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Review Article

Pharmacogenetics and Precision Medicine in Resource-Constrained Settings: Challenges and Prospects

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Abstract

The deployment of emerging technologies and cutting-edge research has been a challenge in resource-constrained environments such as Africa due to several interlinked factors. The field of genomics has redefined biomedical advances since the completion of the first human genome project, showing the huge roles that inter-individual variations play in disease processes and their implication in clinical pharmacology. Until 2019, only about 2% of Genome Wide Association Studies represented Africa. With an estimated population close to one-fifth of the world as generated by the United Nations World Population Prospects in 2022, the underrepresentation of African ancestry in genomic research is concerning. Hence, it is paramount to put a spotlight on pharmacogenetics and precision medicine in Africa, given the genomic diversity that has been discovered so far, and the clinical advantages of tailored pharmacotherapy, even in the presence of traditional medical approaches. In this review, we highlighted the prospect of expanding precision medicine in Africa and the unique challenges that can lead to constraints in a resource-limited environment.

Key Words: *Pharmacogenetics, precision medicine, resource-constrained environment, sub-Saharan Africa.*

INTRODUCTION

Effective healthcare delivery systems are a major focus of several international organizations. The sustainable development goals (SDGs) formulated by the United Nations General Assembly in 2015, proposed: the eradication of extreme poverty, food security, good health, quality education, gender equality, clean water and sanitation, affordable and clean energy, sustainable economic growth and sustainable industrialization among others by the year 2030 (United Nations General Assembly, 2015). While these goals are laudable, implementation continues to be hampered in several resource-constrained settings. Africa was declared, based on the World Bank's analysis, as the world's poorest continent in 2013, accommodating more than 330 million poor people in 2012, which was however reported to have risen to 462 million people living in extreme poverty for the Sub-Saharan region in 2023, influenced by the COVID-19 pandemic, climate issues, and social conflicts (World Bank, 2012; Beegle *et al.*, 2016; World Bank, 2024). Challenges that have been proposed as being responsible for the slow economic growth in many African countries include endemic social unrest, widespread corruption, poor governance, unstable trade policies, and endemic diseases (Ghura *et al.*, 2001; Adeyeye *et al.*, 2023).

The dearth of infrastructure in many developing countries represents one of the most significant limitations to economic growth and the achievement of sustainable development goals (Caldero and Serven, 2010; Gaal and Afran, 2017). Although economic indices in developing nations, particularly in sub-Saharan Africa continue to experience a slow rate of improvement, the impediment that poor infrastructural support and financial systems pose have demonstrable impacts on cutting-edge medical research. Despite the myriads of challenges facing Africa, the emerging field of precision medicine offers a beacon of hope, promising tailored health care solutions to address the continent's complex health issues. Precision medicine is an innovative approach to tailoring disease prevention and treatment that takes into account differences in people's genes, environments, and lifestyles. With the increase in knowledge in molecular biology and pharmacogenetics, precision medicine has rapidly grown in popularity and requires implementation as a potential solution to the healthcare delivery challenges in Africa (Goetz and Schork, 2018). In this review, we have focused on the challenges and prospects of precision medicine in resource-constrained settings of sub-Saharan Africa.

PHARMACOGENETICS

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Pharmacogenetics (PGx) is a scientific tool that aims to improve pharmacotherapy using drug dosing or drug selection adapted towards the genetically determined metabolic profile of the individual to maximize efficacy and safety. Fredrick Vogel in 1959 introduced the term Pharmacogenetics (PGx) which he defined as the study of genetically determined variations in animal species that are revealed by the effects of drugs (Evans and McLeod, 2004). One of the key objectives of pharmacogenetics is to develop rational means of optimizing drug therapy to patients' genotypes. Over the years, published research has shown diverse applications of Pharmacogenetics.

The effect of genetic polymorphism on therapeutic and toxicological responses is dependent upon complex processes involving diverse proteins coded for by the genes. It is thought

that most genes contain variations in their nucleotide sequences developed during their evolution. Single nucleotide polymorphisms (SNPs) are the most common types of genetic variations found in the human genome (Bell, 2002; Abobaker et al., 2021; Guo et al., 2022; Kamal et al., 2024). Although other variations exist, SNPs are the most widely studied variations with many documented applications as shown in Table 1. Ron HN van Schaik and the IFCC Task Force on Pharmacogenetics, in a review article described the clinical applications of pharmacogenetics and PGx testing. In their report, the authors noted that there has been much progress in how genetics and genetic testing may influence drug response. The genetic testings described include applications of Thiopurine S-methyl transferase (TMPT), HLA-B*5701, CYP2D6, CYP2C9/VKORC1, CYP2C19, and others (Table 1).

Table 1:
Developments in Precision Medicine for Clinical Diagnostics

Test	Application	References
Thiopurine S-methyltransferase (TMPT)	TMPT genotyping is done before initiation of Azathioprine (used in Crohn's disease, dermatology, rheumatology, and solid organ transplantation) or 6-mercaptopurine (used in acute lymphoblastic leukemia) therapy.	(van Schaik, 2014)
HLA-B*5701	Testing is done before the initiation of abacavir therapy.	(Mallal et al., 2008)
CYP2D6	Pharmacogenetics testing is advocated as a tool to help in the appropriate dosing of antidepressants and antipsychotics. The testing has also been advocated to guide adjuvant therapy for breast cancer.	(Loovers and van der Weide, 2009; Mrazek, 2010; Murdter et al., 2010)
CYP2C9/VKORC1	Pharmacogenetics testing has been shown to have some benefit in guiding dose recommendations for warfarin therapy.	(Pirmohamed et al., 2013)
CYP2C19	CYP2C19 testing is useful in determining an individual's ability to activate clopidogrel.	(Geisler et al., 2011; Holmes et al., 2011; Zabalza et al., 2012)
CYP3A5	Testing is useful in guiding tacrolimus therapy.	(Elens et al., 2012; Kurzawski and Drozdziak, 2013)
DPYD	Testing has been proposed as a guide to patients receiving 5-Fluorouracil or capecitabine. It has been shown that about 50% of 5-FU and capecitabine toxicity can be predicted by Pharmacogenetics testing.	(van Schaik, 2014)

