Clinical Pharmacology Worldwide: A Global Health Perspective

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Low- and middle-income countries (LMICs) have the highest rates of mortality and morbidity globally, but lag behind high-income countries in the number of clinical trials and trained researchers, as well as research data pertaining to their populations. Lack of local clinical pharmacology and pharmacometrics expertise, limited training opportunities, and lack of local genomic data may contribute to health inequalities and limit the application of precision medicine. Continuing to develop health care infrastructure, including well-designed clinical pharmacology training and data collection in LMICs, can help address these challenges. International collaboration aimed at improving training and infrastructure and encouraging locally driven research and clinical trials will be of benefit. This review describes several examples where clinical pharmacology expertise could be leveraged, including opportunities for pharmacogenomic expertise that could drive improved recommendations for clinical guidelines. Also described are clinical pharmacology and pharmacometrics training programs in Africa, and the personal experience of a Tanzanian researcher currently on a training sabbatical in the United States, as illustrative examples of how training in clinical pharmacology can be effectively implemented in LMICs. These training efforts will benefit from advocacy for employment opportunities and career development pathways for clinical pharmacologists that are gradually being recognized and developed in LMICs. Clinical pharmacologists have a key role to play in global health, and development of training and research infrastructure to advance this expertise in LMICs will be of tremendous benefit.

Increased disease burden from both infectious and non-communicable diseases (NCDs) threatens to overwhelm health-care systems and health workers in low- and middle-income countries (LMICs), which have the highest rates of mortality and morbidity globally (www.healthdata.org), but there are fewer clinical trials and trained researchers in LMICs compared to high-income countries (HICs). Clinical pharmacology expertise is a core skill from drug discovery and development to the postmarketing setting. It has been associated with improved prescribing competencies, better patient therapeutic outcomes, and reduced disease burden. This paper considers global health challenges faced by LMICs and opportunities where clinical pharmacology may be of benefit. In addition, examples of how clinical pharmacology training can be effectively implemented in LMICs, including personal experience with international collaboration, are discussed.

CONDUCTING CLINICAL TRIALS IN LMICS: BARRIERS AND OPPORTUNITIES

Diseases of relevance to HICs are investigated in clinical trials seven to eight times more often than diseases important for LMICs.[1] Per a report on global distribution of clinical trials registered on ClinicalTrials.gov from 2006 to 2012, there were 89,647 clinical trials conducted at 784,585 trial sites in 175 countries. Among those, 652,200 trial sites (83%) were in 25 HICs, whereas 37,195 sites (5%) were in 91 LMICs. Additionally, LMICs operated 19% of phase III trial sites, compared with only 6% of phase I trial sites.[2] Inclusion in clinical trials can directly benefit patients through increased access to otherwise limited health care services, but a correct balance between the interests of trial sponsors and the needs of patients in LMICs must be ensured.[3]

Recent reports on barriers to conducting clinical trials in LMICs highlight challenges, such as lack of skilled study personnel, insufficient funding, ethics committee and regulatory issues (e.g., regulatory processes and uncertain review timelines, and inexperienced reviewers), inadequate research infrastructure, lack of a conducive scientific atmosphere or enabling government policy and institutional hurdles relating to logistics, financial management, and difficulties in patient recruitment. Some authors argue that building a system for broader implementation of trials driven at the local level would address these challenges and encourage opportunities for international collaborations to help build appropriate infrastructure and expertise.[4,5] Creation of trial networks and databases of local sites and qualified investigators has been proposed as a way to encourage this.[6]

There is a precedent for public-academic-private partnerships in Africa to build and strengthen clinical pharmacology research capabilities, resulting in the successful conduct of phase I studies at centers

