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Reservations on the Use of New HIV Prevention Technologies in HIV Prevention in Sub-Saharan Africa

Calvin Gwandure[1] and Thokozile Mayekiso[2]

[1]University of the Witwatersrand, South Africa
[2]Nelson Mandela Metropolitan University, South Africa

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ABSTRACT The aim of the study was to explore the effectiveness of New HIV Prevention Technologies in preventing HIV infection among participants in clinical trials. The study assessed the effectiveness of New HIV Prevention Technologies as reported by researchers on the field. Although it is reported in the media that New HIV Prevention Technologies have made a great deal of progress in HIV prevention, research on the ground indicates that the clinical trials have not managed to reduce HIV infection by a great margin despite the fact that some of the clinical trials have been in place for more than two decades in Sub-Saharan Africa. Most of the clinical trials in HIV prevention have not gone beyond phase III. In this study, it is argued that the use of vaccines, microbicides, antiretroviral therapy for discordant couples, pre-exposure prophylaxis and medical male circumcision in HIV prevention in Sub-Saharan Africa needs a paradigm shift because the results reported so far in clinical trials show more challenges than solutions to the prevention of the HIV pandemic in Sub-Saharan Africa.

INTRODUCTION

The HIV pandemic is showing a gradual decline in new infections, HIV prevalence and AIDS-related deaths in Sub-Saharan Africa (Bateman 2011). Recent reports show that new HIV infections in Sub-Saharan Africa dropped by 25% since 2001 but the demand for treatment is rising (Cohen 2010). It is not clear whether or not the drop in HIV infections and a reduction in AIDS-related health complications are attributable to the efficacy of HIV prevention interventions and AIDS treatment (Cohen 2010). At the moment, researchers attribute the reduction of HIV and AIDS prevalence to prevention education, use of condoms, and the use of New HIV Prevention Technologies. New HIV Prevention Technologies target individuals, groups and the unborn child. In this regard, HIV risk reduction interventions target HIV- positive individuals, people living with AIDS, individuals who do not know their HIV status and HIV-negative individuals. However, there are points of agreement and disagreement about the effectiveness of HIV prevention interventions. Contemporary debate on HIV risk reduction centres on finding the most effective method of reducing HIV and AIDS prevalence in Sub-Saharan Africa (Cohen 2010). Even though new HIV infections have come down, the cost of treating and putting more people living with HIV and AIDS on antiretroviral treatment is prohibitively high in Sub-Saharan Africa (Thairu et al. 201). Recently, HIV and AIDS interventions have changed focus in Sub-Saharan Africa. HIV risk reduction interventions are now targeting and recruiting HIV-negative individuals to participate in New HIV Prevention Technologies clinical trials as a way of "immunising" or "protecting" the public from HIV infection. This paper seeks to critique the use of New HIV Prevention Technologies as an effective method of preventing HIV infection in Sub-Saharan Africa. The paper highlights some of the problems associated with clinical trials and ethical issues relating to the rolling out of New HIV Prevention Technologies in Sub-Saharan Africa. The New HIV Prevention Technologies that are discussed in this paper are vaccines, microbicides, antiretroviral therapy, pre-exposure prophylaxis (PrEP) and medical male circumcision.

**Address for correspondence:*
Dr. Calvin Gwandure
School of Human and Community Development
University of the Witwatersrand
P. O. Box 3 Wits, Johannesburg, 2050, South Africa
E-mail: Calvin.Gwandure@wits.ac.za

PROBLEMS OF CLINICAL TRIALS IN SUB-SAHARAN AFRICA

Sub-Saharan Africa is targeted for HIV clinical trials because of the criterion that is used by

the World Health Organisation to include regions in HIV prevention clinical trials (World Health Organisation 2009). Countries and regions that are selected for clinical trials should have high HIV and AIDS prevalence (World Health Organisation 2009). It is argued that medical research in high-risk countries will ultimately yield benefits for the people and country (White et al. 2011). By participating in clinical trials, communities will facilitate the development of new medicines that could cure HIV (White et al. 2011). The country could realise economic growth by patenting the medicine and selling it to the rest of world, thus bringing in foreign currency. The country could receive foreign direct investment from international HIV and AIDS research organisations working in healthcare business (Tuomi 2011).

The problems of conducting clinical trials in Africa are that the research process itself and funding will be controlled by the organisations sponsoring the studies in the majority of cases (Esser and Bench 2011). Donor funds come with specific instructions on how the money should be used to the satisfaction of the donor (Esser and Bench 2011). Even though the money is earmarked for the host country, the funds might not reach or be utilised by the target population due to bureaucracy and the influence of the donor on programme implementation (Norton-Griffiths 2010). The bulk of the funds in research grants are reported to be used by personnel sent by the donors to the host country and a few local programme implementers (Khan et al. 2010). It is usually alleged that most of the research grants are spent on luxury four-wheel drive vehicles, hotel bills, insurance and medical cover, upmarket offices, residential accommodation, international travel, workshops and conferences. The salaries and benefits of personnel working on donor projects are usually higher than those of civil servants and middle income earners in the private sector (Pillay and Mahlati 2008). High remuneration and benefits could compromise employees' ability to blow the whistle or divulge information to the public about medical risks and casualties such as deaths and infections encountered during clinical trials (Cohen 2004). The sources of funding and accountability of donor funds are usually not transparent enough. Information on income and expenditure of donor funds might not be readily available to the public in some of the donor-funded clinical research projects in Sub-Saharan Africa (Ghosh and Kharas 2011). This could be related to the fact that some governments and local non-governmental organisations in Sub-Saharan Africa tend to rely more on international donor funds to stabilise their balance of payments and operations than their own resources (Morfit 2011). Major donor organisations sometimes accuse governments in Sub-Saharan Africa of interfering and meddling in the clinical trials (Muenning and Su 2011). In situations where government is involved in the clinical trials, the donated money is usually kept and disbursed by non-governmental organisations. It is apparent that major health issues confronting low-income countries are controlled by the politics of developed countries (Park and Sommer 2011). In this case, government might not have full control of the research activities of the programme implementers. International research organisations and donor agencies are usually skeptical of African governments' ability to keep donated money without diverting or misappropriating it (Usher 2010). Researchers might not keep government informed of latest developments on the ground. Such reports could be released by the media and government representatives might be called to participate in launching ceremonies or to inform the public of the good work done in the clinical trials.