The Human Genome Project

Deoxyribose nucleic acid (DNA) contains all of the information required to synthesize cellular and extracellular structures and to regulate molecular processes in an organism. In humans, one copy of the double-stranded DNA is referred to as the haploid genome and consists of approximately 3x10⁹ base pairs in 23 separate molecules, each part of a different chromosome. The DNA directs the synthesis of the protein constituents of the cell through the genetic code. The human genome contains about 3 billion nucleotides with an estimated 30,000 to 40,000 genes which may code for about 100,000 different proteins (Chaffey et al., 2003). The increasing significance of genes in the pathogenesis and

pharmacotherapy of diseases was a major driver of the human genome project.

The human genome project was led by an international group of researchers to comprehensively determine the genetic sequences in the human genome. Planning of the project started in 1984 by the United States government and was launched in 1990. The first draft of the Human Genome, comprising about 85% of the genome was released on the 14th of April, 2003 and the whole genome was declared completed in January 2022 (Nurk et al., 2022). This project has had a tremendous impact on biomedical research globally.

Human genome research has made it possible to recognize the significance of gene mutations in people with various genetic diseases. This science has also been proven to have the potential to identify specific genes linked to various diseases and diverse responses to pharmacotherapeutic interventions. The full implications of the Human Genome Project are still being explored. A great deal of research has been done and is being done by researchers on different methods of using genomic data in the screening, diagnosis, and treatment of human diseases. The breast cancer genes that have been identified as risk factors for the development of breast cancer in genome-wide association studies (GWAS) provide an excellent example (Skol *et al.*, 2016). In a study by the Breast Cancer Association Consortium in *The New England Journal of Medicine* in 2021, 5 Protein-truncating variants in 5 genes (ATM, BRCA1, BRCA2, CHEK2, and PALB2) were associated with a risk of breast cancer. The authors concluded that these were some of the genes that are most clinically useful for inclusion on panels for the prediction of breast cancer risk (Breast Cancer Association Consortium, 2021). These projects have significantly promoted the establishment of what is today known as precision medicine.

Precision medicine and GWAS

Precision medicine enables the tailoring of treatment to the pharmacogenetic profiles of patients. This is based on the dynamics of systems biology and the use of predictive tools to help in the design of health interventions that can reduce disease risk factors and guide precision therapeutics. This concept has continued to receive increasing acceptance globally. Genome-wide association Studies (GWAS) examine unique DNA sequences of particular diseases in the genomes of patients. They have revealed a wide number of links between genomic variations and complex diseases. Machine-learning methods have been programmed to detect GWAS genes associated with known drug targets for several diseases. This approach is potentially useful for identifying drug repurposing opportunities (Cao and Moul, 2014). Johnson *et al.*, 2011 described two genetic loci containing SNPs that reached a genome-wide significance threshold suggesting novel genetic drug targets for blood pressure and hypertension (Chaffey *et al.*, 2003).

The various tools by which precision medicine seeks to achieve its goals are omics, pharmaco-omics, big data, artificial intelligence, machine learning (ML), environmental, social, and behavioural factors, and integration with preventive and public health (Naithani *et al.*, 2021). New chip-based technologies and large-scale sequencing, all based on the availability of human genome databases, have provided reliable information on single nucleotide polymorphisms. Ivan Merelli and colleagues in 2013 proposed a new bioinformatics approach (implemented as a web application named SNPranker 2.0) to support biological data mining in the analysis and interpretation of SNPs associated with pathologies. The system proposed can be used to design customized genotyping chips for disease-oriented studies and to re-evaluate GWAS results for disease-associated prioritization (Merelli *et al.*, 2013). Progress in precision medicine has continued exponentially in developed nations. Increasingly, it is being realized that precision medicine will provide better diagnosis, guide earlier interventions, and support more efficient drug development and better drug therapies.

While precision medicine research has resulted in the generation of vast genomic databases and gene-based technologies in developed nations, the case is different in resource-constrained countries of sub-Saharan Africa. Though there exists extensive literature on genomic research in general, most discussions focus on developed and high-income countries. Regarding the representation of African ancestry, Elizabeth Pennisi reported in a *Science Newsletter* that only about 10,000 whole genomes from Africa have been uncovered relative to over a million whole genome data available globally (Pennisi, 2021). As of 2019, Sirugo and colleagues discovered that only about 2% of African genomic data was represented in global genome-wide association studies (Sirugo *et al.*, 2019). For precision medicine to become a priority in Africa, there is need for more research and genomic databases that are applicable to her indigenous populations.

Precision medicine in Africa

Africa bears the largest burden of resource-constrained settings. The African population exhibits huge ethnic and genetic diversities which can be explored for disease pathogenesis and precision therapeutics. Pharmacogenetics which more specifically studies the impact of variations in a single or few genes on drug response has improved pharmacotherapy. In a 2020 review, Radouani *et al.*, summarized reports of the application of pharmacogenetics in the African population. This review highlighted the limited scope of pharmacogenetics research in Africa which only cuts across a few of the 54 countries despite the continent's immense diversity and population exceeding 1 billion, and captures only 15 of over 300 FDA labelled drugs with pharmacogenomic biomarkers (Radouani *et al.*, 2020). This underrepresentation emphasizes the critical need for extensive research initiatives to ensure optimal therapeutics and improved healthcare outcomes for diverse African populations.

Wood and colleagues in a report in 2005 investigated associations between genetic, linguistic, and geographic variations in Africa (Wood *et al.*, 2005). The authors typed 50Y chromosome SNPs in 1122 individuals from 40 populations representing African geographic and linguistic diversities. The results suggest a wide pattern of differentiation and gene flow in Africa as shown in Figure 1. (Zabalza *et al.*, 2012).



