethical research. Researchers and reviewers must also ask whether there are alternative methodologies that provide the same or better information with an equal or better risk-benefit ratio.\textsuperscript{78,83}

As proposed by Emanuel et al., scientific validity is more than obtaining adequate sample size and unbiased measurements of the outcome. Any study
must fulfil three important benchmarks. Firstly, the study must be designed in such a way that the results obtained will be useful to the health problem in the local setting. The study must be socially, culturally and economically appropriate to the community under study or provide a reliable foundation for conducting subsequent research. In this study several items were used to analyse participant responses to the science used in the studies they were in. The data showed that 91.1% of children reported that the research was sensitive and appropriate to their culture (Item 47 of RRPQ-C and RRPQ-P), compared to 71% of the parents. 83.4% of the children and 67% of parents reported that they like the idea that they contribute to science by participating in the research (items 36 of RRPQ-C and RRPQ-P). Other items tested also revealed significant understanding of validity of the science used in the research they are in in comparison with social, economic and cultural values. Items tested were, “I believe this study will be useful to others”, “I think the research is for good cause”, “I found questionnaire offensive, some questions in the study were hard to understand”, “I felt I was being exploited for scientific purposes”, “investigators explained possible harmful effects to me in ways I understood”, “I gained insight about my experience through research participation and the forms explaining the study were hard to understand”. Evaluating the above items showed that the level of understanding of science used in the research was satisfactory. No significant correlations were found when analysing social demographic data with elements for scientific validity in therapeutic and non-therapeutic groups or the control and the research groups. This suggests that their understanding level was the same regardless of the nature of the research they were in, age, marital status, level of education, age or area they are from.

The second benchmark for scientific validity is the study design in relation to local health care services. In health research, researchers must make sure that the study objectives are neither denying health care services that participants are entitled to nor giving health care services that are not feasible.
or out of the context of the national health care system. As proposed by Emanuel et al., if the study objectives are deemed to be socially valuable, especially to the enrolled participants’ community, demands for providing more comprehensive interventions beyond those to which participants are entitled or beyond those that are feasible and sustainable may be unethical if they undermine the scientific objectives or make the results irrelevant to the community. In this study participants commented thoroughly on the differences in services between the research group and other patients attending health care centres. Diagnostic kits used in research centres were more advanced compared to the general hospitals. The double standards in hospital services were identified by participants as a reason why some members of the community opt to be involved in research. Sustainability of services was also a concern to participants in this study; many felt that the fast-tracked and routine procedures done when they are at the hospitals will no longer be available after research. Their concern is based on a recorded decrease in the services from previous studies done in the community.

The third benchmark is that, the study must be feasible, given the social and cultural environment in which it is being conducted. Feasibility is only ensured if there are sustainable improvements to health care infrastructure, for example, by training personnel, construction of additional facilities or provision of affordable treatments or drugs.

7.5 Social Value

Research in developing countries must have social value, especially research involving minors since they are at higher risk of exploitation. Although generation of knowledge can lead to improvements in health, without social value research exposes participants to risks for no good reason and wastes resources. Even though the process of connecting research into a policy or health care improvements is complex, researchers are obliged to generate
information that is of value to the host community and not the privileged few outside the area under study.\textsuperscript{78,83,84,85}

Social value of research for the host community must explicitly be specified and enhanced. For research to be of best social value, four benchmarks must be assessed.\textsuperscript{78} Firstly, research should determine the beneficiaries of the research, whether local community, host country or people outside the host country. Secondly, the potential value of the research for each prospective beneficiary should be outlined in the research. Each local community or host country has different health priorities hence it is very important to consider their priorities first. Thirdly, mechanisms for improving social value should be strategised. Research dissemination should be arranged to not only policy makers in the host country but to the local community. Collaborative partnership enhances trust and also eases the delivery of health care services. Fourthly, the research conducted should not undermine existing health care services. Supplementary improvements of the existing services are allowed but it should not be to the extent of diminishing the existing service.\textsuperscript{78,81,83}

In this study the level of understanding of the principle of social value was evaluated. In analysing reasons for participation, 188 (91.7\%) of children interviewed reported that their research participation might improve access to health care (Table 3) and 192 (93.7\%) parents/guardians strongly agreed that their participation might improve access to health care (Table 4). 92\% of children and 71\% of parents/guardians reported that the research they were in seemed to be sensitive and appropriate to their culture and that it could transform something that was personally painful into something that might be positive for others (Item 40). Significant positive scores were also observed for items “I think this research is for a good cause” (Item 24), “I believe this study will be useful to others” (Item 18), and “I found participating in this study personally meaningful” (Item 14). No child reported that they felt exploited for scientific purposes and only three parents (1.5\%) felt they were scientifically
exploited. Analysing items above and socio-demographic data, there were no significant correlations noted, suggesting high perceived social value of research participation, unrelated to age, sex, level of education, research group (therapeutic or non-therapeutic), active or control groups.

