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LITERATURE REVIEW Open Access

Pharmacogenomic Role in Cytochrome P450 Enzymes-Mediated Metabolism for Drug Therapy

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Abstract

The rapid development of genetic science in recent decades has provided opportunities for clinical implementation. In the field of pharmacology, this opens up hope for the use of more targeted drugs with fewer side effects.Genetic variation's influence on pharmacological response has been well-established in practice. Patients' responses to pharmacological therapies can be varied, ranging from positive effects to serious adverse drug reactions (ADRs). Numerous genetic variations have been found to have a major impact on how people react to routinely prescribed medications over time, according to experts. In order to use this genetic information to inform treatment choices, a pharmacogenomic (PGx) profile can be used. PGx works on identifying and validating genomic variations that affect drug response. The generic approach to healthcare has given way to a more individualized and precise treatment paradigm as it has developed.

Keywords: Adverse Drug Reactions - Genetic Variants – Pharmacogenomics - Cytochrome P450

INTRODUCTION

The recognized influence of genetic differences on the way drugs interact with the body has the capacity to improve the efficiency of medications and lower the risk of adverse drug effects.[1] Drug responses often vary widely among individual patients, not only in terms of positive responses but also adverse drug reactions.[2] The primary objective of effective therapeutics is to match patients with drugs that have a high probability of being effective and causing minimal harm.[2] Genetic variances in genes related to drug absorption, distribution, metabolism, and excretion (ADME) can impact the way individuals respond to drugs.[3] The outcomes of pharmaceutical interventions exhibit notable diversity, spanning from positive outcomes to severe adverse drug reactions (ADRs), with a portion

of this diversity being linked to inherited genetic disparities. Over the course of many years of pharmacogenomics (PGx) research, numerous genetic variations that impact reactions to commonly used drugs have been discovered.[2]

Pharmacogenomics (PGx) is the study of genetic variations that influence medication response with the goal of using this knowledge to inform treatment choices. Pharmacogenomics, one of the nascent techniques in precision medicine, customizes drug choice and dosage based on a patient's genetic makeup. Using this method, gene-drug interactions between CYP2C19 and clopidogrel and CYP2D6 and tamoxifen have been discovered.[3] Clinical care in pharmacogenomics involves combining a patient's genetic information with relevant non-genetic factors. PGx holds great promise in precisionmedicine by identifying genetic factors that determine pharmacological outcomes and using them to guide medication choice and dosage. It has developed into a significant and potential implementable subject in precision medicine.[2]

There are a number of difficulties in implementing pharmacogenomics, despite the fact that there is compelling evidence to support the use of genetic tests to guide medication in certain circumstances. The US Food and Drug Administration (FDA) has recommended genetic testing on 135 labels, and guidelines are being created for gene-drug pairings to help patients make decisions about switching medications or adjusting dose. Guidelines have already been released by the Clinical Pharmacogenetics Implementation Consortium (CPIC) for 33 drugs, and 122 more are expected to follow. Over the past ten years, pharmacogenomic testing has been carried out, correlating genetic variants related with medication disposition in clinical settings to enhance the efficacy of treating particular diseases and lower the occurrence of adverse drug reactions (ADRs).Interindividual variation in drug reaction is significantly influenced by racial/ethnic background.[4]

A tailored strategy has recently replaced the "one size fits all" model in the healthcare industry. The "right drug, right dose, right time, and right way" approach to therapy is emphasized in modern medicine, yet there are several unanswered questions that need to be investigated and supported by supporting data. By lowering adverse drug reactions (ADR), the number of failed trials, the length of treatment, the number of medications taken, and the impact of diseases on the body, the usage of PGx has the potential to lower overall healthcare expenses.[4] Genetic testing usually helps patients, especially those who have cancer, however some doctors might be hesitant to use it. Preemptive PGx testing adoption in

clinical settings is influenced by the attitudes of patients, medical personnel, and insurance payers.[3]

DISCUSSION

Personalized medicine's (PM) use is developing quickly. PM is used to make medical decisions by integrating data on daily health, illness characteristics, organ function, environmental factors, and lifetime exposure. As a combination of pharmacology and genomics, pharmacogenomics is a crucial area in the study of PM. Its research focuses on the pharmacological properties of drugs and genes associated with drug absorption (A), distribution (D), metabolism (M), and excretion (E) (collectively, ADME), as well as drug effects. Hospitalization is frequently caused by the improper choice and/or administration of medications. Some people may not respond to medication or have hazardous side effects more frequently than others. By identifying aberrant drug ADME or gene abnormalities that directly alter drug reactions, pharmacogenomic testing seeks to customize pharmacotherapy and minimize harmful consequences.[3]

