Pharmacogenomics

ISSN: 1462-2416 (Print) 1744-8042 (Online) Journal homepage: www.tandfonline.com/journals/ipgs20

Considerations for the clinical implementation of DPYD and UGT1A1-guided chemotherapy

Mary-Pearl Ojukwu, Carlos Vegas, Emily J. Cicali, David L. DeRemer & Madeline L. Norris

To cite this article: Mary-Pearl Ojukwu, Carlos Vegas, Emily J. Cicali, David L. DeRemer & Madeline L. Norris (06 Jun 2026): Considerations for the clinical implementation of DPYD and UGT1A1-guided chemotherapy, Pharmacogenomics, DOI: 10.1080/14622416.2026.2685871

To link to this article: https://doi.org/10.1080/14622416.2026.2685871

PHARMACOGENOMICS
https://doi.org/10.1080/14622416.2026.2685871

Taylor & Francis
by informa

REVIEW

Considerations for the clinical implementation of DPYD and UGT1A1-guided chemotherapy

Mary-Pearl Ojukwu[a], Carlos Vegas[a], Emily J. Cicali[a], David L. DeRemer[a,b] and Madeline L. Norris[a]

[a]Center for Pharmacogenomics and Precision Medicine and Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL, USA; [b]Experimental Therapeutics Group, University of Florida Health Cancer Center, Gainesville, FL, USA

ABSTRACT

Existing literature demonstrates the benefits of DPYD and UGT1A1 pharmacogenetic (PGx) testing to reduce toxicity from fluoropyrimidines and irinotecan, respectively. The Food and Drug Administration (FDA) has provided UGT1A1-guided irinotecan dosing for 20 years, and in 2025, the FDA and National Comprehensive Cancer Network both updated their guidance to recommend DPYD testing prior to fluoropyrimidine therapy. As such, there is an increasing interest in testing and a need for guidance describing implementation strategies. This review summarizes conclusions from DPYD and/or UGT1A1 implementation initiatives and describes key takeaways related to perspectives, workflow, cost, and supportive care from 32 included articles. Perspectives toward testing were generally positive, although barriers such as turnaround time and cost concerns were still identified. Workflow integration varied by institution, but a clear delineation of duties was consistently necessary. For both DPYD and UGT1A1, real-world studies and modeling data indicate testing is cost-effective. PGx testing was underutilized for supportive care medications despite its relevance, but there is an opportunity to leverage panel-based approaches to increase utilization without additional workflow burden. Description of these key considerations and takeaways reported by those implementing DPYD and/or UGT1A1 PGx testing would be beneficial to institutions in the early phases of implementation.

ARTICLE HISTORY
Received 22 April 2026
Accepted 3 June 2026

KEYWORDS
DPYD; UGT1A1; fluoropyrimidines; irinotecan; pharmacogenetics; oncology; implementation

1. Introduction

Genetic testing for somatic variations (e.g., *BRAF, RAS, HER2, MSI/dMMR*) has been established as a crucial part of personalized medicine to improve patient care in the oncology setting [1,2]. Somatic testing utilizes tumor DNA to identify actionable mutations that assess tumor characteristics, predict prognosis, and inform selection of targeted chemotherapy. While germline testing analyzes inherited genetic variants in healthy cells, germline testing in the oncology setting is typically used to help select targeted treatment or reveal risk of disease development (e.g., *BRCA1* and *BRCA2*). Despite its utility, germline genetic testing is still underutilized in practice. When performed, it is most commonly done in patients with breast, ovarian, pancreatic, and prostate cancer. Germline DNA may also be used for testing pharmacogenes that predict risk of toxicity with certain chemotherapy or supportive care agents, referred to as pharmacogenetic (PGx) testing. PGx testing is performed at an even lower rate than other germline tests in the oncology setting, and awareness of its availability among patients is low [3]. Specifically, *DPYD* and *UGT1A1* phenotypes predict risk of toxicity with fluoropyrimidines and irinotecan, respectively.

Dihydropyrimidine dehydrogenase (DPD) is an enzyme encoded by the *DPYD* gene that catalyzes the initial and rate-limiting step in fluoropyrimidine (i.e., 5-fluorouracil and its oral prodrug capecitabine) metabolism. Variants in *DPYD* can lead to partial or complete DPD enzyme deficiency, thus diminishing crucial drug metabolism and increasing serum concentrations [4]. DPD enzyme activity may be predicted by directly measuring uracil, an endogenous compound metabolized by DPD, or by screening for the presence of decreased- or no-function *DPYD* variants via genotyping. The latter is more widely available in the United States (US). Individuals who are hetero- or homozygous carriers of decreased-function variants are considered intermediate metabolizers (IM) with an activity score (AS) of 1.5 or 1, respectively, and those heterozygous for a no-function and decreased-function variant or homozygous for no-function variants are considered poor metabolizers (PM) with an AS of 0.5 or 0, respectively [5]. Individuals without decreased- or no-function variants are normal metabolizers (NM). Although variants in the *DPYD* gene exist in only about 5% of the population, DPD deficiency can lead to severe, sometimes fatal, toxicity including neutropenia, diarrhea, and mucositis with fluoropyrimidine therapy [4,6]. There is a substantial amount of evidence linking *DPYD* genotype to toxicity risk with fluoropyrimidines, and preemptive dose reductions reduce this risk [7]. Additionally, treatment outcomes have not been shown to be impacted by initial dose reductions when a subsequent upward titration based on tolerability is performed [8]. International regulatory and professional organizations have long recognized the importance of *DPYD*

CONTACT Madeline L. Norris norris.m@ufl.edu Clinical Assistant Professor, College of Pharmacy, University of Florida, PO Box 100486 1225 Center Drive, Gainesville, FL 32610, USA

Supplemental data for this article can be accessed online at https://doi.org/10.1080/14622416.2026.2685871

Article highlights

- *DPYD* and *UGT1A1* pharmacogenetic (PGx) testing reduces risk of severe, potentially life-threatening toxicity with fluoropyrimidines and irinotecan, respectively. Clinical guidelines from the Clinical Pharmacogenomics Implementation Consortium and the Dutch Pharmacogenomics Working Group are available to inform PGx-guided use of these chemotherapeutics.
- The US Food and Drug Administration and the National Comprehensive Cancer Network have provided guidance for *UGT1A1*-guided irinotecan therapy for many years but just recently strengthened their recommendations to test for *DPYD* prior to fluoropyrimidines administration. With the recent strengthening of recommendations, including the addition of a box warning to fluoropyrimidine drug labels, implementation efforts are likely to expand.
- Implementation of PGx in the oncology setting has a unique set of considerations, and there is a need for additional literature describing the experiences of oncology clinics who have done so thus far.
- Perspectives and attitudes, workflow integration, cost and supportive care utilization were described in this literature review as key considerations for PGx implementation in oncology.
- Providers and patients both generally had positive attitudes toward testing, but providers saw more value in *DPYD* testing than in *UGT1A1*.
- Perceived barriers to implementation included long turnaround times delaying treatment, cost, and a lack of standardized recommendations. Educational efforts, particularly on the literature supporting cost-effectiveness and the availability of clinical guidelines, can mitigate many of these perceived barriers.
- Establishing a workflow that ensures patients are tested pretreatment is especially important in the oncology setting. The interprofessional nature of oncology clinics provides opportunity for nurses, pharmacists, and other staff to help facilitate pretreatment testing.
- Automated clinical decision support tools are effective to help facilitate test ordering and dose reductions when appropriate.
- The cost-effectiveness of genotyping for PGx-guided chemotherapy use is shown in the literature. This plays a key role in obtaining buy-in from an institutional and payer perspective.
- Panel-based PGx testing to inform supportive care medications is underutilized but is relevant to medications commonly prescribed to oncology patients such as antiemetics, PPIs, opioids, and NSAIDs.

