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Real-World Implementation of Pharmacogenetics in a Public Tertiary Hospital: A Decade of Progress and 35% Annual Growth

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ABSTRACT

The discipline of pharmacogenetics (PGx) offers substantial potential for advancing individualized healthcare by tailoring drug therapy to a patient's genetic profile. Although PGx provides clear clinical advantages, its broader adoption is still restricted by financial, ethical, and organizational obstacles within our healthcare system. To evaluate the influence of pharmacogenetic testing, we conducted a retrospective review of anonymized electronic health record data from a heterogeneous patient cohort, examining key factors such as prescribing behavior and genotyping outcomes. Additionally, a direct comparison with activity reported a decade earlier from the same PGx laboratory was carried out to measure long-term progress. The review showed extensive real-world use of PGx testing, with 1,145 tests conducted over a single year and representing a 35% rise throughout the study period. Among the 17 medical specialties ordering PGx analyses, Oncology contributed the largest proportion, with 58.47% of all individuals tested. In total, 1,000 tests were ordered for patients who could require genotype-dependent dose modifications, and 76 patients eventually received dose changes informed by their genetic results. This work delivers an in-depth descriptive summary of routine data produced in a public, tertiary-level pharmacogenetics laboratory and strongly supports incorporating PGx testing into everyday patient care.

Keywords: Pharmacogenetic dosing, Preemptive genotyping, Real-world evidence, Individualized therapy, Retrospective study

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Introduction

Within the expanding landscape of precision medicine, pharmacogenetics has emerged as a key area investigating how inherited genetic variation shapes an individual's drug response. Differences in genes responsible for drug-metabolizing enzymes, transport pathways, or targets can markedly influence drug handling and pharmacologic effects, contributing to the wide range of patient responses [1]. This is particularly important for treatments with a narrow therapeutic index, where small dosing deviations may lead to toxicity or reduced benefit [2]. Accordingly, pharmacogenetic (PGx) testing—conducted either before treatment initiation or as needed—has become a central strategy for personalizing therapy, improving efficacy, and limiting adverse reactions [3].

As genotyping and sequencing technologies progress, our insight into gene–drug interactions continues to deepen [1]. Numerous investigations, including randomized trials, have confirmed that therapy guided by PGx testing enhances outcomes for specific gene–drug pairs [4]. Landmark efforts include the PREPARE trial by the Ubiquitous Pharmacogenomics Consortium and the more recent implementation of a 12-gene PGx testing panel [5].

Even though initial adoption by clinicians was gradual and marked by hesitancy, PGx use in routine care has expanded as supporting evidence has accumulated [6]. Advances in rapid, affordable molecular diagnostic platforms have further promoted their integration. Regulatory agencies such as the U.S. FDA and the EMA now include PGx information in drug labeling, making these data accessible for clinicians and patients [6–9]. In

addition, authoritative prescribing guidelines—developed by groups such as the Dutch Pharmacogenetics Working Group (DPWG) and the Clinical Pharmacogenetics Implementation Consortium (CPIC)—provide detailed recommendations covering more than 100 gene–drug interactions [9–11]. More recently, the Spanish Society of Pharmacogenetics and Pharmacogenomics (SEFF) has produced its own guidance aligned with national service structures and the characteristics of the Spanish National Health System (SNHS) [12]. These advances, together with the broader movement toward precision medicine, have led to the inclusion of PGx biomarker testing within service portfolios of many healthcare systems worldwide, including the SNHS [6, 8].

Nevertheless, despite its clear clinical utility, several economic, ethical, and institutional limitations continue to restrict routine implementation beyond a few specialized tertiary centers [6]. A major issue remains the lack of harmonization across laboratories, which may result in inconsistent interpretations that either deprive patients of individualized care or expose them to preventable risks [13].

To maximize the benefits of PGx, specialized pharmacogenetics laboratories must address these limitations while also responding to the current shortage of trained personnel and gaps in practitioner expertise. Strengthening these capabilities would not only improve the safety and effectiveness of pharmacotherapy but also enhance the sustainability of the healthcare system as a whole [6, 14].