7.6 Favourable Risk-Benefit Ratio
Evaluating and weighing risks in research are among the most challenging and subjective task for health research ethics regulatory bodies.\textsuperscript{82,85} This is even harder when it comes to research involving minors. Many guidelines have highlighted that research involving minors should be of minimal risk. This has created much debate about acceptable research risks for minors.\textsuperscript{82} Minimal risk is very subjective, especially in developing world where cultural perceptions of non-risk and risk differs according to tribes, geographical location, age and sex.\textsuperscript{6,26,78} Due to social inequalities, developing world children are at more risk of being exploited than their counterparts in the developed world.\textsuperscript{85} In evaluating the potential harms or discomfort posed by research in developing countries, researchers should always consider the two recommendations proposed by the U.S. Committee on Clinical Research Involving Children.\textsuperscript{5} Firstly, minimal risk should be interpreted in relation to normal experience of average, healthy, normal children. Secondly, researchers and RECs should make sure that children and parents are given full information regarding risks and benefits of research participation. Benefits must always outweigh the risks; if the risk is slightly higher, then it should be justified by the community on how the scientific knowledge obtained will be helpful to them and the world at large.\textsuperscript{5,78} Previously, researchers were only focusing on taking assent of children age seven or more without respect of their autonomy.\textsuperscript{5} Current teachings focus more on teaching children to become more autonomous by allowing them to make decisions that are informed and useful in improving their social, economic and cultural welfare.\textsuperscript{26,9,12} Children should be enrolled in research after evaluation of their level of understanding of risks, rights and benefits.\textsuperscript{5,78} Decision-making in research involving minors is linked to
understanding of three principles: risks, benefits and rights. A child who can understand the risks or potential benefits of research but not both is unlikely to make good decisions. Understanding of research concepts and decision-making go together, especially in non-beneficial research. In non-beneficial studies children are supposed to be informed to the extent of knowing that it is moral to help others. Asking children whether they want to enrol in research before they develop the concepts of altruism amounts to asking them to accept burdens and risks without knowing. In most cases children less than 10 years can also make the same decision as those above 10 years of age, as long as they understand why they are participating. This study evaluated the level of understanding of risk and benefits of parents/guardians and children involved in research around five centres in Tanzania.

7.6.1 Understanding of risks
In this study several items were used to evaluate the level of understanding of risk involved in research participation. Of 205 of the children interviewed, only 10 (4.9%) of the children reported that being in the respective research studies made them feel upset or sad while only 5% of adults agreed that they felt bad participating in research. Only 8 (3.9%) of the children strongly agreed that when they were told about possible bad effects of participating they didn’t take them seriously while 6 (3%) of the adults strongly agreed. From 205 children and parents interviewed, 4 (1.9%) of the children and 8 (3.9%) of parents/guardians strongly agreed that the research procedure they took/are taking could be risky to others. The lower percentage in each item analysed revealed that a majority of participants believed that they had good understanding of risks involved in research. The same trend was analysed on items, “I feel less suspicious of researchers now”, “I was emotional during the research session”, “participating in this study was inconvenient for me”, “At times the procedure made me feel stupid”, “I found the questionnaire very offensive”, “I experienced intense emotions during research sessions”, “Investigators explained possible harmful effects to me in ways I understood
and when first contacted”, “I had difficulty making a decision about whether or not I should participate in the research”. In analysing level of understanding of on-going risk involved during research, no children reported that they felt exploited for scientific purposes and only 3 parents (1.5%) strongly agreed. The same percentage was observed on item “my condition worsens after participating”. Socio-demographic data and elements of risk showed no significant correlation with all seven socio-demographic measures used in children and parents/guardians ($r=0.000, p=0.001$). The above suggests that age, sex, level of education, religion, marital status, relationship with escorting child/parent occupation did not correlate with understanding of risks involved in research participation in both groups (children and parents/guardians). This means that level of understanding of risks was satisfactory and unrelated to social and demographic factors.

Risk analysis in therapeutic and non-therapeutic groups also revealed no significant correlation with items used to evaluate understanding of ($r=0.000, p=0.001$). The same was observed in the active research groups and the control group (drop-outs). In commenting about their research involvement in general, participants reported that risks were not commonly talked about by the researchers at the time of recruitment. Research risks were only discussed in detail after participants questioned the researchers on potential risks involved. This is more common in non-therapeutic research than therapeutic since interactions between participants and researchers in the latter group are usually more intense and frequent than the former. All participants responded that there must be openness in informing participants about risks involved in research before recruitment.

7.6.2 Understanding of benefits and risks
In most health research it is difficult to outline direct benefits to the participants or the community under study hence it is very important to evaluate both indirect and direct benefits in relation to risks involved (risk-benefit ratio). In
research involving minors, a favourable risk-benefit ratio should be sought. If potential risks outweigh the benefits then social value must justify the risks. As proposed by many research ethics guidelines, two benchmarks must be considered when analysing understanding of favourable risk-benefit ratio. Firstly, the risk-benefit ratio must be favourable to the context of individual life. When a participant is living in an area with higher disease incidence or prevalence then the greater potential benefit might outweigh the risk. This is because the risks taken are for public health interest. Secondly, the risk-benefit ratio to the community involved should also be favourable. The results obtained in the study should be of interest to the community and not just to researchers or other privileged communities.

