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Pharmacogenomics-Guided Drug Dose Adjustment in Personalized Medicine: A Systematic Literature Review

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ABSTRACT

Pharmacogenomics-guided drug dose adjustment is an important approach in personalized medicine because genetic polymorphisms can influence drug metabolism, therapeutic response, dose requirements, and the risk of adverse drug reactions. This systematic literature review synthesized recent evidence on pharmacogenomics-guided dose adjustment, clinically relevant pharmacogenomic biomarkers, and emerging technologies supporting precision medicine. Literature searches were conducted in Scopus and PubMed for studies published between January 2021 and May 2026. Eligible studies were selected using predefined PICOS criteria and synthesized narratively because of heterogeneity in study design, therapeutic area, biomarkers, and reported outcomes. A total of 23 studies were included in the qualitative synthesis. The evidence covered various therapeutic areas, including infectious diseases, neurology, psychiatry, oncology, cardiovascular medicine, and transplantation. Pharmacogenomic-guided dosing was most clearly supported for clinically established gene–drug pairs, including CYP2C9/VKORC1–warfarin, CYP2C19-related therapies, DPYD–fluoropyrimidines, SLCO1B1–statins, CYP2B6–efavirenz, and selected CYP3A5-related immunosuppressant therapies. Other biomarkers, such as ABCB1, APOE, GABRG2, UGT genes, and receptor-related polymorphisms, were associated with treatment response or drug disposition but still require stronger clinical validation for routine dose-adjustment recommendations. Emerging technologies, including clinical decision support systems, model-informed precision dosing, population pharmacokinetic modeling, bioinformatics, artificial intelligence, and machine learning, may strengthen biomarker interpretation and individualized dose optimization. Overall, pharmacogenomic-guided dose adjustment is a promising strategy to support safer and more precise pharmacotherapy, although broader implementation requires standardized guidelines, prospective validation, population-specific evidence, and integration into routine healthcare systems.

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ABSTRAK

Penyesuaian dosis obat berbasis farmakogenomik merupakan pendekatan penting dalam personalized medicine karena polimorfisme genetik dapat memengaruhi metabolisme obat, respons terapi, kebutuhan dosis, dan risiko terjadinya reaksi obat yang tidak diinginkan. Tinjauan literatur sistematis ini mensintesis bukti terkini mengenai penyesuaian dosis berbasis farmakogenomik, biomarker farmakogenomik yang relevan secara klinis, serta teknologi baru yang mendukung precision medicine. Pencarian literatur dilakukan melalui basis data Scopus dan PubMed terhadap artikel yang dipublikasikan antara Januari 2021 hingga Mei 2026. Studi yang memenuhi kriteria dipilih berdasarkan PICOS yang telah ditentukan dan disintesis secara naratif karena adanya heterogenitas desain studi, bidang terapi, biomarker, dan luaran yang dilaporkan. Sebanyak 23 studi dimasukkan dalam sintesis kualitatif. Bukti yang tersedia mencakup berbagai bidang terapi, termasuk penyakit infeksi, neurologi, psikiatri, onkologi, kardiovaskular, dan transplantasi. Penyesuaian dosis berbasis farmakogenomik paling kuat didukung pada pasangan gen–obat yang telah memiliki relevansi klinis, seperti CYP2C9/VKORC1–warfarin, terapi terkait CYP2C19, DPYD–fluoropyrimidines, SLCO1B1–statins, CYP2B6–efavirenz, dan beberapa terapi imunosupresan terkait CYP3A5. Biomarker lain, seperti ABCB1, APOE, GABRG2, gen UGT, dan polimorfisme terkait reseptor, berhubungan dengan respons terapi atau disposisi obat, tetapi masih memerlukan validasi klinis yang lebih kuat sebelum digunakan secara rutin untuk rekomendasi penyesuaian dosis. Teknologi baru, termasuk clinical decision support systems, model-informed precision dosing, population pharmacokinetic modeling, bioinformatika, kecerdasan buatan, dan machine learning, berpotensi memperkuat interpretasi biomarker dan optimalisasi dosis individual. Secara keseluruhan, penyesuaian dosis berbasis farmakogenomik merupakan strategi yang menjanjikan untuk mendukung farmakoterapi yang lebih aman dan presisi, namun implementasi luas masih memerlukan pedoman terstandar, validasi prospektif, bukti spesifik populasi, dan integrasi ke dalam sistem pelayanan kesehatan rutin.

Kata Kunci: Farmakogenomik; Penyesuaian Dosis Obat; Pengobatan yang Dipersonalisasi; Pengobatan Presisi; Biomarker Genetik

1. Introduction

Personalized medicine shifts the therapeutic approach from a one-size-fits-all model to one based on an individual's biological characteristics. By leveraging genomic, molecular, clinical, and environmental data—and supported by next-generation sequencing (NGS) and bioinformatics—this approach improves diagnostic accuracy, optimizes drug selection and dosing, minimizes side effects, and improves clinical outcomes [1].

Despite the growing implementation of personalized medicine, substantial interindividual variability in drug response remains a major clinical challenge. Patients receiving the same drug and dose may experience different therapeutic outcomes due to demographic, physiological, environmental, and clinical factors. Among these, genetic variation is a key determinant, influencing pharmacokinetic and pharmacodynamic processes through polymorphisms in genes encoding drug-metabolizing enzymes,

transporters, and pharmacological targets. These variations affect drug absorption, metabolism, efficacy, toxicity, and dose requirements. Therefore, understanding genetic determinants of drug response is essential to reducing adverse drug reactions, optimizing therapeutic outcomes, and supporting genotype-guided individualized therapy [2].

To address variability in drug response, pharmacogenomics has become a cornerstone of personalized medicine by evaluating how genetic variation influences drug efficacy, safety, and dose requirements. By integrating genomic information into therapeutic decision-making, pharmacogenomics enables clinicians to identify patients who may benefit from specific drugs, require dose adjustments, or have an increased risk of adverse drug reactions before treatment. Advances in genotyping technologies and the reduction of testing costs have accelerated clinical implementation, with several drug–gene pairs incorporated into international guidelines. Pharmacogenomics also supports drug discovery by identifying genetically defined therapeutic targets. However, its widespread adoption remains limited by inadequate healthcare infrastructure, insufficient integration into clinical workflows, limited availability of clinical decision-support systems, and gaps in healthcare professionals' knowledge. These challenges underscore the need for further research to strengthen the evidence base and promote the routine implementation of pharmacogenomics-guided prescribing [3].

