Diversity, equity, and inclusion: translating clinical pharmacology for all

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Diversity, Equity, and Inclusion: Translating Clinical Pharmacology for *All*

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The prospective and purposeful enablement of diversity, equity, and inclusion (DEI) is a critical core competency for today's multidisciplinary continuum of clinical pharmacology and translational science. *Clinical Pharmacology and Therapeutics* (*CPT*) has adopted DEI as core guiding principles in our field.[1,2] Building upon *CPT*'s mini-themes on the topic in October 2021[1] and August 2022[2] and based on positive feedback from our readers and authors, the current issue was designed to showcase the core role of clinical pharmacology in elucidating and harnessing diversity in disease biology and pharmacologic response to enable safe and effective use of therapeutic innovations in *all* patients (**Figure 1**). In this special issue, we highlight the need to enhance diversity and inclusion throughout the clinical development process, including racial and ethnic diversity and diversity in geographical location, disease diagnosis, and demographic factors such as age and gender.

The importance of moving beyond commonly assigned demographic labels and phenotypic approximations when considering population diversity in drug development and clinical practice continues to grow as we better understand the biological basis of diversity at the molecular level as well as the social, economic, and environmental factors that contribute to differences in access to medical care, clinical trials, and drug response.

Research in pharmacogenomics should include diverse populations as genetic polymorphisms that influence drug response may have different allele frequencies in different populations or even be population specific. Inclusive translational and pharmacogenomics research that nurtures participation of historically excluded, admixed, and minority populations across all geographies is imperative.[3–7] In a Perspective, Sitabule *et al.*[8] posit that African populations have more genetic variation than other geographic groups, emphasizing the critical importance of promoting pharmacogenomics research in Africa in the context of the growing burden of both infectious and noninfectious diseases impacting the continent and globe. A major barrier to inclusion in pharmacogenomic research has been a lack of trust particularly from historically excluded populations. Jasper *et al.*[9] and Brown *et al.*[10] raise awareness of the value of building community trust to enhance diversity and inclusion in pharmacogenomics research to include minority groups and vulnerable populations (e.g., pediatrics and pregnant individuals). These consultative and collaborative strategies are designed to enhance trust by facilitating input from community experts to enhance research design, implementation, and dissemination, with the purpose of

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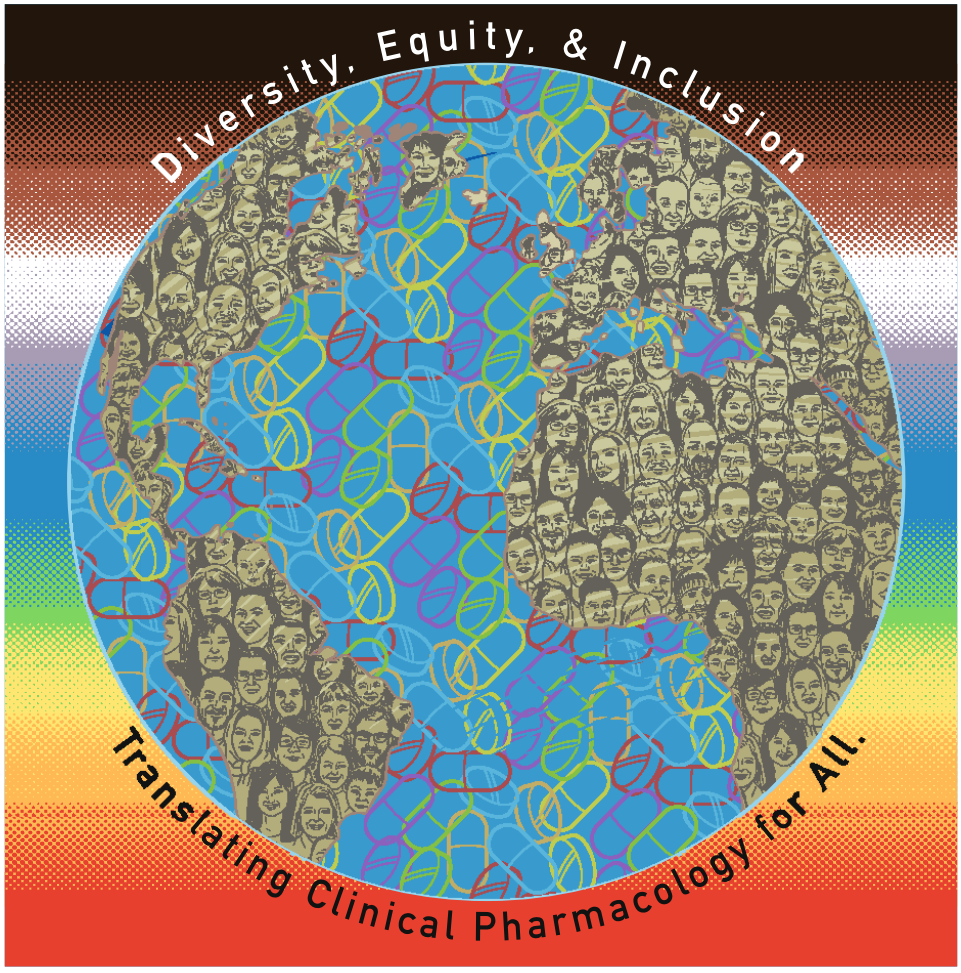

