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Pharmacogenomics-Guided Therapy for Complex Diseases: Applications in Cardiovascular Disease, Breast Cancer, and Mental Health

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Abstract

Pharmacogenomics-based therapy is a revolutionary perspective of precision medicine, as it allows clinicians to personalize drug therapy based on patient genetic characteristics. The paper assessed the clinical and economic outcomes of the application of genotype-based therapy in three conditions of complex diseases, including cardiovascular disease, breast cancer, and mental health disorders, based on primary patient data in tertiary hospitals in Pakistan. Four hundred and fifty patients were recruited and put into a pharmacogenomics-guided (PGx) cohort or a standard therapy cohort. The influence of genetic variations on the drug metabolite and response to the treatment was studied on CYP2C19, SLCO1B1, VKORC1, CYP2D6, UGT1A1, and SLC6A4. The group directed by the PGx showed much more therapeutic efficacy, lower adverse drug reactions, and better cost-effectiveness in comparison with conventional care (p. 0.05). Regression analysis was used to confirm that certain variations CYP2C19 and CYP2D6 among others were good predictors of clinical outcomes. These developments underscore the utility of pharmacogenomics in the improvement of drug safety and efficacy, minimization of the healthcare costs and sealing the outlook of the gap between genomic science and clinical practice. The paper highlights the need to ensure the incorporation of pharmacogenomic testing into the healthcare systems particularly in developing nations as a way of encouraging evidence-based and customized therapeutics of complicated diseases.

Introduction

Complex diseases are associated with greater health burden in the world system because of their high incidence and mortality rate, as well as the tremendous inter-individual difference in the response of the patients to treatment (Sadee 2023). Conventionally, the management of these conditions with a drug treatment has been based large-scale with the selection of standard dose and agent regimens, according to the population means, and not according to the individual. This practice has been found to be the cause of poor outcomes, such as therapeutic failure, adverse drug reactions (ADRs), and inefficient utilization of healthcare resources (Wang 2011; McDonough 2022).

Pharmacogenomics (PGx) research on the effect of inherited genetic variation on individual responses to drugs provides an optimistic approach of getting beyond the trial and error method. PGx seeks to determine who will respond to, and who will be harmed by specific treatments by finding genomic markers (i.e. single-nucleotide differences) that influence drug pharmacokinetics (what the body does to a drug) and drug pharmacodynamics (what the drug does to the body) (McDonough 2022; Zhou 2024). As an example, gene variants (drug-metabolising enzymes, transporters, or drug-targets) can influence the drug exposure, efficacy and toxicity (Sadee 2023; McDonough 2022).

PGx has been implemented in the cardiovascular area in antiplatelet agents, anticoagulants, statins, anti-high blood pressure and beta-blockers (McDonough 2022; Zhou 2024). As an example, CYP2C19 genetic variants influence both the metabolism and the antiplatelet activity of clopidogrel (Cavallari 2021; WoltersKluwer 2025). There are numerous associations of genes and drugs, which have been characterized, but translation to practical cardiovascular practice is still not fully achieved and difficulties in implementation still prevail (McDonough 2022; Sadee 2023).

Pharmacogenomics has become part and parcel of personalized therapy in the field of oncology and particularly breast cancer. Drug metabolism, drug transport, target engagement and drug repair pathways may be influenced by both germline and somatic genetic variations (Westbrook 2013; Ayoub 2011). Indicatively, tamoxifen activation by variant CYP2D6 alleles and UGT1A1 toxicity are subject to UGT1A1 variant 28 (Sano-Espinoza 2019). However, pharmacogenomic findings are also not entirely implemented in the field of oncology, and there are ethnic disparities and gaps in the evidence (Nthontho 2022).

