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GENETIC BIOMARKERS IN PRECISION DRUG THERAPY: EMERGING APPLICATIONS IN NURSING AND MODERN MEDICINE

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ABSTRACT
Genetic biomarkers are increasingly important in precision drug therapy because inherited variation can influence treatment efficacy, toxicity, metabolism, and dosage requirements. This study characterized clinically annotated pharmacogenomic evidence to identify major genetic biomarkers and drug associations relevant to individualized medication management and modern clinical practice. A retrospective secondary-data analysis was conducted using 5,171 unique clinical variant annotations after removal of 21 exact duplicates. Evidence levels, clinical consequence domains, leading genes, and frequently represented drugs or chemicals were summarized descriptively. Level 3 evidence predominated, accounting for 86.27% of annotations, whereas Levels 1A-2B collectively represented 7.76%. Efficacy and toxicity were the principal clinical consequence domains, comprising 38.91% and 36.22% of annotations, respectively. Frequently represented genes included ABCB1, OPRM1, CYP2D6, SLCO1B1, HLA-B, DPYD, CYP2C19, and CYP2C9. Among these, CFTR, DPYD, and CYP2D6 showed comparatively high proportions of Level 1/2 evidence. Fluorouracil, methotrexate, cyclophosphamide, cisplatin, and warfarin were among the most frequently represented therapeutic agents. Overall, the findings show that pharmacogenomic knowledge is broad but heterogeneous in clinical maturity. Precision therapy should therefore prioritize high-evidence gene-drug relationships to support safer prescribing, treatment optimization, adverse-event prevention, and nursing-led medication monitoring.

KEYWORDS: Pharmacogenomics; Genetic biomarkers; Precision medicine; Drug therapy; Nursing practice.

1. INTRODUCTION
The principles of precision medicine have revolutionized traditional pharmacotherapy by acknowledging that there is significant biological variability among people that affects how a drug will work. Pharmacogenomics is a significant aspect of this paradigm, as genetic differences can affect the absorption, metabolism, transport, molecular targeting, efficacy and toxicity of drugs. Pharmacogenomics has evolved from an exploratory research area to a clinically relevant aspect of selecting patient-specific treatments, which has happened over the last few years (Abad-Santos et al., 2024). Genetic biomarkers can give information prior to or during treatment to guide the selection of drugs, dosage, or additional monitoring in patients who should receive different treatments.

Pharmacogenomics has clear clinical relevance particularly with variants that affect drug-metabolizing enzymes, transport proteins, immune-response genes, and therapeutic targets. This variability can lead to significant differences in exposure to the drug and pharmacodynamic response, which can decrease therapeutic failures and prevent unnecessary adverse drug reactions (Sadee et al., 2023). But not all gene-drug associations reported can be adopted for routine use. Translation into clinical practice relies on the quality, consistency, and clinical significance of the pharmacogenomic evidence that is available (Kabbani et al., 2023).

The management of the implementation has thus been an important issue in modern medicine. Although there are increasing efforts and availability of pharmacogenetic testing and evidence-based recommendations, the use of pharmacogenomic services is not optimally integrated throughout health care systems (Medwid & Kim, 2024). There is a need for partnership between physicians, pharmacists, nurses, laboratory specialists, genetic professionals, and health-information teams for clinical implementation. The nurse has a specific role in medication administration, monitoring the therapeutic response, identification of adverse events, patient education and communication in a multidisciplinary care setting, and this is especially so for nurses (Cheek & Walker, 2025).

Genetic results can be further interpreted using digital decision support infrastructure by linking to actionable medication recommendations at the point of care (Farmaki et al., 2024). Additionally, the development of drugs has incorporated biomarker stratification as a tool to identify therapeutic subgroups and better select which patients should receive which therapy (Martínez-Jiménez et al., 2025). However, the implementation of these standards is very different between clinical programs, especially in terms of testing approaches, professional roles, reporting processes, and how it fits into the normal workflow (Luczak et al., 2021).

Structured implementation strategies are thus needed to make pharmacogenetic evidence actionable in an actionable manner (Duong et al. 2020). Another important consideration is education, as it is important that clinicians understand what is possible and what is not before using pharmacogenomic information safely (Kusljic & Luzum, 2024).

