Sacrificing the Poor to Heal the Wealthy

The Reality of Clinical Trials Conducted in Sub-Saharan Africa

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Herman Shaw was a young humble man who lived on a small plot of land and took pride in farming from dusk till dawn to provide for his wife and two kids. When he decided the family needed a new house, he built it himself, hammering away until four or five in the early mornings[1]. Thus, the day he heard about the announcements made in local churches and cotton fields about an opportunity to receive free medical care, he thought it was a reward from God. Herman, along with several of his friends and neighbors, showed up early at the church where the doctors from the U.S. Public Health Service were going to present the program to hundreds of excited men - men who were unaware that the "free medical examination" was a study designed to follow the effect of untreated syphilis in black men, men who were unaware of the high price that would be paid over the next forty years, men who were never told that they had syphilis, a sexually transmitted disease that they were passing to their wives and future children. Throughout this time, Herman did not know why some of his friends were developing sores, while many others were suffering from bone deformities and dying of heart failures and various infections. Even as some men went blind and insane from advanced (tertiary) syphilis, the government doctors withheld treatment, remaining committed to observing their subjects to the study's predetermined "end point": autopsy[2]. To ensure that the families would agree to autopsies, the doctors offered burial allowances and gave them a free meal once a year. This was half a century ago; perhaps we can call it history.

Unfortunately, the racial mythology, the medical exploitation of black bodies for profit, and even the instances of medical sadism that threatened African-Americans in the past, have been exported to Africa[3]. On May 16, 1997, President Clinton stood a few feet away from the last five survivors of the Tuskegee Syphilis Study and made a heart-wrenching apology on behalf of the nation, admitting the injustices that had been committed. In President Clinton's own words, "it was a time when our nation failed to live up to its ideals, when our nation broke the trust… did something that was wrong, deeply, profoundly, morally wrong" [4]. This speech and the work that followed set forth basic ethical principles for medical research involving human subjects, such as the requirement that each subject must give informed consent before participating in an experiment. Undoubtedly, the adoption of informed consent regulations was a critical development. However, in practice, informed consent does not effectively address the needs of research participants who are relatively powerless, such as those who originate from disadvantaged communities, are enduring severe poverty, have limited formal schooling, and lack access to health services to begin with.

For the most part, this description fits research that is being conducted in sub-Saharan countries, where current scientists and scholars from Western institutions have now moved the physical setting of numerous therapeutic studies on vaccines, drugs, or medical devices for the treatment of a disease. In many "developing" countries in sub-Saharan Africa, the heavy burden of disease is combined with a lack of adequate access to healthcare. Institutions in these countries often lack the resources to fund and carry out extensive biomedical research and limited resources are spent mainly on primary health care. This situation leaves a space in which these institutions rely heavily on research sponsored by "developed" countries. The pace of biomedical research is particularly fast in southern Africa, where research ethics capacity is reportedly in danger of falling behind the pace of research activities [5]. Considering this, it is patently clear that there exists an endless possibility for the exploitation of economically disadvantaged minorities in medical research studies. While the concept of informed consent has its advantages in confirming voluntary participation, it does not account for the majority of participants who live in impoverished settings with limited education and support systems, and hence do not have the option to make fully autonomous and non-coerced decisions.

The Controversy of Informed Consent

In the recent discourse around informed consent, biomedical investigations conducted by researchers from "developed' countries in "developing" countries has been, and still is, a topic of significant controversy in regard to medical ethics. On the one hand, as stated by the Code of Medical Ethics of the American Medical Association, the principle objective of the medical profession is to render service to humanity with full respect for the dignity of man [6]. In other words, physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion. On the other hand, some argue that once a promising drug is identified, it is of utmost importance that it goes through clinical trials (i.e. stringent testing on human volunteers). In the modern world, this involves informed consent, a legal requirement and a fundamental part of medical ethics that ensures that the participation of subjects in the study is in fact entirely voluntary. According to the standards set forth by the World Health Organization (WHO) and National Institute of Health (NIH), informed consent involves educating subjects about: their own rights, the purpose of the study, the procedures to be undertaken, potential risks and benefits of participation, the expected duration of study, and the extent of confidentiality for personal identification and demographic data [7]. The remainder of this paper will delve deeper into the prioritization, relevance, application, and consequences of informed consent. Furthermore, this paper aims to provide an introductory evaluation of whether or not most research subjects living rural and impoverished areas in sub-Saharan nations really have the option and ability to refuse participating in research studies.