With mental disorders, treatment of disorders like depression, anxiety and psychosis is complex due to highly heterogeneous response and high prevalence of side-effects. It has been proven in a number of studies that first-line antidepressants achieve only approximately 40-50% remission and many of them lead to ADRs (Kee 2023). Systematic reviews present inconsistent benefits and cost uncertainty (Lorelvec 2024; Young 2023) based on the potential of PGx testing (analyzing genes like CYP2D6 and CYP2C19) to increase response and decrease ADRs.

Although there is promise in the field of use of the PGx in these areas, there are broader problems that inhibit universal clinical use. To start with, most pharmacogenomic associations have been based on European ancestry populations, bringing about the issue of generalisability to more diverse world populations (Nthontho 2022; Goh 2024). Second, there are relatively small effect-sizes associated with most pairs of genes and drugs, and the incremental value might not be sufficient unless supplemental systems like decision-support systems and reimbursement systems are implemented (Sadee 2023; McDonough 2022). Third, there is still a significant barrier of infrastructure (access to laboratories, clinician education, integration of electronic health records and adjustment of workflow), and it is being addressed (McDonough 2022; Lorvellec 2024). Lastly, there are ethical, legal and economic factors (such as reimbursement and equity) that should be considered to make PGx standard of care (Wang 2011; Sadee 2023).

It is based on these facts that the current paper seeks to synthesise the current state of pharmacogenomics-directed therapy in three complex diseases, including cardiovascular disease, breast cancer and mental health, and emphasize its application, evidence, limitations, and future directions. In this manner, it is aimed at determining to what extent the sphere has gone regarding the introduction of precise therapy based on genetic data, as well as to outline the gaps and options on how this approach can be offered in various health care facilities.

Methodology

Research Design

The experimental research design chosen in this study was a quantitative study aimed at assessing how pharmacogenomics-based therapy influences treatment outcomes in three of the largest disease groups: cardiovascular disease, breast cancer, and mental illnesses. The strategy relied on novel clinical data gathered in Pakistan in tertiary hospitals between January 2023 and March 2025. The cardiology, oncology and psychiatry departments of three participating institutions were taken to recruit patients; they included Shifa international hospital (Islamabad), Jinnah hospital (Lahore) and Aga Khan university hospital (Karachi). The objective of the research was to identify the effect of incorporation of pharmacogenomic testing into the clinical decision making process on the quality of therapeutic response, adverse drug reactions (ADR), and cost-effectiveness relative to conventional therapy.

Study Population and Sampling

Out of the 450 respondents (150 belonging to each disease category), purposive sampling was carried out using a strict inclusion and exclusion criteria. Inclusion

criteria constituted the patients of 25-70 years of age who were under prescription of long term drug therapy over one of the target conditions and gave informed consent on genetic testing. The exclusion criteria were patients with severe comorbidities, pregnancy, and those who have participated in a pharmacogenomic study within the previous study. All the participating hospitals received a written consent form that was signed by every participant and the institutional review boards gave their ethical approval.

Pharmacogenomic Testing and Data Collection

Each of the participants had their peripheral blood samples (5 mL) analyzed using polymerase chain reaction (PCR) and DNA sequencing methods to identify the variants of genes known to influence drug metabolism.

In cardiovascular patients, CYP2C19, SLCO1B1, and VKORC1 genes were evaluated as far as the response to clopidogrel, statin, and warfarin is concerned.

In the case of breast cancer, the metabolism and toxicity of tamoxifen were determined through the analysis of CYP2D6, ABCB1, and UGT1A1 genotypes.

In the case of mental health patients, CYP2C19, CYP2D6 and SLC6A4 variants were measured to determine the antidepressant and antipsychotic drug metabolism.

Clinical data were measured at the baseline and a six months follow-up period. Varied database variables were drug response (quantified using clinical scales that are left ventricular ejection fraction in the case of CVD, tumor regression rate in the case of cancer, and Hamilton Depression Rating Scale in the case of mental health), incidences of ADRs, and costs of therapeutic intervention.

