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RESEARCH ARTICLE

Cancer Research in sub-Saharan Africa: Progress in closing the gap

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ABSTRACT

Cancer presents an escalating challenge in Sub-Saharan Africa (SSA), necessitating strategic interventions grounded in regionally relevant evidence-based medicine. Informed decision-making is critical to formulate effective strategies for cancer prevention, diagnosis, funding, and treatment within the SSA population. The aim of this study is to highlight ongoing clinical trials in SSA, emphasizing the continuous initiatives aimed at filling existing knowledge gaps. Further, the study seeks to assess whether SSA is progressing or stagnating in the global landscape of cancer research. A comprehensive review of research papers and online registries on clinical trials was executed, focusing on English-language journal articles retrieved from the PubMed database. Additionally, a quantitative, web-based, retrospective review was conducted on registered cancer studies in SSA over the past decade (2000-2023) from ClinicalTrials.gov and the Pan African Clinical Trials Registry (PACTR) databases. The review resulted in the inclusion of 71 articles from PubMed, alongside 104 and 140 clinical trials from ClinicalTrials.gov and PACTR databases, respectively. Aggregate findings from PubMed and clinical trial databases revealed that East Africa is the predominant contributor (37%) to cancer clinical trials, whereas Central Africa exhibited the lowest contribution (4%). Notably, PubMed indicated a predominant focus on cervical cancer in clinical trials. Between 2000 and 2015, less than 4% of global cancer clinical trials listed on ClinicalTrials.gov were performed in SSA; in subsequent years, there was an observable increase in the percentage of total trials performed in SSA. Analyses of funding sources revealed that 45% and 32% of clinical trials in SSA were supported by the United States and the United Kingdom, respectively. In the last two decades, the formation of entities like the African Consortium for Cancer Clinical Trials, spearheaded by BIO Ventures for Global Health in partnership with African ministries of health, cancer hospitals, private industry, research institutions, and global oncology experts, contributed to increasing the effective implementation of multicenter clinical trials in Africa. Noteworthy instances, such as the Burkitt's lymphoma and HypoAfrica studies, serve as examples of the results arising from these collaborative initiatives, reflecting substantial progress within SSA's cancer research landscape.

Keywords: Clinical trials, sub-Saharan Africa, Cancer research.

Introduction

Cancer has emerged as a major health challenge in Africa, with alarming statistics underscoring its impact. In 2022 alone, Africa witnessed 1,173,771 new cancer cases, with 756,532 cancer-related deaths[1]. This equated to nearly 2,073 lives lost to cancer daily.[1] Predictions for 2040 are worse, with an anticipated 78% increase in new cancer cases. Factors contributing to this surge include population growth, an aging demographic, exposure to carcinogens, unhealthy lifestyles, and tobacco and alcohol use.[1] These alarming mortality and morbidity rates are compounded by various challenges, including a lack of awareness about cancer, limited understanding, negative attitudes towards cancer screening and vaccination, delayed or missed cancer diagnosis, the high cost of cancer care, and misdiagnosis[2].

Clinical research is pivotal to the development of safe and effective cancer treatments and technologies that advance disease management and reduce morbidity and mortality. The capacity of a country to conduct practice-changing cancer clinical trials is associated with improved patient outcomes[3]. The narrative that Sub-Saharan Africa (SSA) cannot conduct cancer research and lags behind other continents is widely believed in the global scientific community. This paper aims to establish whether SSA is making progress or has remained stagnant in cancer research. The discussion includes examples of both completed and ongoing multi-center clinical trials conducted at various sites across the African continent.

A quantitative, web-based, retrospective study of open cancer clinical trials conducted in 2020 revealed that while Africa constitutes about 15% of the global population, it hosts only an estimated 2% of worldwide cancer clinical trials, underscoring disparities in the clinical trials research landscape.[1] The implication of this is that proof of safety and efficacy of cancer treatments given in Africa, which has a population with a distinct genetic and racial profile, is lacking for many cancer treatments[4]. Beyond the imperative of evidence-based interventions, Africans carry a disproportionately heavy burden of certain diseases, including prostate cancer, thus providing an opportunity for efficient recruitment of participants for trials for such diagnoses. This has however not convinced sponsors to carry out clinical trials in Africa. India and China, each with roughly the same population size as Africa, far outpace the continent in research funding. These two nations each have one regulatory jurisdiction for clinical trials while Africa has 54 regulatory jurisdictions, requiring a sponsor to file 54 different applications in order to cover the entire continent.[4] This is a disincentive that would ensure most sponsors continue to prefer working with India and China rather than Africa. Efforts are currently underway to reduce the administrative burden on sponsors, thus making Africa competitive as a clinical trial destination. For example, the establishment of collaboration among national regulatory agencies could potentially enable Africa to be treated as one regulatory jurisdiction[4].

Ntekim and Olopade[5] published comprehensive data on the distribution of clinical trials across the African continent where a total of 368 clinical trials were conducted across 18 African countries,

highlighting an uneven distribution. North Africa hosted 126 trials, with Egypt leading at 99, followed by Morocco, Tunisia, Algeria, and Libya. In SSA, 242 trials took place, with South Africa remarkably on the top with 218 trials. Nigeria, Eswatini (Swaziland), and Uganda collectively had 10 trials. Notably, no French-speaking countries in SSA were involved, raising questions about potential language barriers in articulating needs or accessing funding.

A 2019 review of the National Institutes of Health (NIH) ClinicalTrials.gov website demonstrated that, of the 736 clinical trials conducted on the continent, only 26 focused on cancer-related interventions[1]. Specifically, Egypt, South Africa, and Algeria led with 45, 11, and 10 clinical trials available for inclusion by 2020, respectively. In spite of the fact that cancer related trials in SSA are limited, a number of them have resulted in practice-changing insights. Examples of these are the Burkitt's lymphoma (BL) study and the HypoAfrica study[6,7]. These studies have demonstrated that Africa has the capacity to generate impactful and practice-changing evidence from local research.

