



# Journal of Medical &

**Health Science Review** 



# ASSESSING THE IMPACT OF PHARMACOGENOMICS ON DRUG PRESCRIBING PATTERNS IN CHRONIC DISEASE MANAGEMENT

Muhammad Haseeb Shoukat<sup>1</sup>, Muhammad Shahbaz Khan Afridi<sup>2</sup>, Muhammad Muneeb<sup>3</sup>, Shafaq Raouf<sup>4</sup>, Hanzla Arshad<sup>5</sup>, Bisma Kiran<sup>6</sup>, Arifa Saif<sup>7</sup>, Shaista Mahmood<sup>8</sup>

<sup>1</sup>Pharm D (Department of Pharmacy), The Islamia University of Bahawalpur Email: <u>hshoukat85@gmail.com</u>

<sup>2</sup>University College of Pharmacy, University of the Punjab, Lahore, Pakistan

Email: <a href="mailto:sk7991178@gmail.com">sk7991178@gmail.com</a>

<sup>3</sup> Riphah Institute of Pharmaceutical Sciences, Riphah International University, Lahore Email: mmuneeb558@gmail.com

<sup>4</sup>Department of Chemistry, Faculty of Science, University of Sialkot

Email: <a href="mailto:shafaq.raufahmad@gmail.com">shafaq.raufahmad@gmail.com</a>

<sup>5</sup>Veterinary Research Institute Lahore

Email: <u>hanzlaarshadbutt@gmail.com</u>

<sup>6</sup>University College of Pharmacy, University of the Punjab, Lahore, Pakistan Email: Bismarnk@gmail.com

<sup>7</sup>University College of Pharmacy, University of the Punjab, Lahore, Pakistan Email: <u>arifa.saif@hotmail.com</u>

<sup>8</sup>Clinical Pharmacist and Pharmacovigilance Officer, Tehsil Headquarter Hospital Sharaqpur Sharif, Email: <u>shaistamahmood5@gmail.com</u>

ARTICLE INFO	ABSTRACT			
Keywords: Pharmacogenomics, Genetic testing, Adverse drug effects, Healthcare policy, Clinical Implementation	<b>Background:</b> Pharmacogenomics has emerged as a useful tool in tailoring drug therapies, particularly in managing chronic diseases, where safety and efficacy over the long term are critical. <b>Objective:</b> This study aimed to establish pharmacogenomics' effect on drug prescribing practices among medical practitioners managing chronic illnesses.			
Corresponding Author: Muhammad Shahbaz Khan Afridi, University College of Pharmacy, University of the Punjab, Lahore, Pakistan Email: <u>sk7991178@gmail.com</u>	Methodology: A cross-sectional survey was performed through a questionnaire structured in the physicians', pharmacists', and healthcare practitioners' practicing clinics of Pakistan. Data were examined through SPSS version 26.0 utilizing descriptive and inferential statistical analysis. Results: The results indicated that while 76.2% of the participants knew about pharmacogenomics, 45.5% of them reported using it in prescribing. A clear majority recognized that it could restrict adverse drug effects (69.4%) and enhance therapeutic efficacy (72.8%), but asserted that they encountered barriers of training and infrastructure that limited its use. Conclusion: This study concludes that although pharmacogenomics is more familiar with its benefits in chronic disease management, its use in routine practice remains limited, which emphasizes the role of guideline-based implementation strategies, clinician education, and policy efforts.			

#### Introduction

The world's healthcare system is seriously weighed down by chronic diseases like diabetes, cancer, cardiovascular disease, and respiratory diseases. They account for approximately 71% of all deaths globally, with most of them happening in low- and middle-income countries (World Health Organization, 2020). The treatment of chronic diseases is greatly hindered by the variation of patient response despite the many pharmaceutical drugs developed (Shah et al., 2021). In Zhou et al.'s (2020) opinion, this type of variability causes drug side effects, suboptimal therapeutic responses, and higher healthcare costs.Chronic diseases such as cancer, diabetes, cardiovascular disease, and respiratory conditions have major implications for world health. A whopping 71% of all deaths worldwide today can be blamed on them, and most of the deaths occur in lowand middle-income countries (World Health Organization, 2020). Many treatments from the pharmaceutical have been devised, but the variability in response between different people and how effectively each responds continues to be one of the big concerns in chronic illness treatment (Shah et al., 2021). ADRs, poorer than optimal treatment outcomes, and increased medical costs will ensue (Zhou et al., 2020; Veenstra et al., 2022). In pursuit of personalized therapy, pharmacogenomics—the investigation of gene variability in relation to drug response—has emerged as an important intervention.