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Received February 2, 2021; accepted April 7, 2021. doi:10.1002/cpt.2274

enabled by the partnerships.[7] In addition, the African Academy of Sciences (AAS) recently launched a database of clinical trial sites and capabilities as part of its goal to increase investment in clinical trials in Africa. This project has private and public, international, and local support, including the Bill and Melinda Gates Foundation, the National Institutes of Health (NIH), the biopharmaceutical industry, product development partners, clinical researchers, and African regulatory agencies. Against the backdrop of the generally low prevalence of clinical trials in Africa, the particularly low number of early phase, clinical pharmacology studies, and translational research on the continent provided compelling motivation for this project. Given strong perceptions that regulatory and ethics approval processes are a major bottleneck for conducting clinical trials in Africa, the AAS has partnered with the African Vaccine Regulatory Forum (AVAREF) and the World Health Organization-Africa (WHO-Afro) to seek collaborative solutions (ctc.africa). Talent, competency, and capability development efforts for regulatory scientists in Africa place a strong emphasis on improving clinical pharmacology skills within overall efforts to strengthen regulatory systems.[8]

Globalization of clinical trials requires that the same Good Clinical Practice (GCP) standards, ethical principles, and access to medicine are followed everywhere. However, conducting clinical trials in LMICs is associated with additional challenges, such as the extra care needed to avoid exploitation of vulnerable populations and institutional limitations of infrastructure and logistics. These challenges can lead to study delays and limit patients' access to medicine. International collaborations, development of health care infrastructure, including well-designed clinical pharmacology training and up-skilling local researchers for pharmacogenomic data collection, can help address these challenges. International collaborations should strive for mechanisms to maintain and retain skills and infrastructure after completion of the funded clinical projects, building clinical pharmacology research expertise, and working with local collaborators to incorporate the needs of the local populations.

PHARMACOGENOMIC RESEARCH IN LOW- AND MIDDLE-INCOME COUNTRIES

Pharmacogenomics, the study of DNA and RNA variations that affect drug response,[9] is a valuable tool to optimize clinical outcomes, prevent adverse drug reactions through dose adjustments, and guide the selection of alternative therapies. For example, life-threatening bone marrow toxicity from thioguanines can be avoided by dose reductions in patients with loss-of-function alterations in thiopurine methyltransferase (*TPMT*) gene and nudix hydrolase 15 (*NUDT15*).[10] In recent years, routine care for patients with cancer includes genomic medicine through the identification of specific alterations in patients' tumors, which then guide selection of appropriate therapies. However, the integration of genomic medicine into patient care has not been applied equally across the globe. Part of this inequity is driven by disparities in the availability of genomic data on populations in LMICs, as well as a shortage of experts with experience applying genomic information into clinical care.

In order for LMICs to select their genomic medicine priorities, it is essential to understand the genetic variations present within local patient populations. However, many of the studies that inform drug labeling and clinical practice guidelines have been conducted in HICs in North America, Europe, and Asia.[11] As a result, there is a paucity of information on local and regional variation in important pharmacogenes, particularly in LMICs.[12] Although some genotype-guided treatment studies have been completed in LMICs,[13] it has become clear that increased inclusion of participants from LMICs in studies that inform drug labeling and clinical practice guidelines is not enough to capture the entirety of the world's genomic variations. Indeed, reports on sequencing work conducted at the local level in Colombia, South Africa, and throughout Europe has shown that significant variability exists within discrete populations.[14–17]

Full-scale pharmacogenomics research and implementation is a particular challenge in LMICs. Two potential solutions to this are the selective implementation of pharmacogenomics into clinical care that fits the priorities of a resource-limited country and joining multinational pharmacogenomic organizations. Thailand, for example, prioritized genotyping for the presence of the variant allele human leukocyte antigen HLA-B*15:02, which is strongly associated with increased risk of Stevens–Johnson syndrome and toxic epidermal necrolysis in patients treated with carbamazepine. HLA-B*15:02 is more prevalent in Thailand and other South East Asian populations compared with European countries, and screening patients prior to prescribing carbamazepine was shown to be cost-effective.[18] Another important achievement is the proliferation of multinational organizations focused on the advancement of pharmacogenetics in LMICs. For example, the African Pharmacogenomics Consortium aims to increase awareness, research, training, and implementation of pharmacogenetics in Africa. Organizations such as H3Africa that work with this consortium facilitate training, workshops, capacity building, and fellowship support.[19] In Asia, the Southeast Asian Pharmacogenomics Research Network (SEAPharm; https://www.ims.riken.jp/english/projects/m4.html) was established to support pharmacogenomic implementation by strengthening research among communities within the South East Asian region and beyond.[20] Other global organizations include the Global Genomic Medicine Collaborative (https://g2mc.org/) which aims to create a community of leaders dedicated to advancing genomic medicine implementation in clinical care, and the Genomic Medicine Alliance (http://www.genomicmedicinealliance.org/), which focuses on bringing new research findings into clinical practice in LMICs.[21]

