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Review Article

Unmet Needs in Oncology Clinical Research and Treatment in Africa: Focus on Ghana

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Abstract

Cancer incidence is increasing worldwide and is a major cause of mortality. The relative magnitude of the increase is remarkably high in low human development index (HDI; 95%) and medium HDI (64%) countries. On the African continent, a corresponding increase in cancer burden is predicted, particularly for sub-Saharan Africa. Current epidemiologic data indicate that mortality rates of certain cancers, such as breast and cervical cancers, in sub-Saharan Africa are the highest in the world, and the cancer risks are broadly comparable to the risks in high-income countries, such as the United States and Europe. Although emerging data alludes to the unique genetic profile of cancer in African populations, most cancer therapies are introduced to Africa without confirmatory clinical trials. Therefore, there is an increasing need for clinical trials directed toward prevention, screening, diagnosis, and identification of innovative treatments in the African context. This review will discuss the increasing cancer burden in Africa, with a particular focus on Ghana, unmet clinical needs in cancer, current medical systems, clinical trial regulatory systems, and challenges to clinical trial recruitment.

Key words: Ghana; sub-Saharan Africa; cancer burden; clinical trial; disparities in cancer care.

Implications for Practice

This review reports on the increasing cancer burden, unmet clinical needs in cancer, current medical systems, clinical trial regulatory systems, and challenges to clinical trial recruitment in Ghana. In 2018, GLOBOCAN estimated 18.1 million new cancer cases and 9.6 million cancer deaths. The International Agency for Research on Cancer projects that an estimated 21.7 million cancer cases will be recorded globally by 2030 with cancer-related deaths projected to hit 13 million. The degree of economic development and associated social and lifestyle factors impact the incidence of different cancers across countries. In the African continent, including in Ghana, cancer burden is increasing, and Africa's cancer mortality rate is predicted to double by 2040, underscoring the urgent need for cancer-related initiatives directed toward prevention, screening, diagnosis, and access to treatment innovations.

Globally, cancer incidence is increasing and is a major cause of mortality. In 2020, based on the GLOBOCAN estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer (IARC), an estimated 19.3 million new cancer cases occurred worldwide, resulting in 9.9 million deaths (excluding nonmelanoma skin cancer).[1] The age-standardized cancer incidence rate was estimated to be 201.0 and the age-adjusted mortality rate was 100.7.[2] GLOBOCAN projects that an estimated 28.4 million cancer cases will be recorded globally in 2040, an astronomical 47% increase from 2020, which will likely be paralleled by increases in mortality rates.[1] The relative magnitude of increase is remarkably high in low human development index (HDI; 95%) and medium HDI (64%) countries.[1]

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Cancer Burden in Africa

Africa represents the second largest population in the world; by 2050, more than half of the anticipated growth is projected to occur in Africa, with an estimated 1.3 billion people expected to be added between 2017 and 2050.[3] Cancer burden is increasing in Africa; GLOBOCAN estimated 1 109 209 new cases in the African continent alone in 2020, with 711 429 resultant deaths. The age-standardized cancer incidence rate in Africa is estimated to be 132.1 and age-adjusted mortality rate is 88.8.[2]

Incidence rates of certain cancers are higher in Africa, specifically in sub-Saharan Africa, compared to the United States and Europe. The age-standardized incidence rates of Kaposi's sarcoma (KS) in Africa are approximately 10 times higher than the United States and cervical cancer rates are about 5 times higher, both of which are linked to infectious etiologies (Fig. 1).[2] Higher rates of triple-negative breast cancer are diagnosed in women of African descent than other ethnicities.[4] Malawi in sub-Saharan Africa has the world's highest incidence rate of cervical cancer, with human papilloma virus (HPV), human immunodeficiency virus (HIV), and smoking, implicated as causative factors.[5] Although KS is a relatively rare cancer worldwide, it is endemic in sub-Saharan Africa, with KS-associated herpes virus regarded as the etiologic agent.[6] The incidence rates of liver cancer including hepatocellular cancer and cholangiocarcinoma are high in northern and western Africa.[1]

In terms of cancer-related mortality, rates (all ages) in sub-Saharan Africa are higher for breast cancer, prostate cancer, cervical cancer, liver cancer including cholangiocarcinoma, stomach cancer, esophageal cancer, and KS compared to the United States (Fig. 1).[2] Breast cancer-related mortality rates in sub-Saharan African regions are the highest in the world, which was attributed to weak health infrastructure, leading to late-stage presentation.[1] For example, the 5-year age-standardized breast cancer survival was 66% in sub-Saharan African countries (2008 through 2015). For reference, between 2010 and 2014, the 5-year age-standardized breast cancer survival rate was above 85% for cases diagnosed in the United States and several European countries.[1,7] In terms of late-stage presentation of breast cancer, the majority (77%) of all staged cases in sub-Saharan Africa presented at stage III/IV, highlighting the need to promote early detection followed by timely and appropriate treatment interventions.[8] Disproportionate to incidence rates, prostate cancer is the leading cause of cancer death among men in sub-Saharan Africa.[1] Malawi in sub-Saharan Africa also has the world's highest regional mortality rate from cervical cancer, with lower HDI levels and poverty largely accountable for the global disparity.[1]

Moreover, of concern, an emerging epidemiologic transition indicates that infection-related and poverty-related