testing for fluoropyrimidines, and those in the US have done so more recently. Evidence-based, peer-reviewed guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG) for *DPYD*-guided use of fluoropyrimidines have existed since 2013 and 2011, respectively, and they continue to be updated as new evidence arises [9,10]. Additionally, in a 2020 press release the European Medicines Agency (EMA) mandated testing for DPD deficiency via genotyping or by measuring endogenous uracil concentrations prior to fluoropyrimidine initiation [11]. The US Food and Drug Administration (FDA) did not mandate testing until 2025 when they added a Boxed Warning stating that *DPYD* testing should be performed unless immediate treatment is necessary [12]. Shortly following this label change, the National Comprehensive Cancer Network (NCCN) strengthened the language in their colon and rectal cancer guidelines to align with the FDA [13]. All organizations recommend avoiding the use of fluoropyrimidine medications in those with complete DPD deficiency, and some provide dosing guidance to minimize toxicity in those with partial deficiency (i.e., *DPYD* IMs). Both CPIC and DPWG currently recommend a dose reduction of 50% in all IMs.

The UDP glucuronosyltransferase 1A1 enzyme (UGT1A1) is encoded by the gene of the same name, *UGT1A1*, and is involved in irinotecan metabolism by converting its active metabolite (SN-38) into a water-soluble form for excretion. Toxicity with irinotecan is increased in the presence of genetic variants that reduce UGT1A1 enzyme activity, leading to a buildup of its active metabolite and harmful adverse effects (e.g., neutropenia and diarrhea) [14]. Similar to *DPYD*, an individual with one decreased-function allele is considered an IM and those with two decreased-function alleles are considered a PM. Although IMs have an increased risk of severe adverse effects with irinotecan when compared to NMs, variants in *UGT1A1* are common and about half of the general population are IMs [15]. Unlike *DPYD* and fluoropyrimidines, the concern for an increased risk of severe toxicity with irinotecan is centered around homozygous carriers, or PMs, which make up about 10–15% of the general population. The association between a *UGT1A1* PM phenotype and adverse effects from irinotecan is strongly supported by the literature, particularly in those receiving higher doses (e.g., >150 mg/m^2) [16–18]. Available clinical guidance to inform *UGT1A1*-guided irinotecan therapy is not as robust as *DPYD*-guided fluoropyrimidine use, but there is a growing body of medication recommendations from professional organizations, nonetheless. DPWG most recently published evidence-based *UGT1A1*-irinotecan guidelines in 2022 and recommend an initial dose reduction in *UGT1A1* PMs [19]. The DPWG guidelines also acknowledge that *UGT1A1* NMs will likely tolerate doses increased beyond standard regimens, and this may have a positive impact on treatment outcomes. However, there is currently insufficient evidence to guide specific differences in irinotecan dose requirements in IMs and NMs. Hence, dosing guidance is typically only applied clinically to *UGT1A1* PMs. The FDA drug label for irinotecan has suggested to considering a dose reduction of at least one level (~30%) when administering irinotecan to known PMs since 2005 [20]. Currently, the extent of language in the NCCN guidelines for colon cancer is limited to suggesting additional caution in *UGT1A1* PMs [13].

Despite the availability of multiple evidence-based guidelines, the long-standing recommendation from the FDA for *UGT1A1*-guided use of irinotecan, new boxed warning for preemptive *DPYD* testing with fluoropyrimidines and acknowledgment by NCCN, PGx-guided chemotherapy is not widely acknowledged as standard care. Interest in implementation is growing as the utility of using PGx to reduce toxicity from common chemotherapy regimens is increasingly being recognized by professional organizations. The implementation of PGx in any clinical setting varies greatly between institutions and has been reported on for over two decades, but historical descriptions of its implementation specifically in the oncology setting are more limited. There is a need for more literature describing implementation strategies in this setting. The nature of oncology treatment provides a unique set of concerns for PGx testing, with one of the most important being that no negative impact on treatment outcomes is observed. Additionally, preemptive testing is crucial as subsequent chemotherapy dose adjustments to optimize dosing and achieve a balance of tolerable side effects and treatment effectiveness is already standard practice. Similar to medications in which therapeutic drug monitoring is used, additional dose adjustments following initial dosing are unlikely to be made based

on PGx test results alone. This makes turnaround time and an efficient workflow particularly important. Cancer treatment is also associated with substantial costs to the patient at baseline, so unnecessary charges from the addition of a test not shown to be cost-effective are less likely to be adopted. Workflow integration, stakeholder perspectives, and cost all serve as potential barriers to navigate when implementing PGx in the oncology setting. Thus, a thorough description of these key considerations and takeaways reported by those implementing *DPYD* and/or *UGT1A1* PGx testing would be beneficial to institutions in the early phases of implementation. Herein we describe common *DPYD* and/or *UGT1A1* implementation considerations reported in the literature.

2. Literature search

A literature search in PubMed was performed in April 2025 using keywords and Medical Subject Headings (MeSH) terms to capture descriptions of *DPYD* and *UGT1A1* genotype-guided chemotherapy implementation efforts and perspectives in the real-world oncology clinic setting (Table S1). The search was limited to articles published between 1998 and April 2025, all of which were independently screened for inclusion. Articles describing *DPYD* and *UGT1A1* implementation efforts were included if they addressed at least one of the four predetermined domains: perspectives and attitudes around testing, cost, workflow integration, and supportive care utilization of PGx testing in addition to genotype-guided chemotherapy (Table 1).

Exclusion criteria eliminated review articles, non-human studies, publications not in English, those not related to oncology, and articles which did not address either gene of interest. Articles were screened and categorized by the authors (MPO, CV). Relevant articles known to the authors that did not result, or those published after the date the search was performed, were subsequently included for analysis. Considerations and observed trends among implementation efforts were summarized and are described below. Inclusion criteria were not mutually exclusive; therefore, different aspects of the same article may be described in multiple domains.

The initial search resulted in 518 articles (Figure 1). After author screening, only 23 resulting articles fit inclusion criteria with the most common exclusion reason being that no domain of interest was described. Many of these excluded

Table 1. Categorization of included articles by domain.

Category	Inclusion criteria
Perspectives and attitudes	• Reports opinions on *DPYD* and/or *UGT1A1* implementation from any perspective – provider, patient, etc. • Perceived barriers, benefits, or limitations • Any qualitative aspect of implementation
Workflow integration	• Describes *DPYD* and/or *UGT1A1* testing implementation logistics (e.g., testing method, ordering process or timeline, turnaround time, clinical decision support, medication recommendations)
Cost	• Reports overall cost or cost effectiveness of implementation • Describes willingness to pay
Supportive Care utilization	• Describes testing for PGx genes relevant to supportive care (e.g., *CYP2D6*, *CYP2C19*, *CYP2C9*) in addition to *DPYD* or *UGT1A1* • Describes any *DPYD* or *UGT1A1*-focused implementation effort with a supportive care element (e.g., pain, nausea, reflux, psychiatry)