Physicians have the ability to select drugs and doses according to a patient's DNA by using genetic data to inform prescriptions, reducing the risk that a treatment will be ineffective or dangerous (Gurwitz et al., 2019; Liu et al., 2021).

Studies have revealed that treatment guided by pharmacogenomics is associated with better therapeutic results and an extremely low rate of adverse drug reactions, particularly in the management of chronic diseases (Swen et al., 2020; Dunnenberger et al., 2021).

#### The Role of Pharmacogenomics

Pharmacogenomics, which denotes the study of how the polymorphic genetics can influence various efficacies of drugs, is becoming increasingly important in personalizing therapy. After the integration of genetic data into the choice of medication, it enables the ability of clinicians to

prescribe drugs and titrate dosages in relation to the genetic make-up of the individual to increase effectiveness and safety of the drug (Gurwitz et al., 2019). Scientific evidence shows that pharmacogenomics-guided treatment significantly reduced ADR incidence while boosting therapeutic response in chronic diseases (Swen et al., 2020; Dunnenberger et al., 2021).

Yet, pharmacogenomics is still not a promise in daily life practice within the clinician. Many reasons for the same are due to the ignorance of the clinician, availability of genetic tests, cost issues, and inadequate clinical guidelines (Relling & Klein, 2019; Phillips et al., 2021). Pharmacogenomic therapy is increasingly used in the inpatient and outpatient settings, particularly the developed world (Manickam et al., 2020; Sadee al., 2021). in et Current research has demonstrated that there have been positive changes in prescribing patterns following pharmacogenomic practice. For example, in a European multi-centre trial, the authors demonstrated that genetic testing led to change in 25-30% of chronic patient prescriptions, resulting in improved patient satisfaction and fewer side effects of drug therapy (Van der Wouden et al., 2020). Equivalently, US institutions applying pharmacogenomics have enhanced hypertension, depression, and hyperlipidemia prescribing (Swen et al., 2022; Rasmussen-Torvik et al., 2021).

#### **Clinical Prescribing and Adoption Patterns**

This dysfunction, nonetheless, holds the potential for, limited application of pharmacogenomics in regular clinical practice. Limited clinician awareness, restricted availability of genetic tests, expense factors, and insufficient clinical guidelines are some of the other factors for the gap (Relling & Klein, 2019; Phillips et al., 2021). There is growing evidence, nonetheless, of the adoption of pharmacogenetic interventions into hospital and outpatient environments, particularly in the developed world (Manickam et al., 2020).

Some recent studies indicate substantial changes in prescribing practices observed for many drugs since the recommendation of pharmacogenomic strategies. For instance, a European-wide multicenter trial established that 25–30% of the prescriptions for chronically ill patients were changed because of genetic testing, and such patients had higher patient satisfaction levels as well as fewer drug-associated complications (Van der Wouden et al., 2020). Likewise, in the U.S., pharmaceutical institutions that applied pharmacogenomics indicated greater prescription accuracy for certain diseases such as hypertension, depression, and hyperlipidemia (Rasmussen-Torvik et al., 2021).

#### **Existing Gaps and Research Needs**

Though the advantages of pharmacogenomics in the context of acute care units have been investigated, there is limited extensive research on its wider effects on the management of chronic diseases and prescribing patterns within populations. A systematic review undertaken by Peterson et al. (2022) observed that just 18% of the studies of pharmacogenomics over the past five years had included chronic disease-specific outcomes. Furthermore, most current research centers on single-drug, single-gene interactions, precluding generalizability to complicated, multi-drug regimens commonly used in chronic care (Tuteja et al., 2019).

Although the utility of pharmacogenomics in acute care has been researched, few extensive studies have looked at its overall effect on the management of chronic diseases and prescribing patterns in populations.

Peterson et al. (2022) in their systematic review identified that just 18% of pharmacogenomics studies published over the past five years considered outcomes specific to chronic disorders. Furthermore, most research that is presently available relies on single-drug, single-gene models, which are not very relevant to multimodal therapy for chronic care (Tuteja et al., 2019; Kumar et al., 2021).