Although clinical trials can result in the development of medicine that can cure the disease in the host country, most of the clinical trials that were carried out in Africa did not result in the establishment of pharmaceutical industries in the host countries. Manufacturers of medicines and healthcare products are usually based overseas although local companies could be allowed to make generic medicines (Chaudhuri et al. 2010). International research organisations patent their research findings and sell the medicine back to Africa where the clinical trials were conducted. Africa remains the experimental field for most of the clinical trials and it is a large consumer of HIV prevention and treatment products that are developed abroad (Graboyes 2010).

Local people are usually employed in clinical trials as interpreters for the Principal Investigator appointed by the funding agency (Elmasri 2011). Some of the locals are recruited for data collection, organising conferences and to facilitate training workshops but some will have very little information about the purpose and ultimate

goals of the research (Elmasri 2011; Islam and Sharmin 2011). A few academics from local universities could be involved in the research but they might not be involved in the entire research process. The academics might not be in touch or conversant with the ideology and daily activities of the funding organisation. Activities such as interviewing, social marketing and training of participants are done by health educators. Local health professionals are usually employed to give credence to programme or build trust in participants to participate in clinical trials (Miller 2001). Some African terms could be used to name the research project thereby making the clinical trials more culturally sensitive and acceptable. Some of the promoters of clinical trials could market New HIV Prevention Technologies as "safe" and intended to empower disadvantaged groups, poor people and most-at-risk populations (McMahon et al. 2011). Participants are usually rewarded with meals, drinks and small amounts of money as tokens for participating in clinical trials. The award of money and gifts could be tempting among low-income groups and these could be subtle forms of persuasion and coercion (Ashcroft 2011). The populations of many countries in Sub-Saharan Africa are ravaged by poverty, drought, famine, unemployment and civil unrest to such an extent that very small material incentives could induce large numbers of people to participate in clinical trials irrespective of possible health consequences (Nuffield Council on Bioethics 1999; Emmanuel et al. 2005). Very little information might be available about risks of participating in clinical trials (Klabunde et al. 2011). The use of acronyms such as New "HIV" Technologies or "PrEP" could raise hopes of a cure in the general population. Acronyms change meaning with time and this could attract more participants to clinical trials but without understanding the associated health risks (Orlowski and Christensen 2002). Communities in Sub-Saharan Africa could participate in New HIV Prevention Technologies clinical trials to get small material rewards that fulfill an immediate physiological need at the expense of their future health (Newman et al. 2011).

ESTABLISHMENT OF RESEARCH ETHICS COMMITTEES (RECS) IN SUB-SAHARAN AFRICA

Before clinical trials begin, researchers should get ethical clearance from the National Research Ethics Committee or National Research Ethics Council (Pandey et al. 2011). Each country could have its own terminology with reference to a central authority that is responsible for research ethics in the country. Ideally, all clinical trials must be approved and monitored by an oversight body in order to minimise psychological and medical harm to participants (Chalmers 2011). Most of the countries in Sub-Saharan Africa do not seem to give priority to research ethics. Some countries in Africa do not have a national research ethics council. In situations where Research Ethics Committees could be in place in some of the countries, the committees might not be properly constituted or functional (Bayer et al. 2011). Some of the board members of the Research Ethics Committees might not have qualifications in bioethics and health law or related qualifications in ethics, health, law and human rights. It is common in Africa to find Research Ethics Committees that only appear on paper without corresponding structures on the ground. Such Research Ethics Committees are for window-dressing so that the countries get funding from international donor organisations that support medical research and clinical trials (Rwabihama et al. 2010). In most African countries, it is the Minister of Health who is consulted to give approval to research protocols from local and international organisations seeking permission to carry out clinical trials that involve human subjects in the country. Some politicians could advocate for the fast-tracking of clinical trials in New HIV Prevention Technologies in the country without proper medical advice in order to gain popularity and political mileage (Parker 2010). Medical research does not have to be rushed because it is a life-or-death matter. Research experimentation that involves human life or health should not be fast-tracked or hurried without following due ethical guidelines. The complications of obtaining ethics clearance differ from country to country (Dovey et al. 2011).

Some of the universities in Africa have Research Ethics Committees while others operate without. South Africa has a research ethics statutory body that gives direction to ethical issues in the country. This statutory body is the National Health Research Ethics Council (NHREC). Most of the universities in South Africa have a Research Ethics Committee that approves research protocols for students and

private research organisations. Some universities have Research Ethics Committees that provide consultancy in research ethics to the wider community (Nyika et al. 2009). For example, The South African Research Ethics Training Initiative (SARETI) is based at the University of Kwa Zulu Natal and the University of Pretoria while International Research Ethics Network for Southern Africa (IRENSA) operates from the University of Cape Town. The Training and Resources in Research Ethics Evaluation (TRREE) provides online training on biomedical research ethics and clinical trials in Africa (Nyika et al. 2009). Universities in Sub-Saharan Africa are consulted for advice on getting ethical clearance by international research groups seeking to carry out clinical trials in the region (Adebamowo et al. 2008).

Some African governments work with universities to come up with a regulatory body that oversees the ethical conduct of research organisations in the country (Adebamowo et al. 2008). It is not unusual to find that some of the Research Ethics Committees in Africa have no standard operating procedures on evaluating research protocols (Kass et al. 2007). The World Health Organisation observed that some Member States had no Research Ethics Committees even if they knew that clinical trials required a panel of experts to examine the feasibility and ethical compliance of the study before it commenced (Kaas et al. 2007). In this regard, the World Health Organisation has noted that some clinical trials are being carried out in some of the African countries without subjecting the research protocols to ethics review (Kass et al. 2007). A training needs analysis of the Research Ethics Committees in three African countries, Cameroon, Mali and Tanzania, showed that some of the members of the Research Ethics Committees had not received formal training on evaluating research protocols, which implied that they were not qualified to deal with ethics approval processes (Ateudjeu et al. 2010). It was recommended that the Research Ethics Committees in these countries needed capacity building training to make them functional and more effective (Ateudjeu et al. 2010). There is usually a conflict of interest among members of the Research Ethics Committee in most African universities and independent research ethics organisations. Members of the Research Ethics Committee, as researchers, could at times submit research proposals and budgets for funding to the same organisation that applied for permission to roll out the clinical trials (Kaas et al. 2007). Some academics, independent researchers, executives of private business organisations and top civil servants could form Independent Ethics Committees (IECs) thus running parallel structures that serve the same purpose as the National Health Research Ethics Council. This usually happens as a result of the frustration research organisations experience when they deal with institutional or government bureaucracy to obtain ethical approval for their intended research (Martyn 2003).

