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Review Article

Pharmacogenomics and Precision Medicine: From Genetic Testing to Individualized Pharmacotherapy

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ABSTRACT

Pharmacogenomics (PGx) examines how inherited genetic variation influences drug exposure, efficacy, and toxicity. Genetic results can guide treatment when the gene-drug relationship is clinically valid, actionable, and interpreted in the context of the patient and the intended use. This narrative review summarizes the path from testing and genotype interpretation to individualized pharmacotherapy, highlighting implementation evidence, guideline resources, and barriers to equitable routine care. Established examples include HLA-B*57:01 testing to prevent abacavir hypersensitivity; TPMT and NUDT15-guided thiopurine dosing; CYP2C19-guided selection of antiplatelet therapy; DPYD-informed fluoropyrimidine dosing; and CYP2D6-guided use of codeine and tramadol. The FDA's current pharmacogenetic association table distinguishes associations with therapeutic-management recommendations from those supported only by pharmacokinetic evidence, underscoring that a gene-drug association does not automatically justify testing. The PREPARE implementation trial reported fewer clinically relevant adverse drug reactions among patients with actionable gene-drug pairs receiving a pre-emptive 12-gene panel, while trials in specific settings show that clinical utility varies with population, comparator, outcome, and implementation. Testing alone is insufficient: assay coverage, phenotype translation, ancestry-related allele representation, drug interactions, clinical decision support, result portability, informed consent, and clinician education all influence benefit. PGx is most effective when integrated with medication review, clinical monitoring, patient preferences, and evidence-based guidelines, rather than treated as a stand-alone prescribing algorithm. Further pragmatic research should assess long-term outcomes, costs, equity, and workflow effects across diverse health systems.

Keywords: pharmacogenomics; precision medicine; pharmacogenetics; individualized pharmacotherapy; gene-drug interactions; clinical implementation

1. Introduction

Drug response varies because of genetic and non-genetic factors, including age, organ function, disease state, dose, adherence, diet, and interacting medicines. Pharmacogenomics contributes one component of precision medicine by identifying inherited variants that alter drug metabolism, transport, targets, or immune recognition. The clinical task is to translate a laboratory result into a treatment decision with a favorable balance of benefit, harm, and feasibility. [1,2]

Clinical PGx has moved beyond association studies. Guidelines now provide recommendations for selected gene-drug pairs, but the evidence and actionability differ across pairs. A useful distinction is whether testing is necessary before therapy, whether a pre-existing result can guide prescribing, or whether evidence supports only a pharmacokinetic association without an established clinical outcome. CPIC guidelines primarily explain how to use available results; they do not generally determine whether a test should be ordered. [2,14]

2. Methodology / Literature Search Strategy

This is a narrative review, not a systematic review. A targeted search was conducted on 30 October 2026 using official FDA, CPIC, and ClinPGx resources, PubMed-indexed literature, and major clinical trial reports. Search concepts combined "pharmacogenomics" or "pharmacogenetics" with "precision medicine," "implementation," "clinical utility," "gene-drug guideline," and examples including CYP2C19, HLA-B, TPMT/NUDT15, DPYD, and CYP2D6. Priority was given to current guidance, major implementation trials, systematic evidence, and sources that clarify test interpretation and limitations.

No protocol registration, reproducible database-specific search strings, dual screening, formal risk-of-bias assessment, or quantitative synthesis was undertaken. The source selection is selective and may omit relevant evidence; it should not be read as an exhaustive systematic review. Guideline versions and regulatory statements are described with their dates because recommendations and labeling can change.

3. Background

PGx testing may be targeted to a specific medicine or performed pre-emptively as a panel whose results are stored for future prescribing. Targeted testing can be clinically efficient when treatment is planned and the result is needed promptly. Pre-emptive panels can make results available

across multiple future prescriptions, but create additional requirements for data storage, result interpretation, re-interpretation, and clinical decision support. Testing strategy should reflect local prescribing patterns and evidence of clinical utility.

