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Review Article

Clinical Pharmacology and Genomic Prescription Pathways: Toward a Paradigm Shift in Individualized Drug

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ABSTRACT

Pharmacogenomics (PGx), a key pillar of precision medicine, enables drug therapy customization based on a patient's genetic profile. Pharmacists, as experts in medication, are best placed to organize the use of PGx testing, interpretation, and decision-making about therapeutics in order to optimize therapeutic outcomes. This review identifies actionable gene-drug interactions in the form of CYP2C19-clopidogrel, DPYD-fluoropyridines, and TPMT/NUDT15-thiopurines, which have clinical implications for reducing adverse drug reactions and enhancing the effectiveness. It also explores the international situation of implementing PGx where high-income nations face fragmented data architecture, issues related to guideline harmonization, and lack of reimbursement, and low- and middle-income nations are characterized by poor infrastructure, high costs, and low genomic literacy. Some of the suggested solutions are the incorporation of decision-support tools into the electronic health record, pharmacy curriculum reformation, developing subsidized testing programs, and using AI/ML to support data interpretation. Pharmacists are becoming the primary contributors to precision medicine in the hospital, community and telehealth environment, and can become the solution to making PGx no longer a specialty service provided to a limited set of patients, but the default type of service in most places worldwide.

Keywords: Pharmacogenomics, Precision Medicine, Clinical Pharmacist, Genotype-Guiding Therapy, Implementation Barriers, Decision Support Systems.

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INTRODUCTION

Precision healthcare has influenced medicine radically by enabling individualized care through diagnosis, treatment and prognosis guided by the genetic and molecular profile of the individual (Bustin *et al*., 2023). At the core of this transformation is Pharmacogenomics (PGx), which investigates how genetic differences affect a person's reaction to medication. PGx makes it possible to enhance the effectiveness of drugs, reduce adverse drug responses, and streamline therapies depending on the risk associated with a patient (Sarwar *et al*., 2023). Pharmacogenomics is the linkage between genetic science and clinical therapeutics, where patient-specific genetic information is used to forecast a response to a drug. Pharmacists are ideally positioned as the medication experts to operationalize PGx testing and influence therapeutic optimization. Nonetheless, there is limited integration in real world because of educational, infrastructural and regulatory challenges. The clinical importance of PGx is illustrated by real-life. As an example, CYP2C19 mutations affect the way patients use clopidogrel, which consequently affects clopidogrel efficacy whereas CYP2D6 polymorphisms alter the safety and efficacy of codeine (Youssef *et al*., 2025).

In cancer, cytotoxicity may be life-threatening when fluoropyridine drugs interact with DPYD gene mutations. These cases demonstrate the possibility of pharmacists using PGx data in order to avoid harm and maximize treatment. Nevertheless, the use of PGx is still uneven, due to limited access to testing the absence of the standardized guidelines, and a shorten of genomics-trained specialists (Russmann *et al*., 2021). Pharmacist-led programs, including the University of Florida Personalized Medicine Program and the Clinical Pharmacogenetics Implementation Consortium (CPIC) indicate that pharmacists can also act as successful leaders of precision medicine.

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Increasing integration of pharmacogenomic alerts into Electronic Health Records (EHRs) and the implementation of clinical decision support tools enables pharmacists to make genotype-guided real-time decisions. Implementation of genomics education into pharmacy curricula and continuing education programs are critical to the full achievement of the benefits of the PGx (Manolopoulos *et al*., 2024). Pharmacists are being trained through certification and postgraduate training to assume this more expanded role. With precision medicine coming more to the forefront, pharmacists have the potential to become the key to safer, more effective care in a hospital or community setting (Mai *et al*., 2024).

One of the pillars of personalized medicine is Pharmacogenomics (PGx)-the genetic variations that influence drug response. Such genetic variations justify why people can react differently to the same drug, and that affects its effectiveness as well as a chance of getting adverse effects. The drug metabolism is dependent on the genes CYP2C19, CYP2D6, and CYP3A4, whereas the drug transport and immune reactions are dependent on the SLCO1B1, TPMT, and HLA variants (Amaro-Álvarez *et al*., 2024). These differences classify people into phenotypes such as poor, intermediate, normal or ultra-fast metabolizers, which inform drug choices and dosing. To clinical pharmacists, the implementation of the principles of PGx is paramount to personalized treatment, reduced side effects, and patient-centered care (Rusic *et al*., 2021).