When there is a conflict of interest between the promotion of research ethics and financial gain among members of the Research Ethics Committee, there could be greater chances that ethical misconduct would not be reported. There are numerous medical ethics scandals and unprocedural clinical trials that involve organ transplant, blood samples, tissues, testing of new vaccines, syphilis research and HIV clinical trials reported in Africa and overseas (Hassam and Sole 2011; Dykes 2010). It is reported that poverty in Egypt pushed Egyptians to sell their organs (IRIN 2011). Some clinical trials could be conducted in remote hospitals and clinics run by private and charitable organisations in rural areas (Lorenzo et al. 2010). Medical doctors are paid for their service but it is the organ dealers who would know how much money they will make for selling the organs, for example, kidneys, to desperate patients or international organ traffickers on the black market. Patients, participants and general health workers at the institution might not know that they are involved in shady deals or suspect any wrongdoing because there are few government medical specialists in most of the state-run hospitals and clinics to give medical advice to the public in Sub-Saharan Africa. Such medical ethics breaches by international organisations might be sophisticated to be understood by government inspectors and other statutory bodies that promote medical ethics in the country (Lorenzo et al. 2010).

Some clinical trials target specific races and recommend specific medicines for those races. For example, clinical trials on the cure of syphilis targeted African-Americans as guinea pigs (Beckett 2011). Participants were not offered treatment during the clinical trials resulting in some dying (Beckett 2011). In Guatemala,

researchers from the US Public Health Service injected participants with gonorrhea and syphilis and offered no treatment so that they studied the progression of the diseases among patients housed at the Guatemalan Mental Health Hospital (Reverby 2011). Participants were encouraged by the researchers to infect others or sleep around if they chose to do so as if the disease did not pose health risks (Reverby 2011). Clinical trials on the drug BiDil that was developed to treat heart failure specifically targeted African-Americans as participants (Brody and Hunt 2006). The drug was recommended for use by African-Americans and not other races (Eckstein 2011). The problem with this type of research is that it results in race labelling or stigma. It is argued that the establishment of Institutional Review Boards (IRBs) could curb the use of race and ethnicity as a selection criterion for recruiting participants in medical research. The development of "race-based medicine" is discouraged in global health promotion although there are diseases that affect some races in particular (Eckstein 2011). Medicines should be associated with the diseases they cure and not race. It should be noted that in some cases where patients or participants were exposed to health risks, infection or death, governments and Principal Investigators attempted to cover up the scandal (Eckstein 2011). Some of the breakthroughs in medical research were achieved through scandalous procedures that were not ethically correct (Lederer 2005). In clinical trials, governments could violate participants' or patients' rights to decency, protection from harm and the right to life by recklessly sponsoring or approving high-risk or life-or-death clinical trials (Beckett 2011). The New HIV Prevention Technologies clinical trials in Sub-Saharan Africa are also shrouded in controversy.

NEW HIV PREVENTION TECHNOLOGIES CLINICAL TRIALS

The condom was the main health product that was used to prevent HIV infection over the last three decades before the introduction of New HIV Prevention Technologies. The condom is still used to prevent HIV infection. Presently, public donor funding for condom research has dropped. A larger portion of donor funds is now directed towards the development of New HIV Prevention Technologies (Peters et al. 2010). However, the new HIV prevention methods still use condoms in combination as it is argued by the researchers of New HIV Prevention Technologies that: "No single strategy or technology will be able to solve the AIDS epidemic" (Abdool Karim and Baxter 2010: 268). This study highlights the problems associated with the following New HIV Prevention Technologies in clinical trials: vaccines, microbicides, antiretroviral therapy, pre-exposure prophylaxis and medical male circumcision.

(a) Vaccines

Clinical trials involving vaccines to prevent HIV infection have been going on for the last twenty years with limited success (Abdool Karim and Baxter 2010). It was observed that: " ...The first trial of a vaccine designed to elicit strong cellular immunity has shown no protection against infection. More alarmingly, the vaccine appeared to increase the rate of HIV infection in individuals with prior immunity against the adenovirus vector used in the vaccine" (Sekaly 2008: 7). Furthermore, it was indicated that: "…Results of most of these studies have been disappointing and the development of an HIV vaccine remains elusive" (Abdool Karim and Baxter 2010: 269). For example, it is noted that: "Merck' s adenovirus serotype 5 (Ad5)-based vaccine candidate (MRKAD5), reached an advanced stage of testing in the USA and South Africa but the trials were prematurely stopped in 2007 after an interim analysis by the Data Safety Monitoring Board determined that the vaccine did not offer any protection against HIV infection or reduce viral load in individuals who acquired HIV infection" (Abdool Karim and Baxter 2010: 269). In addition, it was revealed that: "…Subsequent analyses suggest that the vaccine may have enhanced the risk of HIV infection especially in those with pre-existing immunity to the Adenovirus-5 vector" (Abdool Karim and Baxter 2010: 269). The results of a vaccine trial in Thailand (Thai RV144) that were released in 2009 received much world publicity about the efficacy of vaccines in preventing HIV infection among participants. The results showed that:" …vaccine recipients had a 31.2% lower rate of HIV infection than those receiving the placebo" (Abdool Karim and Baxter 2010: 269). Ideally, the vaccines should show a higher rate of HIV prevention. The risk-reduction percentage

should be closer to 100% safety because the research involves protection of human life.