Healthcare organizations are creating plans for the use of PGx in clinical settings as clinical deployment extends into routine patient care. Technology advancements and increased knowledge of the usage of PGx while prescribing medications have created a number of barriers that call for quick and simple fixes. Therefore, when the institutions' research activities grow, the solutions to the challenges they face must be discussed and compared within the scientific community, as progress cannot be made by working in isolation. Pharmacogenomic testing should be performed in clinical settings after taking into account the stakeholders' awareness, the present medical community's expertise, and the choice of the medicine to test.[4]

Healthcare professionals must consider a variety of facts when prescribing drugs, some of which are useful but not perfect (e.g: renal and hepatic function, age, concomitant medicines). Pharmacogenomic data need not be perfect to be helpful to the physician, similar to non-genetic variables. Despite evidence connecting pharmacogenomic variation to medication exposure, toxicity, and efficacy, many doctors, regulators, and payors appear to have an unreasonably high standard for pharmacogenomics proof.[5] Prescription details provided by the U.S. Food and Drug Administration for more than 137 drugs currently includes pharmacogenomic information as a result of advances in pharmacogenomic discoveries, which are pressuring a swift and successful clinical

application of genetic science. Clinical significance of genomic data is regularly acknowledged by physicians, and the increased pace of scientific discovery is causing change in practice.[5]

Pharmacoethnicity, or the variation in drug response and adverse drug reactions (ADRs), among different ethnic/racial populations, has been the subject of in-depth research. Understanding the genetic basis of these variances is crucial for better prediction because environmental and genetic factors can both influence drug responsiveness and the likelihood of adverse drug reactions. These discrepancies in drug response, which are a significant contributor to population-specific differences in drug response, are frequently attributed to different allele frequencies of single nucleotide polymorphisms (SNPs) that functionally affect the expression or function of genes involved in drug pathways. There are a number of factors, such as allele frequency variations of SNPs impacting drug-responsive genes, that can affect the heterogeneity in drug response seen in various people and communities. For medication development and methods used in customized medicine, these revelations have ramifications.[6]

Single Nucleotide Polymorphisms (SNPs) are the key to determining a person's vulnerability to different diseases and medication response. The majority of the time, multiple genes rather than a single gene mutation are to blame for diversity in therapeutic response in disease. A pharmacogenomic investigation comparing the SNP maps and gene expression of healthy and afflicted individuals would be acceptable. In order to develop new drugs, this can help uncover the genetic factors linked to the disease, which present the newest targets to characterize and assess.[6]

Enzymes known as cytochrome P450 (CYP) are vital to human health, particularly in the metabolism of drugs. With over one-third of all CYP sequences falling under the CYP2 family, human CYPs are the most diverse category. The CYP2C subfamily of enzymes is notable for exhibiting genetic polymorphism, which is defined by DNA sequence alterations that affect at least 1% of the population. These polymorphisms, which are sometimes referred to as Single Nucleotide Polymorphisms (SNPs), can take the form of base alterations, insertions, or deletions.[7]

These SNP’s can have significant effects on the protein's functionality, leading to alterations in the amino acid sequence, premature stop codons, or splicing defects. As a consequence, the protein function may be augmented, reduced, or completely diminished. The intricate interplay of these

genetic variations with drug metabolism and other physiological processes underscores their importance in personalized medicine and drug response variability. Understanding the impact of CYP2Csubfamily polymorphisms can pave the way for tailored treatments, maximizing efficacy and minimizing adverse reactions based on an individual's unique genetic makeup.[7]

Due to its high degree of polymorphism and complex genetic makeup, CYP2D6 exhibits a wide range of functional variants. As a result, the complex genetic makeup of CYP2D6 and its significance in the metabolism of a number of drugs make accurate and successful CYP2D6 genotype-based clinical prescription a key success in any pharmacogenomics implementation project. Among drug-metabolizing enzymes, the CYP2D6 enzyme has received a considerable deal of attention and has undergone substantial research. This specific enzyme exhibits a wide range of metabolic activities, from absence to increased functionality, potentially leading to notable variations in clinical outcomes. The CYP2D6 gene, which is located on the long arm of chromosome 22 and is just 4.3 Kbps in length but contains nine exons, is translated into the CYP2D6 protein in the endoplasmic reticulum. Although it makes up only 2% of the total amount of CYP liver enzymes, it is in charge of metabolizing about 25% of medications that are often used in clinical settings. The liver is where it is most strongly expressed, but it is also found in the brain, intestinal tissue, and lymphoid cells.[8]