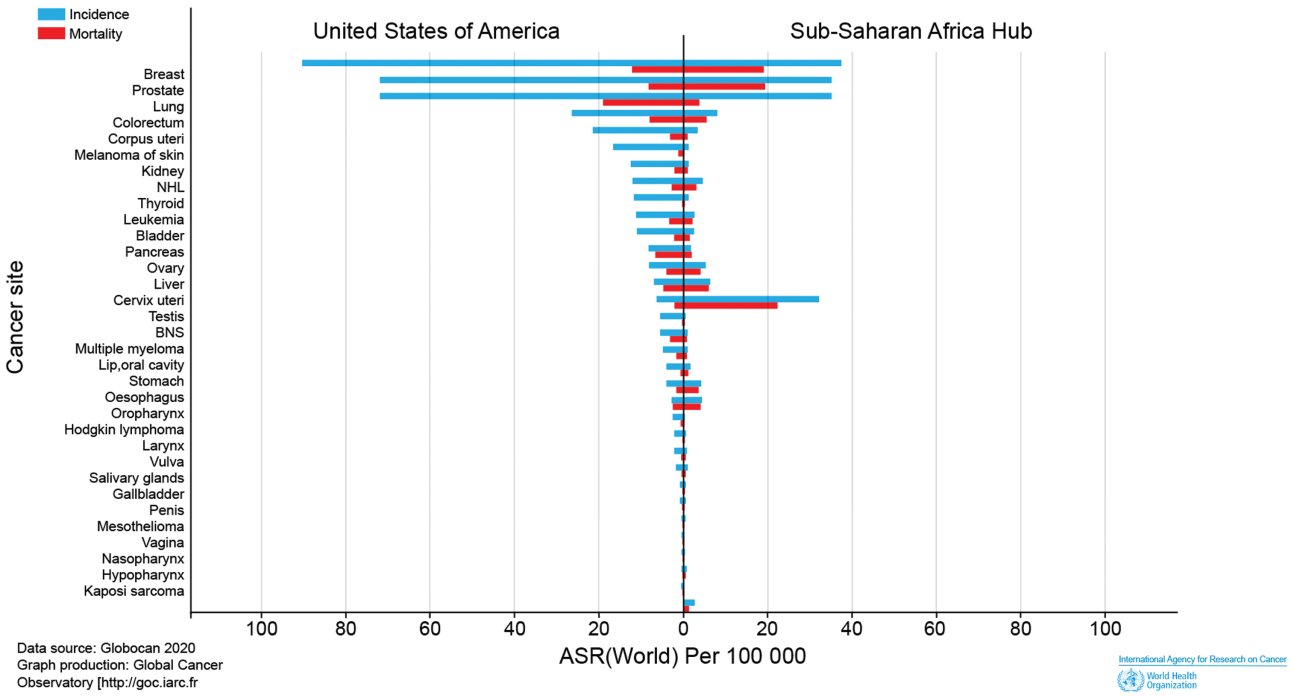

Figure 1. Estimated age-standardized incidence and mortality rates in 2020 (both sexes, all ages).

cancers are being displaced by cancers that are common in developed countries such as cancers of the breast, lung, and prostate, which correlate with marked increases in cancer risk factors of high-income countries such as diabetes, obesity, smoking, and physical inactivity. These trends underscore the need for strong advocacy and concerted efforts to build healthcare infrastructure and programs to facilitate dissemination of cancer prevention measures and the provision of cancer care in transitioning countries such as Ghana.[1]

The grim cancer statistics in Africa may be the result of many complex and interrelated factors, including demographic expansion, aging, changing risk factor profiles, inadequate health care systems and, potentially, the unique tumor genetics and pathobiologies of cancer in individuals of African descent. In Africa, urbanization, dietary patterns, obesity, decreasing physical activity, increasing alcohol consumption, and fertility transitions, characterized by delayed or decreased childbearing, have been implicated in the increasing incidence of cancers.[9-11]

Cancer Burden in Ghana

In a population of more than 31 million Ghanaian people, GLOBOCAN estimated 24 009 new cancer cases in 2020, with 15 802 resultant deaths. The age-standardized cancer incidence rate was estimated to be 115.9 and the age-adjusted mortality rate was 80.6.[2] It is notable that the primary data source for the cancer statistics in Ghana is a single registry (Kumasi Cancer Registry) that was applied to the 2020 population. Therefore, the true cancer burden may be higher than the current cancer incidence and mortality rate estimates, in part because rural communities are under-represented and because there is incomplete coverage of cancer incidence in urban areas and saturation of coverage has not yet been reached. For example, over the past decade, cancer registrations in the Kumasi Cancer Registry have increased each year, as the registry has increased its coverage of healthcare facilities in the metropolis.