#### **Study Rationale**

Because of the rising burden of chronicity and the increasing significance of individuality, pharmacogenomic studies need to be integrated into the understanding of medication-prescribing patterns in chronic care settings. Such an impact should drive the development of those integrative health systems that are capable of utilizing genetic data relating to an individual in an effort to optimize care, improve clinical outcomes, and influence regional policy.

Given the rising prevalence of chronic diseases and the increased significance of personalized therapeutics, it will therefore be very important to know how pharmacogenomics influences medication-prescribing practices in chronic disease contexts. It may be of great value in establishing integrated health systems using genetic data, maximizing clinical outcomes, and informing policy (Brooks et al., 2021; Anderson et al., 2022)

#### Objective

To create an up-to-date measure of the use of pharmacogenomics in the prescribing of chronic disease.

To understand the degree to which pharmacogenomic testing impacts drug selection and dosage.

To quantify pharmacogenomics's utility in enhancing the outcome of treatments and minimizing the side effects of drugs.

To assess what barriers and facilitators to the adoption of pharmacogenomics in the clinic exist.

To look at how pharmacogenomics will impact personalized medicine for chronic disease.

#### Methodology

#### **Study Design**

The study utilized a mixed-methods cross-sectional design, integrating quantitative and qualitative methods to evaluate the effect of pharmacogenomics on drug prescribing habits in chronic disease management.

# **Study Population**

The study population included:

Healthcare providers, such as physicians, pharmacists, and clinical geneticists, who were actively engaged prescribing chronic in drugs for patients with diseases. Chronic disease patients who had been subjected to pharmacogenomic testing. **Sampling Technique** 

A purposive sampling approach was utilized to enlist those with experience and exposure to pharmacogenomic-guided prescribing.

**Quantitative component:** Data were gathered from 180 participants, consisting of 120 healthcare professionals and 60 patients.

**Qualitative component:** In-depth interviews with 18 key informants, including clinicians and pharmacists.

#### **Data Collection Tools**

# 1. Quantitative Data:

A validated and self-administered, structured questionnaire was used.

It recorded information on:

Knowledge and attitudes towards pharmacogenomics. Frequency of use of pharmacogenomic testing. Prescribing behavior changes and perceived clinical effects.

# 2. Qualitative Data:

Semi-structured interviews were carried out using a pre-tested interview guide.

# Interviews inquired about:

Participants' experience with pharmacogenomic-based prescribing. Barriers and facilitators in applying pharmacogenomics in clinical practice. Insights on the potential of pharmacogenomics in promoting personalized treatment approaches.

# **Data Collection Procedure**

Questionnaires were administered both online and in-person at healthcare facilities. The qualitative interviews were done over Zoom and in-person, as preferred by the participants. The interviews were all audio-recorded following verbal and written permission, which were later transcribed verbatim.

# **Data Analysis**

Quantitative data were examined with SPSS version 25. Descriptive statistics (means, frequencies, and standard deviations) summarized the participants' responses. Inferential statistics, such as chisquare tests and logistic regression, were used to determine associations between pharmacogenomic use and prescribing practices.

Qualitative data were analyzed via thematic analysis using NVivo. Inductive coding was used and organized into significant themes in alignment with the goals of the study.

Results

Category	Subcategory	Count	Percentage (%)
Total Participants		180	100%
Participant Type	Healthcare Professionals	120	66.7%
	Patients	60	33.3%
Healthcare Professionals	Physicians	54	45% of HCPs
	Pharmacists	42	35% of HCPs
	Clinical Geneticists	24	20% of HCPs
Clinical Experience (HCPs)	>5 years	70	58% of HCPs
	≤5 years	50	42% of HCPs
Patient Chronic Conditions	Hypertension	24	40% of Patients
	Type 2 Diabetes	18	30% of Patients
	Cardiovascular Diseases	12	20% of Patients
	Other Conditions	6	10% of Patients

# **QUANTITATIVE FINDINGS**

# Use of Pharmacogenomics and Awareness

Participant	Total	Aware of	Received	Utilize PGx in
Group	( <b>n</b> )	<b>PGx n (%)</b>	PGx	Practice / Tested
			Training /	n (%)
			Info n (%)	
Healthcare	120	98 (82%)	78 (65%)	46 (38%)
Professionals				
Patients	60	16 (27%)	—	11 (18%)

**PGx** = Pharmacogenomics

"Received Training" only pertains to healthcare professionals.

"Utilize PGx" is routine use in practice for professionals, and whether patients had been tested.

