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Research Article

The Ethics in Clinical Scientific Research: A Global Challenge in Public Health Dynamics in Low Resource Limited Countries

Estella Tembe Fokunang[1], Marceline Djuidje Ngounoue[2], Marie Therese Obama Ondoua[3] and Charles Fokunang[1]*

[1]Department of Pharmacotoxicology and Pharmacokinetic, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Cameroon

[2]Department of Biochemistry, Faculty of Science, University of Yaoundé 1<, Cameroon

[3]Department of Pediatrics, Faculty of Medicine and Biomedical Sciences, University of Yaounde 1, Cameroon

***Corresponding Author:** Charles Fokunang, Professor, Department of Pharmacotoxicology and Pharmacokinetic, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Cameroon.

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Abstract

The goal of clinical research is to develop generalizable knowledge that improves human health or enhances an understanding the human system. Volunteers who participate in clinical research facilitate the pooling of data that make it possible to secure an understanding of human biology/functioning. The odyssey a new drug or treatment for safety and efficacy, good quality is through clinical testing on patient volunteers. However, creating cohort with some volunteers on placebo with more risk of harm for the good of others is a big challenge demonstrates that clinical research has the potential to exploit patient volunteers. The ethical guidelines in place today were primarily a response to past abuses, the most notorious of which in America was an experiment in Tuskegee, Alabama, in which treatment was withheld from 400 African American men with syphilis so that scientists could study the course of the disease. Various ethical guidelines were developed in the 20th century in response to such studies. The purpose of this review is to exploit the ethical guidelines developed to protect patient volunteers and to preserve the integrity of the science in clinical research.

Keywords: Ethics; Clinical Research; Public Health

Introduction

The origin of clinical research

Modern clinical research may have begun on the 20th of May, 1747, aboard the HMS Salisbury. James Lind, the ship's surgeon, was concerned with the costs scurvy was affecting the British sailors, and was skeptical of some of the interventions, cider, elixir of vitriol, vinegar, sea-water, being used at the time to treat it. Unlike other clinicians of his day, Lind did not simply assume that he was correct and treat his patients accordingly [1,2]. He designed a study with a sample size of 12 sailors from among the 30 on the Salisbury's crew members who were suffering from scurvy, and divided them into six groups of 2 sailors per group. Lind assigned a

different intervention to each of the groups, including two sailors turned research participants who received 2 oranges and 1 lemon each day. Within a week these two were sailors again; the others remained patients, and several were dying [3].

The ethics of clinical research begins by asking how we should think about the fate of these latter sailors. Did Lind treat them appropriately? Do they have a moral claim against Lind? It is widely assumed that physicians should do what they think is best for the patient in front of them. Lind, despite being a physician, did not follow this maxim. He felt strongly that giving sea water to individuals with scurvy was a bad idea, but he gave sea water to 2 of the sailors in his study to test whether he, or others, were right. To put the fundamental concern raised by clinical research in its simplest form: Did Lind sacrifice these two sailors, patients under his care, for the benefit of others? Lind's experiments represent perhaps the first modern clinical trial because he attempted to address one of the primary challenges facing those who set out to evaluate medical treatments [4].

How does one show that any differences in the outcomes of the treatments under study are a result of the treatments themselves, and not a result of the patients who received them, or other differences in the patients' environment or diet? How could Lind be confident that the improvements in the two sailors were the result of the oranges and lemons, and not a result of the fact that he happened to give them to the two patients who occupied the most salutary rooms on the ship? Lind tried to address the challenge of confounding variables by beginning with patients who were as similar as possible [1,5]. He carefully chose the 12 subjects for his experiment from a much larger pool of ailing sailors; he also tried to ensure that all 12 received the same rations each day, apart from the treatments provided as part of his study. It is also worth noting that Lind's dramatic results were largely ignored for decades, leading to uncounted and unnecessary deaths, and highlighting the importance of combining clinical research with effective promulgation and implementation. The Royal Navy did not adopt citrus rations for another 50 years [6], at which point scurvy essentially disappeared from the Royal Navy.

Lind's experiments, despite controlling for a number of factors, did not exclude the possibility that his own choices of which sailors got which treatment influenced the results. More recent experiments, including the first modern randomized, placebo-controlled trial of Streptomycin for Tuberculosis (TB) in 1948 [7], attempt to address this concern by assigning treatments to patients using a random selection process. By randomly assigning patients to treatment groups these studies ushered in the modern era of controlled, clinical trials. And, by taking the choice of which treatment a given patient receives out of the hands of the treating clinician, these trials underscore and, some argue, exacerbate the ethical concerns raised by clinical research [8]. A foundational principle of clinical medicine is the importance of individual judgment. A physician who decides which treatments her patients receive by flipping a coin is guilty of malpractice. A clinical investigator who relies on the same methods receives awards and gets published in elite journals. One might conclude that sacrifice of the interests of some, often sick patients, for the benefit of future patients, is essentially mandated by the scientific method [9].

Clinical research landscape for resource limited settings

Clinical research in resource-limited settings (like much of Sub-Saharan Africa) presents unique ethical dilemmas. While offering critical health data and bringing medical interventions to marginalized populations, systemic inequalities risk participant exploitation. Navigating these challenges requires robust, culturally adapted safeguards to ensure health justice and protect autonomy [4,10].

Key Ethical Challenges in the regions include

Exploitation and Undue Influence: Severe poverty and lack of basic healthcare in host communities make participation highly attractive, potentially undermining voluntary, autonomous consent. Standard of Care Disparities: Debates persist regarding whether experimental trials should offer the "worldwide best" methods or a lower, locally accessible standard of care without compromising safety [11].

Power Imbalances: Power and resource asymmetries between high-income country sponsors/universities and local host institutions often dictate unequal funding and research agendas. To address these global health dynamics to safeguard the international and local regulatory bodies and frameworks there has been an implementation of a mandatory strict operational parameter: Research involving human subjects must align with International Directives like the World Medical Association's, Declaration of Helsinki and the International Ethical Guidelines for health-related research [12].

At the level of Local RECs, the Independent Research Ethics Committees are responsible for evaluating protocols to ensure participant risks are minimized and outweighed by social value to the host community. There is need to enforce Community Engagement by setting up Authentic community advisory boards help translate complicated scientific concepts into local languages and ensure research aligns with local cultural values and health priorities [2,13].

Local regulatory environment (Cameroon)

In Cameroon, clinical trials and the transfer of biological materials are governed by national regulations. Protocols must be approved by the [National Ethics Committee for Health Research (CNERSH)] to ensure compliance with good clinical practices and the protection of local populations. If you are exploring a specific research proposal or wish to understand the approval requirements, tell me:

- What is the primary medical field of your research (e.g., infectious diseases, maternal health)?
- Is this a multinational collaboration or an internationally sponsored trial?
- I can provide the specific regulatory steps and documentation needed to proceed ethically in this region.