Pharmacogenomics is a fundamental component of precision therapy, investigating how inherited genetic variation influences drug absorption, distribution, metabolism, excretion, and pharmacodynamic response. Unlike conventional prescribing, it integrates genomic information into therapeutic decision-making, enabling clinicians to predict treatment response and individualize drug selection and dosing before therapy begins. This approach improves therapeutic efficacy while reducing treatment failure and adverse drug reactions [3],[4]. Its clinical relevance is primarily driven by genetic polymorphisms in drug-metabolizing enzymes, transporter proteins, and pharmacological targets. Variants in the cytochrome P450 (CYP450) family, particularly CYP2D6, CYP2C19, CYP2C9, CYP3A4, and CYP2B6, contribute substantially to variability in drug metabolism, plasma concentrations, therapeutic response, and toxicity. Additional clinically important genes, including DPYD, SLCO1B1, VKORC1, TPMT, and NUDT15, directly influence dose requirements and the risk of severe drug toxicity, making genotype-guided prescribing an evidence-based strategy across multiple therapeutic areas [3],[5].

The implementation of pharmacogenomics has been strengthened by international guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG), which translate genetic test results into actionable prescribing recommendations, facilitating routine clinical integration and advancing precision therapy [6]. The clinical application of pharmacogenomics is most evident in drug dose adjustment, where genetic information is used to optimize therapeutic efficacy and minimize adverse drug reactions. By individualizing drug selection and dosing according to genetic differences in drug metabolism, transport, and pharmacodynamic response, pharmacogenomics-guided prescribing is particularly beneficial for drugs with a narrow therapeutic index or high interindividual variability. Increasing clinical evidence and international guidelines support its implementation in routine practice [7].

Several gene–drug pairs have demonstrated strong clinical utility. Variants in VKORC1 and CYP2C9 influence warfarin dose requirements, while CYP2C19 loss-of-

function variants reduce clopidogrel efficacy. In oncology, DPYD variants predict severe fluoropyrimidine toxicity and support pre-emptive dose reduction. Likewise, CYP2B6 affects efavirenz metabolism, whereas TPMT and NUDT15 polymorphisms guide thiopurine dose reductions to prevent myelosuppression. These examples highlight the transition of pharmacogenomic-guided dosing from research to evidence-based clinical practice [8]. Despite its proven benefits, implementation remains uneven due to limited genetic testing availability, clinician awareness, cost-effectiveness concerns, and challenges integrating pharmacogenomic information into clinical workflows. These limitations emphasize the need to strengthen evidence, validate clinically relevant biomarkers, and improve technologies that support routine genotype-guided prescribing [9].

Despite increasing evidence supporting pharmacogenomics, important knowledge gaps remain. Most published reviews focus on individual diseases, specific drug classes, or single gene–drug pairs, such as CYP2C19–clopidogrel, CYP2C9/VKORC1–warfarin, and DPYD–fluoropyrimidines, resulting in a fragmented understanding of pharmacogenomic-guided dose adjustment across therapeutic areas. In addition, many studies emphasize biomarker identification rather than their implications for individualized dose optimization or comparisons across multiple diseases and medications [3],[8]. Technologies, including model-informed precision dosing (MIPD), clinical decision support systems (CDSS), artificial intelligence (AI), and multigene pharmacogenomic panels, have further advanced precision medicine, but the evidence remains dispersed across clinical disciplines [7].

To address these gaps, this systematic literature review synthesizes recent evidence on pharmacogenomic-guided dose adjustment across diverse therapeutic areas, including neurology, cardiovascular medicine, oncology, infectious diseases, psychiatry, transplantation, and other chronic diseases. It evaluates clinically actionable biomarkers involved in drug metabolism, transport, and pharmacodynamic response, while also examining emerging technologies such as CDSS, population pharmacokinetic modeling, MIPD, bioinformatics, and AI. This review aims to (1) evaluate the influence of genetic variation on drug efficacy, safety, and dose optimization; (2) identify clinically relevant pharmacogenomic biomarkers for genotype-guided prescribing; and (3) assess technologies supporting pharmacogenomic implementation. By integrating evidence published between 2021 and 2026, this review provides an updated reference to advance precision medicine in clinical practice.

2. Methods and Material

Research Question According to the PICOS Strategy

The research question of this systematic literature review was developed using the PICOS (Population, Intervention, Comparator, Outcomes, and Study Design) framework to ensure a structured and transparent review process. The PICOS strategy guided the formulation of the research objectives, eligibility criteria, literature search, and study selection (**Table 1**).

Table 1. PICOS criteria for the current systematic literature review

PICOS Component	Description
Population (P)	Patients of any age, sex, or ethnicity receiving pharmacological treatment in which pharmacogenomic information may influence drug selection or dose adjustment.

Intervention / Exposure (I)	Pharmacogenomic-guided drug therapy, including genotype-guided drug dose adjustment based on clinically relevant pharmacogenomic biomarkers (e.g., CYP2D6, CYP2C19, CYP2C9, CYP2B6, DPYD, SLCO1B1, VKORC1, TPMT, NUDT15, ABCB1, APOE).
Comparator (C)	Conventional dosing strategies, standard clinical care without pharmacogenomic testing, alternative genotype groups, or studies without a comparator, depending on the study design.
Outcomes (O)	Drug dose optimization, therapeutic efficacy, reduction of adverse drug reactions, improvement of treatment safety, individualized pharmacotherapy, and implementation of precision medicine.
Study Design (S)	Original research articles and evidence-based review studies, including randomized controlled trials, observational studies, case-control studies, cohort studies, population pharmacokinetic studies, systematic reviews, clinical practice guidelines, and other eligible studies published in peer-reviewed journals.

Information Sources

The literature search was conducted in Scopus and PubMed (MEDLINE). Duplicate records retrieved from both databases were removed before the screening process. After title/abstract screening and full-text eligibility assessment according to the predefined PICOS criteria, 23 studies were included in the qualitative synthesis

Search Strategy

The literature search was conducted according to the PICOS framework and PRISMA 2020 guidelines using Scopus and PubMed (MEDLINE) to identify studies on pharmacogenomic-guided drug dose adjustment in personalized medicine. The search combined controlled vocabulary and free-text terms related to pharmacogenomics, dose optimization, and personalized medicine, including "pharmacogenomic," "pharmacogenetic," "drug dose adjustment," "dose optimization," "dose individualization," "precision dosing," "genotype-guided dosing," and "personalized medicine." Boolean operators (AND, OR) were used to maximize search sensitivity and specificity, with database-specific syntax adapted for each database.