Standardized implementation frameworks and a shared evidence generation are becoming more supported through international collaboration across healthcare environments (Cavallari et al., 2025).
Another challenge is for pharmacogenomic knowledge to be representative of genetically diverse populations. Many populations are underrepresented and may not enable the generalizability of identified gene-drug associations and help contribute to inequities in precision medicine (Twesigomwe et al., 2025). New AI and multi-omics technologies could facilitate deeper integration of genomic and therapeutic information, thereby facilitating more complex treatment models based on biomarkers (Zack et al., 2025). However, practical challenges related to clinical workflows, evidence translation and accessibility, and provider readiness remain significant barriers to scaling up (Smith et al., 2025).
Thus, the purpose of this study was to explore the landscape of clinically annotated genetic biomarkers that are pertinent to precision drug therapy. It covered evidence levels for pharmacogenomic evidence, therapeutic consequence categories, major genes, and commonly used drugs or chemicals. The aims were to identify highly-represented biomarkers, separate overall frequencies of annotations from the more robust Level 1/2 evidence, assess the relative importance of efficacy, toxicity, metabolism/pharmacokinetics and dose-related outcome groups of the annotations, and discuss the implications for precision medication management, nursing practice and contemporary clinical medicine.

2. METHODOLOGY

2.1 Study Design and Data Source

A secondary data retrospective pharmacogenomic analysis was performed to describe clinically labeled genetic markers for drug response, therapeutic efficacy, toxicity, pharmacokinetics and drug dosing effects. The clinical variant annotations were stored in structured records and all of the other information (e.g. gene, variant, drug/chemical, phenotype, and relationships) was also reviewed to understand the context of the pharmacogenomic annotations.
Clinical variant annotation was the unit of analysis, which describes a documented relationship between a genetic variant and one or more gene(s), drug(s)/chemical(s) and clinical phenotype(s) or pharmacological outcome(s). There are 5,192 records in the original clinical-annotation table. 21 exact duplicate rows were removed before analysis, leaving a final analytical sample of 5,171 unique clinical variant annotations. There were 3,147 distinct genetic variants in those records. The data were separated by gene and drug/chemical, and then analyzed by each gene and each drug/chemical, yielding 1,089 individual genes and 672 individual drugs/chemicals.
The analysis was intended to be descriptive and more of a pharmacogenomic characterization, not a clinical outcome study for patients. Therefore, the individual demographic parameters, treatment period, laboratory parameters, survival parameters or patient level parameters were not available and could not be inferred.

2.2 Variables, Definitions, and Data Processing

The main variables that were retrieved for analyses were the variant identifier, the gene, the clinical annotation type, the level of evidence, the drug/chemical, and the phenotype.
The level of evidence variable was retained based on the available ones: 1A, 1B, 2A, 2B, 3, and 4. For analyses of comparatively stronger evidence in terms of pharmacogenomics, the four levels were grouped together and defined as Level 1/2 evidence.
The clinical annotation variable was first collapsed into mutually exclusive categories: Efficacy, Toxicity, Metabolism/PK, Dosage, Other, PD, Multiple domains. If a record is annotated with a single type of annotation, it has been kept in the same category as the original record. Records in which there was more than one clinical consequence type were assigned to Multiple domains for the Summary analysis. So each of the 5,171 annotations was included once in the denominator in the clinical-consequence distribution.The denominator for calculating the Level 1/2 proportion for each gene/drug/chemical was the number of mentions of that gene/drug/chemical in the annotations:

$$\text{Level } 1/2 \text{ proportion } (\%) = \frac{\text{Level } 1/2 \text{ annotation mentions for the entity}}{\text{Total annotation mentions for the entity}} \times 100.$$

This approach allowed a clinical annotation containing multiple entities to contribute to each explicitly documented entity while preventing the interpretation of these frequencies as patient counts.

2.3 Descriptive Statistical Analysis

All analyses were descriptive because the records represented curated pharmacogenomic annotations rather than independent patient observations. Categorical variables were summarized using frequencies (n) and percentages (%).
For the evidence-level analysis, the denominator was the complete cleaned analytical sample of 5,171 clinical variant annotations. Percentages were calculated as:

$$\text{Percentage } = \frac{\text{Number of annotations in a category}}{5{,}171} \times 100.$$

Distributions of clinical consequence domains were done using the same denominator of 5,171, since the multi-domain records were grouped into the Multiple domains category, and all other annotation categories were assigned to a single clinical consequence category.
Gene level was analysed by counting individual mentions of the gene. All the genes were ranked by the number of annotations mentioned in them and 12 most frequent genes were chosen for comparison presentation. The number and percentage of Level 1/2 annotations were determined for each of these genes. The same was done for the drug/chemical variable where individual items were extracted from multi-agent fields, ranked by number of annotation mentions and the 12 most common drugs/chemicals in terms of Level 1/2 annotations by mentions and within-agent proportions were shown.