Although human experimentation in health research has been in existence for centuries [8], organized efforts to protect human subjects participating in experiments are relatively recent, beginning only in 1947, when the Nuremberg Code banned forced experiments on humans. The origin of consent and malpractice can be traced to a 1767 court case in England where a surgeon was found guilty of using a new instrument without the patient's consent [9]. In this case, the mutual trust between patient and physician, wherein the patient is fully knowledgeable about and consents to the procedures in which they are participating, was broken. One important ethical implication of lack of informed consent in resource poor areas as explained in The Journal of Infectious Diseases, is that there are greater risks to and opportunities for exploitation of communities in "developing" countries, while most of the benefits of the studies may accrue only to people in "developed" countries [10].

Challenges to Obtaining Informed Consent in Sub-Saharan Africa

Despite this, sub-Saharan African nations host countless studies by Western researchers, scientists, and pharmaceutical companies, who clearly see the exigency of doing clinical research in a fairly unregulated and uncompetitive environment. Between 2002 and 2008, the number of U.S. Food and Drug Administration–regulated investigators carrying out biomedical research outside the USA increased by 15% annually, while the number of U.S.-based researchers declined by 5.5% [11]. Just a decade ago, in 2006, research funded by the U.K. Medical Research Council and Rockefeller Foundation conducted an open, randomized Development of Anti-Retroviral Therapy (DART) trial by recruiting 3,300 volunteers in Kampala, Uganda. SOMO, a scientific magazine, later exposed the research: revealing that the study had enrolled patients desperate to get free treatment, had insufficient arrangements for post-trial treatment access, used a drug regimen that is not readily available to the general population, and omitted important risks in the consent forms (9). Once the researchers were forced to switch to acceptable therapy, the situation of the participants deteriorated and some of the patients died during the interruption period. This was because a significant portion of HIV-infected participants were at risk of an undetected mutation that was a result of taking the experimental drug, and these patients developed antiretroviral resistance that compromised their second-line therapy options. These findings have important implications for the broader domain of targeted participants who are struggling to put food on their table and a roof over their heads, making "choice" a tricky concept and "voluntary participation" a potential slippery slope.

In addition to lack of resources, differences in language proficiencies and literacy levels make the process of acquiring informed consent in sub-Saharan Africa even more complicated. To begin with, issues involving communication are the most frequent

root causes of serious adverse events [13]; even after signing a consent form, subjects typically do not understand the risks, benefits and alternatives involved in an experiment. In 2005, Family Health International ran a clinical trial in Cameroon funded by the Bill and Melinda Gates Foundation involving 400 participants, mostly sex workers, who were at high risk of becoming infected with HIV. Before the study was suspended, five women became HIV-infected while enrolled, and NGOs claim that the subjects were not adequately informed about the risks and that only English information was given to mostly French-speaking volunteers. The study's end highlights how certain (and often incorrectly assumed) language comprehension is necessary to understand and complete most consent forms that are required for participation in clinical research studies [14]. It is unreasonable to have a formally uneducated study participant sign a lengthy consent form that they are unable to read, let alone comprehend. Going to even further conservative measures, one could even claim that no matter how extensively researchers verbally explain the details and essence of a particular study, it is virtually impossible for most formally uneducated participants to fully grasp the scientific concept of what is being presented to them and voluntarily join a clinical trial with complete informed consent.

Another factor that can affect the welfare of clinical trials is the culture, politics and socio-economic stability of the particular nation. For instance, recent research shows that participants in developing countries appear to be less likely than those in developed countries to say they can refuse participation in or withdraw from a trial, and are more likely to worry about the consequences of refusal or withdrawal [15]. There is evidence that the act of offering money for participating in human subject research studies can highly distort the judgment of destitute participants and compromise the voluntariness of their informed consent. A deeper analysis shows that the recent history of medical research in sub-Saharan Africa closely parallels that of African-Americans in the United States a few decades ago. As reported by the Berkeley Journal of International Law, sponsors of clinical research tend to search out the least expensive and least burdensome regulatory environment with the lowest liability exposure, in order to avoid litigation in the event of injury to participants [16].