While researchers could be preoccupied with the efficacy of the vaccines, it could be disastrous to deceive participants through the use of placebos in HIV prevention research. The placebo can be made to look like a real drug or it could be water that is given to participants without preventing HIV infection (Miller et al. 2005). The use placebos or deception in clinical trials is controversial because it defeats the purpose of building the doctor-patient relationship. Deception damages the trust between a doctor and a patient (Miller 2001). When participants discover in the end that they were deceived, they might not take the HIV infections that happen during clinical trials as accidental happenings. HIV infection during clinical trials could be construed as deliberate action by the researchers to do harm to the participants (Miller et al. 2005). The use of deception in clinical trials could bring about suspicion and undesirable consequences in Sub-Saharan Africa and Asia where most of the HIV clinical trials are conducted (Martin 2011).

(b) Microbicides

Microbicides are described as "…substances that are able to kill bacteria, viruses and/or parasites" (Abdool Karim and Baxter 2010: 275). They are reported to: "… reduce transmission of sexually transmitted infections, including HIV when applied to either the vagina or rectum" (Abdool Karim and Baxter 2010: 275). Microbicides are meant to protect women because six out of ten new HIV infections occur in women (Abdool Karim and Baxter 2010). It is argued that microbicides will empower women who: "…are unable to successfully negotiate mutual monogamy or male condom use" (Abdool Karim and Baxter 2010: 275). The unequal power relations between men and women in Sub-Saharan Africa can result in men coercing women to have unsafe sex with them (El-Bassel et al. 2011).

There are ongoing clinical trials in Sub-Saharan Africa that seek to develop microbicides into becoming one of the best drugs that can be relied upon in preventing HIV infection. It has been established that microbicides can: "…support normal vaginal defences, destroy surface active pathogens by disrupting membranes, inhibit pathogen entry into mucosal cells by creating a barrier between the pathogen and the vagina, prevent fusion between the membranes of the pathogens and mucosal cells and inhibit a virus from replicating once it has infected the cells that line the vaginal wall" (Abdool Karim and Baxter 2010: 276). For example, Buffergel maintains or mobilises normal vaginal defences while Benzalkonium chloride destroys surface active pathogens by disrupting membranes (Abdool Karim and Baxter 2010). Microbicide PRO2000 gel inhibits pathogen entry into mucosal cells and Maraviroc (CCR5 inhibitor) prevents fusion between the membranes of pathogens and mucosal cells (Abdool Karim and Baxter 2010). The drug UC-781 is a microbicide which inhibits post-fusion replication (Abdool Karim and Baxter 2010).

Microbicide clinical trials in Sub-Saharan Africa have been associated with negative consequences that warrant termination of the research unless safer and risk-free interventions were developed. In South Africa, some of the participants developed side- effects after using microbicide Nonoxynol-9. They developed genital lesions with increased viral loads associated with the lesions (Abdool Karim and Baxter 2010). Most of the clinical trials recruit sex workers as participants. It was reported in Phase 111 of the clinical trials that microbicide Carraguard ® was not effective in preventing male-to-female HIV transmission during vaginal intercourse (Abdool Karim and Baxter 2010). Nonoxynol-9 vaginal gel did not have a protective effect against HIV transmission among a group of sex workers on clinical trials (Abdool Karim and Baxter 2010). Frequent use of the microbicide was found to increase women's risk of HIV infection (Abdool Karim and Baxter 2010). Multiple use of the microbicide Nonoxynol-9 irritates the lining of the vagina (Abdool Karim and Baxter 2010). This could make the women more vulnerable to HIV infection (Abdool Karim and Baxter 2010). The use of Cellulose sulphate (Usher Cell) in HIV prevention clinical trials in Benin, South Africa, Uganda, and India was stopped in 2007 by the study's Independent Data Monitoring Committee (Abdool Karim and Baxter 2010). It was found that the microbicide did not protect women against sexual transmission of HIV and it could have contributed to an increased risk of HIV infection (Abdool Karim and Baxter 2010: 277). However, Buffergel and PRO

2000 showed better results but the microbicides only reduced HIV infection by 30% (Abdool Karim and Baxter 2010). The results were interpreted by clinical researchers as showing promise that: " …a microbicide gel can at least partially reduce a woman's risk of becoming infected with HIV" (Abdool Karim and Baxter 2010: 277). The problem still remains that a greater percentage of participants is more likely to be infected with HIV during clinical trials because the reduction rate is theoretically lower than the rate of exposure. Moreover, the results of clinical trial MDP 301, involving 9 389 women released in 2009 were disappointing in that the microbicide PRO 2000/5 gel failed to show a protective effect against HIV (Abdool Karim and Baxter 2010: 277). A press statement issued in December, 2009 by the Microbicide Development Programme (MDP) indicated that microbicide PRO2000 gel in Phase III of the clinical trials was proven to be ineffective in preventing HIV infection (Microbicide Development Programme 2009; Abdool Karim and Baxter 2010).

Despite these negative results, some private research organisations, non-governmental organisations and some governments in Sub-Saharan Africa are still conducting clinical trials using various types of microbicides in the hope of making a breakthrough in HIV prevention (Abdool Karim and Baxter 2010). The clinical trials that were based in Zambia, Uganda, and Tanzania began in 2005 and ended in 2009. This research endeavor was a partnership of sixteen African and European research institutions (Microbicide Development Programme 2009). Some pharmaceutical organisations are developing microbicide products such as gels, creams, suppositories, films, sponges, and vaginal rings that are given to participants in clinical trials (Abdool Karim and Baxter 2010). Some of the new microbicides that are being tested are Tenofovir gel, VivaGel and Dapivirine but they have not yet reached phases II and III of the clinical trials (Abdool Karim and Baxter 2010). The hope of using microbicides in HIV prevention is dampened by the following statement: "Many microbicidal products are in various stages of development but testing the efficacy and safety of microbicides takes many years and involves a number of carefully phased stages. A safe and effective microbicide is scientifically possible within the next five to seven years" (Abdool Karim and Baxter 2010: 278).