No inferential significance tests were conducted since the aim was to document the distribution and the evidence structure of the pharmacogenomic records. In particular, there were no chi-square tests, t-tests, analysis of variance, correlation tests, or non-parametric hypothesis tests conducted. For the reported analyses, thresholds of statistical significance and confidence intervals were not valid.

2.4 Evidence-Based Gene and Drug Profiling

Two complementary measures were evaluated for each leading gene and drug/chemical: total annotation frequency (number of times the separated annotation mentions occur); and Level 1/2 annotation frequency and proportion (the subset of separated annotation mentions classified as evidence Level 1A, 1B, 2A, 2B). A distinction was needed because the number of annotations does not always reflect the clinical actionability. Evidence in the records was the only evidence considered, and no new composite actionability score or clinical recommendation was assigned.

A multivariable regression analysis was not performed. Logistic regression, linear regression, ordinal regression, survival analysis and predictive modelling were not employed because the analytical units were not individual patients with predictor and outcome measurements, but rather pharmacogenomic annotations. Therefore, the Results do not report regression coefficients, odds ratios, adjusted effect estimates, model-fit statistics or regression-derived p-values. The graphical analysis was carried out in the same way, but using a descriptive approach.

2.5 Missing Data, Quality Control, and Ethical Considerations

Before descriptive analysis, data quality assessment was done. Duplicate records were found on the entire clinical annotation rows and deleted. After removing 21 duplicate records, there were 5,171 left in the data. For each of the primary analytical variables, the extent of missingness was assessed. The phenotype information was not available in 1,007 of 5,171 records (19.47%) and the gene information was not available in 254 of 5,171 records (4.91%). These records were not imputed as there were no categorical pharmacogenomic annotations available that could not be reliably reconstructed without introducing unsupported information.

For all analyses which did not require the gene variable (e.g. evidence-level and clinical-consequence summaries), records with missing gene data were retained. Likewise, records without phenotype data were not excluded from the analytical data set since the four main analyses presented in the Results did not require complete phenotype data. Only the specific variable needed for each entity level analysis was therefore used in available-case processing. No variable deletions were performed for all cases.

Distributions were rounded to two decimal places for overall distributions, and entity-specific proportions were rounded to one decimal place at Level 1/2. The analysis relied on previously compiled non-identifiable secondary pharmacogenomic data and did not require any recruitment, intervention, or collection of biological specimens or access to personally identifiable patient information. Thus there was no immediate risk to human subjects.

3. Results

The analytical dataset had 21 clinical pharmacogenomic variant annotations that were exact duplications and were removed, leaving 5,171 clinical pharmacogenomic variant annotations. After resolving multi-entry fields these equated to 3,147 unique variants, 1,089 individual genes and 672 individual drugs/chemicals. For 1,007 records (19.47%), there was no phenotype information, and for 254 records (4.91%), there was no gene information. The results below represent the evidence base and clinical implications, as well as the primary pharmacogenomics genes and commonly encountered drug-biomarker contexts.

3.1 Distribution of Pharmacogenomic Evidence

The clinical variant annotations were very strongly clustered at evidence Level 3. Of the 5,171 cleaned observations, 4,461 (86.27%) were classified as Level 3. The number of records with high-to-moderate evidence level annotations (Levels 1A, 1B, 2A, and 2B) was 401 (7.76%), with 309 records (5.98%) being marked as Level 4 (Table 1). The 314 annotations at level 1A were a lot higher than the 148, 101 and 23 at levels 1B, 2A and 2B. This distribution shows that while the evidence base is extensive, only a relatively small proportion are at the higher level of evidence that are most applicable to the direct implementation of precision-therapy. This is also reflected in Figure 1, which shows that level 3 annotations are the predominant level of annotation.

Table 1. Distribution of clinical variant annotations according to evidence level

Evidence level	Number of annotations	Percentage (%)
1A	314	6.07
1B	17	0.33
2A	45	0.87
2B	25	0.48
3	4,461	86.27
4	309	5.98

