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REVIEW ARTICLE

Pharmacist-Led Implementation of Oncology Pharmacogenomic Testing of DPYD, UGT1A1, TPMT, and NUDT15 in Community and Rural Hospitals

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Abstract: Chemotherapy is a central modality in cancer care, yet severe adverse events frequently disrupt therapeutic regimens. Substantial interpatient variability in toxicity often arises from inherited polymorphisms in genes encoding drug-metabolizing enzymes. Pre-treatment screening for DPYD, UGT1A1, TPMT, and NUDT15 variants offer a validated mechanism to preempt life-threatening complications through genotype-guided dosing adjustments. Despite robust clinical guidelines from bodies such as the Clinical Pharmacogenetics Implementation Consortium, routine application is largely confined to academic centers, leaving patients in community and rural hospitals without standardized access to precision dosing. Infrastructure limitations, prolonged turnaround times for external laboratory results, and clinical knowledge gaps among providers constitute the primary impediments to widespread adoption. A scalable solution exists through pharmacist-led implementation models that integrate pharmacogenomic screening directly into established chemotherapy order verification workflows. Institutions can identify high-risk candidates by utilizing the pharmacist as a central coordinator and facilitate specimen collection at the point of diagnosis, and translate complex genetic data into actionable dosing modifications. Pre-emptive testing strategies, initiated at the time of cancer diagnosis rather than at the decision to treat, ensure that genomic profiles are available to clinicians before therapy begins. This approach reduces the risk of treatment delays and avoidable hospitalizations while enhancing health equity for underserved populations. Implementation of such screening protocols optimizes patient safety and provides a cost-effective pathway to normalize precision medicine in resource-limited oncology environments.

Keywords: Pharmacogenomics; Precision Oncology; Chemotherapy Toxicity; Pharmacist-led Care; Genotype-guided Dosing.

1. Introduction

Chemotherapy is a foundational element of oncologic management, but its therapeutic window is narrow, and patient response is characterized by significant heterogeneity. While a majority of patients tolerate standard protocols, a distinct subset experiences early-onset, life-threatening toxicities that require hospitalization or permanent treatment discontinuation. This variability is often not stochastic; rather, it is frequently governed by inherited genetic variations that dictate the efficiency of drug metabolism and clearance [1, 2]. Pharmacogenomics (PGx) identifies these germline variations, allowing for the anticipation of adverse outcomes before the first dose is administered [3]. When metabolic pathways are impaired due to genetic deficiency, standard dosages lead to supratherapeutic systemic exposure, escalating the risk of severe hematologic and gastrointestinal injury [4].

The clinical utility of PGx in oncology is supported by a wealth of evidence. The Clinical Pharmacogenetics Implementation Consortium (CPIC) provides validated, peer-reviewed guidelines for several high-priority gene-drug pairs, including DPYD with fluoropyrimidines, UGT1A1 with irinotecan, and the combination of TPMT and NUDT15 with thiopurines [5, 6]. These guidelines are not merely advisory; prospective data indicates that genotype-guided dosing reduces the incidence of severe toxicity without compromising the oncologic efficacy of the treatment [7, 8]. Regulatory bodies such as the U.S. Food and Drug Administration (FDA) have integrated these genomic biomarkers into official drug labeling, solidifying their role in standard clinical practice [9].

Despite the strength of this evidence, a significant implementation gap persists between academic centers and community-based practices. Academic institutions often benefit from centralized molecular laboratories and specialized clinical decision support, whereas community and rural hospitals, where the majority of patients receive care, face severe resource constraints [10]. This disparity leads to a lack of access to routine testing, resulting in avoidable safety risks for patients treated in non-academic settings. Addressing this gap is a matter of clinical necessity and health equity. Patients in rural areas often face existing barriers to specialized care, and the failure to provide PGx-guided dosing represents an additional, preventable layer of risk [11]. Establishing a practice-

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based model that utilizes existing pharmacy workflows offers a pathway to bridge this divide and ensure that precision oncology is accessible to all patients regardless of their geographic location.

2. Molecular Basis and Clinical Rationale for High-Impact Gene-Drug Pairs

The transition toward personalized dosing requires a detailed appreciation of the specific metabolic pathways involved in chemotherapy disposition. Four genes namely DPYD, UGT1A1, TPMT, and NUDT15 account for a substantial portion of predictable chemotherapy toxicity in common solid tumors and hematologic malignancies.

2.1. DPYD and Fluoropyrimidines

Fluoropyrimidines, specifically 5-fluorouracil (5-FU) and its oral prodrug capecitabine, serve as the backbone for treating various gastrointestinal, breast, and head and neck cancers. The metabolic clearance of these agents is almost entirely dependent on the enzyme dihydropyrimidine dehydrogenase (DPD), which is encoded by the DPYD gene. Approximately 80% of an administered dose of 5-FU is inactivated by DPD in the liver [12, 13]. Genetic variations in DPYD that result in reduced or absent DPD activity lead to a profound accumulation of the drug, resulting in severe toxicities such as grade 3 or 4 neutropenia, intractable diarrhea, and extensive mucositis.