Figure 1.

Map of Africa. Contrasting patterns of Y chromosome and mtDNA variation

Figure 1. shows the approximate location of 40 populations typed for Y chromosome markers (●) and 39 populations surveyed for HSV1 sequence data (O). Three shades of grey on the map refer to the distribution of language families: Khoisan (light gray, southwest), Afroasiatic (light gray, north), Niger-Congo (medium gray), and Nilo-Saharan (dark gray). The circled regions include North, West, Central, East, and South Africa. Despite this wide variation in genetic diversity in many resource-constrained settings in Africa, precision medicine research has been slow on account of many challenges.

Precision Medicine in sub-Saharan Africa - Challenges: Poor Representation of African Ancestry

Genome-wide association studies have exposed different population-based genetic variants associated with adverse drug reactions. However, the significance of many variants in people of African descent is unknown due to the paucity of genomic research. This is also coupled with limited utility for reference panels, genotypic arrays, and algorithms that are programmed with robust data of African ancestry (Vergara *et al.*, 2018, O'Connell *et al.*, 2021). There may be the risk of inferring the genetic variation in sub-Saharan Africa from data obtained from Europe and Asia. However, with the discovery of unidentified genetic variants in the African population, this may not be a true reflection of genomes of African origin (Boyer, 2020).

Poverty

Healthcare funding in Africa is mostly patient-sorted, with the insurance system for essential healthcare services still largely limited (Cashin and Dossou, 2021). With the region responsible for an estimated two-thirds of the global extreme poverty level (29% of people in Africa live on \leq \$2.15 a day), the implementation of pharmacogenetics testing and precision medicine without substantial funding is largely constrained (World Poverty Map, 2024). In a review targeted at pharmacogenetics testing in the United Kingdom - a high-income country, cost was perceived as a major barrier to engaging the new medical technology. However, the context in which cost-effectiveness or cost-benefit was perceived was not explored (Jameson *et al.*, 2021). Although there is limited research assessing the cost implication of genetic testing in Africa, another review by Mikkat-Stevens and colleagues which mostly captured high-income countries revealed the costs of genetic testing and lack of insurance coverage as a barrier to precision medicine (Mikat-Stevens, 2015). Hence, the problem of cost is likely to be implicated in the sparing utilization of pharmacogenetics testing and precision medicine in Africa.

The out-of-pocket costs for pharmacogenetics testing for patients with little or no health insurance coverage can significantly limit its utilization, except it is perceived to be of considerable health advantages after failed therapies or adverse reactions. In the case external funding is explored in the sub-Saharan Africa region, delayed implementation due to financial control policies by the government or institution can restrain the transfer of funds between the sponsor and recipient. The possibility of follow-up funding is another unique concern (Baker, 2011; Adebamowo *et al.*, 2018).

Immediate Public Health Challenges

Sub-Saharan Africa accounts for one-quarter of the global disease burden; plagued with an increasing double burden of communicable and non-communicable diseases. The immediate usefulness of precision medicine in complex heterogenic diseases except for the acclaimed success story in oncology, is largely unexplored (Duffy, 2016; Maughan, 2017). Even so, the success of precision medicine technology in oncology is not generalized as its usefulness is limited in some types of cancers (Hogarth *et al.*, 2012; Fojo and Mailankody, 2014). With some of the sub-Saharan African regions still struggling with obtaining essential medicines, the high cost of precision medicine poses greater health inequality, also fueled by sociopolitical disequilibrium. There is the possible shift of precision medicine from population-level health challenges to the development of new drugs for minority groups requiring troubleshooting with their therapies because of unique pharmacogenes. Likewise, the wide-scale applicability of precision medicine may seem conflicting due to the multifaceted nature of public health issues (Ramaswami *et al.*, 2018).

Health system policies

In a workshop on understanding the disparities in access to Genomic Medicine, Katrina Armstrong, the physician-in-chief in the Department of Medicine at Massachusetts General Hospital reiterated the need to establish the effectiveness of pharmacogenetics testing to be able to accelerate the processes required for its implementation (National Academies of Science, 2018). The lack of cost-effectiveness analysis can delay the implementation of pharmacogenetics by primary healthcare policymakers and funders (Rigter *et al.*, 2020). Although South Africa has experienced some form of inclusion with the launch of direct-to-consumer genetic testing laboratories, structures to incorporate pharmacogenetic testing into the routine clinical workflow in hospitals are still lacking in most African nations (Mediclinic Southern Africa, 2024; Dandara *et al.*, 2019). Without the implementation of concrete structures involving physicians and other healthcare professionals, the clinical utility of pharmacogenetics testing may remain limited.

The impact of pharmacogenetic medicines on pharmaceutical industry revenue may present a dilemma. Targeted therapy drugs could potentially reduce revenue from blockbuster drugs, thereby affecting investment in research and development (Eisenberg, 2001, Fahim *et al.*, 2023). Nevertheless, there is an opportunity to leverage pharmacogenetics testing to reevaluate drug candidates that previously failed clinical trials due to safety or efficacy issues, or during post-marketing surveillance. This incentive may prompt the biopharmaceutical industry, one of the key players in delivering precision medicine, to prioritize the adoption of this technology (Jameson and Longo, 2015). However, conflicting interests between patients, funders/insurance companies, clinicians, and the biopharmaceutical industry may considerably limit the utility of precision medicines (Jameson and Longo, 2015).

Diagnostic and Infrastructural Deficiency

Routine laboratory procedures are sometimes neglected due to inadequate infrastructure and personnel, often leading to misdiagnosis; a literal picture of divining without seeds (Okeke, 2011). Hence, it may seem challenging to incorporate pharmacogenetics testing into conventional laboratory

practices. Also, the paucity of pharmacogenetics research output in hospitals and research institutions in Africa limits its standard implementation in clinical practices. Using research output and authorship between 2004 and 2013 as metrics, Adedokun *et al.*, showed the disparity of genomic research output amongst sub-Saharan African countries, with South Africa as the leading country for genomic research attributing to about 40 percent of the general genomic data output in Africa (Adedokun *et al.*, 2016).