Evidence level	Number of annotations	Percentage (%)
Total	5,171	100.00

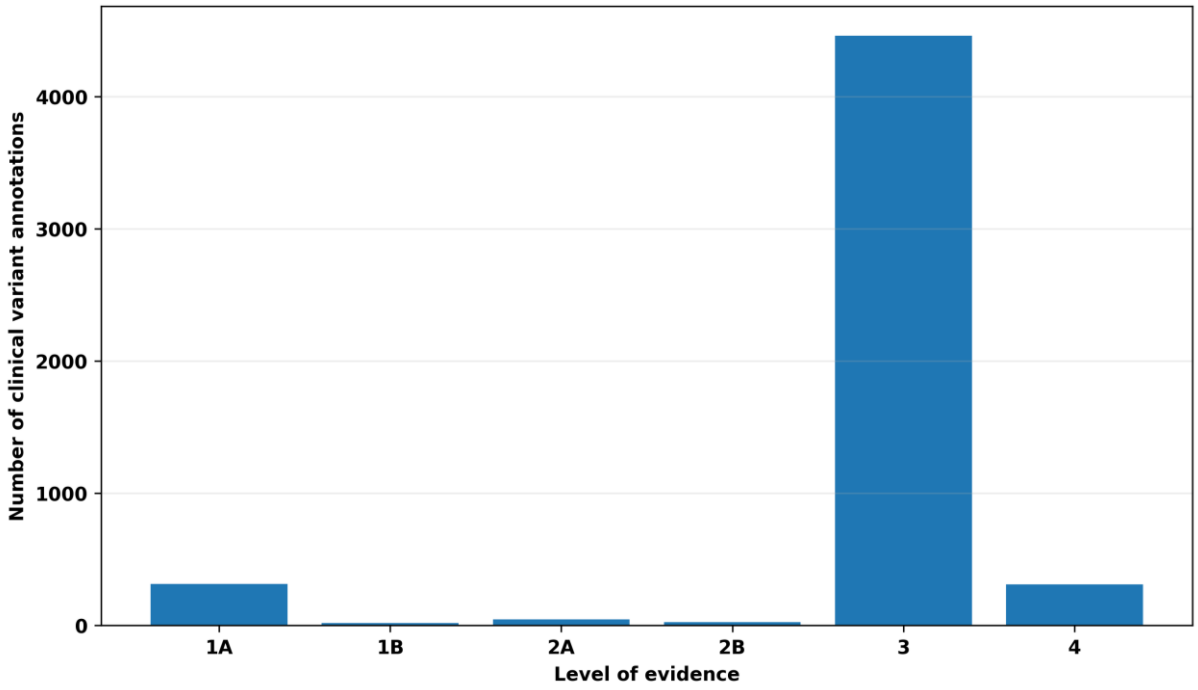


Figure 1. Distribution of Clinical Variant Annotations by Evidence Level

The evidence distribution shown in Figure 1 emphasizes the large separation between Level 3 evidence and the clinically stronger Level 1/2 categories.

3.2 Clinical Consequences of Genetic Variation

Pharmacogenomic annotations were most commonly associated with drug efficacy and toxicity. Efficacy came in next with 2,012 (38.91%) annotations, with toxicity coming in very close with 1,873 (36.22%). There were 649 (12.55%) annotations related to metabolism/pharmacokinetics and 260 (5.03%) dosage-related annotations. Twenty-six other clinical consequences (5.16%) were recorded as other notes. Another 105 annotations (2.03%) contained more than one consequence domain and relatively few had isolated pharmacodynamic annotations (Table 2). Efficacy and toxicity were the two biggest clinical annotations, accounting for 75.13% of all cleaned clinical annotations. These domains were then mapped by their relative distribution are shown in Figure 2.

Table 2. Clinical consequence domains represented in pharmacogenomic annotations

Clinical consequence domain	n	Percentage (%)
Efficacy	2,012	38.91
Toxicity	1,873	36.22
Metabolism/PK	649	12.55
Other	267	5.16
Dosage	260	5.03
Multiple domains	105	2.03
PD	5	0.10
Total	5,171	100.00

Note: Records originally containing more than one consequence type were classified as “Multiple domains” for this summary.