Table 1. High-Impact Oncology Gene–Drug Pairs and Associated Clinical Risks

Gene	Relevant Chemotherapy	Therapeutic Area	Predominant Clinical Toxicity
DPYD	5-Fluorouracil, Capecitabine	GI, Breast, Head & Neck	Severe neutropenia, mucositis, diarrhea
UGT1A1	Irinotecan, Sacituzumab govitecan	Colorectal, Pancreatic, Breast	Neutropenia, life-threatening diarrhea
TPMT	6-Mercaptopurine, Thioguanine	Hematologic Malignancies	Life-threatening myelosuppression
NUDT15	6-Mercaptopurine, Thioguanine	Hematologic Malignancies	Severe myelosuppression, alopecia

Prospective clinical trials have established that pre-treatment screening for common DPYD variants allows for safer initiation of therapy. Patients identified as intermediate or poor metabolizers receive an upfront dose reduction, typically ranging from 25% to 50%, which significantly decreases the risk of hospitalization [8, 14]. The clinical impact of DPYD testing is immediate; by preventing the "first-cycle" toxicity that often occurs in deficient patients, clinicians can maintain the continuity of care and avoid the psychological and physical trauma associated with severe chemotherapy-induced illness.

2.2. UGT1A1 and Irinotecan Disposition

Irinotecan is a topoisomerase I inhibitor frequently utilized in regimens for colorectal and pancreatic cancers. Its activity is mediated by the active metabolite SN-38, which is significantly more potent than the parent compound. Termination of SN-38 activity occurs through glucuronidation by the enzyme UGT1A1 [15]. The most prevalent genetic variation affecting this pathway is a promoter polymorphism known as UGT1A1*28, which results in reduced enzyme expression [16].

Individuals who are homozygous for the UGT1A1*28 allele (the 7/7 genotype) possess a limited capacity to detoxify SN-38, leading to prolonged systemic exposure and an elevated risk of severe neutropenia and life-threatening diarrhea [17]. While the risk is most pronounced at higher doses of irinotecan, even standard-dose regimens can provoke severe reactions in poor metabolizers. CPIC guidelines and FDA labeling suggest that identifying these patients before treatment allows for proactive dose modifications, thereby optimizing the safety profile of irinotecan-containing regimens in routine practice.

2.3. Thiopurines and TPMT, NUDT15

Thiopurine medications, including 6-mercaptopurine and thioguanine, are essential in the management of acute lymphoblastic leukemia and various inflammatory conditions. These agents are converted into cytotoxic thioguanine nucleotides (TGNs) that incorporate into DNA. The regulation of TGN levels is primarily managed by two enzymes: thiopurine S-methyltransferase (TPMT) and nudix hydrolase 15 (NUDT15) [18, 19].

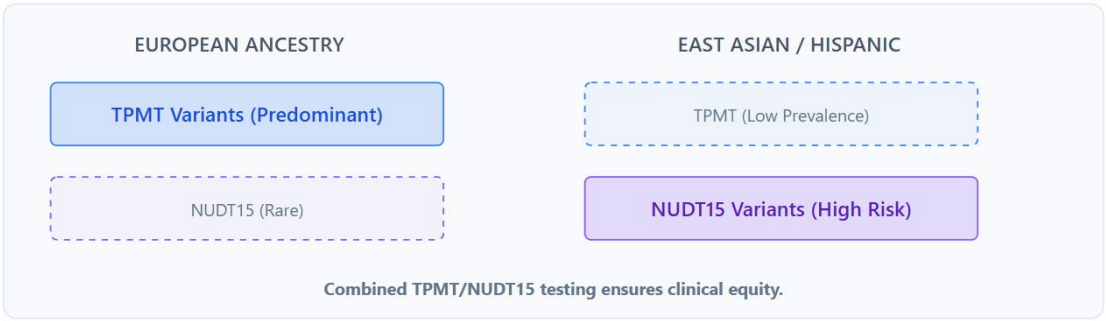

Figure 1. Ancestral variability in thiopurine metabolic pathways requiring dual-gene screening

The importance of testing both TPMT and NUDT15 is rooted in the distinct distribution of genetic variants across different ancestral populations. TPMT deficiency is the primary driver of thiopurine toxicity in individuals of European and African descent. In contrast, NUDT15 variants are the predominant cause of severe myelosuppression and alopecia in East Asian and Hispanic populations [20, 21]. Because many clinical settings serve diverse populations, relying solely on TPMT testing is insufficient and may miss high-risk patients of non-European descent. Guidelines now mandate a combined assessment of both genes to provide an equitable safety assessment, ensuring that dose reductions are applied appropriately based on the patient's comprehensive genetic risk profile [22].

Table 2. Ancestral Distribution and Prevalence of Actionable Variants

Gene	Variant Category	Population Prevalence	Ancestral Association
DPYD	*2A, *13, c.2846A>T	3% – 8%	Primarily European
UGT1A1	*28 (7 repeats)	10% – 15% (homozygous)	European, African
TPMT	*2, *3A, *3C	5% – 10%	European, African
NUDT15	*2, *3, *9	10% – 20%	East Asian, Hispanic

3. Structural and Operational Impediments in Community Oncology

While the evidence supporting genotype-guided dosing is substantial, its translation into routine community oncology practice is hindered by several interconnected barriers. These constraints are often more pronounced in rural and resource-limited settings where specialized molecular support is absent [27].

3.1. Deficiencies in Diagnostic Infrastructure

A primary obstacle is the lack of on-site molecular pathology capabilities. Academic centers frequently maintain internal genotyping platforms, allowing for rapid processing and integrated reporting. In contrast, community hospitals must rely on external reference laboratories. This dependency introduces logistical complexities regarding specimen logistics and specimen integrity [28]. External reports are often delivered as static documents that are not optimized for rapid clinical interpretation, placing an additional cognitive burden on the prescribing clinician to determine how the reported genotype relates to specific dosing adjustments [29].

