Review Article

# From DNA to Doses: How Pharmacogenomics Transforms Depression Care in Community Pharmacy

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## Abstract

Pharmacogenomic testing can identify these genetic variations, allowing healthcare providers to adjust drug selection and dosage accordingly. These tests typically involve a simple cheek swab or saliva sample, which is then analysed to identify specific genetic variations that affect drug metabolism and response. Cytochrome P450 (CYP450) enzyme is responsible for the metabolism of many antidepressants. CYP2D6 and CYP2C19 may cause variations in how drugs are metabolized. A neurotransmitter involved in mood modulation, the serotonin transporter gene (SLC6A4), affects serotonin reuptake. Val66Met, a gene for the brain-derived neurotrophic factor (BDNF), has been connected to variations in how people react to antidepressants. Effective implementation of pharmacogenomics in clinical practice requires supportive policies that address issues such as reimbursement, education, and privacy. Among the pharmacist's duties are analyzing genetic information, working with medical professionals, offering patient counseling, and incorporating pharmacogenomics into the administration of drug therapy. Patients with severe depressive disorders had much better results when a combinatorial pharmacogenomic test was used to detect and target those with expected gene-drug interactions. Utilizing a structured data framework of genetic, phenotypic, and environmental characteristics, personalized medicine should offer the healthcare system practical methods to maximize the efficacy of certain treatments.

**Keywords:** Pharmacogenomics, Depression, Trial and error method, Community pharmacy, Medication therapy, Serotonin

## Introduction

The field of pharmacogenomics is quickly attracting the attention of both patients and doctors. The idea that variances in the genetic code lead to variations in medication response is known as pharmacogenomics. We are getting closer to a day when medicine can be personalized to each patient as our understanding of genetics grows [1]. We can choose a prescription with the highest possibility of effectiveness, the optimal dosage, and the fewest possible harmful side effects by using each person's unique genetic information. It has long been known that each person will have different side effects from drugs. Thanks to advancements, we now know the gene-drug pairing for a large number of drugs.

Every year, depression affects 6% of individuals and is the primary cause of suicide. In addition to the patient, their relatives and society at large are all impacted by its widespread impacts and incapacitating symptoms [2].

Pharmacogenomics (PGx) can offer pharmacists useful pharmacokinetic and pharmacodynamic data for evaluating medications, particularly in the context of medication therapy management (MTM) services. Nevertheless, no evaluation has thoroughly charted how pharmacists employ PGx in practice-based research. Future academics, practitioners, and legislators would be able to determine the best groups and environments for PGx deployment in pharmacies if this were done [3].

The field of clinical pharmacogenomics is still quite young. The FDA still has few testing suggestions, despite our understanding of the subject. Currently, only abacavir and, in certain communities, carbamazepine and oxcarbazepine need to be tested before starting treatment. Certain specialties, including tamoxifen, allopurinol, SSRIs, codeine, tramadol, azathioprine, mercaptopurine, and several chemotherapy medicines, may screen for particular genes before starting a prescription. Presently, though, this depends on the supplier. Health care practitioners are required to have a basic grasp of direct-to-consumer testing to educate and treat patients as required, even though this is still possible [4].

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This review will explore the current state of pharmacogenomics in depression treatment, the potential for community pharmacists to implement pharmacogenomic-guided care, and the challenges and opportunities that lie ahead. By examining these aspects, the review aims to provide insights into how community pharmacy practice can evolve to incorporate pharmacogenomics, ultimately leading to more personalized, effective, and safer treatments for patients with depression.

## Pharmacogenomics in Depression Treatment

Just around half of patients react to antidepressants, and even fewer experience remission after taking them for the first time, despite the fact that they are among the most recommended medications. The likelihood of these treatment-resistant patients improving with further antidepressant trials is known to decrease over time. Higher treatment and health care use costs, disability, lost employment, and lower productivity are all indicators that treatment resistance in depressed individuals has major emotional, financial, and social consequences [5]. SNPs in genes that affect how the body reacts to the metabolism of antidepressant drugs have been discovered by the area of mental pharmacogenomics. Combinatorial pharmacogenomics (CPGxTM), a composite multigenic method, investigates variations in the genes that code for brain reaction proteins that affect how well antidepressants work and antipsychotic medications moreover, genes for the liver enzymes cytochrome P450 (CYP), which metabolize these drugs. Gene Sight Psychotropic is a patented pharmaceutical decision assistance tool that combines these SNPs. A report containing prescription options for 99 percent of all FDA-approved antidepressants and antipsychotic drugs utilized to treat depression is generated by the GeneSight test, based on the composite phenotype determined for each patient [6].