GLOBOCAN estimated the top 6 cancers in Ghana in 2020 to be breast, liver, cervical, prostate, non-Hodgkin's lymphoma, and ovarian cancers.[2] A single-institution study in Ghana found breast cancer affected mostly young pre-menopausal women who have unfavorable prognostic features and are unlikely to respond to hormonal therapy.[12] HPV infection is known to be the primary cause of cervical cancer among sexually active women in Ghana.[9]

Major Cancer Risk Factors and Barriers to Cancer Care in Ghana

Several cancer risk factors have been identified in Ghana; higher prevalence of chronic viral hepatitis B (HBV) and hepatitis C, KS, HPV, cytomegalovirus, and Epstein-Barr virus infections have been reported, correlating with etiologies of certain cancer types such as liver, KS, and cervical cancer.[13,14] In Ghana, a report indicates that 33.2% of men and women are affected by overweight or obesity, more than 85% of the population consume less than the recommended 5 daily servings of fruits and vegetables, and over 65% of those living in rural areas use alcohol and tobacco products.[9,15] Also, geographical location, occupational settings, heavy metal contamination, and second-hand smoking have been identified as risk factors for cancer in Ghana.[16]

A recurring theme in Africa, including Ghana, is that many of the prevalent cancers are either preventable (eg, cervical cancer, liver cancer, and KS) or could be managed more effectively with early detection and treatment (eg, breast cancer, liver cancer, colorectal cancer, and prostate cancer). With strong public education and vaccination programs these preventable cancers, although they cannot be completely eliminated, could be substantially reduced by better control of risk factors. For cancers that can be more easily detected by screening, stronger advocacy for early detection may improve outcomes. However, the majority of Ghanaian women with cervical cancer present with advanced disease; similarly, women with breast cancer also present with late-stage disease; and liver cancer is usually diagnosed at a near-terminal stage. The delayed presentation may be attributed to the lack of national breast, cervical, and liver cancer screening programs, the poor healthcare system and infrastructure, low coverage of screening services, and lack of access to health facilities in Ghana. Although HBV vaccination is becoming an integral part of Ghana's immunization program and may contribute to reducing the incidence of liver cancer, the birth dose of HBV vaccine is still not included in the national vaccination strategy. Uptake of HPV vaccination for prevention of cervical cancer has also been found to be low.[17] Contributing socioeconomic factors may include low levels of education, lack of awareness of disease and appropriate screening practices, perceptions and attitudes based on cultural and religious beliefs, and ease of access to faith healers and traditional and herbal practitioners even in the urban and semi-urban communities.[17,18] For example, despite the high prevalence of prostate cancer in Ghana, low awareness of the signs and symptoms of prostate cancer persists among Ghanaian men.[18]

Molecular Profiling

In Ghana, molecular and genetic profiling are not routinely conducted in clinical practice, and is restricted to certain cancers. For example, clinical biomarker testing for hormone receptor status in breast cancer is not routinely offered in clinical practice in Ghana, which is largely attributed to limited local expertise in immunohistochemistry and the perceived expense of testing and partly due to lack of adoption of test standardization and quality assurance approaches.[19] Consequently, molecular/genetic tests are typically sent to out-of-country laboratories, which are associated with higher costs, underscoring the need for local testing facilities.[19] The lack of investment in molecular profiling also creates a substantial barrier to the adoption of targeted approaches based on precision medicine that have revolutionized cancer care across the globe.[20]

Inequity in Data Availability in Africa

At present, there is a major inequity in the availability of high-quality, local health data in Africa in general, including in Ghana, which has direct consequences for the corresponding robustness of cancer statistical data. Cancer registries are the primary sources of cancer statistics, so the accuracy of estimates and predictions is dependent on the quality of data in these source registries. In response to a global initiative for cancer registry development, the African Cancer Registry Network (AFCRN) was established in 2012 as a regional consortium to support African cancer registries with expertise and to help them surmount challenges and barriers.

Data sources for epidemiological analyses are from 2 main types of cancer registries, hospital-based and population-based. While hospital-based cancer registries (HBCR) track cancer diagnosis and/or treatment with pertinent patient demographic and disease information to map the types of cancer occurring in the community, they may not capture differences in the patterns of cancer occurring in the population as a whole. This is largely because many patients lack access to hospital care or are not treated in hospitals for a host of reasons. Population-based cancer registries (PBCR) track cancer cases occurring in a population and represent the gold standard for cancer incidence reporting. Unlike HBCRs, they collect data through outreach to all potential places a patient might seek cancer care, including physicians' offices, clinics, and laboratories. While PBCRs are desirable, it is well-recognized that establishing PBCRs is challenging in developing countries and HBCRs can be useful in that context.

Indeed, PBCRs cover only 1% of Africa's population compared to most other world regions; 100% population coverage was reported in 47 countries in Europe, Asia, Central and South America, Oceania, and Africa.[7,21] Also, registry coverage (PBCR and/or HBCR) among African countries is highly variable and ranges from approximately 2.3% of the population in Kenya to 100% in Gambia. Ghana scored 8 out of 10 (worst) in terms of the quality of national incidence data reflecting that estimates of incidence are based only on local data on the relative frequency of different cancers.[22] The GLOBOCAN review of cancer incidence across 5 continents indicated that the quality of the incidence estimate for Ghana was F, the lowest classification for inclusion, signifying the worst data quality for inclusion in the analysis.[22]

Recognizing the importance of reducing the incidence and impact of cancer in Ghana, a policy document for cancer control strategy between 2012 and 2016 was published that outlines the establishment of PBCR to form the basis of cancer data research and surveillance.[9]

Medical Systems in Ghana

The current medical system in Ghana encompasses national comprehensive care centers as well as public, regional, private, and university medical centers. Currently, there are 2 comprehensive public cancer care centers, Komfo Anokye Teaching Hospital (KATH, Kumasi) and Korle Bu Teaching Hospital (KBTH, Accra). These 2 national comprehensive cancer hospitals serve as the main conduits for 2 national registries in Ghana, the Kumasi Cancer Registry and the Accra Cancer Registry, which are members of the AFCRN. The Kumasi Cancer Registry includes KATH and was established as the first PBCR in Ghana in 2012 to provide information on cancer cases seen in the city of Kumasi in the Ashanti Region of Ghana, which has a coverage population of 5 924 498 (based on the 2020 census data made available by the Ghana Statistical Service).[23] The Accra Cancer Registry covers the Greater Accra region, with a population of 5 055 883 (based on 2020 Ghana Statistical Service census data)[23]; its primary source is the KBTH followed by the Ghana Sweden Medical Center.[22] The 2 registries collect data routinely for cancers reported among residents in their coverage area from multiple sources, including KATH and KBTH, major public hospitals in the region, pathology laboratories (private and public), and the Births and Deaths Registry.