3.2. The Temporal Mismatch: Turnaround Time Constraints

The most critical operational bottleneck is the mismatch between laboratory turnaround times and the clinical urgency of chemotherapy initiation. Conventional pharmacogenomic testing often requires several days to over a week for results to be finalized. In many oncologic scenarios, particularly in aggressive solid tumors or hematologic malignancies, treatment initiation cannot be delayed without risking disease progression [30]. This forces a difficult choice: delaying therapy to await results or proceeding with standard dosing and risking severe toxicity. The lack of rapid, point-of-care testing solutions in most community settings essentially renders reactive testing ordering a test only after a treatment decision is made operationally unfeasible for many patients [31, 32].

3.3. Clinical Knowledge Gaps and Interpretive Challenges

A significant proportion of oncology providers report limited confidence in interpreting pharmacogenomic data [33]. While many are aware of the DPYD and UGT1A1 associations, the translation of a specific diplotype into a precise dose reduction requires

specialized knowledge. In the absence of integrated clinical decision support (CDS) within the electronic health record (EHR), the identification of at-risk patients depends entirely on individual clinician vigilance [34]. Without standardized protocols or expert consultation available on-site, pharmacogenomic results may be overlooked or misapplied, leading to either sub-therapeutic dosing or continued exposure to toxicity risks [35, 36].

Table 3. Tactical Solutions for Overcoming Implementation Barriers in Community Settings

Implementation Barrier	Strategic Practice-Based Solution	Outcome
Infrastructure Gap	Utilization of CLIA-certified external reference laboratories	Eliminates need for on-site molecular diagnostics
Turnaround Time	Transition to pre-emptive testing at the point of diagnosis	Results available before treatment planning
Provider Knowledge	Pharmacist-led interpretation and actionable dosing memos	Reduces interpretive burden on oncologists
IT/EHR Limitations	Documentation of results in standardized discrete fields	Ensures longitudinal accessibility of genomic data

4. Proposed Pharmacist-Led Practice Framework

To overcome these structural barriers, we propose a practice-based framework that redefines the pharmacist's role from a passive recipient of genetic data to a central implementation driver. This model is designed to be scalable and does not require institutional investment in specialized molecular infrastructure.

4.1. The Pharmacist as the Central PGx Coordinator

Pharmacists are uniquely positioned to manage the pharmacogenomic lifecycle because they already serve as the final safety checkpoint in the chemotherapy order verification process. Health care institutions can ensure that every order for a high-risk agent (fluoropyrimidines, irinotecan, thiopurines) triggers an automatic review of the patient's genomic profile by embedding PGx screening into this existing workflow [37].

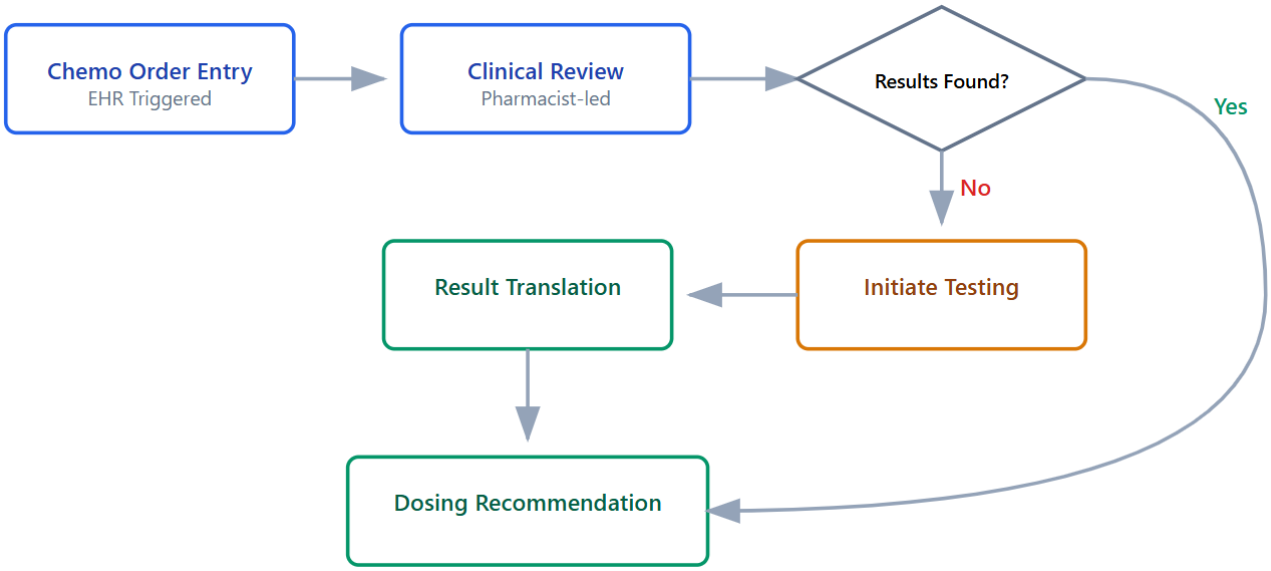

Figure 2. Standardizing the pharmacogenomic lifecycle within pharmacy order verification

The framework begins with the establishment of a "trigger medication" list approved by the Pharmacy and Therapeutics (P&T) committee. When an order for an agent on this list is entered into the system, the pharmacist verifies if actionable results are already present in the patient's record. If no data exists, the pharmacist is empowered via institutional protocol to initiate testing or provide an immediate recommendation to the oncologist to facilitate specimen collection [38, 39].

4.2. Transitioning to a Preemptive Testing Model

The solution to the turnaround time dilemma lies in shifting from reactive to preemptive testing. This framework advocates for initiating pharmacogenomic screening at the time of cancer diagnosis or during the initial oncology consultation, rather than waiting for a specific treatment decision [40, 41].