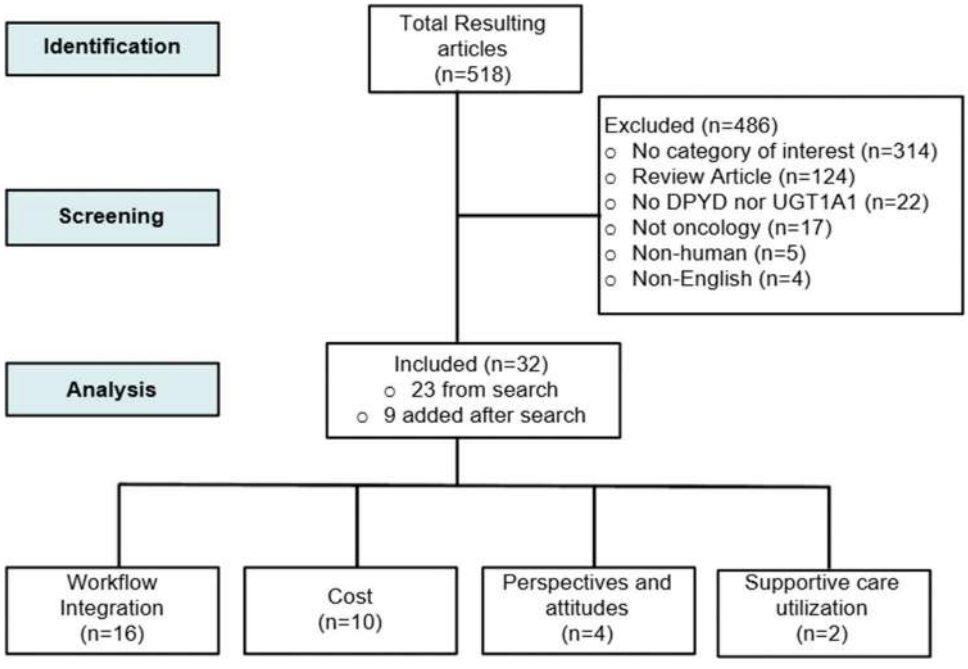

Figure 1. Consort diagram of article identification, screening, and analysis.

articles described the relationship between *DPYD* and/or *UGT1A1* genotype and pharmacokinetics or chemotherapy toxicity but did not describe implementation specifics. An additional nine relevant articles known to the authors were added for analysis following the formal literature search. Most articles ($n = 16$) included aspects of the institution's workflow integration, ($n = 10$) investigated overall cost or cost-effectiveness, and fewer described patient and/or provider perspectives ($n = 4$) and supportive care utilization ($n = 2$). Herein we describe the key take aways from these four domains.

3. Perspectives and attitudes

Several surveys have been performed assessing perspectives and attitudes around PGx testing in the oncology setting from both the patient and provider perspective [21–24]. Attitudes around *UGT1A1* testing were less frequently described in the literature than that of *DPYD*, which exemplifies how the current conversation around PGx testing to guide chemotherapy agents is largely dominated by *DPYD* and fluoropyrimidines. In fact, one 2024 survey distributed to 156 clinicians reported that 22% of respondents routinely test for *DPYD*, while only 1% routinely test for *UGT1A1* [23]. More clinicians reported finding value in having *DPYD* results available prior to fluoropyrimidine administration (77%) than *UGT1A1* for irinotecan (53%). Additionally, a large disparity existed in the perceived value of *DPYD* and *UGT1A1* genotyping for those who responded "Unsure"; 30% of respondents were unsure of *UGT1A1's* value, while this was the case for only 15% when asked about *DPYD's* value. Opinions on when performing PGx testing is appropriate were also dependent on treatment setting, with more clinicians being willing to dose reduce fluoropyrimidines and irinotecan in the palliative care setting than curative.

In a study assessing healthcare providers' perspectives on the clinical utility of PGx testing in general, hematology/oncology physicians were among those most familiar with PGx testing (57.2%), only second to psychiatrists (80%) [25]. They also reported that pediatric hematology/oncology had the highest proportion of physicians perceiving benefits of PGx testing (63.8%), followed by anesthesiology/pain/surgery and psychiatry. These general perceptions of PGx testing by oncologists are consistent with the values summarized in included articles that specifically inquired about *DPYD* and *UGT1A1* genotyping (77%–83% for *DPYD* and 53%–83% for *UGT1A1*) [22,23].

Overall, oncologists are receptive to PGx implementation efforts and perceive a benefit in doing so. In fact, one pharmacist-led PGx screening pilot program reported that 96% of oncologists were willing to offer PGx testing to their patients beyond the trial period [22]. However, several perceived barriers were consistently reported in the literature. A lack of clear dosing guidance and potential liability were significant concerns expressed by clinicians, especially for those at institutions in the pre-implementation phase. Even when clinicians became aware of updated guidance from organizations such as the FDA, a desire for more definitive and clear language was expressed, particularly for a specific assay recommendation to use for testing. Factors such as cost/reimbursement, a lack of infrastructure, patient identification, and turnaround time became more prominent perceived barriers post-implementation. A wide range of acceptable turnaround times have been reported, ranging anywhere from 2 to 21 days [24]. This range also depended on the treatment setting, however, with one survey indicating that most clinicians believed up to 7 business days were acceptable in palliative settings, while only 5 business days were acceptable in the curative setting.

Patient perspectives are equally important considerations for implementing PGx testing. Two surveys explicitly described attitudes and perspectives on *DPYD* and *UGT1A1* PGx testing reported by patients [21,22]. Similar to clinician perspectives, cost was noted as being among the most significant factors of consideration for patients being offered *DPYD* and/or *UGT1A1* genotyping for their care. One focus group found that many patients were unaware of the existence of PGx testing initially but noted that their understanding was improved by conversations with their care team [21]. Importantly, they consistently preferred to learn about their PGx test results from either an oncologist or pharmacist but felt that verbal conversations about testing via phone, telehealth, or in person were all appropriate methods. One survey of patients who previously received *DPYD* and/or *UGT1A1* testing found that nearly 90% of respondents felt that their PGx test was either 'extremely' or 'quite a bit' relevant and valuable to their cancer treatment. Still, only 46% of these patients reported not worrying about the impact of test results on their dosing regimen. Patients that expressed concern described a fear that dose adjustments could reduce the efficacy of their treatment, a concern that has been echoed by clinicians.

4. Workflow integration

4.1. Gene ordering and sample collection

Across published PGx implementation efforts, the ordering and collection processes for *DPYD* and *UGT1A1* testing varied depending on institutional resources, laboratory access, and clinical culture, yet several consistent themes have emerged.

As expected, nearly all programs attempted to perform preemptive genotyping to ensure actionable results were available prior to drug initiation. Most implementation initiatives reported oncologists as the team member responsible for placing PGx orders; however, several institutions have successfully incorporated pharmacists and, less frequently, nurses or research coordinators as being responsible for helping to initiate PGx test orders [26–28]. These models also utilized nurse coordinators or research staff to initiate consent and sample collection in parallel with treatment planning [27,29]. The need for standardized consent processes and patient education is stressed, as unfamiliarity with germline testing occasionally slowed ordering during initial rollout phases [27,30]. Across diverse health systems, from academic hospitals in Europe and Asia to community and rural centers in North America and Australia, the most effective workflows were those embedding PGx orders directly into chemotherapy planning and leveraging multidisciplinary collaboration to sustain timely preemptive testing [24,26–28,31–34].

Blood and buccal samples were the only sample types noted in the summarized implementation efforts, although assays do exist for other sample types (e.g., saliva and skin biopsy) [35,36]. Blood and buccal sampling each provide unique pros and cons, and selection largely depended on lab capabilities and institutional workflow. Blood sampling via peripheral venipuncture was the most common collection method, accounting for over 70% of reported workflows [37–39]. This was favored by many institutions considering it could easily be incorporated into routine pre-treatment laboratory draws completed by infusion nurses, thus minimizing additional clinic visits and time. Several programs, however, described using buccal swab samples. This method is less invasive and, in some settings, may be a logistically simpler alternative [30,32]. This was particularly the case in outpatient and rural settings where phlebotomy access is not immediately available. Buccal collection was generally performed by nurses or pharmacists at the point of care, taking less than 5 minutes, and was valued for enabling patient self-collection when blood draws were delayed. One multicenter initiative reported using telehealth services and providing patients with self-sampling cheek swab kits [31]. They showed that buccal swab genotyping achieved a 100% sample success rate with no recollections being warranted, despite blood samples generally yielding higher quality DNA.