In this study 18 items were used to analyse understanding of risks and benefits of being involved in research. Of 205 responses, 193 (94.1%) children involved in the research reported that their research participation was beneficial to them, 167 (81.5%) parents/guardians strongly agreed; 192 (93.7%) parents/guardians and 188 (91.7%) children felt that their participation might improve access to health care. Evaluating their reactions in participation, 186 (90.7%) children and 82 (40%) parents/guardians reported that they felt good about helping others. Long-term benefits were analysed separately. In the study 181 (88.3%) children and 167 (81.5%) parents reported that they like the idea that they contributed to science by participating in research. In analysing the data in general it can be concluded that participants’ level of understanding of benefits involved in the research was satisfactory because participants scored very highly on positive appraisal items for benefits and low in positive appraisal values for risks. Among the items evaluated to justify the analysis above were: “I think this research is for a good cause”, “I believe the study will be useful to others”, “I gained insight about my experience through research participation and I gained something positive from participating.”
Research social value was also analysed as part of risk-benefit analysis. One hundred and forty (68.3%) children and 173 (84.4%) parents/guardians reported that the research they were involved in was sensitive and appropriate to their culture and also felt that participation in the project was worth it despite any inconveniences experienced. Appropriateness of research to social value is something important to be considered in health research. This is because in developing countries research is not well understood, hence contributing to greater risk of research exploitation. Many participants in discussion reported that they were concerned with losing services when the research ended. The debate on when to stop supporting research communities after the termination of a study has been going on for the past two decades. Since most studies cannot give ongoing direct benefit to research participants, improvements of health care infrastructure and services have been used by many investigators as a tool for recruiting research participants. The level of understanding of risk and benefits involved in research in this study were very high compared to understanding of other ethical concepts. This could be due to the fact that the research participants were well prepared by the respective research teams, or awareness has increased due to level of education or development. But evaluating the items on benefits and socio-demographic measures revealed the opposite. In this study there was no significant relationship between the level of understanding of benefits and rights of participation to sex, age, level of education, marital status, occupation or living areas (urban or rural). No significant correlation was observed in therapeutic and non-therapeutic groups when compared to items used in analysing understanding of research benefits in research participants ($r=0.000$, $p=0.001$). The same was analysed in the research active group and the control group (the drop-outs).
8. CONCLUSION AND RECOMMENDATIONS

Overall, this study suggests that perceptions of rights, risks and benefits of research participation and other ethical concepts did not correlate with level of education, age, sex, occupation, demographic distribution, marital status or type of research study (therapeutic or non-therapeutic) participants had been involved in. It would appear that if participants are given standard information required to make a decision whether to participate or not, they believe they can decide reasonably regardless of their demographic backgrounds.

The results of this study support the maxim that even minors, if presented with information in an age-appropriate format, can understand and respond appropriately to key ethical issues in health research ethics. Children's abilities to understand complex information should not be underestimated. The same applies to rural and uneducated parents/guardians. The results of this study also suggest that all individuals, regardless of age, sex, level of education, occupation, demographic locations or type of research trial they are enrolled in can understand and differentiate research options, and the associated risks and benefits. As opposed to some previous studies done in developing countries, this study has shown that for health research involving minors to be ethical then children should be evaluated as whether they possess several factors. Firstly, they must at least have a basic understanding of the facts presented in research; secondly, they must be given a chance to make appropriate choices without interference or undue influence (that means they must be very comfortable with their choices).

The study was not without limitations. Firstly, the Instrument RRPQ-P and RRPQ-C used was developed and previously used only in trauma-related research. This study is the first to use the same instrument in research not related to trauma, hence creating some difficulties in transforming trauma-related concepts into a general research ethics tool. The questionnaire
contained more than 100 items that needed thorough analysis. The data collected from 205 participants was very detailed. It was difficult to rank the most and least important findings. Balancing negative and positive appraisal items in the questionnaire and analysis was time consuming. There were many repetitions of concepts in some items. All these made analysis time consuming and difficult. The questionnaire was not validated in Tanzania nor in any other African setting.

In trauma studies more than one child in the household was recruited for the research as long as they met the same research inclusion criteria. Our inclusion criteria excluded the possibility of having more than one child from the same family participating in research. Only one child per parent/guardian was enrolled.

Due to limited time some of the parents/guardians were present at the time of the interview; this was to assure the child that his/her participation in the research was well supported by the accompanying family member. Parent’s/guardian’s presence during the interview could have influenced children’s decisions. Researchers have tried to limit this bias but it is a factor that should not be ignored in future studies.

This study assessed participants’ immediate reactions to research participation, so a follow-up assessment might augment our understanding of any longer lasting perceived costs or benefits of research participation.

This study did not control for participants who had been in several or only one previous study. These factors could influence the results.

This study also underlines the need for independent regulatory bodies in protecting groups at risk. The current Tanzania national research regulation only gives constitutional regulatory mandate to Ministry of Health (MOH) and
National Institute of Medical Research (NIMR). A separate guideline which
focuses on groups at risk of research exploitation should be developed instead
of using the blanket/general guideline currently used by NIMR and MOH.

Thorough education should be given to research communities prior to and
during research participation. This will help to clear many concerns expressed
by participants in this study. The current model of only including few members
of the community (CAB) is not enough. The UNAIDS AVAC GPP guidelines are
helpful in this respect.87

Finally, this research hopefully highlighted the new knowledge in research
involving minors in developing countries. This is due to the fact that the existing
literature in research ethics in developing countries focuses mainly on informed
consent and standard of care. Research investigating risks, benefits and rights
of research participants in developing countries remains an essential area of
focus for future studies. Research of this nature will provide a more accurate
understanding of risks, benefits and rights in health research involving minors in
developing countries.


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82. Informed consent. ACOG committee opinion No 439, August 2009.


84. Research involving children. UCL research ethics committee guidance note 1. 2006.


Appendix I:

REACTIONS TO RESEARCH PARTICIPATION QUESTIONNAIRE (RRPQ) – PARENTS.