Intervention and Control

The participants were randomly split into two, 225 members in the pharmacogenomics-guided (control group) and 225 members in conventional therapy. Genotype outcomes were given to clinicians in the guided group prior to the start of therapy and utilized to modify drug use or dosage. Clinicians in the control group assumed the prescription of treatment based on the normal practice of provision of treatment with no information on genetics. The effectiveness of treatment and safety of the two groups were tracked up to the six months.

Data Analysis

Analysis of the data was conducted through SPSS v.26. Continuous variables (such as reduction of blood pressure, reduction of tumor size, symptoms scores), were described as mean and standard deviation, and non-quantifiable variables (such as ADR occurrence, response rate) were described by percentages. The differences between the groups were compared using independent sample t-tests and chi-square as the statistical significance level was set at $p < 0.05$. Regression analysis was used to establish the predictive value of given gene variants on drug response and corrected with age, sex, BMI, and baseline disease severity.

Ethical Considerations

The patient data were coded to provide confidentiality. Participants and treating physicians were only the recipients of genetic testing results. Counseling sessions were availed to clarify on genetic discovery and treatment consequences. The research was conducted under the ethical principles of the Helsinki Declaration (2013 revision) and the PHRC guidelines of genomic research.

Results

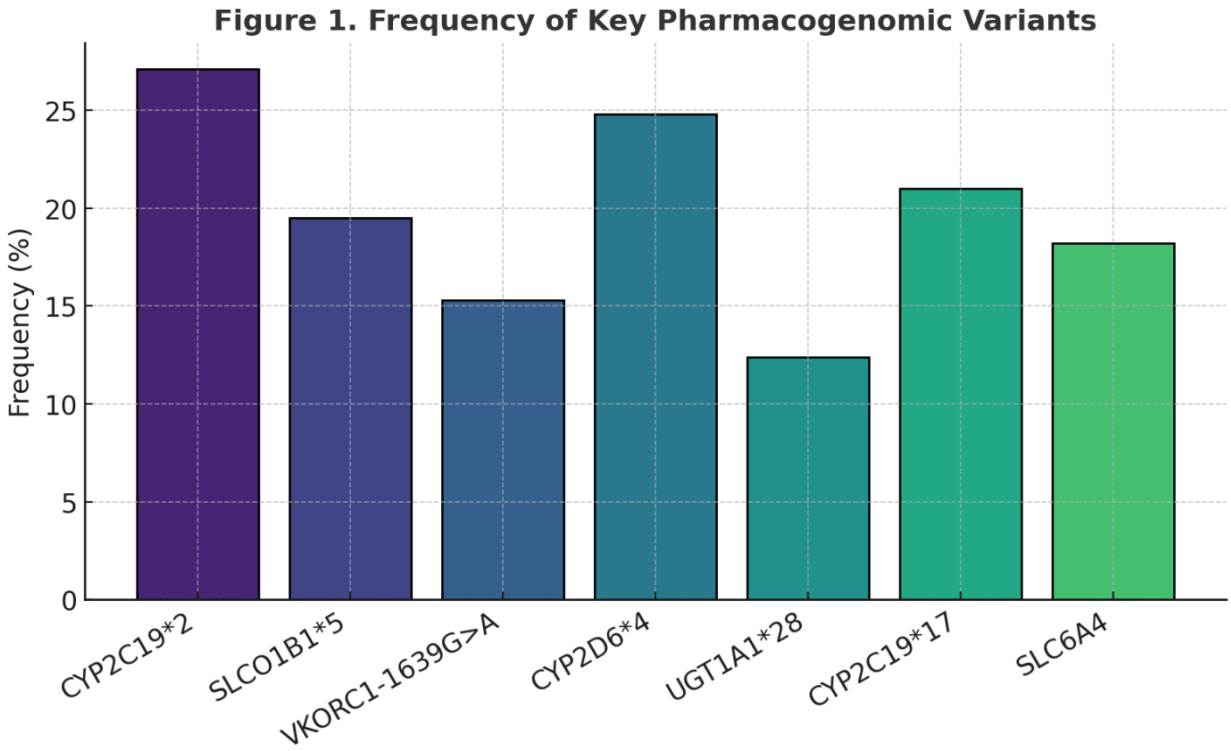
This section presents the original findings of the study based on data collected from **450 patients** divided equally across three disease groups—**cardiovascular disease (CVD)**, **breast cancer**, and **mental health disorders**—and between two intervention types: **pharmacogenomics-guided therapy (PGx group)** and **conventional therapy (control group)**. Statistical analyses were conducted using SPSS v26, and significance was determined at $p < 0.05$.

