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# Pharmacogenomics using Whole-Exome Sequencing in Oncology Clinics: Clinical Workflows, Outcomes, and Cost-Effectiveness

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## ABSTRACT

Pharmacogenomics leverages genomic information to optimize drug therapy, improving efficacy and minimizing toxicity in oncology patients. Whole-exome sequencing (WES) provides a comprehensive platform for identifying clinically actionable variants in germline and tumor DNA, enabling personalized treatment selection and dose adjustment. WES-based pharmacogenomic workflows encompass patient selection, informed consent, sample acquisition, sequencing, variant annotation, clinical reporting, and integration into multidisciplinary care. Evidence indicates that pharmacogenomic-guided therapy can reduce adverse drug reactions, maintain chemotherapy dose intensity, and enhance targeted therapy outcomes. Economic analyses suggest potential cost savings through the prevention of drug-related complications, though formal cost-effectiveness remains context-dependent. Despite technical and methodological challenges, WES-guided pharmacogenomics represents a promising approach to precision oncology, with ongoing data accumulation likely to expand its clinical utility and integration into routine care.

**Keywords**: Pharmacogenomics, Whole-Exome Sequencing, Precision Oncology, Clinical Workflows, and Cost-Effectiveness.

## INTRODUCTION

Pharmacogenomics is an important aspect of personalized medicine for cancer patients. Its main goal is to improve therapeutic efficacy, safety, and tolerability of anticancer agents by tailoring drug administration to the subject's genomic makeup, especially single-nucleotide variants (SNVs) or copy number variants (CNVs) in genes implicated in drug efficacy or toxicity [1]. Whole-exome sequencing (WES) offers a powerful practical approach to implement pharmacogenomics, as it targets only the exonic portion of the genome for sequencing. Pharmacogenomic WES clinical services start with patient selection [2]. When a therapeutic option exists with evidence-level 1A to 1B patient-specific assay is considered. When other drug-indication combinations applicable to standard therapy are not available, the service may also be used. Patient-oriented engagement at all stages increases the likelihood of informed consent [3]. Bioinformatics also emphasizes critical explanations for pharmacogenomic genes; anchoring facts about drugs without laboratory support is essential to reveal the true added value of genomics [4]. Pharmacogenomics can directly guide the selection of anticancer drugs. Clinically relevant variants in pharmacogenomic genes may occur in three scenarios [5]. Variants modifying the biotransformation of the prodrug capecitabine may dictate the choice of this drug in subjects with various tumors. Variants in the DDR protein BRCA1 lead to a strong recommendation of olaparib in both breast and ovarian cancers. CNVs and non-template-encoded DNA appear to affect 5-fluorouracil activity in the adjuvant setting of colorectal cancer, and recommendations are based primarily on these engineering studies [6]. However, no analysis of pharmacogenomic WES-guided clinical trials is currently available.

### Conceptual Framework of Pharmacogenomics in Oncology

Pharmacogenomics, the branch of genomics concerned with how genes affect an individual's response to drugs, has emerged as a promising tool to enhance patient benefit and reduce harm from drug therapy [7]. The field is particularly pertinent in oncology due to the extensive use of targeted therapies, which have specific recommended dosing and monitoring that genetic variation can significantly influence [8]. Multiple cancer-associated genetic

variants have been identified with clinically actionable drug interventions [9]. Recently, whole-exome sequencing (WES) and targeted next-generation sequencing (NGS) have been incorporated into various pharmacogenomic workflows in oncology clinics [10]. These approaches are expected to provide a more comprehensive pharmacogenomic profiling than conventional single-gene approaches [8]. Among guidelines and recommendations, the Clinical Pharmacogenetics Implementation Consortium (CPIC) has published an extensive list of pharmacogenes linked to drugs with established recommendations accounting for dosage and alternative choices, as well as an increasing number of pharmacogene–drug pairs where evidence is still evolving [9]. Pharmacogenomic actionability addresses drug-gene pairs with sufficient evidence supporting a clinical recommendation to modify prescribing when variants meet specific criteria [10]. Actionability remains a vital yet fluid aspect as knowledge continues to accumulate and more polygenic traits are recognized in pharmacogenomic studies [11].

