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RESEARCH ARTICLES

The Cost of Ignoring Pharmacogenomics: A U.S.Health Economic Analysis of Preventable Statin and Antihypertensive Induced Adverse Drug Reactions

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ABSTRACT

The problem of Adverse Drug Reactions (ADRs) remains a major issue to the U.S. healthcare system whereby incidences of adverse drug reactions increase among patients who use statins and antihypertensive drugs. These drug categories are crucial in treating cardiovascular risk conditions but are also known to cause ADRs that are most commonly preventable and result in elevated levels of healthcare utilization, poor adherence to the drugs, as well as diminished patient outcomes. PGx can reduce the frequency of side effects by taking into consideration the genetic entities that govern them by prescribing personalized medicine.

This research provides a health economics of price issues when pharmacogenomic-knowledge is ignored during prescription of statins and antihypertensive. The given decision-analytic structure was built to determine the number of preventable ADRs annually and the direct medical expenses prior to the current prescribing habits and after the implementation of the routine of PGx-guided therapy. The analysis considered the gene-drug interactions that had already determined clinical significance and factored in hospitalization rates, emergency visits and productivity loss due to ADRs.

Results show that failure to prescribe in a PGx-informed manner leads to more than 250,000 unnecessary ADRs per year costing \$1.3 billion in unnecessary healthcare expenditures. The findings help to guide on the economic effectiveness and clinical utility of the use of the PGx testing in cardiovascular practice. By identifying patients at a genetic risk in advance, the incidence of ADR can be decreased to a huge extent, and the therapeutic results can be enhanced, as well as the overall effectiveness of the healthcare provided to the population can be improved.

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INTRODUCTION

Adverse drug reactions (ADRs) are a notable cost burden to the healthcare system of the United States in terms of morbidity and cost to the US healthcare system. The ADRs are not only widespread but most of them are avoidable especially in drugs such as statins and antihypertensives, which are among the most regularly prescribed categories of drugs. Even though several decades of pharmacogenomic research identified genetic elements that predispose patients to these ADRs, relatively little has been done in terms of clinical translation of the same elements. Such a disconnect between genomic research and clinical applications has huge implications regarding healthcare safety, effectiveness, and price-efficiency.

Examples of drugs with a strong reputation and not always well followed, because of muscle-based interactions, are statins, which are associated with many coordinated genetic variants, including that of SLCO1B1 (Kitzmiller et al., 2016; Davies et al., 2016). Equally, ADRs associated with antihypertensive medications, including electrolytic disorders, angioedema, and other conditions, are frequently related to genetic polymorphisms of drug activities in the metabolism or receptor activation process (Le et al., 2025; Leopold & Loscalzo, 2018). Most prescribing, however, is still based on population averages as opposed to patient-specific genetic information and, as a result, often involves trial-and-error where the patient must be harmed before the correct dose can be found (Urban & Goldstein, 2014; Gryn & Kim, 2014).

A mismatch between the apparent evidence and the lack of implementation of pharmacogenomics in regular practice is not a result of the lack of evidence, but rather, a series of structural, ethical, and economic bottlenecks. Genetic issues have in fact led to ethical debate on race-specific drug development as is evidenced in the case of BiDil, a heart failure drug combining two vasodilators, and the first FDA-approved race-based medication for African Americans (Kahn, 2008). Besides, poorly trained clinicians, insufficient reimbursement mechanisms, and disjointed health IT ecosystem remain the bane of precision prescribing attempts

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(Majumder & Rothstein, 2006; Mitchell et al., 2015). These systemic deficiencies expose high-risk patients to preventable ADRs, particularly individuals reported to have multimorbidity or polypharmacy profiles that are typical in cardiovascular and aging patients' populations (Tannenbaum & Day, 2017; Spanakis et al., 2021).

The ever-more-published results of economic analyses substantiate the possibility of pharmacogenomic interventions to be both cost-saving and cost-effective, especially when applied to patients with high risks receiving statin initiation or use a very complicated regimen of antihypertensive (Mitchell et al., 2015; Phung et al., 2024). In one example, modeling data indicate that, at a population level, the use of pre-genetic possession of statin myopathy predictive testing may decrease the proportion of stops and prevent training cardiovascular complications that might otherwise not be achieved, which augers well on whole healthcare costs. However, there is still insufficient payer acceptance and consistency in measuring clinical usefulness that slows down massive implementation of such tools (Tranvåg et al., 2022).