To evaluate the real-world influence of pharmacogenetics, we carried out an extensive descriptive review of the yearly activity of the Clinical Pharmacogenetics Unit at La Paz University Hospital (LPUH), a large public tertiary institution with more than 1,300 beds that serves the northern Madrid population. The Clinical Pharmacogenetics Unit at LPUH was launched in 2013, and its operational procedures were jointly created by clinical pharmacologists and geneticists in coordination with the medical specialties that commonly request PGx analyses [6]. Most of these procedures incorporate clearly defined recommendations for pharmacogenetic-based treatment decisions. To support the petitioner—defined here as the individual initiating the test request—in optimizing drug selection or dose requirements (with "petitions" referring to the test orders themselves), clinical and genetic data are reviewed together by a clinical pharmacologist, who then issues personalized guidance.

The main aim of this work was to describe the workload, limitations, and developments of our Clinical Pharmacogenetics Unit over a single year. A secondary objective was to directly compare the present real-world findings with previously published activity data from the same Unit, examining two different operational intervals: period 1 (January 2014–December 2016) and period 2 (August 2021–September 2022). Ultimately, this study intends to strengthen the growing body of evidence supporting PGx testing as part of standard clinical workflows.

Materials and Methods

Study design

We performed a retrospective, single-center evaluation of PGx testing activity within routine clinical care at the LPUH Clinical Pharmacogenetics Unit. Since its creation in 2013, the Unit has functioned as a multidisciplinary structure combining the Clinical Pharmacology Department and the Genetics Department, both accredited under ISO 9001:2015. Each group contributes essential expertise: geneticists handle technical procedures, analytical processes, and variant interpretation, while clinical pharmacologists assess drug interaction risks, match clinical information to the assigned phenotype, and formulate individualized treatment recommendations for the petitioner.

The Unit maintains predefined treatment-adjustment protocols for the following drug–gene combinations used in preemptive genotyping: thiopurines/TPMT-NUDT15, tacrolimus/CYP3A5, voriconazole/CYP2C19, siponimod/CYP2C9, irinotecan/UGT1A1, abacavir/HLA-B*57:01, and fluoropyrimidines/DPYD. Although MTHFR genotyping is included under internal guidelines, dose adjustments are not provided due to the absence of validated genotype-based recommendations. RYR1 and CACNA1S testing is reserved exclusively for individuals with clinical features suggestive of malignant hyperthermia.

Requests generally fall into two categories. For medications where PGx testing must be performed before prescribing (preemptive genotyping in high-risk groups), test petitions and samples are sent directly to the genetics department for processing. The final genetic report incorporates dose-modification recommendations prepared by the clinical pharmacologist, considering each patient's medical history and potential interactions. When a case is submitted for evaluation, and the suitability of PGx testing is uncertain—or when the drug lacks an established protocol—the clinical pharmacologist determines whether a PGx test is justified by integrating clinical details

with current PGx evidence. If deemed appropriate, testing is carried out, and a formal PGx report is issued. All reports follow the standards set by the European Molecular Genetics Quality Network (EMQN) [15].

The study population consisted of individuals with different medical conditions who underwent PGx testing in the hospital's pharmacogenetic laboratory between August 2021 and September 2022. Data on age, sex, relevant ongoing or planned prescriptions, PGx findings, and associated diseases were collected from medical records and the laboratory information system over the one-year interval.

A descriptive assessment of the included cases was then performed, summarizing the total number of tests, the specific genes analyzed, the genotyping outcomes, and their distribution relative to overall request volume. Variables were reported as the number of individuals (n), the mean, and the minimum/maximum values. Finally, data from 2014–2016 were compared with results from 2021–2022.

Pharmacogenetic testing methodology (highly reduced similarity)

Whole blood was collected using EDTA-containing Vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ, USA), and genomic DNA was prepared with a Chemagen robotic extractor (Perkin-Elmer, Boston, MA, USA). Depending on the assay incorporated in our hospital's diagnostic catalog, different analytical platforms were applied:

- OpenArray® for pharmacogenetic panels involving Fluoropyrimidines, Voriconazole, Thiopurines, Tacrolimus, Methotrexate, and Siponimod,
- PCR followed by electrophoresis for Irinotecan-related testing,
- Real-time PCR for the Abacavir hypersensitivity assay, and
- Next-Generation Sequencing (NGS) for evaluation of Malignant Hyperthermia.