## Whole-Exome Sequencing in Clinical Oncology: Technical Foundations

Massively parallel sequencing approaches, such as whole-exome sequencing (WES), have elucidated genetic alterations in many tumor types and revealed biological insights [12]. The increased availability and decreased cost of tumor genomic profiling have created opportunities to test the precision medicine hypothesis in clinical oncology. WES may inform treatment choices and therapeutic discovery efforts by identifying alterations in the coding regions of all genes [13]. Challenges to clinical WES include generating high-quality data from archival FFPE tumor material and interpreting WES data for clinical use. An approach has been developed to produce high-quality WES data from archival tumor tissue, validated with frozen tissue, and combined with a heuristic algorithm for clinical interpretation [14]. This method has been applied in a cohort of 511 cases, enabling biological discovery and clinical trial enrollment [15]. With the decrease in sequencing costs, clinical testing has shifted from single-gene analysis to gene panels and now to WES and whole-genome sequencing (WGS). Clinical laboratories are rapidly adopting NGS-based WES and WGS [16]. It is critical to design and validate these assays properly, ensuring performance meets specifications before implementation. WES is used for broad gene enrichment and targeted analysis for specific disorders [17]. From an analytical perspective, WES generates approximately 30,000 variants per exome, and WGS over 3 million variants per genome [18]. WES and WGS can also identify pathogenic variants in genes unrelated to the primary phenotype under investigation [19].

## Clinical Workflows for Pharmacogenomic Testing in Oncology

Pharmacogenomics relies on understanding how a patient's genetic makeup affects drug efficacy, toxicity, and drug–drug interactions to guide drug choice and dosing and minimize adverse effects [20]. Rapid advances in next-generation sequencing have facilitated the identification of thousands of somatic mutations in cancer. Whole-exome sequencing (WES) characterizes the coding regions of the genome, providing a reasonable compromise between cost, interpretability, and coverage of relevant pharmacogenomic variation [13]. Whole-exome sequencing (WES) characterizes the coding regions of the genome, providing a cost-effective compromise for analyzing relevant pharmacogenomic variation [15]. Algorithmic methods identify somatic mutations that drive cell transformation, specifying targeted drugs associated with a greater likelihood of response [16]. Mutations are not uniformly distributed, and pharmacogenomic analysis identifies variants linked to metabolic drug interactions, toxicity, and treatment response regardless of the therapeutic approach [7]. These variant classes are common and demonstrate extensive overlap among cancers, justifying the inclusion of recurrently mutated genes in pharmacogenomic assessment [18]. Other non-exome techniques target variant classes more epidemiologically characterized or employ panels designed to guide anticancer therapy, but WES offers broader coverage at a reasonable price and with established community standards from which to develop tumor-normal pipelines. However, despite extensive CRISPR–Cas9 screens and transcriptomic analyses that highlight signaling pathways involved in cancer cell proliferation, global gene-essentiality maps for HTPR and HTPF remain scarce. HTPR sustains diverse human cancers, and proteomic studies establish the kinase as a critical regulator of cancer cell growth, validated using pharmacological inhibitors of the enzyme [18]. The relative fitness of dependent cells is limited by mitochondrial quantity and function tied to the glycolytic axis of the Warburg effect and tumorigenesis [11].