In terms of national health infrastructure, the 2017 *Facts and Figures* released by the Ghana Health Service indicates that there are 267 national hospitals, 855 health centers, and 1003 clinics in Ghana. Of note, the Women's Cancer Center at HopeXchange Medical Center (Kumasi) is a modern hospital, research center, and medical training facility that is designed to serve as a regional hub for medical training, research, and patient care to address public health priorities in sub-Saharan Africa. Cape Coast Teaching Hospital, Ho Teaching Hospital, and Tamale Teaching Hospital are 3 other major referral hospitals in Ghana.[24]

Clinical Trial Participation Among African Countries

It is well-established that oncology clinical trials are needed to develop innovative interventions for cancer prevention, screening, diagnosis, treatment, and survivorship. In the context of evidence suggesting that the genetic basis of cancer in individuals of African ancestry may be different from their counterparts from other races and ethnicities, it is imperative that clinical trials are conducted in this population. Deep whole-genome sequencing of 910 individuals of African descent showed that the African pan-genome contains approximately 10% more DNA than the current human reference genome, indicating that the standard human reference genome lacks a substantial amount of DNA sequence compared with the African population.[25] Therefore, drugs tested in European/American or Asian populations cannot be assumed to be effective in the African population. However, the majority of cancer therapies are introduced to Africa without supportive clinical trials to confirm their safety and efficacy in the African context, thereby limiting optimal cancer prevention and treatment decisions for individuals of African descent.

Unfortunately, despite the growing cancer burden in Africa, individuals of African descent are significantly underrepresented in cancer clinical trials in general. Even in the United States, the US Food and Drug Administration (FDA) estimated that only 5% of patients enrolled in clinical trials that led to the approval of new cancer drugs in 2020 were of African descent.[26] In total, there were only 109 open, active and registered African oncology trials identified in 2019 on multiple online registries including ClinicalTrials.gov, Pan African Clinical Trials Registry, South African National Clinical Trial Register, World Health Organization International Clinical Trials Registry Platform, and European Union Clinical Trials Register.[27] By comparison, 7557 active (recruiting) oncology clinical trials are registered in the United States (at the time of drafting the manuscript, July 2021) on ClinicalTrials.gov alone, reflecting the global disparities of clinical trials relating to cancer in the African population.[28]

Of the 109 open African oncology clinical trials, the majority were conducted in Egypt (n = 45), South Africa (n = 11), Algeria (n = 10), and Kenya (n = 9); there were only 2 trials registered in Ghana.[27] Nearly half of the African oncology clinical trials were sponsored by academic institutions defined as sole universities and university-affiliated hospitals (n = 52), which were primarily institutions in the United States and Europe; 33 trials were sponsored by pharmaceutical companies, and 10 trials by research organizations.

Challenges of Conducting Clinical Trials in Africa

The challenges of conducting clinical trials in Africa are manifold but largely relate to 2 overarching factors: system level

(eg, disparities in research priorities, funding, regulatory standards, research and development capacities, availability of skilled personnel, inadequate infrastructure needed to manage clinical trials) and patient level (eg, low awareness, culture, traditional medicine).

A major barrier to conducting clinical trials is inadequate funding due to low prioritization, both for oncology and the conduct of clinical trials in general, and disparity in health resource allocation. Despite the increasing cancer burden, many sub-Saharan African countries consider infectious diseases such as HIV/AIDS, tuberculosis, and malaria to be the main priority for clinical research, which are accompanied by government policies in place for the control of these diseases.[29] Moreover, government funding was reported to be restricted to indirect support such as staff salaries, infrastructure, and provision of subsidized equipment, and did not extend to funding health research programs.[29] It is estimated that only a fraction of the cost needed to sustain the public health sector in Africa is available for cancer research.[30]

International funding for oncology clinical trials in Africa is predominantly from the European and Developing Countries Clinical Trials Partnership, the Bill & Melinda Gates Foundation, and the US National Institutes of Health (NIH); however, such funding is often available only to African countries with a strong clinical trial presence and does not extend to other sub-Saharan African countries, such as Ghana. For example, South Africa is the most frequent recipient of NIH funding.[27] Moreover, it must be noted that the regulatory needs and funding received also differs based on whether the clinical trials are prevention or therapeutic trials. For example, the Bill & Melinda Gates Foundation primarily funds African clinical trials that are focused on cervical cancer prevention.