A number of gene-drug combinations are clinically actionable and validated and listed in international guidelines. Evidence-based recommendations on a variety of interactions are available in the Clinical Pharmacogenetics Implementation Consortium (CPIC) and Dutch Pharmacogenetics Working Group (DPWG) (Dash *et al*., 2024). The most important pharmacogenomic interactions are summarized in Table 1 and show that genotype-directed prescribing can positively change the efficacy and decrease adverse effects.

Global Landscape of pharmacogenomics implementation

Clinical pharmacists are emerging as key players in the implementation of Pharmacogenomics (PGx) as it shifts its gear to being applied on clinical practice (Ahmed *et al*., 2016). They are well trained in pharmacokinetics, pharmacodynamics and drug interactions as well as patient counseling and therefore they are in a better position to lead genotype-guided therapy in different healthcare facilities (Brouwer *et al*., 2022). In addition to their traditional role of dispensing medicines, pharmacists have become crucial participants in the interpretation of PGx test results, optimization of therapy on the basis of genotype data, The education of both patients and healthcare providers is integral to the precision medicine ecosystem driving changes across clinical practice (Manson *et al*., 2024).

Historically, pharmacists were ensuring the medication safety; however, with the introduction of a Pharmacogenomic (PGx) testing, it has become their primary mission. Currently, clinical pharmacists would explain the results of genetic tests, provide adjustments to the therapy with evidence-based parameters, and train healthcare units and individuals on PGx consequences. The evidence on the potential impact of PGx interventions led directly by pharmacists demonstrated in practice is flagged by real world programs: the IGNITE Network in the U.S., the U-PGx Initiative in Europe, along with the Mayo Clinic RIGHT Protocol (Hippman *et al*., 2019). These programs show that the role of the pharmacist in precision medicine is increasingly important, as it does not only involve knowledge of genomics but also close connections with prescribers, lab specialists, and genetic counselors. Table 2 includes a list of selected pharmacogenomics databases and digital tools which assist in clinical decision-making, providing access to genotype specific drug prescription guidelines, allele frequencies, and drug-gene interaction databases that form the principal data for translation of precision medicine to everyday clinical practice (Singh *et al*., 2017).

Core Competencies in pharmacogenomics

To provide the Pharmacogenomics (PGx)-enabled care successfully, pharmacists should have an integrative set of knowledge, analytical, and communication skills. They should be able to know how genetic variants, metabolizer phenotypes, gene-drug interactions work and translate test results into clinically actionable recommendations. The ability to convey the findings of PGx research effectively to both staff and patients is equally essential. Pharmacist preparation associations such as ACCP, ESCP and ASHP also provide certification programs in the areas of pharmacogenomics, as well as continuing education programs (Wang *et al*., 2025).

A successful implementation strategy should include the integration of pharmacists into interdisciplinary teams, making their contribution at all levels, including a stage of pre-test counseling, interpreting results, and maximizing therapy and monitoring outcomes. Being integrated into the electronic health records and Clinical Decision Support Systems (CDSS) and built into the clinical decision support, ensures that insights of the PGx become a part of real-time decisions (Haga *et al*., 2023). Adoption can be slowed, however, by challenges to adoption such as limited reimbursement, fragmented data systems, low prescriber awareness, Ethical concerns. They can be addressed through the intervention of pharmacists by encouraging the introduction of value-based reimbursement, encouraging education, and ethical utilization of the genetic information (Blagec *et al*., 2022).

New models are being developed in which pharmacists are in charge of PGx. These are specific pharmacogenomics clinics and embedded positions in high-risk specialties such as oncology or psychiatry as well as PGx-based Medication Therapy Management

(MTM). These models emphasize the role shift of pharmacists by making them front runners in the delivery of personalized and genomics-guided care (Wondrasek *et al*., 2024).