(c) Antiretroviral Therapy

Antiretroviral prophylaxis has proved to be effective in preventing HIV transmission (Abdool Karim and Baxter 2010). Antiretroviral drugs suppress HIV replication in people living with HIV. It has been found that low viral load in individuals living with HIV was associated with low HIV transmission rate among couples in Uganda (Abdool Karim and Baxter 2010). Discordant couple studies show that partners can prevent HIV infection by taking antiretroviral drugs (Anglemyer et al. 2011). Clinical trials are underway to assess the effectiveness of antiretroviral therapy in preventing heterosexual transmission of HIV in sero-discordant couples (Abdool Karim and Baxter 2010). In this case, antiretroviral therapy is used to prevent HIV transmission from the infected partner to the HIV-negative partner.

The problem of this approach to HIV prevention is that couples might not use condoms consistently once they are told that the partner living with HIV has a low viral load that might not endanger the other partner. The HIV-negative partner might not understand the logic of taking antiretroviral medicine when they are not HIV-positive thus resulting in non-adherence to safer sexual practices. People living with HIV might look for HIV- negative partners and give them the impression that antiretroviral therapy eliminates HIV transmission and yet it only reduces the viral load. In Sub-Saharan Africa, where most of the societies are patriarchal and male-dominated, women might have low negotiation skills for safer sex (Wandera et al. 2011). For example, the sexual behaviour of participants in a three-year clinical trial of antiretroviral therapy in Uganda showed that more women than men, engaged in unprotected sex (Wandera et al. 2011). The partner who was initially HIV-negative sometimes ends up being infected due to the belief that a reduction of the chances of HIV transmission is enough to prevent HIV infection (Wandera et al. 2011). Some individuals on antiretroviral treatment might not disclose their status to their partners due to the misconception that they would not infect their partners with HIV (Wandera et al. 2011). The argument of this paper is that although antiretroviral therapy is effective in reducing HIV transmission, partners should not be tempted to have unprotected sex under the illusion that risk sexual behaviour will not result in HIV infection.

(d) Pre-exposure Prophylaxis (PrEP)

Pre-exposure prophylaxis (PrEP) is an HIV prevention measure that involves taking one antiretroviral pill or a combination of antiretroviral drugs per day in order to lower the risk of infection among HIV-negative individuals (Dolgin 2011). This method of HIV prevention targets high risk groups. Prophylaxis refers to any medical or public health measure that is taken to prevent the occurrence of a disease. The idea behind prophylaxis in health promotion is that prevention is better than cure or treatment (Buchbinder and Liu 2011). At the moment, major HIV research donors are torn between increasing funding for HIV prevention or allocating more resources for the treatment of HIV and AIDS (Nguyen et al. 2011). Pre-exposure prophylaxis was found to reduce HIV infection by 44% in clinical trials that had men who have sex with men as participants (Dolgin 2011). Even though pre-exposure prophylaxis reduced HIV infection in most-at-risk populations during clinical trials, some of the participants were infected with HIV (Dolgin 2011). In Sub-Saharan Africa, results from phase II safety trial conducted in Ghana, Cameroon, and Nigeria have shown reduced toxicity among participants but the technology has not yet shown positive results in phase III of the clinical trials (Abdool Karim and Baxter 2010). This HIV prevention procedure exposes participants to HIV infection (Celentano et al. 2010).

The problem with pre-exposure prophylaxis is that it recruits HIV-negative participants to the clinical trials. It targets high-risk groups such as sex workers, intravenous drug users, men who have sex with men and people who are at risk of HIV infection (Dolgin 2011). The ethical concern is that healthy people are attracted to the clinical trials and some of the participants become infected as a result of participating in the study. Most of the clinical trials for other diseases target people living with the medical condition or disease as participants and such individuals normally volunteer to be participants in the hope that a cure could be found to treat them. Even if a cure is not found, they are less likely to blame organisers of the clinical trials because such participants would accept that they contracted the disease before they participated in the research.

(e) Medical Male Circumcision

Of all the New HIV Prevention Technologies, medical male circumcision is the only one that is reported to reduce HIV infection by 50% up to 60% (Celentano et al. 2010; Abdool Karim and Baxter 2010). Clinical trials for medical male circumcision target countries or regions of countries where the prevalence of circumcision is low and HIV prevalence is high. The World Health Organisation states in the Executive Summary of a paper on circumcision that: "Priority countries for the scale-up of male circumcision for HIV prevention have high HIV prevalence and low levels of male circumcision (World Health Organisation 2009: 2). The position of the World Health Organisation is that: "In general, the countries and communities where traditional male circumcision is performed are not those with high HIV prevalence and low levels of male circumcision" (World Health Organisation 2009: 2). Most of the cited clinical studies about the effectiveness of medical male circumcision in HIV prevention were carried out in Kenya, South Africa and Uganda (World Health Organisation 2009; Herman et al. 2011).

The reason why researchers in Sub-Saharan Africa should have reservations about rolling out circumcision as an HIV prevention method is that circumcision is not a new concept in Africa (World Health Organisation 2009). It has been shown that medical male circumcision does not protect women or transgender men from HIV infection (World Health Organisation 2009; Abdool Karim and Baxter 2010). Even if it was proven scientifically that medical male circumcision can reduce HIV infection; the exposure to infection is still too high to warrant certification of the technology as an effective HIV prevention method (Senel et al. 2011). Partial protection makes participants uneasy about their safety and protection from harm in clinical trials (Newman et al. 2011).

All the New HIV Prevention Technologies highlighted in this study require participants in clinical trials to use condoms. The reduction in HIV infection could be attributed to the effectiveness of condoms since condoms have an HIV prevention rate that is closer to 100%; that is, from 90% and above (Hearst and Chen 2004). Manufacturers of condoms do not develop their products in a way that accommodates New HIV Prevention Technologies. It is

not appropriate for developers of New HIV Prevention Technologies to base the efficacy of their products on condoms. New HIV Prevention Technologies should be able to prevent HIV infection without condoms (Gwandure 2011). In case of failure, developers of New HIV Prevention Technologies could deny responsibility and blame condom manufacturers or blame participants for inconsistent use or any other reason to avoid taking responsibility for HIV infection. The promoters of New HIV Prevention Technologies should be able to report product performance, weaknesses, failure and consequences. It is now evident that New HIV Prevention Technologies clinical trials are also contributing to the rise in HIV infections and numbers of people living with AIDS. There is evidence that in most of the research sites in Sub-Saharan Africa there are participants who get infected with HIV and some develop AIDS due to non-availability or inadequacy of antiretroviral treatment.