Figure 1 *Clinical Pharmacology & Therapeutics* March 2023 cover image: Diversity, Equity, and Inclusion: Translating Clinical Pharmacology for *All*.

enabling equitable access to clinical trials and delivery of innovation for people who have historically been left out of biomedical research. In their comprehensive review of methodologies for population pharmacogenomics research, Yang *et al*.[11] offer a landscape analysis of multi-omics technologies across the spectrum from the genome to transcriptome, proteome and metabolome, with a specific focus on database resources and analytics that maximize the ability to discover variants of pathophysiologic and pharmacological significance in minority and admixed populations.

Race continues to play a role in medical care—diagnosis, treatment, and practice—and is utilized in the medical curriculum. On behalf of the European Open Platform for prescribing Education (EurOP^{2}E) consortium, Bakkum *et al*. illustrate the unintended consequences of race-based medical guidelines.[12] The authors offer a call to action for the teaching community to be cognizant of the nuanced and incomplete overlaps between self-assigned labels of race and the true biological drivers of variation in disease biology and pharmacologic response to therapeutics, cautioning against the use of clinical case vignettes containing oversimplification and stereotyping. Equally important to appreciate for successful personalization of therapeutics and dosing across diverse populations is the multiplicity of intrinsic and extrinsic determinants of benefit/risk of drugs and our often incomplete understanding of the role of these factors, particularly in under-represented racial groups, as reviewed for direct oral anticoagulants by Thompson *et al*.[13] With the exponential increase in our ability to harness multi-modal data and digital technologies, translation of our understanding of population sources of variability to precision dosing solutions for *all* patients is an opportunity for intelligent clinical decision support systems, as reviewed by Hughes *et al*.[14] We are witnessing substantial progress in the science and technology required to develop

intelligent, continuously learning precision dosing systems driven by population pharmacology models built from clinical trial and real-world data in diverse populations.[14–16] Translating scientific and medical advances to equity in health care will, however, need to consider and address the critically important extrinsic factor of *Social Determinants of Health* through innovative health system, public health, and policy-level interventions, as eloquently discussed by Golden[17]—reflecting her compelling State of the Art lecture at the ASCPT 2022 Annual Meeting.