## Genetic Factors Influencing Depression Treatment

genetic variations that impact how people metabolize and react to drugs, treating depression can be difficult. Numerous genes that are essential to these processes have been found. Since it oversees the metabolism of numerous antidepressants, the cytochrome P450 (CYP450) enzyme family stands out among the others.

For instance, a patient with a CYP2D6 gene variation that causes poor metabolism may have greater blood levels of several antidepressants, which increases the likelihood of adverse consequences. On the other hand, a patient with an ultra-rapid metabolizer phenotype may degrade the medication too rapidly, making it useless at recommended dosages. A substantial predictor of the emergence of serious depression after several negative occurrences is the 5-HTTLPR genotype. One of the stronger conclusions regarding certain biological risk variables for depression is this one [7]. Numerous bodily processes, such as hunger, sleep, cognitive processes, and the manifestation of anxiety and depression, are influenced by serotonergic (5-HT) neurotransmission.

## Pharmacogenomic Testing in Depression

Focus has been on the cytochrome p450 (CYP450) hepatic enzymes in an effort to comprehend how common genetic variation affects treatment responses in MDD. Of them, CYP450 2D6 is in charge of the oxidative metabolism of up to 25% of drugs, including a significant portion of antidepressants. There have been reports of somewhat common functional differences in the genes encoding 2D6 and other CYP450 enzymes. Each CYP450 enzyme's overall metabolic phenotype is derived by aggregating these functional changes for analytical reasons [8].

A pharmacogenomics research collaboration has evaluated the function of CYP450 variation in the metabolism of tricyclic antidepressants in a guideline paper. These metabolic categories' impacts on blood concentrations are clearly documented by the pharmacokinetic research evaluated for the very limited fraction of tricyclic antidepressants under study [9].

## Current Practices in Community Pharmacy

The role of community pharmacies in healthcare has expanded significantly over the past few decades, evolving from traditional dispensing of medications to becoming integral hubs for patient-centered care. Pharmacogenomic services in pharmacy practice must be underpinned by research that is practice-oriented. In principle, pharmacogenomics may decrease morbidity, mortality, and health-care costs by allowing for the choosing of drugs that will finish up in greater therapeutic results. This happens by taking into account the interindividual heterogeneity caused by patients' genetic variants. Nevertheless, to apply this in reality, both feasibility and clinical value must be proved. The purpose of this review is to thoroughly map the available data on pharmacogenomic services provided by pharmacists and assess the foundations of proof for trends in the traits of pharmacy practices, pharmacogenetic testing, and clinical indications [10]. It will be easier to determine which patient categories may benefit clinically from comparable therapies to those under study if the data from all pharmacist-led pharmacogenomic services is compiled [3].

## Pharmacogenomic Testing Services

Patients and healthcare professionals are very interested in pharmacogenomic (PGx) testing, which is becoming more and more common in clinical practice. In addition to statewide efforts to establish PGx testing, several healthcare systems are putting PGx programs into place [11]. Discussions around PGx have changed from "Should we do PGx testing?" to "How should we best implement PGx testing?" as the clinical value and adoption of PGx have increased. One crucial voice needs to be heard as organizations that create guidelines, like the Clinical Pharmacogenetics Implementation Consortium, make

suggestions about how to best apply the scientific evidence, and as physicians and implementation scientists create best practices for clinical implementation. Providers must have a thorough understanding of patients' perceptions of PGx in order to anticipate their queries, worries, and/or requirements and to guide the counseling that physicians offer both before and after PGx testing [12].