Current literature indicates that the genetic basis of cancers in individuals of African ancestry is different from that of other races and ethnicities[8]. Further, compared to Europe and North America, people in Africa exhibit distinct responses to cancer treatment influenced by factors such as cancer biology, nutritional status, and HIV coinfection[3]. Notably, the diverse genetic makeup among individuals of African ancestry implies a need for region-specific clinical trials to optimize cancer treatment outcomes[9].

THE BARRIERS FOR CONDUCTING CANCER RESEARCH IN SSA

Among the studies explored for this review, over 40 quotes were extracted relating to different types of challenges to conducting clinical trials. The major challenges include financial and human capacity limitations, ethical and regulatory obstacles, lack of infrastructure to conduct research, operational barriers, and competing demands[10].

FINANCIAL AND LOGISTICAL BARRIERS

The Amafrica study in Ivory Coast found financial burden to be the most common reason for patient refusal and abandonment of treatment[11]. A South Africa cervical cancer screening study ran out of funding leading to a collapse of the human papillomavirus (HPV) typing and testing by the month 12 visit, leading to a further challenge[12]. The funding difficulties in the South African study created a further challenge - loss of follow up, which was higher in the treatment arm compared to the observational arm. A study in Kenya also noted the lack of funds as an important cause of loss of to follow up in one of the study groups[13].

METHODOLOGICAL, OPERATIONAL AND TECHNICAL CHALLENGES

A primary concern in conducting trials in Africa is methodological inexperience. For example, a study comparing the effects of cryotherapy versus loop electrosurgical excision procedure (LEEP) on cervical disease recurrence, highlighted limitations related to the region including the fact the trial was conducted in a single urban care facility where all treatment procedures were administered by a singular clinician[14]. While this ensured internal consistency in outcomes, it raises

questions regarding the generalizability of results in varied and less controlled settings. Another study in Uganda employed several measures that were specifically developed for the research, in addition to which the small sample size potentially affects the generalizability of the results[15]. A randomized trial conducted (RCT) in Tanzania experienced various challenges starting from a need to switch to a new SMS system halfway through the trial due to discrepancies due to errors in transferring laboratory reports to study investigators and inability to conduct active post-trial follow-up[16]. In South Africa and Zimbabwe a radiotherapy trial identified methodology issues coupled with infrastructure limits, specifically difficulty ensuring appropriate radiotherapy delivery and maintaining consistent quality assurance across different centers[17]. Other factors such as data submission delays and the lack of electronic methods for data submission impacting the timeliness and efficiency of data processing and analysis also occurred. An open label, multi-centre safety study in 44 countries, including some in SSA countries, posited that the direct involvement of a sponsor in formulating and analyzing oncology clinical trials can present both obstacles and advantages[18,19].

PATIENT RECRUITMENT AND RETENTION ISSUES

Clinical trials in various African countries have notably faced challenges relating to participant communication, engagement, and follow-up[20-22]. A prostate cancer study in Nigeria faced constraints in managing losses to follow-up[23]. A South African study found challenges related to therapeutic misconceptions with most participants consenting to participate primarily for self-benefit, despite more than half having a poor understanding of the specificity of the Phase 3 of the clinical trial[24]. Almost half of the trial participants believed that the clinical trial posed no significant risk to them, indicating a gap in understanding the potential risks and experimental nature of the trial. A study in Ethiopia encountered difficulty in communicating with participants, as over half of the women could not be reached by phone to receive their test results[25]. Researchers in Kenya noted a high proportion of potential participants were excluded primarily due to the anticipated likelihood that they would not return for follow-up, suggesting challenges in ensuring long-term participant commitment. These factors collectively point to critical gaps in participant management and follow-up in the research process[26]. A study using an SMS-based intervention in Tanzania to increase attendance and follow up noted challenges in technical and logistical aspects of the implementation[27].

CULTURAL AND COMMUNITY BARRIERS

Socio-cultural norms are a documented barrier to clinical trials hesitancy in Africa. A study in Cameroon found that 5.6% of the participants held religious beliefs that they perceived to conflict with conducting HPV self-sampling, while 17.3% of participants reported the necessity of obtaining their partner's approval before performing HPV self-sampling[28]. In a Tanzanian study, parents perceived associated a higher number of doses of the HPV vaccine as providing increased protection. This belief, however, posed challenges in comprehending the concept of randomization by dosage, especially in the context of dose reduction in

administered vaccines[29]. Children tended to defer to their parents in interviews, making it difficult to extract independent views from the younger participants.

INFRASTRUCTURE AND HUMAN RESOURCES SHORTAGE

One of the major challenges related to conducting clinical trials in Africa is the limited resources and gaps in the research ecosystem, including the lack of available skilled human resources and infrastructure within the health systems[5,30]. Fewer than 2% of worldwide cancer clinical trials take place in Africa, with the majority of trial sponsors being non-African institutions. Ntekim and Olopade[5] identified several key deficiencies in the academic and research infrastructure: shortage of faculty and research leaders, limited training facilities and infrastructure, and scarcity of postdoctoral training or fellowship opportunities. Additionally, there is a significant lack of experience in conducting clinical trials, compounded by substantial deficiencies in bioinformatics and data science. Further, most healthcare facilities in SSA are primarily designed for delivering healthcare and thus lack dedicated spaces for research activities.

THE FACILITATORS FOR CONDUCTING CANCER TRIALS IN SSA

Governmental commitments to funding research have been increasing with a current positive trend in increased globalization of clinical trials and collaborations that favor Africa. These are driven by factors such as a need to access wider pools of study participants, reduce research timelines and operational costs, address the global burden of disease, increase healthcare market size, and build or strengthen research capacity in countries with limited capacity[4].

COLLABORATION AND CAPACITY BUILDING

The pivotal recommendations of the 1st All Africa Clinical Trial Summit for advancing clinical research across the continent, along with the Operational Strategy for Clinical Trials in Nigeria Summit, can serve as a strategic opportunity for transforming oncology clinical research in Africa. The experts at the summit advocated for increased funding to support trials, improvements in transparent clinical trial regulatory infrastructure, and consistent enforcement[31]. There is a call for capacity building through international pharmaceutical company engagement for instance, development of a robust African database of clinical sites, and enhancement of clinical trial capacity.