A seminal *CPT* publication in 2021 systematically reviewed the available data on sex and gender differences in clinical pharmacology, identifying knowledge gaps and opportunities to optimize pharmacotherapy in the transgender population.[18] The authors of this State of the Art review were recognized with the 2022 *CPT* Award. In the current issue, Webster raises awareness of the critical importance of optimizing healthcare for this population in a patient perspective based on an interview with a transgender woman and her lived experiences with accessing gender-affirming medical care.[19] In addition to giving voice to the experiences of transgender individuals navigating the US healthcare system, this perspective outlines necessary steps to improve the quality of transgender patient care and recommendations for researchers. Cirrincione *et al*.[20] offer insights for enabling participation of transgender individuals in phase III clinical trials through community engagement and recruitment efforts, reflecting on experience in the HIV prevention clinical trial setting which intentionally included transgender and gender diverse people.

In addition to describing the scientific, environmental, and socioeconomic reasons for inclusion of diverse populations in clinical pharmacology studies, this issue of *CPT* also includes manuscripts that focus on mechanisms to facilitate recruitment of diverse populations into clinical studies. We are pleased to highlight a series of contributions in this issue of *CPT* that provide expert recommendations from across sectors of practice to enable enhancement of diversity and inclusion in clinical trials. Johnson-Williams *et al*.[21] offer a vision for patient-centered multistakeholder continuous engagement throughout the drug discovery, development, and utilization spectrum to ultimately help close the existing gaps that contribute to health disparities in underserved communities. As articulated by the authors, the purpose is simple—ensuring that the clinical trial population reflects the diversity of patients likely to take a medical product if it is approved. In their White Paper outlining the findings from qualitative research by the Clinical Trials Transformation Initiative (CTTI) Diversity Team, Corneli and colleagues[22] present the insights gained from interviews with leaders at institutions that conduct clinical trials that were designed to explore perspectives on organizational-level practices that promote diversity and inclusion in clinical trials. Washington *et al*.[23] review facilitators for actionable enhancement of diversity, equity, and inclusion (DEI) at all stages of clinical development—planning/design, protocol generation, accrual/enrollment, study conduct, analysis of results, and evidence generation for regulatory review. Of note, some of the identified strategies, like decentralization and technology-driven flexibility in data collection, are notable opportunities to leverage quantitative clinical pharmacology methods for design optimization and analysis applying principles of model-informed drug development. Mohan and Freedman[24] review three exemplary clinical trials in diverse therapeutic areas—coronavirus disease 2019 (COVID-19), multiple sclerosis, and diabetic macular edema—where an emphasis on inclusion or exclusive enrollment of historically underrepresented racial and ethnic groups was a key focus of design and operationalization. The authors discuss community engagement, site selection strategy, patient-centered approaches to communication, and breaking barriers to participation as key enablers, in resonance with several of the recommendations offered through insights from CTTI's qualitative research,[22] the roadmap presented by Washington *et al*.,[23] and MacLennan *et al*.'s[25] survey of site-level clinical research professionals. Regulatory frameworks that nurture DEI are the subject of two mini-reviews in this issue of *CPT*. Ramamoorthy and co-workers[26] provide a broad overview of select US Food and Drug Administration (FDA) initiatives aimed at promoting clinical trial diversity. From a European Medicines Agency perspective, Cerreta *et al*.[27] outline the Agency's approach to assess data on older adult patients in medicines registration dossiers in alignment with the International Conference on Harmonization (ICH) E7 geriatrics guidance.

As articulated by Brown *et al*.[28] in their Call to Action contributed by a diverse group of members of the American Society for Clinical Pharmacology and Therapeutics (ASCPT) working across sectors of practice and scientific

disciplines, prioritization of DEI across all facets of our work should be a priority for the clinical pharmacology community. This applies not only to increasing diversity in clinical research, but further for broadening the diversity in our workforce—nurturing authenticity, empathy, and continuous evolution—with benefits ranging from better business performance to improved decision making. The release of this issue of *CPT* in March 2023 will coincide with the Annual Meeting of ASCPT, themed *Translating Clinical Pharmacology for All*. We trust that the content in this month's *CPT* issue, together with the scientific program of the Annual Meeting, will galvanize our multidisciplinary and cross-sector community of clinical pharmacologists as they engage and network during the Annual Meeting and beyond, to advance clinical pharmacology, translational science, and therapeutics for the benefit of patients and society.

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