4.2. Turnaround time

Average and median turnaround times (TAT) varied per implementation effort and ranged greatly from as quickly as 3 days to as long as 2 weeks. In some cases, TAT varied by location type in the same institution, with urban sites having faster result times compared to suburban sites (10 vs 13 days) [40].

Testing location was a significant workflow determinant affecting TAT for PGx results. In-house laboratories, typically institutional molecular diagnostics or clinical pharmacology units, offered the advantage of short turnaround times, often reporting results within 3–7 business days with a mean of 6 days [32,33,41]. Additionally, in-house testing offered greater control over PGx interpretation reports and allelic coverage [27,33]. In contrast, institutions performing send-out testing to commercial laboratories came at the cost of longer turnaround times, averaging 8–10 days, and occasional treatment delays if tests were ordered too close to planned therapy initiation [27]. Although send out tests were consistently done through accredited laboratories, some programs noted that courier schedules and sample batching likely added further lag compared to in-house processing [24].

Despite a consistent emphasis on performing preemptive testing, there was a wide range (57–96%) in the percent of results that returned prior to chemotherapy. Some programs reported up to 96% of results returning prior to chemotherapy, while others observed only 57% of tests resulting preemptively [28,31,32,40]. Results from one large community-based health system in the US found that a total of 72.5% of tests resulted were interpreted and communicated to the provider prior to the scheduled start of the patient's chemotherapy regimen [28]. This was likely a result of the variable turnaround times reported among institutions but also influenced by institution-specific processes and procedures.

4.3. Clinical decision support

Clinical decision support (CDS) tools have been designed in the electronic health record (EHR) to prompt the ordering of PGx tests, to warn the clinician team of patients with drug–gene interaction, to interpret PGx test results, and to provide recommended dose adjustments [27,29,32,40,42,43]. Epic's Genomic Module, particularly the Genomic Indicators feature, was specifically noted in some cases to effectively help facilitate CDS development and implementation [29]. To support the test ordering workflow, either embedded pretest alerts or standardized order sets were used once a fluoropyrimidine or irinotecan-containing regimen was selected. Integrating pretest alerts early within the prescribing process allows pharmacists, nurses, or research coordinators to be involved in helping to facilitate test ordering by "pending" tests for an oncologist's co-signature [27,29,40]. Sites that lacked automated test prompts reported lower preemptive testing rates and occasional chemotherapy delays [27,32]. A 2024 survey found that about 50% of sites surveyed currently implementing *DPYD*-guided fluoropyrimidines still relied on individual clinicians to remember to order testing without the assistance of any electronic reminders integrated into their workflow [27]. Posttest CDS tools were also integrated into the EHR and relied on discrete resulting of genotype. Hospitals with established local or in-house testing described coordinated electronic workflows in which results automatically populated structured fields in the EHR and thus were able to automatically trigger CDS alerts [29,32,40]. Both interruptive pop-up alerts and non-interruptive in-line warnings were reported being set up at time of order entry and/or verification showcasing the many possible approaches to CDS infrastructure, which depends on institution-specific workflows and preferences [29,32].

In many cases, dose recommendations were provided via CDS tools and largely supported by a pharmacy team. In multidisciplinary settings, one survey found that pharmacists provide PGx-guided chemotherapy dosing services and patient education at about 75% of sites implementing PGx in the oncology setting [27]. Some of these recommendations are documented as a consultation note to remain as a permanent part of the patient's health record, while others reported that dose recommendations were emailed directly to the treating oncologist [32]. In all cases, the ultimate prescribing decision was still left at the discretion of the treating oncologist.

DPYD genotype-guided fluoropyrimidine dose recommendations were nearly all in line with current CPIC and DPWG guidelines; to perform a 50% dose reduction in IMs and to avoid fluoropyrimidines in PMs. CPIC guidelines were updated in 2018 to strengthen the dose recommendation for IMs with an AS = 1.5 from 25–50% to 50% after additional evidence suggested that a 25% dose reduction was insufficient at reducing adverse effects in this patient population. The one institution who reported recommending a 25% dose reduction in IMs with an AS = 1.5 adjusted this in 2019 to align with CPIC's update [44]. As expected, no institution recommended use of

fluoropyrimidines in known *DPYD* PMs. However, consistent with CPIC guidelines, a strong dose reduction of at least 75% was provided as an alternative option for PMs with an AS = 0.5.

There are currently no existing CPIC guidelines for *UGT1A1* and irinotecan. Hence, most irinotecan dose reductions described were made according to DPWG clinical guidelines and/or the FDA drug label. In most cases, no dose recommendation was given for *UGT1A1* NMs and IMs (e.g., *1/*28 or *1/*6), and a 30% initial dose reduction was given for PMs (e.g., *28/*28 or *6/*6). One institution, however, also recommended a 25–30% dose reduction in IMs who received doses >180 mg/m^2 [28]. Importantly, upward dose titrations based on patient tolerability following the initial PGx-guided dose reduction of fluoropyrimidines or irinotecan were consistently encouraged across implementation efforts.

5. Cost

Beyond clinical outcomes, financial viability is fundamental pillar of adoption in the health system. The upfront cost of testing, lack of standardized reimbursement, and unclear payer coverage are consistently cited as the primary barriers preventing the widespread clinical implementation of PGx testing. Coverage varies by insurer, reimbursement policy, and by accepted societal willingness to pay (WTP) thresholds, which in the U.S. have historically been evaluated between $50,000 and $100,000 per quality-adjusted life year (QALY) [45,46]. More recent US-based cost-effective analyses, however, reference an acceptable WTP threshold range between $100,000 and $150,000. Cancer-related analyses in particular were significantly more likely to use the higher threshold of $150,000 than non-cancer-related analyses [47].

For both *DPYD* and *UGT1A1*-guided chemotherapy, real-world implementation data and modeling show fewer costly toxicities without loss of efficacy, though the economic value falls into two distinct categories; cost-saving or cost-effective. Several studies conclude that preemptive genotyping is strictly cost-saving, meaning the upfront assay costs are completely recouped by the prevention of severe toxicities [48–50]. Conversely, other models classify testing as highly cost-effective, indicating that while it may marginally increase initial expenditures, the clinical benefit falls well below standard societal willingness-to-pay thresholds [45,51]. It is important to distinguish between these two types of evidence: economic modeling (such as Markov models) simulates hypothetical patient cohorts over time to predict theoretical cost-effectiveness based on assumed perfect adherence [45,46]. Real-world implementation studies, however, capture actual clinical resource utilization and reflect how testing performs amidst human error and logistical challenges, confirming that theoretical savings translate into actual reduced hospitalization costs [50,52]. Rather than simply reporting isolated cost-effectiveness ratios, these economic models reveal the critical clinical thresholds required for PGx testing to remain viable in practice. First, cost-effectiveness is highly dependent on the assumption that genotype-guided dose reductions maintain efficacy. For example, if reducing the irinotecan dose in *UGT1A1* homozygotes compromises survival by even a small margin, preemptive testing may lose its economic advantage [46,49]. Furthermore, patient ancestry and the local prevalence of genetic variants directly dictate value. Because *UGT1A1* variant frequencies differ globally, genotyping is highly cost-saving for populations of African and European descent but explicitly not cost-effective for populations of Asian descent, where the variant frequency falls below the ~9% threshold for economic viability [49]. Finally, institutional dosing schedules matter; while testing is highly valuable prior to high-dose, infrequent irinotecan regimens, institutions utilizing low-dose weekly regimens may not see the same economic justification.