A typical translation pathway moves from genotype (observed alleles) to predicted function or phenotype (for example, poor, intermediate, normal, rapid, or ultrarapid metabolizer), then to a drug-specific recommendation. Allele function and phenotype assignment are gene-specific; a "poor metabolizer" label cannot be interpreted identically across all genes. Assays may miss rare or structural variants, copy-number changes, or ancestry-relevant alleles. Results need a clear test method, coverage statement, and laboratory interpretation. [2,3]

Clinical implementation relies on curated guidance, including CPIC, the Dutch Pharmacogenetics Working Group (DPWG), PharmGKB/ClinPGx, and regulator-approved product labeling. These sources are complementary and may differ in scope or recommendation strength. The FDA cautions that inclusion of an association in its pharmacogenetic table does not necessarily mean that pre-prescription testing is recommended; many listed associations have not been evaluated for improved clinical outcomes. Clinicians should consult the current label and applicable guideline. [1,4]

4. Current Evidence

4.1 High-actionability examples

HLA-B*57:01 and abacavir provide a well-established example of prospective testing to prevent a specific immune-mediated adverse reaction. In PREDICT-1, screening and exclusion of allele-positive patients markedly reduced immunologically confirmed hypersensitivity, supporting a treatment decision before exposure. [5] HLA-B*15:02 and carbamazepine or related aromatic antiseizure medicines illustrate a gene-associated risk of severe cutaneous reactions; allele prevalence varies by ancestry, so recommendations and testing strategies must be applied with clinical and population context. [6]

TPMT and NUDT15 variants can increase thiopurine toxicity by reducing safe handling of active metabolites. CPIC's 2025 update provides dosing guidance and addresses compound intermediate metabolizers, emphasizing that combined reduced function may require larger dose reductions than a single-gene result. Genotype-guided starting doses do not remove the need for blood-count monitoring and titration. [3,7]

CYP2C19 loss-of-function alleles reduce clopidogrel activation. CPIC recommends considering alternative antiplatelet therapy for intermediate and poor metabolizers in relevant acute coronary syndrome or percutaneous coronary intervention settings when clinically suitable. However, outcome evidence is context-sensitive: TAILOR-PCI did not meet statistical significance for its prespecified primary comparison at 12 months, despite a numerically lower event rate in the genotype-guided group. [4,8]

Reduced DPYD function can cause severe fluoropyrimidine toxicity. CPIC guidance supports reduced starting doses for intermediate metabolizers and avoiding fluoropyrimidines in poor metabolizers when alternatives are appropriate, with cautious titration guided by tolerance. The guideline is under revision; a July 2026 ClinPGx update clarifies an allele value for the HapB3 causal variant and a corresponding starting-dose recommendation. Local labeling and the current guideline should be checked before prescribing. [9,10]

4.2 Implementation and clinical utility

In PREPARE, an open-label, multicentre, cluster-randomised crossover study across seven European countries, a pre-emptive 12-gene panel was used to guide treatment. The trial reported a 30% reduction in clinically relevant adverse drug reactions among patients with an actionable gene-drug interaction compared with usual care. Its findings support implementation potential, but interpretation should consider the trial design, the composite of adverse reactions, duration, gene-drug mix, and transferability to other settings. [11]

Clinical utility is not uniform across PGx. PREDICT-1 demonstrates prevention of a defined adverse reaction through avoiding a drug in test-positive patients. PREPARE evaluates a multi-gene service across several medicines. TAILOR-PCI evaluates a particular prescribing strategy and endpoint in a cardiovascular population. These examples cannot be collapsed into a claim that all testing improves outcomes. Utility depends on whether the result changes care, whether the alternative is effective and safe, and whether implementation reaches the patient at the right time.

5. Clinical Applications

Gene / drug example	Clinical interpretation	Potential prescribing action	Important caveat
HLA-B*57:01 / abacavir	Increased risk of abacavir hypersensitivity	Test before initiation; avoid abacavir if positive	A negative result does not exclude every hypersensitivity syndrome
TPMT, NUDT15 / thiopurines	Reduced function increases myelosuppression risk	Lower starting dose or choose alternative based on phenotype	Monitor blood counts; genotype does not replace titration
CYP2C19 / clopidogrel	Loss of function reduces active metabolite formation	Consider alternative P2Y12 inhibitor in actionable settings	Balance ischemic and bleeding risks; follow current guideline
DPYD / 5-FU, capecitabine	Reduced DPD activity increases severe toxicity risk	Reduce initial dose or avoid based on activity score	Check current CPIC/label; titrate by tolerance and monitor

Gene / drug example	Clinical interpretation	Potential prescribing action	Important caveat
CYP2D6 / codeine, tramadol	Altered formation of active opioid metabolites	Avoid codeine/tramadol for poor or ultrarapid phenotypes per guidance	Pain response, age, co-medications, and alternatives matter
CYP2C9, VKORC1 / warfarin	Variants affect dose requirements	Use validated genotype-plus-clinical dosing algorithm if results available	INR monitoring remains essential; ancestry-specific alleles matter

Table 1. Examples of actionable gene-drug pairs. Recommendations are summaries for review purposes; apply current local guidance, product labeling, clinical factors, and specialist advice. Sources include CPIC guidelines and key clinical studies. [4–13]

6. Safety and Limitations

Analytical validity and assay scope. A result is only useful if the test reliably detects the relevant variants and structural changes. Panels differ in allele coverage and may not capture rare alleles, copy-number variation, or variants more prevalent in particular ancestry groups. Laboratories should report limitations and follow recognized quality standards; clinicians should not infer that an untested allele is absent.