Eligibility Criteria

Eligibility criteria were predefined according to the research objectives and PICOS framework to identify studies relevant to pharmacogenomic-guided drug dose adjustment in personalized medicine. Studies were screened using predefined inclusion and exclusion criteria, and only those evaluating the clinical application of pharmacogenomic biomarkers for dose optimization or individualized pharmacotherapy were included in the qualitative synthesis (**Table 2**).

Table 2. Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
Original research articles and evidence-based review articles published in peer-reviewed journals	Editorials, letters, commentaries, conference abstracts, book chapters, dissertations, and non-peer-reviewed publications
Published between January 2021 and May 2026	Articles published before January 2021
Articles published in English	Articles published in languages other than English
Full-text articles available	Articles without accessible full text
Human studies involving patients receiving pharmacological therapy	Animal studies, in vitro studies, or preclinical studies

Studies evaluating pharmacogenomic-guided drug dose adjustment, genotype-guided prescribing, dose optimization, or individualized pharmacotherapy	Studies evaluating pharmacogenomic biomarkers without clinical implications for drug dosing or individualized therapy
Studies reporting clinically relevant pharmacogenomic biomarkers.	Studies lacking pharmacogenomic data or not reporting clinically relevant biomarkers
Studies reporting outcomes related to therapeutic efficacy, drug safety, adverse drug reactions, or dose optimization	Studies without relevant clinical outcomes or insufficient data for qualitative synthesis
RCTs, observational studies, population PK studies, implementation studies, and evidence-based reviews.	Duplicates, retracted articles, study protocols, or incomplete methodological reports.

Study Selection

Study selection followed the PRISMA 2020 guidelines. After duplicate removal, two reviewers independently screened titles, abstracts, and full texts using predefined eligibility criteria. Disagreements were resolved by consensus. Studies with insufficient data, duplicate publications, or retracted articles were excluded. The complete selection process is presented in the PRISMA 2020 flow diagram (**Figure 1**).

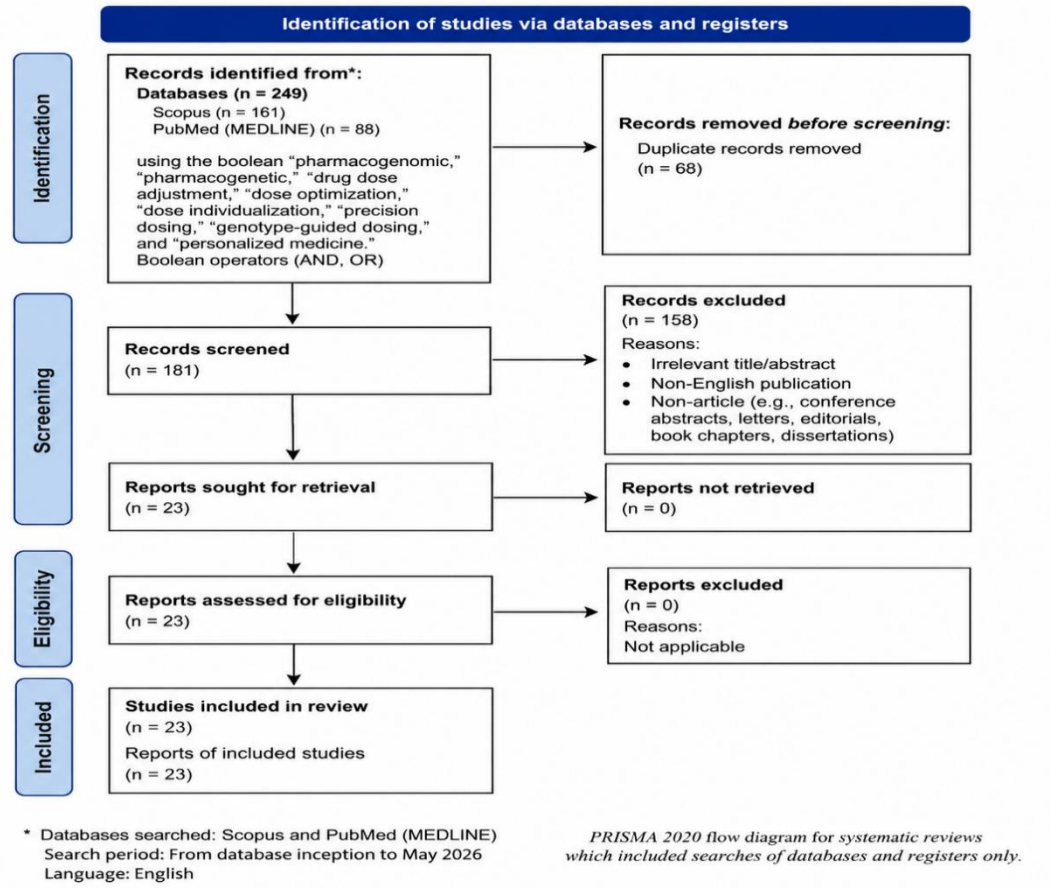

Figure 1. PRISMA flowchart of study selection process

Methodological Quality Assessment

The methodological quality of the included studies was assessed using the appraisal tool appropriate for each study design. Systematic reviews, randomized controlled trials, case-control studies, and observational studies were critically appraised using the corresponding Joanna Briggs Institute (JBI) Critical Appraisal Checklists. Narrative reviews, hypothesis papers, and clinical practice guidelines were included to provide contextual and translational evidence but were not subjected to formal critical appraisal because no validated appraisal tool is available for these publication types. These articles were synthesized qualitatively. The detailed quality assessment results are presented in **Table 3**.