The absolute cost of the PGx assay itself is one of the primary drivers of the extent of cost-effectiveness; models indicate that *DPYD* testing becomes a dominant, cost-saving strategy if the assay cost drops below $96 but exceeds acceptable cost-effectiveness thresholds if the price rises above $286 [45]. It is worth noting that the acceptable WTP per QALY threshold used in this study was $50,000, which is much lower than updated estimations in the United States. If evaluated at these higher thresholds, *DPYD* testing priced > $286 would still be considered cost-effective. Similarly, cost-effectiveness is highly sensitive to the background costs of treating severe toxicities within a specific healthcare system. Because the primary economic benefit of PGx testing in the oncology setting is hospitalization avoidance, institutions with higher standard fees for treating events like febrile neutropenia will see a magnified economic benefit from preemptive screening. For instance, *DPYD* testing becomes universally cost-saving if the local cost of a toxicity-related hospitalization exceeds $27,778 [45].

Overall, pharmacoeconomic literature of preemptive testing *DPYD* and *UGT1A1* demonstrates significant value. As preemptive testing becomes more routine in oncology, the expanding use of multi-gene panels further strengthens this economic rationale. Specifically, single-gene testing costs reported in these models range from $174+ for *DPYD* to between $102 and $375 for *UGT1A1*. However, the cost of a multi-gene panel closely mirrors the cumulative cost of ordering these single-gene tests sequentially. By proactively integrating a wider array of actionable genetic data into the electronic health record, panel-based testing offsets the future financial and administrative burdens of ordering sequential single-gene tests, follow-up office visits for therapeutic inefficacy, and costly emergency department admissions for adverse drug reactions [53]. Because these panels evaluate multiple genes simultaneously, which is particularly crucial in gastrointestinal cancers where patients frequently receive fluoropyrimidines, irinotecan, and supportive care medications, they may offer superior economic value.

6. Supportive care utilization

Only two institutions explicitly reported their use of panel-based PGx testing to inform supporting care medications in the oncology setting, indicating that this practice is not yet widespread even among those who are actively performing PGx testing for chemotherapy agents. Relevant PGx-informed medications include nausea (ondansetron), pain (opioids and

NSAIDs), acid-reflux (proton-pump inhibitors), anxiety (SSRI/SNRIs), infections (voriconazole), and anticoagulation (warfarin). Cicali et al. observed that the overall prevalence of individual supportive care medications informed by PGx testing was lower than the investigators anticipated when excluding antiemetics (i.e., less than 50%), but only 4.9% of patients were not on any PGx-informed supportive care medication [54]. Nearly all (>90%) patients were on the antiemetic informed by CYP2D6 genotype, ondansetron, as was expected, and it is worth noting the rate of use for relevant opioids (31.2%), proton pump inhibitors (23.6%), and antidepressants (18.6%). The patient population described from this institution included two cohorts, an intervention arm who received supportive care medication recommendations based on PGx results and a control arm who did not. Of the 72 patients in the intervention arm, there was a low rate of provider action to adjust medications based on PGx results within 2 weeks of initiating chemotherapy. The authors noted that reoccurring provider education may be necessary to ensure that appropriate adjustments are performed beyond chemotherapy regimens when actionable genetic results relevant to supportive care are available.

Kasi et al. demonstrated the feasibility of integrating PGx testing with a panel of pharmacogenes to reduce adverse effects from both supportive care and chemotherapy agents at their institution [42]. Buccal samples were collected at point of care, and the OneOme RightMed genotyping panel of 27 genes was performed. Both chemotherapy (e.g., *UGT1A1, DPYD*) and supportive care genes (e.g., *CYP2D6*, *CYP2C19*, *CYP2C9*) were included in this single panel, so obtaining the necessary genetic information to inform supportive care medications did not add any additional steps to their proposed workflow. At this institution, pharmacists were the primary personnel responsible for interpreting test results and developing specific medication recommendations for physicians involved in various aspects of a patient's care. Ultimately, dose adjustments performed were still the discretion of the medical oncologist.

7. Future perspectives

Most, if not all, oncology institutions have an established workflow for performing somatic genetic testing as a part of standard care, but they lack the same for preemptive PGx testing. PGx testing is not yet widespread standard of care, particularly in the oncology setting. Despite the broad date range of eligible publication dates in the initial search, 75% of included articles were published in 2021 or later, exemplifying the rapidly growing relevance of PGx implementation in oncology. As more institutions embark on the beginning phases of implementation, learning from the challenges and achievements of others will be key for sustained success. The main takeaways and considerations for each domain analyzed in this review are summarized in Table 2. Many of the resulting implementation efforts were performed in the US. Considerations, particularly those related to cost, are therefore most applicable to health systems based in the US in which private insurance is the primary payer. Further analyses focused on public healthcare models would help inform *DPYD* and *UGT1A1* implementation on a global scale.

Clinicians generally perceive value in performing PGx testing prior to chemotherapy, although more so for *DPYD* testing

Table 2. Takeaways per relevant consideration for implementing PGx-guided chemotherapy.

Consideration	Main takeaway(s)
Patient and Provider Perspective	• Perspectives and attitudes toward testing were generally positive across all stakeholders. • Patients prefer to have initial discussions around PGx testing in person with their oncologist or pharmacist. • Perceived barriers to address include treatment delay due to turnaround time, lack of standardized recommendations, and cost. • Perceived value of testing is higher for *DPYD* than *UGT1A1*, but can be improved by educational efforts.
Workflow Integration: Gene Ordering and Sample Collection Processes	• Establishing a process for *pre-emptive* testing is more critical in oncology than other clinical areas where *reactive* testing may be acceptable. • With large, interprofessional teams being common in the oncology setting, there is opportunity to involve various healthcare professionals in the gene ordering and sample collection processes. This may minimize the workload burden on a single individual, but a clear delineation of duties is necessary. • Blood sample collection methods may easily integrate into standard lab draw already being performed, but buccal samples provide a less invasive technique without compromising result accuracy.
Workflow Integration: Turnaround Time	• Although fast turnaround times are ideal, tracking and understanding institution-specific result turnaround times help to proactively plan a workflow that allows adequate time for result return. • Longer turnaround times are generally more acceptable in the palliative care setting than curative.
Workflow Integration: Clinical Decision Support	• Automated pre-test alerts effectively facilitate PGx test ordering. • Dose recommendations were generally consistent among institutions and in-line with professional guidance (e.g., CPIC, DPWG). • Pharmacists are a key team member for providing medication guidance based on *DPYD* and/or *UGT1A1* phenotype.
Cost	• Establishing cost-effectiveness is a key factor influencing stakeholder buy-in for implementation, particularly on the institutional and payer level. • Growing recognition by professional organizations is likely to improve reimbursement rates.
Supportive Care Utilization	• Nearly all chemotherapy recipients receive at least one supportive care medication informed by PGx results, most commonly ondansetron. • Panel-based testing provides comprehensive opportunities for improving patient care without adding steps to the ordering process nor a significant additional cost. • Continued oncologist education is needed to improve acceptance rate of PGx-guided supportive care medication recommendations.

than that of *UGT1A1*. There is a clear need for continued clinician education, as medical oncologists' unfamiliarity with testing options, interpretation, and guideline-directed dose modifications is a primary barrier to widespread clinical adoption [27,40]. Patients are also generally unfamiliar with PGx testing, but they report seeing its value once educated. Verbal education provided by either an oncologist or pharmacist on pharmacogenetic testing was preferred by patients. Developing a collaborative environment between PGx specialists and the oncology care team will incorporate an educational resource for both treating clinicians and patients. This helps provide oncologists with necessary background information on clinical utility, increases uptake in testing, ensures appropriate dose modifications are being made, and improves patient comfortability with their care. All of which contribute to improved patient care outcomes.