Pharmacogenomics has become a widely used tool to improve therapeutic outcomes and reduce healthcare costs. Although much of the initial discovery work has been performed in HICs, the clinical implications can have increased impact in LMICs. Encouragingly, pharmacogenomics and genomic medicine are expanding in LMICs through integration of high-priority tests into relevant countries and the growth of multinational partnerships. As a result, opportunities for clinical pharmacologists in LMICs to gain pharmacogenomic experience are likely to increase.

CLINICAL PHARMACOLOGY AND PHARMACOMETRICS TRAINING: EXAMPLES FROM AFRICA

Clinical pharmacology and pharmacometrics offer an opportunity to improve the use of medications to reduce the burden of

diseases in Africa.[22] Older medicines were typically developed without modern methods of dose selection and optimization. The growing prevalence of NCD in Africa presents the additional challenge of polypharmacy for patients with comorbidities and varying nutritional status, adding complexity due to possible drug-drug interactions. These issues can be best managed by healthcare personnel with a strong understanding of clinical pharmacology. Although pharmacometrics is a well-established scientific discipline in HICs, there is a need to increase expertise in LMICs. The next few paragraphs provide examples from post-graduate and on-line pharmacometrics training in Africa.

Formal postgraduate training on pharmacometrics in African countries is essentially nonexistent. To expand and accelerate the efforts of academic and industry clinical pharmacologists to develop pharmacometrics in Africa, Pharmacometrics Africa (www.pmxafrica.org) was established using grant funds from the Bill & Melinda Gates Foundation. The aims are to attract students into clinical pharmacology by providing research programs, to advocate application of model-based techniques in clinical trials among experienced clinical researchers, and to raise awareness for applying quantitative methods among healthcare professionals. The platform allows collaboration, learning, and interaction among students, faculty members, scientists, and healthcare professionals from across the world using local data and relevant clinical pharmacology questions.

A 10–12 week clinical pharmacology and pharmacometrics training was taught using the Moodle Virtual Learning Environment (VLE) located at the Infectious Diseases Institute at Makerere University in Kampala, Uganda, and more recently at Strathmore University in Nairobi, Kenya. The curriculum included concepts in pharmacokinetics (PK), pharmacodynamics (PD), and biostatistics, and visualization of PK and PD models in the Berkeley-Madonna modeling software. Each week commenced with self-study lessons that included videos, guided reading, and self-assessment exercises. The week culminated with a live webinar tutorial where faculty members discussed the week's materials and exercises. Tutorials were recorded for off-line use by those who might have had difficulties with internet connectivity. Students were assigned to small groups led by international and local subject matter experts (see Acknowledgments) who monitored progress, provided guidance, and acted as mentors. Four iterations of the course have been successfully completed, reaching over 350 participants, mainly from multiple African countries (**Figure 1**). The participants included pharmacists, medical officers, statisticians, mathematicians, and scientists with backgrounds in biology, drug regulation, pharmaceutics, and pharmacogenetics. Students who qualified to receive certificates of course completion were invited to attend one of several hands-on nonlinear mixed-effects modeling face-to-face (F2F) workshops. These were typically under 5 days duration and were hosted in various African countries to maximize attendance by local scientists.