Consequently, the required infrastructure for clinical trial conduct in the majority of African countries is suboptimal and personnel training is inadequate. Lack of human resources was considered to be a critical factor, with a shortage of skilled research staff that was attributable to few opportunities to gain experience and few local experts who could train staff.[29,31,32] A lack of laboratory capacity, regulatory and pharmacovigilance systems, and local training programs were also reported among stakeholders in sub-Saharan African governments, research institutions, and international organizations.[30]

Due to the constraints relating to human, financial, and infrastructural resources, quality assurance in African clinical trials can be an important issue. The capabilities of African clinical research teams to meet international Good Clinical Practice (GCP) standards, including institutional review boards (IRBs), are limited.[27] According to the American Society of Clinical Oncology (ASCO) statement on *Minimum Standards and Exemplary Attributes of Clinical Trial Sites*, a quality research site complies with the International Conference on Harmonization (ICH) GCP guidelines, the internationally accepted gold standard for designing, conducting, recording, and reporting clinical trials.[33] The ICH-GCP seeks to protect the rights, safety, and well-being of participants and ensures clinical trial data quality and integrity. Supplemental attributes of a clinical trial site include diversification of the clinical trial site portfolio to offer a broad range of options and fully utilize site resources, high accrual activity, stakeholder participation in the trial development process that facilitates understanding of trial processes and fosters sharing of resources and support, maintenance of high educational standards via appropriate certifications and continuing education, quality assurance using routine self-audits for continuous improvement, multidisciplinary involvement in the clinical trial process to increase the site's capacity and optimal patient care, and promotion of clinical trial awareness programs among physicians.[33]

However, despite adopting the International Ethical Guidelines for Biomedical Research involving Human Subjects as the minimum requirement in 2001, these guidelines are not universally used in Africa and different countries in sub-Saharan Africa follow different practices.[34] Although all African countries have functioning medicine review agencies, clinical trial oversight authority is available in only 17 of 55 African countries, underscoring the need for more mature regulatory frameworks at the institutional and national levels.[35]

Moreover, following GCP guidelines with the informed consent procedure presents logistical challenges in Africa due to several reasons. Readability and comprehension of the informed consent document can pose an issue due to literacy variance among participants and challenges of translating the document into several languages and dialects spoken in the continent.[36] An interview-based study of 60 clinical trial staff at different levels in clinical research centers indicated that the guideline's requirements for informed consent are unimplementable, too restrictive, and impractical for the African population.[37] Major difficulties were cited in obtaining written and individual consent in a population with an oral culture, finding impartial witnesses for less-educated individuals or legally acceptable representatives for children, and guaranteeing voluntariness and full understanding of the consent given.[37] Additional oversight above and beyond what a general IRB would consider may be required for this vulnerable patient population.

Moreover, patient recruitment might represent a challenge. Compared to the Western world where clinical trial information can be accessed from platforms such as ClinicalTrials.gov, the European Union Clinical Trials Register, or social media platforms, information on open oncology clinical trials is not easily accessible to the general public in Africa, including both clinicians and patients.[27] This may largely be related to the socioeconomic and cultural landscape of Africa; in particular, the internet penetration rate, although increasing, is low (eg, only 50% in Ghana in 2021).[38] A relatively high preference for alternative traditional medicine is recognized in sub-Saharan Africa.[39] Traditional medicine is largely used due to its perceived low cost, alignment with sociocultural, religious, and spiritual values, and dissatisfaction with modern healthcare.[39]

There may also be ethical implications of conducting clinical trials in Africa. Patients in limited resource settings such as Africa are a vulnerable population that may consent to clinical trial participation in the hope of obtaining access to ancillary care provided by clinical trials.[40,41] They may have an optimistic expectation of better outcomes from clinical trials, without full comprehension of the associated risks and the inherently experimental nature of clinical trials.[42] Patient interest in enrollment in clinical trials may also be motivated by lack of insurance coverage and exorbitantly high out-of-pocket costs of cancer drugs. It has been estimated that cancer care out-of-pocket cost might be as high as Egyptian Pound 50 000 (US $5 600) per month, which most underprivileged patients in developing countries in sub-Saharan Africa cannot afford.[27]

Pharmaceutical Company-Sponsored Clinical Trials

Despite the identified challenges to conducting clinical trials in Africa, there is increased interest in pharmaceutical-company sponsored clinical trials, which has been attributed to (1) a fast-growing, largely uninsured, and treatment-naïve population; (2) the large pool of diseases within the population; (3) limited but attractive research infrastructure; (4) lower costs of conducting trials.[43]

However, a recent study found that pharmaceutical companies sponsored only 33 of 109 oncology clinical trials in Africa; by contrast, 3133 of 7557 active oncology clinical trials were registered on ClinicalTrials.gov as industry-sponsored in the United States at the time of manuscript writing. Industry-sponsored clinical trials were generally not conducted in most countries in sub-Saharan Africa and were primarily restricted to South Africa and a few countries in the northern region, including Egypt, Algeria, Nigeria, and Kenya.[27,28] Higher pharmaceutical company engagement in these countries was attributed to heavier investment of these countries in their overall research capacity and infrastructure development to host and manage clinical trials, including the presence of established IRBs, Medicines Regulatory Authorities, Clinical Trial Units, and GCP quality management systems. The larger number of cancer trials in these countries attests to the value boost added by quality assurance.[27]

Recommendations to Pharmaceutical Companies

Recognizing the unique challenges that sponsors of oncology clinical trials in Africa would have to face, key experts have defined strategies and recommendations to mitigate challenges and encourage sponsors to conduct clinical trials in Africa, which were broadly classified into funding, regulation, capacity building, an Africa-centric approach, and patient engagement (Fig. 2).[35] It is imperative that adequate funding to conduct clinical trials in the African continent be obtained, sourced from either the government, academic institutions, or pharmaceutical sponsors. It was recommended that sponsors facilitate capacity building at all levels of cancer care including infrastructure investment, healthcare provider training, and establishment of African sites capable of conducting clinical trials that meet international standards. Given the entrenchment of traditional medicine in the African healthcare landscape and often times being the first point of contact for many cancer patients, the relationship with traditional medicine practitioners may be leveraged for capacity building in clinical trials.