Challenges of clinical research

Clinical research attempts to address public health, human biology issues that are straightforward, and some important challenges. Such challenges deals with how to determine whether one medical intervention is better than another, whether it offers greater clinical benefit and/or poses fewer risks [14]. Clinicians are constantly may one day be able to answer these questions by relying on computer models, thereby avoiding reliance on clinical research and the ethical concerns it raises. Until that day, clinical researchers begin by testing potential new medical interventions in the laboratory, and often in animals. While these methods can provide valuable information and, in the case of animal research, raise important ethical issues of their own, potential new interventions eventually must be tested in human beings. Interventions which work miracles in test tubes and in mice, often leave humans untouched, or worse off [9,15].

Ethical guidelines and regulation of clinical research have seen significant evolution based on some of the international influential codes of ethics and regulations that guide ethical clinical research such as; The: Nuremberg Code (1947), the Belmont Report (1979), U.S. Common Rule (1991, the Declaration of Helsinki (2000) and CIOMS (2002). Using these sources of guidance and others there seven main ethical principles that is considered for any clinical research to be ethical. This principles include; Social and clinical value, Scientific validity, Fair subject selection, Favorable risk-benefit ratio. Independent review, Informed consent and the Respect for potential and enrolled subjects [2,15].

Social and clinical value

Every clinical research study design is linked a specific research question. The answer to the questions will have a significant value for society or for present or future patients with a particular illness. An answer to the research question should be important or valuable enough to justify asking people to accept some risk or inconvenience for others. In other words, answers to the research question should contribute to scientific understanding of health or improve our ways of preventing, treating, or caring for people with a given disease. Only if society will gain useful knowledge which requires sharing results, both negative and positive can exposing human subjects to the risk and burden of research be justified [16,17].

Scientific validity

A study should be designed in a way that will get an understandable answer to the valuable research question. This includes considering whether the question researchers are asking is answerable, whether the research methods are valid and feasible, and whether the study is designed with a clear scientific objective and using accepted principles, methods, and reliable practices. It is also important that statistical plans be of sufficient power to definitively test the objective, for example, and for data analysis. Invalid research is unethical because it is a waste of resources and exposes people to risk for no purpose [18].

Fair subject selection

Who does the study need to include, to answer the question it is asking? The primary basis for recruiting and enrolling groups and individuals should be the scientific goals of the study — not vulnerability, privilege, or other factors unrelated to the purposes of the study. Consistent with the scientific purpose, people should be chosen in a way that minimizes risks and enhances benefits to indi-

viduals and society [11,19]. Groups and individuals who accept the risks and burdens of research should be in a position to enjoy its benefits, and those who may benefit should share some of the risks and burdens. Specific groups or individuals (for example, women or children) should not be excluded from the opportunity to participate in research without a good scientific reason or a particular susceptibility to risk [20].

Favorable risk-benefit ratio

Uncertainty about the degree of risks and benefits associated with a drug, device, or procedure being tested is inherent in clinical research otherwise there would be little point to doing the research. And by definition, there is more uncertainty about risks and benefits in early-phase research than in later research. Depending on the particulars of a study, research risks might be trivial or serious, might cause transient discomfort or long-term changes. Risks can be physical (death, disability, infection), psychological (depression, anxiety), economic (job loss), or social (for example, discrimination or stigma from participating in a certain trial). Has everything been done to minimize the risks and inconvenience to research subjects, to maximize the potential benefits, and to determine that the potential benefits to individuals and society are proportionate to, or outweigh, the risks? Research volunteers often receive some health services and benefits in the course of participating, yet the purpose of clinical research is not to provide health services [21,22].

Independent review

To minimize potential conflicts of interest and make sure a study is ethically acceptable before it even starts, an independent review panel with no vested interest in the particular study should review the proposal and ask important questions, including: Are those conducting the trial sufficiently free of bias? Is the study doing all it can to protect research volunteers? Has the trial been ethically designed and is the risk–benefit ratio favorable? In the United States, independent evaluation of research projects is done through granting agencies, local institutional review boards (IRBs), and data and safety monitoring boards. These groups also monitor a study while it is ongoing [6,24].

Informed consent

For research to be ethical, most agree that individuals should make their own decision about whether they want to participate or continue participating in research. This is done through a process of informed consent in which individuals (1) are accurately informed of the purpose, methods, risks, benefits, and alternatives to the research, (2) understand this information and how it relates to their own clinical situation or interests, and (3) make a voluntary decision about whether to participate [25].

There are exceptions to the need for informed consent from the individual — for example, in the case of a child, of an adult with severe Alzheimer's, of an adult unconscious by head trauma, or of someone with limited mental capacity. Ensuring that the individual's research participation is consistent with his or her values and interests usually entails empowering a proxy decision maker to decide about participation, usually based on what research decision the subject would have made, if doing so were possible [14].

Respect for potential and enrolled subjects

Individuals should be treated with respect from the time they are approached for possible participation in a study, even if they refuse enrollment in the study throughout their participation and after their participation ends. Those important respect should include.

Respect for privacy and confidentiality of their private information

- Respect of the right of volunteers to change their mind, to decide that the research does not match their interests, and to withdraw without penalty.
- The right to inform volunteers of new information that might emerge in the course of research, which might change their assessment of the risks and benefits of participating.
- The right to monitoring the welfare of participants, if they experience adverse reactions, untoward events, or changes in clinical status, ensuring appropriate treatment and, when necessary, removal from the study.
- The right to inform participants about the research outcome. Most researchers comply to ethical guidelines obligations by the ethics committees and IRBs by monitoring the volunteers' welfare and making sure they are well informed of the study. However, they are not always good at distributing the study results [26,27].

Ethical challenges in clinical research

Testing medical interventions in humans typically poses some risks to the participants, no matter how many laboratory and animal tests precede it. In this way, the process of collecting data through clinical trials to improve health and well-being inevitably exposes research participants to some risks for the benefit of future patients. This brings us to the central ethical challenge posed by clinical research: When is it ethically permissible to expose research participants to risks of harm for the benefit of others? The present entry focuses on this concern, and canvasses the most prominent attempts to address it. The present entry largely brackets the range of interesting and important ethical challenges that arise in the course of conducting clinical research:

How should a clinical research study be reviewed? Who may conduct it? What must potential participants understand to give valid consent? May it be conducted in countries that will not be able to afford the intervention being tested? Do investigators have any obligations to treat unrelated medical conditions in participants that they uncover during the course of their research?

