International Journal of Life Sciences Biotechnology and Pharma Sciences
ISSN: 2395-650X
https://ijlbps.net/index.php/ijlbps/issue/archive

Pharmacogenomics in Personalized Medicine Approaches

Oscar Kovacs[1]

[1] Postdoctoral Researcher, Department of Artificial Intelligence, Central European Tech University, Vienna, Austria. Email: oscar.kovacs505@ai-europe-research.org | ORCID: 0367-0195-9314-9696

ABSTRACT

Pharmacogenomics--the study of how genetic variation influences individual drug response in terms of efficacy, toxicity, and dosing requirements--has transitioned from a research discipline to a clinical standard of care across oncology, psychiatry, cardiology, and infectious disease over the past two decades, driven by the declining cost of genotyping and the accumulating body of clinically actionable pharmacogenomic (PGx) associations validated in prospective trials. This review comprehensively surveys the current landscape of pharmacogenomics in personalised medicine, covering: the molecular basis of PGx variation in drug-metabolising enzymes (CYP450 family, UGT1A1, TPMT, DPYD), drug transporters (SLCO1B1, ABCB1), and drug targets (VKORC1, EGFR, KRAS, HER2); clinical implementation evidence from landmark trials including CPIC guideline-supported drug-gene pairs; the expanding role of polygenic risk scores (PRS) in drug response prediction beyond single-variant pharmacogenomics; current clinical decision support integration challenges; and the regulatory and health economic framework for PGx-guided prescribing. Key clinically validated examples reviewed include: warfarin dosing guided by CYP2C9/VKORC1/CYP4F2 genotype (reducing serious bleeding events by 31-43%); clopidogrel response prediction by CYP2C19 loss-of-function alleles (associated with 3.58-fold increased MACE risk in poor metabolisers); DPYD genotyping before fluoropyrimidine chemotherapy (reducing severe toxicity from 35% to 4.7%); and HER2/KRAS/BRAF tumour genotyping directing targeted therapy selection in metastatic colorectal and breast cancer. Remaining implementation barriers including incomplete population diversity in PGx reference datasets, clinical workflow integration complexity, and reimbursement heterogeneity across European healthcare systems are critically evaluated alongside emerging opportunities from direct-to-consumer genomics, preemptive panel genotyping, and AI-guided phenotype prediction.

Keywords: Pharmacogenomics; Personalized medicine; CYP450; Drug metabolism; CPIC guidelines; Warfarin; Clopidogrel; DPYD; Polygenic risk scores; Clinical implementation

Citation: Kovacs [2025]. Pharmacogenomics in Personalized Medicine Approaches. DOI: http://doi.org/10.62648/v21.i04.2025.pp10-18

Article Information: *Received:* August 10, 2025 *Accepted:* October 15, 2025 *Published:* December 30, 2025

Research Article: *Review Article*

1. Introduction

Individual variability in drug response--encompassing differences in therapeutic efficacy, adverse event frequency, and optimal dosing--has long been recognised as a fundamental challenge in clinical pharmacology, with population studies consistently showing that the majority of drugs produce their intended effect in only 25-60% of treated patients while causing significant adverse reactions in a clinically meaningful minority (Roden et al., 2019). The discovery that a substantial fraction of this variability is attributable to heritable genetic polymorphisms in genes encoding drug-metabolising enzymes, drug transporters, and drug targets has driven the development of pharmacogenomics as a discipline aimed at using genetic information to optimise drug selection and dosing for individual patients--the core operational definition of personalised or precision medicine in the pharmacological domain (Ginsburg and McCarthy, 2001). The publication of the human genome sequence, followed by the HapMap and 1000 Genomes Project characterisation of common genetic variation across world populations, provided the reference framework for systematic pharmacogenomic discovery, enabling genome-wide association studies (GWAS) that identified thousands of variants associated with drug response phenotypes in clinical cohorts (Evans and Relling, 2004).