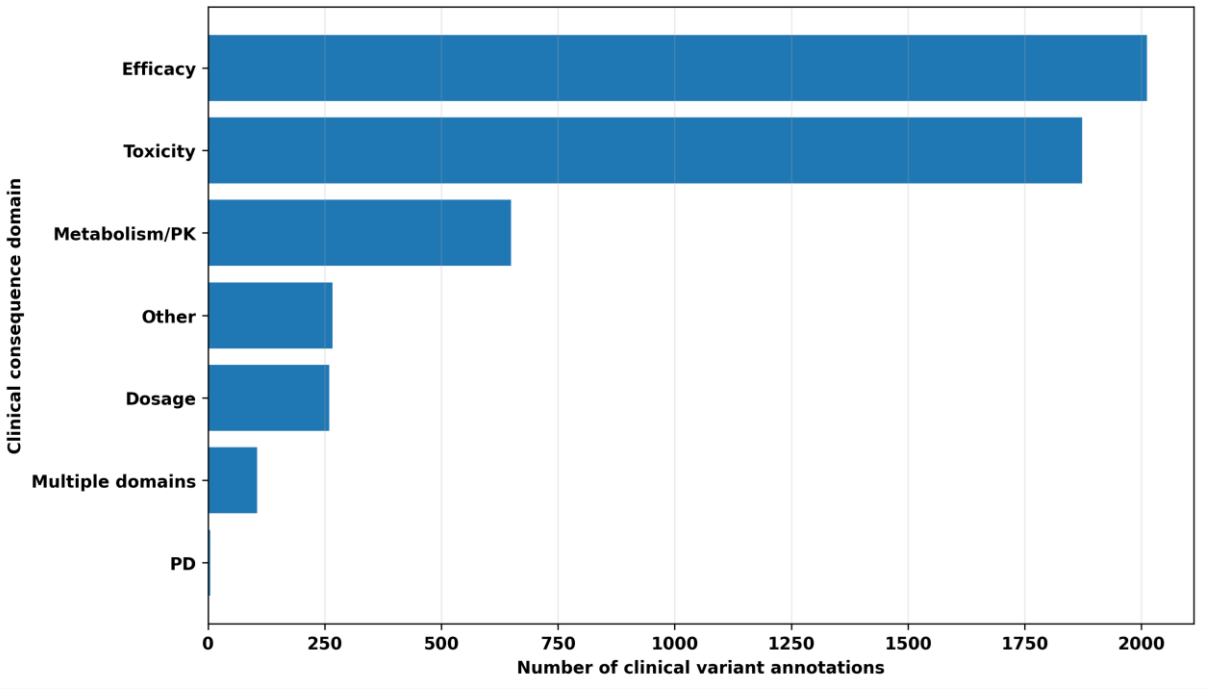


Figure 2. Clinical Consequence Profile of Pharmacogenomic Annotations

As illustrated in Figure 2, efficacy and toxicity substantially exceed metabolism/PK and dosage annotations, reinforcing the clinical relevance of genetic biomarkers to treatment response and medication safety.

3.3 Major Genetic Biomarkers and Their Evidence Strength

A few genes appeared multiple times in the clinical variant annotations. Overall, the highest frequencies of annotations were for ABCB1 (246), followed by OPRM1 (133) and CYP2D6 (122). But there was not a direct correlation between frequency and greater clinical evidence. In contrast, a number of established pharmacogenes showed a high percentage of higher-evidence associations in their high-frequency records, and neither ABCB1 nor OPRM1 had any Level 1/2 annotations in their high-frequency records. The most common genes with Level 1/2 annotations (among the most frequently mentioned genes) were CFTR (62.8%) and DPYD (51.8%). There were 48 high evidence annotations in CYP2D6, representing 39.3% of the total number of annotations. Prominent are also clinically important genes involved in drug-metabolism such as CYP2C9, CYP2C19, SLCO1B1, HLA-B, CYP2B6, CYP3A4 and CYP3A5 genes (Table 3). This is reflected in Figure 3.

Table 3. Leading pharmacogenomic genes and proportion supported by Level 1/2 evidence

Gene	Total annotation mentions	Level 1/2 annotations	Level 1/2 proportion (%)
ABCB1	246	0	0.0
OPRM1	133	0	0.0
CYP2D6	122	48	39.3
SLCO1B1	95	27	28.4
HLA-B	89	12	13.5
DPYD	83	43	51.8
CFTR	78	49	62.8
CYP2C19	77	22	28.6

Gene	Total annotation mentions	Level 1/2 annotations	Level 1/2 proportion (%)
CYP2C9	73	19	26.0
CYP3A4	69	6	8.7
CYP2B6	68	10	14.7
CYP3A5	67	4	6.0

Note: Multi-gene annotations were separated into individual gene mentions. Level 1/2 includes evidence Levels 1A, 1B, 2A, and 2B.