While initiatives such as Human Heredity and Health in Africa established by the National Institutes of Health and the Wellcome Trust have expanded the reach of genomic expertise since inception, equitable access to research centres and standard laboratories and bioinformaticians still require scaling (Morris, 2023; World Health Organization, 2024). It is also notable that most of these initiatives focus primarily on the genomics of disease, and the field of pharmacogenomics remains largely unexplored (Dandara *et al.*, 2019). Likewise, there is a dearth of expertise in setting up bioethics procedures for sampling and carrying out the actual genetic testing and analysis.

Recommendations

Expanding Laboratory capacities and expertise

Limited diagnostic testing, routine use of empiricism, and underutilization of the available clinical tests are a common problem in most of sub-Saharan Africa. Likewise, the dearth of resources in diagnostic laboratories in sub-Saharan Africa, attrition of human capital, and the problem of misdiagnosis require a multidisciplinary approach of funding, training, and expansion of skilled healthcare workforce (Cohen, 2002; Petti *et al.*, 2006; Okeke, 2011). Otherwise, Pharmacogenetics testing which should be operated as a supplementary diagnostic tool for precision medicine, and not as replacement for conventional medical practices would suffer similar neglect as a problem of a bigger picture (Duffy, 2016).

Integrating awareness and training programmes within existing health systems to update clinicians, bioinformaticians and other healthcare professionals' knowledge of pharmacogenetics tests and regulations will improve the recommendation of precision medicine to patients when required (Zhong *et al.*, 2012; Jongeneel *et al.*, 2022). Pharmacists-led pharmacogenetic services can be explored to assist clinicians with their prescribing decisions and also expand the reach of information to patients (Pasternak *et al.*, 2020). Online genomics modules adapted by Mayor Clinic Centre for Individualized Medicines can be tested and modified to suit needs in sub-Saharan Africa to equip pharmacists on drug-gene interaction management (Formea *et al.*, 2014). Such training models can also be expanded to incorporate clinicians, nurses, and other medical scientists. African institutions should include innovative courses on pharmacogenetics and equip their clinical pharmacology departments with in-depth bio-analytical capabilities (Radouani *et al.*, 2020). More networks across research centres and academic health centers within the sub-Saharan Africa region with the inclusion of local investigators can help to enlarge the genomic research capacity.

Prioritizing Large Scale Pharmacogenetics Research

Large-scale initiatives in research and testing in pharmacogenetics are required for the smooth running of precision medicine in sub-Saharan Africa. Although there have been some studies to assess the prospect of pharmacogenetics testing in a few countries in sub-Saharan

Africa, general information on the clinical utility across regions is scarce (Tata and Ambele, 2020). Prescribers urgently need to acquire adequate and relevant knowledge of drug-drug, drug-gene, and drug-drug-gene interactions for the successful takeoff and continuous implementation of precision medicine in sub-Saharan Africa. While large-scale research is necessary to uncover novel gene variations and their frequency in different subregions, priority pharmacogenes of the cytochrome P450 family which have been documented to encode protein responsible for metabolizing about 90% of commonly prescribed medications should be given considerable attention (Wood *et al.*, 2005).

Structures to guide randomized clinical trials on pharmacogenetics biomarkers in research institutions and hospitals should be established to track the clinical effectiveness of pharmacogenetics implementation (Cavallari, 2017). Likewise, properly organized medical record systems is necessary for the implementation of pre-emptive pharmacogenetics testing (Tata and Ambele, 2020). Ajogbasile, 2022 and co-authors explored the discovery of biomarkers for artemisinin resistance of *Plasmodium falciparum* in Nigeria (Ajogbasile *et al.*, 2022). Expanding such clinical research and testing across sub-Saharan African regions, especially where the disease is endemic would be of great advantage.

Developing Simplified Bioinformatics Workflow

Lack of bioinformatics capacity has been an impeding factor to quality high-throughput research output and a vital aspect of precision medicine in resource-constraint settings. With the need for optimal data sharing and robust genetic mapping, it is imperative to document unique genetic variants of African origin with simplified bioinformatics workflows and computational platforms. The switch from text-based operating systems to graphical user interface (GUI) models which can be used with minimal coding experience, and hence more accessible to a wider range of users including clinicians and biologists, has been proposed to reduce repetitive menial workload and redirect the efforts of pure bioinformaticians to optimize useful analytical tools for precision medicine (Duffy, 2016).

Efforts such as the initiation of H3ABioNET as an extension of bioinformatics capacity building by the H3Africa program, the African Society for Human Genetics (AfSHG), the African Human Genome Initiative, and MalariaGEN are commendable. The African Pharmacogenomics Consortium aims to develop infrastructures that are equipped for pharmacogenomics phenotype analysis and genomic characterization. The reach of these initiatives is still limited to a few countries in the sub-Saharan African region and requires expansion across research institutions and laboratories in the region (Dandara *et al.*, 2019).

Strengthening Data Storage, Sharing, and Privacy

Genomic initiatives to harmonize pharmacogenetics data in sub-Saharan Africa are required urgently; this is suggested to ensure fluidity of information and data flow among researchers for the collective good. However, with this need arises the social, legal, and ethical challenges of data storage and usage. Drawing from the backdrop of scientific disparities and the concerns of genomic data ownership, it is imperative to establish standard policies governing genomic data sharing to bolster confidence in sample collection and its associated procedures (Christoffels and Abayomi, 2020). Likewise, fundamental training on African ethics as regards biobanking

should be undertaken by researchers and genetics specialists. So far, there have been efforts to guide procedures on biobanking by the H3Africa, 54Gene, and H3Africa (Christoffels and Abayomi, 2020).