Within the African community, partnership with local health facilities to integrate research within existing health service using a study design that ensures no impact on the clinical part comes up as a good opportunity. A randomized trial on early breast cancer diagnosis in Rwandan rural districts used the opportunity of existing routine health services to integrate their study and managed to minimize impact on the clinical care through the randomization[32].

Many articles mentioned the need for collaboration to go beyond the barriers, and discussed how public private partnerships could fill in the funding and well-equipped human resources gaps as well as a way to build and sustain regional networks of clinical trials for knowledge and resources sharing. Atara et al.[5] highlighted that "Each team should partner with multiple stakeholders,

including foundations and industry partners, because of the significant research infrastructure, education, and training needs in low- and middle-income countries."

From Africa to the world, a multi group collaboration, including research institutions, industry and hospitals, is a key opportunity to share knowledge, implement a context-based expertise, and to succeed in implementing trials.

Several African institutions are establishing units for clinical trials via partnerships with foreign organizations/institutions[5]. For example, the West African Breast Cancer Study group achieved success using a collaborative strategy between Novartis Biomedical Research Institute; the University of Chicago in the United States; and the University College Hospital, Ibadan, Nigeria, and Lagos State University Teaching Hospital, Lagos, Nigeria. In Ivory Coast, collaborators from the Toulouse University Medical Center (France) and the Abidjan University Medical Center (Ivory Coast) demonstrated that the use of a patient navigator improved adherence to chemotherapy and reduced rates of refusal and abandonment of treatment[11].

A comprehensive review of the trials conducted across Africa show a disparity in trial distribution across countries where the northern region of Africa hosted nearly a third of the total trials. Within SSA, countries like South Africa lead with 90% of the total trials[5]. Such data suggests the potential for building stronger research networks across Africa where collaboration can be the backbone of research with institutions in countries like Egypt, Morocco, South Africa, and Nigeria, which could provide valuable insights and resources for conducting trials in lesser-represented regions. Ntekim and Olopade[5] highlighted that the investments in regional comprehensive cancer centers and the formation of cancer clinical trial coordinating centers is an opportunity to foster pooling and sharing of resources to enable increased clinical trial activities in a sustainable manner. A paper on survival improvement in a collaborative project highlighted the use of collaborative strategy in the context of multi-centre studies for data sharing, and using a local context-based consensus treatment guideline[29].

COMMUNITY ENGAGEMENT AND CULTURAL SENSITIVITY

Two cervical cancer screening studies in Kenya and Tanzania emphasized the need for building clinical trials that engages community members such as community health workers to both address care workers shortages and enhance community participation in culturally sensitive studies[27,33]. This is an example of an approach to accelerate clinical trial participation among populations in low- and middle-income countries or low-resource settings common in Africa. It supports the recruitment and retention of patients[5]. Another approach is to leverage or expand upon existing networks. Examples of such networks include the African Consortium for Cancer Clinical Trials (AC^{3}T) launched by BIO Ventures for Global Health (BVGH), the Association for Good Clinical Practice in Nigeria, the African Clinical Trial Consortium, and the Prostate Cancer Transatlantic Consortium[31].

AFRICAN CONTEXT-BASED DESIGN OF TRIALS

The African continent is large and diverse presenting an opportunity to have diversified clinical trials that consider such diversity of the population's needs and their expression of

different cancers. A 2019 AIDS Malignancy Consortium study on advanced cervical cancer in South Africa and Zimbabwe underscored the importance of designing clinical studies that are tailored to the specific needs and contexts of African populations, particularly in terms of disease prevalence and stages[34]. The recommendations of the Operational Strategy for Clinical Trials in Nigeria Summit emphasized an Africa-centric approach by encouraging local innovations, including traditional medicines, and the establishment of an Africa-wide clinical trial network for better collaboration[31].

STRONG REGULATORY AUTHORITIES

Many African institutions have strong institutional review boards and national medicine registration agencies with relevant experience in regulating clinical trials, reducing the need for external intervention[5].

LEVERAGING EXISTING EXPERIENCE

Odedina et al.[35] noted that there is a substantial pool of professionals in Africa with extensive experience in conducting clinical trials for diseases like malaria, tuberculosis, HIV, and more; upon which oncology trials could leverage. A study on innovative strategies suggested outsourcing functions requiring facilities such as "certified clinical laboratories and imaging centers"[5].

TECHNOLOGY AND DIGITAL HEALTH

As Africa is home for decreasing costs of mobile phones with a notable improvement of the mobile network capability, penetration of mobile technology in SSA opens innovative avenues for developing clinical trials using digital health for a more sustainable and effective impact[30]. Mobile technology can enhance patient recruitment to a wider and more diverse audience for generalization of results. It can also enhance study retention and mitigate challenges to patient follow up. mHealth applications can be a powerful tool for timely and accurate data collection and monitoring of patient reported-outcomes[36]. Okunade et al.[36] highlighted the opportunity for research to apply mHealth for interventions that can increase screening uptake. A 2014 pre-cervical cancer study in Nigeria addressed operational challenges by switching to a practical approach online cloud SMS demonstrating adaptability using technology and digital health[37]. The Operational Strategy for Clinical Trials in Nigeria Summit recommended the use of technology to enhance clinical trial efficiency boost patient recruitment and retention[31].

LEARNING FROM THE CLINICAL TRIALS GEOGRAPHICAL DISTRIBUTION DATA

Exploring Untapped Regions: The lack of trials in French-speaking countries in SSA suggests a significant opportunity for conducting trials in these regions, which could address the gap in research and provide insights into the unique challenges and needs of these populations, especially in psycho-oncology[38].