COMPENSATION FOR HIV SERO CONVERSION DURING CLINICAL TRIALS

Individuals who choose to participate in clinical trials are given information about the research procedures before they volunteer to participate (Omosa-Manyonyi et al. 2011). HIV is incurable hence prospective participants should be informed that they will leave the clinical trials being HIV-negative or HIV-positive. Promoters of New HIV Prevention Technologies debrief participants about what is involved but provide little information on monetary compensation for medical injury (Gwandure 2011). Mostly, participants are told that should they get infected with HIV, they will receive antiretroviral treatment and that should HIV infection happens it should be treated like any other unfortunate happening such as occupational injury. Individuals and communities in Sub-Saharan Africa generally respect medical professionals and the service they provide without having doubts about the safety of the procedure (Riley 2010). In New HIV Prevention Technologies participants in Sub-Saharan Africa are less likely to suspect that they could be infected with HIV during clinical trials because medical doctors have always been associated with helping people (Kent et al. 2004). It is argued in this study that monetary compensation should be pursued in cases of seroconversion during clinical trials.

It is not fair to ask infected participants to look for treatment on their own and queue with others at public hospitals that sometimes run out of antiretroviral drugs (Barsdorf et al. 2010; Kulkarni et al. 2011). It is a human right to access medical care when sick. Some organisations running the clinical trials provide first help to infected participants while others advise participants to look for treatment elsewhere (Barsdorf et al. 2010). Some of the participants in rural areas and low income groups fall sick and die as a result of failure to get antiretroviral therapy. The project leaders of clinical trials should take care of sick participants considering that they volunteered to participate as healthy and uninfected individuals.

There should be health insurance to compensate participants in monetary terms. Project leaders of clinical trials should be accountable and transparent enough to report the number of participants who contract HIV on a monthly, biannual and annual basis at each site of the clinical trials so that the public and participants are kept abreast of their safety in the clinical trials (Kent et al. 2004; Roujeau and Le Pallec 2011). Countries in Sub-Saharan Africa should pass legislation that asks Principal Investigators to disclose casualties to the public (Newman et al. 2011). Participants infected in clinical trials should be invited to share their experiences with the public on national television, radio and the print media so that prospective participants can join clinical trials fully informed of what happened to other participants before. It is standard procedure in many developed countries for patients and participants to litigate for medical injury compensation during clinical trials (Davis et al. 2002). The position of this paper is that there should be medical and monetary legislation on compensation for HIV infection during clinical trials in Sub-Saharan Africa. Countries in Sub-Saharan Africa in which clinical trials are conducted should ask research organisations and their Principal Investigators to provide evidence of ability to pay for HIV infection compensation and post-exposure care during clinical trials. Governments in Sub-Saharan Africa should take the lead in promoting civil societies, local human rights organisations and legal entities that work for the protection, compensation and treatment of participants in HIV clinical trials (Norton-Griffiths 2010).

CONCLUSION

Even though there is evidence that some countries in Sub-Saharan Africa have oversight committees that are put in place to approve research protocols, monitor the conduct of clinical trials and evaluate the progress made in clinical trials, it is apparent that these committees need to be more functional and visible in controlling HIV infection in clinical trials. Although ground-breaking findings are reported about the reduction of HIV transmission in clinical trials, it is disappointing to note that the results show a low HIV prevention rate among participants in clinical trials. It is also worrying that New HIV Prevention Technologies clinical trials invite people who are HIV-negative to participate in research activities that result in some of the participants being infected with HIV. The media and non-governmental organisations that support New HIV Prevention Technologies tend to exaggerate their efficacy in HIV prevention and hardly report of failures, infections and human suffering due to seroconversion in clinical trials. Even though medical male circumcision is reported to show better results as compared to the other New HIV Prevention Technologies, it can cause medical complications that will require participants to be on medical cover or health insurance to cater for medical costs associated operation complications such as excessive bleeding, infection, and wound-healing. It is advised in this study that countries in Sub-Saharan Africa with ongoing New HIV Prevention Technologies clinical trials should challenge their Research Ethics Committees (RECs), Institutional Review Boards (IRBs), Independent Ethics Committees (IECs), Ethical Review Boards (ERBs) and Data and Safety Monitoring Boards (DSMBs) to review their roles and achievements made so far in protecting their participants from HIV infection since the beginning of the clinical trials.

REFERENCES

Abdool Karim SS, Baxter C 2010. New prevention strategies under development and investigation. In: SS Abdool Karim, Q Abdool Karim (Eds.): *HIV/AIDS in South Africa*. Cape Town: Cambridge University Press, pp. 268-282.

Adebamowo CA, Mate MA, Yakubu AA, Adekeye JM, Jiya JY 2008. Developing Ethical Oversight of Research in Developing Countries: A Case Study of Nigeria. *Paper presented at the Ethics for Public Health Research in Africa in Abuja, Nigeria,* April 21 to 23, 2008.

Anglemyer A, Rutherford GW, Egger M, Siegfried N 2011. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Cochraine Database of Systematic Reviews (in press).*

Ashcroft RE 2011. Personal financial incentives in health promotion: Where do they fit in an ethic of autonomy. *Health Expectations,* 14:191-200.

Ateudjeu J, Williams J, Hirtle M, Baume C, Ikingura J, Niare A, Sprumont D 2010. Training needs, assessment in research ethics evaluation among research ethics committee members in three African countries: Cameroon, Malawi and Tanzania. *Developing World Bioethics,* 10: 88-98.

Barsdorf N, Maman S, Kass N, Slack C 2010. Access to treatment in HIV prevention trials: Perspectives from a South African community. *Developing World Bioethics,*10: 78-87.

Bateman C 2011. HIV prevalence in Zimbabwe dropping like a stone. *South African Medical Journal,* 101:10-11.

Bayer R, Greco DB, Ramachandran R 2011. The ethics of clinical and epidemiological research. *The International Journal of Tuberculosis and Lung Disease,* 15: 525-529.