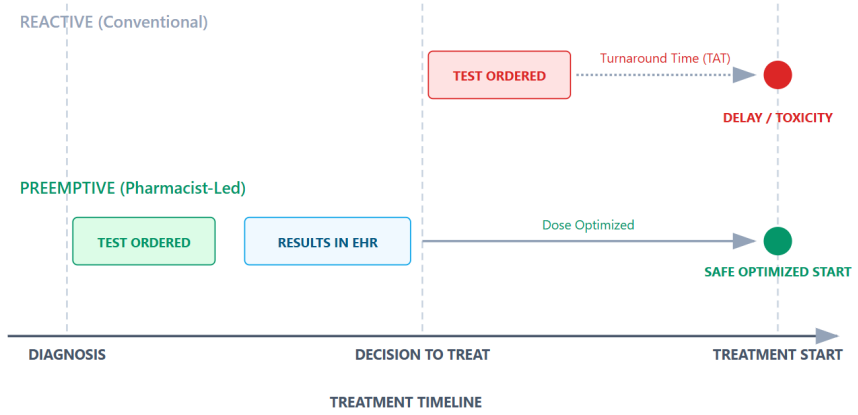

Figure 3. Alignment of PGx data availability with clinical decision-making milestones

Most patients undergo a period of diagnostic workup and staging before chemotherapy begins. Pharmacists can coordinate specimen collection (typically via non-invasive buccal swabs) early in the patient's journey by utilizing this diagnostic window. This ensures that the genomic data is available and documented in the EHR before the clinician even begins treatment planning. Preemptive testing reframes the pharmacogenomic profile as a permanent clinical asset that informs not just the first line of therapy, but all subsequent treatment decisions throughout the patient's lifetime [42, 43].

4.3. Data Translation and Clinical Communication

Effective implementation requires that genetic data be delivered to the oncologist in a format that is immediately actionable. In this model, the pharmacist assumes the responsibility for result interpretation. Upon receipt of the laboratory report, the pharmacist assigns the metabolizer phenotype (e.g., DPD intermediate metabolizer) and calculates the specific dose adjustment based on CPIC guidelines [44, 45].

Table 4. Pharmacist-Led Clinical Decision Support: Actionable Dosing Adjustments

Gene	Metabolizer Phenotype	CPIC/FDA Recommended Dosing Action
DPYD	Intermediate Metabolizer	Reduce starting dose by 25% – 50%
DPYD	Poor Metabolizer	Avoid fluoropyrimidines; use alternative therapy
UGT1A1	Poor Metabolizer (*28/*28)	Reduce starting dose of irinotecan by 25%
TPMT	Intermediate Metabolizer	Reduce starting dose by 30% – 70%
NUDT15	Intermediate Metabolizer	Reduce starting dose by 30% – 80%
TPMT/NUDT15	Poor Metabolizer	Reduce dose by 90% or switch to alternative

Instead of providing a complex genetic report, the pharmacist communicates a clear, concise recommendation: "Patient identified as DPYD *2A carrier; recommend 50% reduction in starting dose of capecitabine to prevent severe toxicity." This approach reduces the interpretive burden on oncologists and facilitates rapid, evidence-based decision-making. Documentation of these results in a standardized section of the EHR ensures that the information is accessible to all members of the multidisciplinary care team [46, 47, 48].

5. Equitable Access and Scalability

This framework is particularly vital for rural and tribal communities where access to academic-level precision medicine is limited. Community hospitals can provide the same level of safety and precision as large academic centers by utilizing external reference laboratories and utilizing existing pharmacy staff [49, 50]. The model's reliance on established pharmacy workflows makes it highly

scalable and adaptable to various institutional sizes, offering a pragmatic pathway to eliminate the geographic disparities currently seen in pharmacogenomic adoption [51].

5.1. Bridging the Geographic Gap in Precision Oncology

The equitable delivery of personalized medicine is frequently compromised by the centralization of molecular pathology resources in major metropolitan academic hubs. Patients residing in rural or tribal communities face significant logistical and financial hurdles that often preclude them from accessing advanced genomic screening. This creates a disparity where safety-enhancing dose modifications are less likely to be applied in resource-constrained settings. Community hospitals can effectively bypass the need for on-site molecular specialists or high-capital infrastructure by using a pharmacist-led framework that utilizes external reference laboratories. This decentralization allows local facilities to provide a standard of treatment safety and precision that is functionally equivalent to that of leading academic cancer centers [49, 50].

Table 5. Comparative Analysis of Reactive vs. Preemptive Testing

Feature	Reactive (Post-Decision)	Preemptive (At Diagnosis)
Timing of Order	After chemotherapy selection	During initial oncology workup
Result Availability	Often delayed (7–14 days)	Immediate (Available in EHR)
Treatment Delay	High risk of delay or empiric dosing	Negligible risk
Workload Impact	Urgent, non-standard workflow	Integrated, predictable workflow
Clinical Confidence	Clinician uncertainty at initiation	Data-informed precision dosing

5.2. Operational Scalability across Diverse Resource Settings

The success of pharmacogenomic integration depends on a model's ability to adapt to varying institutional sizes and existing staffing levels. The proposed framework relies on established medication-use processes, making it highly scalable and flexible. Because the workflow is built into the standard chemotherapy verification routine, it does not require the creation of parallel systems or the recruitment of dedicated genomic counselors. This efficiency ensures that the model can be scaled from small outpatient clinics to larger regional health systems with minimal disruption. Such adaptability offers a realistic and pragmatic pathway for the broad elimination of geographic disparities in pharmacogenomic utilization, ensuring that high-risk chemotherapy is optimized for safety regardless of the patient's location or the institution's resource level [51].