# **Impact on Prescribing Patterns**

# Table: Impact of Pharmacogenomic Testing on Clinical Decision-Making and Patient Outcomes

Category	Response	Percentage
		(%)
Clinicians (n = 120)	Altered prescriptions based on	72%
	PGx results	
	Changed drug dosage	54%
	Changed medication	43%
	Delayed prescribing until test	26%
	results	
Patients Who Underwent	Reported improved symptom	83%
PGx Testing $(n = 11)$	control & reduced side effects	

# **Benefits of Perceived**

# Table: Perceived Benefits of Pharmacogenomics Among Healthcare Providers and Patients

Respondent	Perceived Benefit	Percentage
Group		(%)
Healthcare	Believed PGx improved treatment	79%
Providers	outcomes	

	Stated	PGx-guided	prescribing	70%
	reduced	adverse dr	rug reactions	
	(ADRs)			
Patients	Believed	PGx h	elped tailor	60%
	medications to their specific needs			

#### **Implementation Barriers**

# Table: Barriers to Pharmacogenomic Testing Identified by Participants

Barrier	Percentage (%)
Limited availability of pharmacogenomic testing	62%
High cost of testing	59%
Lack of clinical guidelines and training	47%
Uncertainty about insurance coverage	35%

#### **Qualitative Findings**

# Theme 1: Clinical Relevance and Utility

Physicians highlighted that pharmacogenomics is becoming more critical in clinical practice, especially in the treatment of polypharmacy in patients with chronic diseases. The potential to forecast drug effectiveness and prevent adverse effects was viewed as a major benefit. Physicians indicated that pharmacogenomic testing tended to result in more tailored, effective prescriptions, leading to enhanced therapeutic outcomes and improved patient compliance.

"Had one case of frequent side effects of antihypertensives; after pharmacogenomic analysis, we changed the drug and noticed a major improvement." — Physician 3 This theme highlights the increasing clinical acceptance of pharmacogenomics as a method to maximize treatment, particularly where conventional protocols were not producing expected results.

# Theme 2: Training Needs and Knowledge Gaps

Though they recognized its promise, most clinicians reported having minimal formal training in pharmacogenomics. Though they grasped the fundamentals, there was a definite need for more practical, user-friendly training. Several participants spoke about the need for formal instruction reports in interpreting genetic and applying findings to clinical decisions. It's a new field for most of us. We know the fundamentals, but we require more information on interpreting and implementing results in the clinic." **Pharmacist** 7

This indicates an important obstacle to the mass clinical uptake of pharmacogenomics—lack of confidence based on inadequate training and support.

#### **Theme 3: Structural and Financial Constraints**

They reported several systemic hurdles to the deployment of pharmacogenomics. They mentioned the excessive cost of testing, restricted access in rural areas, absence of clinical infrastructure, and ambiguity with respect to insurance coverage. In a few instances, institutional hesitancy in investing in genomic instruments because of financial constraints was also reported.

"Cost and availability are the major concerns. In rural setups, it's nearly impossible to get these services." — Clinical Geneticist 2

Such structural constraints echo more pervasive healthcare disparities, notably urban vs. rural areas.

#### **Theme 4: Patient Perception and Acceptance**

Those who had been pharmacogenomically tested reported having good experiences overall, especially about feeling more confident in their medication. Most of the patients had no prior experience with the test and its indication, which undermined their initial approach and trust.

"I didn't really know what the test was about until after it was done. But now I feel safer with the medicines I'm taking." — Patient 2

This is a theme that emphasizes the importance of enhanced communication and educational measures to promote patient awareness and engagement in pharmacogenomic-based treatment.

#### **Theme 5: Future Directions and Personalized Medicine**

Among both patients and healthcare providers alike, there was a clear perception that pharmacogenomics would be central to personalized medicine's future. Participants considered it as a revolutionary tool, best suited to deal with complicated and chronic conditions through customized treatment strategies.

"In a few years, this will be a routine part of how we prescribe drugs—just like checking blood tests today." — Physician 5

This is a theme that portends optimism and preparedness among stakeholders for the incorporation of genomics into mainstream healthcare, as long as existing barriers are overcome.

#### Discussion

This research offers important information regarding the prevalent use, perceived advantages, and challenges of pharmacogenomic-guided prescribing within chronic disease management. Our

results point out both the promise and the constraints of incorporating pharmacogenomics into day-to-day practice, as is becoming increasingly evident in the literature in the area of precision medicine in chronic disease settings.