## Patient Selection and Consent

Pharmacogenomics has been defined as "the branch of pharmacology concerned with the effects of genetic factors on responses to drugs [5]." Personalized therapy has revolutionized the practice of medical oncology, especially in targeted therapies, lock-key mechanisms that match the right drug to a patient's cancer. However, efficacy and toxicity of treatment can differ even when such target mutations exist [6]. Exome sequencing of both tumor and germline provides a comprehensive survey of genes that play a role in drug disposition and action, allowing further refinement of treatment selection to improve patient outcomes [7]. Patients with a newly diagnosed malignancy and those with acquired resistance after initial targeted therapy are selected. Informed consent is obtained using a team with experience in the consent process for high-complexity genomic studies 6. The limitations of currently actionable alterations, additional detected variants, and implications for relatives are

emphasized [8]. The consent process is collaborative, engaging the patient and family in a dialogue about their own risks and interests. Specific consent for germline analysis is obtained, although tumor analysis proceeds regardless [10]. Test results that implicate hereditary cancer susceptibility-germline variants with well-defined clinical actionability from the outset are relayed to the treating physician within the standard clinical nomenclature, ensuring rapid care adjustment when appropriate [7].

**Sample Acquisition and Sequencing**

Before sample collection, qualified clinical staff review the patient's case and determine whether pharmacogenomic whole-exome sequencing is indicated [6]. The request is forwarded to the laboratory, where sample requisition forms are prepared [5]. Along with the forms, an information pamphlet about the test, detailing its purpose and theoretical boundaries, is sent to the patient's physician for discussion with the patient [3]. As a general guide, requests for sequencing are accepted when a compound screening test has not previously been carried out. Once the physician decides to proceed with the test, he or she also addresses the information pamphlet to the patient in a non-technical manner and submits a signed requisition form [6]. This constitutes consent to perform the test [8].

**Variant Annotation and Interpretation**

Acquired test metrics are processed through web-based ClinVar access 8. Variants flagged as "pathogenic" or "likely pathogenic" having conflicting classifications were omitted [21]. No restrictions apply to institutional or group domain selections. Exome capture was predominantly performed using the Agilent SureSelect kit, with Flex Exome v3 targeting ~24,000 regions of the genome, and NovaSeq or HiSeq technology applied on an Illumina platform [18]. The deployment of the search tool CAVATICA-BRAID accelerates the detection of variants. Datasets are open-access, enabling submission through the Genomic Data Commons. A processing pipeline develops the results from primary analysis to structured clinical reporting while retaining flexibility for laboratory requirements [21]. Moreover, VCF, alignment files, and coverage metrics have been released, assisting in the self-developed analytic implementation. The accessibility of instructional videos and analysis frameworks via GitHub has further enhanced the documentation of the pipeline [22].

**Reporting and Clinical Decision Support**

Integration of pharmacogenomics into clinical practice generates specific demands for reporting and clinical decision support [15]. Pharmacogenomics relies on well-curated, openly accessible databases for gene-drug pair interpretations, detailing relevant variants, clinical significance, affected processes, and recommended domain-specific actions [17]. A comprehensive report on gene-drug relationships and treatment options, including the mutations detected, their classification according to established standards, and the clinical support provided, enhances refinement of the pharmacogenomic report [18]. Automated pipelines incorporating Artificial Intelligence and natural language processing can improve and accelerate the reporting process [19].

**Integration into Multidisciplinary Care**

Pharmacogenomic testing typically requires specialist input, especially for cancer cases that need rapid turnaround of a test result [16]. The workflow, therefore, must support integration into multidisciplinary management as well as a predominantly single-specialty approach [13]. Strategic working arrangements at the participating sites enabled either simultaneous or staggered integration for paediatric and adult oncology cases, with two experienced medical oncologists critical to patient selection and test coordination, and also to report production, supported by the broader genomic workforce [8].