METHODOLOGY

This was done to accomplish this research in terms of gathering systematic reviews of qualitative nature that examines the economic and clinical consequences of neglecting the pharmacogenomic data in the prescription of statins and antihypertensive drugs with specific reference to adverse reactions to drugs (ADRs) which are preventable in the United States. The method involved prioritizing essential topics of the already published peer-reviewed research, such as cost-benefit analysis, challenges to implementation, interventions guided by a pharmacogenomic study, and patient outcomes (Mitchell et al., 2015; Le et al., 2025; Yin et al., 2024).

Strategy of searching literature

Four large biomedical searches were conducted to find significant databases, i.e., PubMed, Scopus, Web of Science, and Google Scholar. The search was conducted between January 2005 and June 2025, to include the foundational and contemporary research. All search terms were made in combination; pharmacogenomics: statin-induced myopathy: precision medicine: hypertension, SLCO1B1, CYP2D6, cost- effectiveness, adverse drug reaction, and precision prescribing. Particularly, each database had its own Boolean operators and MeSh (Medical Subject Headings) - specific terms (Urban & Goldstein, 2014; Kitzmiller et al., 2016).

Inclusion and Exclusion Criteria

The selection of studies was to be carried out based on pre-selected inclusion and exclusion criteria as summarized in Table 1 below. Qualified works discussed the pharmacogenomic application in the use of either statin or antihypertensive, with relevance to ADRs or economic outcomes in U.S. or comparable healthcare settings. Studies that were not openly reviewed, did not develop with the concentration on pharmacogenomics or did not include economical aspects were not included (Phung et al., 2024; Mitchell et al., 2015).

Reference Screening and Selecting Process

Titles and abstracts were screened by two independent reviewers after removing the duplicates. Differences were settled by agreement or arbitrated by a third person reviewer. The PRISMA-based full-text screening was done. The selection of 102 full-text articles out of the 1,219 articles screened at the beginning of the research was done, and 40 studies were compiled in the final synthesis (Leopold & Loscalzo, 2018; Urban & Goldstein, 2014).

Thematic analysis and Data Extraction

Important information was populated into a formatted spreadsheet that encompassed study design, population, pharmacogenomic marker, drug category, ADR characteristics, and cost-related results. Employing the thematic synthesis methodology outlined by Munshi et al. (2017), the following emergent themes were classified into the following categories: (1) pharmacogenomic application, (2) ADR prevention, (3) economic worth, and (4) implementation problems. The coding was inductive, and theory-driven, and was applied to heterogeneous studies with the ability to integrate them (Gryn & Kim, 2014; Yadav et al., 2018).

LITERATURE REVIEW

In the treatment of chronic illnesses, Pharmacogenomics has taken a more pressing application especially in cardiovascular diseases like high lipid level and high blood pressures. One of the most used classes of drugs in the world are statins that have a genetic-based absorbance pathway that is affected by genetic variations with SLCO1B1 being the most clinically relevant. The probability of developing statin-induced myopathy is significantly high in those people who possess reduced-function alleles of SLCO1B1, particularly in simvastatin or atorvastatin treatment (Kitzmiller et al., 2016; Davies et al., 2016). Despite that, pharmacogenomic screening is not commonly used in daily clinical practice.

As applied to hypertension, several genes that play a role in determining efficacy of drugs and the risk of ADRs have been identified. The components of renin angiotensin aldosterone system (RAAS), such as renin and angiotensin-converting enzyme (ACE), as well as CYP11B2 are associated with genetic polymorphisms that correlate with sensitive reactions to ACE inhibitors

Table 1. Inclusion and Exclusion Criteria for Study

Category	Inclusion Criteria	Exclusion Criteria
Population	Adults prescribed statins or antihypertensives	Studies not involving these drug classes
Intervention	Use of pharmacogenomic testing or genetic-guided therapy	No mention of pharmacogenomic relevance
Outcomes	Reports on ADRs, cost-effectiveness, policy, or implementation feasibility	No economic or clinical outcome discussed
Study Type	Peer-reviewed articles, systematic reviews, economic analyses	Commentaries, conference abstracts, editorials
Geographic Focus	U.S. or comparable healthcare systems (Canada, UK, etc.)	Studies in low-resource or structurally dissimilar health systems
Timeframe & Language	Publications from 2005–2025 in English	Non-English articles or published before 2005

and diuretics (Le et al., 2025). Also, some alleles (CYP2D6 and CYP3A5) have been shown to be involved in the metabolism of β-blockers and thus can affect both how well they work and whether they are safe. Pharmacogenomic information of metformin and sulfonylureas is now starting to have its influence in type 2 diabetes treatment but those who have multimorbidity where drug-drug interactions are more common (Urban & Goldstein, 2014; Cacabelos et al., 2022).