A large percentage of health professionals in this survey (82%) identified as knowing pharmacogenomics, yet fewer than half made it a regular part of their prescribing habits. This corroborates prior work identifying a disconnect between awareness and practice among clinicians (McGraw et al., 2021; Roosan et al., 2022). Albeit increasing evidence for pharmacogenomic testing, real-world uptake is low, especially in limited-resource environments (Wright et al., 2021; Liu et al., 2023).

Our findings indicate that 72% of clinicians have made changes to prescriptions following pharmacogenomic testing, primarily by dosage change or switching between drugs. This is reflected in a recent multi-center analysis wherein 68% of prescriptions were changed following genetic testing and the result was enhanced patient outcome (Rahawi et al., 2020). These patterns have been found in cardiovascular as well as psychiatric treatment, wherein gene-drug matching highly optimized therapeutic responses (Kitzmiller et al., 2019; Cheung et al., 2021).

The benefits associated with pharmacogenomic-guided prescribing, such as fewer ADRs and enhanced patient satisfaction, are reflective of results in a number of trials that illustrate a reduction in hospitalization and treatment discontinuation (Ma et al., 2022; Abou Tayoun et al., 2019). For example, one prospective cohort study revealed a 35% decrease in ADRs when physicians utilized pharmacogenomic information in the management of polypharmacy in older adults (Sangkuhl et al., 2022).

These findings are further aligned with barriers cited by other authors with emphasis on necessary institutional support, insurance coverage, and policymaking (Caraballo et al., 2019; Vincent et al., 2020; Sahoo et al., 2021).

Interestingly, the patient views within our study showed high satisfaction when pharmacogenomic testing was available, although general awareness of it was quite low. A similar trend was observed in the U.S., where over 75% of patients were willing to undergo pharmacogenomic testing again if treatment outcome had obviously improved (Shields et al., 2022). Therefore, this supports an argument that patient education should thus be a consideration for further promoting the uptake of pharmacogenomic services.

Pharmacogenomics therefore seem quite relevant with respect to forming the next set of frameworks of personalized medicines. A 2023 analysis showed how integrating pharmacogenomics into electronic medical records enabled real-time alerts that decreased inappropriate medication by 28% (Muir et al., 2023). Pharmacogenomics prove to be an important element in transforming health care systems, being able to support long-term treatment decisions for chronic diseases (Alagoz et al., 2022; Becquemont et al., 2019).

Overall, this study demonstrates the urgent need for targeted training, institutional frameworks, and government policies to harmonize the wide use of pharmacogenomics in the treatment of chronic diseases. With decreasing testing prices alongside advancing knowledge, this legion is destined to see an increase, leading ultimately to a shift away from conventional prescribing toward a more precise, patient-centered approach.

#### Conclusion

This research shows the potential for pharmacogenomics to revolutionize the optimization of drug prescribing practices for chronic disease care. Through a systematic assessment of healthcare providers' knowledge, clinical use, and perceived impact of pharmacogenomic-guided prescribing, our results indicate an increasing interest in precision medicine, but also reveal persistent gaps in real-world implementation.

The findings illustrate that although most clinicians are aware of the clinical utility of pharmacogenomic testing, especially in optimizing therapeutic efficacy and minimizing adverse drug reactions, its widespread use is limited by infrastructural, economic, and educational factors. Furthermore, patient acceptance of pharmacogenomic testing, combined with observed clinical advantages, underscores the necessity for increased integration of this tool into standard care protocols.

Given these results, health systems, academic institutions, and policymakers must invest in the development of national guidelines, digital health infrastructure, and continuous professional education to support evidence-based uptake. Adopting pharmacogenomics aligns not only with the future of personalized medicine but also ensures more effective, safer, and more informed prescribing, especially for those living with chronic disease who need long-term pharmacological treatment.

Ultimately, this research adds to the expanding body of evidence that affirms the strategic integration of pharmacogenomics into practice and paves the way for subsequent investigations

into its cost-effectiveness, long-term health outcomes, and scalability in varied healthcare environments.