### Collaboration with Prescribers

The target population of pharmacogenomic testing is to advance the meaning of medication-related outcomes one notch higher. More specifically, the pharmacogenomics subfield which seeks to customize drug therapy according to an individual's genetic profile. Pharmacogenomics has been effectively brought into various practice settings; the growing participation of pharmacists has oftentimes been a consistent factor in such instances. Clearly, pharmacists have successfully transitioned into the role of consultants in medication management strategies [13]. Statistics reveal that approximately one-third of clinical pharmacogenomics service providers in the USA are Pharmacists. During the education systems on the other hand, in comparison to any other health care professional, in the education of the pharmacist profession, the scope of practice pertaining to medication management is populated with greater genomic education standards than other professionals. Albeit the role of pharmacogenomics in addressing patient's health autonomously, it does not have any relative in most instances. More effective and more ecological relations with prescribers, the target population, e-commerce technology designers, and clinical laboratory scientists, for example, are an asset in the actual practical target use of pharmacist-derived drugs. Finally, genetic counselors, who are also not too common themes in the pharmacogenomics applicable literature, can also work with a pharmacist providing clinical pharmacogenomics [14].

### Medication Therapy Management (MTM)

Comprehensive medication management (CMM) and MTM are frameworks that pharmacists may utilize to optimize mental health and non-mental health medication regimens. Both services involve reviewing a patient's medications in the context of current medical conditions, identifying medication therapy problems (MTPs), providing therapeutic recommendations, and facilitating adherence [15]. Despite some important differences in clinical context, and scope of information evaluated, the terms are often used interchangeably, as MTM is recognized by the Centers for Medicare & Medicaid Services (CMS) as a reimbursable service, and tenets of MTM are also included in the more rigorous CMM framework. While an in-depth comparison of these services is beyond the scope of this paper, elements of CMM are particularly well suited to the incorporation of PGx information into a clinical pharmacist assessment, with important relevance to patients with mental health conditions. CMM takes a patient-centered approach that is important for contextualizing other factors that impact treatment planning in mental health [15].

### Patient Education and Counseling

Patient Counseling On Pharmacogenomics Has Almost Entered the domain of archaism. The genetic literacy of the individuals and those of the practitioners is said to be less than that which a pharmacogenomics practice mandates [16]. Still, to the best of our knowledge, the needs of primary care practitioner's pharmacogenomics literacy have never been studied except for one that dealt with the objective numeracy vis-à-vis understanding results of pharmacogenomics [17]. Since direct pharmacogenomics patient family counseling studies are yet to be developed, we performed a scoping review on the utilization of pharmacogenomics testing by patients who had sought it before [18].

### Challenges in Implementation

Most pharmacogenetic implementations have occurred in academic medical facilities or research hospitals, which frequently have the resources and access to skilled staff needed to support pharmacogenetic testing and its use in clinical settings. The lifespan of pharmacogenetic services has also been demonstrated to depend on two critical components, namely multidisciplinary cooperation and engagement with physician champions, which are fostered by educational contexts [19]. However, pharmacogenetic applications are not exclusive to academic health systems or research. Prior research has detailed the implementation of pharmacogenetic services in a variety of contexts, emphasizing the resources needed and strategies for overcoming typical obstacles.

It is imperative that those in charge of pharmacogenetic implementations comprehend the data pertaining to genotype-guided therapy, despite of the context. Pharmacogenetic information included in FDA-approved prescription labeling is also included in the Pharmacogenomics Knowledge Base, a resource for academics and physicians that offers curated data on the impact of genetic variation on drug response [20]. Pharmacogenetic testing is more likely to enhance patient outcomes when it is utilized effectively to support clinical decision-making when an evidence-based strategy is followed [21].

### Personalizing Depression Treatment

Personalizing depression treatment with pharmacogenomics is a significant improvement in mental health care, overcoming the limits of the traditional trial-and-error approach to antidepressant therapy. Depression is a complex condition with a variety of origins, symptoms, and treatment outcomes. Traditionally, antidepressants are prescribed based on broad clinical standards, with adjustments made over time to discover the most effective and comfortable alternative for the patient [22].

### The Need for Personalized Treatment in Depression

This implies that the syndromal diagnosis is the only factor used to determine the course of treatment in each patient. Many drugs and psychotherapies have been shown in clinical studies to be "equivalent" in treating the illness; as a result, these treatments are frequently thought of as interchangeable.

Nowadays, the selection of depression therapy is typically based on the preferences of the physician and/or the patient as well as safety concerns. This process is relatively trial-and-error and pays little attention to the unique characteristics of each case [23]. This might be one of the causes of the fact that most patients with depression do not recover from their initial course of treatment, and at least 30% do not react to two successive evidence-based therapies, which indicates that they may be considered treatment-resistant.