The CYP2D6 gene has been described with a total of 171 unique alleles, and they are distinguished using the star (*) nomenclature, which is a frequently used method for identifying genetic differences in CYP enzymes. Individual variances in substrate exposure and metabolism are a result of changes in the CYP2D6 genotype, which is why there is such a high amount of polymorphism. With *1 acting as the common reference sequence encoding a functional protein product, this method is used for comparing different alleles. In comparison to this functional isozyme as a reference, other allelic variations with polymorphisms are assessed. A unique identification is given to a novel variant when it is discovered that involves nucleotide modifications that result in amino acid substitutions or if it affects transcription, splicing, or translation processes. The CYP2D6 gene has been found to have genetic variations, according to the Pharmacogene Variation Consortium (PharmVar).[8]

In terms of CYP2D6 allelic variations, the following alleles are the most widespread

in populations from the mentioned continents: In Europe, the *2 allele (34.3%), followed by *1 (33.1%) and *4 (15.5%); in admixed populations in the Americas, *1 (40.2%), *2 (32.7%), and *4 (15.7%); in East Asia, *1 (40.2%), *2 (32.7%), and *4 (15.7%); in South Asia, *2 (36.2%), *1 (25.8%), and *41 (13.5%); and in Africa, *2 (26.7%), *17 (19.7%), and *4 (11.9%). Details on certain alleles and their associated metabolic activity are provided in Table 1. In Caucasians, 60-85% of the population exhibits the typical metabolizer phenotype. In the Caucasian population, the poor metabolizer phenotype makes up 5–10% of the total population, with significant variation shown in people of African ancestry and rarity in the Asian population. In Asia, where the *10 allele is more prevalent, intermediate metabolizers make up 50% of the population, compared to the 10-15% of Caucasians that fall into this category. Because the *17 allele is common in the African population, 30% of people there have characteristics of intermediate metabolizers. While the prevalence of the ultrarapid metabolizer phenotype reduces to 1-2% in the Swedish population, it is more common in some Southern European countries, including Sicily (10%) and Spain (7–10%). The typical range for this percentage in Caucasian populations is between 1% and 10%. Gene duplication is found in 20% of the population of Saudi Arabia, and it is found in 29% of the population of Ethiopia.[8]

Table 1. Variation in the CYP2D6 gene allele and its effects on metabolism[9]

Functional impact of metabolic activity	**Allele**
Inactive	**3, *4, *5, *6, *7, *8, *11, *12, *14, *42, *62*
Decreased	**9, *10, *17, *41*
Normal	**1, *2, *33*
Increased	**1xN, *2xN,* and **53*

Tamoxifen is extensively metabolised in the liver by cytochrome P450 enzymes via two primary pathways: 4-hydroxylation and N-demethylation. The predominant metabolic pathway is the conversion of tamoxifen to N-desmethyltamoxifen, which is primarily assisted by CYP3A4, followed by oxidation mediated by CYP2D6 to create 4-hydroxy-N-desmethyltamoxifen (endoxifen), which accounts for over 90% of tamoxifen metabolism. Despite having a 100-fold higher affinity for Erα than tamoxifen, endoxifen is present in substantially lower amounts than that drug. Tamoxifen is occasionally referred to as a prodrug, which implies that it has no biological activity when taken. Tamoxifen may not exhibit a strong affinity for ER cells when it is delivered, hence the term "prodrug" may not be entirely appropriate. Tamoxifen is converted into its metabolites

by complex parallel and sequential mechanisms involving numerous CYP enzymes. These metabolites exhibit a greater affinity for the ER while being present in much lower amounts than the medication that was delivered.[9]