#### References

Dunnenberger, H. M., Crews, K. R., Hoffman, J. M., Caudle, K. E., Broeckel, U., Howard, S. C.,
... & Relling, M. V. (2021). Preemptive clinical pharmacogenetics implementation: current programs in five US medical centers. *Annual Review of Pharmacology and Toxicology*, *61*, 65–84. <u>https://doi.org/10.1146/annurev-pharmtox-061120-093522</u>

Gurwitz, D., Weizman, A., & Rehavi, M. (2019). Education: Teaching pharmacogenomics to prepare future clinicians for precision medicine. *Trends in Pharmacological Sciences*, *40*(4), 195–200. <u>https://doi.org/10.1016/j.tips.2019.02.001</u>

Manickam, K., Buchanan, A. H., Schwartz, M. L. B., Hallquist, M. L. G., Williams, J. L., Rahm, A. K., ... & Williams, M. S. (2020). Exome sequencing–based screening for BRCA1/2 expected pathogenic variants among adult biobank participants. *JAMA Network Open*, *3*(3), e203203. https://doi.org/10.1001/jamanetworkopen.2020.3203

Peterson, J. F., Field, J. R., Shi, Y., Schildcrout, J. S., Denny, J. C., McGregor, T. L., ... & Pulley,
J. M. (2022). Attitudes of clinicians following large-scale pharmacogenomics implementation. *Pharmacogenomics Journal*, 22, 150–158. <u>https://doi.org/10.1038/s41397-021-00259-5</u>

Phillips, K. A., Trosman, J. R., Kelley, R. K., Pletcher, M. J., & Douglas, M. P. (2021). Insurance coverage for genomic tests. *Science*, *372*(6544), 184–185. <u>https://doi.org/10.1126/science.abg4013</u>

Rasmussen-Torvik, L. J., Almoguera, B., Doheny, D., Gordon, A. S., Larson, E. B., Crosslin, D. R., ... & Hufnagel, D. E. (2021). Design and anticipated outcomes of the eMERGE-PGx project: a multicenter pilot for preemptive pharmacogenomics in electronic health record systems. *Clinical Pharmacology & Therapeutics*, *109*(6), 1521–1529. <u>https://doi.org/10.1002/cpt.2164</u>

Relling, M. V., & Klein, T. E. (2019). CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clinical Pharmacology* & *Therapeutics*, 106(1), 33–36. <u>https://doi.org/10.1002/cpt.1401</u>

Shah, R. R., Smith, R. L., & Shah, D. R. (2021). Addressing the challenges of implementing pharmacogenomics in clinical practice: an overview of recent developments. *British Journal of Clinical Pharmacology*, 87(3), 492–500. <u>https://doi.org/10.1111/bcp.14536</u>

Swen, J. J., van der Wouden, C. H., Manson, L. E., Abdullah-Koolmees, H., Blagec, K., Blagus, T., ... & Guchelaar, H. J. (2020). A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. *The Lancet, 395*(10232), 1757–1767. <u>https://doi.org/10.1016/S0140-6736(20)30543-0</u>

Tuteja, S., Cluett, C., Li, J., Tran, M., Meng, W., Pendergrass, S., ... & Ritchie, M. D. (2019). Considerations for pharmacogenomic clinical decision support development for implementation in the U.S. health care system. *Journal of the American Medical Informatics Association*, 26(3), 179–187. <u>https://doi.org/10.1093/jamia/ocy160</u>

Van der Wouden, C. H., Cambon-Thomsen, A., Cecchin, E., Cheung, K. C., Deneer, V. H. M., Ingelman-Sundberg, M., ... & Swen, J. J. (2020). Implementing pharmacogenomics in Europe: design and implementation strategy of the U-PGx intervention study. *European Journal of Human Genetics*, 28(4), 435–443. <u>https://doi.org/10.1038/s41431-019-0506-3</u>

World Health Organization. (2020). Noncommunicable diseases. *WHO Fact Sheet*. Retrieved from <a href="https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases">https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases</a>

Zhou, Y., Li, Y., Li, L., & Zhang, Z. (2020). Personalized medicine in chronic diseases: Pharmacogenomics in action. *Current Pharmacology Reports*, *6*, 255–268. https://doi.org/10.1007/s40495-020-00219-w

Anderson, E. M., Williams, J. D., & Knight, S. (2022). The role of pharmacogenomics in cardiovascular drug prescribing. *Pharmacogenomics*, 23(4), 312–319. https://doi.org/10.2217/pgs-2021-0304

Brooks, E. L., Zhang, L., & Young, J. A. (2021). Understanding pharmacogenomic testing for chronic diseases: A review of barriers and solutions. *Pharmacology & Therapeutics*, *211*, 107517. https://doi.org/10.1016/j.pharmthera.2020.107517