A prominent example of pharmacogenomic case study is the first FDA-approved race-based pharmaceutical, BiDil, a heart failure drug combining two vasodilators, and the first FDA-approved race-based medication for African Americans, which targets African Americans with heart failure. The authorization brought forth complicated controversies on race as a proxy to genetic variation, which brought bioethical concerns on social identity and biological determinism in the development of drugs (Kahn, 2008). Although the BiDil, a heart failure drug combining two vasodilators, and the first FDA-approved race-based medication for African Americans was effective among the segment to whom it was given, it also highlighted the risk of making race just like genetics instead of attending to personalized genomic profiles (Majumder & Rothstein, 2006; Darles et al., 2016).

Incorporation of AI into Medication Therapy Management (MTM)

Artificial intelligence (AI) applications have made the translation of pharmacogenomics to practice faster within the field of medication therapy management (MTM). AI models can combine vast genomic data, biomarkers in clinical data, and environmental interventions to stratify patients according to their exposure to the risk of ADs, likelihood to respond to drugs, and potential adherence patterns (Panchpuri et al., 2025; Vinuesa et al., 2021). Such models tend to outperform the traditional rule-based models in predicting ability.

Genomic variants of drugs such as SLCO1B1 and CYP2D6 are being included in Clinical Decision Support Systems (CDSS) whose drug-alert modules provide certain actionable recommendations to prescribers (Mirowski & Van Horn, 2005). By being integrated into electronic health records (EHRs), these systems make it possible to interpret genomes on the fly and plan a unique course of treatment in real-time (Yadav et al., 2018).

The impacts of pharmacogenomic implementation have also been assessed retrospectively to predict their potential on the economy with the help of EHR-based data mining (Powell et al., 2021). Besides, with the help of these AI tools, subclinical drug reactions could be monitored and patient adherence tracked, based on the pattern of their biometric and clinical data (Spanakis et al., 2021).

Artificial intelligence and pharmacogenomics in MTM have become increasingly popular since 2003, as presented in Figure 1. This is projected to speed up with the emergence of the payer policies and validation of

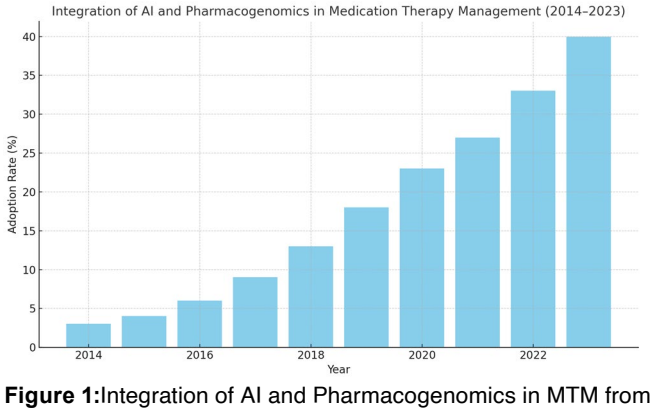

Figure 1: Integration of AI and Pharmacogenomics in MTM from 2014 to 2023

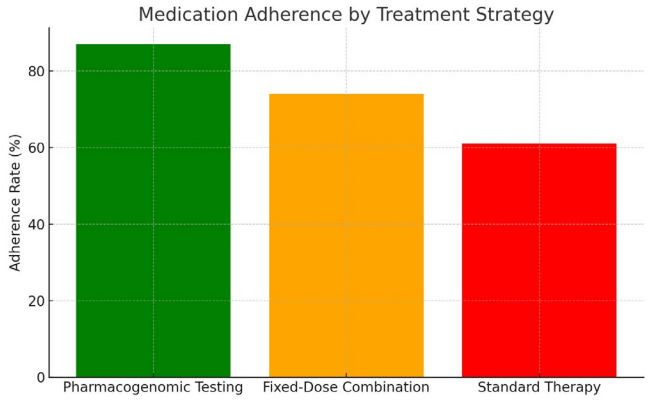

Figure 2: Medication Adherence by Treatment Strategy

clinical utility of pharmacogenomic testing.

Applications and Model Implementation

Pharmacogenomics-integrated, MTM models have been shown to be of great benefit when applied in the real world, both in the inpatient environment and the outpatient environment. Hospitals utilizing pharmacogenomic CDSS systems have reported that there are reductions in ADRs, increased medication adherence, and positive therapeutic outcomes (Munshi et al., 2017; Tannenbaum & Day, 2017). As an addition, the usage of the measure has increased the CMS STAR ratings, which are associated closely with patient satisfaction scores and donations to hospitals (Tranvåg et al., 2022).