Investigating Regional Disparities: South Africa is leading the way in developing and conducting multiple trials - 218 out of 242 in SSA) and could potentially uncover structural and economic factors, and policy implications and political will that facilitate or hinder clinical research. This is an important opportunity for South Africa to share their knowledge to inform strategies to boost trials in other African regions and countries[5,39].

Objectives

The primary aim of this paper is to establish whether sub-Sahara Africa is catching up or

losing out in cancer research globally. The secondary aim is to highlight and share successful examples of completed and ongoing multi centre clinical trials conducted in different sites in Africa.

Methods

To establish whether sub-Sahara Africa is catching up or losing out in cancer research globally (primary aim), an in-depth review of research papers and online registries of cancer clinical trials was conducted.

DATABASES SEARCH

We identified and analyzed the opportunities and challenges associated with cancer clinical trials in Africa, following the updated guidelines for reporting systematic reviews outlined by the Preferred Reporting Items for Systematic Reviews (PRISMA) checklist[40]. Firstly, the study focused on journal articles written in English from the PubMed database from the past decade (2000-2023). With an advanced search strategy employed we used PubMed, utilizing keywords such as "Clinical Trials," "Cancer," "Oncology", "Africa," "Opportunities," and "Challenges." A snowballing technique to broaden our search scope from the identified articles was also incorporated. The selection process began with screening the titles and abstracts of articles to determine relevance. This initial screening was followed by a full-text review of selected studies to ascertain their eligibility for inclusion in our analysis. Additionally, the search terms "name of country," "Africa," "oncology," "cancer," and "clinical trials" were employed in clinical trials registries.

Subsequently, a quantitative, web-based, retrospective review of registered cancer studies in SSA was conducted between 2000 and 2023 in clinical trial registries. Online clinical trial registries for all open clinical trials in SSA were reviewed. The online registries included Clinicaltrials.gov (https://clinialtrials.gov) and the Pan African Clinical Trials Registry (http://www.pactr.org). A search of private and public funding agencies, including pharmaceutical companies was also performed. The review included studies conducted in Africa and globally focused studies that enrolled patients in some SSA countries.

DATA COLLECTION

The data extraction concentrated on several key areas: types of cancer being studied, the geographical distribution of the trials, sources of funding, impact of the clinical trials, and a detailed examination of both the opportunities and challenges presented or inferred within these trials. Furthermore, a web-based review was used to identify public and private registries of oncology clinical trials based in Africa.

The following data were collected from open oncology clinical trials in Africa: information source for the trials; country; type of cancer; a summary of study; sponsor(s) name and country; study type; estimated enrollment; allocation; official title of study; primary purpose of study; study start date and end date; and age and sex eligibility. Two authors (F.B.I and L.K) independently performed data retrieval from PubMed. Furthermore, four research coordinators who are Co- PIs in the HypoAfrica Prostate Cancer Clinical trial based in Uganda, Nigeria, Tanzania and South Africa captured data. Each of the data collectors was preassigned countries in their region to focus on for the data retrieval.

Subsequently, all data were validated by authors A.M, A.J and M.T. Discrepancies were resolved through collaborative group discussions at the weekly meeting. Data validation and quality checks involved using the information source identified by data collectors to confirm the clinical trials in the database. In addition, the research coordinator checked for double entry to ensure unique entry. Following an agreed-upon template, both reviewers (F.B.I and L.K) independently extracted data from all selected studies. The final reference list was generated based on its relevance to the broad scope of this review.

DATA ANALYSIS

The R studio software was used for data analyses and reporting. Descriptive analyses, including frequency analysis and descriptions of findings, were used to summarize findings.

Results

The literature search from PubMed database yielded 152 articles, of which 88 studies met the inclusion criteria for this study, following a full text review using the snowball method, 71 articles were incorporated, while 11 were excluded. Subsequent searches conducted on clinicaltrial.gov and PACTR revealed an additional 104 and 140 studies, respectively (Figure 1).

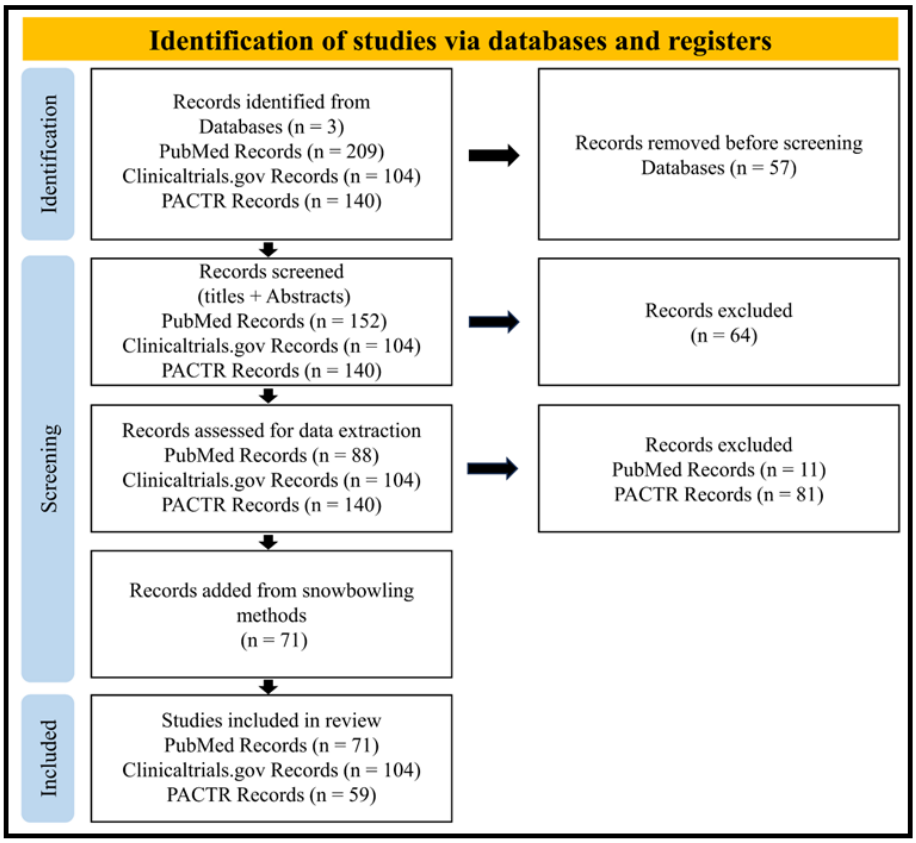

Figure 1: Schematic guideline on studies conducted from PubMed, Clinicaltrial.gov and Pan African Clinical Trials Registries (PACTR) as adopted from M.J., McKenzie, J.E., Bossuyt, P.M. et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews[40].