Table 3. Methodological quality assessment of the included studies using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists

No.	First Author (Year)	Study Design	JBI Checklist Used	JBI Score	Overall Quality
1	Hardi (2025)	Systematic Review	JBI SR (11 items)	10/11	High Quality
2	Climacosa (2025)	Systematic Review	JBI SR (11 items)	9/11	High Quality
3	Biswas (2024)	Narrative Review	JBI SR (11 items)	9/11	High Quality
4	Anghel (2024)	Narrative Review	JBI SR (11 items)	9/11	High Quality
5	Hausman-Cohen (2022)	Hypothesis and Theory (Proof-of-Concept with Case Reports)	N/A	N/A	Not Appraised
6	Ortolan (2021)	Systematic Literature Review	JBI SR (11 items)	10/11	High Quality
7	Jarrar (2021)	Narrative Review	N/A	N/A	Not Appraised
8	Lu (2021)	Retrospective Cohort Study	JBI Cohort (11 items)	9/11	High Quality
9	Aypek (2025)	Narrative Review	N/A	N/A	Not Appraised
10	Delage (2022)	Retrospective Observational Study	JBI Cross-Sectional (8 items)	07/8	High Quality
11	Shen (2022)	Retrospective Cohort / Population Pharmacokinetic Study	JBI Cohort (11 items)	10/11	High Quality
12	Rezayi (2022)	Systematic Review	JBI SR (11 items)	10/11	High Quality
13	Khong (2025)	Randomized Controlled Trial (Phase II)	JBI RCT (13 items)	12/13	High Quality

14	Lima (2021)	Clinical Practice Guideline (CPIC Guideline)	N/A	N/A	Not Appraised
15	Stocker (2025)	Narrative Review	N/A	N/A	Not Appraised
16	Bigossi (2023)	Case-Control Study (Genetic Association Study)	JBI Case-Control (10 items)	09/10	High Quality
17	Marques (2024)	Narrative Review	N/A	N/A	Not Appraised
18	Polasek (2024)	Narrative Review	N/A	N/A	Not Appraised
19	Goutelle (2023)	Methodological Modeling Study (Simulation Study)	N/A	N/A	Not Appraised
20	Karthikeyan (2026)	Narrative Review	N/A	N/A	Not Appraised
21	Sahu (2026)	Narrative Review	N/A	N/A	Not Appraised
22	Maslarinou (2023)	Narrative Review	N/A	N/A	Not Appraised
23	Ngabea (2026)	Narrative Review	N/A	N/A	Not Appraised

Data Synthesis

The extracted data were synthesized using a narrative approach because of the heterogeneity among the included studies in terms of study design, disease conditions, therapeutic agents, pharmacogenomic biomarkers, and reported outcomes, which precluded quantitative meta-analysis. The findings were summarized descriptively and organized into thematic categories based on the objectives of this review, including study characteristics, disease and drug distribution, pharmacogenomic biomarkers, pharmacogenomic-guided dose adjustment, and emerging technologies supporting personalized medicine.

3. Results and Discussion

Characteristics of Included Studies

A total of 23 studies published between 2021 and 2026 met the eligibility criteria and were included following the PRISMA 2020 guidelines. The evidence comprised systematic reviews, a randomized controlled trial, observational and population pharmacokinetic studies, a clinical practice guideline, a case-based article, and narrative reviews, reflecting the multidisciplinary nature of pharmacogenomic research (**Table 4**).

The included studies covered infectious, neurological, psychiatric, cardiovascular, oncological, and transplant diseases. Pharmacogenomic-guided dosing was evaluated across diverse therapeutic areas, particularly for long-term therapies and drugs with narrow therapeutic indices, including anti-infectives, antiepileptics, psychotropics, anticoagulants, statins, proton pump inhibitors, fluoropyrimidines, tyrosine kinase inhibitors, and immunosuppressants.

The most frequently investigated biomarkers were cytochrome P450 genes (CYP2D6, CYP2C19, CYP2B6, CYP2C9, CYP3A4, and CYP2A6), together with DPYD, SLCO1B1, ABCB1, VKORC1, APOE, GABRG2, UGT family genes, and receptor-related polymorphisms. These biomarkers were associated with variability in drug metabolism, pharmacological response, and adverse drug reactions. Overall, the studies demonstrated that integrating pharmacogenomic information with clinical decision support systems, model-informed precision dosing, artificial intelligence, machine learning, and polygenic algorithms can optimize drug dosing, improve therapeutic outcomes, reduce toxicity, and advance personalized medicine.

Table 4. Characteristics and Evidence Synthesis of Included Studies on Pharmacogenomics-Guided Drug Dose Adjustment in Personalized Medicine

No	First Author (Year)	Disease/Drug	Biomarkers	Dose Adjustment	Clinical Outcome
1	Hardi (2025)	Tuberculosis-HIV coinfection; Efavirenz, Isoniazid, Rifapentine, Dolutegravir	CYP2B6, NAT2, AADAC, PXR, CYP2A6, CYP1A2	CYP2B6 and NAT2 guide personalized efavirenz and isoniazid dosing.	Genotyping improves dosing accuracy and reduces treatment toxicity [10].
2	Climacosa (2025)	Alzheimer's disease; Donepezil, Rivastigmine, Galantamine, Memantine	APOE, CYP2D6, ABCA1, CHRNA7, CHRFAM7A, CHAT, ACE, IL6, IDE	APOE and CYP2D6 variants influence donepezil response and dosing.	Testing supports personalized Alzheimer's therapy and safer dosing [11].
3	Biswas (2024)	Autism Spectrum Disorder; Risperidone, Aripiprazole	CYP2D6, DRD2	CYP2D6 variants affect risperidone exposure, efficacy, and adverse effects.	CYP2D6-guided dosing improves risperidone efficacy and safety [12].
4	Anghel (2024)	Multiple diseases involving receptor-targeted therapies (GPCR and RTK-targeting drugs)	GPCR variants, EGFR, VKORC1, CYP2C9 and other receptor polymorphisms	Receptor variants affect drug response; dosing evidence remains limited.	Routine receptor-guided dosing requires stronger clinical evidence [13].
5	Hausman-Cohen (2022)	Mild Cognitive Impairment & Cognitive Decline; Personalized multi-component interventions	APOE ε4 and multiple genomic variants.	Genomic CDS improved personalized therapy without direct dose adjustment.	Supports precision medicine beyond pharmacogenomic dose optimization [14].