One might attempt to address the central ethical challenge by limiting clinical research to the medical setting, offering experimental interventions to patients who want to try them. This approach, which has the virtue of evaluating interventions in the process of trying to help individual patients, makes sense for comparisons of two or more interventions that are widely accepted and already in clinical use [28,29]. In contrast, this approach poses enormous scientific and practical problems with respect to testing new drugs or interventions. On the practical side, who would be willing to manufacture a new drug or chemical entity, without knowing whether it works? What dose should be used? How often should the new drug be taken? More importantly, this approach might not yield reliable information as to whether the new treatment is useful or harmful until hundreds, perhaps thousands of people have received it [19,30].

Clinical research is designed to address these concerns by systematically assessing potential new treatments in a small number of individuals, including very sick ones, before offering them more widely. With our normal daily activities and challenges, we are predisposed to predictable and un predictable risks of harm. Despite the fact that these practices pervade our lives, there has been surprisingly little philosophical analysis of the conditions under which they are acceptable [31]. In addition to being of value in its own right, evaluation of the central ethical challenge posed by clinical research thus provides an opportunity to consider one of the more fundamental concerns in moral theory: when is it acceptable to expose some individuals to risks of harm? In order to understand the importance of ethics in clinical research we have to address and understand the concepts that is our interest of discussion.

Concept of clinical research

Human subjects research is concern with the study of humans and related illnesses, as opposed to animals and microorganisms. Clinical research refers to the subset of human volunteers' research that evaluates the impact interventions have on human beings with the goal of assessing whether they might help to improve human health and well-being [32,33]. The present study focuses on research that is designed to improve human health and well-being though the identification of better methods of treatment, cure or prevention of illness or disease. This focus is intended to address the question of whether research on improvement that might better our well-being by making us feel better than normal, allowing us to remember more or worry less, without treating, curing, or preventing illness or disease qualifies as clinical research [34].

It attempts to also answer the question of whether quality improvement and quality assurance studies qualify as clinical research. To briefly consider the type of research at the centre of this discussion, it is worth considering a hospital which proposes to evaluate the impact of checklists on the quality of patient care [35].

Half the nurses in the hospital are told to continue to provide care as usual; the other half are provided with a checklist and instructed to mechanically check off each item as they complete it when caring for their patients. The question of whether this activity constitutes clinical research is of theoretical interest as a means to clarifying the precise boundaries of the concept. Should we say that this is not clinical research because the checklist is used by the nurses, not administered to the patients? Or should we say this is clinical research because it involves the systematic testing of a hypothesis which is answered by collecting data on patient outcomes? The answer has significant practical implications, determining whether these activities must satisfy existing regulations for clinical research, including whether the clinicians need to obtain patients' informed consent before the nurses taking care of them can use the checklist. With the improvement of clinical medi-

cine than it was a century ago, there are still many diseases such as malaria, chronic diseases against which current clinical medicine offers an inadequate response. The social value of clinical research lies in its ability to collect information that might be useful for identifying improved methods to address these conditions [36,37]. Yet, it is the rare study which definitively establishes that a particular method is effective and safe for treating, curing or preventing some illness. The success of specific research studies more commonly lies in the gathering of information that, together with the results of many other studies, may yield these improvements. For example, prior to establishing the efficacy of a new treatment for a given condition, researchers typically need to identify the cause of the condition, possible mechanisms for treating it, a safe and effective dose, and ways of testing whether the drug alters the course of the disease. The process of testing potential new treatments can take 10–15 years, and is standardly divided into phases [38].

Phases of clinical trials study

Phase 0

Formalized phase 0 studies are a relatively recent phenomenon involving the testing of interventions and methods which might be used in later phase studies. A phase 0 study might be designed to determine the mechanism of action of a particular drug and evaluate different ways to administer it.

Phase 1

Phase 1 studies are the earliest tests of a new intervention and are conducted in small numbers of individuals. Phase 1 studies are designed to evaluate the pharmacokinetics and pharmacodynamics of new treatments, essentially evaluating how the drug influences the human body and how the human body influences the drug [39,40]. Phase 1 studies also evaluate the risks of the treatment and attempt to identify an appropriate dose to be used in subsequent phase 2 studies. Phase 1 studies pose risks and frequently offer little if any potential for clinical benefit to participants. As a result, a significant amount of the ethical concern over clinical research focuses on phase 1 studies.

If phase 1 testing is successful, potential new treatments go on to larger phase 2 studies which are designed to further assess risks and also to evaluate whether there is any evidence that the treatment might be beneficial.

Phase 2 and 3

Successful phase 2 studies are followed by phase 3 studies which involve hundreds, sometimes thousands of patients. Phase 3 studies are designed to provide a rigorous test of the efficacy of a treatment and frequently involve randomization of participants to the new treatment or a control, which might be the current treatment or a placebo.

Phase 4

Finally, post-marketing or phase 4 studies evaluate the use of interventions in clinical practice. The first three phases of clinical trials typically include purely research procedures, such as blood draws, imaging scans, or biopsies, that are included in the study to collect data regarding the treatment under study. Analysis of the central ethical challenge posed by clinical research thus focuses on three related risk-benefit profiles: (a) the risk-benefit profile of the interventions(s) under study; (b) the risk-benefit profile of the included research procedures; and (c) the risk-benefit profile of the study as a whole [41-43].

Clinical research which poses net risks raises important ethical concern. Net-risk studies raise concern that participants are being used as mere means to collect information to benefit future patients. Research procedures that pose net risks may seem to raise less concern when they are embedded within a study which offers a favorable risk-benefit profile overall. Yet, since these procedures pose net risks, and since the investigators could provide participants with the new potential treatment alone, they require justification. An investigator who is about to insert a needle into a research participant to obtain some blood purely for laboratory purposes faces the question of whether doing so is ethically justified, even when the procedure is included in a study that offers participants the potential for important medical benefit. The goal of ethical analyses of clinical research is to provide an answer [44-46].

Net risk of clinical research

Clinical research poses three types of net risks: absolute, relative, and indirect [5].

Absolute net risks arise when the risks of an intervention or procedure are not justified by its potential clinical benefits. Most commentators focus on this possibility with respect to research

procedures which pose some risks and offer (essentially) no chance of clinical benefit, such as blood draws to obtain cells for laboratory studies. Research with healthy volunteers is another example which frequently offers no chance for clinical benefit. Clinical research also poses absolute net risks when it offers a chance for clinical benefit which is not sufficient to justify the risks participants face. A kidney biopsy to obtain tissue from presumed healthy volunteers may offer some very low chance of identifying an unrecognized and treatable pathology. This intervention nonetheless poses net risks if the chance for clinical benefit for the participants is not sufficient to justify the risks of their undergoing the biopsy [47].