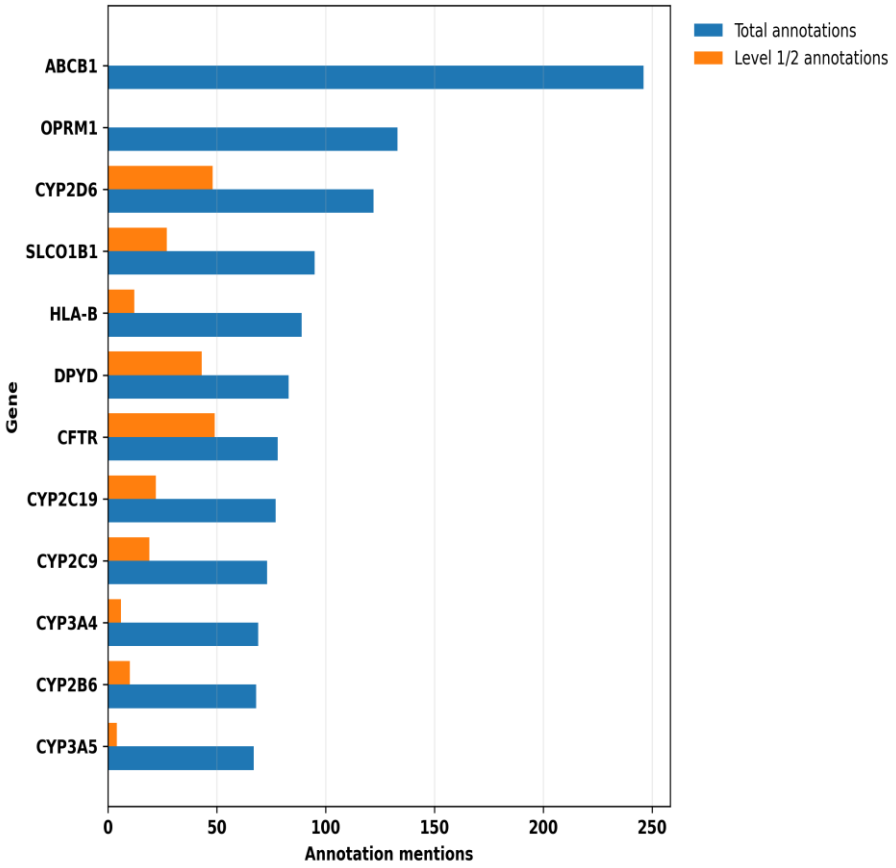


Figure 3. Most Frequently Represented Pharmacogenomic Genes

Figure 3 demonstrates that the genes with the largest numbers of reported associations are not necessarily those with the largest proportion of clinically stronger evidence. CFTR, DPYD, CYP2D6, SLCO1B1, CYP2C19, and CYP2C9 showed particularly notable Level 1/2 representation.

3.4 Drug-Biomarker Representation and Precision-Therapy Relevance

A wide variety of pharmacologic agents were included in the clinical annotations. Multi-agent fields were cleared of individual drugs/chemicals and then fluorouracil was the most common drug represented with 198 annotation mentions, followed by methotrexate (n = 174), nicotine (n = 134), cyclophosphamide (n = 124), and cisplatin (n = 122). Other common therapeutic exposures were methadone, opioids, gemcitabine, warfarin, docetaxel and platinum agents (Table 4). The distribution of higher evidence also varied significantly between the medicines. With fewer total annotations, warfaracil's 29 Level 1/2 annotations were more than warfarin's 17. There were 4 Level 1/2 annotations to Methotrexate. Larger evidence annotations, on the other hand, were more prevalent for several agents that are often studied, such as cyclophosphamide and cisplatin. Figure 4 thus separates the overall amount of pharmacogenomic evidence from that which has been classified as Level 1/2 evidence.

Table 4. Most frequently represented drugs/chemicals and Level 1/2 pharmacogenomic evidence

Drug/chemical	Total annotation mentions	Level 1/2 annotations	Level 1/2 proportion (%)
Fluorouracil	198	29	14.6
Methotrexate	174	4	2.3
Nicotine	134	2	1.5
Cyclophosphamide	124	0	0.0
Cisplatin	122	0	0.0
Methadone	99	1	1.0
Opioids	97	0	0.0
Ethanol	93	1	1.1
Gemcitabine	90	0	0.0
Warfarin	87	17	19.5
Docetaxel	81	0	0.0
Platinum compounds	79	1	1.3

Note: Multi-agent fields were separated into individual drug/chemical mentions. Level 1/2 includes Levels 1A, 1B, 2A, and 2B.