GEOGRAPHICAL DISTRIBUTION OF TRIALS

The papers analyzed primarily focused on clinical trials conducted within African countries. Regarding regional distribution, the average data from PubMed, ClinicalTrials.gov, and PACTR indicated that East Africa emerged as the leading contributor of cancer clinical trials, accounting for 36.6%, followed by West Africa (21.2%), and Southern Africa (15.3%). Central Africa exhibited the lowest number of clinical trials, representing only 4.1% (Table 1).

Table 1: Geographical distribution of studies according to PubMed, Clinicaltrials.gov and Pan African Clinical Trials Registry (PACTR).

African Region	SSA Countries	PubMed; Clinicaltrials.gov and PACTR (%)
East Africa	Kenya, Ethiopia, Uganda, Burundi, Tanzania and Rwanda	36.6
Central Africa	Cameroon and Congo	4.1
Southern Africa	Botswana, Malawi, Mozambique, Namibia, South Africa and Zimbabwe	15.3
West Africa	Benin, Gambia, Ghana, Ivory coast, Mali, Nigeria and Senegal	21.2

AN INDICATION OF INDIVIDUAL COUNTRIES' CONTRIBUTIONS TO THE CLINICAL TRIALS

Most representation comes from Kenya (19%), followed by South Africa and Ethiopia, each comprising 13%. Nigeria also contributes significantly with 10%. In contrast, the Ivory Coast, Mali, Benin, Democratic Republic of Congo (DRC), Namibia, Mozambique, Cote d'Ivoire, and Botswana were least active in cancer clinical trials, with each accounting for 1%.

On the other hand, clinicaltrials.gov documented most clinical trials in Kenya (28.16%) and Nigeria (24.27%). Notably, 5-10% of clinical trials were registered in Malawi (9.71%), Botswana (6.8%), Ghana (5.83%), Cameroon (5.83%), and Burkina Faso (5.83%). Though, countries such as Rwanda (3.88%), Ethiopia (2.91%), Madagascar (1.94%), Burundi (0.98%), Code d'Ivoire (0.98%), DRC (0.98%), Mozambique (0.98%), and Uganda (0.98%) reported less than 5% of clinical trials conducted in Africa (Figure 2).

In contrast, PACTR documented that most clinical trials were performed in Kenya (12.13%). Countries with less than 10% of clinical trials performed in Sub-Saharan Africa included Nigeria (6.43%), Ethiopia (5.71%), Tanzania (5%), South Africa (4.29%), Uganda (3.6%), Ghana (2.14%), Zimbabwe (1.4%), Malawi (0.71%), Gambia (0.71%) and Cameroon (0.71%) (Figure 2).

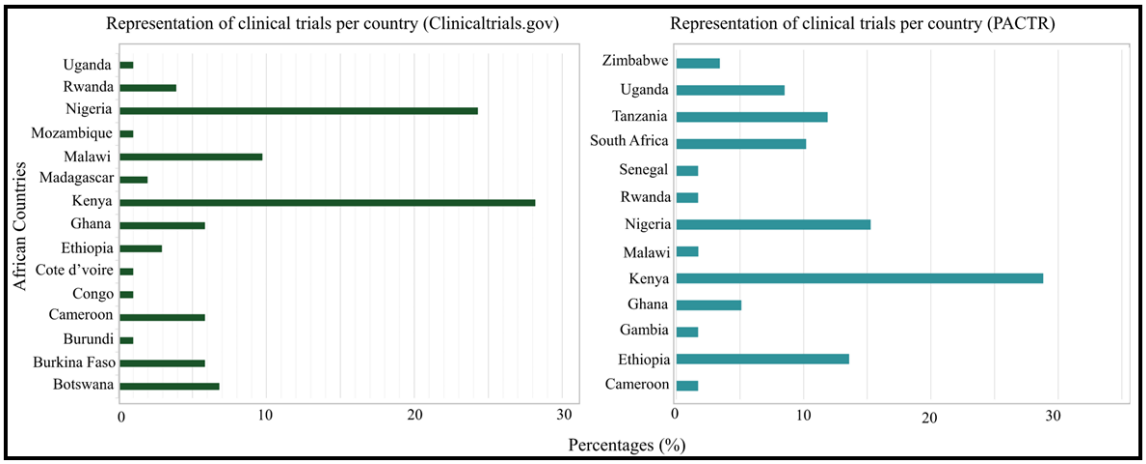

Figure 2: A representation of Clinical Trials performed per country according to Clinicaltrials.gov and Pan African Clinical Trials Registry (PACTR).

TYPES OF CANCER REPRESENTED

Our analysis revealed that the most prevalent clinical trials focused on cervical cancer (44.8% of the studies), followed by breast cancer (10.3%) and prostate cancer (5.2%). Malignant lymphoma, hepatocellular carcinoma, and non-Hodgkin lymphoma each comprised 1.7% of the trials.