<table>
<thead>
<tr>
<th>Serial Number</th>
<th>Centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region</td>
<td>Type of research/trial</td>
</tr>
<tr>
<td>Title of research</td>
<td></td>
</tr>
</tbody>
</table>

_We want to know your opinion about what it is like for you to be in the study that you are participating/have participated. Your answers will help us understand how children feel about being in studies like the one you are participating/have participate. We REALLY want to hear your opinions, even if there were things you did not like._

_For each section below, please complete the questionnaire as instructed by investigator. There is no right or wrong answers._

I: The following questions aim at gathering your personal information;

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Level of education</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Marital status  
Religion  
Occupation  
Relation with accompanied child  

II The following question aims at gathering your reasons for participation;

From list below, please rank the top three reasons why you decided to participate (1=Most important, 2=second most important, 3=third most important).

I was curious  
I don’t know  
Felt I had to  
To help others  
Thought it might improve my access to health care  
For the money  
To help my self  
I didn’t want to say no  

III: The following questions deal with your reactions to participation. Please circle.

<table>
<thead>
<tr>
<th>Question</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neutral (may be)</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I gained something positive from participating.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Participation upsets me more than I expected.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Knowing what I know now, would participate in this study if given the opportunity.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. The investigators explained possible harmful effects to me in ways I understood.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. When first contacted, I had difficulty making a decision about whether or not I should participate in the research.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. The research raised emotional issues for me that I had not expected.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. I gained insight about my experience through research participation.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. I found participation to be interesting.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>9. The research made me think about things I didn’t want to think about.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>10. I felt free to skip questions and/or parts of the study.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11. I found questions too personal</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>12. Participation took my mind off my problems.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>13. I not sure I trust the</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
research staff.

14. I found participating in this study personally meaningful.

15. The forms explaining the study were hard to understand.

16. I liked knowing someone was paying attention to my thought and feelings.

17. I felt pressured to participate.

18. I believe this study will be useful to others

19. I trust that my replies will be kept private.

20. In this study, my choices were respected.

21. I am concerned why I was selected for this study.

22. I experienced intense emotions during research session.

23. I trust the research staff

24. I think this research is for a good cause.

25. I was treated with respect and dignity.

26. I understood the consent form

27. I felt like I couldn’t say “no” to participation.

28. I found the questionnaire offensive.

29. At times the procedures made me feel stupid.

30. I felt calm after participating.

31. I found participation beneficial to me

32. I felt real out of control after participating.

33. Volunteering made me feel good about myself
<table>
<thead>
<tr>
<th>Number</th>
<th>Statement</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>34.</td>
<td>Some of the questions in the study were hard to understand.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>35.</td>
<td>I was glad to be asked to participate</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>36.</td>
<td>I like the idea that I contribute to science.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>37.</td>
<td>My condition worsens after Participating.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>38.</td>
<td>Information received before participating accurately described what I was required to do and my reaction to it</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>39.</td>
<td>I felt that I was being exploited for scientific purpose.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>40.</td>
<td>The research let me transform something that was personally painful into something that might be positive for others.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>41.</td>
<td>I regret agreeing to participate.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>42.</td>
<td>I was emotional during the research session.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>43.</td>
<td>I am concerned this procedure could be risky to others.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>44.</td>
<td>I felt I could stop at any time.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>45.</td>
<td>I feel less suspicious of researchers now.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>46.</td>
<td>I found the experience of participating to be stressful.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>47.</td>
<td>The research seemed to be sensitive and appropriate to my culture.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>48.</td>
<td>When they told me possible bad effects of participating, I didn’t take them seriously.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>49.</td>
<td>I felt able to ask</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Question</td>
<td>Rating</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>--------</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>questions when wanted.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50. I am worried that my answers won’t stay private.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51. I found participating boring.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52. My condition improved after participating.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>53. The study procedures took too long</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>54. Participating in this study was incontinent for me.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55. Participation made me feel like someone understands my problems.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56. I found myself really enjoying the procedures.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57. Participating in the project was worth it to me despite any inconvenience I experienced.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58. I felt calm while participating.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>59. Had I known in advance what participating would be like for me, I still would have agreed.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60. I learned something new about myself by participating.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**DO YOU HAVE ANY COMMENTS OR SUGGESTIONS FOR THE RESEARCHERS?** (Please write here or on the back of the this sheet)
Appendix II:

REACTIONS TO RESEARCH PARTICIPATION QUESTIONNAIRE (RRPQ) – CHILDREN

**Serial Number**
**Region**
**Title of research**
**Centre**
**Type of research/trial**

*We want to know your opinion about what it is like for you to be in the study that you are participating/have participated. Your answers will help us understand how children feel about being in studies like the one you are participating /have participate. We REALLY want to hear your opinions, even if there were things you did not like.*

*For each section below, please complete the questionnaire as instructed by investigator. There is no right or wrong answers.*

**I:** The following questions aim at gathering your personal information.

Age_______ Sex____ Level of education(F/I) and standard/form___________
Religion________
Relation with escorting adult

II The following question aims at gathering your reasons for participation;

From list below, please rank the top three reasons why you decided to participate (1=Most important, 2=second most important,3=third most important).

I was curious _______
I don’t know_________
Felt I had to_________
To help others_______
Thought it might improve my access to health care
For the money
To help my self
I didn’t want to say no

III: The following questions deal with your reaction to participation. Please circle the number that best describe your response.