**Clinical Outcomes Associated with Pharmacogenomic-Guided Therapy**

Among patients with cancer, pharmacogenomics mapping based on germline DNA sequences can identify genomic variants associated with drug safety, tolerability, efficacy, and drug interactions [9]. Pharmacogenomics testing at the time of diagnosis and during the disease course can support treatment selection, optimization, and dose adjustments [10]. Genomic variants associated with severe drug-related toxicities can be particularly useful at the outset of an oncology treatment regimen [8]. Evidence from adult patients with cancer indicates that pharmacogenomics mapping reduces the risk of severe toxicity and symptom burden during established chemotherapy regimens by supporting the selection of non- or less-harmful alternatives [7]. Mid-course genomic controls may facilitate the dose adjustment or selection of drugs less likely to induce severe or bothersome adverse effects [2]. Pharmacogenomics mapping can help maintain chemotherapy dose intensity and compliance, potentially improving treatment outcomes [15]. Germline pharmacogenomics guidance applied at the time a pharmacologically active oncology drug is introduced, rather than germline genotyping for solely predictive genes, has been termed "pharmacogenomics-guided therapy"[16]. Initial pharmacological agents in oncology often provide proof of concept and determine the guidelines for subsequent therapy [17].

**Efficacy Outcomes in Targeted Therapies**

Acquired resistance to targeted therapies for oncogenic drivers is a common phenomenon across multiple tumor types, and in selected malignancies, treatment can be changed in response to the emergence of resistance mutations without prolonged interruptions in therapy [17]. The direct readout of efficacy would therefore be the duration of response following initiation of a targeted therapy [18]. Unfortunately, clinical trials assessing this

endpoint are rare, as most exome-based pharmacogenomics projects focus on an exploratory or wild-type pipeline [18]. Moreover, data from other modalities might not be forthcoming, or temporal considerations may preclude the completion of the requisite studies within the pharmacogenomic program timeframe [10]. Additionally, certain drugs for which active pharmacogenomic projects exist do not lend themselves easily to efficacy analyses [19].

**Toxicity and Safety Profiles**

Pharmacogenomic guidance may improve patient safety in clinical oncology [1]. Pharmacogenomic markers help clinicians select medications that optimize therapeutic effectiveness while limiting adverse events by understanding drug metabolism [4]. Common drug-gene interactions for cancer treatment target several drug classes, particularly anti-cancer drugs [14]. Several VUSs associated with adverse events in cancer therapies have been associated with medications used in supportive care and treatment of co-morbid conditions [6]. Nonetheless, definitive evidence supporting the strong predictive value of individual variants is still pending. Although therapeutic outcomes are the most direct method for assessing the clinical and economic value of pharmacogenomics, concern about drug safety remains critical [7, 9]. Toxicity arising from pharmacogenomic-guided therapy is a major impediment to optimized treatment yet may prevent the full realization of pharmacogenomic benefits, leading to bias against exome-based pharmacogenomics [17].

**Treatment Optimization and Dose Individualization**

Through the principle of precision medicine, pharmacogenomic testing aims to personalize cancer therapy by maximizing the therapeutic benefit while minimizing the risk of adverse drug reactions [5]. Among available genomic information, gene variants that affect drug metabolism are frequently investigated [7]. A pharmacogenomic approach has been assessed in 178 cases involving exome-based testing [10]. In accordance with the Clinical Pharmacogenetics Implementation Consortium guidelines, only alterations in germline variants were subject to a test that included approved or investigational therapies matched to 131 drugs [16]. Implementation of the test influenced treatment decisions in over one-third of cases, and pharmacogenomic-guided therapy enabled a significant extension of the time to treatment failure and a markedly better safety profile compared with the alternative in patients undergoing targeted therapy [17].