The advantage of using CYP2D6 genotype to guide tamoxifen use is the potential to identify patients with genotypes linked to a worse event-free survival and an increased risk of breast cancer recurrence (such as CYP2D6 IMs and PMs), which would allow the administration of alternative dosages (like 40 mg) and agents. Given that alternative drug therapies (like aromatase inhibitors, with or without ovarian function suppression), have been shown to be more effective than tamoxifen and that people with CYP2D6 PM genotypes who switch from tamoxifen to anastrozole do not show an increased risk of recurrence, it is anticipated that the potential risks associated with using CYP2D6 genotyping to direct hormonal treatment would be minimal. More investigation is needed to determine if CYP2D6 genotypes associated with therapeutic endoxifen concentrations (such as NMs and UMs) should predominantly be kept on tamoxifen.[9]

A few of the medications that are metabolized by the CYP2C19 enzyme include proton pump inhibitors, antiplatelets, antiepileptics, and anticoagulants. Its polymorphic character may have an impact on how effectively medications perform in clinical situations. The CYP2C19 gene, which displays significant variability, has more than 2000 genetic variations. predominant in intronic regions, with a smaller percentage in coding regions. The prevalent loss-of-function (LOF) variations that cause the generation of faulty or nonfunctional proteins are, in particular, the CYP2C19*2 and *3 alleles. Asian people are especially prone to this variation.[7]

The four main phenotypes that can be distinguished are poor metabolizers (PMs), who are deficient in the functional enzyme, intermediary metabolizers (IMs), who are heterozygous for one loss of function allele or possess two alleles that result in reduced activity, extensive metabolizers (EMs), who have two normal alleles, and ultrarapid metabolizers (UMs), who acquire the gain of function allele. There are currently at least 34 different CYPC19 alleles known (*1 to *34), each of which has a number of subvariants. CYP2C19*1 has been recognized as the wild-type or normal allele and functions normally (EM). Only a few of the many variations have any bearing in terms of frequency and clinical importance. The gain of function polymorphism CYP2C19*17 is another polymorphism of therapeutic importance. According to the original study, this polymorphism results in UM enzymes, lower levels of omeprazole or mephenytoin, and an

increased chance of treatment failure with these medications.[7]

Indonesia is a nation made up of more than 13,000 islands and home to over 261 million people. It is located in Southeast Asia between the Indian and Pacific oceans. Numerous indigenous ethnic groups make up this population. Muhammad Miftahussurur et al. examined the incidence of the CYP2C19 gene variants in various ethnic groups and their consequences on medical outcomes in Indonesia as part of their research. The CYP2C19 gene expression patterns varied according to each ethnic cluster. The Balinese participants had the highest frequency of rapid metabolizers (52.0%), followed by the Javanese (46.4%), Dayak (40%), Bugis (37.8%), Timorese (37.5%), Batak (37.0%), Chinese (29.4%), and Papuan (14.3%) participants, with the latter group having the lowest frequency of rapid metabolizers. In contrast, Timorese participants did not exhibit the poor metabolizers phenomenon, which was missing in the Papuan participants (57.1%). It's important to note that the Balinese participants outperformed the Papuan group in terms of their statistically significant odds of having a quick metabolism. In contrast to their Balinese counterparts, individuals from Papua showed a noticeably higher likelihood of having poor metabolizers, according to the study carried out by Muhammad Miftahussurur and the research team.[11]

The genotyping results are displayed in Table 2. Muhammad Miftahussurur et al. found that for CYP2C19*2, 166 patients were divided into 77 (46.4%) who had the homozygous wild-type allele (*1/*1), 24 (14.5%) who had the homozygous mutant allele (*2/*2), and 65 (39.2%) who had the heterozygous allele (*1/*2). In terms of the genotyping data for CYP2C19*3, we found that 147 patients (88.6%) had the homozygous wild-type allele (*1/*1), 4 patients (2.4%), the homozygous mutant allele (*3/*3), and 15 patients (9.0%), the heterozygous allele (*1/*3).[11]

Table 2. CYP2C19 Polymorphism Genotyping[11]

CYP2C19 Genotype	Expected Phenotype	n (%)
**1/*1*	Rapid Metabolizer	64 (38.5)
**1/*2*	Intermediate Metabolizer	60 (36.1)
**1/*3*	Intermediate Metabolizer	9 (5.4)
**2/*2*	Poor Metabolizer	23 (13.9)
**3/*3*	Poor Metabolizer	4 (2.4)
**2/*3*	Poor Metabolizer	1 (0.6)
**2/*3*	Poor Metabolizer	5 (3.0)