6. Projected Clinical and Economic Impact

The adoption of a pharmacist-led pharmacogenomic (PGx) framework in community settings carries significant implications for both patient outcomes and healthcare resource utilization. Institutions can transform the safety profile of high-risk chemotherapy regimens by standardizing the application of genotype-guided dosing.

6.1. Clinical Outcomes and Patient Safety

The prevalence of actionable genetic variants for DPYD, UGT1A1, TPMT, and NUDT15 is substantial across diverse populations. Collectively, it is estimated that approximately 15% to 25% of patients initiating fluoropyrimidine, irinotecan, or thiopurine therapies carry at least one high-risk allele [52, 53]. In the absence of pre-treatment screening, these individuals are at a significantly higher risk for grade 3 or 4 toxicities, which often lead to emergency department visits, prolonged hospitalizations, and permanent dose reductions that may compromise oncologic control [54].

Implementation of the proposed framework allows for the preemptive identification of these "at-risk" patients. Prospective data from early adopters suggests that genotype-guided dosing can reduce the incidence of severe treatment-related toxicity by up to 30% [55]. In community and rural settings, where patients may have limited access to intensive supportive care, the prevention of severe neutropenia or intractable diarrhea is particularly critical for maintaining treatment continuity and improving the overall quality of life during therapy [56].

6.2. Economic Evaluation and Cost Avoidance

While the upfront cost of multi-gene pharmacogenomic testing typically ranging from $250 to $500 is a common point of discussion, it must be weighed against the substantial costs associated with managing preventable adverse events [57]. The financial burden of a single hospitalization for chemotherapy-induced febrile neutropenia or severe gastrointestinal toxicity can exceed $15,000 to $20,000 [58].

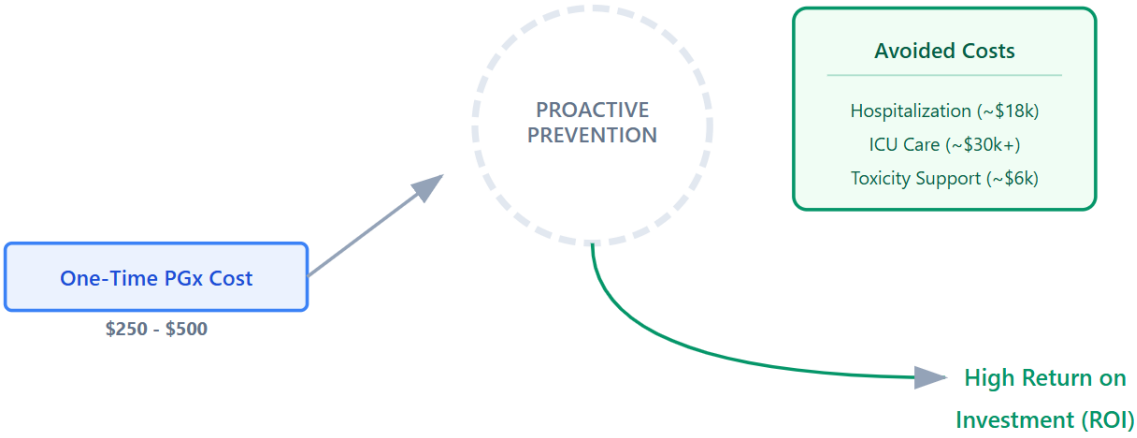

Figure 4. Economic rationale for preemptive testing based on the prevention of high-cost adverse clinical events

Economic modeling indicates that for high-risk gene-drug pairs like DPYD and fluoropyrimidines, pre-treatment screening is not only clinically beneficial but also cost-neutral or cost-saving at the population level [59]. The cost of testing a large cohort of patients is offset by the reduction in emergency care and inpatient services by avoiding even a small percentage of severe toxicities. The use of a pharmacist-led model minimizes institutional overhead by utilizing existing personnel and standardizing the workflow within current operational budgets [60].

Table 6. Projected Economic Impact and Hospital Resource Avoidance

Clinical Event	Severity	Estimated Cost per Event (USD)	PGx Prevention Potential
PGx Multi-Gene Panel	Diagnostic	$250 – $500	N/A (Upfront Investment)
Febrile Neutropenia	Hospitalization	$15,000 – $22,000	25% – 30% risk reduction
Severe Mucositis	Support Care	$5,000 – $8,000	Significant reduction in DPYD carriers
ICU Admission	Critical Care	$30,000+	Avoidance of extreme toxicity cases
Treatment Interruption	Logistical	Indirect productivity loss	Enhanced therapy adherence

7. Policy and Practice Implications

The transition of pharmacogenomics from an academic luxury to a community standard of care requires alignment across institutional policy, provider education, and reimbursement structures.

7.1. Advancing Health Equity in Precision Medicine

A central tenet of this framework is the reduction of geographic disparities in cancer care. Historically, precision medicine initiatives have been concentrated in well-funded urban centers, inadvertently widening the gap in outcomes for rural and underserved populations [61]. This framework ensures that patients in rural communities receive the same genomic-informed safety checks as those in major metropolitan areas by providing a scalable model that relies on external reference laboratories and local pharmacy expertise [62]. This is particularly relevant for variants such as NUDT15, where the failure to test in diverse populations represents a significant oversight in equitable care delivery [63].