Relative net risks arise when the risks of a research intervention are justified by its potential clinical benefits, but the intervention's risk-benefit ratio is less favorable than the risk-benefit profile of one or more available alternatives. Imagine that investigators propose a randomized, controlled trial to compare an inexpensive drug against an expensive and somewhat more effective drug. Such trials make sense when, in the absence of a direct comparison, it is unclear whether the increased effectiveness of the more expensive drug justifies its costs. In this case, receipt of the cheaper drug would be contrary to participants' interest in comparison to receiving the more expensive drug. The trial thus poses relative net risks to participants [48-50].

Indirect net risks arise when a research intervention has a favorable risk-benefit ratio, but the intervention diminishes the risk-benefit profile of other interventions provided as part of or in parallel to the study. For example, an experimental drug for tuberculosis might undermine the effectiveness of other drugs individuals are taking for their condition. The risks of research participation can be compounded if the indicated response to the harm in question poses additional risks. Kidney damage suffered as the result of research participation might lead to the need for short-term dialysis which poses additional risks to the individual; a participant who experiences a post lumbar puncture headache might need a 'blood patch' which poses some risk of blood entering the epidural space which would call for a further response which carries additional risks [51].

While investigators tend to focus on the risks of physical harm, participation in clinical research can pose other types of risks as well, including psychological, economic, and social risks. Depending on the study and the circumstances, individuals who are injured as the result of participating in research might incur significant expenses. Most guidelines and regulations stipulate that evaluation of the acceptability of clinical research studies should take into account all the different risks to which participants are exposed [52].

Ethical evaluation of risk of participants

To assess the ethics of exposing research participants to risks, one needs an account of why exposing others to risks raises ethical concern in the first place. Being exposed to risks obviously raises concern to the extent that the potential harm to which the risk refers is realized: the chance of a headache turns into an actual headache. Being exposed to risks also can lead to negative consequences as a result of the recognition that one is at risk of harm. Individuals who recognize that they face a risk may become frightened; they also may take costly or burdensome measures to protect themselves [53]. On the contrary, the information on the ethics of clinical research implicitly assumes that being exposed to risks is not necessarily harmful. The fact that participants are exposed to risks is not regarded as necessarily contrary to their interests. It depends on whether the risk is realized in an actual harm. It is well and good to expose a consenting adult to risks to save the health or life of an identified and present other, particularly when the two individuals are first degree relatives [15,54].

It is another thing, and seems too many to be another thing, to expose consenting individuals to risks to help unknown and unidentified, and possibly future others. Almost no one objects to operating on a healthy, consenting adult to obtain a kidney that might save a present and ailing sibling, even though the operation poses some risk of serious harm and offers the donor no potential for clinical benefit. Attempts to obtain a kidney from a healthy, consenting adult and give it to an unidentified individual are met with greater ethical concern [55]. The extent of the concern increases as the path from risk exposure to benefit becomes longer and more complex. Many clinical research studies expose participants to risks in order to collect generalizable information which, if combined with the results of other, as yet non-existent studies, may eventually benefit future patients through the identification of a new intervention, assuming the appropriate regulatory authorities approve it. Some companies or major actor in research chooses to manufacture new interventions that patients can afford

to purchase it. The potential benefits of clinical research may thus be realized someday, but the risks and burdens are clear and present [56].

Clinical research misconducts, abuses and regulatory guidelines

The history of clinical research is marked with abuses. It is worth noting that the history of pediatric research is "largely one of child abuse" [7,56]. This history has had a significant impact on how research ethicists understand the concerns raised by clinical research and on how policy makers attempt to address them. In particular, policy makers have responded to previous abuses by developing guidelines intended to prevent their recurrence.

The most influential abuses in history were the horrific experiments conducted by Nazi physicians during World War II (WW II). The abuses perpetrated by the Japanese physicians were also horrific, but have received significantly less attention). Response to these abuses led to the Nuremberg Code [57-59], which is frequently regarded as the first set of formal guidelines for clinical research, an ironic claim on two counts. First, there is some debate over whether the Nuremberg Code was intended to apply generally to clinical research or whether, as a legal ruling in a specific trial, it was intended to address only the cases before the court [60]. Second, the Germans themselves had developed systematic research guidelines as early as 1931 [35]. These guidelines were still legally in force at the time of the Nazi atrocities and clearly prohibited a great deal of what the Nazi doctors did.

The declaration of Helsinki

World Medical Organization [43] allows individuals who cannot consent to be enrolled in clinical research based on the permission of the participant's representative. The U.S. federal regulations governing clinical research aligns with a similar approach. These regulations are not laws in the strict sense of being passed by Congress and applying to all research conducted on U.S. soil. Instead, the regulations represent administrative laws which effectively attach to clinical research at the beginning and the end. Research conducted using U.S. federal monies, for instance, research funded by the NIH, or research involving NIH researchers, must follow the U.S. regulations [47]. Research that is included as part of an application for approval from the U.S. FDA also must have been conducted according to FDA regulations which, except for a few exceptions, are essentially the same. Although many countries now have their own national regulations [46], the U.S. regulations continue to exert enormous influence around the world because so much clinical research is conducted using U.S. federal money and U.S. federal investigators, and the developers of medical treatments often want to obtain approval for the U.S. market.

Tuskegee abuses

The abuses perpetrated as part of the infamous Tuskegee syphilis study were made public in 1972, 40 years after the study was initiated. The resulting outcry led to the formation of the U.S. National Commission, which was charged with evaluating the ethics of clinical research with humans and developing recommendations for appropriate safeguards. These deliberations resulted in a series of recommendations for the conduct of clinical research, which became the framework for existing U.S. regulations [20,32]. The U.S. regulations, like many regulations, place no clear limits on the risks to which competent and consenting adults may be exposed. In contrast, strict limits are placed on the level of research risks to which those unable to consent may be exposed, particularly children. In the case of pediatric research, the standard process for review and approval is limited to studies that offer a 'prospect of direct' benefit and research that poses minimal risk or a minor increase over minimal risk. Studies that cannot be approved in one of these categories must be reviewed by an expert panel and approved by a high government official. While this 4th category offers important flexibility, it implies that, at least in principle, U.S. regulations do not mandate a ceiling on the risks to which pediatric research participants may be exposed for the benefit of others. This reinforces the importance of considering how we might justify exposing participants to research risks, both minimal and greater than minimal, for the benefit of others [7,41].