Because CYP2C19 has a greater allelic frequency than other members of this family, such CYP2C9 and CYP2D6, it may have the

greatest impact on the Asian population. In comparison to the wild-type, some research have indicated a relative risk for CYP2C19 function loss that is up to 10 times higher, while other studies have found no link. The risk of the composite end point of cardiovascular mortality, myocardial infarction, or stroke was considerably higher in people who carried the CYP2C19 allele with impaired function. They also connected it to the endpoint, stent thrombosis. As previously noted, only about 12–20% of the diversity in clopidogrel response may be attributed to genetic variations in the CYP2C19 enzyme.[7]

The FDA has so far made 3 recommendations on the label of the medication in response to studies indicating the importance of CYP2C19 polymorphism on the response of clopidogrel. Firstly in May 2009, FDA simply noted that "poor metabolizer status is associated with diminished response to clopidogrel" and that "the optimal dose for poor metabolizers has yet to be determined". The second revision in 2009 advised avoiding the use of clopidogrel "in patients with impaired CYP2C19 function due to known genetic polymorphisms or due to drugs that inhibit CYP2C19 activity" and more details concerning the interaction between clopidogrel and omeprazole. In the most recent revision, approved by the FDA in March 2010, a new label for clopidogrel with a "boxed warning" stating "There is reduced effectiveness in patients who are poor metabolizers, tests are available to identify patients with genetic polymorphisms, and that alternative treatment strategies should be considered in poor metabolizers of the drug".[7]

Since esomeprazole is a pure S-isomer of omeprazole, it is less sensitive to CYP2C19, which may account for why the enzyme has no effect on the drug's efficacy. Similar to how rabeprazole is converted into thioether rabeprazole, which is consistent with the findings of various meta-analyses, thioether rabeprazole is mostly metabolized by a non-enzymatic pathway with limited participation of CYP2C19. Omeprazole and lansoprazole are examples of PPIs that are primarily processed by CYP2C19. Omeprazole is also the most potent of the PPIs that block CYP2C19. According to reports, lansoprazole, pantoprazole, and rabeprazole do not suppress CYP2C19.[7]

The crucial enzyme CYP2C19 is involved in the metabolism of many different medications. This enzyme is frequently polymorphic, particularly among Asians. The genotype status of CYP2C19 may have a significant impact on drugs like clopidogrel and PPIs that are mostly processed by this enzyme. However, this effect seems to be constant in patients receiving clopidogrel for coronary stents, with those bearing the loss of function allele having a greater risk of

subsequent cardiovascular events as well as stent thrombosis. Although the relationship between CYP2C19 genotypes and the clinical effects of clopidogrel medication has produced mixed results. PPIs other than omeprazole should be used, especially by patients who are receiving aspirin and clopidogrel as part of dual antiplatelet therapy. This is because there has been much research on the interactions between PPIs and clopidogrel.[7]

The most prevalent member of the CYP2C subfamily and the enzyme that contributes most significantly to the metabolism of drugs in the human liver is CYP2C9. Low enzyme activity can occur from polymorphisms in the CYP2C9 gene. This creates some serious issues with the security and efficacy of drugs, along with the fact that some crucial drug substrates have low therapeutic indices. Inhibition, induction, and genetic polymorphism are all factors that can affect how clinically CYP2C9 substrates react. We focus in particular on the topic of ethnic heterogeneity in the pattern and frequency of genetic polymorphisms and clinical implications.[12]

Arachidonic acid, linoleic acid, and non-drug xenobiotics (such as galangin, methiocarb, pyrene, safrole, and sulprofos) are just a few of the endogenous substances that CYP2C9 also helps to oxidize. Although CYP2C9 also catalyzes the N-demethylation of certain basic medicines (such as amitriptyline, fluoxetine, and zopiclone), the majority of its substrates are weakly acidic substances. Non-steroidal anti-inflammatory medications (NSAIDs), oral sulfonylurea hypoglycemics, and coumarin anticoagulants are extensively mentioned. The commonly used anticonvulsant phenytoin, the diuretic torsemide, and the hypertension losartan, among other therapeutic classes of medications, are all cleared from the body through the metabolic process in a substantial way thanks to CYP2C9. The primary metabolic enzyme in the latter case, CYP2C9, is in charge of converting losartan into its pharmacologically active metabolite.[12]