7.2. Educational and Institutional Requirements

Successful adoption requires a shift in institutional culture. Pharmacy and Therapeutics (P&T) committees must move toward formalizing PGx-guided dosing as a standard safety protocol rather than an optional adjunct. Continuous professional development for oncology pharmacists is essential to ensure they remain proficient in the evolving landscape of genomic biomarkers and clinical guidelines [64]. Advocating for consistent insurance coverage for germline PGx testing remains a priority for policy leaders to ensure that financial barriers do not impede the delivery of safe, evidence-based care [65].

8. Conclusion

The evidence supporting pharmacogenomic-guided dosing for DPYD, UGT1A1, TPMT, and NUDT15 is mature and clinically robust. The persistence of severe, preventable chemotherapy toxicity in the face of this evidence represents a critical implementation gap in modern oncology. The pharmacist-led, preemptive implementation discussed here offers a pragmatic and scalable solution for community and rural hospitals to bridge this divide. Health institutions can overcome the traditional barriers of turnaround time and clinical knowledge gaps by utilizing the pharmacist's unique position in the medication-use process and shifting testing upstream to the point of diagnosis. Normalizing pharmacogenomic screening in routine oncology practice is a vital step toward a safer, more equitable, and more efficient healthcare system where treatment is precisely tailored to the individual's unique genetic blueprint.

References

[1] Anand U, Dey A, Chandel AKS, Sanyal R, Mishra A, Pandey DK, et al. Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. Genes Dis. 2022;10(4):1367–401.

[2] Amjad MT, Chidharla A, Kasi A. Cancer Chemotherapy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: http://www.ncbi.nlm.nih.gov/books/NBK564367/

[3] Zhang XT, Blacutt J, Lloyd T, Mencer M, Pratt V, Kotha J, et al. Enhancing clinical research with pharmacogenomics: a practical perspective. Bioanalysis. 2025;17(6):399–411.

[4] Porrogi P. The Environmental and Global Impact of Pharmacogenomics: Advancing Green Pharmacy Toward Sustainable and Inclusive Precision Medicine. J Pers Med. 2024;16(4).

[5] Tremmel R, Hübschmann D, Schaeffeler E, Pirmann S, Fröhling S, Schwab M. Innovation in cancer pharmacotherapy through integrative consideration of germline and tumor genomes. Pharmacol Rev. 2025;77(1):100014.

[6] Abdullah-Koolmees H, van Keulen AM, Nijenhuis M, Deneer VHM. Pharmacogenetics Guidelines: Overview and Comparison of the DPWG, CPIC, CPNDS, and RNPGx Guidelines. Front Pharmacol. 2021;11.

[7] Wu A, Anderson H, Hughesman C, Young S, Lohrisch C, Ross CJD, et al. Implementation of pharmacogenetic testing in oncology: DPYD-guided dosing to prevent fluoropyrimidine toxicity in British Columbia. Front Pharmacol. 2023;14:1257745.

[8] Rodríguez-García M, Salvador-Martín S, Piedra MSR, Bravo A, Vidal M, Gutierrez CF, et al. Genetic Variants Associated with Fluoropyrimidine-Induced Toxicity in Real-World Patients After Pre-Emptive DPYD Pharmacogenetic Testing. Pharmaceuticals. 2024;19(3).

[9] Food and Drug Administration (FDA). Table of Pharmacogenomic Biomarkers in Drug Labeling. [Internet]. Silver Spring (MD): FDA; 2024. Available from: https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling

[10] Unger JM, McAneny BL, Osarogiagbon RU. Cancer in rural America: Improving access to clinical trials and quality of oncologic care. CA Cancer J Clin. 2025;75(4):341–61.

[11] Hippman C, Nislow C. Pharmacogenomic Testing: Clinical Evidence and Implementation Challenges. J Pers Med. 2019;9(3):40.

[12] Otero-Torres S, Rodríguez-Mauriz R, Fort-Casamartina E, Clopés-Estela A, Soler-Rotllant F, Fontanals-Martínez S, et al. DPYD Genotyping, Fluoropyrimidine Dosage and Toxicity: An Umbrella Review of Systematic Reviews. Pharmaceuticals. 2025;18(5).

[13] Maslarinou A, Manolopoulos VG, Ragia G. Pharmacogenomic-guided dosing of fluoropyrimidines beyond DPYD: time for a polygenic algorithm? Front Pharmacol. 2023;14.

[14] Henricks LM, Lunenburg CATC, de Man FM, Meulendijks D, van Kuilenburg ABP, Boink BP, et al. DPYD genotype-guided dose individualisation of fluoropyrimidine therapy in routine clinical care: a prospective, multicentre, safety analysis. Lancet Oncol. 2018;19(11):1459-1467.

[15] Díaz-Villamarín X, Nieto-Sánchez MT, Martínez-Pérez M, Novo-González P, Fernández-Varón E, Torres-García A, et al. Dose-Limiting Toxicities and the Maximum Tolerated Dose of Irinotecan Based on UGT1A1 Genotypes: A Systematic Review. Pharmaceutics. 2025;17(5).

[16] Martínez-Pérez M, Nieto-Sánchez MT, Díaz-Villamarín X, Torres-García A, Fernández-Varón E, Prados-Carmona A, et al. The Early Safety Signal of Sacituzumab Govitecan-Related Toxicity and the UGT1A1*28 Genotype in Metastatic Breast Cancer: A Real-World Preliminary Report. J Clin Med. 2026;15(5).

[17] Karas S, Innocenti F. All You Need to Know About UGT1A1 Genetic Testing for Patients Treated With Irinotecan: A Practitioner-Friendly Guide. JCO Oncol Pract. 2022;18(4):270–7.

