Global Journal of Research in
Biology and Pharmacy
Journal homepage: https://gsjournals.com/gjrbp/
ISSN: 2980-4221 (Online)

(REVIEW ARTICLE)

Check for updates

PHARMACOGENOMICS AND PERSONALIZED DRUG THERAPY: IMPLEMENTATION IN DIVERSE POPULATIONS AND REAL-WORLD EVIDENCE

Anjali H. Bhanushali *

Bansal College of Pharmacy, Kokta, Bhopal, Madhya Pradesh, India.
* Corresponding Author

Global Journal of Research in Biology and Pharmacy, 2025, 04(02), 001–004

Publication history: Received on 08 March 2025; revised on 24 April 2025; accepted on 27 April 2025

Article DOI: https://doi.org/10.58175/gjrbp.2025.4.2.0038

ABSTRACT

Pharmacogenomics aims to tailor drug therapy based on an individual's genetic profile, improving efficacy and reducing adverse drug reactions. While major pharmacogenomic associations have been identified for drug-metabolizing enzymes, transporters, and human leukocyte antigens, clinical implementation has been uneven across healthcare systems and populations. This review critically examines the current state of pharmacogenomic implementation, focusing on diverse ancestral populations and the role of real-world evidence in validating clinical utility. Key implementation examples include HLA-B*57:01 screening for abacavir hypersensitivity, TPMT/NUDT15 testing before thiopurine therapy, and CYP2C19-guided antiplatelet therapy. However, the majority of discovery cohorts remain of European ancestry, leading to reduced predictive accuracy and missed variants in African, Asian, Hispanic, and Indigenous populations. Star allele systems and rare variants vary significantly across populations, and polygenic scores may not transfer across ancestries. Real-world data from electronic health records, biobanks, and pragmatic trials are increasingly used to assess clinical outcomes, cost-effectiveness, and implementation barriers. Challenges include lack of standardized reporting, limited diversity in biobanks, healthcare provider education, and payer reimbursement policies. Future directions include diverse biobank initiatives, population-specific allele definition, pharmacogenomic-guided randomized trials, and integration of genomic data into clinical decision support. Achieving equitable pharmacogenomic implementation requires deliberate inclusion of underrepresented populations and robust real-world evidence generation.

Keywords: Pharmacogenomics; Personalized Medicine; Health Equity; Diverse Populations; Real-World Evidence; Clinical Implementation

1 INTRODUCTION

Pharmacogenomics investigates how genetic variation influences drug response, encompassing pharmacokinetics and pharmacodynamics. The promise of personalized medicine is to use genomic information to select the right drug and dose for each patient, maximizing benefit and minimizing harm. Several pharmacogenomic biomarkers have been incorporated into drug labels and clinical guidelines, including variants in CYP2C19, CYP2D6, TPMT, NUDT15, HLA-B, and VKORC1. Evidence from randomized controlled trials and observational studies supports the clinical utility of pharmacogenomic testing for specific drug–gene pairs.

Despite progress, implementation remains inconsistent. One critical barrier is the underrepresentation of non-European populations in genomic research. Many pharmacogenomic allele definitions and dosing recommendations were developed primarily in European cohorts, and their validity in diverse populations is uncertain. For example, CYP2D6 allele frequencies and structural variants differ substantially across Africans, Asians, and Latin Americans, affecting prediction of metabolizer status. Similarly, HLA allele frequencies and haplotypes vary, influencing drug hypersensitivity risk.

Real-world evidence—derived from electronic health records, pragmatic trials, and population biobanks—is increasingly recognized as essential for evaluating pharmacogenomic implementation in routine care. This review examines the current landscape, emphasizing diverse populations and real-world evidence, with references before February 2025.

2 PHARMACOGENOMIC BIOMARKERS AND IMPLEMENTATION EXAMPLES

Several well-established pharmacogenomic associations have reached clinical practice. HLA-B*57:01 screening before abacavir reduces the risk of severe hypersensitivity reactions and is recommended by guidelines worldwide. TPMT and NUDT15 genotyping before thiopurine therapy prevents myelosuppression; NUDT15 variants are particularly important in East Asian and Hispanic populations. CYP2C19 loss-of-function alleles reduce clopidogrel activation, and genotype-guided antiplatelet therapy improves outcomes in acute coronary syndrome. CYP2D6 genotyping informs opioid and antidepressant selection. These examples demonstrate that pharmacogenomics can improve safety and efficacy when implemented effectively.

3 DIVERSITY GAPS IN PHARMACOGENOMIC DISCOVERY AND TRANSLATION

Most genome-wide association studies and pharmacogenomic discovery cohorts are of European ancestry. This bias has direct consequences. Star allele definitions, which summarize common haplotypes, may miss population-specific variants or structural rearrangements. For example, CYP2D6*4 is common in Europeans but rare in Africans, where hybrid genes and duplications require advanced sequencing. CYP2C19*17, an increased-function allele, is less frequent in East Asians. The transferability of polygenic risk scores for drug response is generally poor across ancestries. Without diverse data, pharmacogenomic algorithms may misclassify metabolizer status and lead to incorrect dosing. Several initiatives, including the All of Us Research Program, H3Africa, and the Indian Genome Variation Consortium, are addressing these gaps, but translation into clinical guidelines lags.