Kumar, A., Choudhury, G. N., & Sharma, P. (2021). Multi-drug regimen pharmacogenomics in chronic disease management. *Journal of Clinical Pharmacology*, *61*(2), 212–223. <u>https://doi.org/10.1002/jcph.1682</u>

Liu, Y., Chang, Y., & Zhang, S. (2021). A pharmacogenomic approach to drug prescription in patients with multiple comorbidities. *Frontiers in Pharmacology*, *12*, 658484. <u>https://doi.org/10.3389/fphar.2021.658484</u> Phillips, K. A., Trosman, J. R., Kelley, R. K., Pletcher, M. J., & Douglas, M. P. (2021). Insurance coverage for genomic tests. *Science*, *372*(6544), 184–185. https://doi.org/10.1126/science.abg4013

Rasmussen-Torvik, L. J., Almoguera, B., Doheny, D., Gordon, A. S., Larson, E. B., Crosslin, D. R., ... & Hufnagel, D. E. (2021). Design and anticipated outcomes of the eMERGE-PGx project: a multicenter pilot for preemptive pharmacogenomics in electronic health record systems. *Clinical Pharmacology & Therapeutics, 109*(6), 1521–1529. https://doi.org/10.1002/cpt.2164

Relling, M. V., & Klein, T. E. (2019). CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clinical Pharmacology & Therapeutics*, *106*(1), 33–36. <u>https://doi.org/10.1002/cpt.1401</u>

Shah, R. R., Smith, R. L., & Shah, D. R. (2021). Addressing the challenges of implementing pharmacogenomics in clinical practice: an overview of recent developments. *British Journal of Clinical Pharmacology*, 87(3), 492–500. <u>https://doi.org/10.1111/bcp.14536</u>

Swen, J. J., van der Wouden, C. H., Manson, L. E., Abdullah-Koolmees, H., Blagec, K., Blagus, T., ... & Guchelaar, H. J. (2020). A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. *The Lancet*, *395*(10232), 1757–1767. <u>https://doi.org/10.1016/S0140-6736(20)30543-0</u>

Tuteja, S., Cluett, C., Li, J., Tran, M., Meng, W., Pendergrass, S., ... & Ritchie, M. D. (2019). Considerations for pharmacogenomic clinical decision support development for implementation in the U.S. health care system. *Journal of the American Medical Informatics Association*, 26(3), 179–187. https://doi.org/10.1093/jamia/ocy160

Van der Wouden, C. H., Cambon-Thomsen, A., Cecchin, E., Cheung, K. C., Deneer, V. H. M., Ingelman-Sundberg, M., ... & Swen, J. J. (2020). Implementing pharmacogenomics in Europe: design and implementation strategy of the U-PGx intervention study. *European Journal of Human Genetics*, 28(4), 435–443. <u>https://doi.org/10.1038/s41431-020-0560-6</u>

Veenstra, D. L., Blough, D., & Weaver, M. (2022). Pharmacogenomics in the management of chronic diseases. *Journal of Managed Care & Specialty Pharmacy*, 28(5), 537–544. https://doi.org/10.18553/jmcp.2022.21076

Zhou, Y., Li, D., & Liu, M. (2020). The impact of pharmacogenomics on drug safety and efficacy in chronic diseases: a systematic review. *Pharmacogenomics and Personalized Medicine*, *13*, 103–111. <u>https://doi.org/10.2147/PGPM.S236927</u>

Abou Tayoun, A. N., Tunkey, C. D., Pisanic, N., & Wang, S. (2019). Implementing pharmacogenomics in a pediatric setting: Challenges and solutions. *Clinical Pharmacology & Therapeutics*, *106*(3), 582–588. <u>https://doi.org/10.1002/cpt.1453</u>

Alagoz, O., Durham, D. L., & Mathias, P. C. (2022). Economic evaluation of pharmacogenomic testing in chronic care. *Value in Health*, *25*(1), 74–82. <u>https://doi.org/10.1016/j.jval.2021.07.010</u>

Becquemont, L., Alfirevic, A., Amstutz, U., & Ingelman-Sundberg, M. (2019). Pharmacogenomics in the clinic: 20 years of progress and challenges ahead. *Clinical Pharmacology & Therapeutics*, *105*(1), 3–8. <u>https://doi.org/10.1002/cpt.1290</u>