Institutional efforts consistently showed that the success of test implementation depended not only on assay result timing, but also on interpersonal coordination. The most effective workflows were those embedding pharmacogenomic orders directly into chemotherapy plans and leveraging multidisciplinary collaboration to sustain timely preemptive testing. Oncology clinic visits, particularly in the early phases of care when PGx is most likely to be ordered, involve a large, multidisciplinary team. The success of test implementation in oncology settings requires having a clear delineation of ordering responsibility and sample handling among the many personnel involved in a single patient's care. In contrast, PGx implementation efforts done in typical clinical settings such as primary care may have minimal personnel (e.g., only a nurse and a physician) involved in a patient's clinic visit. The responsibility for lab ordering will often clearly fall on a single individual in these settings. Institutions with clear protocols describing the responsibility for test ordering reported this as a contributing factor to successfully obtaining results prior to initiating chemotherapy. A wide range of acceptable turnaround times of PGx testing have been reported, but all clinicians agree that avoiding a delay in chemotherapy is ideal. Understanding nuances of institution-specific workflows will allow implementers to design a system in which testing is offered at the earliest possible timepoint in care when fluoropyrimidine and/or irinotecan therapy is deemed likely. By offering testing as soon as possible following patient identification, longer turnaround times based on individual laboratory capabilities may be worked around. Pre-treatment ordering led by oncologists, supported by pharmacists, nurses, and other personnel, and synchronized with baseline laboratory collection represents a highly effective model for implementing *DPYD* and *UGT1A1* testing. CDS tools may also be leveraged to optimize nearly all aspects of the workflow to prompt the ordering of PGx tests, to provide test result interpretations, warn clinicians when gene–drug interactions are present, and to provide standard recommended dose adjustments. Feasibility outcomes suffered when relying on individuals to remember to order testing without CDS and therefore have shown to be another key factor for successful implementation.

Institutions performing testing in-house achieved markedly faster results, often reporting within 3–7 days, enabling same-week therapy initiation, while send-out models require more robust coordination. Aligning sample collection with routine laboratory draws was repeatedly underscored as a low-cost, high-yield efficiency measure due to its easy integration into already established processes. Blood sampling was the most common approach, but buccal swabs provide a practical alternative that can facilitate at-home self-sampling and telehealth consultations where access to local clinics is limited. Sample preference should be chosen based on lab capabilities and individual preference, as both methods yield equally accurate results. Ultimately, those performing the sample collection (e.g., nurses) should be at the forefront of these discussions to ensure a smooth integration into their workflow.

Recognition and clinical guidelines from professional organizations are a major factor when gaining stakeholder support for PGx implementation in the oncology setting. Although concern for a lack of dosing guidance among clinicians has been cited, both *UGT1A1*-guided irinotecan and *DPYD*-guided fluoropyrimidine therapy have multiple reliable, evidence-based sources to base adjustments on. *DPYD* is acknowledged by the FDA, NCCN, and CPIC, while there is less clinical guidance available for *UGT1A1*. This likely played a role in the lower perceived value of *UGT1A1* genotyping compared to *DPYD* among clinicians. *UGT1A1*-guided irinotecan use is described in both the FDA's drug label and in guidelines from a highly respected international PGx resource, DPWG, yet most clinicians are likely minimally aware of its clinical utility. An emphasis should be placed on providing strong educational background on the available evidence and guidance from professional organizations that are available in the early phases of implementation. Nearly all current implementation efforts are providing consistent medication recommendations established by CPIC, the FDA, and/or DPWG, and this widespread consistency among institutions may help facilitate gaining internal stakeholder support for those just getting started.

Not only does guidance from professional organizations improve stakeholder support, but it also influences testing cost and reimbursement rates. While CPIC guidelines (*DPYD*) and the FDA labeling guidance (*DPYD* and *UGT1A1*) have existed for years, payer coverage policies in the U.S. remain inconsistent [53]. In contrast, recommendations from the European Medicines Agency have driven more systematic reimbursement and integration across European healthcare systems [50,55]. The landscape of professional guidance in the US has still rapidly changed in the last year, and reimbursement rates, particularly for *DPYD* genotyping, are expected to improve with the significant strengthening of language from the FDA and NCCN since October 2025. This would have a positive impact on one of the major perceived barriers to test implementation, cost, and reimbursement. Support from professional organizations is not the only factor influencing insurance coverage, however. Payers frequently cite the lack of robust cost-effectiveness data as a primary reason for refusing to reimburse testing [50]. They place an emphasis on determining whether upfront coverage for testing will ultimately decrease downstream healthcare expenditures. Showing that preemptive genotyping reduces costly treatment failures, severe adverse events, and hospitalizations provides the compelling economic

argument payers require [49,53]. As cost is among the most commonly cited barriers to clinical use of PGx-guided chemotherapy, familiarity with the current landscape is crucial for new implementation efforts. Individuals have little opportunity to change testing costs outside of participating in advocacy groups for improved reimbursement, but knowledge of general cost, demonstrations of cost-effectiveness, reimbursement rates, and trends in coverage will allow those working to achieve stakeholder buy-in to participate in engaging conversations.

Nearly all chemotherapy recipients will require some form of supportive care medication management to mitigate the severity of or prevent adverse effects associated with chemotherapy. Despite the current lack of widespread use in the oncology setting, NCCN® guidelines do support the use of PGx in certain supportive care settings and recommend consulting a PGx specialist to aid in the appropriate interpretation and use of results. The NCCN® guidelines for adult cancer pain reference published CPIC recommendations to provide specific medication guidance when prescribing opioids (*CYP2D6*), tricyclic antidepressants (*CYP2D6* and *CYP2C19*) and NSAIDs (*CYP2C9*) [56]. Additionally, the NCCN® guidelines for the prevention and treatment of cancer-related infections and cancer-associated venous thromboembolic disease acknowledge that genetic variability may impact dose requirements of voriconazole and warfarin, respectively. Typical cost for panel-based pharmacogenetic testing ranges from $300 to $600, compared to approximately $200–$400 for single-gene tests [57]. This cost continues to decline as genotyping technology evolves. The increasing availability and improving financial feasibility of shifting from single-gene testing to inform only chemotherapy agents to panel-based testing for both chemotherapy and supportive care medications are likely to expand its use. It is reasonable to anticipate that panel-based testing will increase as general interest in PGx testing to inform chemotherapy agents continues to grow.

Author contributions

MLN performed the literature search, MPO and CV screened articles and performed the initial analysis. Writing original draft was completed by MPO, CV, and MLN. Writing review and editing were performed by EJC and DLD.

Disclosure statement

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Funding

This paper was not funded.