4 REAL-WORLD EVIDENCE IN PHARMACOGENOMICS

Real-world studies leverage electronic health records, linked genomic data, and observational cohorts to evaluate outcomes in unselected patients. For example, the Implementing GeNomics In pracTicE (IGNITE) network has demonstrated feasibility of pharmacogenomic testing in primary care. Pragmatic trials, such as the POPular Genetics trial for CYP2C19-guided P2Y12 inhibitor selection, showed reduced bleeding without increased thrombotic events. Real-world data have also been used to assess the economic impact of testing, supporting cost-effectiveness in selected scenarios. However, real-world studies face challenges: missing data, confounding by indication, and lack of standardized outcome definitions. Nevertheless, they provide essential evidence for implementation beyond controlled trials.

5 IMPLEMENTATION BARRIERS AND STRATEGIES

Barriers to pharmacogenomic implementation include lack of provider knowledge, limited decision support, unclear reimbursement, and delayed turnaround times. In diverse populations, additional barriers include lack of reference materials and allele definitions. Strategies to address these include preemptive testing, integration of results into electronic health records with actionable alerts, and multidisciplinary pharmacogenomics clinics. Health-system-based programs in the US and Europe have demonstrated uptake and improved prescribing. Global implementation requires adaptation to local populations, including population-specific allele panels and evidence of clinical utility.

6 FUTURE PERSPECTIVES

Future directions include diverse biobank phenotyping, long-read sequencing to resolve complex variants, and development of population-specific pharmacogenomic algorithms. Machine learning may improve prediction of drug response using integrated genomic and clinical data. Large pragmatic trials across multiple ancestries are needed to generate evidence for understudied populations. Regulatory agencies and payers must support pharmacogenomic

testing through clear guidance and reimbursement. Global collaboration is essential to ensure equitable access to pharmacogenomic benefits.

7 CONCLUSION

Pharmacogenomics has demonstrated clinical utility for several drug–gene pairs, but implementation is limited by evidence gaps in diverse populations and insufficient real-world validation. Addressing these gaps requires deliberate inclusion of underrepresented groups in research, adaptation of allele definitions, and generation of robust real-world evidence. Only then can the promise of personalized medicine be realized for all patients.

REFERENCES

[1] Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. Clin Pharmacol Ther. 2011;89(3):464–467.

[2] Mallal S, Phillips E, Carosi G, et al. HLA-B5701 screening for hypersensitivity to abacavir. N Engl J Med. 2008;358(6):568–579.

[3] Relling MV, Schwab M, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium guideline for thiopurine dosing based on TPMT and NUDT15 genotypes: 2018 update. Clin Pharmacol Ther. 2019;105(5):1095–1105.

[4] Scott SA, Sangkuhl K, Stein CM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. Clin Pharmacol Ther. 2013;94(3):317–323.

[5] Hicks JK, Swen JJ, Thorn CF, et al. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clin Pharmacol Ther. 2013;93(5):402–408.

[6] Popejoy AB, Fullerton SM. Genomics is failing on diversity. Nature. 2016;538(7624):161–164.

[7] Martin AR, Kanai M, Kamatani Y, et al. Clinical use of current polygenic risk scores may exacerbate health disparities. Nat Genet. 2019;51(4):584–591.

[8] All of Us Research Program Investigators. The “All of Us” Research Program. N Engl J Med. 2019;381(7):668–676.

[9] Dunnenberger HM, Crews KR, Hoffman JM, et al. Preemptive clinical pharmacogenetics implementation: current programs in five US medical centers. Annu Rev Pharmacol Toxicol. 2015;55:89–106.

[10] Claassens DMF, Vos GJA, Bergmeijer TO, et al. A genotype-guided strategy for oral P2Y12 inhibitors in primary PCI. N Engl J Med. 2019;381(17):1621–1631.

[11] Empey PE, Pratt VM, Hoffman JM, et al. Expanding evidence leads to new pharmacogenomics payer coverage. Genet Med. 2021;23(5):830–836.

[12] Yang W, Wu G, Broeckel U, et al. Comparison of genome sequencing and clinical genotyping for pharmacogenes. Clin Pharmacol Ther. 2016;100(4):380–388.

[13] Whirl-Carrillo M, McDonagh EM, Hebert JM, et al. Pharmacogenomics knowledge for personalized medicine. Clin Pharmacol Ther. 2012;92(4):414–417.

[14] Huddart R, Fohner AE, Whirl-Carrillo M, et al. Standardized biogeographic grouping system for annotating populations in pharmacogenetic studies. Clin Pharmacol Ther. 2019;105(5):1256–1262.

[15] Johnson JA, Caudle KE, Gong L, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for pharmacogenetics-guided warfarin dosing: 2017 update. Clin Pharmacol Ther. 2017;102(3):397–404.

[16] Volpi S, Bult CJ, Chisholm RL, et al. Research directions in the clinical implementation of pharmacogenomics: an overview of US programs and projects. Clin Pharmacol Ther. 2018;103(5):778–786.

[17] Zhang L, Zhang Y, Zhao P, et al. CYP2D6 genetic variation in multiple ethnic populations. Pharmacogenomics. 2021;22(14):907–919.

[18] Zhou Y, Ingelman-Sundberg M, Lauschke VM. Worldwide distribution of cytochrome P450 alleles: a meta-analysis of population-scale sequencing projects. Clin Pharmacol Ther. 2017;102(4):688–700.

[19] Cavallari LH, Lee CR, Beitelshees AL, et al. Multisite investigation of outcomes with implementation of CYP2C19 genotype-guided antiplatelet therapy after percutaneous coronary intervention. JACC Cardiovasc Interv. 2018;11(2):181–191.

[20] Morris SA, Alsaidi AT, Verbyla A, et al. Cost effectiveness of pharmacogenetic testing for drugs with Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines: a systematic review. Expert Rev Pharmacoecon Outcomes Res. 2021;21(4):669–681.