6	Ortolan (2021)	Spondyloarthritis ; TNF inhibitors (adalimumab, etanercept, infliximab), methotrexate	TNFRSF1A, TNFRSF1B, TNF-α, PDE3A, DHFR variants.	Genetic variants predict TNF inhibitor response and treatment optimization.	Testing may optimize therapy pending stronger clinical validation [15].
7	Lu (2021)	Pediatric Epilepsy; Valproic Acid	GABRG2 rs211037	GABRG2 genotype predicts valproate response and adverse effects.	Testing supports safer, individualized valproate therapy [16].
8	Jarrar (2021)	Multiple diseases / UGT substrate drugs.	UGT1A/UGT2B genetic variants.	UGT1A1 and other UGT variants influence drug metabolism, efficacy, and toxicity.	UGT genotyping enables personalized dosing to improve efficacy and reduce toxicity [17].
9	Aypek (2025)	Pancreas–Kidney Transplantation; Immunosuppressive therapy	HLA, non-HLA polymorphisms, cytokine genes, immune-regulatory genes, MICA, HLA-G, SNPs	Genomic risk stratification improves transplant outcome prediction but not immunosuppressant dose adjustment.	Genomic profiling supports personalized transplantation but not yet routine pharmacogenomic-guided dosing [18].
10	Delage (2022)	Psychiatric Disorders; Psychotropic medications	CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, P-glycoprotein (ABCB1) phenotypes	CYP and P-gp phenotyping guided dose adjustment and therapy selection, improving clinical outcomes.	Phenotype-guided psychotropic dosing improves efficacy and reduces adverse drug reactions [19].
11	Shen (2022)	Pediatric epilepsy treated with valproic acid (VPA)	ABCB1 rs3789243	ABCB1 genotype and age guided individualized VPA dosing using a pharmacogenetic population PK model.	ABCB1 genotype–guided VPA dosing improves individualized therapy and therapeutic drug monitoring [16].

12	Rezayi (2022)	Cancer / Precision Medicine (multiple anticancer therapies)	Multiple genomic and pharmacoge nomic biomarkers	AI-guided genomic models personalize therapy without directly informing dose adjustment.	AI-integrated pharmacogenomics enables personalized oncology therapy and dose optimization [20].
13	Khong (2025)	Liver transplantation treated with tacrolimus	Phenotypic biomarker only (tacrolimus trough concentratio n).	Phenotype-guided tacrolimus dosing improved exposure and safety.	Supports phenotype-guided dosing but is outside pharmacogenomic optimization.. [21].
14	Lima (2021)	Acid-related disorders / PPIs	CYP2C19	CYP2C19-guided PPI dosing optimizes efficacy and minimizes toxicity.	Supports routine CYP2C19-guided PPI prescribing for safer, more effective therapy [22].
15	Stocker (2025)	Multiple therapeutic areas (e.g., clopidogrel, warfarin, thiopurines, allopurinol, abacavir)	CYP2C19, CYP2C9, VKORC1, TPMT, HLA-B57:01, HLA-B58:01	Reviews clinical implementation of pharmacogenomics-guided prescribing, including CYP2C19, CYP2C9/VKORC1, TPMT, and HLA-based therapy optimizatio	Pharmacogenomic testing enhances treatment safety and efficacy through personalized drug therapy [23].
16	Bigossi (2023)	Hypercholesterol emia / Statin therapy	SLCO1B1 missense variants (Val174Ala, Asn130Asp, Pro155Thr, Leu643Phe).	SLCO1B1 gene risk scoring improved prediction of statin intolerance and myopathy, particularly in patients receiving high-dose statins.	SLCO1B1 genotyping enables personalized statin dosing and selection to reduce adverse drug reactions [24].
17	Marques (2024)	Precision medicine across multiple diseases and drug therapies	Multiple PGx biomarkers integrated with multi-omics and AI.	Supports integrated pharmacogenomics and digital health technologies for more accurate individualized dose optimization	Supports integrated pharmacogenomic decision-support systems for optimized drug selection and dosing [25].

18	Polasek (2024)	Multiple therapeutic areas / Precision dosing across diverse drug classes.	Integrated PGx, PK/PD biomarkers.	Supports biomarker-integrated precision dosing beyond conventional dosing strategies.	Supports biomarker-integrated precision dosing to maximize efficacy and minimize toxicity [26].
19	Goutelle (2023)	Chronic Myeloid Leukemia (CML) & Gastrointestinal Stromal Tumor (GIST) / Imatinib	None; PK-based precision dosing using Cmin.	Model-informed TID outperformed conventional fixed-dose imatinib therapy.	Supports model-informed TDM without pharmacogenomic biomarkers [27].
20	Karthikeyan (2026)	Multiple diseases / Warfarin, Clopidogrel, Antidepressants, Chemotherapy, Tacrolimus, Cyclosporine	Major PGx markers (CYP2C9, VKORC1, CYP2C19, CYP2D6, CYP3A5).	Pharmacogenomic-guided dosing improves efficacy and safety but requires broader clinical implementation.	Supports AI-integrated pharmacogenomic-guided dosing to improve outcomes and reduce healthcare costs [28].
21	Maslarinou (2023)	Solid tumors treated with fluoropyrimidines (5-fluorouracil, capecitabine, tegafur)	DPYD and multiple fluoropyrimidine-related PGx genes.	DPYD-guided dosing may be enhanced by integrating additional PK/PD genes for individualized dose optimization.	Supports polygenic PGx-guided dosing for safer, more precise chemotherapy [29].
22	Sahu (2026)	Multiple diseases / Warfarin, clopidogrel, statins, psychotropics, thiopurines, abacavir.	CYP2D6, CYP2C19, CYP2C9, VKORC1, TPMT, HLA-B*57:01, SLCO1B1, HTR2A, SLC6A4	Genotype-guided therapy improves treatment efficacy and safety.	Pharmacogenomics supports safer, more effective precision medicine [30].
23	Ngabea (2026)	Cardiovascular diseases; warfarin, clopidogrel, simvastatin, ACE inhibitors, mavacamten	CYP2C9, VKORC1, CYP2C19, SLCO1B1, CYP2D6, CYP3A4	Improves cardiovascular therapy, but implementation remains limited by resource constraints.	Supports safer, more effective cardiovascular therapy, but broader implementation is needed [31].

Disease and Drug Distribution

The 23 included studies covered diverse diseases and therapeutic areas, highlighting the broad application of pharmacogenomic-guided dose adjustment in personalized medicine (**Table 5**). Commonly investigated conditions included neurological, cardiovascular, infectious, psychiatric, oncological, autoimmune, and transplant-related diseases requiring individualized pharmacotherapy [11],[19],[24],[32],.

Neurological disorders were a major focus, with studies evaluating pharmacogenomic influences on acetylcholinesterase inhibitors, NMDA receptor antagonists, valproic acid, psychotropics, and stimulant medications [11],[12],[16],[32]. Cardiovascular research investigated genotype-guided therapy for warfarin, clopidogrel, statins, beta-blockers, and proton pump inhibitors, whereas psychiatric studies focused on optimizing antidepressant, antipsychotic, and mood stabilizer therapy [19],[25],[31].