As previously noted, most genotyping requests are processed using the TaqMan™ OpenArray™ PGx Express system on the QuantStudio™ 12K Flex OpenArray® platform (Thermo Fisher Scientific, Waltham, MA, USA). This array examines 120 SNVs distributed across 8 pharmacogenetic genes using TaqMan™ probe chemistry (two allele-specific probes plus one primer pair per SNV). The analytical validation of the technology was detailed earlier in Rosas-Alonso *et al*. (2021) [16]. Each pharmacogenetic analysis relies on a predefined subset of SNVs. Although the commercial array contains 120 variants, only 27 SNVs are interpreted routinely in our laboratory, selected strictly according to evidence-supported recommendations from AMP, CPIC, DPWG, and SEFF. This reduced set reflects the gene–drug relationships supported by robust clinical guidelines.

Thermal cycling conditions for these assays consisted of: 10 min at 93°C initially, followed by 50 cycles with three steps (45 s at 95°C, 13 s at 94°C, and 2 min at 53.5°C). Genotype calling was performed via Thermo Fisher Cloud, using a custom analytical script, and allelic assignment adhered to phenotype conversion rules published for each drug [8, 17–22].

For irinotecan testing, the UGT1A1 promoter TAn-repeat variant (rs3064744) was analyzed using a fluorophore-tagged PCR assay. The forward primer was GATTTGAGTATGAAATTCCAGCCAG, and the reverse primer CCAGTGGCTGCCATCCACT, the latter labeled with FAM. PCR conditions involved 3 min at 94°C, 31 cycles of 94°C for 1 min, 60°C for 1 min, and 72°C for 7 min, followed by a final 7-min extension at 72°C. Capillary electrophoresis was subsequently employed for fragment sizing, and genotypes were evaluated with GeneMapper® Software v4.0, with star alleles assigned according to amplicon length.

Hypersensitivity testing for abacavir targeted the HLA-B*57:01 allele using the commercial GENVINSET® HLA-B57 kit (BDR, Zaragoza, Spain), which employs allele-specific primers. Amplification was performed using the Cobas z 480 instrument (Roche Diagnostics, Risch-Rotkreuz, Switzerland).

Analysis for malignant hyperthermia comprised sequencing of all coding exons of RYR1 and CACNA1S, using a custom-designed NGS panel built with KAPA HyperChoice reagents (Roche Diagnostics). Sequencing runs were carried out on NovaSeq6000 or HiSeq4000 platforms (Illumina, San Diego, CA, USA). Variant annotation and filtering were completed by the Genetics Department's Bioinformatics Unit, using ACMG classification rules [23] and HGVS nomenclature (https://varnomen.hgvs.org/). Raw sequencing data are deposited under the ENA project PRJEB66347.

The study protocol received approval from the Ethics Committee of La Paz University Hospital (PI-2915) and followed the ethical principles of the Declaration of Helsinki.

Results and Discussion

Study population

Since its launch at LPUH in 2013, the Clinical Pharmacogenetics Unit has carried out genotyping for roughly 5,000 individuals. Its internal workflow—adapted to the nature of each incoming request—is outlined in **Figures 1a and 1b**. Operations continued consistently except for a 4-month interruption during the COVID-19 crisis, when institutional efforts were redirected to meet hospital-wide demands.

Between August 2021 and September 2022, a total of 1,145 pharmacogenetic assessments were processed for 655 patients. The mean age of this cohort was 55.58 years (range 0–94), with 43.7% (286/655) aged 65 or older. Men represented 55.8% of those evaluated. LPUH, a public center serving northern Madrid, treats a population that is predominantly Caucasian.

Referrals to the Pharmacogenetics Unit encompass multiple clinical contexts, including: oncology cases requiring fluoropyrimidines or irinotecan; pre- and post-transplant patients receiving tacrolimus; candidates for voriconazole therapy or those diagnosed with aspergillosis; dermatologic, rheumatologic, and gastrointestinal immune-mediated disorders in which tacrolimus may be used; patients slated for methotrexate; and individuals with suspected anesthetic-related reactions or a familial predisposition to malignant hyperthermia.