Based on requests from students and advice from faculty, a beta version of a self-paced course was introduced in June 2020 (https://www.pmxafrica.org/phm-self-paced-overview). Preliminary observations suggested high interest (clicks on the site), but low rates of completion. It is possible that students consulted specific lessons rather than the full course end-to-end. A revised full release of the course will allow tracking of usage patterns.

A webinar series with open-access resources and materials on topics of global health relevance was also introduced. These topics

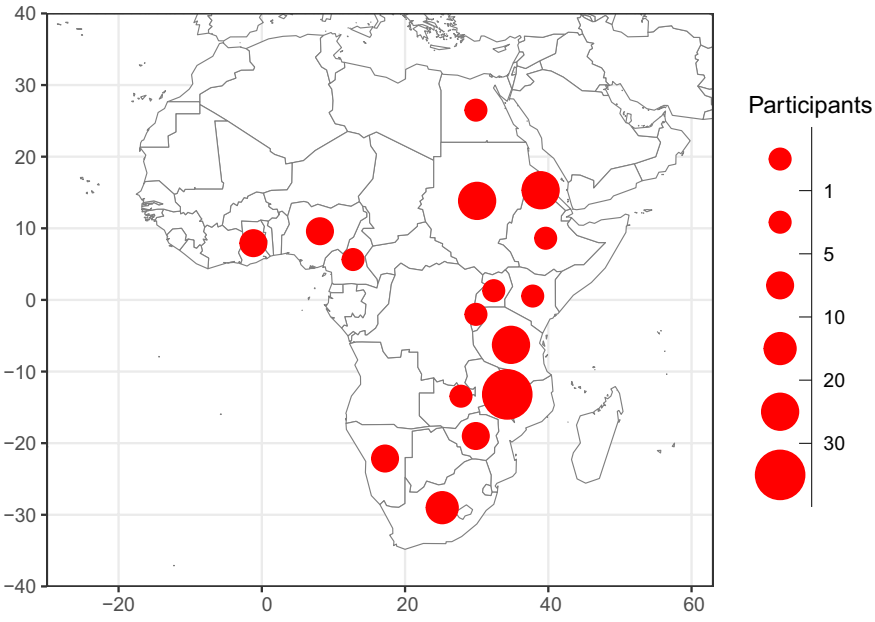

Figure 1 Geographic distribution of > 350 African participants in an on-line clinical pharmacology and pharmacometrics training program. Participants from non-African countries (not shown) included seven from Brazil, two from India, and one each from Argentina, Germany, and The Netherlands.

included malaria vaccine modeling, data integrity during PK/PD analyses, pharmacometrics considerations in pediatric trial designs, exploratory and noncompartmental analysis of PK/PD data, and more recently topics related to coronavirus disease 2019 (COVID-19). All webinars were of < 2 hours duration and targeted a global audience.

Under the assumption that long-term sustainability of the clinical pharmacology and pharmacometrics capacity development efforts might be facilitated if incorporated into University postgraduate degree programs, local academic subject matter experts drawn mainly from pharmacy, medicine, and mathematics departments were engaged in curriculum development, course delivery, and delegate selection in the suite of training programs. They are gradually working on incorporating teaching content into postgraduate degree programs. Although the processing timelines for new course offerings and degree programs are slow and bureaucratic, there is optimism that the following aspects will facilitate success for these nascent efforts: modular on-line course structure allowing for incorporation into existing degree programs, standalone lessons allowing for adjustment of content to meet local needs (e.g., incorporation of local case studies), and advocacy sparked by hosting in-person training events at universities across the continent.

THE VALUE OF PHARMACOMETRICS EXPERTISE IN AFRICAN COUNTRIES

Although there are diseases, such as malaria, where most clinical trials are conducted in African countries, these studies are typically designed and analyzed by non-African scientists, and do not always address the needs of local populations. Improving the clinical and pharmacometric research capacity of African researchers will ultimately facilitate and accelerate drug development in Africa, reduce dependency on Western countries, and empower African researchers to set research agendas that most benefit their communities.