1. I gained something positive from participating.
   No  May be (In the middle)  yes
   1  3  5

2. Participation upsets me more than I expected.
   1  3  5

3. Knowing what I know now, would participate in this study if given the opportunity.
   1  3  5

4. The investigators explained possible harmful effects to me in ways I understood.
   1  3  5
5. When first contacted, I had difficulty making a decision about whether or not I should participate in the research.  
6. The research raised emotional issues for me that I had not expected.  
7. I gained insight about my experience through research participation.  
8. I found participation to be interesting.  
9. The research made me think about things I didn’t want to think about.  
10. I felt free to skip questions and/or parts of the study.  
11. I found questions too personal  
12. Participation took my mind off my problems.  
13. I not sure I trust the research staff.  
14. I found participating in this study personally meaningful.  
15. The forms explaining the study were hard to understand.  
16. I liked knowing someone was paying attention to my thought and feelings.  
17. I felt pressured to participate.  
18. I believe this study will be useful to others  
19. I trust that my replies will be kept private.  
20. In this study, my choices were respected.  
21. I am concerned why I was selected for this study.  
22. I experienced intense emotions during research session.  
23. I trust the research staff  
24. I think this research is for a good cause.  
25. I was treated with respect and dignity.  
26. I understood the consent form
27. I felt like I couldn’t say “no” to participation.  
28. I found the questionnaire offensive.  
29. At times the procedures made me feel stupid.  
30. I felt calm after participating.  
31. I found participation beneficial to me  
32. I felt real out of control after participating.  
33. Volunteering made me feel good about myself.  
34. Some of the questions in the study were hard to understand.  
35. I was glad to be asked to participate.  
36. I like the idea that I contribute to science.  
37. My condition worsens after participating.  
38. Information received before participating accurately described what I was required to do and my reaction to it.  
39. I felt I that I was being exploited for scientific purpose.  
40. The research let me transform something that was personally painful into something that might be positive for others.  
41. I regret agreeing to participate.  
42. I was emotional during the research session.  
43. I am concerned this procedure could be risky to others.  
44. I felt I could stop at any time.  
45. I feel less suspicious of researchers now.  
46. I found the experience of participating to be stressful.  
47. The research seemed to be sensitive and appropriate to my culture.  
48. When they told me possible bad effects of participating, I didn’t
<table>
<thead>
<tr>
<th>Question</th>
<th>1</th>
<th>3</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>49. I felt able to ask questions when wanted.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50. I am worried that my answers won’t stay private.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51. I found participating boring.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52. My condition improved after participating.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>53. The study procedures took too long</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>54. Participating in this study was incontinent for me.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55. Participation made me feel like someone understands my problems.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56. I found myself really enjoying the procedures.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57. Participating in the project was worth it to me despite any</td>
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<tr>
<td>inconveniencene I experienced.</td>
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<td></td>
</tr>
<tr>
<td>58. I felt calm while participating.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>59. Had I known in advance what participating would be like for me, I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>still would have agreed.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60. I learned something new about myself by participating.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DO YOU HAVE ANY COMMENTS OR SUGGESTIONS FOR THE RESEARCHERS?** (Please write here or on the back of this sheet.)
Appendix III:

REACTIONS TO RESEARCH PARTICIPATION SCALE

1. Participation
   I like the idea that I contributed to science.
   I was glad to be asked to participate.
   *Include in future testing:* I felt I could stop participating at any time.
   *Recommended new item:* Participation was a choice I freely made.

2. Personal Benefits
   I gained insight about my experiences through research participation.
   I gained something positive from participating.
   I found participating beneficial to me.
   I found participating in this study personally meaningful.

3. Emotional Reactions
   The research raised emotional issues for me that I had not expected.
   I experienced intense emotions during the research session.
   I was emotional during the research session.
   The research made me think about things I didn’t want to think about.

4. Perceived Drawbacks
   The study procedures took too long.
   Participating in this study was inconvenient for me.
   I found participating boring.
   I found the questions too personal.
   *Include in future testing:* Knowing what I know now, I would participate in this study again if given the opportunity. (Reverse score)
   *Include in future testing:* Had I known in advance what participating would be like I still would have agreed to participate. (Reverse score)

5. Global evaluation
   I think this research is for a good cause.
   I believe this study’s results will be useful to others.
   I was treated with respect and dignity
   I trust that my replies will be kept private.
   *Include in future testing:* I understood the consent form.
Appendix IV:

INFORMATION SHEET AND CONSENT TO PARTICIPATE IN RESEARCH

CHILDRENS’ AND PARENTS’/GUARDIANS’ UNDERSTANDINGS OF RIGHTS, RISKS AND BENEFITS ASSOCIATED WITH RESEARCH INVOLVING MINORS.

Dear Participant

1) INTRODUCTION
We invite you to participate in a research study. This information leaflet will help you to decide if you want to participate. Before you agree to take part you should fully understand what is involved. If you have any questions that this leaflet does not fully explain, please do not hesitate to ask the interviewer

2) THE NATURE AND PURPOSE OF THIS STUDY
The aim of this study is to evaluate community understanding of risks, rights and benefits associated with research involving minors. You as a client are a very important source of information on the research area since you are currently participating in a research.

3) EXPLANATION OF PROCEDURES TO BE FOLLOWED
This study involves accessing your perception on various topics relating to research participation, especially research which involves minors. We will ask you some questions about rights, risks and benefits of participating in a research including one which you are involved now.

4) RISK AND DISCOMFORT INVOLVED
Some of the questions we are going to ask you may make you feel uncomfortable, but you need not answer them if you don't want to. The interview will take about 20 minutes of your time.

5) POSSIBLE BENEFITS OF THIS STUDY
Although you will not benefit directly from the study, the results of the study will enable us to prepare guidelines and policies on research involving minors.