Concept of clinical research and clinical care

Lind's experiments on scurvy exemplify the fact that clinical research is often conducted by clinicians and often is conducted on patients. Many commentators have thus assumed that clinical research should be governed by the ethics of clinical care, and the methods of research should not diverge from the methods that are acceptable in clinical care. On this approach, participants should not be denied any beneficial treatments available in the clinical setting and they should not be exposed to any risks not present in the clinical setting [11].

Some researchers [35], argue that this approach is implied by the kind of treatment that patients, understood as individuals who have a condition or illness needing treatment, are owed. Such individuals are owed treatment that promotes, or at least is consistent with their medical interests. Others [19,55] argue that the norms of clinical research derive largely from the obligations that bear on clinicians. These commentators argue that it is unacceptable for a physician to participate in, or even support the participation of her patients in a clinical trial unless that trial is consistent with the patients' medical interests. To do less is to provide substandard medical treatment and to violate one's obligations as a clinician.

The claim that the treatment of research participants should be consistent with the norms which govern clinical care has been applied most prominently to the ethics of randomized clinical trials [57]. Randomized trials determine which treatment a given research participant receives based on a random process, not based on clinical judgment of which treatment would be best for that patient. Lind assigned the different existing treatments for scurvy to the sailors in his study based not on what he thought was best for them, but based on what he thought would yield an effective comparative test. Lind did not give each intervention to the same number of sailors because he thought that all the interventions had an equal chance of being effective. To the contrary, he did this because he was confident that several of the interventions were harmful and this design was the best way to show it. Contemporary clinical researchers go even further, assigning participants to treatments randomly. Because this aspect of clinical research represents a clear departure from the practice of clinical medicine it appears to sacrifice the interests of participants in order to collect valid data [30,39].

Critics respond that even when clinical equipoise obtains for the population of patients, the specific circumstances of individual patients within that population might imply that one of the treatments under investigation is better for them [21]. A specific patient may have reduced liver function which places her at greater risk of harm if she receives a treatment metabolized by the liver. And some patients may have personal preferences which incline them toward one treatment over another (e.g., they may prefer a one-time riskier procedure to multiple, lower risk procedures which pose the same collective risk). Current debate focuses on whether randomized clinical trials can take these possibilities into account in a way that is consistent with the norms of clinical medicine [51].

The problem with the distinction between therapeutic and non-therapeutic research so defined is that research itself often is defined as a practice designed to collect generalizable knowledge and conducted by investigators who intend to achieve this end [27]. On this definition, all research qualifies as non-therapeutic. Conversely, most investigators intend to benefit their participants in some way or other. Perhaps they design the study in a way that provides participants with clinically useful findings, or they provide minor care not required for research purposes, or referrals to colleagues. Even if proponents can make good on the distinction between therapeutic and non-therapeutic research in theory, these practices appear to render it irrelevant to the practice of clinical research. More importantly, it is not clear why investigators' responsibilities to patients, or patients' claims on investigators, should vary as a function of this distinction [14]. Why think that investigators are allowed to expose patients to some risks for the benefit of others, but only in the context of research that is not designed to benefit the participants? To apply this proposed resolution to pediatric research, why might it be acceptable to expose infants to risks for the benefit of others, but only in the context of studies which offer the infants no chance for personal benefit?

Critics argue that these problems highlight the fundamental confusion that results when one attempts to evaluate clinical research based on norms appropriate to clinical medicine. They instead distinguish between the ethics of clinical research and the ethics of clinical care, arguing that it is inappropriate to assume that investigators are subject to the claims and obligations which apply to physicians, despite the fact that the individuals who conduct clinical research often are physicians [23,40].

The claim that clinical research should satisfy the norms of clinical medicine has this strong virtue: it provides a clear method to protect individual research participants and reassure the public that they are being so protected. If research participants are treated consistent with their medical interests, we can be reasonably confident that improvements in clinical medicine will not be won at the expense of exploiting them. Most accounts of the ethics of clinical research now recognize the limitations of this approach and search for ways to ensure that research participants are not exposed to excessive risks without assuming that the claims of clinical medicine apply to clinical researchers [39-42]. Dismissal of the distinction between therapeutic and non-therapeutic research thus yields an

increase in both conceptual clarity and concern regarding the potential for abuse of research participants.

Libertarian principles

It is documented that advocates and experts in bioethics and health research ethics actors are more concerned with the fundamental principle of respect for individual autonomy. This view of bioethicists is reflected in the upholding of the high esteem accorded in the field to the requirement of obtaining individual informed consent and the regular effort made to resolve bioethical challenges. We can therefore make some assumptions that this view within bioethics imply an implicit endorsement of a libertarian principle according to which it is permissible for competent and informed individuals to do whatever they prefer, provided those with whom they interact are competent, informed and in agreement. According to Mill [22,38], investigators should be permitted to conduct research and expose participants to risks provided they obtain their "free, voluntary, and undeceived consent and participation" [9,50]. Putting aside the question of whether this view accurately tie in with bioethics and bioethicists generally, in practice it is not applicable to the vast majority of the work done on the ethics of clinical research. There is no dispute in the field that it is permissible for investigators to conduct any research they want provided they obtain the free and informed consent of those they enroll [25].

Modern day research ethics lay emphasis on informed consent, many regulatory guidelines developed to deal with the requirement for informed consent. Using the example of the response to the Nuremberg Code, almost no one regards informed consent as necessary and sufficient for ethical research. Most regulations and guidelines, starting with the Declaration of Helsinki, first adopted in 1964 [11,17], allow investigators to conduct research on humans only when it has been approved by an independent group charged with ensuring that the study is ethically acceptable. Most regulations further place limits on the types of research that independent ethics committees may approve. They must find that the research has important social value and the risks have been minimized, thereby restricting the types of research to which even competent adults may consent [9]. Are these requirements justified, or are they inappropriate infringements on the free actions of competent individuals? The importance of answering this question goes beyond its relevance to debates over Libertarianism.

Issues of understanding of randomization by competent adults

To consider an example which is much discussed in the research ethics literature, it is commonly assumed that valid consent for randomized clinical trials requires individuals to understand randomization [3,36]. It requires individuals to understand that the treatment they will receive, if they enroll in the study, will be determined by a process which does not take into account which of the treatments is better for them [51]. Significant data mining has shown individuals who participate in clinical research do not understand randomization [17,60]. The data also suggest that these failures of understanding often are resistant to educational interventions.

With this in mind, one may consider the limitations on research with competent adults as betraying the paternalism embedded in most approaches to the ethics of clinical research [45]. Although the charge of paternalism often carries with it some degree of condemnation, there is a strong history of what is regarded as appropriate paternalism in the context of clinical research. This too may have evolved from clinical medicine. Clinicians are charged with protecting and promoting the interests of the patient under their care. Clinician researchers, who frequently begin their careers as clinicians, may regard themselves as similarly charged.