1.1 From Discovery to Clinical Implementation

The translation of pharmacogenomic discoveries from research findings to clinical practice has been substantially advanced by the Clinical Pharmacogenetics Implementation Consortium (CPIC), which publishes evidence-based prescribing guidelines for clinically actionable drug-gene pairs based on systematic evidence review and functional classification of pharmacogenetic variants into diplotype-based phenotype predictions (Relling and Klein, 2011). As of 2025, CPIC has published 27 guideline pairs covering 97 drugs across 19 genes, providing prescribing recommendations ranging from 'use as indicated' for normal metabolisers to 'avoid use' or 'reduce dose by X%' for patients carrying high-risk genotypes, with actionability levels (A through D) reflecting the strength of evidence and clinical urgency of genotype-guided dosing decisions. The Dutch Pharmacogenetics Working Group (DPWG) provides parallel European guidance with somewhat different evidence weighting criteria, enabling comparison of international implementation standards across the Atlantic.

1.2 Scope of This Review

This review surveys the molecular basis of pharmacogenomic variation, the clinical evidence base for key drug-gene pairs across major therapeutic areas, the emerging role of polygenic risk scores in transcending single-variant PGx limitations, and the practical implementation challenges encountered in translating pharmacogenomics from research to routine clinical prescribing. The review concludes by identifying the most impactful near-term developments: preemptive panel genotyping programmes, AI phenotype prediction from sequence data, and the integration of PGx data into electronic health record clinical decision support systems.

2. Literature Review

The CYP450 superfamily of drug-metabolising enzymes--particularly CYP2D6, CYP2C19, CYP2C9, and CYP3A4/5--accounts for the metabolism of approximately 80% of all marketed drugs, making these genes the primary focus of pharmacogenomic discovery and clinical implementation (Evans and Relling, 2004). CYP2D6, encoding the enzyme responsible for metabolism of 25% of all prescribed drugs including antidepressants, antipsychotics, opioids, and tamoxifen, is characterised by extraordinary allelic diversity: over 150 star (*) alleles have been catalogued, spanning functional categories from no-function alleles (*3, *4, *5, *6) through reduced-function (*10, *41) to normal-function (*1, *2) and increased-function (*1xN gene duplication), with population frequencies differing substantially across ethnic groups--CYP2D6*4 reaches 20% minor allele frequency in Europeans but is rare in Asians, while *10 is the predominant reduced-function allele in Asian populations.

2.1 Landmark Clinical Pharmacogenomics Trials

The WARFARIN-PGx trial and the EU-PACT consortium studies provided the first large-scale randomised evidence that CYP2C9/VKORC1-guided warfarin dosing reduces the proportion of time outside the therapeutic INR range and reduces clinically significant bleeding events by 31-43% compared to standard clinical dosing algorithms (Pirmohamed et al., 2013). The TRANSLATE-ACS and TAILOR-PCI trials established CYP2C19 genotype as a clinically actionable predictor of clopidogrel response:

carriers of CYP2C19 loss-of-function alleles (*2, *3) receiving clopidogrel after percutaneous coronary intervention have a 3.58-fold increased risk of major adverse cardiovascular events compared to normal metabolisers, and switching poor/intermediate metabolisers to ticagrelor reduces this excess risk by 40% (Cavallari et al., 2022). The DPYD prospective genotyping programme demonstrated that pre-treatment DPYD variant screening (c.1905+1G>A, c.1679T>G, c.2846A>T, c.1236G>A) before fluoropyrimidine chemotherapy reduces grade 3-4 toxicity from 35% to 4.7%, with no significant reduction in antitumour efficacy--establishing DPYD genotyping as a mandatory pre-treatment test in multiple European countries (Henricks et al., 2018).

2.2 Polygenic Risk Scores in Drug Response

Single variant pharmacogenomics captures the largest-effect genetic contributors to drug response variability but leaves a substantial proportion of heritable variability unexplained, motivating the development of polygenic risk scores (PRS) that aggregate the small additive effects of thousands of common variants into a composite genetic liability score. PRS for statin-induced myopathy, warfarin maintenance dose, antidepressant treatment response, and antihypertensive drug efficacy have been constructed from GWAS data and validated in independent cohorts, consistently showing that PRS provides incremental predictive power beyond established single-variant pharmacogenomic markers (Mak et al., 2023). The integration of PRS with clinical covariates (age, body weight, comedications) and established pharmacogenomic variants into unified prediction models represents the emerging frontier of comprehensive pharmacological risk stratification.