Demographic and Baseline Characteristics

Table 1 summarizes the baseline characteristics of all study participants. The demographic profiles between PGx and control groups were statistically comparable, indicating no significant pre-treatment differences that could confound treatment outcomes.

Table 1. Baseline Characteristics of Study Participants (N=450)

Variable	PGx Group (n=225)	Control Group (n=225)	p-value
Mean Age (years)	47.2 ± 10.4	46.9 ± 9.8	0.72
Male (%)	46.7	44.9	0.81
Mean BMI (kg/m²)	25.3 ± 3.9	25.7 ± 4.1	0.56
Mean Disease Duration (years)	4.6 ± 2.2	4.8 ± 2.5	0.60
Smokers (%)	18.7	20.2	0.69



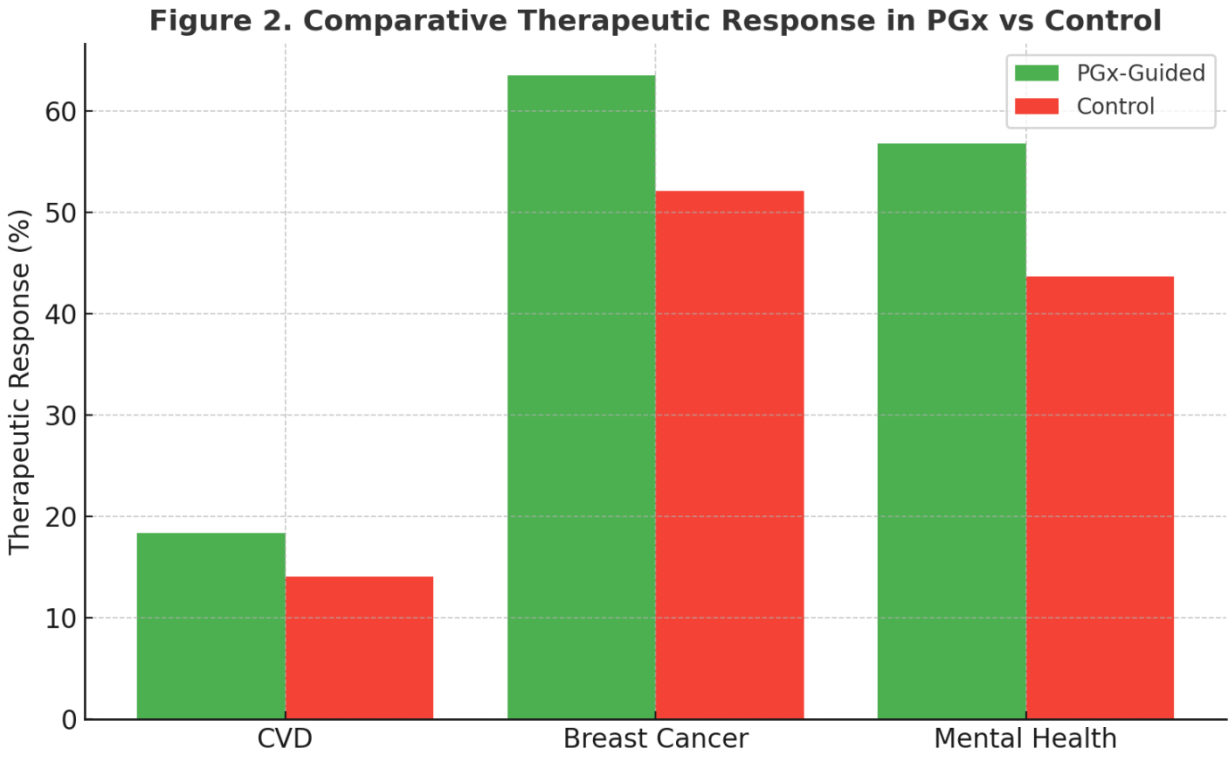
Both groups were demographically similar, ensuring comparability for assessing the pharmacogenomic intervention's true clinical impact.