References

1. Casolino R, Beer PA, Chakravarty D, et al. Interpreting and integrating genomic tests results in clinical cancer care: overview and practical guidance. CA Cancer J Clin. 2024;74(3):264–285. doi: 10.3322/caac.21825
2. Chakravarty D, Johnson A, Sklar J, et al. Somatic Genomic testing in patients with metastatic or advanced cancer: ASCO provisional clinical opinion. J Clin Oncol. 2022;40(11):1231–1258. doi: 10.1200/JCO.21.02767
3. Shriver SP, Long S, Fleury ME. Views toward pharmacogenomic testing among patients with cancer. JAMA Netw Open. 2025;8(8):e2526714. doi: 10.1001/jamanetworkopen.2025.26714
4. Amstutz U, Froehlich TK, Largiadèr CR. Dihydropyrimidine dehydrogenase gene as a major predictor of severe 5-fluorouracil toxicity. Pharmacogenomics. 2011;12(9):1321–1336. doi: 10.2217/pgs.11.72
5. Henricks LM, Lunenburg CA, Meulendijks D, et al. Translating DPYD genotype into DPD phenotype: using the DPYD gene activity score. Pharmacogenomics. 2015;16(11):1277–1286. doi: 10.2217/pgs.15.70
6. CPIC. CPIC guideline for fluoropyrimidines and DPYD; DPYD frequency table. [cited 2026 Apr 21]. Available from: https://cpicpgx.org/guidelines/guideline-for-fluoropyrimidines-and-dpyd/
7. Otero-Torres S, Rodríguez-Mauriz R, Fort-Casamartina E, et al. DPYD genotyping, fluoropyrimidine dosage and toxicity: an umbrella review of systematic reviews. Pharmaceuticals (Basel). 2025;18(5). doi: 10.3390/ph18050727
8. Knikman JE, Wilting TA, Lopez-Yurda M, et al. Survival of patients with cancer with survival of patients with cancer with DPYD variant alleles and dose-individualized fluoropyrimidine therapy-A matched-pair analysis. J Clin Oncol. 2023;41(35):5411–5421.
9. Amstutz U, Henricks LM, Offer SM, et al. Clinical pharmacogenetics implementation consortium (CPIC) guideline for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing: 2017 update. Clin Pharmacol Ther. 2018;103(2):210–216. doi: 10.1002/cpt.911
10. Lunenburg CATC, van der Wouden CH, Nijenhuis M, et al. Dutch pharmacogenetics working group (DPWG) guideline for the gene-drug interaction of DPYD and fluoropyrimidines. Eur J Hum Genet. 2020;28(4):508–517. doi: 10.1038/s41431-019-0540-0
11. (EMA) EMA. EMA recommendations on DPD testing prior to treatment with fluorouracil, capecitabine, tegafur and flucytosine. 2020 [cited 2026 Apr 10]. Available from: https://www.ema.europa.eu/en/documents/press-release/ema-recommendations-dpd-testing-prior-treatment-fluorouracil-capecitabine-tegafur-and-flucytosine_en.pdf
12. H2-Pharma, LLC. Xeloda (capecitabine) [package insert]. U.S. Food and Drug Administration. Revised 2025 Oct [cited 2026 Apr].
13. National Comprehensive Cancer Network I. NCCN clinical practice guidelines in oncology (NCCN guidelines®) for colon cancer. V.2.2026. 2026.
14. Dean L. Irinotecan therapy and UGT1A1 genotype. In: Pratt VM, Scott SA, Pirmohamed M, et al., editors. Medical genetics summaries [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2015 May 27 [cited 2018 Apr 4]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK294473/
15. Nelson RS, Seligson ND, Bottiglieri S, et al. Guided cancer therapy: review of the evidence and considerations for clinical implementation. Cancers (Basel). 2021;13(7):1566. doi: 10.3390/cancers13071566
16. Liu X, Cheng D, Kuang Q, et al. Association of UGT1A1*28 polymorphisms with irinotecan-induced toxicities in colorectal cancer: a meta-analysis in Caucasians. Pharmacogenomics J. 2014;14(2):120–129. doi: 10.1038/tpj.2013.10
17. Fujita K, Sparreboom A. Pharmacogenetics of irinotecan disposition and toxicity: a review. Curr Clin Pharmacol. 2010;5(3):209–217. doi: 10.2174/157488410791498806
18. Hoskins JM, Goldberg RM, Qu P, et al. UGT1A1*28 genotype and irinotecan-induced neutropenia: dose matters. J Natl Cancer Inst. 2007;99(17):1290–1295. doi: 10.1093/jnci/djm115