Paternalism

Paternalism involves interfering with the liberty of agents for their own benefit (Feinberg 1986). As the terms are used in the present debate, 'soft' paternalism involves interfering with the liberty of an individual in order to promote their interests on the grounds that the action being interfered with is the result of impaired decision-making: "A freedom-restricting intervention is based on soft paternalism only when the target's decision-making is substantially impaired, when the agent lacks (or we have reason to suspect that he lacks) the information or capacity to protect his own interests—as when *A* prevents *B* from drinking the liquid in a glass because *A* knows it contains poison but *B* does not" [21,49]. 'Hard' paternalism, in contrast, involves interfering with the liberty of an individual in order to promote their interests, despite the fact that the action being interfered with is the result of an informed and voluntary choice by a competent individual.

If many restrictions on clinical research were justified on the basis of hard paternalism they would represent restrictions on individuals' autonomous actions. However, the data on the extent

to which otherwise competent adults fail to understand what they need to understand to provide valid consent suggests that the limitations can instead be justified on the grounds of soft paternalism. This suggests that while the restrictions may limit the liberty of adult research participants, they do not limit their autonomy [35]. In this case, one may regard many of the regulations on clinical research not as inconsistent with the libertarian ideal, but instead as starting from that ideal and recognizing that otherwise competent adults often fail to attain it.

Even when most research participants have sufficient understanding to provide valid consent, it in some cases do not imply that there should be no limitations on research with competent adults. The conditions on what one individual may do to another are not exhausted by what the second individual consents to. Perhaps some individuals may choose for themselves to be treated with a lack of respect, even tortured. It does not follow that it is acceptable for us to treat them accordingly. As independent moral agents we need sufficient reason to believe that our actions, especially the ways in which we treat others, are appropriate, and this evaluation concerns, in typical cases, more than just the fact that the affected individuals consented to them [7,40].

Exposure of participants to risk

It seems clear that researchers may not expose research participants to risks without sufficient justification, and also clear that this claim applies even to those who provide free and informed consent. The current challenge then is to develop an analysis of the conditions under which it is acceptable for investigators to expose participants to risks and determine to what extent current regulations need to be modified to reflect this analysis. To consider briefly the extent of this challenge, and to underscore and clarify the claim that the ethics of clinical research go beyond the protection of research participants to include the independent consideration of what constitutes appropriate behaviour on the part of investigators, consider an example [53].

Physical and emotional abuse cause enormous suffering, and a good deal of research is designed to study various methods to reduce instances of abuse and also to help victims recover from being abused. Imagine that a team of investigators establishes a laboratory to promote the specific abuse line of research. The investigators will enroll consenting adults and, to mimic the experience of extended periods of abuse in real life, they will abuse their participants emotionally and physically for a week. The abused participants will then be used in studies to evaluate the efficacy of different methods for helping victims to cope with the effects of abuse [11].

The proper response to this proposal is not to claim that the study is acceptable because the participants are competent and they gave informed consent. The proper response is to point out that, while these considerations are undoubtedly important, they do not establish that the study is ethically acceptable. One needs to consider many other things. Is the experiment sufficiently similar to real life abuse that its results will have external validity? Are there less risky ways to obtain the same results? Finally, even if these questions are answered in a way that supports the research, the question remains whether investigators may ethically treat their participants in this way. The fact that essentially everyone working in research ethics would hold that this study is unethical, investigators are not permitted to treat participants in this way, suggests that research ethics, both in terms of how it is practiced and possibly how it should be practiced, goes beyond respect for individual autonomy to include independent standards on investigator behaviour. Defining those standards represents one of the more important challenges for research ethics [31,55].

Ethical challenges of defining standard

As exemplified by Lind's experiments on treatments for scurvy, clinical research studies were first conducted by clinicians wondering whether the methods they were using were effective. To answer this question, the clinicians altered the ways in which they treated their patients in order to yield information that would allow them to assess their methods. In this way, clinical research studies initially were part of, but an exception to standard clinical practice. As a result, clinical research came to be seen as an essentially unique activity. And widespread recognition of clinical research's scandals and abuses led to the view that this activity needed its own extensive regulations [11,34].

More recently, some commentators have come to question the view that clinical research is a unique human activity, as well as the regulations and guidelines which result from this view. In particular, it has been argued that this view has led to overly restrictive requirements on clinical research, requirements that hinder scientists' ability to improve medical care for future patients, and also fail to respect the liberty of potential research participants. This

view is often described in terms of the claim that many regulations and guidelines for clinical research are based on an unjustified 'research exceptionalism' [6,42,47].

The central ethical concern raised by clinical research involves the practice of exposing participants to risks for the benefit of others. Yet, as noted previously, we are constantly exposing individuals to risks for our benefit and the benefit of others. When you drive to the store, you expose your neighbors to some increased risk of pollution for the benefits you derive from shopping; speeding ambulances expose pedestrians to risks for the benefit of the patients they carry; factories expose their workers to risks for the benefit of their customers; charities expose volunteers to risks for the benefit of recipients. Despite this similarity, clinical research is widely regarded as ethically problematic and is subject to significantly greater regulation, review, and oversight [39]. Almost no one regards driving, ambulances, charities, or factories as inherently problematic.

Contract theory

A few reporters [7,45,60] try to justify exposing research participants to risks for the benefit of others by citing an obligation to participate in clinical research. At least all individuals who have access to medical care have benefited from the efforts of previous research participants in the form of effective vaccines and better medical treatments. One might try to argue that these benefits oblige us to participate in clinical research. Current participation in clinical research typically benefits future patients although if we incur an obligation for the benefits that are due to previous research studies, we presumably are obliged to the patients who participated in those studies, an obligation we cannot discharge by participating in current studies. This approach also does not provide a way to justify the very first clinical trials, such as Lind's, which of necessity enrolled participants who had never benefited from previous clinical research [7,26].

Alternatively, one might argue that the obligation to participate does not trace to the benefits we receive from the efforts of previous research participants. Rather, the obligation is to the overall social system of which clinical research is a part [6]. For example, one might argue that individuals acquire this obligation as the result of being raised in the context of a cooperative scheme or society. We are obligated to do our part because of the many benefits we have enjoyed as a result of living within such a scheme.

The first challenge for this view is to explain why the mere enjoyment of benefits, without some prospective agreement to respond in kind, obliges individuals to help others. Presumably, your doing a nice thing for me yesterday, without my knowledge or invitation, does not oblige me to do you a good turn today. This concern seems even greater with respect to pediatric research. Children certainly benefit from previous research studies, but typically do so unknowingly and often with vigorous opposition. The example of pediatric research makes the further point that justification of clinical research on straightforward contractualist grounds will be difficult at best. Contract theories have difficulties with those groups, such as children, who do not accept in any meaningful way the benefits of the social system under which they live [45].