Beyond the appropriate biobanking of samples, it is also necessary for sub-Saharan Africa to document robust metadata for optimal data representation which would help influence precision medicine policies in healthcare. The African Pharmacogenomics Consortium survey showed poor pharmacovigilance data which facilitates the dearth of information on the influence of genetic variants in adverse drug reactions (Dandara et al., 2019). The underrepresentation of Africa in the global case individual case safety reports submission to VigiBase, a database set up by the World Health Organization for international drug monitoring needs to be improved to track the growing number of gene-drug interactions. It is also expedient to complement the paper documentation with efficient clinical electronic record systems suitable for the African environment plagued with poor internet and electricity access (Odekunle et al., 2017). This would also help to better direct the efforts of pharmacogenetics testing and precision medicines in Africa (Ampadu et al., 2016).

Fostering Collaborations

Isolated research is not optimal for inferring global outcomes. One of the key outcomes of the Human Genome Project (HGP) was to pool over 2000 researchers from several countries and disciplines for collective results. Stemming from shared insights of a rich 25 years of big biology experience, a multidisciplinary approach is required to navigate the challenges that accompany biomedical research (Green et al., 2015). Likewise, this applies to the clinical translation of pharmacogenetics testing and personalized drug therapy (Zierhut et al., 2017).

African researchers should benefit from improving partnerships amongst themselves and globally to help troubleshoot systems and scale workable models for pharmacogenetics. Initiatives for collaboration within Africa which bodies like the H3Africa Initiative have chaperoned should be expanded to reach more countries in sub-Saharan Africa (Collins et al., 2003). Likewise, collaboration between genetics specialists and primary health care providers can help facilitate the transfer of knowledge to the community, and increase the chance of referrals of patients that require the genetic service (Kabata and Thaladar, 2023). Also, it is imperative to navigate the data-sharing barrier or genomic sovereignty policies that impede collaboration. Genomic sovereignty policy treats genomic material and data as a national heritage and regulates and restricts access to such outside the confines of the country's jurisdiction except with a government permit. This policy, which has operated in some sub-Saharan African countries like South Africa, has been argued to stall international collaboration and funding due to limitations such as the lack of clarity of the final authority in charge of granting access to data (Odekunle et al., 2017).

The Bermuda principle initiated by the Human Genome Project group which facilitates the sharing of large genome-data assemblies in public databases can be modified and integrated to suit pharmacogenetics in sub-Saharan Africa (Cook-Deegan et al., 2017). This can help balance the practice of genomic sovereignty as practiced in some countries as a means of protecting local data. This calls for partnership between bioethicists and local communities to ensure that sociocultural differences are considered in policy-making, the

usage of data, and necessary standards for informed consent design.

Conclusion

The emerging field of precision medicine offers a beacon of hope, promising tailored healthcare solutions to addressing the complex health issues in sub-Saharan Africa. However, there are challenges as highlighted in this write-up. These challenges surrounding the implementation of Pharmacogenetics and Precision Medicine in a resource-constrained environment such as Africa and the lack of genomic data for such an ethnically diverse population may lead to the lack of replication and clinical applicability of such revolutionary technologies. This may hamper the full realization of the value of genome architecture in disease processes and responses to pharmacotherapies in resource-constrained settings. It is thus paramount to intensify efforts on bridging genomic data gaps and exploring precision medicine in these settings.

Conflict of Interest

Authors declare no conflict of interest

REFERENCES

- Abobaker, A., Nagib, T. and Alsoufi, A., 2021. The impact of certain genetic variants (single nucleotide polymorphisms) on incidence and severity of COVID-19. *The Journal of Gene Medicine*, 23(2).
- Adebamowo, S.N., V. Francis, E. Tambo, S.H. Diallo G. Landouré, V. Nembaware, E. Dareng B.Muhamed, M. Odotola, T. Akeredolu, and B. Nerima. 2018. Implementation of genomics research in Africa: challenges and recommendations. *Global Health Action*, 11(1):1419033.
- Adedokun, B.O., C.O., Olopade, and O.I. Olopade. 2016. Building local capacity for genomics research in Africa: recommendations from analysis of publications in Sub-Saharan Africa from 2004 to 2013. *Global Health Action*, 9(1):31026.
- Adeyeye, S.A.O., T.J. Ashaolu, O.T. Bolaji, T.A. Abegunde, and A.O. Omoyajowo. 2023. Africa and the Nexus of poverty, malnutrition and diseases. *Critical Reviews in Food Science and Nutrition*, 63(5):641-656.
- Ajogbasile, F.V., P.E. Oluniyi, A.T. Kayode, K.O. Akano, B.B. Adegboyega, C. Philip, N. Ogbulafor, H.U.Okafor, S. Oguche, R.D.Wammanda, and , A.O. Mokuolu. 2022. Molecular profiling of the artemisinin resistance Kelch 13 gene in Plasmodium falciparum from Nigeria. *PLoS One*, 17(2):e0264548.
- Ampadu, H.H., J. Hoekman, M.L. de Bruin, S.N. Pal, S. Olsson, D. Sartori, H.D. H.G. Leufkens, and A.N. Dodoo. 2016. Adverse drug reaction reporting in Africa and a comparison of individual case safety report characteristics between Africa and the rest of the world: analyses of spontaneous reports in VigiBase®. *Drug safety*, 39:335-45.
- Baker, S. 2011. Genomic medicine has failed the poor. *Nature*, 478(7369):287.
- Beegle, K., Christiaensen, L., Dabalen, A., & Gaddis, I., 2016. Poverty in a Rising Africa. Washington, DC: World Bank. The World Bank, <https://openknowledge.worldbank.org/handle/10986/22575> License: CC BY 3.0 IGO. [Assessed 04 April, 2025]