Ghana and other sub-Saharan African countries have regulatory guidelines and agencies that enforce them. Establishing or following existing regulatory guidelines is thought to be a top priority for sponsors favoring clinical trials in Africa. Initiating earlier and improved communication with regulatory bodies at a national level was recommended to ensure a smooth clinical trial process.[31] Ghana has incorporated clinical trial regulations and oversight authorities into its national health and research systems, with the establishment of the Ghana Food and Drug Authority.[44] The Ghana FDA currently regulates all clinical trial activities in the country and must issue a clinical trial authorization certificate before a clinical study can commence.

It is imperative that clinical trial sponsors in Africa foster partnerships with government departments of health and academic institutions to align with oncology research priorities.[27] Lack of understanding of the importance and benefits of research by policymakers has been cited as a major barrier to the development of clinical research.[29] Coordinated engagement with all relevant stakeholders, including African government agencies and cancer clinicians, pharmaceutical companies, international cancer experts, and patients with cancer may be necessary.

Recognizing the unique and varied cultural and socioeconomic fabric of Africa, an Africa-focused strategy for clinical trial management is encouraged. To promote stakeholder engagement, it is of pivotal importance that the existing burden of cancer and unmet needs in African countries is aligned with the research priorities of oncology clinical trials. As the adoption of digital technologies in Africa

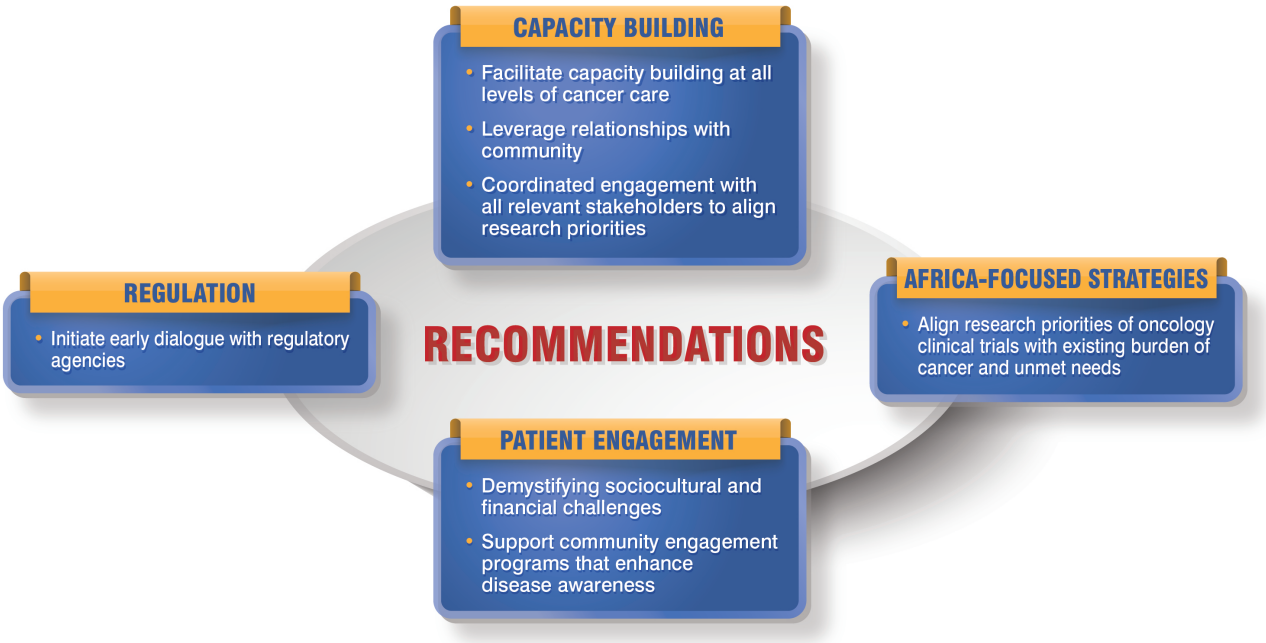

Figure 2. Recommendations to pharmaceutical companies.

increases, pharmaceutical companies may follow the trend and consider sponsoring/adopting digital health approaches to clinical trials.

Patient engagement is critical to demystifying sociocultural and financial challenges, improving patient education and awareness, and promoting patient recruitment and retention in clinical trials. Patient education measures are encouraged to dispel myths, misconceptions, and stigma associated with cancer, cancer research, and cancer clinical trials. Sociocultural barriers may be mitigated by collaborating with community healthcare providers. Since nurses are the frontline health workers who are in regular contact with patients in many of these communities, engaging in nurse-led patient navigation models to help engender trust, provide patient education, mitigate barriers relating to language and sociocultural beliefs and initiate other targeted interventions is recommended. Community engagement programs that enhance disease awareness and provide a patient voice must be established.