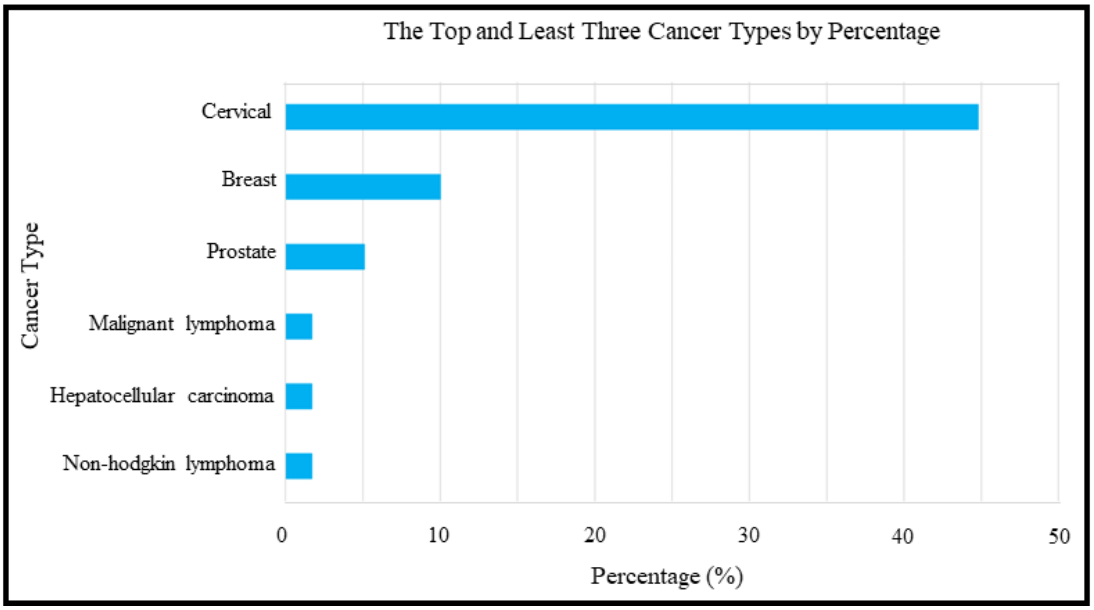

Figure 3: A representation of the top and least three cancer types identified in SSA

The analysis revealed that the most prevalent clinical trials focused on Cervical Cancer, accounting for 44.83% of the studies, followed by Breast Cancer and Prostate Cancer, representing 10.34% and 5.17% respectively. On the other hand, Malignant Lymphoma, Hepatocellular Carcinoma, and Non-Hodgkin Lymphoma each comprised 1.72% of the trials.

CLINICAL TRIALS OVER TIME

As per clinicaltrials.gov, cancer clinical trials conducted in SSA between the years 2000 to 2015 accounted for less than 4% of the

worldwide total. Notably, there was a substantial increase in clinical trial activity in subsequent years. The year 2021 recorded the highest number of clinical trials in SSA, constituting 15.8% of the total. Following closely, the year 2020 contributed 11.9%, while 2016 and 2023 both accounted for 9.9% each. The year 2022 represented 8.9% of clinical trials, and 2017 and 2018 contributed 6.9% each to the overall distribution (Figure 4).

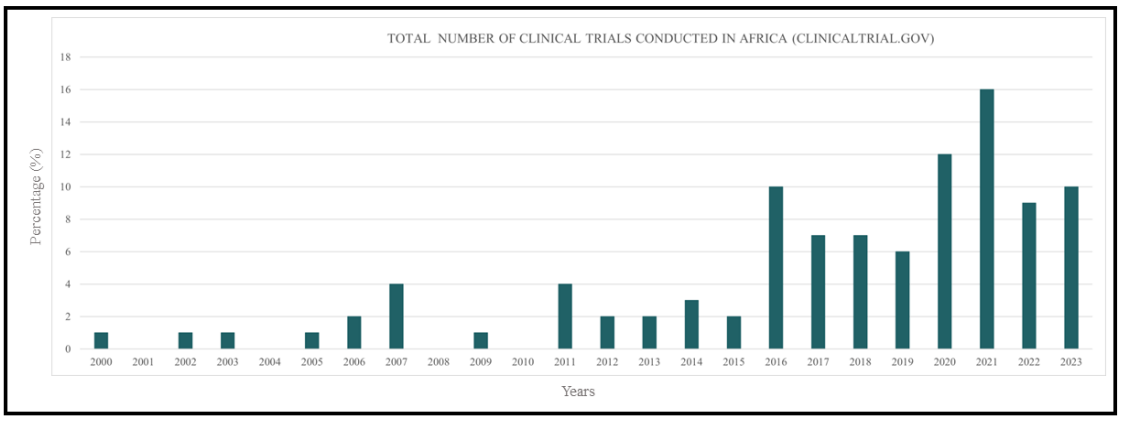

Figure 4: An illustration of clinical trials from the year 2000 to 2023

CLINICAL TRIALS FUNDING SOURCES

Regarding the source of funding for the studies from articles we reviewed, the largest funding comes from institutions in the United States, which represents the largest proportion of funders with 45.2% of total mentions. This is followed closely by the United Kingdom, contributing 32.3% of the total funding institutions. Germany also plays a significant role, accounting for 6.5% of the funders. Other notable contributions come from diverse geographic locations, including the European Union, Denmark, Switzerland South Africa, India, Kenya, Nigeria, and China.

Table 2: Depiction of organisation that funded clinical trial research in Africa with their country of origin. Information obtained from research papers and clinicaltrial.gov database.

Institution/Organization	Country
Abramson Cancer Center at Penn Medicine	United States
Albert Einstein College of Medicine	United States
ANRS, Emerging Infectious Diseases	France
AIDS Clinical Trials Group	United States
AIDS Community Research Initiative of America	United States
AIDS Malignancy Consortium	United States
American Cancer Society	United States
Amsterdam UMC	The Netherlands
Beth Israel Deaconess Medical Center	United States
Bill and Melinda Gates Foundation	United States
Breast Cancer Research Foundation	United States
Brigham and Women's Hospital	United States
Caring Cancer Trust	United Kingdom
Centers for Disease Control and Prevention	United States
Chief Scientist Office (Scotland)	United Kingdom