19. Hulshof EC, Deenen MJ, Nijenhuis M, et al. Dutch pharmacogenetics working group (DPWG) guideline for the gene-drug interaction between UGT1A1 and irinotecan. Eur J Hum Genet. 2023;31(9):982–987. doi: 10.1038/s41431-022-01243-2
20. IRINOTECAN HYDROCHLORIDE- irinotecan hydrochloride injection [package insert]. Orlando F (USA): Ingenus Pharmaceuticals. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d04f2471-3085-4fc8-a657-bb3918d48e6euAf
21. Wittner V, Purcell J, Cayabyab M, et al. Patient and provider perspectives on the implementation of DPYD testing in oncology care clinics in an academic health system. J Am Pharm Assoc (2003). 2026;66(1):102990. doi: 10.1016/j.japh.2025.102990
22. Glewis S, Krishnasamy M, Lingaratnam S, et al. Patient and healthcare professional acceptability of pharmacogenetic screening for DPYD and UGT1A1: a cross sectional survey. Clin Transl Sci. 2023;16(12):2700–2708. doi: 10.1111/cts.13664
23. Glewis S, Lingaratnam S, Krishnasamy M, et al. Pharmacogenetics testing (DPYD and UGT1A1) for fluoropyrimidine and irinotecan in routine clinical care: perspectives of medical oncologists and oncology pharmacists. J Oncol Pharm Pract. 2024;30(1):30–37. doi: 10.1177/10781552231167554
24. White C, Paul C, Liet E, et al. Implementing DPYD genotyping to predict chemotherapy toxicity in Australia: a feasibility study. Intern Med J. 2025;55(5):741–748. doi: 10.1111/imj.16576
25. Liko I, Lee YM, Stutzman DL, et al. Providers' perspectives on the clinical utility of pharmacogenomic testing in pediatric patients. Pharmacogenomics. 2021;22(5):263–274. doi: 10.2217/pgs-2020-0112
26. Green JK, Hackett LJ, Green DC, et al. Implementation of a pharmacist-guided pharmacogenomics dosing service at a rural NCI-designated comprehensive cancer center. J Oncol Pharm Pract. 2025;31(8):1264–1269. doi: 10.1177/10781552241281936
27. Tracksdorf T, Smith DM, Pearse S, et al. Strategies for DPYD testing prior to fluoropyrimidine chemotherapy in the US. Support Care Cancer. 2024;32(8):497. doi: 10.1007/s00520-024-08674-1
28. Luczak TS, Schillo PJ, Renier CM, et al. Feasibility of preemptive pharmacogenetic testing in colorectal cancer patients within a community oncology setting. J Oncol Pharm Pract. 2022;28(4):842–849. doi: 10.1177/10781552211005529
29. Varughese LA, Bhupathiraju M, Hoffecker G, et al. Implementing pharmacogenetic testing in gastrointestinal cancers (IMPACT-GI): study protocol for a pragmatic implementation trial for Establishing. Front Oncol. 2022;12:859846. doi: 10.3389/fonc.2022.859846
30. Hertz DL, Glatz A, Pasternak AL, et al. Integration of germline Pharmacogenetics into a tumor sequencing program. JCO Precis Oncol. 2018;2(2):1–15. doi: 10.1200/PO.18.00011
31. Glewis S, Lingaratnam S, Lee B, et al. Pharmacogenetic-guided dosing for fluoropyrimidine (DPYD) and irinotecan (UGT1A1*28) chemotherapies for patients with cancer (PACIFIC-PGx): a multicenter clinical trial. Clin Transl Sci. 2024;17(12):e70083. doi: 10.1111/cts.70083
32. Nguyen DG, Morris SA, Hamilton A, et al. Real-world impact of an in-house dihydropyrimidine dehydrogenase. JCO Precis Oncol. 2024;8(8):e2300623. doi: 10.1200/PO.23.00623
33. Saarenheimo J, Wahid N, Eigeliene N, et al. Preemptive screening of DPYD as part of clinical practice: high prevalence of a novel exon 4 deletion in the Finnish population. Cancer Chemother Pharmacol. 2021;87(5):657–663. doi: 10.1007/s00280-021-04236-y
34. Satoh T, Ura T, Yamada Y, et al. Genotype-directed, dose-finding study of irinotecan in cancer patients with UGT1A1*28 and/or UGT1A1*6 polymorphisms. Cancer Sci. 2011;102(10):1868–1873. doi: 10.1111/j.1349-7006.2011.02030.x
35. Laboratories MC. UDP-glucuronosyltransferase 1A1 (UGT1A1), full gene sequencing, varies. [cited 2026 Apr 22]. Available from: https://www.mayocliniclabs.com/test-catalog/overview/610064#specimen
36. Laboratories MC. Dihydropyrimidine dehydrogenase, DPYD full gene sequencing, varies. [cited 2026 Apr 22]. Available from: https://www.mayocliniclabs.com/test-catalog/overview/610051#specimen
37. Anai S, Iwama E, Yoneshima Y, et al. Association of nephrotoxicity during platinum-etoposide doublet therapy with UGT1A1 polymorphisms in small cell lung cancer patients. Lung Cancer. 2018;126:156–161. doi: 10.1016/j.lungcan.2018.11.002
38. Páez D, Tobeña M, Fernández-Plana J, et al. Pharmacogenetic clinical randomised phase II trial to evaluate the efficacy and safety of FOLFIRI with high-dose irinotecan (HD-FOLFIRI) in metastatic colorectal cancer patients according to their UGT1A 1 genotype. Br J Cancer. 2019;120(2):190–195. doi: 10.1038/s41416-018-0348-7
39. Lui G, Treluyer JM, Fresneau B, et al. A pharmacokinetic and pharmacogenetic analysis of osteosarcoma patients treated with high-dose methotrexate: data from the OS2006/sarcoma-09 trial. J Clin Pharmacol. 2018;58(12):1541–1549. doi: 10.1002/jcph.1252
40. Tuteja S, Cayabyab MAS, Hoffecker G, et al. Implementation of DPYD and UGT1A1 testing in patients with GI cancer: a prospective, nonrandomized clinical trial. JCO Precis Oncol. 2025;9. doi: 10.1200/PO-25-00086
41. Wu F, Lu S, Zhang D, et al. Clinical implementation and outcome evaluation of dihydropyrimidine dehydrogenase (DPYD) pharmacogenomic testing for fluoropyrimidine dosing in a Canadian provincial healthcare center. Clin Biochem. 2025;140:111008. doi: 10.1016/j.clinbiochem.2025.111008
42. Kasi PM, Koep T, Schnettler E, et al. Feasibility of integrating panel-based Pharmacogenomics testing for chemotherapy and supportive care in patients with colorectal cancer. Technol Cancer Res Treat. 2019;18:1533033819873924. doi: 10.1177/1533033819873924
43. Paulsen NH, Pfeiffer P, Ewertz M, et al. Implementation and clinical benefit of DPYD genotyping in a Danish cancer population. ESMO Open. 2023;8(1):100782. doi: 10.1016/j.esmoop.2023.100782
44. van Kan AHE, Harmsze AM, Herbschleb K, et al. Optimizing fluoropyrimidine therapy: real-world impact of DPYD genotype-based dosing on severe toxicity rates. Br J Clin Pharmacol. 2026;92(1):269–279. doi: 10.1002/bcp.70266
45. Brooks GA, Tapp S, Daly AT, et al. Cost-effectiveness of DPYD genotyping prior to fluoropyrimidine-based adjuvant chemotherapy for colon cancer. Clin Colorectal Cancer. 2022;21(3):e189–e195. doi: 10.1016/j.clcc.2022.05.001
46. Gold HT, Hall MJ, Blinder V, et al. Cost effectiveness of pharmacogenetic testing for uridine diphosphate glucuronosyltransferase 1A1 before irinotecan administration for metastatic colorectal cancer. Cancer. 2009;115(17):3858–3867. doi: 10.1002/cncr.24428
47. Neumann PJ, Kim DD. Cost-effectiveness thresholds used by study authors, 1990–2021. JAMA. 2023;329(15):1312–1314. doi: 10.1001/jama.2023.1792
48. Hulshof EC, de with M, de Man FM, et al. UGT1A1 genotype-guided dosing of irinotecan: a prospective safety and cost analysis in poor metaboliser patients. Eur J Cancer. 2022;162:148–157. doi: 10.1016/j.ejca.2021.12.009
49. Obradovic M, Mrhar A, Kos M. Cost-effectiveness of UGT1A1 genotyping in second-line, high-dose, once every 3 weeks irinotecan monotherapy treatment of colorectal cancer. Pharmacogenomics. 2008;9(5):539–549. doi: 10.2217/14622416.9.5.539
50. Fragoulakis V, Roncato R, Bignucolo A, et al. Cost-utility analysis and cross-country comparison of pharmacogenomics-guided treatment in colorectal cancer patients participating in the U-PGx PREPARE study. Pharmacol Res. 2023;197:106949. doi: 10.1016/j.phrs.2023.106949
51. Pichereau S, Le Louarn A, Lecomte T, et al. Cost-effectiveness of UGT1A1*28 genotyping in preventing severe neutropenia following FOLFIRI therapy in colorectal cancer. J Pharm Pharm Sci. 2010;13(4):615–625. doi: 10.18433/J3WK5S
52. Toffoli G, Innocenti F, Polesel J, et al. The genotype for DPYD risk variants in patients with colorectal cancer and the related toxicity management costs in clinical practice. Clin Pharmacol Ther. 2019;105(4):994–1002. doi: 10.1002/cpt.1257
53. Abushanab D, Mohamed S, Abdel-Latif R, et al. Dihydropyrimidine dehydrogenase deficiency (DPYD) genotyping-guided fluoropyrimidine-based adjuvant chemotherapy for breast cancer. A cost-effectiveness analysis.

Clin Drug Investig. 2025;45(3):151–163. doi: 10.1007/s40261-024-01413-8
54. Cicali EJ, Eddy E, Gong Y, et al. Implementation of a pharmacogenetic panel-based test for pharmacotherapy-based supportive care in an adult oncology clinic. Clin Transl Sci. 2024;17(7):e13890. doi: 10.1111/cts.13890
55. Roncato R, Bignucolo A, Peruzzi E, et al. Clinical benefits and utility of pretherapeutic DPYD and UGT1A1 testing in gastrointestinal cancer: a secondary analysis of the PREPARE randomized clinical trial. JAMA Netw Open. 2024;7(12):e2449441. doi: 10.1001/jamanetworkopen.2024.49441
56. (NCCN) NCCN. Adult cancer pain guidelines (version 1.2026). 2026.
57. Apted T, Huff A. Pharmacogenomics for improved outcomes and decreased costs in health care. Am J Manag Care. 2023 [cited 2026 Apr 10]. Available from: https://www.ajmc.com/view/pharmacogenomics-for-improved-outcomes-and-decreased-costs-in-health-care#:~:text=Results%20showed%20that%2C%20accounting%20for,28%2C29