Clinical validity versus utility. A statistically robust association with drug concentration or response does not automatically establish that testing improves outcomes. FDA tables explicitly separate evidence supporting therapeutic management from pharmacokinetic associations and potential effects. Action should be grounded in guideline strength, clinical context, and current labeling. [1,4]

Ancestry and equity. Allele frequencies differ among populations, and many discovery cohorts have overrepresented European ancestry. Limited variant coverage can yield less informative results in underrepresented groups. This creates risks of false reassurance, unequal access, and inappropriate extrapolation. Equitable implementation requires diverse validation cohorts, transparent test coverage, accessible counseling, and monitoring of who is tested and who benefits.

Phenoconversion and dynamic context. Enzyme activity can be altered by inhibitors, inducers, inflammation, organ dysfunction, age, and other clinical factors, so genetically predicted phenotype may not match current functional phenotype. Genotype is generally stable, but its clinical interpretation can change with co-medications and health status. Medication reconciliation and clinical monitoring remain necessary.

Workflow, privacy, and result portability. Results may be unavailable when a medicine is prescribed, buried in the record, or disconnected from clinical decision support. Pre-emptive testing requires durable storage, interoperable formats, consent and privacy safeguards, and processes for reanalysis as evidence changes. Alerts should be concise, relevant, and linked to the source result and guideline version to limit alert fatigue.

7. Emerging Advances

Pre-emptive panel testing, point-of-care genotyping, and implementation through health-system biobanks are expanding access to results beyond one prescribing episode. Genome sequencing may reveal pharmacogenomic variants incidentally, while electronic decision support can retrieve recommendations at prescribing time. Research is exploring polygenic scores and integration of genomic, clinical, and therapeutic drug-monitoring data, but these approaches require prospective validation before broad clinical use.

Guidelines are also evolving: CPIC's 2025 thiopurine update added guidance for compound intermediate metabolizers, and ClinPGx published a July 2026 DPYD allele interpretation update while the full guideline revision remains in development. This highlights the need for version-aware decision support and mechanisms to update stored phenotype interpretations without losing the original laboratory result. [7,10]

8. Pharmacist's Role

Pharmacists connect the genetic result to the medication regimen. They can verify the test and phenotype, reconcile current medicines for enzyme inhibitors or inducers, compare the result with the current label and guideline, assess therapeutic alternatives, and coordinate dosing, monitoring, and follow-up. Their medication expertise is particularly important when multiple gene-drug pairs, organ impairment, interacting medicines, or narrow therapeutic windows coexist.

Pharmacist activity	Application in precision pharmacotherapy
Medication review	Identify current and planned medicines affected by PGx and review interactions, indication, organ function, and prior response.
Result interpretation	Confirm gene, diplotype, phenotype, assay coverage, and applicable guideline version; clarify uncertain or incomplete results.
Therapy planning	Discuss alternatives, starting dose, titration, monitoring, and patient preferences with the prescriber and care team.
Implementation	Support EHR decision support, documentation, result portability, and follow-up after prescribing changes.
Education and equity	Explain what a result does and does not predict; support informed consent and identify access or coverage barriers.

Table 2. Pharmacist contributions across the PGx testing-to-treatment pathway.

9. Research Gaps

Evidence gaps include long-term outcomes, effectiveness across diverse ancestry groups, clinical utility for less-established gene-drug pairs, and comparative evaluation of targeted versus pre-emptive testing. Many studies rely on intermediate outcomes, short follow-up, or trial settings with resources not routinely available. Economic findings depend on test cost, turnaround time, prescribing patterns, health-system structure, and avoided adverse events; they may not transfer across jurisdictions.

Implementation research should report uptake, result availability at prescribing, clinician response, patient experience, downstream monitoring, and unintended effects. Common outcome definitions and transparent subgroup reporting would improve synthesis. Research should also compare clinical decision support strategies and evaluate how reclassification, rare variants, and pharmacogenomic data from exome or genome sequencing are handled over time.