Minimizing risks in clinical research

Limits on risks are a central part of almost all current research regulations and guidelines. With respect to those who can consent, there is an essentially implicit agreement that the risks should not be too high (as noted earlier, some argue that there should not be any net risks to even competent adults in the context of so-called therapeutic research). However, there is no consensus regarding how to determine which risks are acceptable in this context. With respect to those who cannot consent, many commentators argue that clinical research is acceptable when the net risks are very low. The challenge, currently faced by many in clinical research, is to identify a standard, and find a reliable way to implement it, for what constitutes a sufficiently low risk in this context. An interesting and important question in this regard is whether the level of acceptable risks varies depending on the particular class of individuals who cannot consent. Is the level of acceptable risks the same for individuals who were once competent, such as previously competent adults with Alzheimer disease, individuals who are not now but are expected to become competent, such as healthy children, and individuals who are not now and likely never will be competent, such as individuals born with severe cognitive disabilities?

Some argue that the risks of clinical research qualify as sufficiently low when they are 'negligible', understood as risks that do not pose any chance of serious harm [19,60]. Researchers who ask children a few questions for research purposes may expose them to

risks no more worrisome than that of being mildly upset for a few minutes. Exposing participants to a risk of minor harm for the benefit of others does not seem to raise ethical concern. Or one might argue that the ethical concerns it raises do not merit serious ethical concern. Despite the plausibility of these views, very few studies satisfy the negligible risk standard. Even routine procedures that are widely accepted in pediatric research, such as single blood draws, pose some, typically very low risk of more than negligible harm.

Industry actors of clinical research

The fundamental ethical challenge posed by clinical research is whether it is acceptable to expose some to research risks for the benefit of others. In the standard formulation, the one we have been considering to this point, the benefits that others enjoy as the result of participants' participation in clinical research are medical and health benefits, better treatments for disease, better methods to prevent disease. Industry funded research introduces the potential for a very different sort of benefit and thereby potentially alters, in a fundamental way, the moral concerns raised by clinical research. Pharmaceutical companies typically focus on generating profit and increasing stock price and market share. Indeed, it is sometimes argued that corporations have an obligation to their shareholders to pursue increased market share and share price [41]. This approach may well lead companies to pursue new medical treatments which have little or no potential to improve overall health and well-being [25,49]. "Me-too" drugs are the classic example here. These are drugs identical in all clinically relevant respects to approved drugs already in use. The development of a me-too drug offers the potential to redistribute market share without increasing overall health and well-being.

There is considerable debate regarding how many me-too drugs there really are and what is required for a drug to qualify as effectively identical [56]. For example, if the existing treatment needs to be taken with meals, but a new treatment need not, is that a clinically relevant advance? Bracketing these questions, a drug company may well be interested in a drug which clearly qualifies as a me-too drug. The company may be able, by relying on a savvy marketing department, to convince physicians to prescribe, and consumers to request the new one, thus increasing profit for the company without advancing health and well-being.

The majority of clinical research was once conducted by governmental agencies. For example, the US NIH is likely the largest governmental sponsor of clinical research in the world. However, its research budget has declined over the past 20 years [6,33], and it is estimated that a majority, perhaps a significant majority of clinical research studies are now conducted by industry: "as recently as 1991 eighty per cent of industry-sponsored trials were conducted in academic health centers…Impatient with the slow pace of academic bureaucracies, pharmaceutical companies have moved trials to the private sector, where more than seventy per cent of them are now conducted" [11,28].

.Understanding the public health care

Like most early clinical research, James Lind's experiments on treatments for scurvy took place in the clinical setting, with a physician evaluating different possible treatments in his patients. This practice eventually led to concern that it did not offer sufficient protection for patients who were frequently unaware that they were involved in research. And this concern led to separating clinical research from clinical care and subjecting it to significantly more extensive regulations, including independent review and extensive consent [9,45]. This approach offered greater protections for research participants and likely led to more sophisticated clinical trials as the result of being conducted by dedicated researchers rather than clinicians in their spare time. This segregation of clinical research from clinical care has also had significant drawbacks. It makes clinical research much more expensive and much more difficult to conduct. Given that studies are conducted in specialized environments, this approach has also undermined to some extent the relevance that the findings of clinical trials have for clinical care. For example, clinical trials assessing possible new treatments for hypertension are conducted in individuals who are aware that the trials exist and take the time to find out what is required to enroll. These studies frequently have trouble enrolling sufficient numbers of participants and take years to complete. At the same time, on the other side of the clinical research/clinical care divide, millions of patients with hypertension who might be eligible for a clinical trial are obtaining care from their doctors. Moreover, the countless data points generated by these encounters, what dose did the patient receive, did they experience any side effects, how long did they last, end up gathering dust in the patients' medical records rather than being systematically collected and used to inform future practice [21-24].

The segregated model of clinical research was designed to protect research participants from exploitation. The primary drawbacks are that it is inefficient and it raises concerns over free riders, allowing patients to realize the benefits of improved clinical care without having to accept any of the risks associated with its generation. Learning health care systems are intended to address the problem of inefficiency. Given that all the members of learning health care systems are possible research participants and also beneficiaries of research, they may, in the process, address concerns over free riders [2,11].

Ethical issues of exclusion of vulnerable population in clinical research

Excluding vulnerable populations from clinical trials creates significant ethical dilemmas, primarily by compromising justice and beneficence. While these groups are shielded from potential harms, this exclusion yields a lack of safety data, forcing these populations to rely on off-label treatments and widening healthcare disparities [55].

Key ethical issues include

- **The Therapeutic Orphan**: Excluding groups like children and pregnant individuals' leaves them without evidence-based dosing or treatments, meaning they receive interventions that have not been adequately studied for their specific physiological needs [6,56]
- **Compromised Autonomy and Coercion:** Institutionalized individuals, such as prisoners, are often protected from exploitation. However, total exclusion denies them the right to participate in trials that could offer access to better medical care, undermining their autonomy [14,57].
- **Distributive Justice:** Broad exclusion means these populations do not benefit from the medical advancements derived from publicly and privately funded research [15,58].
- **Generalizability:** When trials only include healthy adults, the resulting data may not apply to the very elderly with multimorbidity, leading to dangerous adverse effects when these therapies are eventually prescribed in the real world [17,59].