Recent efforts by the pharmaceutical industry to build skills in drug discovery and clinical development,[23] and efforts by the Medicines for Malaria Venture (MMV), who launched a postdoctoral fellowship program to build physiology-based population PK modeling and simulation skills, will allow experiential learning on real-world data. The WorldWide Antimalarial Resistance Network (WWARN) is a part of the Infectious Diseases Data Observatory and has become an important source of data sharing for training, as evidenced by analyses conducted on WWARN data.[24] More funding should be allocated for fellowships that promote collaboration with local researchers to make sure the capacity that is built remains sustainable. Providing access to PK/PD data for training is another way to build pharmacometric expertise because these data are often not available to LMIC scientists.

MY PERSONAL EXPERIENCE AS A TANZANIAN PHARMACOMETRICIAN TRAINED IN THE UNITED STATES OF AMERICA (ALI MOHAMED ALI)

Providing opportunities for researchers from LMICs to learn innovative skills in clinical pharmacology and pharmacometrics is key to building global health-related research capacity in Tanzania. Therefore, my reason to obtain training in pharmacometrics was to acquire the knowledge and skills necessary to establish a quantitative pharmacology unit in Ifakara Health Institute in Tanzania and to provide training to African researchers and their international collaborators. Recognizing that pharmacometrics expertise is scarce in LMICs, I took up a postdoctoral academic fellowship, titled "Building Pharmacometric Capacity in Africa," at the University of California San Francisco (UCSF). As part of my fellowship, I have been examining the interplay between malaria and linear growth in young children at high risk of malaria. To describe associations between antimalarial drug use for malaria chemoprevention, malaria risk, and the impact of malaria and malaria prevention on growth, I developed advanced PK/PD modeling skills in a larger team of experts that were not available at my institution. These skills are a much-needed complement to the long-standing malaria research expertise at my institute spanning over 50 years in patients with all stages of malaria. For example, as part of my pharmacometrics training at UCSF, I analyzed data from an African setting and found that adherence to the drug regimen was the largest barrier for the study. Improved data collection on adherence could have been implemented earlier, and coupled with drug exposure data collected during study implementation would have made important contributions to the topic of forgiveness of drug treatment regimens as done by researchers in Rwanda.[25] When I return to the institute at the end of my fellowship, I see myself filling gaps, which include providing methodological expertise in designing, conducting, and analyzing clinical pharmacology studies.

CAREER DEVELOPMENT PATHWAYS AND EMPLOYMENT OPPORTUNITIES

Clinical pharmacologists in LMICs are typically used in healthcare practice (e.g., medical doctors or pharmacists), and in academia (e.g., teaching or as research staff). They might also find employment in clinical research organizations (e.g., working to design, analyze, and interpret drug interventional trials), or in pharmaceutical companies as research or regulatory scientists. However, there are far fewer opportunities for these roles in LMICs than in HICs given the lower presence of commercial research-based entities. A recent paper by authors, including experienced regulators, acknowledges the critical importance of clinical pharmacology skills for regulatory scientists in Africa.[8] They suggest linking education, training, and research with career development and a competency framework comprising a learning context (academic and training institutions) and a performance context (regulatory agencies and industry) as a means of strengthening African regulatory ecosystems while also improving careers in the agencies.

CONCLUSIONS/DISCUSSION

A lack of clinical pharmacology and pharmacometrics expertise presents multiple barriers that impact health care in LMICs. These countries would benefit from international collaboration aimed at improving training and infrastructure and encouraging locally driven research and clinical trials. The programs described in this paper illustrate opportunities for application of clinical pharmacology expertise in the field

of pharmacogenomics in LMICs. In addition, successful training programs in Africa were presented, which can be applied in other areas of the world. The personal experience of one of the authors speaks to the impact of international clinical pharmacology and pharmacometrics training as the acquired knowledge and skills provide two-way learning to the host organization and local institutions.