Oncology studies emphasized individualized dosing of fluoropyrimidines and imatinib using model-informed precision dosing. Infectious disease research focused on genotype-guided efavirenz therapy for tuberculosis-HIV coinfection, whereas transplantation studies evaluated personalized immunosuppressive therapy [10],[27],[29],[18]. Overall, pharmacogenomic-guided dose adjustment has expanded across multiple medical specialties, consistently aiming to optimize drug selection and dosing, improve therapeutic efficacy, reduce adverse drug reactions, and advance personalized medicine. The characteristics of the included studies are presented in the following table

Table 5. Distribution of Diseases, Therapeutic Agents, and Pharmacogenomic Biomarkers Across Included Studies

Disease / Clinical Condition	Drug(s) / Drug Class	Major Pharmacogenomic Biomarker(s)	No. of Studies	Ref
Tuberculosis–HIV coinfection	Efavirenz, Rifampicin-based therapy	CYP2B6, CYP2A6, ABCB1	1	[10]
Alzheimer's disease	Donepezil, Rivastigmine, Galantamine, Memantine	APOE, CYP2D6, CYP3A4, ABCB1	1	[11]
Epilepsy [32] [16]	Valproic acid	ABCB1, GABRG2	2	[16],[32]
Autism spectrum disorder	Antipsychotics, Antidepressants, Stimulants	CYP2D6, CYP2C19, SLC6A4	1	[12]
Psychiatric disorders	Antidepressants, Antipsychotics, Mood stabilizers	CYP2D6, CYP2C19, CYP3A4, CYP1A2	2	[19] [26]
Spondyloarthritis	NSAIDs, TNF inhibitors, DMARDs	TNF, IL23R, ERAP1, HLA-B27	1	[19]
Cancer	Fluoropyrimidines, Imatinib	DPYD, TYMS, MTHFR, CYP3A5	3	[20],[27],[29]
Cardiovascular diseases	Warfarin, Clopidogrel, Statins, β-blockers	CYP2C9, CYP2C19, VKORC1, SLCO1B1	3	[22],[24],[31]
Organ transplantation	Immunosuppressants (Tacrolimus, etc.)	CYP3A5, ABCB1	1	[18]
Multiple chronic diseases / Precision medicine	Multiple medications	Multi-gene pharmacogenomic panel	6	[13],[14],[17], [23],[30]

Pharmacogenomic Biomarkers

Pharmacogenomic biomarkers identified across the 23 included studies were mainly genes involved in drug metabolism, transport, pharmacodynamic response, and therapeutic targets (**Table 6**). The most frequently investigated biomarkers were CYP450 enzymes, particularly CYP2D6, CYP2C19, CYP2B6, CYP2C9, CYP3A4, CYP3A5, and CYP2A6, which influenced drug exposure, therapeutic response, and adverse drug reactions across multiple drug classes [11],[10],[12],[19],[22],[31].

Other key biomarkers included ABCB1, SLCO1B1, VKORC1, DPYD, APOE, GABRG2, and UGT family genes, which were associated with drug pharmacokinetics, treatment response, toxicity, and genotype-guided dose optimization [16],[24][17][29]. Recent studies also demonstrated a shift from single-gene testing to multigene and polygenic approaches integrated with population pharmacokinetic models and clinical decision support systems to improve individualized dosing and advance precision medicine [20],[23],[27].

Table 6. Major Pharmacogenomic Biomarkers Identified Across the Included Studies

Biomarker Category	Major Gene(s)	Primary Drug(s)	Clinical Relevance
Drug-metabolizing enzymes	CYP2D6, CYP2C19, CYP2B6, CYP2C9, CYP3A4, CYP3A5, CYP2A6	Antidepressants, Antipsychotics, Efavirenz, Warfarin, PPIs	Determines drug metabolism and dose requirements
Drug transporters	ABCB1, SLCO1B1	Valproic acid, Statins, Efavirenz	Influences drug absorption, distribution, and toxicity
Drug targets	VKORC1	Warfarin	Predicts anticoagulant dose requirements
Toxicity-related genes	DPYD	Fluoropyrimidines	Predicts severe chemotherapy toxicity and guides dose reduction
Disease-specific biomarkers	APOE, GABRG2	Donepezil, Valproic acid	Associated with treatment response and clinical outcomes
Phase II metabolism genes	UGT family	Multiple drugs	Influences glucuronidation and drug clearance
Polygenic biomarkers	Multi-gene panels	Multiple drugs	Supports comprehensive precision dosing and personalized therapy

Pharmacogenomic-Guided Dose Adjustment

The included studies consistently demonstrated that pharmacogenomic-guided dose adjustment has become an essential component of personalized medicine by enabling individualized drug therapy based on genetic variability (**Table 7**). Across different therapeutic areas, genetic polymorphisms were shown to influence drug metabolism, pharmacokinetics, pharmacodynamics, and susceptibility to adverse drug reactions, thereby affecting optimal dose selection and treatment outcomes. Although the specific pharmacogenomic biomarkers varied among diseases and medications, the primary objective remained consistent: to maximize therapeutic efficacy while minimizing toxicity through individualized dosing strategies[10],[15],[20].

Dose reduction was the most common pharmacogenomic-guided strategy to prevent toxicity in patients carrying reduced-function or poor-metabolizer variants. This approach was particularly evident for fluoropyrimidines, where DPYD variants supported pre-emptive dose reduction to minimize severe toxicity. Similarly, polymorphisms affecting drug metabolism required lower maintenance doses to reduce adverse drug reactions while maintaining therapeutic efficacy [11],[29].

Conversely, several studies demonstrated the need for dose escalation or alternative therapeutic strategies in patients with rapid or ultra-rapid drug metabolism. For example, polymorphisms in CYP2B6 were consistently associated with altered efavirenz exposure among patients with tuberculosis-HIV coinfection, while variants in CYP2D6 and CYP2C19 influenced the clinical response to psychotropic medications and several neurological therapies. These findings emphasize that genetically determined metabolic capacity should be considered during dose selection to avoid both subtherapeutic drug exposure and treatment failure [10],[12],[19].