10. Future Perspectives

A practical implementation should begin with a defined clinical use case, a validated assay, a trusted guideline, a workflow that returns results before prescribing, and a plan for monitoring and outcome evaluation. Health systems should specify responsibilities for test ordering, interpretation, documentation, result sharing, and update management. Clinicians should be able to see the evidence and recommendation source, not only an automated dose suggestion.

Precision prescribing will increasingly combine PGx with clinical factors, therapeutic drug monitoring, and patient preferences. This integration should preserve uncertainty: a genotype is a probabilistic predictor, not a complete account of an individual's response. Implementation should be evaluated for clinical benefit, safety, cost-effectiveness, and equity in routine practice, with guideline updates incorporated through transparent governance.

11. Conclusion

Pharmacogenomics can make pharmacotherapy more individualized when a well-supported gene-drug relationship changes treatment and the result is correctly interpreted and acted on. Examples such as HLA-B*57:01 with abacavir, TPMT/NUDT15 with thiopurines, CYP2C19 with clopidogrel, and DPYD with fluoropyrimidines show how genetic information can inform safer or more effective prescribing. Benefits depend on validated testing, current guidance, clinical context, accessible workflows, and ongoing monitoring. The next phase requires implementation evidence across diverse populations and health systems, with pharmacists and multidisciplinary teams helping translate genetic results into informed, patient-centered care.

12. Declarations

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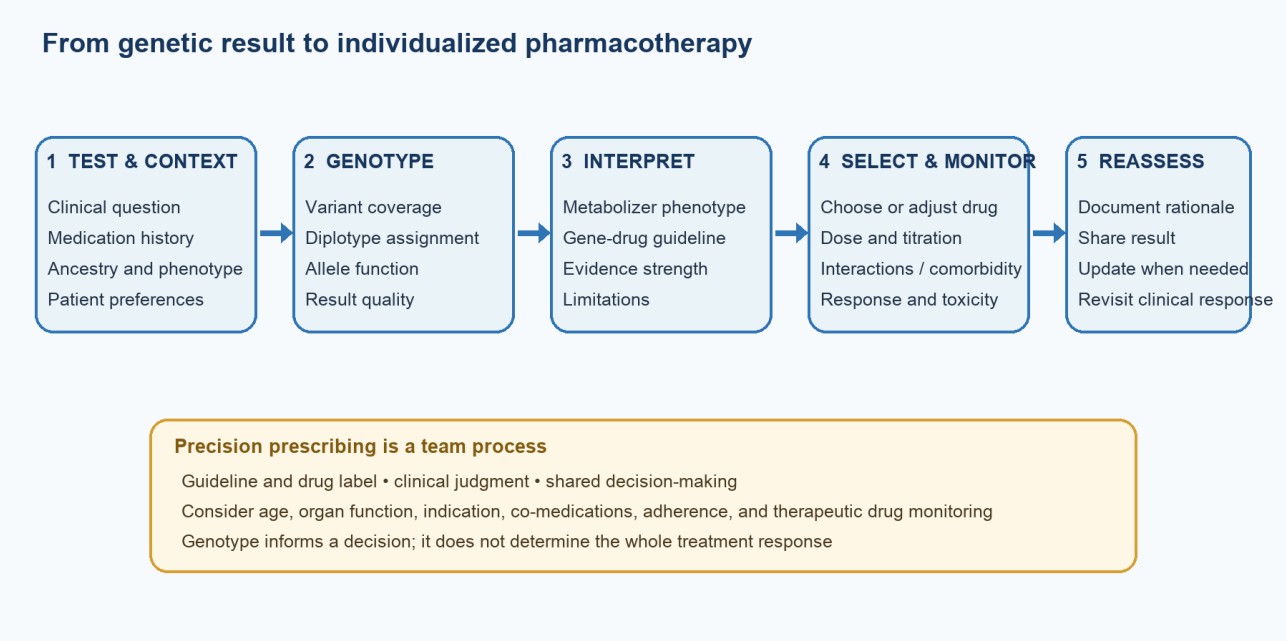
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14. Figures

Figure 1. Conceptual pathway from pharmacogenomic testing to individualized prescribing, including the clinical and workflow context needed for safe use.



Abbreviations: CPIC, Clinical Pharmacogenetics Implementation Consortium; DPWG, Dutch Pharmacogenetics Working Group; EHR, electronic health record; PGx, pharmacogenomics.