Ongoing (rather than once-and-done) training, connections, application, and collaboration are keys to successful programs with lasting impact—expertise must be maintained through continuing work after training. Little data are available so far on how many trainees go on to pursue careers in clinical pharmacology, pharmacometrics, or pharmacogenomics, but such follow-up information would be extremely valuable to judge the impact of these programs. Although we have presented isolated examples, a systematic analysis across multiple programs might further illuminate strengths and weaknesses of these efforts in LMICs. In summary, clinical pharmacologists play a key role in global health, pharmacogenomics, and design and conduct of clinical trials. Continued development of training in clinical pharmacology, pharmacometrics, and pharmacogenomics will be of tremendous benefit for improving patient care in these countries. For maximum benefit, several components must come together, including increased funding for research and trials in LMICs, increased opportunities for inclusion in multinational trials, and ongoing commitment to increased training centered around real projects via fellowships and other employment opportunities that leverage this training. We call on professional societies such as ASCPT, as well as other international collaborations, to aid in empowering local expertise and locally driven research, and to strive to include expert and trainee clinical pharmacologists from LMICs in ongoing conversations about advancing global health.

ACKNOWLEDGMENTS

The following people from the Pharmacometrics Africa team contributed to the training programs described: Leon Aarons, Noha Abdelgawad, Ahmed Abulfathi, Anthony Afum-Adjei Awuah, Linda Chaba, Emmanuel Chigutsa, Maxwell Tawanda Chirehwa, Paolo Denti, Edmund Ekuadzi, Pius Fasinu, Lufina Tsirani Galileya, Kamunkwala Gausi, Eva Maria Hodel, Aida Kawuma, Eliford Ngaimisi Kitabi, Gary Maartens, Collen Masimirembwa, Lydia Caroline Nalule, Verrah Odhiambo, Kayode Ogungbenro, Bernhards Ogutu, Adeniyi Olagunju, Evans Omondi, Roslyn Thelingwini, and Simbarashe Zvada.

Erika Wallender, MD assisted with editing the sections on The Value of Pharmacometrics Expertise in African Countries and Personal Experience.

FUNDING

Pharmacometrics Africa receives funding from the Bill & Melinda Gates Foundation. A.M.A is a postdoctoral fellow in a program that is funded by the Bill & Melinda Gates Foundation.

CONFLICT OF INTEREST

L.W. is an employee of Merck & Co., Inc. and owns stock in Merck & Co., Inc. K.I. is an employee of Shire, a Takeda company, and owns stock in Takeda. G.P. is a consultant on capacity/capability programs for LMICs and owns stock in Novartis Pharma. J.E.H. is an employee of Pfizer, Inc. and owns stock or stock options in Pfizer. All other authors declared no competing interests for this work.