Another major application of pharmacogenomic-guided dosing involved the prevention of adverse drug reactions (ADRs). Studies investigating SLCO1B1, ABCB1, and VKORC1 demonstrated that genetic polymorphisms substantially influenced drug toxicity, transport, and pharmacodynamic response. In particular, SLCO1B1 variants were associated with statin intolerance, whereas VKORC1 polymorphisms contributed to variability in warfarin dose requirements. Incorporating these biomarkers into prescribing decisions has the potential to reduce serious drug-related complications and improve medication safety in routine clinical practice Furthermore [16],[22],[24].

Recent studies highlighted the integration of **model-informed precision dosing (MIPD), population pharmacokinetic modeling, and clinical decision support systems (CDSS) into pharmacogenomic-guided therapy. By combining genetic, clinical, laboratory, and pharmacokinetic data, these approaches generated individualized dosing recommendations and improved dose optimization compared with conventional empirical dosing, particularly in oncology, epilepsy, and precision pharmacotherapy [16],[20],[27].

Overall, the evidence synthesized in this review indicates that pharmacogenomic-guided dose adjustment extends beyond simple genotype-based dose modification. Contemporary precision medicine increasingly integrates genetic biomarkers with pharmacokinetic modeling, clinical algorithms, and digital decision-support technologies to optimize drug selection, determine individualized dosing regimens, reduce adverse drug reactions, and improve long-term therapeutic outcomes across diverse disease settings.

Table 7. Pharmacogenomic-Guided Dose Adjustment Strategies Identified Across the Included Studies

Dose Adjustment Strategy	Representative Biomarker(s)	Drug(s)	Expected Clinical Benefit
Dose reduction	DPYD, CYP2B6	Fluoropyrimidines, Efavirenz	Reduced toxicity while maintaining efficacy
Dose escalation	CYP2D6, CYP2C19	Antidepressants, Antipsychotics	Improved therapeutic response in rapid metabolizers
Individualized maintenance dose	VKORC1, CYP2C9	Warfarin	Optimized anticoagulation and reduced bleeding risk

Prevention of adverse drug reactions	SLCO1B1, ABCB1	Statins, Valproic acid	Reduced drug-induced toxicity and improved medication safety
Model-informed precision dosing	Multiple pharmacogenes	Imatinib, Valproic acid	Personalized dose optimization using pharmacokinetic models
Clinical decision support	Multi-gene panels	Multiple therapeutic classes	Improved precision prescribing and clinical decision-making

Emerging Technologies Supporting Personalized Medicine

Recent advances in pharmacogenomics extend beyond identifying individual genetic variants toward integrating emerging technologies that support personalized drug therapy (**Table 8**). The included studies highlighted the combination of pharmacogenomic data with computational models, bioinformatics, Clinical Decision Support Systems (CDSS), and model-informed precision dosing (MIPD) to improve individualized therapeutic decision-making. These technologies facilitate the translation of genomic information into clinically actionable dosing recommendations and promote the routine implementation of precision medicine [20],[23],[27].

CDSS provide**Table 8.** Emerging Technologies Supporting Pharmacogenomic-Guided Personalized Medicine

Emerging Technology	Primary Function	Clinical Application	Ref
Clinical Decision Support System (CDSS)	Integrates pharmacogenomic results with clinical data	Drug selection and genotype-guided dose recommendations	[14][20]
Model-Informed Precision Dosing (MIPD)	Combines pharmacogenomics with pharmacokinetic modeling	Individualized dose optimization	[16]
Population Pharmacokinetic (PopPK) Modeling	Predicts individualized drug exposure	Precision dosing for narrow therapeutic index drugs	[16]
Bioinformatics Platforms	Integrates multi-omics and pharmacogenomic datasets	Biomarker discovery and clinical interpretation	[20][23]
Polygenic Algorithms / Multi-gene Panels	Simultaneous evaluation of multiple pharmacogenes	Comprehensive genotype-guided therapy	[29]
Artificial Intelligence (AI) & Machine Learning	Predictive modeling for individualized therapy	Automated pharmacogenomic interpretation and dose prediction	[25][30]

Clinical Significance of Genetic Variability in Pharmacogenomic-Guided Drug Dose Adjustment

This review demonstrates that genetic variability is the principal biological factor underlying interindividual differences in drug response, reinforcing the central role of

pharmacogenomics in precision medicine. Although the included studies covered diverse diseases, therapeutic agents, and study designs, they consistently showed that inherited genetic variation influences drug metabolism, pharmacokinetics, pharmacodynamics, and susceptibility to adverse drug reactions. These findings support the concept that genotype-guided prescribing is more effective than empirical dose selection in optimizing treatment efficacy while minimizing drug-related toxicity [10] [11],[16],[19],[23],[30].

An important finding of this review is that not all pharmacogenomic biomarkers have equivalent clinical utility. Biomarkers involved in drug metabolism and disposition, particularly CYP2C9, CYP2C19, VKORC1, DPYD, and SLCO1B1, have accumulated sufficient clinical evidence to support genotype-guided prescribing and have been incorporated into international pharmacogenomic recommendations. In contrast, biomarkers such as APOE, ABCB1, GABRG2, and receptor-related polymorphisms were more frequently associated with variability in treatment response than with validated dose-adjustment strategies, indicating that biological association alone is insufficient for routine clinical implementation [11],[13],[16],[22],[24],[29],[31]. This distinction emphasizes that successful translation into clinical practice depends not only on identifying statistically significant genetic associations but also on demonstrating consistent improvements in clinically relevant outcomes.

Another notable trend identified across the included studies is the evolution of pharmacogenomics from single-gene testing toward integrated precision dosing strategies. Rather than relying solely on individual genetic variants, recent evidence supports combining pharmacogenomic biomarkers with clinical characteristics, therapeutic drug monitoring, population pharmacokinetic modeling, and clinical decision support systems to improve dose prediction and treatment optimization [16],[20],[25],[26],[27] . This integrated approach recognizes that drug response is determined by the interaction of genetic and non-genetic factors, suggesting that future precision pharmacotherapy will increasingly depend on comprehensive predictive models capable of supporting individualized prescribing in routine clinical practice.

Clinically Actionable Gene–Drug Pairs in Precision Pharmacotherapy

One of the most important findings of this review is that only a limited number of pharmacogenomic biomarkers currently provide sufficient evidence to support routine genotype-guided prescribing. Among the included studies, CYP2C9–VKORC1, CYP2C19, DPYD, and SLCO1B1 consistently demonstrated the strongest clinical utility because their genetic variants directly influence drug exposure, therapeutic efficacy, or the risk of serious adverse drug reactions. Consequently, these gene–drug pairs have been incorporated into international pharmacogenomic recommendations and represent the most mature examples of precision pharmacotherapy [22],[23],[24],[29],[30],[31].