**Economic Considerations: Cost-Effectiveness of Exome-Based Pharmacogenomics**

At the point of care, drug-related problems (DRPs) can be associated with patient inefficacy, safety, adherence, and other aspects. When treatment is not optimized, it is associated with poorer health outcomes and higher healthcare costs [11]. Adverse drug reactions (ADRs) are among the ten leading causes of death in Canada, leading to 1 out of every 12 hospitalizations and 34,000 annually. Drug-related problems (DRPs) are among the biggest reasons for medication errors [10]. Pharmacogenomic (PGx) testing and screening can reduce ADRs, optimize therapy, and achieve better-targeted drug therapy. Community pharmacists are considered well-positioned to address these problems, with a high degree of both training and patient engagement, and the 200 PHeDEx tests conducted show the pharmacogenomics community should be addressed where its practice by clinicians expedites treatment choice [12]. The approach of using exome-scale data for dosing accuracy is known when seeking information on, for example, abacavir (well-characterized), clopidogrel (polymorphic), codeine (non-DME), carbamazepine (starting dose), and irinotecan (huge inter-patient variability)[11]. With over 380 actionable drugs, 13, it is appropriate to consider high throughput, population, and exome data involved (OncoKBC). Abacavir PGx information influenced approximately 12% of all patients [14].

**Cost Components and Reimbursement Landscape**

Integrating pharmacogenomics into comprehensive clinical and economic evaluations provides opportunities to increase adoption levels across different healthcare systems within the oncology community [11]. With adequate technical capabilities, sophisticated systems for information management, and adequate consideration of patient and societal value, the community can leverage pharmacogenomics to optimize the delivery and overall value of cancer therapy [13, 14].

**Health Economic Modeling and Value Assessment**

Pharmacogenomics Exome Sequencing in Oncology Clinics: Clinical Workflows, Outcomes, and Cost-Effectiveness [3]. Health economic modeling and value assessment are crucial for evaluating the cost-effectiveness of pharmacogenomic testing in clinical oncology and hematology [3]. Modeling studies typically adopt a micro-costing framework to estimate the overall costs associated with a pharmacogenomic test through the various time-consuming and resource-intensive steps required for its integration into routine oncology practice. Modeling the health economic impact of pharmacogenomic testing also examines the value of pre-test genomic prioritization strategies and provides insights on the costs incurred by supplementary laboratory workflows focused on the standardization of variant annotation and interpretation efforts [15]. Overall, these studies highlight the importance of establishing standardized operational procedures, developing appropriate cost-estimation methodologies, and considering the key principles of each national health-care system's financing model to maximize the successful implementation of pharmacogenomic diagnostics within a broad range of health-care

contexts [10]. Unlike alternative models of whole-exome sequencing aimed explicitly at maximizing pharmacogenomic coverage or overall clinical utility, health economic models specific to pharmacogenomic oncology workflows take a distinctly counterproductive approach by focusing exclusively on a single class of clinically relevant genomics[9]. Moreover, pharmacogenomic oncology models uniquely consider the costs incurred by interventions intended to enhance the performance of exome-based genomics, including those directed toward an initial pre-test prioritization activity aimed at augmenting the exome interpretation workflow and providing notably rapid results [8]. Modeling studies further highlight the comparative-targeted nature of exome-based pharmacogenomic workflows, which also lend themselves to substantial savings by permitting the continued unencumbered operation of pre-existing universal genomic workflows and standardizing assay reagent-pooling practices across rather than within the pre-test and post-test phases of integrated laboratories [16].

**Comparative Effectiveness versus Standard Care**

Compared with standard care, exome-based pharmacogenomics is unlikely to provide a clinical or economic advantage [15]. Clinical guidelines recommend pharmacogenomic testing only when evidence establishes an effect on health outcomes, yet patients are receiving prescriptions directed by pharmacogenomic results [12]. Most of the evidence cited by advocates for heterogeneous cancer patient cohorts linked to pharmacogenomic activity remains associative, spanning from examining summary statistics to acquisition [1]. Overall, outcome evaluation is impeded by a study design preferring prospective evaluation complemented by heterogeneous methodologies and patient biases, including minorities [3]. Estimation of utility valuation by consideration of explicit preference offers advantages over simplified modelling. While exome-based pharmacogenomic testing is commonly implemented, the underlying scientific evidence associated with patient benefit continues to form and develop [5].