- Bell JI. 2002. Single nucleotide polymorphisms and disease gene mapping. 2002. *Arthritis Research & Therapy*, 4:1-6.
- Boyer, O. 2020. Africa's people must be able to write their own genomics agenda. *Nature*, 29;586.
- Breast Cancer Association Consortium, 2021. Breast cancer risk genes—association analysis in more than 113,000 women. *New England Journal of Medicine*, 384(5), pp.428-439.
- Calderón, C., and L. Servén. 2010. Infrastructure and economic development in Sub-Saharan Africa. *Journal of African Economies*, 19(suppl_1);i13-87.
- Cao, C. and J. Moul. 2014. GWAS and drug targets. *BMC Genomics*, 15:1-4.
- Cashin, C. and J.P. Dossou. 2021. Can national health insurance pave the way to universal health coverage in sub-Saharan Africa? *Health Systems & Reform*, 7(1): e2006122.
- Cavallari, L.H., A.L. Beitelshes, K.V. Blake, L.G. Dressler, J.D. Duarte, A. Elsey, J.N. Eichmeyer, P.E. Empey, J.P. Franciosi, J.K. Hicks, and A.M. Holmes. 2017. The IGNITE Pharmacogenetics Working Group: an opportunity for building evidence with pharmacogenetic implementation in a real-world setting. *Clinical and Translational Science*, 10(3):143.
- Chaffey, N., B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter. 2003. Molecular biology of the cell. 4th edn. *Annals of Botany*. 91(31), 401. doi: 10.1093/aob/mcg023
- Christoffels, A.G., and A. Abayomi. 2020. Careful governance of African biobanks. *The Lancet*, 395(10217), 29–30. doi:10.1016/s0140-6736(19)32624-8
- Cohen, D. 2022. Human capital and the HIV epidemic in sub-Saharan Africa. ILO Programme on HIV/AIDS and the World of Work
- Collins, F.S., M. Morgan, and A. Patrinos 2003 The Human Genome Project: lessons from large-scale biology. *Science*, 300(5617):286-90.
- Cook-Deegan, R., R.A. Ankeny, and K. Maxson Jones. 2017. Sharing data to build a medical information commons: from Bermuda to the Global Alliance. *Annual Review of Genomics and Human Genetics*, 18:389-415.
- Dandara, C., C. Masimirembwa, Y.Z. Haffani, B. Ogutu, J. Mabuka, E. Aklillu, and O. Bolaji. 2019. African Pharmacogenomics Consortium: consolidating pharmacogenomics knowledge, capacity development and translation in Africa: consolidating pharmacogenomics knowledge, capacity development and translation in Africa. AAS Open Research
- Duffy, D.J. 2016. Problems, challenges and promises: perspectives on precision medicine. *Briefings in Bioinformatics*, 17(3):494-504.
- Eisenberg, R.S. 2001. The shifting functional balance of patents and drug regulation. *Health Affairs*, 20(5):119-35.
- Elens, L., D.A. Hesselink, R.H. van Schaik, and T. van Gelder. 2012. Pharmacogenetics in kidney transplantation: recent updates and potential clinical applications. *Molecular Diagnosis & Therapy*, 16:331-45.
- Evans, W.E., and H.L. McLeod. 2003. Pharmacogenomics—drug disposition, drug targets, and side effects. *New England Journal of Medicine*, 348(6):538-49.
- Fahim, S.M., C.S. Alexander, J. Qian, S. Ngorsuraches, N.S. Hohmann, K.B. Lloyd, A. Reagan, L. Hart, N. McCormick, and S.C. Westrick. 2023. Current published evidence on barriers and proposed strategies for genetic testing implementation in healthcare settings: A scoping review. *Journal of the American Pharmacists Association*, 63(4):998-1016.
- Gojo, T., S.L. Mailankody. 2014. A. Unintended consequences of expensive cancer therapeutics—the pursuit of marginal indications and a me-too mentality that stifles innovation and creativity: the John Conley Lecture. *JAMA Otolaryngology–Head & Neck Surgery*, 140(12):1225-36.
- Formea, C.M., W.T. Nicholson, K.B. McCullough, K.D. Berg, M.L. Berg, J.L. Cunningham, J.A. Merten, N. N. Ou, and J.L. Stollings .2013. Development and Evaluation of a Pharmacogenomics Educational Program for Pharmacists. *American Journal of Pharmaceutical Education*, 77 (1) doi.org/10.5688/ajpe77110.
- Formea, C.M., W.T. Nicholson, and C.R. Vitek. 2015. An inter-professional approach to personalized medicine education: one institution's experience. *Personalized medicine*, 12(2):129-38.
- Gaal, H.O., N.A. and N.A. Afrah. 2017. Lack of Infrastructure: The Impact on Economic Development as a case of Benadir region and Hir-shabelle, Somalia. *Developing Country Studies*, 7(1);49-55
- Geisler, T., B. Bigalke, and M. Schwab. 2011. CYP2C19 genotype and outcomes of clopidogrel treatment. *The New England Journal of Medicine*, 364(5):481.
- Ghura, D., A. Basu, and A.E. Calamitsis. 2001. Promoting growth in sub-Saharan Africa: Learning what works. In Promoting growth in sub-saharan Africa. *International Monetary Fund*
- Goetz, L.H., and N.J. Schork. 2018. Personalized medicine: motivation, challenges, and progress. *Fertility and sterility*, 109(6):952-63.
- Green, E.D., J.D. Watson, and F.S. Collins. 2015. Human Genome Project: Twenty-five years of big biology. *Nature*, 526(7571):29-31.
- Guo, Z., Y.J. Wang, B.S. He, and J. Zhou. 2022. Linc00312 single nucleotide polymorphism as biomarker for chemoradiotherapy induced hematotoxicity in nasopharyngeal carcinoma patients. *Disease Markers*, 2022(1), p.6707821.
- Hardy, B.J. 2012. Bridging the genomics gap: The role of large-scale genotyping projects in the developing world and the importance of genomic sovereignty (Doctoral dissertation, University of Toronto). <http://hdl.handle.net/1807/42497>. [Assessed 04 Jan., 2025]
- Hogarth, S., M.M. Hopkins, and V. Rodriguez. 2012. A molecular monopoly? HPV testing, the Pap smear and the molecularisation of cervical cancer screening in the USA. *Sociology of Health & Illness*, 34(2):234-50.
- Holmes, M.V., P. Perel, T. Shah, A.D. Hingorani, and J.P. Casas. 2011.. CYP2C19 genotype, clopidogrel metabolism, platelet function, and cardiovascular events: a systematic review and meta-analysis. *JAMA*, 306(24):2704-14.
- Jameson, A., B. Fylan, G.C. Bristow, G.S. Sagoo, C. Dalton, A. Cardno, J. Sohal, and S.L. McLean. 2021. What are the barriers and enablers to the implementation of pharmacogenetic testing in mental health care settings? *Frontiers in Genetics*, 12:740216.
- Jameson, J.L., and DL. Longo. 2011. Precision medicine—personalized, problematic, and promising. *Obstetrical & Gynecological Survey*, 70(10):612-4.
- Johnson, A.D., C. Newton-Cheh, D.I. Chasman, G.B. Ehret, T. Johnson, L. Rose, K. Rice, G.C. Verwoert, L.J. Launer, V. Gudnason, and M.G. Larson. 2011. Association of hypertension drug target genes with blood pressure and