6) WHAT ARE YOUR RIGHTS AS A PARTICIPANT?
Your participation in this study is entirely voluntary. You can refuse to participate or stop at any time during the study without giving any reason. Your withdrawal will not affect you or your current management or research enrolment.

7) HAS THE STUDY RECEIVED ETHICAL APPROVAL?
This study has received written approval from the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria and National Institute of Medical Research (NIMR). Copies of the approval letters are available if you wish to have one.

8) INFORMATION AND CONTACT PERSON
The contact person for the study is Dr Lumuli Mbonile. If you have any questions about the study please contact him at cell 0717 542898.

9) COMPENSATION
Your participation is voluntary. No compensation will be given for your participation.

10) CONFIDENTIALITY
All information that you give will be kept strictly confidential. Once we have analyzed the information no one will be able to identify you. Research reports and articles in scientific journals will not include any information that may identify you.

CONSENT TO PARTICIPATE IN THIS STUDY
I confirm that the person asking my consent to take part in this study has told me about nature, process, risks, discomforts and benefits of the study. I have also received, read and understood the above written information (Information Leaflet and Informed Consent) regarding the study. I am aware that the results of the study, including personal details, will be anonymously processed into research reports. I am participating willingly. I have had time to ask questions and have no objection to participate in the study. I understand that there is no penalty should I wish to discontinue with the study and my withdrawal will not affect any management or research enrolment.

I have received a signed copy of this informed consent agreement.

Participant's name ...........................................................................................................(Please print)
Participant's signature: .................................... Date..............................
Investigator's name ...........................................................................................................(Please print)
Investigator's signature ........................................ Date..............................
Witness's Name ...........................................................................................................(Please print)
Witness's signature .............................................. Date..............................

VERBAL INFORMED CONSENT
I, the undersigned, have read and have fully explained the participant information leaflet, which explains the nature, process, risks, discomforts and benefits of the study to the participant whom I have asked to participate in the study children's’
and parents’ understanding on rights, risks and benefits associated with research involving minors.

The participant indicates that s/he understands that the results of the study, including personal details regarding the interview will be anonymously processed into a research report. The participant indicates that s/he has had time to ask questions and has no objection to participate in the interview. S/he understands that there is no penalty should s/he wish to discontinue with the study and his/her withdrawal will not affect any management or research enrolment (current research). I hereby certify that the client has agreed to participate in this study.

Participant's Name ..............................................................(Please print)
Person seeking consent ...........................................................(Please print)
Signature ..................................................................................Date ..................................
Witness's name ..........................................................................(Please print)
Signature ..................................................................................Date ..........................
Appendix V:

Assent Form

CHILDRENS’ AND PARENTS’/GUARDIANS’ UNDERSTANDINGS OF RIGHTS, RISKS AND BENEFITS ASSOCIATED WITH RESEARCH INVOLVING MINORS.
Investigator: Dr Lumuli Milline Mbonile.

The investigators named above are doing a research study.

These are some things we want you to know about research studies:
We are asking you to be in a research study. Research is a way to test new ideas. Research helps us learn new things. Whether or not to be in this research is your choice. You can say Yes or No. Whatever you decide is OK. We will still take good care of you and you will continue with other activities in this centre as usual.

Why am I being asked to be in this research study?
You are being asked to be in the study because you are also participating to one or more studies organized by this centre.

What is the study about?
The Investigator need to learn more about community understanding on risks, rights and benefits of being involved in research, especially research that involve your age group. The Knowledge gained in this research will give researcher and other an opportunity to prepare programs that will guarantees protection of minor’s like you once you are involved in research.

What will happen during this study?
If you agree to be in this study, you will ask you some questions which are very simple and relating to the research you are involved now. Most of these questions will ask about benefits, rights and risks of being involved in a research.

Will the study hurt?
You will not get hurt in anyway. The researcher will only ask few questions regarding your current research. You are free to stop answering questions anytime without interfering your activities/management at this centre.

What else should I know about the study?
If you feel sick or afraid that something is wrong with you or questions asked, tell an adult at once. You do not have to answer any questions that are asked of you if you not comfortable.
What are the good things that might happen?
People may have good things happen to them because they are in a research study. These are called “benefits.” This study will not have a direct benefit to you but it will assist researchers and other stakeholders to prepare programs and policies to protect minors like you once you are involved in research.

What if I don’t want to be in this study?
You do not have to be in the study if you do not want to. The doctors/nurse/researchers will still take care of you. If you don’t want to be in this study, you can continue to get your medical care/can continue to participate in previous research.

Who should I ask if I have any questions?
If you have any questions about this study, you or your parents can call Dr. Lumuli Mbonile at +255 717 542898

Do I have to be in the study?
No, you do not have to be in the study. Even if you say yes now, you can change your mind later. It is up to you. No one will be mad at you if you don’t want to do this

Now that I have asked my questions and think I know about the study and what it means, here is what I decided:

_________OK, I’ll be in the study. _________ No, I do not want to be in the study.

The researchers have told me about the research. I had a chance to ask questions. I know I can ask questions at any time. I want to be in the research.

If you sign your name below, it means that you agree to take part in this research study.