Beckett J 2011. Elaine scarry. Rule of law, misrule of men. *Administrative Theory and Praxis,* 33: 149-153.

Brody H, Hunt 2006. Assessing a race-based pharmaceutical. *Annals of Family Medicine,* 4: 556-560.

Buchbinder SP, Liu A 2011. Pre-exposure prophylaxis and the promise of combination prevention approaches. *AIDS and Behaviour,* 15: 72-79.

Chalmers D 2011. Are the research ethics committees working in the best interests of participants in an increasingly globalised research environment? *Journal of Internal Medicine,* 269: 392-395.

Chaudhuri S, Mackintosh M, Mujinja PGM 2010. Indian generic producers, access to essential medicines and local production in Africa: An argument with reference to Tanzania. *European Journal of Development Research,* 22:451-468.

Celentano DD, Davis WW, Beyrer C 2010. Biomedical prevention: What is the current status? *Asian Biomedicine,* 4: 679-682.

Cohen J 2004. Allegations raise fears of backlash against AIDS prevention strategy. *Science,* 306: 2168-2169.

Cohen J 2008. Where have all the dollars gone? *Science,* 321: 520-520.

Cohen J 2010. New HIV infections drop but treatment demands rise. *Science,* 330: 1301-1301.

Davis P, Lay-Yee R, Fitzjohn J, Hider P, Briant R, Schug S 2002. Compensation for medical injury in New Zealand: Does "no-fault" increase the level of claims making and reduce social and clinical selectivity? *Journal of Health Politics, Policy and Law,* 27: 833-854.

Dolgin E 2011. Trial success spurs planning for rollout of HIV prevention pills. *Nature Medicine,* 17: 392-392.

Dovey S, Katherine H, Makeham M, Rosser W, Kuzel A, Van Weel C, Esmail A, Phillips R 2011. Seeking ethical approval for an international study in primary care patient safety. *British Journal of General Practice,* 61: 197-204.

Dykes BM 2010. US Apologises to Guatemalans for Secret STD Experiments. The Upshot, October 1, 2010. From< http://news.yahoo.com/guatemalans-secret std-experiments.html.> (Retrieved November 21, 2011).

Eckstein L 2011. Beyond racial and ethnic analyses of clinical research. A proposed model for institutional review boards. *Food and Drug Law Journal,* 66: 243-263.

El-Bassel N, Gilbert L, Witte S, Wu E, Chang M 2011. Intimate partner violence and HIV among drug-involved women: Contexts linking these two epidemics-challenges and implications for prevention and treatment. *Substance Use and Misuse,* 46: 295-306.

Elmasri M 2011. Mental health beyond the crises. *Bulletin of the World Health Organisation,* 89: 326-327.

Emmanuel EJ, Currie XE, Herman A 2005. Undue inducement in clinical research in developing countries: Is it a worry? *The Lancet,* 366: 336-340.

Esser DE, Bench KK 2011. Does global health funding respond to recipients needs? Comparing public and private donors' allocations in 2005-2007. *World Development.* (In press).

Ghosh A, Kharas H 2011. *The Money Trail: Ranking Donor Transparency in Foreign Aid.*Washington DC: Brookings Institution.

Graboyes M 2010. Fines, orders, fears…and consent? Medical research in East Africa, C. 1950s. *Developing World Bioethics,* 10: 34-41.

Gwandure C 2011. The ethical concerns of using medical male circumcision in HIV prevention in Sub-Saharan Africa. *South African Journal of Bioethics and Law. In press*

Hassan F, Sole S 2011. Kidneygate: What the Netcare Bosses Really Knew. *Mail and Guardian,* April 29, 2011.

Hearst N, Chen S 2004. Condom promotion for AIDS prevention in the developing world: Is it working? *Studies in Family Planning,* 35: 39-47.

Herman-Roloff A, Llewellyn E, Obiero W, Agot K, Ndinya-Achola J, Muraguri N, Bailey RC 2011. Implementing voluntary medical male circumcision for HIV prevention in Nyanza Province, Kenya: Lessons learned during the first year. *PLOS ONE,* 6: 18299-18299.

Islam MR, Sharmin K 2011. Social exclusion in non-governmental organisations' (NGOs) development activities in Bangladesh. *Sociology of Mind,* 2: 36-44.

IRIN 2011. *Poverty Pushes Poor Egyptians to Sell Their Organs.* Geneva: UN Office for the Co-ordination of Humanitarian Affairs.

Kass NE, Hyder AA, Ajuwon A, Appiah-Poku J, Barsdorf N, Elsayed DE, Mokhachane M, Mupenda B, Ndebele P, Ndossi G, Sikateyo B, Tangwa G, Tindana P 2007. The structure and function of research ethics committees in Africa: A case study. *PLOS Medicine,* 4: 3-3.

Kent DM, Mwamburi DM, Bennish M, Kupelnick B, Ioannidis JPA 2004. Clinical trials in sub-Saharan Africa and establishment standards of care: A systematic review of HIV, tuberculosis and malaria trials. *JAMA,* 292:237-242.

Khan FR, Westhood R, Boje D 2010. "I feel like a foreign agent": NGOs and corporate social responsibility interventions into Third World child labour. *Human Relations,* 63: 1417-1438.

Klabunde CN, Keating NL, Potosky AL, Ambs, A, He Y, Hornbrook ML, Ganz PA 2011. A population-based assessment of specialty physician involvement in cancer clinical trials. *Journal of the National Cancer Institute,* 103: 384-397.

Kukarni H, Okulicz JF, Grandits G, Crum-Cianflone NF, Landrum ML, Hale B, Wortman G, Tramont E, Polis M, Dolan M, Lifson AR, Agan BK, Ahuja SK, Marconi VC 2011. Early post seroconversion CD4 cell counts independently predict CD4 cell count recovery in HIV-1-positive subjects receiving antiretroviral therapy. *JAIDS,* (in press).

Lederer S 2005. Experimentation on human beings. *Organisations of American Historians: Magazine of History,* 19: 20-22.

Lorenzo C, Garrafa V, Solbakk, JH, Vidal S 2010. Hidden risks associated with clinical trials in developing countries. *Journal of Medical Ethics,* 36: 111-115.