[18] Lubis IS, Anggadiredja K, Artarini AA, Sari NM, Suryawan N, Zazuli Z. NUDT15 Pharmacogenetics in Acute Lymphoblastic Leukemia: Synthesizing Progress for Personalized Thiopurine Therapy. Med Sci. 2025;13(3).

[19] Bayoumy AB, Crouwel F, Chanda N, Florin THJ, Buiter HJC, Mulder CJJ, et al. Advances in Thiopurine Drug Delivery: The Current State-of-the-Art. Eur J Drug Metab Pharmacokinet. 2021;46(6):743–58.

[20] Venugopal J, Sivadasan S, Aiyalu R. Optimizing mercaptopurine therapy in indian pediatric ALL: The role of TPMT and NUDT15 genetic polymorphisms. Cancer Treat Res Commun. 2026;47:101173.

[21] Maillard M, Schwab M, Whirl-Carrillo M, Moyer AM, Suarez-Kurtz G, Pui CH, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2025 Update. Clin Pharmacol Ther. 2026;119(4):916–27.

[22] Relling MV, Schwab M, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. Clin Pharmacol Ther. 2019;105(5):1095-1105.

[23] Wang RC, Wang Z. Precision Medicine: Disease Subtyping and Tailored Treatment. Cancers. 2023;15(15).

[24] Dean L, Kane M. Capecitabine Therapy and DPYD Genotype. In: Medical Genetics Summaries [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2012. Available from: http://www.ncbi.nlm.nih.gov/books/NBK385155/

[25] Hicks JK. Towards UGT1A1 guided irinotecan dosing. Eur J Hum Genet. 2023;31(9):980–1.

[26] Nguyen CM, Mendes MAS, Ma JD. Thiopurine methyltransferase (TPMT) genotyping to predict myelosuppression risk. PLoS Curr. 2011;3:RRN1236.

[27] Nelson H, Song JT, Kinshella MLW, Cochrane J, Mooder K, Hassani K, et al. A qualitative systematic review of barriers and facilitators to the implementation of community-based molecular diagnostics for infectious diseases. PLoS One. 2025;20(5):e0321690.

[28] Varughese LA, Bhupathiraju M, Hoffecker G, Terek S, Harr M, Hakonarson H, et al. Implementing Pharmacogenetic Testing in Gastrointestinal Cancers (IMPACT-GI): Study Protocol for a Pragmatic Implementation Trial for Establishing DPYD and UGT1A1 Screening to Guide Chemotherapy Dosing. Front Oncol. 2022;12:859846.

[29] Giri S, Lamichhane G, Pandey J, Khadayat R, K. C. S, Devkota HP, et al. Immune Modulation and Immunotherapy in Solid Tumors: Mechanisms of Resistance and Potential Therapeutic Strategies. Int J Mol Sci. 2025;26(7).

[30] Caraballo PJ, Sutton JA, Giri J, Wright JA, Nicholson WT, Kullo IJ, et al. Integrating pharmacogenomics into the electronic health record by implementing genomic indicators. J Am Med Inform Assoc. 2019;27(1):154–8.

[31] Newsom KJ, Hall B, Martinez KA, Nelson S, Starostik P, Nguyen K. Integration of pharmacogenetic data in epic genomic module drives clinical decision support alerts. Front Pharmacol. 2024;15.

[32] Lemke LK, Alam B, Williams R, Starostik P, Cavallari LH, Cicali EJ, et al. Reimbursement of pharmacogenetic tests at a tertiary academic medical center in the United States. Front Pharmacol. 2023;14:1179364.

[33] Smith DM, Douglas MP, Aquilante CL, Deverka PA, Devine B, Dunnenberger HM, et al. Progress in Pharmacogenomics Implementation in the United States: Barrier Erosion and Remaining Challenges. Clin Pharmacol Ther. 2025;118(4):778–89.

[34] Thottunkal S, Spahn C, Wang B, Rohatgi N, Hong J, Khandelwal A, et al. Clinician Experiences at the Frontier of Pharmacogenomics and Future Directions. J Pers Med. 2025;15(7):294.

[35] Wouden CH van der, Paasman E, Teichert M, Crone MR, Guchelaar HJ, Swen JJ. Assessing the Implementation of Pharmacogenomic Panel-Testing in Primary Care in the Netherlands Utilizing a Theoretical Framework. J Clin Med. 2020;9(3).

[36] Montrasio C, Cheli S, Clementi E. Pharmacogenetic Practice of Anticancer Drugs: Multiple Approaches for an Accurate and Comprehensive Genotyping. Pharmgenomics Pers Med. 2023;16:739–46.

[37] Shugg T, Tillman EM, Breman AM, Hodge JC, McDonald CA, Ly RC, et al. Development of a Multifaceted Program for Pharmacogenetics Adoption at an Academic Medical Center: Practical Considerations and Lessons Learned. Clin Pharmacol Ther. 2024;116(4):914–31.

[38] Bryan EG, Lunsford K, Mullis MD, McFarlane A, Elwood E, Gawronski BE, et al. Enhancing the Integration of Pre-Emptive Pharmacogenetic (PGx) Testing in Primary Care: Prioritizing Underserved Patients' Preferences in Implementation. J Pers Med. 2024;14(12).

[39] Franceschini N, Frick A, Kopp JB. Genetic Testing in Clinical Settings. Am J Kidney Dis. 2018;72(4):569–81.

[40] Perezcano C. The critical need to implement pharmacogenomics in public health services: Mexico in the global picture. Front Public Health. 2026;14.