_________________________________   _____  __________________
Your Name (Printed)             Age       Date

_________________________________
Your Signature                   Date

_________________________________
Signature of Witness             Date

_________________________________
Signature of Person Obtaining Consent
Appendix VI:

Parental Consent for Children under 18

CHILDRENS’ AND PARENTS’/GUARDIANS’ UNDERSTANDINGS OF RIGHTS, RISKS AND BENEFITS ASSOCIATED WITH RESEARCH INVOLVING

1) INTRODUCTION
Your child is invited to participate in a research project being conducted by Dr Lumuli Milline Mbonile from Mbeya Referral Hospital. This information leaflet will help you to decide if you want him/ her to participate. Before you agree you should fully understand what is involved. If you have any questions that this leaflet does not fully explain, please do not hesitate to ask the interviewer

2) THE NATURE AND PURPOSE OF THIS STUDY
The aim of this study is to evaluate community understanding of risks, rights and benefits associated with research involving minors. Your child is very important source of information on the research area since him/her currently participating in a research.

3) EXPLANATION OF PROCEDURES TO BE FOLLOWED
This study involves accessing his/her perception on various topics relating to research participation, especially research which involves minors. We will ask him/her some questions about rights, risks and benefits of participating in a research including one which he/she involved now.

4) RISK AND DISCOMFORT INVOLVED
Some of the questions we are going to ask may make him/her feel uncomfortable, but he/she need not answer them if he/she doesn’t want to. The interview will take about 20 minutes of his/her time

5) POSSIBLE BENEFITS OF THIS STUDY
Although he/she will not benefit directly from the study, the results of the study will enable us to prepare guidelines and policies on research involving minors.

6) WHAT ARE HIS/HER RIGHTS AS A PARTICIPANT?
Following your consent, participation of your child in this study remains voluntary. Your child will also be asked to provide assent to participate and may refuse even if you consent. Your child can also refuse to answer any questions and may withdraw from the study at any time without penalty

7) HAS THE STUDY RECEIVED ETHICAL APPROVAL?
This study has received written approval from the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria and National Institute of
Medical Research (NIMR). Copies of the approval letters are available if you wish to have one.

8) INFORMATION AND CONTACT PERSON
The contact person for the study is Dr Lumuli Mbonile. If you have any questions about the study please contact him at cell 0717 542898.

9) COMPENSATION
His/her participation is voluntary. No compensation will be given for his/her participation.

10) CONFIDENTIALITY
No identifying information will be included in the data your child provides. Your signed consent form, and their assent form, will be kept separate from the data, and nobody will be able to link their responses to them.

Any identifying information collected will be kept in a secure location and only the researchers will have access to the data. Participants will not be individually identified in any publication or presentation of the research results. Only aggregate data will be used. Your signed consent form and your child’s assent form will be kept separate from the data, and nobody will be able to link their responses to them.

I have read the information provided above and all of my questions have been answered. I voluntarily agree to the participation of my child in this study. I will receive a copy of this consent form for my information.


Parent / Legal Guardian Signature
Parent / Legal Guardian Signature
Name of Child _______________________________
Appendix VII:

THE UNITED REPUBLIC OF TANZANIA

National Institute for Medical Research
P.O. Box 9653
Dar es Salaam
Tel: 255 22 2121400/390
Fax: 255 22 2121380/2121360
E-mail: headquarters@nimr.or.tz
NIMR/HQ/R1/Vol. IX/1014

Ministry of Health and Social Welfare
P.O. Box 9083
Dar es Salaam
Tel: 255 22 2120262-7
Fax: 255 22 2110986
29th September 2010

Dr Lumuli Mbonile
Mbeya Referral Hospital
P.O.Box 419,
MBEYA

CLEARANCE CERTIFICATE FOR CONDUCTING
MEDICAL RESEARCH IN TANZANIA

This is to certify that the research entitled: Children’s and Parent/Guardian’s Understanding of Rights, Risks and Benefits Associated with Research Involving Minors in Tanzania, (Mbonile L. et al), has been granted ethics clearance to be conducted in Tanzania.

The Principal Investigator of the study must ensure that the following conditions are fulfilled:

1. Annual Progress report is submitted to the Ministry of Health and the National Institute for Medical Research, Regional and District Medical Officers.
2. Permission to publish the results is obtained from National Institute for Medical Research.
3. Copies of final publications are made available to the Ministry of Health & Social Welfare and the National Institute for Medical Research.
4. Any researcher, who contravenes or fails to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine; NIMR Act No. 23 of 1979, PART III Section 10(2).
5. Approval is for one year: 29th September 2010 to 28th September 2011.

Name: Dr Mwelecle N Malecela

Signature

ACTING CHAIRPERSON
MEDICAL RESEARCH
COORDINATING COMMITTEE

CC: RMO
DMO

Name: Dr Deo M Mtsaiva

Signature

CHIEF MEDICAL OFFICER
MINISTRY OF HEALTH, SOCIAL WELFARE

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Appendix VIII:

NATIONAL INSTITUTE FOR MEDICAL RESEARCH
HQ/DAR ES SALAAM

No. 8044

Date: 28/6/2010

RECEIVED from: Dr. Lumulii Kivumbi
The sum of Shillings: One hundred Thirty Seven Thousand only.
Being Payment of Ethical Clearance Fee.
Shs: 137,000-
Cash / Cheque No.

Signature: [signature]
for Director General
N.I.M.R.
Appendix IX:

The Research Ethics Committee, Faculty Health Sciences, University of Pretoria complies with ICH-GCP guidelines and has US Federal wide Assurance.