**Current Evidence Gaps and Methodological Challenges**

Whole-exome sequencing (WES)-based pharmacogenomics in oncology provides an opportunity to select life-extending therapies and to avoid drugs with an unfavorable risk-benefit profile [13]. In addition to current evidence gaps and methodological challenges limiting clinical adoption, the identification of targetable events for precision treatment adds complexities to the workflow [14]. Even when exome sequencing and pharmacogenomics deliver analytical and clinical validity, uncertainty remains regarding their clinical utility and added value compared to standard care [15]. Nonetheless, ongoing accumulation of pharmacogenomic evidence continues to expand the spectrum of pharmacogenomic guidance of antitumor therapy in a growing number of cancers, including combination therapies, neoadjuvant options, and immunotherapy [12]. Therefore, in oncology, even pharmacogenomic schemes that only half fill the evidence-data cycle of analytical and clinical validity still offer an attractive proposition [11]. Furthermore, WES provides wider access to additional clinically relevant genomic information beyond traditional pharmacogenomic data and allows cyclotherapy and the evaluation of drug combination synergies and antitumor resistance mechanisms an innovative and clinically applicable scope emerging in other areas [17].

**Study Design Limitations in Pharmacogenomic Oncology**

The pharmacogenomic approach to alteration-guided therapy is imperfectly addressed under the stringent criteria for evidence-based medicine that prioritizes randomized clinical trials [7]. Such studies, readily feasible and informative in phases when treatment does not target distinct lesions, remain elusive and unviable after the focus shifts to specific modifications of oncogenesis [6]. Conducting randomized trials that counterpose pharmacotherapy based on mutational versus nonmutational lesions challenges current paradigms about the iterative nature of cancer evolution [18]. While therapeutic interventions are plausible candidates for maintenance and redirected therapy after sequential relapses, exome sequencing routinely reveals additional nongenotoxic alterations. Their annotation as potential therapeutic objectives and comparable classifications of treatments unrelated to these mechanisms would require a circular examination of typology analysis. Reliable estimates for such protocols also remain unavailable [16]. The concordance of anticipated prescriptions with subsequent decisions becomes increasingly uncertain when the initial target after de novo onset is absent from the pretherapy catalogue or other nongenotoxic mutations are involved. The addition of new features to morphologic descriptors similarly hampers the identification of observational sets still amenable to straight analysis without circularity [19]. Once therapy is initiated, the cycle is unlikely to be resumed for cases where the prescription stems from the exome [14].

**Data Sharing, Privacy, and Generalizability**

The paradigm of pharmacogenomics seeks to enhance health outcomes and minimize adverse effects associated with cancer therapy [4]. To achieve such goals, the strategic and coordinated assessment of genetic information, integrating functional knowledge of the drug, gene, and disease pathways, is crucial for patient stratification in therapy selection, guidance for precision dosing, and identification of safety monitoring needs [7]. Despite expectations that the lack of enhancement of the pharmacogenomics paradigm in oncology would limit the immediate deployment of clinical-grade whole-exome sequencing (WES) of germline DNA for cancer patients, analysis across the WES-generation patient cohort indicates broad application; pharmacogenomically pertinent

drug-gene interactions were identified in more than 80% of patients at the time of analysis. Three elements facilitated such emergence: [1] the extension of pharmacogenomic concepts beyond 8 wording present in pivotal investigations into drug-drug or drug-disease interactions of current and future therapeutic relevance, [2] the establishment of standardized coding convention for the elaboration of the indication or reasoning justifying the need for continued or alternative therapy, and [3] patients often previously receiving therapy without variant-level assessment enabled coordinated pharmacogenomic effort prior to an anticipated new change in therapy[6].
WES-generation data remain centralized in the originating academic institution with attendant limitations toward generalization of pharmacogenomic observations to entities outside the institution [20]. Need therefore arises for strategies maximizing dissemination while permitting adjunct local collection to domain-generalize clinical impact [17]. Sharing requires a modality permitting full comprehension of pharmacogenomic components as decoupled from assigned identifiers such as cookie, patient, or specimen processing URN to ensure unauthorized linkage cannot occur [13]. Consideration of sharing approaches soundly focused on these dimensions does occur in the clinical literature and general bioinformatics domain [20].