Pharmacogenomics in Pharmacy Practice

Pharmacogenomics (PGx) transforms the future of precision medicine, and its successful implementation into pharmacy practice has emerged a key element toward provision of precision therapeutics. Their role as the medication experts with easy access are in the best position to implement PGx-guided interventions in the various clinical settings (Koufaki *et al*., 2023). This transformation however is based on systematic workflow, superior decision-support systems as well as well-defined roles in the hospital and community pharmacy settings. The process of integration will start with a patient-centered approach which shall begin with pre-test counseling, whereby the pharmacists shall engage the patients in discussions on the purposes, effectiveness, Constraints to the functions as well as the confidentiality of PGx test so that informed consent is granted before proceeding. They arrange collection of samples like buccal swabs or blood samples and subsequently, give meaning to test results with the help of protocols like CPIC or DPWG to determine clinical significance (Niazkhani *et al*., 2020).

Depending on the genotype of the patient, pharmacists suggest treatment adjustments, e.g., one should not use clopidogrel in poor metabolizers of the CYP2C19 enzyme, and can cooperate with prescribers to individualize treatment to optimize safety and treatment responses. Informatics tools are central to this effort. Some EHRs include embedded Clinical Decision Support (CDS) systems which are used to notify clinicians in real-time on genotype-specific considerations, e.g. thiopurine dose in TPMT defect individuals (Raheem *et al*., 2020). It is common practice to have pharmacists provide the service of interpreting the results of PGx and advising the prescriber and writing the recommendations in the patient record. More often than not, institutions are being built to have secure pharmacogenomic data repositories that aid continuity of care and retrospective quality improvement. The role of a pharmacist in hospital practice and in the community is quite different (Primorac *et al*., 2020). Figure 1 shows that the adoption of PGx tools into the healthcare routine is significantly simplified - once genetic testing order is placed, the process is as convenient as that of having a pharmacist conduct a decision support-based review resulting in a clearly regulated genotype-directed prescription targeted at each patient (Olakotan *et al*., 2021).

Pharmacists may work within a multidisciplinary team in the hospitals and have access to EHR and lab records to lead high-risk drug prescribers and education at the bedside. Academic hospitals are also the places where PGx innovation and pilot projects are conducted (Ellithi *et al*., 2020). The community-based pharmacists, in turn, have no or limited access to genomic data and CDS technology yet play critical roles in initiating PGx testing and interpreting Direct-to-Consumer (DTC) reports, and sharing them with patients or referring to specialist care. They also have an opportunity to modify therapies on the spot in states where collaborative practice agreements are operational (Obeng *et al*., 2019). Although such contextual issues differ, hospital and community pharmacists have a significant role to play in the development of PGx literacy, providing education to patients and medics, as well as promoting policies that would facilitate genome-informed prescribing. Combined, they are the spearhead in mainstreaming of PGx in healthcare in order to provide safer, more effective, and precise pharmacotherapy (Klein *et al*.,2017).

Case Studies as well as Practical Applications

The evidence-based practice in the real-world setting of Pharmacogenomics (PGx) supports the potential of precision medicine as facilitated by pharmacists in enhancing patient outcomes, minimizing Adverse Drug Reactions (ADRs) and refinement of therapeutic regiments (Tafazoli *et al*., 2021). The adoption at St. Jude Children's Research Hospital is a landmark, in which a combination of genotyping using preemptive Thiopurine Methyltransferase (TPMT) and the integration of PGx in pediatric oncology occurred. The adverse effects of the drug were decreased by genotype-based dose adjustments of TPMT-deficient patients, who are at risk of severe myelosuppression to standard doses of 6-mercaptopurine, facilitated by pharmacists (Haga *et al*., 2021). The result of this successful proactive strategy was the substantially lowered hematologic toxicity, decreased hospitalization, and higher adherence to treatment without reducing efficacy serving as a model for other countries in the world. On the same note, psychiatric pharmacogenomics has been picking pace where the pharmacist and the clinician will reduce the trial and error method in prescribing antidepressants and antipsychotics. An example of preemptive PGx in a U.S. Veterans Affairs (VA) mental health system showed that when veterans with treatment-resistant depression were given the option of PGx testing, clinical pharmacists were instrumental in interpreting genotypic data, especially of the CYP2D6 and CYP2C19 polymorphisms, and making practical recommendations to the psychiatrists (Jameson *et al*., 2024). Genotype-guided psychopharmacology with adjustments based on metabolizer status also promoted faster remission, adherence, less polypharmacy, and Other DPYD variants were found with a deleterious result leading to low doses or alternative treatment.