Institution/Organization	Country
Chinese University of Hong Kong	China
Cipla-M (Triomune donation)	India
Columbia University–Southern African Fogarty AIDS International Training and Research Programme	United States
Danish International Development Agency (Danida)	Denmark
Doris Duke Charitable Foundation	United States
European Union (part of the EDCTP2 programme)	European Union
ESTHER University and Hospital Partnership Initiative of German International Cooperation	Germany
ETOP IBCSG Partners Foundation	Switzerland
French Africa Pediatric Oncology Group	France
Fogarty International Center, National Institutes of Health	United States
German Ministry for Economic and Development Cooperation (BMZ)	Germany
GlaxoSmithKline	United States
Harvard School of Public Health (HSPH)	United States
Irene Diamond Fund	United States
International Atomic Energy Agency	Austria
International Agency for Research on Cancer	France
International Breast Cancer Research Foundation	United States
Janice Cholerton Research Fund/East Africa Medical Trust (EAMT)	United Kingdom
Jhpiego	Brazil
Lilly (Inst)	United States
M.D. Anderson Cancer Center	United States
Medical Research Council	United Kingdom
Memorial Sloan Kettering Cancer Center	United States
Moi University	Kenya
Montefiore Medical Center	United States
National Cancer Institute	United States
National Cancer Institute AIDS Malignancy Consortium	United States
National Institute of Allergy and Infectious Diseases (NIAID) of the NIH	United States
National Research Foundation Thuthuka	South Africa
Obafemi Awolowo University Teaching Hospital	Nigeria
President's Emergency Plan for AIDS Relief	United States
Quest Cancer Research	United Kingdom
The Cancer Prevention Research Trust	United Kingdom
The Humane Research Trust	United Kingdom
United-in-Cancer Charitable Trust	United Kingdom
UK Department for International Development (DFID)	United Kingdom
UK Medical Research Council	United Kingdom
UNC Lineberger Comprehensive Cancer Center	United States
University College Hospital, Ibadan	Nigeria
University of Chicago	United States
University of Southern Denmark	Denmark

Discussions

Over the past two decades, clinical trials have been instrumental in enhancing survival rates among cancer patients in high-income countries (HICs)[41,42]. Notably, in England, cancer patients participating in clinical trials exhibit substantially elevated survival rates compared to their counterparts who are not enrolled in such trials[42,43]. The National Comprehensive Cancer Network has stated that clinical trials are the best way to manage patients with cancer[31,44]. Unfortunately, clinical trial as a way of managing cancer patients in Africa has not been adopted because of infrastructure and human resources shortage, financial and logistical barriers, patient recruitment and retention issues, methodological, operational and technical challenges, and cultural /community barriers. To improve the landscape of cancer research in Africa all these factors should be addressed. The best way to do this is to consider these factors as symptoms of a root cause, which is lack of African governments commitment to funding research. The solution therefore has to come from Africa, and this is beginning to happen for example Tanzania commits 1% of its gross domestic product for research. The experts during the 1st All Africa Clinical Trial Summit for advancing clinical research across the continent, along with the Operational Strategy for Clinical Trials in Nigeria advocated for funding to support clinical trials, improvements in transparent clinical trial regulatory infrastructure, and consistent enforcement[31]. The Africa Centre for Disease Control (CDC) established seven years ago created an Institute for Workforce Development, which conducts a course on proposal writing to provide guidance on how participants can transform their ideas into strong grant proposals, and search grant markets for potential funders. It covers the mechanics of grant writing, including the scientific and administrative components and using didactic and applied training to build competency in developing proposals for public health programs or research projects. It equips trainees with the skills to identify a suitable funding opportunity, distinguish between different types of funding mechanisms and funding agencies, to fit their ideas to the funding agency's guidelines, and to navigate the grant review process.

However, Africa cannot do this alone. Collaborations and partnerships must be established to complement the efforts of African governments. The creation of AC^{3}T by BVGH, in partnership with African ministries of health and cancer hospitals, private industry, and global oncology experts, has been an important opportunity for countries aiming to develop research collaborations. In the last ten years many other initiatives committed to strengthening cancer research in Africa have been established. These include African Organization for Research and Training in Cancer (AORTIC), the AFROX-Harvard-Oxford-UPenn and Hopkins Consortium, Harvard Global Catalyst Initiative, Global Oncology University, US NIH International Network for Cancer Treatment and Research (INCTR), International Prevention Research Institute (iPRI), Innovation for Cancer Care in Africa (ICCA), American Society of Clinical Oncology (ASCO), American Cancer Society (ACS), and more. All these consortia have a mission to build research capacity in Africa. From the Africa point of view, all of the above initiatives serve as strategic opportunities to

strengthen health systems[45,46] and transform cancer clinical research in Africa.

EXAMPLE OF SUCCESSFUL CLINICAL TRIAL CONDUCTED BY AFRICAN PI'S

Two examples of successful multi-center clinical trials conducted in Africa as a result of collaborative efforts include the Burkitt's lymphoma and HypoAfrica clinical studies.

BURKITT'S LYMPHOMA CLINICAL STUDY

Study rationale

In 2004, the INCTR convened a group of African physicians from three countries, subsequently referred to as INCTR's "African Burkitt's lymphoma (BL) Strategy Group," to discuss their results in the treatment of BL and to design a joint treatment protocol[6]. BL is particularly important in Africa, as it the most common childhood cancer in SSA, accounting for 30–50% of all cancer cases in children less than 15 years of age. The strategy group physicians were all using combinations of cyclophosphamide (CTX), methotrexate (MTX), and vincristine (VCR), but with varying doses of systemic agents and different regimens of intrathecal therapy. Because follow-up was very poor, it was not possible to determine event-free survival (EFS) or overall survival (OS) rates. However, there was little doubt that these were very low, due to a variety of factors, including treatment abandonment, the inability of families to afford therapy, failure to treat recurrent disease and/or poor supportive care. The objectives were to attempt to precisely define response and toxicity to this therapy in order to provide a solid baseline with which other regimens for the treatment of BL iAfrica could be compared[6].

Study Team

INCTR BL Strategy Group was composed of a team of diverse oncology professionals, including experts in medical oncology, data management, and clinical trial management. The Strategy Group was supported by an advisory panel and PIs from Tanzania, Nigeria, and Kenya.