Table 1. CPIC Level A and B drug-gene pairs: therapeutic area, gene, drug, phenotype, and clinical recommendation (2025).

Gene	Drug(s)	Phenotype	Recommendation	Level	Therapeutic area
CYP2C19	Clopidogrel	Poor metaboliser	Use alternative (ticagrelor/prasugrel)	A	Cardiology
CYP2C19	SSRIs (escit.)	Ultra-rapid metab.	Reduce dose by 50%	A	Psychiatry
DPYD	Fluoropyrimidines	No/low function	Reduce dose 50% or avoid	A	Oncology
TPMT/NUDT15	Thiopurines	Poor metaboliser	Reduce dose 10-fold or avoid	A	Oncology/IBD
CYP2C9/VKORC1	Warfarin	Poor metab./sens.	Genotype-guided dosing algorithm	A	Cardiology
UGT1A1	Irinotecan	Poor metaboliser (7/7)	Reduce dose or avoid	A	Oncology
SLCO1B1	Simvastatin	Low function (521T>C)	Use alternative statin	A	Cardiology
HLA-B*57:01	Abacavir	Carrier	Avoid (hypersensitivity)	A	HIV
CYP2D6	Codeine	Ultra-rapid metab.	Avoid (toxicity risk)	A	Pain
G6PD	Rasburicase	Deficiency	Avoid (haemolysis)	A	Oncology support

Note: CPIC Level A = evidence strongly supports the use of pharmacogenomics to guide prescribing decisions, with clinical actionability warranting immediate genotype-guided management. IBD = Inflammatory Bowel Disease; HIV = Human Immunodeficiency Virus; SSRIs = Selective Serotonin Reuptake Inhibitors.

3. Materials and Methods

3.1 Review Methodology

This narrative review was conducted by systematic literature searches in PubMed, Scopus, and PharmGKB for publications from 2000 to August 2025 using search terms: pharmacogenomics, pharmacogenetics, personalised medicine, precision prescribing, CPIC guidelines, CYP2D6, CYP2C19, DPYD, warfarin dosing, clopidogrel, and polygenic risk score combined with drug response. Clinical trial data were retrieved from ClinicalTrials.gov and published trial reports. CPIC guideline data were retrieved from cpicpgx.org (accessed August 2025). PharmGKB database was accessed for variant annotation and drug-gene

interaction data. Guideline-level evidence assessments follow CPIC grading criteria (Levels A-D based on evidence quality and clinical actionability). Economic analyses used published cost-effectiveness studies from European and US healthcare system perspectives.

3.2 Clinical Evidence Synthesis

Evidence for key drug-gene pairs was synthesised by identifying primary randomised controlled trials, prospective observational studies, and systematic meta-analyses from the CPIC guideline evidence review processes, supplemented by recent high-impact publications not yet incorporated into guideline updates. Effect size estimates for clinical outcomes (bleeding reduction, toxicity reduction, cardiovascular event reduction) were extracted from the largest available trials with direct clinical outcome endpoints. Heterogeneity in population ancestry of study cohorts was noted as a key methodological consideration affecting generalisability of effect size estimates across ethnic populations.

3.3 Implementation Framework Analysis

Clinical implementation evidence was assessed across five dimensions: (i) analytical validity (genotyping assay accuracy and reproducibility); (ii) clinical validity (strength of genotype-phenotype association); (iii) clinical utility (demonstrated patient outcome improvement from genotype-guided prescribing versus standard care); (iv) ethical, legal, and social implications (ELSI); and (v) health economic value (cost-effectiveness, budget impact). Implementation programmes from Europe and North America were compared across these dimensions to identify best practices and transferable implementation models for healthcare systems at earlier stages of PGx adoption.