Pharmacists took care of the logistic and interpretive part of testing and coordinated the implementation into electronic health records. In the outpatient setup, pharmacist-led PGx has provided a lifesaving service to the community as well as reducing hospitalization rates, and grade 3,4 toxicities by 60-70% frequencies and maintaining the effectiveness of therapeutic benefits (Omar *et al*.,2025). In the Netherlands, a pilot project involving pharmacists learning to interpret the results of

Table 1: Clinically Actionable Gene-Drug Pairs with Clinical Recommendations.

Gene	Drug(s)	Genetic Variant(s)	Clinical Implication	Recommended action
CYP2C19	Clopidogrel	*2, *3 (loss-of-function)	Reduced antiplatelet response- increase risk of thrombosis.	Use ticagrelor or prasugrel.
DPYD	5-FU, Capecitabine	*2A, *13, etc.	Impaired metabolism-severe toxicity.	Reduce dose or avoid
TPMT/NUDT15	Azathioprine, Mercaptopurine	Low/deficient activity alleles	Increase risk of myelosuppression.	Reduce starting dose, frequent monitoring.
CYP2D6	Codeine	PM or UM variants	PM: no analgesia; UM: increase morphine- toxicity.	Avoid codeine, use alternative opioids.
HLA-B15: 02*	Carbamazepine	Present (especially in Asians).	Increase risk of SJS/ TEN.	Avoid carbamazepine

preemptive genotyping and make statin, antiplatelet, and beta-blocker medication adjustments, based on clinical decision support systems, had a striking effect on clopidogrel therapy, with ADRs being reduced by adjustments based on CYP2C19 genotype (Jiang *et al.*, 2015). Figure 1 visualizes the universal geography of pharmacogenomics application, where geographic variation of clinical practice implementation, presence of national guidelines, and rapid increase of pharmacist-led programs within the framework of developed and developing medical systems are noted.

CHALLENGES AND BARRIERS

Although the role of Pharmacogenomics (PGx) is increasingly receiving interest globally, there remain various obstacles to widespread implementation, and these obstacles vary markedly between High-Income Countries (HICs) and Low-/ Middle-Income Countries (LMICs) (Jayatilleke *et al.*,2020).

In High-Income Countries

In HICs, barriers are less about infrastructure and more about integration and optimization. HICs have access to accredited, procedural Pharmacogenomic (PGx) testing laboratories, some of the most sophisticated electronic health records (EHR) and Clinical Decision Support Systems (CDS) (Caraballo *et al.*,2020). Nevertheless, lack of awareness of clinicians, disjointed information sharing, and unreliable adoption of guidelines (e.g., CPIC vs. DPWG) prevents adoption. Legal and regulatory barriers to pharmacist autonomy in recommending therapy changes exist in parts of the world, and reimbursement of pharmacist-led services based on PGx is uneven as well. Secondly, despite a well-funded environment, there are still some difficulties in probabilistic GX result interpretation, harmonization of reporting, and ethical concerns including data privacy and consent (Torres *et al.*, 2022).

In Low- and Middle-Income Countries

Barriers are more basic and comprise of poor accessibility to testing facilities, high out-of-pocket expenses and untrained professionals of genomic nature. PGx testing is not readily accessible beyond urban areas, and the results are seldom incorporated into EHR systems, and pharmacists have to operate with fixed reports that slow decision-making (Bryan *et al.*,2024). There is low coverage of reimbursement and insurance which results in poor uptake of patients. Other limitations to clinical utility are infrastructure gaps, including a lack of secure storage of genetic data and CDS tools. The policy frameworks that embrace pharmacist led-PGx services are underdeveloped and investment in pharmacy curriculum reforms to develop genomic literacy is often limited (Adler *et al.*,2022).