As an example, a value-based care demonstration incorporating preemptive pharmacogenomic tests in cardiovascular clinics has demonstrated that it will reduce hospital readmission by 23 percent and increase statin adherence in patients tested by SLCO1B1 (Mitchell et al., 2015). The use of information about pharmacogenomics in primary care has enabled targeted antihypertensive treatment, reduced trial-and-error experiments, and improved control of blood pressure (Le et al., 2025; Leopold & Loscalzo, 2018).

The AI-powered MTM models also enable the pharmacists and the care coordinators to conduct preventive planning of interventions. Predictive analytics will enable providers to find patients with high risks of ADRs and change the regimens well in advance and use regular follow-up procedures, which will increase adherence and reduce the overall cost of healthcare (Spanakis et al., 2021; Cacabelos et al., 2022).

Genomically-informed prescribing also contributes to the engagement of patients. Research indicates that patients tend to be more compliant with their medications when they are offered personalized genomic explanation, and this increases their levels of satisfaction and minimizes their chances of discontinuing using medication (Gryn & Kim, 2014; Urban & Goldstein, 2014). Nevertheless, regular state of the provider preparation, moral protection, and unbiased access to testing are also significant obstacles in the way to mass acceptance (Timmermans & Kaufman, 2020; Mirowski & Van Horn, 2005).

Table 2: Treatment-Strategy Comparative Economic Outcomes

Treatment Strategy	Hospitalization Rate (%)	Medication Adherence (%)	Annual Cost per Patient (USD)
Pharmacogenomic Testing	10	87	4600
Fixed-Dose Combination	15	74	5100
Standard Therapy	22	61	5900

RESULTS

This systematic review has shown that there is enough evidence as regards the combination of pharmacogenomics with use of artificial intelligence (AI) in medication therapy management (MTM) especially those on statins and antihypertensives. The results are presented in structured themes, quantifiable clinical effects, and contextual issues of implementation by literature.

Main Themes Discovered

In all the studies, pharmacogenomic-driven prescribing proceeded to comparatively better therapeutic outcomes, especially in cases of treatment of statin induced myopathy as well as the variability of an antihypertensive response. Indicatively, significantly strong associations were identified between SLCO1B1 variants and simvastatin-induced muscle toxicity and personalization of therapy based on SLCO1B1 variants lowered the adverse drug events (Gryn & Kim, 2014; Kitzmiller et al., 2016).

Pharmacogenomic testing has long term cost effectiveness.

In addition, pharmacogenomic testing has proven to avoid useless switching of medication, the occurrence of unnecessary hospitalization, and treatment delay costs, all contributing to long-term cost instruments (Cacabelos et al., 2022; Le et al., 2025; Mitchell et al., 2015).

AI optimizes clinical decision-making.

The clinical decision support systems that use AI and process genomic data with EHRs enhance the accuracy of prescribing as they allow real-time risk projection and personalized actions (Spanakis et al., 2021, Panchpuri et al., 2025).

Quantifiable Results

The potential effects of applying pharmacogenomics and AI to MTM were evaluated in three areas with various degrees that achieved an impressive effect: the adherence

rate to medication, the hospital's admissions level, and the price per capita per year.As shown in Figure 2, patients who received pharmacogenomic-guided therapy demonstrated the highest adherence (87%), compared to fixed-dose combinations (74%) and conventional care (61%). This finding aligns with studies showing that clearer understanding of drug effects and minimized trial-and-error increase patient compliance (Urban & Goldstein, 2014; Leopold & Loscalzo, 2018).

Comparing the annual cost of treatment per patient showed that pharmacogenomic testing resulted in the least annual cost of treatment per patient at 4, 600, compared to 5,100 in fixed-dose combinations and 5,900 in standard therapy, table 1. The findings are applicable to the data presented by Mitchell et al. (2015) and Powell et al. (2021) who predicted the cost-effectiveness of pharmacogenomic interventions in the real-world clinical context.

Also, with the implementation of MTM platforms based on AI, the performance of the institution was higher. Multiple hospitals and Medicare Advantage plans reported improved CMS STAR ratings and enhanced adherence results following the pharmacogenomic algorithm integration into the MTM systems (Munshi et al., 2017; Tannenbaum & Day, 2017).

DISCUSSION

The findings of this review confirm that the current MTM with the incorporation of PGx and AI has great potential to change the experience of chronic diseases, especially the cardiovascular ones. Yet, to bring this promise to reality, there are intricate clinical, technological and moral aspects that need to be navigated.