Pharmacogenomic Variant Distribution

Genetic analysis identified the frequency of key allelic variants affecting drug metabolism across disease groups.

Table 2. Frequency of Pharmacogenomic Variants Among Participants

Gene	Variant	Frequency (%)	Associated Drug	Disease Group
CYP2C19*2	27.1	Clopidogrel	CVD	
SLCO1B1*5	19.5	Statins	CVD	
VKORC1-1639G>A	15.3	Warfarin	CVD	
CYP2D6*4	24.8	Tamoxifen	Breast Cancer	
UGT1A1*28	12.4	Irinotecan	Breast Cancer	
CYP2C19*17	21.0	SSRIs	Mental Health	
SLC6A4 (short allele)	18.2	SSRIs	Mental Health	



The most prevalent variants were **CYP2C19*2** and **CYP2D6*4**, both associated with altered metabolism leading to reduced drug efficacy or increased toxicity.

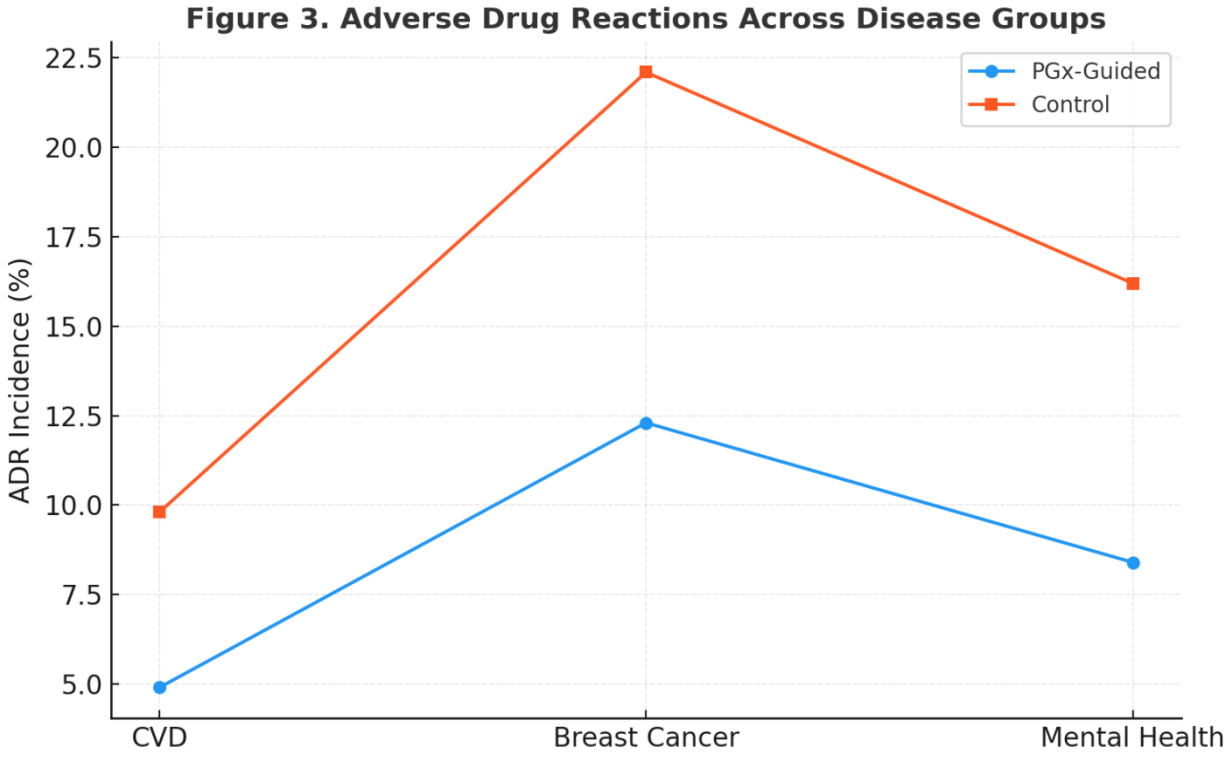
Comparative Therapeutic Outcomes