Cross-Cutting Challenges

Pharmacists around the world encounter variation in education of the pharmacogenomic theory, the absence of standard training models, and a deficiency in interprofessional relationships with prescribers and geneticists. Clinical decision-making is difficult because of polypharmacy and comorbidity, as well as the complexity of the genotype-phenotype interpretation. The ethical issues including patient consent and data confidentiality are not fully addressed in most of the settings (Reisberg *et al.*,2019).

Strategies to Overcome these Barriers

Barriers to the implementation of Pharmacogenomics (PGx) cannot be overcome through general approaches that could be applicable across High-Income Countries (HICs) and Low or Middle-Income Countries (LMICs) (Tata *et al.*, 2020). HICs are encouraged to work on increasing pharmacist training, integrating real-time clinical-decision-support into interoperable EHRs, aligning guidelines, and developing reimbursement schemes that reward pharmacist-led PGx services. LMICs should have baseline investments such as low-cost decentralized testing centers, state-subsidized high impact therapy programs, pharmacy curriculum change and mobile health technology to enhance access (Heeney *et al.*, 2023). Pilot programs that have proven clinical and economic usefulness, and where consent and data sharing have been ethically and legally well defined, can be used across the world to instill confidence and expedite

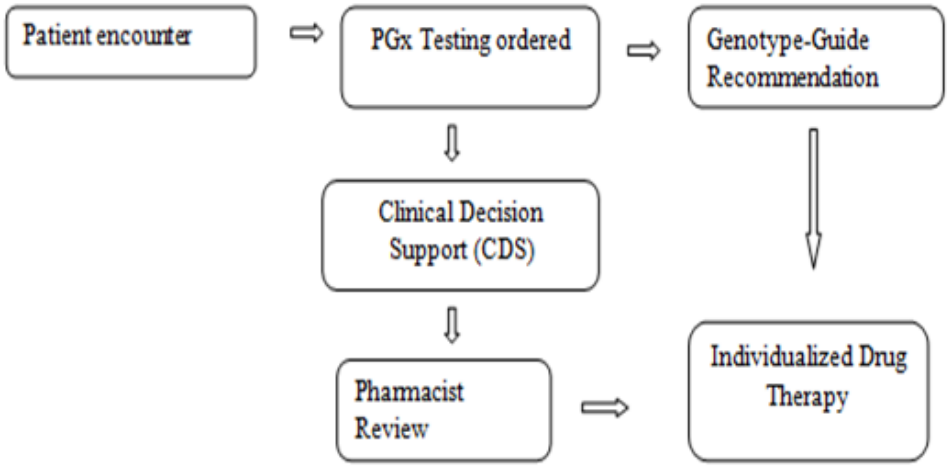

Figure 1: Integration of PGx Tools in Clinical Workflow.

its implementation. Collectively, these measures will help pharmacists shift away from the conventional dispensing activities to become catalysts of genotype-oriented, patient-focused therapy (Mackey *et al.*,2019).

FUTURE DIRECTIONS

The field of precision medicine is developing so rapidly that it is in the best interest of pharmacists as key stakeholders in Pharmacogenomics (PGx), which needs genomic literacy, interpretive, and digital skills. To achieve it, pharmacy education has to be reformed PGx must become a core, immersive PharmD/DPharm curricular aspect. In order to maintain current science, postgraduate certifications of organizations, such as ASHP, AACP, or CPIC, and continuous education will be needed (Thomas *et al.*,2024).

Pharmacists should also embrace such technologies as Artificial Intelligence (AI) and Machine Learning (ML) which contribute to simplifying the use of complex omics data, e.g., when predicting statin-induced myopathy based on SLCO1B1 genotypes, or when selecting antidepressants based on CYP2C19/CYP2D6 profiling. This gives them a very unique opportunity to confirm and qualify these AI-proposed insights by putting them into perspective (van *et al.*, 2023).