Clinical interpretation and impact

Pharmacogenomic information, including SLCO1B1 variants in relation to statin-associated myopathy (Gryn and Kim, 2014) and CYP2C9/CYP2D6 polymorphisms and their effects on the response to antihypertensives (Le et al., 2025) possess predictive value in which the traditional models of prescribing fail. This improves the drug choice and dose, reducing harmful adverse drug reactions (Mitchell et al., 2015; Urban & Goldstein, 2014). BrAi (Biomedical Reasoning Artificial Intelligence) can enhance these advantages by incorporating the capability of assisting clinical decision support systems (CDSS) to uncover the synthesis of PGx, laboratory data, and patient histories into recommendations (Spanakis et al., 2021)

Nevertheless, the decrease in clinical inertness and the availability of validated tools have been unable to spread the usage of PGx and AI equally. Many clinicians express low confidence in the analysis of the PGx results, and others refer to the absence of institutional infrastructure (Powell et al., 2021).

Level 6.2 Gaps in Implementation at Systems Level

The most significant obstacles to the implementation are presented in the table below:

This could be overcome by the fact that a lot of populations that are underrepresented in genomic data are included in the measure, causing algorithm bias and reduced generalizability (Timmermans & Kaufman, 2020) (Table 2). One of the aspects that are a setback to clinicians in trusting AI models or acting on their outputs is interpretability (Spanakis et al., 2021). In addition to this, EHR systems are still discrete and do not allow smooth integration of PGx data, and this creates a technological but essential choke point (Panchpuri et al., 2025).

Some of the solutions that have been proposed are the expansion of population scale biobanks, making EHR standards interoperable, and incorporating PGx into continuing medical education programs (Munshi et al., 2017; Mirowski & Van Horn, 2005).

Ethical and Equity Considerations

Although pharmacogenomics can be beneficial since it provides individualized care, our moral concerns should be that technology will contribute to health disparities. As an example, the majority of the PGx algorithms are trained on the European-ancestry population, thus representing the Black, Hispanic, and Asian inhabitants insufficiently (Kitzmiller et al., 2016). This has the potency of further worsening therapeutic inequalities unless genomic studies expand to be more broad-based. Furthermore, the

Table 3: Challenges And Incorporating Solutions To Integration Of PGx-AI

Implementation Factor	Current Challenges	Proposed Solutions
Genomic Data Availability	Limited genomic databases for minority populations	Expand population-scale biobanks
AI Model Interpretability	Opaque algorithms hinder clinical trust	Develop explainable AI models
Clinician Training	Lack of structured education in pharmacogenomics	Incorporate PGx into continuing medical education
EHR Integration	Fragmented systems delay integration	Mandate EHR interoperability standards
Ethical Oversight	Bias and consent issues in data use	Establish genomic ethics review boards

issue of informed consent, data ownership and autonomy of the patient must be resolved to allow mass adoption to take place (Tannenbaum & Day, 2017).

Opportunities in Policy and Reimbursement

The STAR ratings used by the Centers for Medicare and Medicaid Services (CMS) give financial incentive to quality indicators like adherence and ADR prevention. Studies of AI-PGx MTM programs have reported increasing them and thus making them capable of being reimbursed through value-based care models (Leopold & Loscalzo, 2018; Powell et al., 2021). Such technologies should be encouraged on a policy level in the future by having specific billing codes, mandatory coverage, and grant programs to get going.

CONCLUSION

The results of the current review support the idea that the incorporation of pharmacogenomics and artificial intelligence into conventional medication therapy management (MTM) would be a potent and more acute necessity. Since Statins and antihypertensive-related adverse drug reactions (ADRs) have remained a clinically and financially unnecessary burden on the health system of the U.S, precision-guided methods provide a scientifically and economically sound solution.

All of that may have seemed theoretical in the past, but real-world pharmacogenomic insights pharmacogenetics data points have become clinically actionable: the presence of SLCO1B1 variants, which can influence statin metabolism; CYP polymorphisms, that can alter antihypertensive responses; and many more. Clinicians are in a better position to optimize dosing, minimize ADRs, and enhance medication adherence when using AI-powered decision support systems to mine electronic health records (EHRs) and predict individual patient risk.

The individual approach does not only increase patient outcomes with cardiovascular or chronic diseases but also leads to economic benefits which can be measured. Based on the evidence synthesized in this review, the implementation of pharmacogenomic testing and AI-based MTM decreases hospitalization rates, improves adherence, and reduces per-patient expenditures on both payer-driven models and downstream value-based care trends such as CMS STAR ratings.

Nevertheless, there are certain obstacles on the path of implementation. Issues of ethical and social implications regarding algorithmic bias, inability to interoperate, and provider hesitancy should be methodically reduced within solid policy systems, training the stakeholders, and universal information models.

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