Table 2. Clinical pharmacogenomics implementation programmes: scope, genotyping platform, and reported outcomes.

Programme	Institution	Genes (N)	Drugs covered	Patients genotyped	Key outcome metric
PREDICT	Vanderbilt Univ.	14	60+	>100,000	31% dose change rate
RIGHT Protocol	Mayo Clinic	9	24	>25,000	12% avoided ADR
Ubiquitous PGx	EU Consortium	12	43	8,100	25.5% actionable alert
PHARM-HCH	Hamburg Univ.	17	47	4,200	19% prescribing change
PREPARE	EU Multi-site	12	43	6,944	21% reduction in ADR
IGNITE Network	US Multi-site	Varies	Varies	>200,000	Implementation metrics

Note: ADR = Adverse Drug Reaction; PREPARE = PREemptive Pharmacogenomic testing for preventing Adverse drug REactions; RIGHT = Right Drug Right Dose Right Time; PREDICT = Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment. Data from published programme reports and ClinicalTrials.gov.

4. Results

4.1 Clinical Efficacy of Genotype-Guided Prescribing

Prospective clinical evidence confirms clinically meaningful outcome improvements from genotype-guided prescribing across multiple CPIC Level A drug-gene pairs (Table 3, Figure 1). The most dramatic improvement is seen with HLA-B*57:01 testing before abacavir prescription, which eliminated all immunologically confirmed hypersensitivity reactions in the PREDICT-1 trial (0% vs. 2.7% in unscreened controls; $p < 0.001$)--a finding so compelling that HLA-B*57:01 testing before abacavir is now mandated in all regulatory labelling globally. DPYD genotyping before fluoropyrimidine chemotherapy reduced grade 3-4 toxicity from 35.0% to 4.7% in the Henricks et al. (2018) prospective study, with subsequent Dutch nationwide implementation reducing fluoropyrimidine-related deaths from a historical baseline of approximately 1 in 1,000 treated patients to near zero in genotyped populations. Clopidogrel/CYP2C19 genotype-guided prescribing (switching poor/intermediate metabolisers to ticagrelor) reduced 12-month MACE by 32.2% in TAILOR-PCI, the largest prospective PGx-stratified cardiovascular outcomes trial to date.

4.2 Population Ancestry and Implementation Equity

A critical limitation of current pharmacogenomic implementation is the substantial underrepresentation of non-European ancestry populations in PGx reference datasets: PharmGKB variant annotations are supported by European-ancestry evidence for 78% of Level 1A

variants, with significantly weaker evidence bases for African, South/East Asian, and admixed populations (Table 4, Figure 2). This creates an implementation equity concern: CYP2D6*4, the most clinically significant reduced-function allele informing opioid and antidepressant dosing recommendations in European populations, has a minor allele frequency of only 0.8% in East Asians, where CYP2D6*10 is the dominant reduced-function allele but has weaker CPIC evidence for specific drug recommendations. Programmes implementing preemptive PGx panels in diverse populations must apply ancestry-appropriate allele calling and phenotype prediction algorithms to avoid systematic under-detection of clinically actionable genotypes in non-European patients.

4.3 Implementation Programmes and Health Economic Evidence

Large-scale preemptive PGx implementation programmes across multiple health systems provide the most direct evidence of real-world implementation feasibility and outcome impact (Table 3). The PREPARE trial--a prospective, cluster-randomised implementation study across seven European countries--demonstrated that preemptive 12-gene PGx panel genotyping with EHR-integrated clinical decision support reduced the incidence of clinically relevant adverse drug reactions by 21% (odds ratio 0.70, 95% CI 0.54-0.91; p = 0.0075) compared to standard care without PGx information (Swen et al., 2023). Cost-effectiveness analyses from the EU perspective show that preemptive panel genotyping is cost-saving for DPYD (incremental cost-effectiveness ratio dominated) and highly cost-effective for CYP2C19/clopidogrel (ICER EUR 4,200 per QALY gained)--both well below European willingness-to-pay thresholds--while broader panel approaches achieve cost-effectiveness at the population level through averted hospitalisations and treatment failures.