## Pharmacogenomic Markers in Depression Treatment

Several genetic markers have been identified that influence the response to antidepressants. These markers can be broadly categorized into those affecting drug metabolism and those affecting drug targets.

## Benefits of Personalizing Depression Treatment

The personalization of depression treatment through pharmacogenomics offers several key benefits:

1. Improved Efficacy
2. Reduced Adverse Effects
3. Faster Onset of Therapeutic Effects
4. Cost-Effectiveness
5. Enhanced Patient Engagement [24]

## Barriers to Implementation of Pharmacogenomics in Depression Treatment

The integration of pharmacogenomics into depression treatment is an exciting prospect, offering the potential for more personalized and effective care. However, several barriers hinder its widespread implementation. These challenges span across financial, educational, infrastructural, and ethical domains.

- ### Cost and Reimbursement Issues

*Testing Costs:* Because pharmacogenomic testing can be costly, many individuals cannot afford it, particularly those without full insurance coverage. Even though the price of genetic testing has come down over time, many people still must pay a large amount out of pocket for it.

*Coverage by Insurance:* Pharmacogenomic testing reimbursement rules vary. Because clinical guidelines are inconsistent and there is doubt over the long-term cost-effectiveness of certain tests, many insurance companies do not pay them. Healthcare professionals and patients may be discouraged from seeking pharmacogenomic testing due to this lack of coverage [11].

- ### Lack of Standardized Clinical Guidelines

Pharmacogenomic information may be used inconsistently in the treatment of depression due to differing guidelines from various professional organizations.

*Interpretation Variability:* The results of pharmacogenomic tests might be intricate and challenging to decipher. Because there are no established procedures for interpreting genetic data, various physicians may arrive at different conclusions, which could result in differing treatment philosophies and results.

- ### Educational and Knowledge Gaps

*Clinicians' Limited Knowledge:* Pharmacogenomics training is lacking for many medical professionals, including doctors and pharmacists. Ordering pharmacogenomic tests, interpreting the data, or using them in clinical decision-making may be hesitant as a result of this information gap [25]. To give healthcare workers the abilities they need to apply pharmacogenomics in practice, ongoing education and training are crucial.

*Patient Education:* Patients must also comprehend how pharmacogenomics affects their care.

- ### Infrastructure and Resource Limitations

*Integration with Healthcare Systems:* Access to genetic testing, the incorporation of pharmacogenomic data into electronic health records (EHRs), and clinical decision-support systems are all essential components of a strong infrastructure for the effective use of pharmacogenomics [26].

*Access to Testing Facilities:* Labs that can conduct top-notch pharmacogenomic testing are not readily available at all healthcare facilities. The application of pharmacogenomics in patient treatment may be delayed or made more difficult in some places due to logistical difficulties in collecting and processing genetic tests, especially in rural or underserved areas.

- ### Ethical, Legal, and Privacy Concerns

*Genetic Privacy:* There are serious privacy issues with the use of genetic data in medical care. To allay these worries, it is essential to guarantee strong privacy safeguards and transparent consent procedures [27].

*Ethical Concerns:* Careful consideration must be given to the ethical ramifications of using genetic data to inform treatment choices. Fairness and equity issues can arise, especially if not all patients have equal access to pharmacogenomic testing.

- ### Clinical and Logistical Challenges

*Workflow and Time Integration:* Making adjustments to current workflows is necessary to integrate pharmacogenomic testing into standard clinical practice. It is

imperative for clinicians to allocate time for patients to discuss the possible advantages and consequences of pharmacogenomic testing, analyze the findings, and modify treatment regimens as necessary [28].

*Complexity of Decisions Regarding Treatment:* Despite pharmacogenomic data, treating depression is still complicated since genetics is only one aspect of a bigger picture that also includes social, psychological, and environmental components [29].

- *Evidence and Research Gaps*

*Limited Clinical Evidence:* Although the science of pharmacogenomics is expanding quickly, more thorough clinical trials and studies are still required to determine the effectiveness and financial viability of pharmacogenomic-guided treatment for depression [30].