- hypertension in 86 588 individuals. *Hypertension*, 57(5):903-10.
- Jongeneel, C.V., M.J. Kotze, A. Bhaw-Luximon, F.M. Fadlelmola, Y.J. Fakim, Y. Hamdi, S.K. Kassim, J. Kumuthini, V. Nembaware, F. Radouani, and N.Tiffin N2022. A view on genomic medicine activities in Africa: implications for policy. *Frontiers in Genetics*, 13:769919.
- Kabata, F., D. Thaldar. 2023. Regulating human genomic research in Africa: why a human rights approach is a more promising conceptual framework than genomic sovereignty. *Frontiers in Genetics*, 14:1208606.
- Kamal, M.M., M.N. Islam, M.G. Rabby, M.A. Zahid, and M.M. Hasan, 2024. In silico functional and structural analysis of non-synonymous single nucleotide polymorphisms (nsSNPs) in human paired box 4 gene. *Biochemical Genetics*, 62(4), pp.2975-2998.
- Kurzwaski, M., and M. Drożdżik. 2013. Pharmacogenetics in solid organ transplantation: genes involved in mechanism of action and pharmacokinetics of immunosuppressive drugs. *Pharmacogenomics*, 14(9):1099-118.
- Loovers, H.M., and J. van der Weide. 2009. Implementation of CYP2D6 genotyping in psychiatry. *Expert Opinion on Drug Metabolism & Toxicology*, 5(9):1065-77.
- Mallal, S., E. Phillips, G. Carosi, J.M. Molina, C. Workman, J. Tomažič, E. Jägel-Guedes, S. Rugina, O. Kozyrev, J.F. Cid, and P. Hay P. 2008. HLA-B* 5701 screening for hypersensitivity to abacavir. *New England Journal of Medicine*, 358(6):568-79.
- Maugham, T., 2017. The promise and the hype of 'personalised medicine'. *The New Bioethics*, 23(1):13-20.
- Mediclinic Southern Africa. [Internet]. Mediclinic Southern Africa; [cited 2024 May 10]. Available from: <https://www.mediclinic.co.za/en/corporate/aboutmediclinic-southern-africa.html>
- Merelli, I., A. Calabria, P. Cozzi, F. Viti, E. Mosca, and L. Milanese. 2013. SNPPranker 2.0: a gene-centric data mining tool for diseases associated SNP prioritization in GWAS. *BMC Bioinformatics*, 14:1-2.
- Mikat-Stevens, N.A., I.A. Larson, and B.A. Tarini. 2015. Primary-care providers' perceived barriers to integration of genetics services: a systematic review of the literature. *Genetics in Medicine*, 17(3):169-76.
- Morris., M. 2023. Growing Bioinformatics Capacity in Africa. Available from: <https://doi.org/10.1038/d44148-023-00210-3> [Accessed 10 May 2024].
- Mrazek., D.A. 2010. Psychiatric pharmacogenomic testing in clinical practice. *Dialogues in Clinical Neuroscience*, 12(1):69-76.
- Mürdter, T.E., W. Schroth, L. Bacchus-Gerybadze, S. Winter, G. Heinkele, W. Simon, P.A. Fasching, T. Fehm, German Tamoxifen and AI Clinicians Group, M. Eichelbaum, and M. Schwab. 2011. Activity levels of tamoxifen metabolites at the estrogen receptor and the impact of genetic polymorphisms of phase I and II enzymes on their concentration levels in plasma. *Clinical Pharmacology & Therapeutics*, 89(5):708-17.
- Naithani, N., S. Sinha, P. Misra, B. Vasudevan, and R. Sahu. 2021. Precision medicine: Concept and tools. *Medical Journal Armed Forces India*, 77(3):249-57.
- National Academies of Sciences, Engineering, and Medicine. 2018. Understanding disparities in access to genomic medicine: Proceedings of a workshop. Washington, DC: *The National Academies Press*. doi: <https://doi.org/10.17226/25277>. [Assessed 04 Jan., 2025]
- Nurk, S., S. Koren, A. Rhie, M. Rautiainen, A.V. Bzikadze, A. Mikheenko, M.R. Vollger, N. Altomose, L. Uralsky, A. Gershman, and S. Aganezov. 2022. The complete sequence of a human genome. *Science*, 376(6588):44-53.
- O'Connell, J., T. Yun, M. Moreno, H. Li, N. Litterman, A. Kolesnikov, E. Noblin, P.C. Chang, A. Shastri, E. H. Dorfman, and S. Shringarpure. 2021. A population-specific reference panel for improved genotype imputation in African Americans. *Communications Biology*, 4(1):1269.
- Odekunle, F.F., R.O. Odekunle, and S. Shankar. 2017. Why sub-Saharan Africa lags in electronic health record adoption and possible strategies to increase its adoption in this region. *International Journal of Health Sciences*, 11(4):59.
- Okeke, I.N. 2011. Divining without seeds: the case for strengthening laboratory medicine in Africa. *Cornell University Press*.
- Pasternak, A.L., K.M. Ward, M.B. Ateya, H.M. Choe, A.N. Thompson, J.S. Clark, and V. Ellingrod. 2020. Establishment of a pharmacogenetics service focused on optimizing existing pharmacogenetic testing at a large academic health center. *Journal of Personalized Medicine*, 10(4):154.
- Pennisi, E. 2021. Africans have begun to study their continent's rich human diversity—but what comes after current grants end. Available online at: <https://www.science.org/content/article/africans-begin-take-reins-research-their-own-genomes> [Assessed 06 Jan., 2025]
- Petti, C.A., C.R. Polage, T.C. Quinn, A.R. Ronald, and M.A. Sande. 2006. Laboratory medicine in Africa: a barrier to effective health care. *Clinical Infectious Diseases*, 42(3):377-82.
- Pirmohamed, M., G. Burnside, N. Eriksson, A.L. Jorgensen, C.H. Toh, T. Nicholson, P. Kesteven, C. Christersson, B. Wahlström, C. Stafberg, and J. E. Zhang. 2013. A randomized trial of genotype-guided dosing of warfarin. *New England Journal of Medicine*, 369(24):2294-303.
- Radouani, F., L. Zass, Y. Hamdi, J.D. Rocha, R. Sallam, S. Abdelhak, S. Ahmed, MAzzouzi, I. Benamri, A. Benkahla, and B. Bouhaouala-Zahar. 2020. A review of clinical pharmacogenetics Studies in African populations. *Personalized Medicine*, 17(2):155-70.
- Ramaswami, R., R. Bayer, and S. Galea. 2018. Precision medicine from a public health perspective. *Annual Review of Public Health*, 39:153-68.
- Resolution, A. RES/70/1. 2015. Transforming our world: the 2030 agenda for sustainable development. Seventieth United Nations General Assembly, New York, 25:86-97.
- Rigter, T., M.E. Jansen, J.M. Groot, S.W. Janssen, W. Rodenburg, and M.C. Cornel. 2020. Implementation of pharmacogenetics in primary care: a multi-stakeholder perspective. *Frontiers in Genetics*, 11:10.
- Sirugo, G., S.M. Williams, and S.A. Tishkoff. 2019. The missing diversity in human genetic studies. *Cell*, 177(1):26-31.
- Skol, A.D., M.M. Sasaki, and k. Onel. 2016. The genetics of breast cancer risk in the post-genome era: thoughts on study design to move past BRCA and towards clinical relevance. *Breast Cancer Research*, 18:1-8.
- van Schaik, R.H., 2014. On Pharmacogenetics IT, IT MF, GER MN, UK MP, NL HJ. Clinical application of pharmacogenetics: where are we now? *Ejifcc*, 24(3):105.
- Tata, E.A., and M.S. Ambele. 2020. Pepper M. Barriers to Implementing Clinical Pharmacogenetics Testing in Sub-Saharan Africa. A Critical Review. *Pharmaceutics*, 12(9):809.