Martin P 2011. Part 1: Long after Tuskegee, Blacks still Leary of Clinical Trials. From<http://health-equity.pitt.edu/2669/> (Retrieved November 21, 2011).

Martyn C 2003. The ethical bureaucracy. *QJM: An International Journal of Medicine,* 96: 323-324.

McMahon JM, Morrow KM, Weeks M, Morrison-Beedy D, Coyle A 2011. Vaginal microbicides and HIV risk. *Journal of the Association of Nurses in AIDS Care,* 22: 9-16.

Microbicide Development Programme 2009. HIV 'Prevention' Gel PRO 2000 Proven Ineffective.From<http://www. healthandwelfare. idaho.gov/LinkClick. asp?fileticket= BVpbUi JUEtE% 3D&tabid=390&mid=2960> (Retrieved November 21, 2011).

Miller FH 2001. Trusting doctors: Tricky business when it comes to clinical research. *Boston University Law Review,* 81: 423-444.

Miller FG, Wendler D, Swartzman LC 2005. Deception in research on the placebo effect. *PLOS Medicine,* 2: 262-262.

Morfit NS 2011. "AIDS is money": How donor preferences reconfigure local realities. *World Development,* 39: 64-76.

Muennig P, Su C 2011. The politics of global aid. In: R Parker, M Sommer (Eds.): *Routledge Handbook in Global Public Health*. New York: Routldege, pp.282-290.

Newman PA, Yim S, Daley A, Walliser R, Halpenny R, Cunningham W, Louffy M 2011. "Once bitten twice shy": Participant perspectives in the aftermath of early HIV vaccine trial termination. *Vaccine,* 29: 451-458.

Nguyen VK, Bajos N, Dubois-Arber F, O'Malley J, Pirkle C 2011. Remedicalizing an epidemic: From HIV treatment as prevention to HIV treatment is prevention. *AIDS,* 25: 291-293.

Norton-Griffiths M 2010. The growing involvement of foreign NGOs in setting policy agendas and political decision-making in Africa. *Economic Affairs,* 30: 29-34.

Nuffield Council on Bioethics 1999. *The Ethics of Clinical Research in Developing Countries*. London: Nuffield Council on Bioethics.

Nyika A, Kilama W, Chilengi R, Tangwa G, Tindana P, Ndebele P, Ikingura J 2009. Composition, training needs and independence of ethics review committees acrossAfrica: Are the gate-keepers rising to the emerging challenges. *Journal of Medical Ethics*, 35, 189-193.

Omosa-Manyonyi GS, Jaoko W, Onzala O, Ogutu H, Wakasiaka S, Malogo R, Nyange J, Njuguna P, Ndinya-Achola J, Bhatt K, Farah B, Oyaro M, Schmidt C, Priddy F, Fast P 2011. Reasons for ineligibility in phase 1 and 2A HIV vaccine clinical trials at Kenya AIDS vaccine (KAVI), Kenya. *PLOS ONE*, 14580-14580.

Orlowski JP, Christensen JA 2002. Potentially coercive nature of some clinical research trials acronyms. *Chest*, 121: 2023-2028.

Pandey A, Aggarwal A, Seth SD, Maulik M, Juneja A 2011. Strengthening ethics in research. *International Journal of Medical Research*, 133:339-340.

Parker R, Sommer M 2011. *Routledge Handbook in Global Public Health*. New York: Routledge

Parker F 2010. Fast-track Anti-HIV Gel, Says Minister. From < http://mg.co.za/article/2010-07-23-fast-track-antihiv-gel-says-minister> (Retrieved November 21, 2011).

Peters AJTP, Scharf MM, van Driel FTM, Hansen WHM 2010. Where does public funding for HIV prevention go to? The case of condoms versus microbicides and vaccines. *Globalization and Health*, 6, 23-23.

Pillay V, Mahlati P 2008. Health workers' salaries and incomes in sub-Saharan Africa. *The Lancet*, 371: 632-634.

Reverby SM 2011. "Normal exposure" and inoculation syphilis: A PHS "Tuskegee" doctor in Guatemala, 1946-1948. *Journal of Policy History*, 23: 6-28.

Riley V 2010. Women and HIV: Ethics and laws. *Clinical Risk*, 16:25-29.

Roujeau JC, Le Pallec S 2011. Who should support the costs of severe adverse drug reactions? *Therapeutic Advances in Drug Safety*, 2: 5-8.

Rwabihama JP, Girre C, Duquest AM 2010. Ethics committees for biomedical research in some African emerging countries: Which establishment for which independence? A comparison with the USA and Canada. *Journal of Medical Ethics*, 36: 243-249.

Sekaly RP 2008. The failed HIV Merck vaccine study: A step back or a launching point for future vaccine development. *JEM*, 205:7-12.

Senel FM 2011. Mass circumcision with a novel plastic clamp technique. *Urology*, (in press).

Thairu L, Katzenstein D, Israelski D 2011. Operational challenges in delivering CD4 diagnostics in Sub-Saharan Africa. *AIDS Care*, (in press).

Tuomi K 2011. The role of the investment climate and tax incentives in foreign direct investment decision: Evidence from South Africa. *Journal of African Business*, 12:133-147.

Usher AD 2010. Donors lose faith in Zambia Health Ministry. *The Lancet*, 376, 403-404.

Wainberg MA 2011. AIDS: Drugs that prevent HIV infection. *Nature*, 469:306-307.

Wandera B, Kamya MR, Castelnuovo B, Kiragga A, Kambugu A, Wanyama JN, Easterbrook P, Sethi AK 2011. Sexual behaviours over a 3-year period among individual with advanced HIV/AIDS receiving antiretroviral therapy in an urban HIV clinic in Kampala, Uganda. *JAIDS*, 57: 62-68.

White R, Chileshe M, Dawson L, Donnell D, Hillier S, Morar N, Noguchi L, Dixon D 2011.Fostering community understanding of sufficient benefit and early stopping for a phase 2B HIV prevention clinical trial in Africa. *Clinical Trials*, 8: 103-111.

World Health Organisation 2009. *Traditional male circumcision among young people: A public health perspective in the context of HIV prevention*. Geneva: Author.