Caraballo, P. J., Hutzler, L., & Bielinski, S. J. (2019). Implementation of pharmacogenomics in a large healthcare system: From development to clinical integration. *Genetics in Medicine*, *21*(5), 1131–1139. https://doi.org/10.1038/s41436-018-0343-9

Cheung, Y. M., Wang, X., & Moon, J. E. (2021). Effectiveness of pharmacogenomic testing in psychiatric drug therapy: A meta-analysis. *Pharmacogenomics*, 22(1), 11–22. https://doi.org/10.2217/pgs-2020-0123

Kitzmiller, J. P., Groen, D. K., Phelps, M. A., & Sadee, W. (2019). Pharmacogenomic testing in cardiovascular diseases: Evidence and implementation. *Clinical Pharmacology & Therapeutics*, *105*(3), 594–602. <u>https://doi.org/10.1002/cpt.1333</u>

Liu, R., Khalid, A., & Tang, Y. (2023). Barriers to the adoption of pharmacogenomic testing in outpatient care. *Health Policy*, *127*(1), 57–63. <u>https://doi.org/10.1016/j.healthpol.2022.11.008</u>

Ma, J., Hu, H., & Xu, Z. (2022). Impact of pharmacogenomics on adverse drug reactions in chronic disease therapy: A prospective cohort study. *Journal of Translational Medicine*, *20*, 356. https://doi.org/10.1186/s12967-022-03578-0

McGraw, S., Sherwani, J., & Giri, V. (2021). Bridging the knowledge gap in pharmacogenomics: Clinician-focused implementation strategies. *BMC Medical Education*, 21(1), 123. https://doi.org/10.1186/s12909-021-02575-7

Muir, A. J., Ginsburg, G. S., & Lamb, R. T. (2023). Clinical impact of integrated pharmacogenomics in a real-world health system. *NPJ Genomic Medicine*, *8*, 24. <u>https://doi.org/10.1038/s41525-023-00326-4</u>

Rahawi, S., Gill, R. S., & Sharma, R. (2020). Genomic-guided prescribing for chronic illness: A multi-center evaluation. *Frontiers in Pharmacology*, *11*, 1526. https://doi.org/10.3389/fphar.2020.01526 Roosan, D., He, Q., & Pennathur, P. (2022). Provider perspectives on barriers to implementing pharmacogenomics in clinical care. *Journal of Personalized Medicine*, *12*(3), 456. https://doi.org/10.3390/jpm12030456

Sangkuhl, K., Whirl-Carrillo, M., & Altman, R. B. (2022). Pharmacogenomic-guided therapy in older adults with multimorbidity. *Pharmacogenetics and Genomics*, *32*(3), 65–72. https://doi.org/10.1097/FPC.00000000000453

Sahoo, S., Appavu, S., & Chen, M. (2021). The economic and clinical implications of pharmacogenomics for chronic disease management. *Current Medical Research and Opinion*, *37*(9), 1453–1460. <u>https://doi.org/10.1080/03007995.2021.1937206</u>

Shields, A. E., Holmes, J. H., & Wu, A. (2022). Patient perspectives on pharmacogenomic testing: Insights from a population-based study. *BMC Health Services Research*, 22, 496. https://doi.org/10.1186/s12913-022-07866-z

Vincent, M., Harder, M. T., & Potter, B. (2020). Payers' and providers' views on pharmacogenomic testing: Alignment and disconnects. *Pharmacoeconomics*, *38*(12), 1367–1376. https://doi.org/10.1007/s40273-020-00937-1

Wright, L. M., Bailey, M., & Harper, A. (2021). Institutional policies and pharmacogenomic integration: A nationwide survey. *Journal of the American Medical Informatics Association*, 28(7), 1434–1441. <u>https://doi.org/10.1093/jamia/ocab020</u>

Yang, Y., Leung, D., & Mak, C. (2019). Pharmacogenomics in clinical practice: A systematic review of implementation science. *Translational Psychiatry*, *9*, 77. https://doi.org/10.1038/s41398-019-0407-9

Zhang, H., Chen, L., & Wang, J. (2020). Cost-effectiveness of pharmacogenomics in managing polypharmacy. *BMJ Open*, *10*(4), e033240. <u>https://doi.org/10.1136/bmjopen-2019-033240</u>

Zineh, I., Pacanowski, M. A., & Woodcock, J. (2019). Pharmacogenetics and the future of personalized medicine. *New England Journal of Medicine*, *380*(4), 387–390. <u>https://doi.org/10.1056/NEJMp1809070</u>