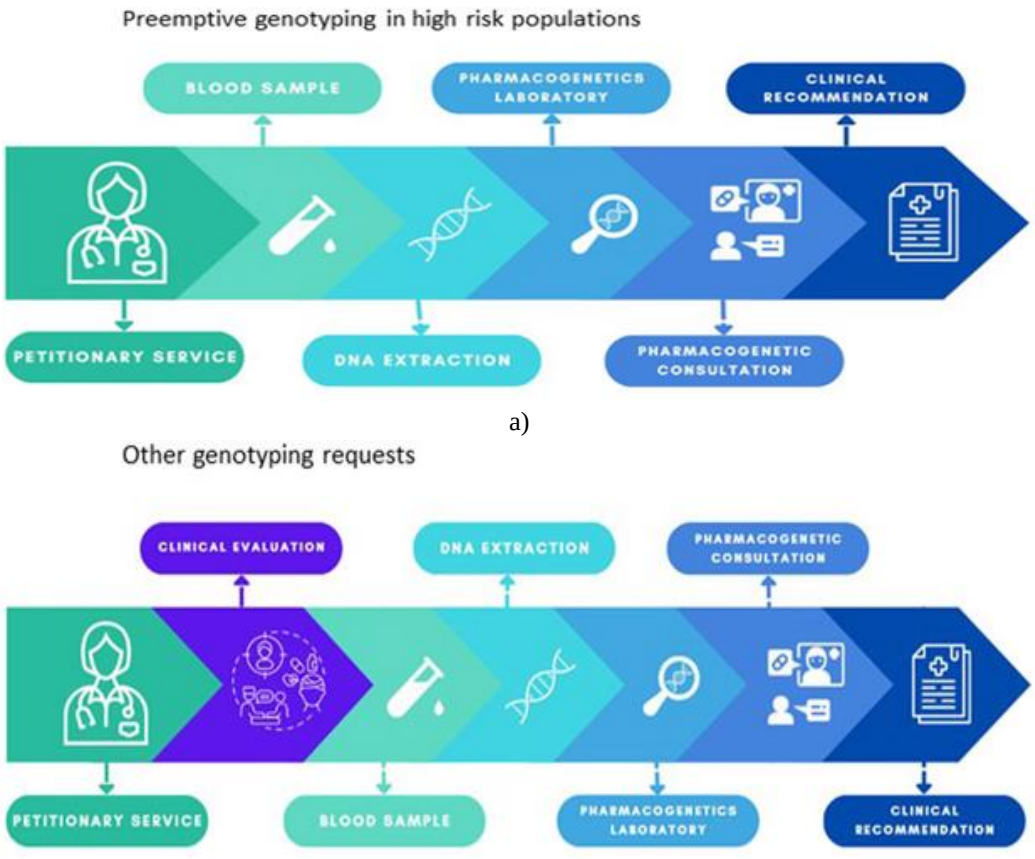
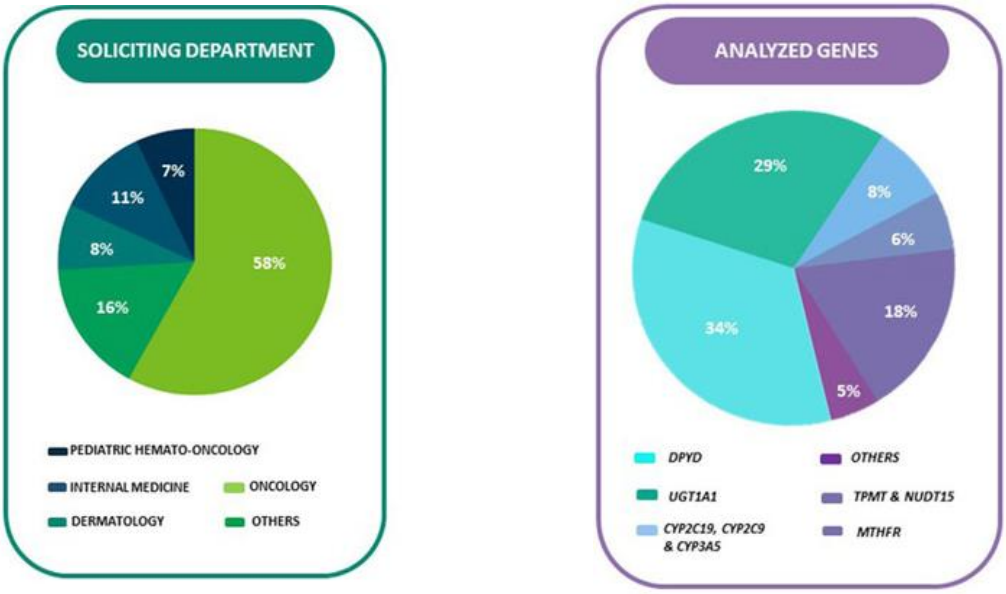