[41] Cicali EJ, Eddy E, Gong Y, Elchynski AL, Pena del Aguila K, Basha T, et al. Implementation of a pharmacogenetic panel-based test for pharmacotherapy-based supportive care in an adult oncology clinic. Clin Transl Sci. 2024;17(7):e13890.

[42] Hicks JK, El Rouby N, Ong HH, Schildcrout JS, Ramsey LB, Shi Y, et al. Opportunity for Genotype-Guided Prescribing Among Adult Patients in 11 U.S. Health Systems. Clin Pharmacol Ther. 2021;110(1):179–88.

[43] Wu A, Anderson H, Hughesman C, Young S, Lohrisch C, Ross CJD, et al. Implementation of pharmacogenetic testing in oncology: DPYD-guided dosing to prevent fluoropyrimidine toxicity in British Columbia. Front Pharmacol. 2023;14:1257745.

[44] Kelley EF, Snyder EM, Alkhatib NS, Snyder SC, Sprissler R, Olson TP, et al. Economic evaluation of a pharmacogenomic multi-gene panel test to optimize anti-hypertension therapy: simulation study. J Med Econ. 2018;21(12):1246–53.

[45] Glewis S, Fagery M, Lingaratnam S, Harris S, Georgiou C, Underhill C, et al. Cost-Effectiveness of Pre-emptive DPYD Genotyping Compared to Standard of Care Among Patients Receiving Fluoropyrimidine-Based Anti-cancer Treatment in Australia. Clin Drug Investig. 2025;45(12):945–56.

[46] Reizine N, Vokes EE, Liu P, Truong TM, Nanda R, Fleming GF, et al. Implementation of pharmacogenomic testing in oncology care (PhOCus): study protocol of a pragmatic, randomized clinical trial. Ther Adv Med Oncol. 2020;12:1758835920974118.

[47] Green JK, Hackett LJ, Green DC, Deharvengt SJ, Brooks GA, Khan WA, et al. Implementation of a Pharmacist-Guided Pharmacogenomics Dosing Service at a Rural NCI-Designated Comprehensive Cancer Center. J Oncol Pharm Pract. 2025;31(8):1264–9.

[48] Lau-Min KS, Varughese LA, Nelson MN, Cambareri C, Reddy NJ, Oyer RA, et al. Preemptive pharmacogenetic testing to guide chemotherapy dosing in patients with gastrointestinal malignancies: a qualitative study of barriers to implementation. BMC Cancer. 2022;22:47.

[49] Leitch TM, Killam SR, Brown KE, Katseanes KC, George KM, Schwanke C, et al. Ensuring equity: Pharmacogenetic implementation in rural and tribal communities. Front Pharmacol. 2022;13:953142.

[50] Maruf AA, Aziz MA. The Potential Roles of Pharmacists in the Clinical Implementation of Pharmacogenomics. Pharmacy (Basel). 2023;11(6):180.

[51] Swen JJ, van der Wouden CH, Manson LE, et al. A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, stepped-wedge, cluster-randomised-controlled trial. Lancet. 2023;401(10374):347-356.

[52] Cicali EJ, Gong Y, et al. Implementation of a pharmacogenetic panel-based test for pharmacotherapy-based supportive care in an adult oncology clinic. Clin Transl Sci. 2024;17(7):e13890.

[53] Hicks JK, Rouby NE, et al. Opportunity for Genotype-Guided Prescribing Among Adult Patients in 11 U.S. Health Systems. Clin Pharmacol Ther. 2021;110(1):179-188.

[54] Meulendijks D, Henricks LM, et al. Clinical relevance of DPYD variants last updated in 2020. Pharmacological Reviews. 2025;77(1):100014.

[55] Wu A, Anderson H, et al. Implementation of pharmacogenetic testing in oncology: DPYD-guided dosing to prevent fluoropyrimidine toxicity in British Columbia. Front Pharmacol. 2023;14:1257745.

[56] Henricks LM, et al. DPYD genotype-guided dose individualisation of fluoropyrimidine therapy in routine clinical care. Lancet Oncol. 2018;19(11):1459-1467.

[57] Glewis S, Fagery M, et al. Cost-Effectiveness of Pre-emptive DPYD Genotyping Compared to Standard of Care. Clin Drug Investig. 2025;45(12):945-956.

[58] Berm EJJ, de Looff M, et al. Economic Evaluations of Pharmacogenetic and Pharmacogenomic Screening Tests: A Systematic Review. PLOS ONE. 2016;11(1):e0146262.

[59] Faruque F, Noh H, et al. Economic Value of Pharmacogenetic Testing for Cancer Drugs with Clinically Relevant Drug-Gene Associations. J Manag Care Spec Pharm. 2019;25(2):260-271.

[60] Haidar CE, Crews KR, et al. Advancing Pharmacogenomics from Single-Gene to Preemptive Testing. Annu Rev Genomics Hum Genet. 2022;23:449-473.

[61] Leitch TM, et al. Ensuring equity: Pharmacogenetic implementation in rural and tribal communities. Front Pharmacol. 2022;13:953142.

[62] Kabbani D, Akika R, et al. Pharmacogenomics in practice: a review and implementation guide. Front Pharmacol. 2023;14:1189976.

[63] Maillard M, et al. CPIC Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2025 Update. Clin Pharmacol Ther. 2026;119(4):916-927.

[64] Maruf AA, Aziz MA. The Potential Roles of Pharmacists in the Clinical Implementation of Pharmacogenomics. Pharmacy. 2023;11(6):180.

[65] Smith DM, et al. Progress in Pharmacogenomics Implementation in the United States: Barrier Erosion and Remaining Challenges. Clin Pharmacol Ther. 2025;118(4):778-789.