The greatest clinical impact was observed in cardiovascular medicine and oncology. Variants in CYP2C9 and VKORC1 explain a substantial proportion of variability in warfarin dose requirements, allowing individualized anticoagulant therapy that reduces bleeding complications while maintaining therapeutic effectiveness. Likewise, CYP2C19 polymorphisms identify patients with reduced clopidogrel activation who may require alternative antiplatelet strategies to avoid treatment failure. In oncology, DPYD genotyping enables pre-treatment dose reduction of fluoropyrimidines, thereby minimizing life-threatening toxicity without compromising treatment efficacy, whereas SLCO1B1 variants improve prediction of statin intolerance and support safer lipid-lowering therapy [22],[23],[24][,29],[30],[31] . These findings

illustrate that the greatest clinical benefit is achieved when genetic testing informs therapeutic decisions before treatment initiation, rather than after adverse events have occurred.

In contrast, biomarkers such as APOE, GABRG2, ABCB1, and several receptor-related polymorphisms were primarily associated with variability in treatment response or pharmacokinetic characteristics but lacked sufficient evidence to support standardized dose-adjustment recommendations [11],[13],[16],[19]. This difference highlights that statistical associations alone are insufficient for clinical implementation. Pharmacogenomic biomarkers become clinically actionable only when supported by reproducible evidence demonstrating improved patient outcomes, validated dosing recommendations, and integration into evidence-based clinical guidelines. Therefore, future research should focus on validating emerging biomarkers through prospective multicenter studies while expanding the clinical application of established gene–drug pairs.

Emerging Technologies Supporting Pharmacogenomic-Guided Dose Adjustment

An important trend identified in this review is the evolution of pharmacogenomic-guided dosing from genotype-based prescribing toward technology-assisted precision pharmacotherapy. Rather than relying solely on genetic information, recent studies have demonstrated that integrating pharmacogenomic biomarkers with clinical decision support systems (CDSS), model-informed precision dosing (MIPD), population Pharmacokinetic (PopPK) modeling, bioinformatics, and artificial intelligence (AI) can substantially improve individualized dosing recommendations by incorporating both genetic and clinical variables [13],[18],[19],[20],[21].

Among these technologies, AI and machine learning have emerged as promising tools for supporting clinical decision-making by identifying complex relationships between genetic variants, patient characteristics, and therapeutic outcomes that are difficult to detect using conventional approaches. In parallel, MIPD and PopPK modeling provide dynamic dose optimization by combining pharmacogenomic data with drug concentration monitoring and patient-specific pharmacokinetic parameters, thereby improving dosing precision in complex clinical settings, including oncology and transplantation [13],[18],[19],[20],[21].

Despite these advances, the included studies consistently emphasized that technological innovation should complement, rather than replace, clinical judgment. The successful implementation of AI-assisted pharmacogenomics depends on high-quality clinical datasets, external validation across diverse populations, interoperability with electronic health records, and standardized clinical workflows. Therefore, future precision pharmacotherapy will require multidisciplinary collaboration among clinicians, pharmacologists, geneticists, bioinformaticians, and data scientists to ensure that emerging technologies can be translated into safe, effective, and clinically applicable decision-support tools [13],[18],[19],[20],[21].

Challenges and Future Perspectives

Despite the growing evidence supporting pharmacogenomic-guided dose adjustment, several barriers continue to limit its implementation in routine clinical practice. The included studies highlighted challenges related to the accessibility and cost of pharmacogenomic testing, variability in genetic profiles across populations, insufficient clinician education, and the limited integration of pharmacogenomic data into clinical decision support systems and electronic health records [17],[20],[22],[29],[30]. Furthermore, while gene–drug pairs such as CYP2C9–VKORC1, CYP2C19, DPYD, and SLCO1B1 have demonstrated strong clinical utility, many emerging biomarkers still

require prospective validation before widespread clinical adoption [22],[23],[24],[29], [30],[31].

Future advances in precision pharmacotherapy will depend on integrating validated pharmacogenomic biomarkers with digital health technologies, including artificial intelligence, clinical decision support systems, and model-informed precision dosing. Continued multicenter studies, standardized implementation strategies, and interdisciplinary collaboration will be essential to facilitate the broader adoption of pharmacogenomic-guided dosing in routine healthcare [18], [19], [20], [21].

Strengths and Limitations

This systematic literature review provides a comprehensive overview of recent advances in pharmacogenomic-guided drug dose adjustment by synthesizing evidence across multiple therapeutic areas, pharmacogenomic biomarkers, and emerging precision medicine technologies. However, this review has several limitations. Only studies indexed in Scopus and PubMed were included, potentially excluding relevant evidence from other databases. Additionally, methodological heterogeneity across study designs, therapeutic areas, and reported outcomes precluded quantitative meta-analysis. Some included publications were narrative reviews and clinical practice guidelines that could not be formally appraised using the Joanna Briggs Institute (JBI) critical appraisal tools. Therefore, further high-quality prospective multicenter studies are needed to strengthen the evidence for broader clinical implementation of pharmacogenomic-guided dosing.

4. Conclusion

This systematic literature review shows that pharmacogenomic-guided dose adjustment is a promising approach to support personalized medicine by improving drug selection, dose optimization, treatment safety, and therapeutic precision. Across the 23 included studies, the strongest clinical relevance was observed for established gene–drug pairs such as CYP2C9/VKORC1–warfarin, CYP2C19-related therapies, DPYD–fluoropyrimidines, SLCO1B1–statins, CYP2B6–efavirenz, and selected CYP3A5-related immunosuppressant therapies. However, the strength of evidence varied across biomarkers, therapeutic areas, and study designs, indicating that some biomarkers still require stronger prospective validation before routine clinical implementation. Emerging technologies, including clinical decision support systems, model-informed precision dosing, population pharmacokinetic modeling, bioinformatics, artificial intelligence, and machine learning, may further support individualized pharmacotherapy. Broader implementation requires standardized guidelines, population-specific evidence, affordable genetic testing, integration into routine healthcare systems, and careful protection of genetic data.

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Conflict of Interest:

The authors declare no conflict of interest.

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