Conclusion

Despite the recognized high cancer burden in Africa, there is a dearth of oncology trials overall in the continent, including Ghana, and substantial underrepresentation of individuals of African descent in oncology clinical trials globally. Clinical trials are imperative to confirm the safety and efficacy of currently approved drugs in the African population and develop novel personalized therapies specific to individuals of African descent. Several challenges and barriers to conducting clinical trials in Africa are recognized in the context of inadequate funding, infrastructure, appropriately trained clinical staff, adherence to GCP guidelines, and regulatory hurdles as well as impediments relating to socioeconomic and cultural factors. Prospective sponsors of clinical trials, whether pharmaceutical companies or academic institutions, must adequately address these challenges to further oncology clinical research in Africa, including Ghana.

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Conflict of Interest

Lewis Roberts: Ariad Pharmaceuticals, Bayer, BTG International, Exact Sciences, Gilead Sciences, Glycotest Inc., RedHill, TARGET PharmaSolutions, Wako Diagnostics, QED Therapeutics, TAVEC, AstraZeneca, Merck (C/A, RF); **Clayton Yates:** Riptide Biosciences (C/A, RF, OI, IP), Amgen (H), QED Therapeutics (C/A); **Lisa Newman:** Genentech (RF); **Melissa Davis:** Patent pending for DARC as a tumor immunological marker (IP), Genentech, Touch Black Breast Cancer Patient Advocacy group, Bridge Bio Therapeutics (SAB); **Adalynn Harris:** Inivata Ltd (E); QED Therapeutics, Ipsen Biopharmaceuticals (E, formerly). The other authors indicated no financial relationships.

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Author Contributions

Conception/design, data analysis and interpretation, manuscript writing, and final approval of manuscript: All authors.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. Sung H, Ferlay J, Siegel R, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249.
2. International Agency for Research on Cancer fact sheets. Accessed September 7, 2021. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
3. United Nations. *World Population Prospects*; 2017.
4. Newman LA, Kaljee L. Health disparities and triple-negative breast cancer in African American women: a review. *JAMA Surg*. 2017;152(5):485-493.
5. Singh GK, Azuine RE, Siahpush M. Global inequalities in cervical cancer incidence and mortality are linked to deprivation, low socioeconomic status, and human development. *Int J MCH AIDS*. 2012;1:17-30. https://doi.org/10.10.21106/ijma.12
6. Cesarman E, Damania B, Krown SE, et al. Kaposi sarcoma. *Nat Rev Dis Primers*. 2019;5(1):9. https://doi.org/10.1038/s41572-019-0060-9
7. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37,513,025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. 2018;391:1023-1075. https://doi.org/10.1016/S0140-6736(17)33326-3
8. Jedy-Agba E, McCormack V, Adebamowo C, et al. Stage at diagnosis of breast cancer in sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Glob Health*. 2016;4:e923-e935.
9. Fei N, Choo-Kang C, Reutrakul S, et al. Gut microbiota alterations in response to sleep length among African-origin adults. *PLoS One*. 2021;16(9):e0255323. https://doi.org/10.1371/journal.pone.0255323
10. Moultrie TA, Sayi TS, Timæus IM. Birth intervals, postponement, and fertility decline in Africa: a new type of transition. *Popul Stud (Camb)*. 2012;66(3):241-258. https://doi.org/10.1080/00324728.2012.701660
11. Ajayi IO, Adebamowo C, Adami HO, et al. Urban-rural and geographic differences in overweight and obesity in four sub-Saharan African adult populations: a multi-country cross-sectional study. *BMC Public Health*. 2016;16(1):1126. https://doi.org/10.1186/s12889-016-3789-z
12. Ohene-Yeboah M, Adjei A. Breast cancer in Ghana. *Ghana Med J*. 2012;46:8-13.
13. Domfeh A, Wiredu E, Adjei A, et al. Cervical human papillomavirus infection in Accra, Ghana. *Ghana Med J*. 2008;42(2):71-78. https://doi.org/10.4314/gmj.v42i2.43596
14. Adjei AA, Armah HB, Gbagbo F, et al. Seroprevalence of HHV-8, CMV, and EBV among the general population in Ghana, West Africa. *BMC Infect Dis*. 2008;8(1):111. https://doi.org/10.1186/1471-2334-8-111