Faculty of Health Sciences Research Ethics Committee
Fakulteit Gesondheidswetenskappe Navorsingsetiekkomitee

<table>
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<tr>
<th>PROTOCOL NO.</th>
<th>126/2010</th>
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<tr>
<td>PROTOCOL TITLE</td>
<td>Children's And Parents/Guardian's Understanding Of Rights, Risks And Benefits Associated With Research Involving Minors</td>
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<tr>
<td>INVESTIGATOR</td>
<td>Principal Investigator: Dr Lumuli Mbonile</td>
</tr>
<tr>
<td>SUBINVESTIGATOR</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>SUPERVISOR</td>
<td>Prof Douglas R. Wassenaar</td>
</tr>
<tr>
<td>DEPARTMENT</td>
<td>Dept: SARETI Phone: 033 2606162 Fax: 033 2606809 E-Mail: <a href="mailto:wassemaa@ukzn.ac.za">wassemaa@ukzn.ac.za</a></td>
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<tr>
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<tr>
<td>MEETING DATE</td>
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DATE: 20/07/201

The Protocol and Informed Consent Document were Provisionally approved on 30/06/201 properly constituted meeting of the Ethics Committee subject to the following conditions:

1. Patient Informed Leaflet to be done editorial, and
2. The approval is valid for 2 years period, and
3. The approval is conditional on the receipt of 6 monthly written Progress Reports, and
4. The approval is conditional on the research being conducted as stipulated by the details of the documents submitted to and approved by the Committee. In the event that a change arises who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

Members of the Research Ethics Committees:

- Prof M J Bester (female) BSc (Chemistry and Biochemistry); BSc(Hons)(Biochemistry); MSc(Biochemistry); PhD (Medical Biochemistry); M Ed Coordinated Education
- Prof R Delport (female) BA et Scien, B Curationis (Hons) (Intensive Care Nursing), M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Prof VOL Karusiteit (female) BSc(Chemistry); BSc(Biochemistry); MSc(Biochemistry); PhD (Medical Biochemistry); M Ed Coordinated Education
- Prof JA Kriel (female) BSc(Hons)(Maths); MMed(Hons); MD - Vice-Dean (ex officio)
- Dr NK Likibi (female) BSc(Hons)(Maths); MMed(Hons); MD - Vice-Dean (ex officio)
- Prof TS Marcus (female) BSc(Hons)(Maths); BSc(Biochemistry); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Dr MP Mathebula (female) Department of Clinical Sciences; BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Prof A Nienaber (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Mrs MC Nzeku (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Prof L M Ntsho (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Mr SRJ Phatoli (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Dr R. Reinders (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Dr T Rossouw (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Dr L Schoeman (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education
- Mr Y Silwewiya (female) BSc(Hons)(Maths); MSc(Biochemistry); M Sc (Physics), PhD (Medicine), M Ed Coordinated Education

MS: dd 2016/08/03  
C:\Documents and Settings\user\My Documents\Protocol\Grade briefs\Letters 2016/126-Provisionally.doc

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Dr R Sommers
Prof TJP Swart
Prof CW van Staden

(female) MBchB; MMed(imm); MPharmMed – Deputy Chairperson
BChD, MSc (Odont), MChD (Oral Path), PGCHET – School of Dentistry representative
MBchB; MMed (Psych); MD, FCPsych; FTCL; UPLM – Chairperson

Dr R Sommers

Deputy Chairperson of the Faculty of Health Sciences Research Ethics Committee, University of Pretoria
Appendix X:

Suggested Classification of Risk in Relation to Research Ethics Applications (Brunel University)

The following are suggested criteria for determining risk levels. They should be used in a way that takes full account of circumstances faced by the researcher.

Low Risk
Based on research methods drawn up to elicit data where, for example:-

- Topics have very low risk of causing distress
- Respondents are not classed as being from a potentially vulnerable group (e.g., children), or include clients of the researcher.
- Questionnaires are to be completed solely by the respondent and administered and returned anonymously
- Focus groups with low likelihood of causing distress
- Risk to researcher and respondent of carrying out the research process are negligible, in terms of likelihood of occurrence and severity of outcome – e.g., researcher has no direct contact with respondents
- If a gatekeeper is involved, their permission is already in place.

Medium Risk
- Topics and methods that may cause moderate distress to respondents – sources of help available should be detailed
- Research involving respondents from a potentially vulnerable group – how the ethical issues arising will be dealt with must be detailed. Some vulnerable groups may be high risk
- Researcher will directly collect data from respondents in a medium risk setting, such as a public place or office of an organisation with the organisation’s knowledge and consent – full risk assessment details required
- Material inducements/incentive will be offered to participants
- Setting unfamiliar to researcher – this may also be classed as high risk.

High Risk
- Any research involving:
  - Human tissue or other biological material – Human Tissue Act applies
  - People using social care services
  - Those whose ability to consent is in doubt – legal competence to consent
  - Members of any vulnerable groups, including refugees and asylum seekers, children in care or at risk of going into care or where potential respondents could be considered in a dependent position (e.g., researcher’s own students or clients/patients)
• Research where the risk of distress, or the potential level of distress, embarrassment or harm, that might be caused to the participants or researcher is particularly high. Topics such as death and bereavement or sexuality would probably come into this category, at least in most settings.

• Research that may touch on, or elicit information about:
  • Illegal behaviours by the respondent or others
  • Risky behaviours by the respondent or others
  • Focus groups where the researcher is the sole facilitator – how they will deal with problems such as if one person becomes distressed, or requires attention need addressing
  • Research overseas where the setting is unfamiliar to the researcher
  • Lone working by researcher – particularly if the researcher is planning to visit the home of the respondents.

**NOTE:** None of these higher risks would necessarily preclude research being carried out, but merely require that all matters had been adequately thought through, and sufficient measures taken in response to risks that might have been identified.