- Vergara, C., M.M. Parker, L. Franco, M.H. Cho, A.V. Valencia-Duarte, T.H. Beaty, and P. Duggal. 2018. Genotype imputation performance of three reference panels using African ancestry individuals. *Human Genetics*, 137:281-92.
- Wood, E.T., D.A. Stover, C. Ehret, G. Destro-Bisol, G. Spedini, H. McLeod, L. Louie, M. Bamshad, B.I. Strassmann, H. Soodyall, and M.F. Hammer. 2021. Contrasting patterns of Y chromosome and mtDNA variation in Africa: evidence for sex-biased demographic processes. *European Journal of Human Genetics*, 13(7):867-76.
- World Bank. Africa Overview [Internet]. World Bank. 2024. Available from: <https://www.worldbank.org/en/region/afr/overview#:~:text=About%20462%20million%20people%20in,has%20expected%20this%20debt%20surge>
- World Bank. 2021. Despite Global Slowdown, African Economies Growing Strongly; World Bank Urges Countries to Spend New Oil, Gas, Mineral Wealth Wisely [Internet]. Available from: https://www.worldbank.org/en/news/press-release/2012/10/04/despite-global-slowdown-african-economies-growing-strongly-world-bank-urges-countries-spend-new-oil-gas-mineral-wealth-wisely?cid=EXT_WBEmailShare_EXT [Assessed 06 Jan., 2025]
- World Health Organization. Scaling up genomic sequencing in Nigeria [Internet]. World Health Organization; 2024. Available from: <https://www.afro.who.int/photo-story/scaling-genomic-sequencing-nigeria>
- World Poverty Map. [Internet]. World Poverty Map; 2024. Available from: <https://worldpoverty.io/map>
- Zabalza, M., I. Subirana, J. Sala, C. Lluís-Ganella, G. Lucas, M. Tomás, R. Masiá, J. Marrugat, R. Brugada, R. Elosua. 2012. Meta-analyses of the association between cytochrome CYP2C19 loss-and gain-of-function polymorphisms and cardiovascular outcomes in patients with coronary artery disease treated with clopidogrel. *Heart*, 98(2):100-8.
- Zhong, A., B. Darren, B. Loiseau, L.Q. He, T. Chang, J. Hill, and H. Dimaras. 2021. Ethical, social, and cultural issues related to clinical genetic testing and counseling in low-and middle-income countries: a systematic review. *Genetics in Medicine*, (12):2270-80.
- Zierhut, H.A., C.A. Campbell, A.G. Mitchell, A.A. Lemke, R. Mills, and J.R. Bishop. 2017. Collaborative counseling considerations for pharmacogenomic tests. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 37(9):990-9.