The emergence of Direct-to-Consumer (DTC) genetic testing has in further changed pharmacists into frontline genomic interpreters, making it a requirement that genomic interpreters be ethically trained and capable of communicating effectively, particularly in rural areas. Future models presuppose decentralized, pharmacist-led PGx clinics as a part of primary care that would offer genotyping, counseling, EHR-based prescribing, even telepharmacy services, especially in the area of oncology, cardiology, and psychiatry (Kostakou *et al.*,2019).

Table 2: Pharmacogenomics Databases and Tools Supporting Clinical Practice.

Resource	Functionality	Key Features
CPIC	Clinical prescribing guidelines.	Peer-reviewed, genotype-phenotype recommendations.
PharmGKB	PGx knowledge base	Drug pathways, gene-drug labels, curated annotations.
PGxPOP	Population-level PGx variant analysis.	Allele frequency viewer, ethnic stratification.
FDA Table of Pharmacogenomic Biomarkers.	Regulatory resource for PGx labeling.	More than 300 drug labels with biomarker information.
Pharos	Genomic and drug interaction exploration.	Interactive, translational science resource.

In order to achieve this vision, there is a need to have favorable policy and interprofessional collaboration. Pharmacists should collaborate with genetics researchers, clinicians, and informaticians to convert the genomic insights into clinical practice and contribute to the development of efficient Clinical Decision Support (CDS) systems. Pharmacist-led PGx services should be covered in formulary through national policies, establish reimbursement channels, and require pharmacists to have a seat on precision medicine governance boards.

Publicly-available internationally-oriented models, including Dutch DPWG and U.S. CPIC, provide scaling solution frameworks regarding the inclusion of pharmacists as part of PGx delivery. Singapore and India are pilot locations to establish pharmacists-led initiatives, and global consortia are seeking to harmonize the standards (Okpete *et al.*, 2024).

CONCLUSION

Pharmacogenomics (PGx) is transforming the future of precision medicine, and pharmacists are best placed to change genetic understanding into practical, patient-focused treatment. To achieve this potential the high-income countries, have to optimize infrastructure, combine decision-support tools and assure reimbursement pathways whereas the low-income and middle-income countries should focus on access to cost-effective testing, curriculum reform and policy support. These efforts will require pilot programs, interprofessional cooperation, and ethical systems of data use to be expanded on a long-term basis. Through spearheading the implementation of PGx in hospital, community, and digital health environments, pharmacists can decrease the number of adverse drug reactions, enhance the quality of therapy, and make precision medicine a care standard on the global scale.

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ABBREVIATIONS

PGx: Pharmacogenomics; **EHRs:** Electronic Health Records; **CPIC:** Clinical Pharmacogenetics Implementation Consortium; **DPWG:** Dutch Pharmacogenetics Working Group; **ADRs:** Adverse Drug Reactions; **CDDS:** Clinical Decision Support Systems; **MTM:** Medication Therapy Management; **TPMT:** Thiopurine Methyltransferase; **VA:** Veterans Affairs, **AI:** Artificial Intelligence; **ML:** Machine Learning.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

SUMMARY

This review highlights the significant place of pharmacists in the translation of genotype-guided, patient-centered therapy to clinical practice by utilizing Pharmacogenomics (PGx). It lays emphasis on actionable gene-drug interactions and how they affect the maximization of treatment outcome and medication-drug interactions. Through electronic health records and clinical decision support systems, pharmacists organize the testing of the PSG and interpretation of the results as well as consult the prescribers. Programs such as IGNITE and U-PGx have yielded evidence of better adherence, reduced toxicities, and better therapeutic efficacy. The barriers are fragmented data and reimbursement gaps in the high-income countries and inadequate infrastructure and genomic literacy in the low- and middle-income countries. The review recommends unified guidelines, pharmacist education, cost-effective testing, and artificial intelligence-assisted tools that will be used to achieve faster adoption rates and make pharmacists central to mainstreaming of precision medicine in different countries across the world.

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