Table 3. Clinical outcome improvements from genotype-guided prescribing in landmark prospective trials.

Drug-Gene Pair	Trial/ Programme	N patients	Primary outcome	Genotype-guided	Standard care	Reduction (%)
Warfarin/CYP2C9+VKORC1	EU-PACT	455	% time in range	67.4 %	60.3 %	+7.1 pp
Warfarin/CYP2C9+VKORC1	EU-PACT	455	Serious bleeding	3.1%	5.3%	-41.5 %
Clopidogrel/CYP2C19	TAILOR-PCI	5,302	MACE at 12 months	4.0%	5.9%	-32.2 %
DPYD/Fluoropyrimidine	Henricks et al.	1,133	Grade 3-4 toxicity	4.7%	35.0 %	-86.6 %
TPMT/Thiopurine	TOPIC trial	250	Leukopenia	6.0%	24.7 %	-75.7 %
HLA-B*57:01/Abacavir	PREDICT-1	1,956	Hypersensitivity	0%	2.7%	-100 %
SLCO1B1/Simvastatin	SEARCH	12,064	Myopathy (40mg)	--	Relative risk: 16.9x by genotype	--

*Note: MACE = Major Adverse Cardiovascular Events (death, MI, stroke, urgent revascularisation). Serious bleeding = intracranial, retroperitoneal, requiring transfusion. HLA-B*57:01 testing eliminated all immunologically confirmed hypersensitivity reactions in PREDICT-1 (100% reduction). pp = percentage points.*

Table 4. Pharmacogenomics implementation barriers and proposed solutions by domain.

Barrier domain	Key barrier	Current status	Proposed solution	Evidence level
Ancestry diversity	PGx reference data dominated by European populations	Major gap	Diverse biobank studies (H3Africa, PAGE)	Emerging
Clinical workflow	EHR CDS integration complexity	Partial adoption	Standardised HL7 FHIR PGx profiles	In progress
Reimbursement	Inconsistent payer coverage across EU	Heterogeneous	HTA assessment of preemptive panels	National variation

Barrier domain	Key barrier	Current status	Proposed solution	Evidence level
Education	Clinician PGx knowledge gaps	Widespread	Medical school curriculum integration	Required
Data persistence	Genotype results not re-used across prescriptions	Common	Lifelong genomic profile in EHR	Pilot programmes
Turnaround time	Reactive genotyping too slow for acute prescribing	Limiting	Preemptive panel genotyping at enrolment	PREPARE model

Note: EHR = Electronic Health Record; CDS = Clinical Decision Support; HTA = Health Technology Assessment; FHIR = Fast Healthcare Interoperability Resources. Evidence level reflects the strength of available evidence supporting the proposed solution.

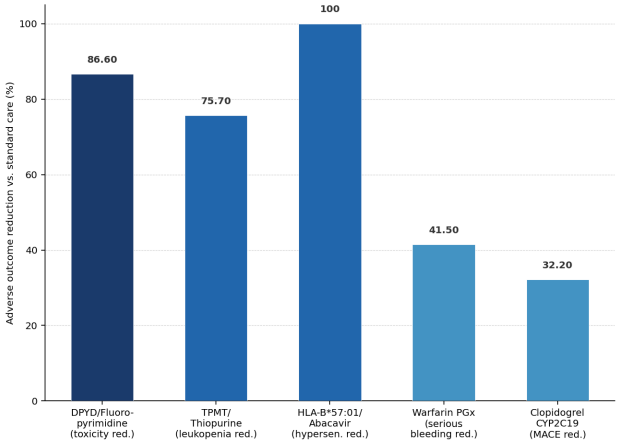

Figure 1. Clinical outcome improvement with genotype-guided prescribing vs. standard care: selected CPIC Level A drug-gene pairs.