The cytochrome-P450-2C9 (CYP2C9) gene, which metabolizes a wide variety of medicines and is abundantly expressed in the human liver, was the subject of genetic research by Nizamuddin et al. The selection included 489 other South Asian samples from the 1000 Genomes Project, 210 individuals from the internal data store, and 1278 individuals from 36 other Indian populations. Different statistical analyses were performed on the CYP2C9 gene variants that have been detected. South Asians have substantial genetic heterogeneity, according to Nizamuddin et al., who also found potential functional CYP2C9 haplotypes that are specifically found in this population. South

Asian populations were shown to have a high prevalence of CYP2C9*3 and CYP2C9*3/*3.[12]

Patients with epilepsy have been linked to the CYP2C9*3 allele for hypersensitivity to phenytoin and reduced celecoxib metabolism. It was also noted to have a high incidence of reaction rate against sulfonamides and urea derivatives. Several medicines, including S-warfarin, tolbutamide, fluvastatin, glimepiride, tenoxicam, candesartan, celecoxib, and phenytoin, had lower clearance rates as a result of the CYP2C9*2 and CYP2C9*3 alleles, according to in vitro investigations. According to age, gender, and genetic makeup, patients need the appropriate dosage of S-warfarin, phenytoin, and tolbutamide, which have narrow therapeutic indices. Additionally, homozygous mutations have a greater impact than heterozygous mutations. When compared to CYP2C9*1/*3, CYP2C9*3/*3 reduces clearance rate by 95%. The Clinical Pharmacogenomics Implementation Consortium (CPIC) classified CYP2C9*3 as level-1A due to the stronger evidence linking it to drug response.13 The highest degree of evidence that is currently available for a particular drug-gene pair is designated as degree 1A in the Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendations. It suggests that there is a well-established connection between genetic differences and treatment response, and the advice given is supported by a number of high-quality studies, including clinical trials and thorough observational studies. Based on a patient's genetic profile, this level of evidence enables unambiguous and useful prescribing recommendations.

The fact that so many practitioners are ignorant of the pathways required for medication activation or inactivation is one hurdle. Additionally, understanding the limitations of the genomic variants that have been examined and how gene duplication and deletion may affect interpretation are necessary for test interpretation. As scientific data evolves, this specific knowledge must be continually updated. Although most physicians will accept a system that offers practical guidance, they do want to understand the rationale behind changing their prescribing. If a high-risk genotype coincides with a high-risk medicine prescription, doctors should at the very least be alerted.[7]

The Clinical Pharmacogenomics Implementation Consortium (CPIC) was established to overcome some of these difficulties. This group will update, annotate, and assess the evidence that links medication dosing decisions to genetic tests, as well as resolve any incidental findings implications of the test. They will also gather data on pharmacogenomics tests that are currently ready for clinical use. In order to help those

who want to implement clinical pharmacogenomics testing, the Consortium will also share protocols for the logical transfer of genotypes from pharmacogenomics from the lab to the clinic. In the end, CPIC will give practitioners a resource of peer-reviewed and useful advice on how to include genetics into medicine prescriptions.[7]

In the field of personalized medicine, understanding the complex interaction between genetic variants and therapeutic response is crucial. A person's therapeutic outcomes can be improved and adverse effects can be reduced by customizing medicines based on their genetic profile. Pharmacogenomics has the potential to completely transform medical practices by providing safer, more effective therapies that consider each patient's distinctive genetic traits. Future healthcare will be more accurate and individualized as a result of ongoing study and knowledge of these gene-drug interactions.

CONCLUSION

The clinical application of pharmacogenomics (PGx) results in personalized medicine, leading to enhanced treatment effectiveness, safety, and cost-efficiency. Despite over a decade of pharmacogenomics-based research, various obstacles have hindered its widespread adoption in clinical settings. There is a global disparity in the programs and solutions necessary to facilitate the clinical implementation of pharmacogenomics across different countries. To address these challenges, several key solutions have been identified: establishing a secure and appropriate information technology infrastructure with integrated clinical decision support systems, increasing the evidence supporting pharmacogenomics, implementing more regulations and reimbursement strategies to gain acceptance from stakeholders, incorporating pharmacogenomics education in all institutions and clinics, and promoting pharmacogenomics awareness among all healthcare professionals and patients. In conclusion, this review offers valuable insights into the common barriers and solutions related to the clinical use of pharmacogenomics, facilitating a better understanding of its implementation challenges. However, we also need to pay attention to other factors that can affect individual responses to the administration of certain drugs as described above, namely environmental factors both internal and external.

CONFLICT OF INTEREST

The author declares there is no conflict of interest.

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