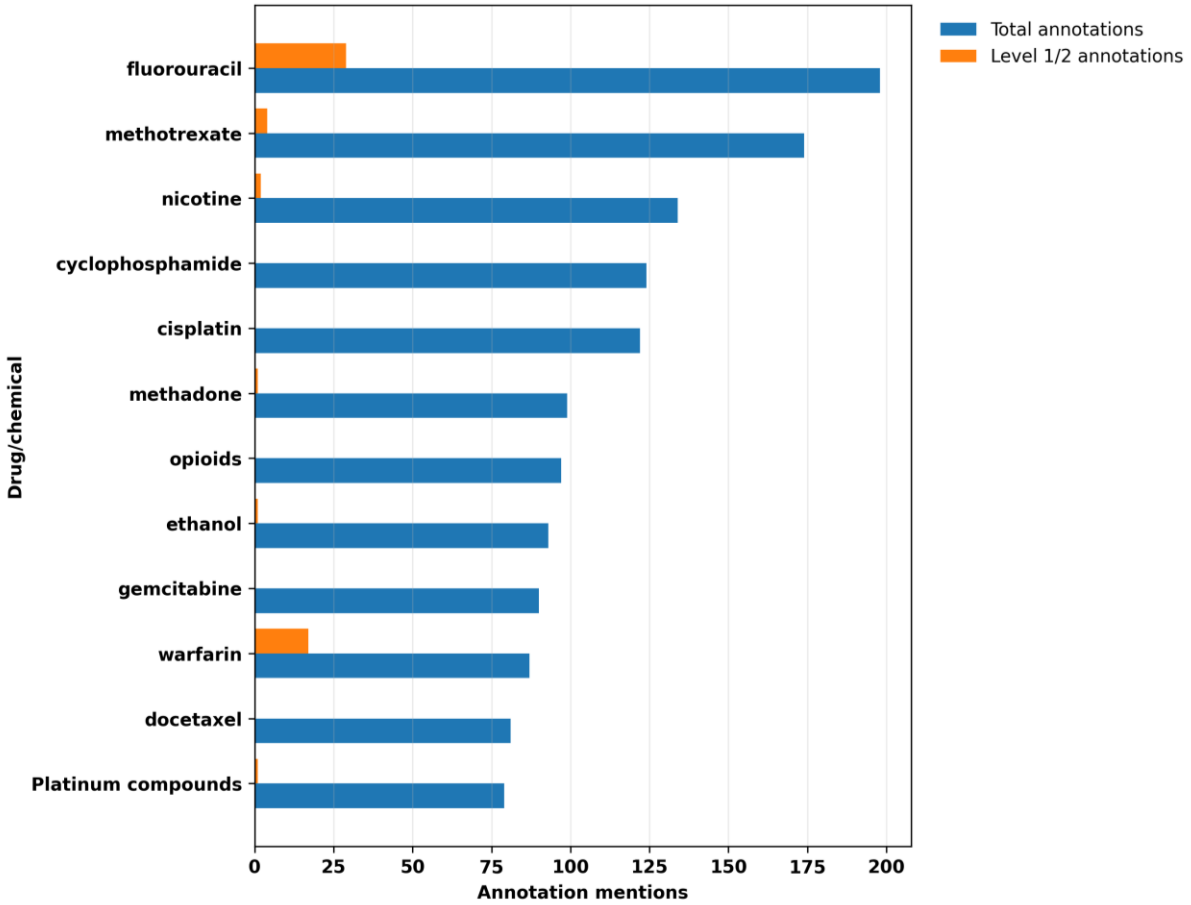


Figure 4. Most Frequently Represented Drugs/Chemicals in Clinical Variant Annotations

The pharmacogenomic literature covered by the data is quite extensive for oncology-related therapy drugs, with the number of annotations having different levels of evidence ranging widely from agent to agent as illustrated in Figure 4.

This distinction is crucial because it is well to not mistakenly equate high volume of gene-drug associations with high clinical actionability.

4. DISCUSSION

The present analysis shows that the available pharmacogenomic information is vast, but that there is significant variability in the degree of evidence that backs it up. From the 5,171 unique clinical variant annotations, 86.27% were associated with Level 3, and Levels 1A-2B were associated with only 7.76%. In compliance with this concept, pharmacogenomic resources not only carry clinically mature evidence, as well as emerging ones, but the volume of the annotations does not necessarily mean clinical actionability. Evidence hierarchies are required, therefore, when deciding if there is enough evidence of a gene-drug relationship to guide therapeutic decisions (Whirl-Carrillo et al., 2021). Structured pharmacogenomic resources can be particularly beneficial as they link variants, genes, drugs, phenotypes and clinical evidence in an integrated knowledge landscape (Gong et al. 2021).

The most common consequence categories were efficacy (38.91% annotations) and toxicity (36.22% annotations). Their combined share of the analyzed records was over three-quarters of all records. The key clinical uses that emerged in these findings involve maximizing the therapeutic benefit and minimizing the harm of treatment. This interpretation is directly supported by evidence that pre-emptive pharmacogenetic panels have the potential to prevent clinically relevant adverse drug reactions (Swen et al., 2023).