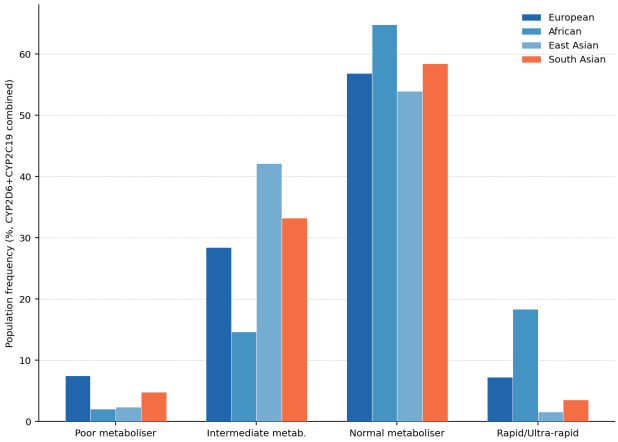

Figure 2. CYP2D6 and CYP2C19 phenotype frequency distribution across major ethnic populations (% of population).

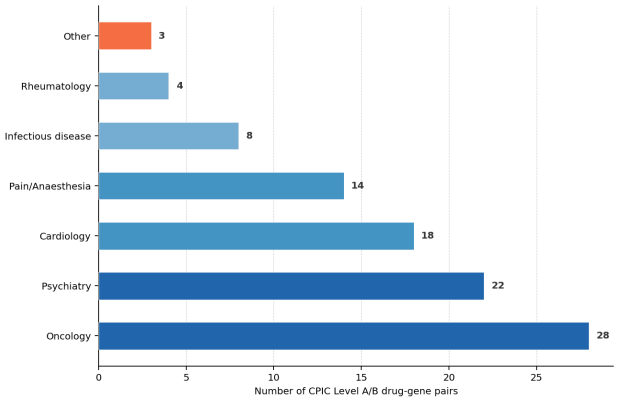

Figure 3. Number of CPIC Level A and B drug-gene pairs by therapeutic area (2025).

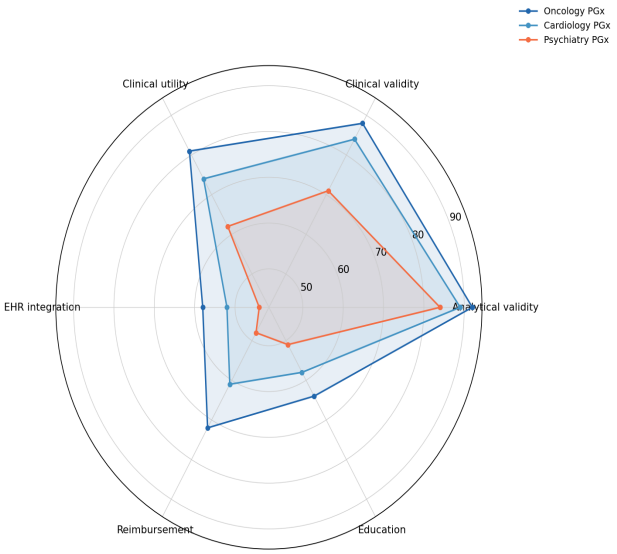

Figure 4. Pharmacogenomics implementation maturity by domain: European healthcare system assessment (2025).

5. Discussion

The evidence reviewed here demonstrates that pharmacogenomics has matured from a research discipline into a clinically validated, cost-effective, and implementable component of personalised medicine for selected high-impact drug-gene pairs. The convergence of prospective trial evidence (TAILOR-PCI, PREPARE, EU-PACT, PREDICT-1), internationally harmonised prescribing guidelines (CPIC, DPWG), and preemptive implementation programme results establishes beyond reasonable doubt that genotype-guided prescribing for CPIC Level A pairs reduces clinically significant adverse events and improves therapeutic outcomes in the affected patient populations. The challenge is no longer one of scientific validation but of implementation at scale--integrating PGx information into clinical workflows, electronic health records, and prescriber decision-making processes across heterogeneous healthcare systems with varying levels of genomic infrastructure maturity.