1. Rottingen, J.A. *et al*. Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory? *Lancet* **382**, 1286–1307 (2013).
2. Drain, P.K., Parker, R.A., Robine, M., Holmes, K.K. & Bassett, I.V. Global migration of clinical research during the era of trial registration. *PLoS One* **13**, e0192413 (2018).
3. Weigmann, K. The ethics of global clinical trials in developing countries, participation in clinical trials is sometimes the only way to access medical treatment. What should be done to avoid exploitation of disadvantaged populations? *EMBO Rep.* **16**, 566–570 (2015).
4. Alemayehu, C., Mitchell, G. & Nikles, J. Barriers for conducting clinical trials in developing countries- a systematic review. *Int. J. Equity Health* **17**, 37 (2018).
5. Gyawali, B., Bouche, G., Crisp, N. & André, N. Challenges and opportunities for cancer clinical trials in low- and middle-income countries. *Nature Cancer* **1**, 142–145 (2020).
6. Graef, K.M., Okoye, I., Ohene Oti, N.O., Dent, J. & Odedina, F.T. Operational strategies for clinical trials in Africa. *JCO Glob. Oncol.* **6**, 973–982 (2020).
7. Gutierrez, M.M. *et al*. Building capability for clinical pharmacology research in Sub-Saharan Africa. *Clin. Pharmacol. Ther.* **102**, 786–795 (2017).
8. Semete-Makokotlela, B. *et al*. Needs driven talent and competency development for the next generation of regulatory scientists in Africa. *Authorea* https://doi.org/10.22541/au.161429668.84136777/v1.
9. Roden, D.M. *et al*. Pharmacogenomics. *Lancet* **394**, 521–532 (2019).
10. Relling, M.V. *et al*. Clinical pharmacogenetics implementation consortium guideline for thiopurine dosing based on TPMT and NUDT15 genotypes: 2018 update. *Clin. Pharmacol. Ther.* **105**, 1095–1105 (2019).
11. Knepper, T.C. & McLeod, H.L. When will clinical trials finally reflect diversity? *Nature* **557**, 157–159 (2018).
12. Popejoy, A.B. & Fullerton, S.M. Genomics is failing on diversity. *Nature* **538**, 161–164 (2016).
13. Mukonzo, J.K., Bisaso, R.K., Ogwal-Okeng, J., Gustafsson, L.L., Owen, J.S. & Aklillu, E. CYP2B6 genotype-based efavirenz dose recommendations during rifampicin-based antituberculosis cotreatment for a sub-Saharan Africa population. *Pharmacogenomics* **17**, 603–613 (2016).
14. Nagar, S.D. *et al*. Population pharmacogenomics for precision public health in Colombia. *Front. Genet.* **10**, 241 (2019).
15. Warnich, L., Drogemoller, B.I., Pepper, M.S., Dandara, C. & Wright, G.E. Pharmacogenomic research in South Africa: Lessons learned and future opportunities in the rainbow nation. *Curr. Pharmacogenomics Person. Med.* **9**, 191–207 (2011).
16. Patrinos, G.P. Sketching the prevalence of pharmacogenomic biomarkers among populations for clinical pharmacogenomics. *Eur. J. Hum. Genet.* **28**, 1–3 (2020).
17. Rajman, I., Knapp, L., Morgan, T. & Masimirembwa, C. African genetic diversity: implications for cytochrome P450-mediated drug metabolism and drug development. *EBioMedicine* **17**, 67–74 (2017).
18. Rattanavipapong, W., Koopitakkajorn, T., Praditsitthikorn, N., Mahasirimongkol, S. & Teerawattananon, Y. Economic evaluation of HLA-B*15:02 screening for carbamazepine-induced severe adverse drug reactions in Thailand. *Epilepsia* **54**, 1628–1638 (2013).
19. Dandara, C. *et al*. African Pharmacogenomics Consortium: Consolidating pharmacogenomics knowledge, capacity development and translation in Africa: consolidating pharmacogenomics knowledge, capacity development and translation in Africa. *AAS Open Res.* **2**, 19 (2019).
20. Chumnumwat, S. *et al*. Southeast Asian Pharmacogenomics Research Network (SEAPharm): current status and perspectives. *Public Health Genomics* **22**, 132–139 (2019).
21. Cooper, D.N. *et al*. Bridging genomics research between developed and developing countries: the Genomic Medicine Alliance. *Per. Med.* **11**, 615–623 (2014).

22. Pillai, G. *et al*. Pharmacometrics: opportunity for reducing disease burden in the developing world: the case of Africa. *CPT Pharmacometrics Syst. Pharmacol.* **2**, e69 (2013).
23. Pillai, G. *et al*. The Next Generation Scientist program: capacity-building for future scientific leaders in low- and middle-income countries. *BMC Med. Educ.* **18**, 233 (2018).
24. Ali, A.M. *et al*. Population pharmacokinetics of the antimalarial amodiaquine: a pooled analysis to optimize dosing. *Antimicrob. Agents Chemother.* **62**, e02193–17 (2018).
25. Twagirumukiza, M. *et al*. Evaluation of medication adherence methods in the treatment of malaria in Rwandan infants. *Malar. J.* **9**, 206 (2010).