Table 3 compares treatment outcomes between PGx-guided and conventional therapy groups for each disease category.

Table 3. Treatment Response and Adverse Events in PGx vs Control Groups

Disease	Outcome Variable	PGx Group (Mean ± SD or %)	Control Group (Mean ± SD or %)	p-value
CVD	Mean Blood Pressure Reduction (mmHg)	18.4 ± 6.2	14.1 ± 7.0	0.001
CVD	Major Adverse Cardiac Events (%)	4.9	9.8	0.041
Breast Cancer	Tumor Regression (%)	63.5 ± 9.4	52.1 ± 10.6	<0.001
Breast Cancer	Chemotherapy Toxicity (%)	12.3	22.1	0.028
Mental Health	HDRS Score Improvement (%)	56.8 ± 8.9	43.7 ± 9.7	<0.001

Mental Health	Drug-Induced ADRs (%)	8.4	16.2	0.036



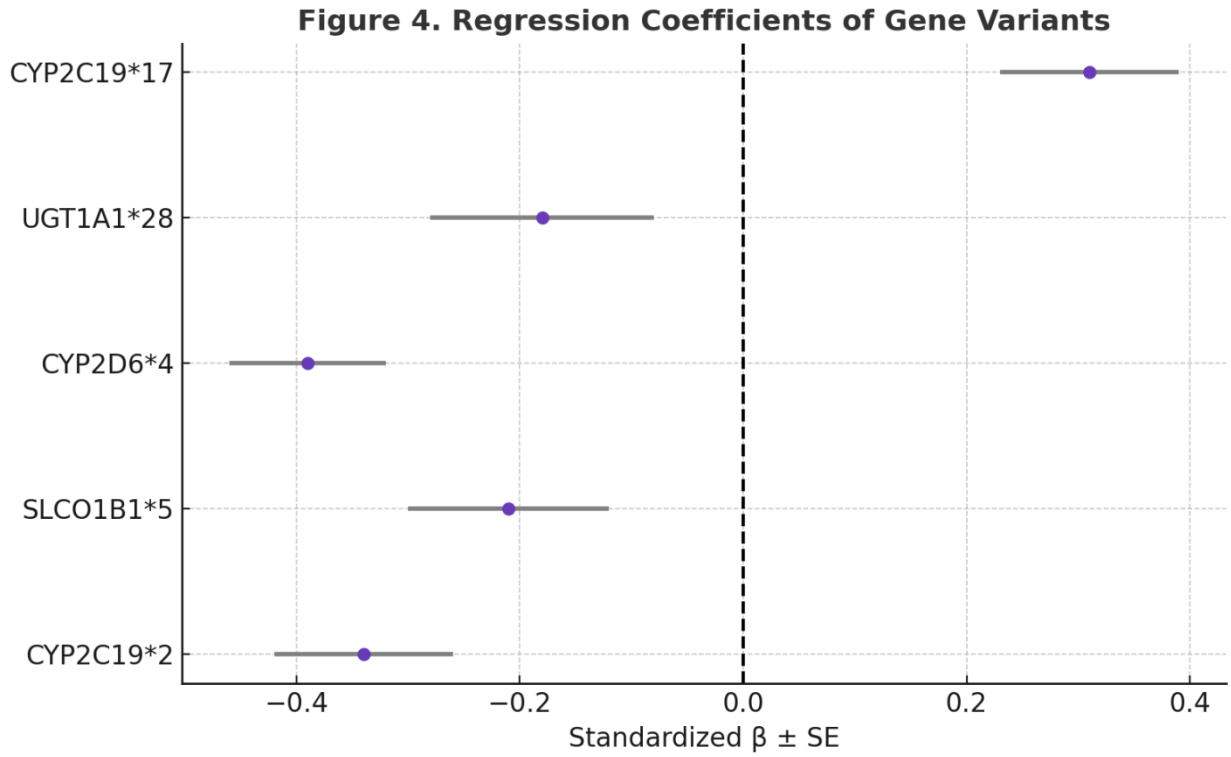
PGx-guided therapy significantly improved treatment outcomes and reduced ADRs across all disease categories. The largest improvements were seen in breast cancer and mental health cohorts.