Study Design

The INCTR BL Strategy Group designed a standard regimen based on the three drugs they were all using (CTX, MTX, VCR) in addition to IT therapy spread over multiple cycles. In order to gain the maximal amount of information possible from the trial, a new combination of drugs (ifosfamide, mesna, etoposide, and cytarabine [salvage therapy]) was tested in patients who failed to achieve a complete response to first-line therapy or relapsed early.[6] This combination was based on similar combinations shown to be effective and feasible (albeit with differences in drug doses) in the USA, Egypt and India[47,48,49,50] If non-cross resistant and feasible, in terms of toxicity, in the African setting, the combination could be incorporated into first-line therapy in high-risk patients in a future treatment regimen, with potentially improved survival rates

Study Findings

Prior to the introduction of the INCTR BL study protocol in 2012, survival of patients with BL at four tertiary care centres in Tanzania, Kenya and Nigeria was probably no more than 10–20%. The INCTR BL results reported after recruiting 356 patients and treating them with the study protocol then following them up for two years demonstrated marked improvement in survival through the use of the uniform treatment protocol. Overall

survival rates of 67% and 62% were observed at 1 and 2 years (relapse is rare after one year). Of interest was the small impact of cerebrospinal fluid (CSF) and bone marrow involvement on outcomes.

HYPOAFRICA STUDY

Study Rationale

Due to the inadequate number of radiotherapy machines and centers in Africa, approaches that maximize machine usage and minimize cost – such as the use of hypofractionated radiotherapy (HFRT) – were recommended by the Lancet Oncology Commission for SSA[51]. In response, a multi-center study to evaluate the feasibility of applying moderate HFRT for the treatment of localized prostate cancer in the African context (HypoAfrica) was launched in 2022.

Study Team

HypoAfrica is led by PIs based at four sites in Nigeria (NSIA-LUTH Cancer Center [NLCC] in Lagos), South Africa (Inkosi Albert Luthuli Central Hospital [IALCH] in Durban), Tanzania (Ocean Road Cancer Institute [ORCI] in Dar es Salaam), and Uganda (Uganda Cancer Institute [UCI] in Kampala). The trial sites are supported by PIs in the Netherlands (Erasmus Medical Center) and USA (Johns Hopkins Medicine) and an international team of diverse oncology professionals, including experts in radiation oncology, medical physics, data management, and clinical trial management. Each week, the HypoAfrica team holds weekly Zoom meetings to share updates, review study proceedings, and troubleshoot problems. Ad hoc meetings between team members - including between staff at the four trial sites - are held as needed.

Study Design

In preparation for the HypoAfrica trial, a survey was conducted among various African radiotherapy centers to ascertain their interests in conducting cancer clinical trials and their radiotherapy capabilities, infrastructure, and equipment. The results of the survey were reviewed by senior leaders from HypoAfrica team and two sites NLCC and ORCI were selected. The trial was designed as a collaborative initiative between the project leader and PI of the HYPRO trial, the Director of Global Health Catalyst (GHC), and senior radiation oncologists from ORCI and NLCC[52,53]. Ethics approval was received by both trial sites and research funding was provided by BVGH. The trial was launched in early 2022, with the third trial site (IALCH) joining shortly thereafter and UCI joining in 2023.

To ensure the quality of radiotherapy practices and to standardize quality assurance across the trial sites, members of the American Association of Physicists in Medicine (AAPM) International Council were recruited to advise the sites' medical physics teams. A data management expert from University of Ljubljana, Slovenia was engaged to provide support in clinical trial data management tools to streamline and standardize the trial sites' data collection and management.

Designed to mirror the European CHHiP study, patients with histologically-confirmed localized non-metastatic prostate cancer are enrolled to receive a HFRT total dose of either 60Gy (low- and intermediate-risk prostate cancer) or 62Gy (high-risk prostate cancer) delivered in 20 fractions.[54] Gastrointestinal (GI) and genitourinary (GU) toxicities are assessed using Radiation Therapy Oncology Group and the European Organization for

Research and Treatment of Cancer (RTOG-EORTC) and Common Terminology Criteria for Adverse Events (CTCAE) criteria before the start and upon completion of radiotherapy and at 3-, 12-, and 24-months post completion of radiotherapy.

Study Findings

Of the 163 patients enrolled to date, 132 (mean age: 70 years, range 50-82 years) have finished radiotherapy and 92 of those have completed their 3-month post-radiotherapy assessment. Fifty-two percent received 60Gy (n=69) and 48% (n=63) received 62Gy. At completion of radiotherapy, ≥2 grade toxicity was reported by 5% (n=6) of participants for GI and 7% (n=9) for GU, whereas at three months following completion of radiotherapy, ≥2 grade toxicity was reported by none and 1% (n=1) of participants for GI and GU, respectively.

Beyond the valuable information on the utility of HFRT in African populations, the HypoAfrica study has also provided a crucible for identifying barriers and facilitators to implementing HFRT and conducting high-quality multicenter - or otherwise large-scale - clinical trials in Africa that involve HFRT. The HypoAfrica team has reported the challenges encountered during this study and the solutions employed to overcome these challenges[7]. These findings can be considered in facilitating the broader adoption of HFRT in Africa and other low-resource settings[7]. The preliminary work using telehealth for the HypoAfrica trial has highlighted barriers and facilitators to such a telemedicine approach for radiotherapy.

Conclusion

- Africa's progress in cancer research is linked to government commitment and the increasing number of research partnerships and collaborations. In the past 20 years, many higher learning institutions in sub-Sahara Africa have developed mutually beneficial research collaborations with universities and research institutes in high income countries. These collaborations have enabled universities in SSA to apply for grants funded by funding agencies in the High Income Countries.
- Another positive development is the commitment of African governments to provide funding and conducive environments for research. Overall, there are all the signs that SSA is catching up in cancer research.

Conflict of Interest:

None of the authors has any conflict of interest to disclose.

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