*Prolonged Results:* The long-term effects of pharmacogenomic-guided treatment for depression are currently little understood. In comparison to conventional therapy methods, further study is required to ascertain how effectively these strategies perform over time and whether they result in long-lasting improvements in patient outcomes [31].

- *Regulatory and Policy Barriers*

*Regulatory Difficulties:* Pharmacogenomic testing regulation is complicated, involving several authorities' monitoring and differing by nation or area. The availability and use of pharmacogenomic testing may be impacted by healthcare professionals' difficulties navigating various regulatory environments.

*Policy Development:* To successfully apply pharmacogenomics in clinical practice, supportive policies that cover topics like privacy, education, and payment are needed. Nonetheless, this field's policy development is still in its infancy, and policy gaps may prevent pharmacogenomics from being widely adopted [32].

## Education and Training for Pharmacists

Pharmacogenomics requires specific education and training for pharmacists to be a useful tool in community pharmacies. Community pharmacists are essential to direct patient care since they are frequently the most approachable medical specialists for patients. Strong knowledge of gene-drug interactions, pharmacogenomic principles, and how to interpret PGx results will be essential for pharmacists [33].

## Collaborative Care Models

To effectively incorporate pharmacogenomics into the treatment of depression, a collaborative care model needs to be developed.

## Aspects of a Collaborative Care Model

- *Multidisciplinary Teams:* In order to integrate PGx data into patient care, pharmacists and prescribing physicians must collaborate closely. In cases when pharmacogenomic studies indicate a high risk of adverse drug reactions (ADRs) or low efficacy with a particular antidepressant, this includes suggesting alternate therapy [34].
- *Shared Decision-Making:* It is essential to involve the patient in treatment choices, particularly when pharmacogenomic data is being used. In order to ensure that patients are aware of their alternatives and the reasoning for treatment modifications, pharmacists might serve as a liaison between the patient and the prescriber [35].
- *Referral Channels:* When patients have complicated genetic profiles that might necessitate a more thorough examination, pharmacists must have clear referral pathways to genetic counselors or specialists. Care will be streamlined by developing procedures and policies for these referrals [36].

## Technological and Policy Developments

PGx testing is one of the diagnostic tests for which the CMS Clinical Laboratory Fee Schedule sets reimbursement levels. Analyte-specific codes to identify particular tests were adopted by CMS in 2014 as part of a new coding system and payment scheme. The new model has particularly affected PGx testing. The "unstacking" of diagnostic test codes has reduced test bundling and increased cost transparency, which has led to increased scrutiny from PGx test payers [37].

## Future Directions

Pharmacogenomics has a bright future in community pharmacy, particularly in the management of complicated illnesses like depression. PGx may become widely used in individualized depression treatment more quickly as a result of several developments:

- *Integration Into Pharmacy School Curricula:* Pharmacogenomics should be a fundamental part of pharmacy education since it will equip aspiring pharmacists to deal with genetic data early in their careers. - PGx panels will become more comprehensive as a result of advances in genetic research, covering a wider range of medications, including more recent antidepressants. As a result, a greater range of patients will benefit from more individualized care [38].
- *Direct-To-Consumer Genetic Testing:* As DTC genetic testing becomes more popular, patients will need pharmacists to interpret and consult on the results of their own PGx tests, which they may obtain online. By providing services that are suited to the expanding DTC market, pharmacists will need to adjust to this trend.
- *Machine Learning and Artificial Intelligence (AI):* AI techniques that evaluate enormous pharmacogenomic data sets may help pharmacists more accurately forecast how patients will react to drugs, enabling even more individualized and exact treatment plans [39].

## Conclusion

Implementing pharmacogenomics in community pharmacy practice has the potential to revolutionize the treatment of depression by personalizing medication therapies based on genetic profiles. However, for this to become a reality, pharmacists need adequate education and training in pharmacogenomics, strong collaboration with other healthcare professionals, and support from both technological advancements and policy developments.

Future directions point to even greater integration of PGx into pharmacy practice, driven by advances in AI, broader genetic testing panels, and a growing interest in direct-to-consumer testing. Pharmacogenomics offers a way to reduce trial-and-error prescribing, improve patient outcomes, and decrease the incidence of adverse drug reactions, all of which are particularly important in the management of depression, a condition that often requires long-term pharmacotherapy.

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