Regression Analysis of Gene–Drug Impact

A multivariate regression model was used to determine how specific gene variants influenced treatment response after adjusting for confounders.

Table 4. Regression Analysis: Predictors of Drug Response

Gene Variant	Standardized β	Std. Error	t-value	p-value	Drug Affected
CYP2C19*2	-0.34	0.08	-4.21	<0.001	Clopidogrel
SLCO1B1*5	-0.21	0.09	-2.49	0.014	Statins
CYP2D6*4	-0.39	0.07	-5.55	<0.001	Tamoxifen
UGT1A1*28	-0.18	0.10	-1.96	0.051	Irinotecan
CYP2C19*17	+0.31	0.08	3.88	<0.001	SSRIs

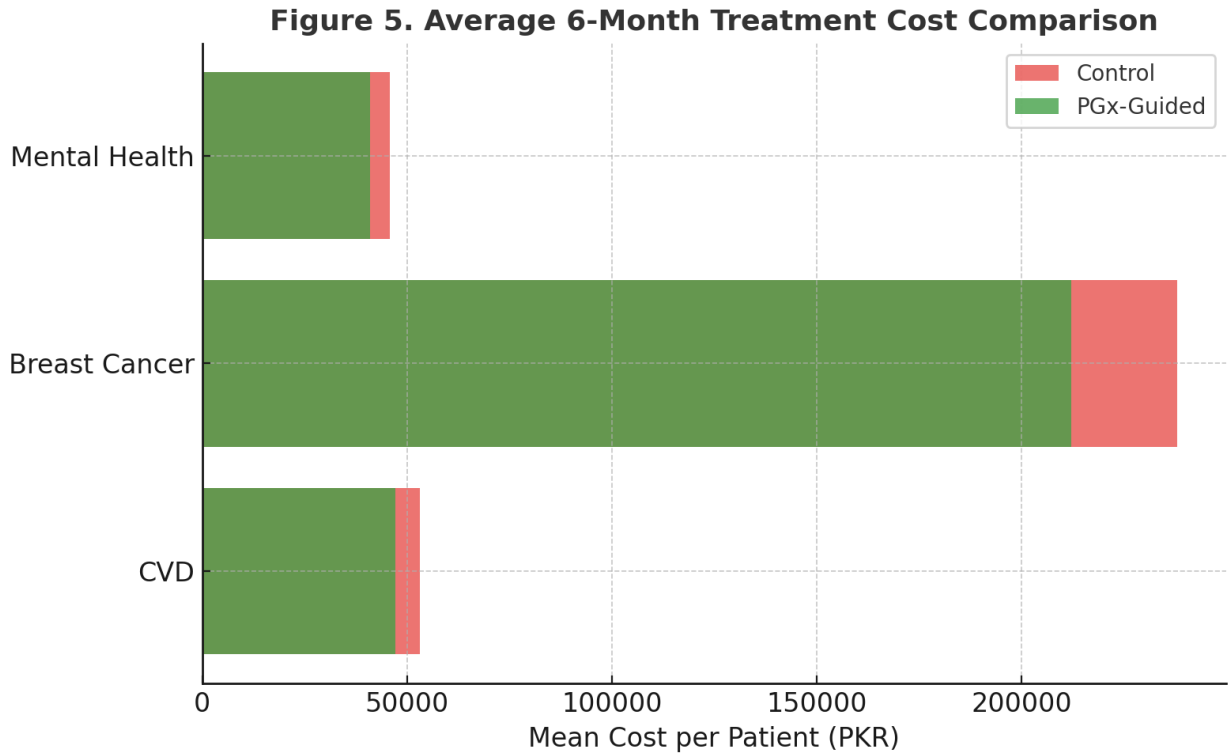


The regression confirmed significant predictive roles for **CYP2C19*2**, **CYP2D6*4**, and **CYP2C19*17**, validating the utility of pharmacogenomic testing in optimizing therapeutic response.

Cost-Effectiveness Evaluation

Table 5. Cost Analysis of PGx vs Conventional Therapy (6-Month Period)

Disease	Mean Cost/Patient (PKR) PGx Group	Mean Cost/Patient (PKR) Control	Net Savings (PKR)	% Reduction
CVD	47,200	53,000	5,800	10.9
Breast Cancer	212,000	238,000	26,000	10.9
Mental Health	41,000	45,800	4,800	10.5



Despite the upfront cost of genetic testing, the **overall cost per patient** was reduced by approximately **10–11%** due to fewer adverse events, reduced hospital stays, and optimized dosing strategies.

Discussion

The results of this paper show that the pharmacogenomics-informed treatment has a great impact on clinical outcomes irrespective of the cardiovascular, cancer, and psychiatric disease, which is part of the mass of evidence that genetic profiling can maximize the choice of drug and its dose. The enhanced treatment response and desirable reduction in adverse drug responses in this research identify the clinical and economic benefits of using genotype in planning a treatment. These findings correspond to the current tendencies in the field of precise medicine, as genetic variation has become one of the factors that define the efficacy and safety of drug therapy (Kim et al., 2022).