The use of placebo in clinical trials

A placebo is a substance provided to a patient that the physician believes has no specific pharmacological effect on the condition being treated. The use of placebo, when consistent with good medical care, is distinct from interventions that lack scientific foundation. A placebo may still be effective if the patient knows it will be used but cannot identify it and does not know the precise timing of its use. In the clinical setting, the use of a placebo without the patient's knowledge may undermine trust, compromise the patient-physician relationship, and result in medical harm to the patient. Physicians may use placebos for diagnosis or treatment only if they: (a) Enlist the patient's cooperation [56]. The physician should explain that it can be possible to achieve a better understanding of the medical condition by evaluating the effects of different medications, including the placebo. (b) Obtain the patient's general consent to administer a placebo. The physician does not need to identify precisely when the placebo will be administered. In this way, the physician respects the patient autonomy and fosters a trusting relationship, while the patient may still benefit from the placebo effect. (c) Avoid giving a placebo merely to mollify a difficult patient. Giving a placebo for such reasons places the convenience of the physician above the welfare of the patient. Physicians can produce a placebo-like effect through the skillful use of reassurance and encouragement, thereby building respect and trust, promoting the patient-physician relationship, and improving health outcomes Using a placebo that withholds essential care from patients is highly controversial and generally unethical. The primary ethical dilemma lies in the conflict between scientific advancement and the physician's fundamental duty to provide optimal, proven care to every individual [56,57].

The core ethical arguments

Arguments Against Placebos (Withholding Care):

- **Beneficence and Non-Maleficence:** Medical ethics demand that providers act in the patient's best interest (beneficence) and do no harm (non-maleficence). Withholding effective treatments especially for severe or life-threatening conditions—risks irreversible deterioration or suffering [3,58].
- **Violation of Clinical Equipoise:** Ethicists argue that a placebo should only be used if there is genuine uncertainty in the medical community about whether the new treatment or the standard treatment is better. If a proven, effective therapy already exists, equipoise is lost, making it unethical to randomize patients to an inactive placebo [41,59].

- **Patient Autonomy and Deception:** In everyday clinical practice, giving a placebo while allowing the patient to believe they are receiving active medication undermines the doctor-patient relationship, breaks trust, and violates patient autonomy [40].

When is placebo use considered ethical?

According to foundational medical guidelines like the World Medical Association Declaration of Helsinki, there are very narrow situations where a placebo control is permissible: [56].

- **No Proven Alternative:** If there is no established, proven treatment for the condition under study [55].
- **Negligible Risk:** If the condition is mild (e.g., the common cold, mild headaches) and withholding active care poses no risk of serious or permanent harm to the patient [57].
- **Add-On Trials:** When all participants receive the proven standard of care, and the placebo is simply used alongside it to test an additional intervention [31,57].

Evolving perspectives on placebos

In clinical research, "active-control" trials (testing a new drug against an already proven drug rather than a placebo) are becoming the preferred ethical standard when treatments exist. Meanwhile, some ethicists argue that placebos can be used more ethically if patients are fully informed beforehand (meaning no deception), or through the use of "open-label" placebos, which have been shown to sometimes elicit physical improvements despite the patient knowing they are inactive [3,27].

Virtual clinical trials (decentralized trials) rely on telehealth, remote monitoring, and wearables to conduct medical research. By bringing studies into participants' homes, this model avoids risks like pandemic-related disruptions, geographical dropouts, and exposure to contagious clinical environments. It also diversifies participant pools and improves patient compliance [6,57].

While virtual trials excel at eliminating logistical and exposure risks, they introduce their own unique set of vulnerabilities that researchers must manage: [45]

- **Technology and Data Failures:** Relying on mobile health apps and remote medical devices means a higher chance of connectivity issues, hardware malfunctions, or lost data streams [60].
- **Privacy Risks:** Transmitting sensitive health data online increases the risk of accidental disclosures and requires stringent cybersecurity compliance [1,19].
- **Safety Monitoring Lags:** Because participants are not seen face-to-face, it can be harder for investigators to instantly verify patient identity, observe physical symptoms, or address adverse events as they happen [35,57].
- **Not a Universal Solution**: Complex imaging, high-risk interventions, or intensive monitoring still require traditional, on-site infrastructure [18].

Landscape of ethics in clinical research in Cameroon

Ethics in clinical research in Cameroon are strictly governed by Law N° 2022/08, which mandates rigorous participant protections, voluntary informed consent, and independent ethical review. Researchers must submit protocols to the CNERSH or regional committees, ensuring human dignity and minimizing risks, especially for vulnerable populations [18].

Core ethical requirements in Cameroon

Research involving human subjects in Cameroon must align with established national guidelines and international best practices:

- **Informed Consent**: Participants must be informed in a language they understand regarding the study's purpose, risks, and benefits. Consent must be given freely, without coercion, and documented in writing.
- **Risk-Benefit Analysis**: Investigators and sponsors are required to maximize benefits and minimize physical, psychological, and social risks to participants.
- **Fair Participant Selection**: Inclusion criteria must be scientifically justified rather than based on vulnerability or easy availability, and vulnerable populations (such as children and pregnant women) require special protections [19,20].
- **Confidentiality**: Researchers must enforce strict data protection mechanisms to maintain participant privacy and confidentiality.

The approval process

To conduct a clinical trial or health study, researchers must follow a specific regulatory pathway

- **Protocol Submission:** Research protocols are submitted to the Cameroon National Ethics Committee for Research in Human Health (CNERSH) or relevant regional ethics committees (e.g., Littoral, West, North, or North West).
- **Ethical Clearance:** The committee will review the documentation and provide a decision (Approved, Rejected, or Additional Data Required).
- **Administrative Clearance:** After securing ethical approval, researchers cannot commence the study without administrative clearance from the Ministry of Public Health (MINSANTE).

Conclusion

Clinical trials in low-resource settings necessitate robust ethical frameworks that prioritize participant protection, fair standards of care, and community benefits to prevent exploitation. Effective research requires culturally tailored informed consent, strengthened local research capacity, and guaranteed post-trial provisions. The ethical challenge within the health care systems on clinical research faces some challenges especially whether it is possible to do away with the segregated model, along with its regulations and practices, without reintroducing the potential for participant exploitation. Should an individual in clinical research be told that their data might be used for research purposes? Should they be notified when it is? To what extent can patients in be exposed to added risks for the purposes of research? Should they be permitted to decline being so exposed? In the end, then, on-going attempts to address the concerns raised by clinical research raise new ethical concerns and, thereby, offer opportunities for researchers and other stakeholders to look for proper regulatory sound ways to address ethical issues in clinical research.

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Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

FCN, MDG, ETF are the main conceptor of this article and searched for funding, conceived and supervised the activities and wrote the entire article, CF, MTOO, did data mining and search for regulation documents. All the authors read and corrected the manuscript. All the authors read and approved the final manuscript.

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