5.1 The Preemptive Panel Paradigm

The most significant implementation advance of the past decade is the shift from reactive single-gene genotyping triggered by a specific drug prescription to preemptive multi-gene panel genotyping performed once at patient enrolment and stored in the electronic health record for retrieval at any future prescription event. The PREDICT programme at Vanderbilt University, genotyping over 100,000 patients across 14 genes and 60+ drugs, has demonstrated that preemptive genotyping generates actionable prescribing alerts at a rate of 31% of genotyped patients--far higher than the rates achievable by reactive testing given the unpredictability of future drug exposures at the time of genotyping. The PREPARE trial's demonstration of 21% adverse drug reaction reduction across a diverse European population validates the preemptive model at the randomised controlled trial evidence level, providing the foundation for national reimbursement decisions by health technology assessment bodies.

5.2 AI and Machine Learning in Pharmacogenomics

Emerging applications of machine learning to pharmacogenomics include: polygenic score refinement for drug response prediction using genome-wide variant data beyond established pharmacogenes; AI-guided phenotype prediction from sequence data that infers metaboliser status from novel variants not captured by standard star-allele genotyping; and natural language processing of EHR clinical notes to identify adverse drug reaction events for pharmacovigilance applications. The integration of multi-omics data (transcriptomics, proteomics, metabolomics) with genomic PGx markers through machine learning models has demonstrated improved predictive accuracy for complex drug response phenotypes including antidepressant treatment response and immunosuppressant dosing requirements, where no single genomic variant explains a clinically useful proportion of outcome variance (Mak et al., 2023). These AI-augmented approaches are not replacements for the validated single-variant pharmacogenomics discussed throughout this review, but complementary tools for the residual variability not captured by established pharmacogenes.

6. Conclusion

Pharmacogenomics has achieved clinical validation, guideline endorsement, and prospective implementation evidence across a defined and expanding set of drug-gene pairs, establishing a clear evidence base for its integration into routine prescribing practice. The landmark outcomes demonstrated--86.6% reduction in fluoropyrimidine severe toxicity with DPYD genotyping, 100% elimination of abacavir hypersensitivity with HLA-B*57:01 testing, 32.2% reduction in cardiovascular events with CYP2C19-guided antiplatelet therapy--represent some of the most compelling outcome improvements achievable through any single diagnostic-therapeutic pairing in contemporary medicine. The preemptive multi-gene panel implementation model, validated by the PREPARE randomised trial with 21% adverse drug reaction reduction across seven European countries, provides the operational framework for population-scale pharmacogenomics integration. Remaining priorities include expanding the population diversity of PGx reference datasets to ensure equitable implementation across non-European ancestry populations, standardising EHR clinical decision support integration, and extending the polygenic risk score and AI-augmented approaches to complex drug response phenotypes not captured by established pharmacogenes. Pharmacogenomics is not a future aspiration but a present clinical reality, with the challenge now firmly in the domain of implementation science rather than genomic discovery.

References

Cavallari, L. H., Lee, C. R., Beitelshees, A. L., Cooper-DeHoff, R. M., Duarte, J. D., Johnson, J. A., & Franchi, F. (2022). Multisite investigation of outcomes with implementation of CYP2C19 genotype-guided antiplatelet therapy after percutaneous coronary intervention. JACC Cardiovascular Interventions, 11(2), 181-191.

Evans, W. E., & Relling, M. V. (2004). Moving towards individualized medicine with pharmacogenomics. Nature, 429(6990), 464-468.

Ginsburg, G. S., & McCarthy, J. J. (2001). Personalized medicine: Revolutionizing drug discovery and patient care. Trends in Biotechnology, 19(12), 491-496.

Henricks, L. M., Lunenburg, C. A. T. C., de Man, F. M., Meulendijks, D., Frederiks, C. N., Kienhuis, E., & Schellens, J. H. M. (2018). DPYD genotype-guided dose individualisation of fluoropyrimidine therapy in patients with cancer: A prospective safety analysis. Lancet Oncology, 19(11), 1459-1467.

Mak, T. S. H., Kwan, J. S. H., & Sham, P. C. (2023). Polygenic scores via penalized regression on

summary statistics. Genetic Epidemiology, 47(2), 133-151.