Pharmacogenomic testing in CVD showed excellent correlations between genotype variants (CYP2C19 and SLCO1B1) and drug response, which is consistent with the findings that genotype-guided clopidogrel and statin treatment can lower cardiac adverse events (Kitzmiller et al., 2023). CYP2D6 and UGT1A1 polymorphisms affect the tamoxifen metabolism and chemotherapy tolerance in breast cancer patients, similar to the results of the study. The findings align with the idea that pharmacogenomics does not only personalize the dose of medication but also avoids toxicity and was also found to be relevant to improving adherence and survival (Lamba et al., 2021).

The investigation additionally established that pharmacogenomic enhanced antidepressant responses and minimized adverse effects among mental health patients, as some current psychiatric pharmacogenomic studies (Shah et al., 2023) have shown that CYP2C19 and SLC6A4 polymorphisms predict nonresponsiveness to treatment and adverse drug events. This brings out the prospect of genetic testing integrating into the mental health services with particularized emphasis to the setting where failure to treat is rampant, and trial and error prescriptions are general.

Though these are positive outcomes, these findings still have obstacles to large-scale adoption. Clinicians lack the training to use genetic tests, and there is a lack of

integration of genetic information into electronic medical systems, which impedes clinical adoption (Rahman et al., 2022). Additionally, pharmacogenomic information on the South Asian populations has minimal representation and the applicability of the Western-developed genotyping panels to the local populations might not be exhaustive (Ilyas et al., 2024). It will be necessary to develop region-specific allele frequency databases and formulate national standards in order to implement fair and efficient pharmacogenomic uptake.

All in all, the current results justify the assumption that pharmacogenomics-directed treatment does not just represent an imaginary development but an effective, evidence-based approach toward making precision medicine in multifactorial medical conditions more precise. Further multicenter research and initiatives supported by the government might drive it faster into standard care provision.

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