In the book, Medical Apartheid: The Dark History of Medical Experimentation on Black Americans from Colonial Times to the Present, Harriet Washington writes about the cultural memory of medical experimentation, abuse, research and the complex relationship between racism and medicine. Washington claims that U.S. researchers who can no longer conduct trials at home without intense scrutiny from the FDA and the news media have moved their operations to sub-Saharan Africa to exploit the public-health vacuum that once condemned black Americans [17]. Consider the scandalous experiment piloted in 1996 by Pfizer, the world's largest research-based pharmaceutical company, which conducted an unregistered drug trial in Kano, Nigeria, during one of the nation's worst meningitis epidemics. Pfizer came along with other international organizations such as Doctors without Borders "to assist and treat patients." The study immediately recruited two hundred children and conducted a clinical trial that involved ingesting one of three oral antibiotics: Trovan, Ceftriaxone or Chloramphenicol. Pfizer was sued after 11 children died within three weeks of the clinical trial and others developed conditions including brain damage, paralysis, and slurred speech. The allegations against Pfizer included:

1. Pfizer never obtained ethical clearance before conducting the study;

2. Pfizer did not obtain informed consent before recruiting participants and did not inform the study participants that the drug was an experimental drug;

3. Pfizer capitalized on the poor, illiterate, and desperate situation of the participants and their communities; and,

4. Pfizer left the town after conducting the study despite the fact that the epidemic was still ongoing [18].

Understandably, some may claim that, currently, clinical trials are firmly regulated and researchers attempt to comply with ethical requirements to the best of their ability while maintaining high scientific standards. In fact, some scholars might challenge this paper by insisting that as long as participants are accurately informed of the purpose, methods, risks, benefits, and alternatives to the research, they are able to understand the information and can make a voluntary decision about whether to participate or not. By focusing on the general definition of informed consent, such critics overlook the deeper

problem at hand, which is the fact that clinical trials have become a big business with the imperative of getting the work done as quickly as possible with minimal obstacles is prioritized [19]. The examples mentioned in the previous paragraphs of incidents in Uganda, Cameroon and Nigeria are current case studies that clearly illustrate the ethical challenges that may arise in conducting clinical trials in "developing" countries. Though I concede that clinical trials are extremely useful tools that are much needed to address the burden of disease and have yielded exciting results that have improved health care, I maintain that many studies that are done in sub-Saharan Africa could never be conducted in the countries sponsoring the work.

Future Directions

Despite the existence of international guidelines, standards, and protocols that govern biomedical researches, many gaps and challenges relating to ethical issues still need to be addressed to ensure a fair, transparent, and moral research processes. The first step is to create awareness about the grossly immoral injustices that are inflicted on the most vulnerable of populations. The difficulties in finding scientifically published unethical clinical trials, despite the numerous reports and research that are being conducted, suggests that we are aware of a small fraction of the number of abuses that occur as many go unreported. Domestically, there is a huge prospect for laws to be successfully applied and upheld to protect participants from persecution and exploitation in clinical trials. Eventually, we have to admit that it has come to a point where we, sub-Saharan Africans, need to take a stand and stop allowing this perpetuation of exploitation from continuing. The fact that only Malawi and South Africa contain a provision which makes specific reference to clinical research [20] is clear evidence that civilians and local governments need to work harder to uphold the guarantees of human right protections written on their constitutions.

The goal of clinical research is to develop information that improves human health and increases the understanding of life. In order to achieve this, researchers need to understand that the act of a participant signing a consent form does not necessarily equate granting full informed consent. Signing the form is only part of the process, the most important part being the conversation with the patient, which allows for informed consent. It is of utmost importance that the content of these trials is given to the potential participants in linguistically and culturally acceptable formats. This might mean something as simple as improving the presentation through the use of instructional graphics and accompanying videos, or something more complicated, such as involving local communities in establishing the criteria for recruiting participants, as well as determining the incentives for participation. Furthermore, research must begin with a clear plan for what will happen to the participants once the trial has ended. In order to accomplish these goals, we need to hold researchers to a higher standard of moral conscience and ensure that funding agencies are giving money to ethically sound research. Ultimately, while we need all the cures we can find for HIV, malaria, TB and countless other diseases, it is imperative that we conduct our clinical trials in a humane way.

The blood, sweat and tears of people like Herman Shaw has brought us to a time where there exists a law that any U.S. organization conducting federally funded research must have an institutional review board (IRB) to ensure compliance with federal regulations [21]. Despite their good intentions, even such guidelines have proved to be inadequate in ensuring the safety of human subjects. It is a shame that after all the extremely painful lessons we learnt from the Tuskegee Syphilis Study, we are still targeting populations who are defenseless to fight for their own interests against high-risk research. For some of us today, breakthroughs in medicine can no longer bring the joy and celebration they used to, as they remind us of the mandatory preface to such achievements, their commercialization, and how it has frequently brought pain to many families in sub-Saharan Africa. I challenge you to be part of the movement; As you close the lid of your laptop and walk towards your top drawer to grab riboflavin to deal with the aftereffects of a bright screen, to just take a moment and appreciate the shoulders of the unfortunate people it took to develop the drug. Perhaps then, there will be a spark of hope for a positive change.

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