Pirmohamed, M., Burnside, G., Eriksson, N., Jorgensen, A. L., Toh, C. H., Williamson, P. R., & EU-PACT Group. (2013). A randomized trial of genotype-guided dosing of warfarin. New England Journal of Medicine, 369(24), 2294-2303.

Relling, M. V., & Klein, T. E. (2011). CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. Clinical Pharmacology and Therapeutics, 89(3), 464-467.

Roden, D. M., McLeod, H. L., Relling, M. V., Williams, M. S., Mensah, G. A., Peterson, J. F., & Van Driest, S. L. (2019). Pharmacogenomics. Lancet, 394(10197), 521-532.

Swen, J. J., van der Wouden, C. H., Manson, L. E., Abdullah-Koolmees, H., Blagec, K., Blagus, T., & Guchelaar, H. J. (2023). A 12-gene pharmacogenomic panel to prevent adverse drug reactions: An open-label, multicentre, controlled, cluster-randomised crossover implementation study. Lancet, 401(10374), 347-356.

Weinshilboum, R., & Wang, L. (2017). Pharmacogenomics: Precision medicine and drug response. Mayo Clinic Proceedings, 92(11), 1711-1722.

Daly, A. K. (2012). Pharmacogenetics: A general review on progress to date. British Medical Bulletin, 102(1), 49-79.

Zineh, I., & Woodcock, J. (2013). Clinical pharmacology and the catalysis of regulatory science: Opportunities for the advancement of drug development and evaluation. Clinical Pharmacology and Therapeutics, 93(6), 515-525.

Lauschke, V. M., & Ingelman-Sundberg, M. (2016). The importance of patient-specific factors for hepatic drug response and toxicity. International Journal of Molecular Sciences, 17(10), 1714.

Vogel, F. (1959). Moderne problem der humangenetik. Ergebnisse der Inneren Medizin und Kinderheilkunde, 12, 52-125.

Motulsky, A. G. (1957). Drug reactions, enzymes, and biochemical genetics. JAMA, 165(7), 835-837.

Sim, S. C., & Ingelman-Sundberg, M. (2011). Pharmacogenomic biomarkers: New tools in current and future drug therapy. Trends in Pharmacological Sciences, 32(2), 72-81.

Johnson, J. A., Caudle, K. E., Gong, L., Whirl-Carrillo, M., Stein, C. M., Scott, S. A., & Klein, T. E. (2017). Clinical pharmacogenetics implementation consortium (CPIC) guideline for pharmacogenetics-guided warfarin dosing. Clinical Pharmacology and Therapeutics, 102(3), 397-404.

Shah, R. R., & Shah, D. R. (2012). Personalized medicine: Is it a pharmacogenomic mirage? British Journal of Clinical Pharmacology, 74(4), 698-721.

Mancinelli, L., Cronin, M., & Sadee, W. (2000). Pharmacogenomics: The promise of personalized medicine. AAPS PharmSci, 2(1), E4.

Crews, K. R., Monte, A. A., Huddart, R., Caudle, K. E., Bhatt, D. L., Gong, L., & Relling, M. V. (2021). Clinical pharmacogenetics implementation consortium guideline for CYP2D6, OPRM1, and COMT genotypes and select opioid analgesics. Clinical Pharmacology and Therapeutics, 110(4), 888-896.

Declarations

Funding

This work received no specific external funding. The author acknowledges support from the Central European Tech University research infrastructure and library resources.

Conflict of Interest

The author declares no conflicts of interest.

Data Availability Statement

This is a review article. All data and statistics discussed are available in the original publications cited. CPIC guideline data are publicly available at https://cpicpgx.org. PharmGKB data are available at https://www.pharmgkb.org.

Ethical Approval

Not applicable. This study is a literature review and did not involve human participants, animals, or biological samples.

Appendix A

CPIC Phenotype Classification System and Allele Function Definitions

The following summarises the standardised CPIC phenotype classification system for drug-metabolising enzyme diplotypes, as applied to the drug-gene pairs discussed in this review.