15. Ministry of Health. *National Strategy for Cancer Control in Ghana*; 2011.
16. Armah FA, Gyeabour EK. Health risks to children and adults residing in riverine environments where surficial sediments contain metals generated by active gold mining in Ghana. *Toxicol Res*. 2013;29(1):69-79. doi:10.5487/TR.2013.29.1.069.
17. Calys-Tagoe BNL, Aheto JMK, Mensah G, et al. Cervical cancer screening practices among women in Ghana: evidence from wave 2 of the WHO study on global AGEing and adult health. *BMC Women's Health*. 2020;20:49. https://doi.org/10.1186/s12905-020-00915-9
18. Yeboah-Asiamah B. Perceptions and attitudes about prostate cancer among male teachers in the Sunyani Municipality. *Afr J Urol*. 2017;23:184-191. https://doi.org/10.1016/j.afju.2016.12.003
19. Sayed S, Moloo Z, Wasike R, et al. Is breast cancer from Sub Saharan Africa truly receptor poor? Prevalence of ER/PR/HER2 in breast cancer from Kenya. *Breast*. 2014;23:591-596. https://doi.org/10.1016/j.breast.2014.06.006
20. Drake TM, Knight SR, Harrison EM, et al. Global inequities in precision medicine and molecular cancer research. *Front Oncol*. 2018;8:346. https://doi.org/10.3389/fonc.2018.00346
21. Bray F, Colombet M, Mery L, et al. *Cancer Incidence in Five Continents, Vol. XI (Electronic Version)*. International Agency for Research on Cancer; 2017.
22. Yarney J, Oti NOO, Calys-Tagoe BNL, et al. Establishing a cancer registry in a resource-constrained region: process experience from Ghana. *JCO Glob Oncol*. 2020;6:610-616.
23. Ghana Statistical Services. Accessed September 20, 2021. https://statsghana.gov.gh
24. Country Policy and Information Note - Ghana: Medical and healthcare issues. Accessed June 1, 2022. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/812958/Ghana_-_Medical_and_Healthcare_-_CPIN_-_v1.0__GOV.UK_.pdf https://www.ghanahealthservice.org/downloads/FACTS+FIGURES_2017.pdf
25. Sherman RM, Forman J, Antonescu V, et al. Assembly of a pan-genome from deep sequencing of 910 humans of African descent. *Nat Genet*. 2019;51:30-35. https://doi.org/10.1038/s41588-018-0273-y
26. US Food and Drug Administration: *2020 Drug Trials Snapshots Summary Report*. US Food and Drug Administration; 2019. Accessed September 20, 2021. https://www.fda.gov/media/145718/download
27. Odedina F, Shamley D, Okaye I, et al. Landscape of oncology clinical trials in Africa. *JCO Global Oncol*. 2020;6:932-941.
28. *Clinicaltrials.gov Industry-Sponsored*. Accessed July 6, 2021. clinicaltrials.gov/ct2/results?cond=cancer&term=&cntry=US&state=&city=&dist=&recrs=a
29. European & Developing Countries Clinical Trials Partnership (EDCTP). *African Mapping: Current State of Health Research on Poverty-Related and Neglected Infectious Diseases in sub-Saharan Africa*. Accessed September 20, 2021. http://www.edctp.org/web/app/uploads/2015/01/Report_on_the_current_state_of_health_research_-_Africa.pdf
30. Mellstedt H. Cancer initiatives in developing countries. *Ann Oncol*. 2006;17(Suppl 8):viii24-viii31. https://doi.org/10.1093/annonc/mdl984
31. Conradie A, Duys R, Forget P, et al. Barriers to clinical research in Africa: a quantitative and qualitative survey of clinical researchers in 27 African countries. *Br J Anaesth*. 2018;121(14):813-821. https://doi.org/10.1016/j.bja.2018.06.013
32. Franzen SR, Chandler C, Enquselassie F, et al. Understanding the investigators: a qualitative study investigating the barriers and enablers to the implementation of local investigator-initiated clinical trials in Ethiopia. *BMJ Open*. 2013;3(11):e003616. https://doi.org/10.1136/bmjopen-2013-003616
33. Zon R, Meropol NJ, Catalano RB, et al. American Society of Clinical Oncology statement on minimum standards and exemplary attributes of clinical trial sites. *J Clin Oncol*. 2008;26(15):2562-2567.
34. Puppalwar G, Mourya M, Kadhe G, et al. Conducting clinical trials in emerging markets of sub-Saharan Africa: review of guidelines and resources for foreign sponsors. *J Clin Trials*. 2015;7:23-34.
35. Graef FT, Okaye I, Oti NOO, et al. Operational strategies for clinical trials in Africa. *JCO Glob Oncol*. 2020;6:973-982.
36. Somers R, Van Staden C, Steffens F. Views of clinical trial participants on the readability and their understanding of informed consent documents. *AJOB Empir Bioeth*. 2017;8:277-284. https://doi.org/10.1080/23294515.2017.1401563.
37. Vischer N, Pfeiffer N, Joller A, et al. The Good Clinical Practice guideline and its interpretation –perceptions of clinical trial teams in sub-Saharan Africa. *Trop Med Int Health*. 2016;21(8):1040-1048.
38. Sasu DD. *Penetration Rate of Internet Users in Ghana 2017-2021*. Accessed July 6, 2021. https://www.statista.com/statistics/1171435/internet-penetration-rate-ghana/
39. James PB, Wardle J, Steel A, et al. Traditional, complementary and alternative medicine use in Sub-Saharan Africa: a systematic review. *BMJ Glob Health*. 2018;3:e000895e00089. https://doi.org/10.1136/bmjgh-2018-000895
40. Mfutso-Bengo J, Ndebele P, Jumbe V, et al. Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi. *Malawi Med J*. 2018;20:37-41.
41. Mensah KB, Mensah ABB. Cancer control in Ghana: a narrative review in global context. *Heliyon*. 2020;4;6(8):e04564.
42. Malan T, Moodley K. Phase 3 oncology clinical trials in South Africa: experimentation or therapeutic misconception? *J Empir Res Hum Res Ethics*. 2016;11(1):47-56. https://doi.org/10.1177/1556264616637736
43. Wemos Health Unlimited. *Clinical Trials in Africa: The Cases of Egypt, Kenya, Zimbabwe, and South Africa*. Accessed August 31, 2021. https://www.wemos.nl/wp-content/uploads/2017/07/JH_Wemos_Clinical-Trials_v5_def.pdf
44. Ghanaian FDA. *Regulation of Clinical Trials in Ghana*. Accessed September 20, 2021. http://www.fdaghana.gov.gh/images/stories/pdfs/Clinical%20Trials/REGULATION%20OF%20CLINICAL%20TRIALS%20IN%20GHANA.pdf