There was a good representation of several major pharmacogenes, but no strong relationship between their frequency and the evidence. There were 122 mentions of CYP2D6 in the annotations (48 were at Level 1/2). It has also been used in clinical contexts, such as antidepressant use, where genetic differences in metabolism may guide selection of antidepressant and dosing considerations (Bousman et al., 2023). SLCO1B1 was also represented strongly, which was in agreement with its known association with statin-associated musculoskeletal toxicity (Cooper-DeHoff et al., 2022). The representation of OPRM1 and CYP2D6 is also a result of ongoing research on genotype guided opioid use (Crews et al., 2021).

There were 77 mentions of CYP2C19 in the annotations, with 22 supported by Level 1/2 evidence. Clinically relevant as activation and effectiveness of clopidogrel is affected by CYP2C19 genotype (Lee et al., 2022). The general trend was the same for DPYD, which had one of the highest percentages of Level 1/2 annotations (43/83). This is similar to the known association between DPYD variation and fluoropyrimidine associated toxicity and dose individualisation (Lunenburg et al., 2020). Additionally, the high occurrence of fluorouracil in the current drug level analysis highlights the clinical significance of DPYD-guided treatment strategies (Ho et al., 2025). Consequently, standardization of DPYD testing has become more and more important when it comes to routine implementation (Pratt et al., 2024).

HLA-B was also well-represented. HLA-associated pharmacogenomics is unique in that alleles can be used to identify a person who is at a significantly higher risk of having a severe immune-mediated adverse reaction to a drug, such as carbamazepine and oxcarbazepine reactions (Phillips et al., 2018). The inherited variation also directly affects drug exposure and hematologic toxicity, as is the case for thiopurine dosing through TPMT and NUDT15.This is also true for thiopurine dosing by TPMT and NUDT15 (Relling et al., 2019). The dynamic nature of clinically actionable pharmacogenomic evidence is illustrated by continued refinement of such recommendations (Maillard et al., 2026).

Highly active pharmacogenomic activity was seen in oncology and other high-risk therapeutic areas, as fluorouracil, methotrexate, cyclophosphamide, cisplatin, warfarin and other drugs were commonly represented at the drug level. One interesting finding was that although the total number of annotations was lower than the number for some other agents, 19.5% of these were at Level 1/2 evidence for warfarin. This is a reminder of the need to appraise the quality of evidence not just its frequency. At a more general level, having pre-emptive pharmacogenetic information available to prescribers has been linked to opportunities for enhancing prescribing and clinical outcomes (Roden et al., 2018).

These findings underscore the need for the practitioner to know what clinically meaningful biomarkers are present when giving a medication, watching for therapeutic responses, being aware of adverse responses, and counseling patients in nursing and multidisciplinary practice. The overwhelming majority of the evidence that exists is also of low quality, which serves as a warning to not take all reported associations as immediate action. Therefore, there is a need to focus on validated gene-drug relationships, interpretation according to guidelines, communication between disciplines, and ongoing reassessment of the interpretation as the evidence on pharmacogenomics continues to develop.

5. CONCLUSION

This study illustrates that there is a wealth of pharmacogenomic evidence available for precision drug therapy that is not necessarily equally developed. Of the 5,171 unique clinical variant annotations, the majority were annotated at Level 3, while smaller proportions were annotated at Level 1A-2B, reflecting that there remains a large volume of clinical drug-gene associations that need further validation to enable their routine use in the clinic. The most prevalent consequence domains of pharmacogenomics were efficacy and toxicity, which reflects the centrality of genetic markers to improving the therapeutic effect and minimizing adverse drug reactions. A significant number of clinically relevant genes were represented, such as CYP2D6, DPYD, CYP2C19, SLCO1B1, HLA-B, and CYP2C9, and a large number of drugs and other high risk therapies were annotated. Importantly, the genes/drugs that were most commonly used were not necessarily the ones with the highest proportion of stronger evidence, which highlights the importance of separating out the number of annotations and their clinical actionability. The results are in tune with the expanding use of pharmacogenomics in personalized drug treatment, drug safety, and drug monitoring. Clinically validated biomarkers have the potential to enhance patient education, adverse event monitoring and communication on genotype-based therapy in the field of nursing and multidisciplinary practice. Implementation in the future needs to focus on high-evidence gene-drug

relationships, standardized interpretation, representation of a diverse range of populations, and incremental updating of pharmacogenomic knowledge as new evidence becomes available.

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