## Technical Variability in Exome Sequencing

Pre-analytical, analytical, and post-analytical factors can significantly affect the cost, performance, and outcome of WES-based pharmacogenomics, although no suitable standardized guidelines prioritize key aspects of the process [8]. Collectively, these factors introduce technical variability that remains uncharacterized and unquantified in the literature [7].

## Clinical Utility versus Analytical Validity

Implementation of the genomic knowledge obtained through whole-exome sequencing (WES) into routine oncology clinical practice requires consideration of not only the analytical validity of the generated data at the test level but also the clinical validity and clinical utility associated with patient-level interpretation and resulting clinical action [14]. Analytical validity, which assesses the accuracy of genotypes predicted from the sequencing data generated, is routinely evaluated and reported for WES tests in general, including those specifically used in oncology [13]. Nevertheless, the clinical validity associated with pharmacogenomic data in oncology remains inadequately characterized, which hinders the establishment of clinical utility and broader acceptance of the use of pharmacogenomic guidance following exomic tests in practice [15]. Consequently, many organizations have characterized the validity of variantly pharmacogenomically actionable exomic variants at the clinical utility level, which in turn serves as a clear indicator of the clinical utility expected from pharmacogenomic–guided therapy in oncology [1].

## Ethical, Legal, and Social Implications

The rapid advances in DNA sequencing technologies, such as exome sequencing, have made it possible to obtain, store, and analyze an individual's entire genetic code [19]. These developments have triggered an ethical and legal quandary regarding the use of whole-exome sequencing data for pharmacogenomic analysis. While pharmaceutical compounds are developed and regulated on the basis of an exposition–response paradigm, the concept of a pharmaceutical compound, as defined by state and federal laws, has become blurred with the advancement of individualized therapies based on genetic data [20]. Millions of people are already receiving personalized drugs, with unlimited opportunities for similar services and products [21]. A unique proportion of actionable variants affecting drug exposition, response, and toxicity can be extracted from exome sequencing data [20]. The U.S. Food and Drug Administration posts several compendium action tables and guidelines for genetic variants within a specific group of drugs [18]. Government and professional societies, however, seldom provide a scientific study to clarify the provision. Consequently, it is crucial to provide guidance to avoid regulatory or legal action in such services for over a decade [17]. The process of universally utilizing pharmacogenomic information toward patient care soon after exome sequencing needs to be precisely described beforehand in order to implement exome-based personalized patient care [21].

## Future Directions and Recommendations for Practice

Pharmacogenomics using whole exome sequencing (WES) in oncology clinics holds great promise for improving outcomes, yet many evidence gaps remain to be addressed to support broad implementation[22-24]. Data sharing and technology standardization will enhance study robustness, return of information protocols will strengthen practice recommendations, and systematic economic appraisals will clarify the true cost-effectiveness of the approach [25-27]. Furthermore, fostering collaboration among healthcare professionals and stakeholders can facilitate the integration of WES-based pharmacogenomics into existing clinical workflows [28].

# CONCLUSION

Whole-exome sequencing enables the implementation of pharmacogenomics in oncology, providing actionable insights for personalized therapy. It supports optimized drug selection, improved safety profiles, and potential cost savings, while facilitating integration into multidisciplinary clinical workflows. Although evidence gaps and methodological challenges remain, the continued accumulation of pharmacogenomic data and standardization of

analytical pipelines are likely to enhance clinical utility. WES-based pharmacogenomics offers a promising pathway toward precision oncology, advancing both patient outcomes and healthcare efficiency.

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