Figure 1. (a) Workflow for medications requiring mandatory PGx assessment prior to prescribing (preemptive testing in elevated-risk groups).
(b) Workflow when a clinical case is submitted for potential PGx evaluation or when testing is requested for a medication without established institutional guidelines.

Pharmacogenetic genotyping results

From January 2014 to December 2016, the same laboratory reported 2,539 PGx analyses (~846 annually) [6]. When compared with the current period, this reflects an approximate 35% rise in yearly testing over six years.

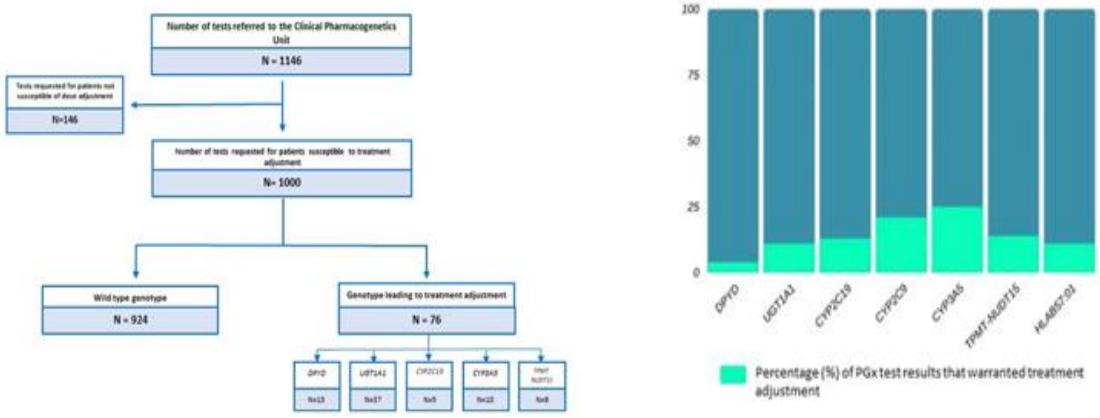
Earlier data indicated that Internal Medicine/Infectious Diseases generated 76.3% (1,939/2,539) of actionable marker requests. In contrast, in the present dataset—including 17 departments requesting testing—Oncology accounted for the majority, contributing 58.47% (383/655) of all genotyped patients **(Figure 2a)**.



a) b)

Figure 2. (a) Proportion (%) of genes analyzed in the complete dataset. (b) Proportion (%) of genes analyzed in the complete dataset.

DPYD (95.36%, 370/388) and UGT1A1 (92.55%, 311/336) testing was almost entirely initiated by Oncology. Dermatology generated the largest share of combined TPMT-NUDT15 requests (29.41%, 30/102). Dermatology and Pediatric Hemato-Oncology each represented 26.15% (17/65) of MTHFR test requests. Pediatric Hemato-Oncology accounted for the vast majority (88.23%, 30/34) of voriconazole-related PGx evaluations. Pediatric Nephrology submitted the highest proportion of CYP3A5 requests (46.15%, 18/39). All CYP2C9 analyses (100%, 15/15) originated from Neurology. The Internal Medicine HIV Clinic exclusively requested HLA B57:01 tests.
More than one-third of the 1,145 PGx tests performed (33.89%, 388/1,145) corresponded to DPYD **(Figure 2b)**. UGT1A1 was the second most frequent (29.34%, 336/1,145). TPMT/NUDT15 accounted for 17.82% (204/1,145), MTHFR for 5.68% (65/1,145), HLA B57:01 for 4.63% (53/1,145), CYP3A5 for 3.41% (39/1,145), and CYP2C19 (voriconazole) for 3.32% (38/1,145). The least frequent tests were CYP2C9 at 1.22% (14/1,145) and malignant hyperthermia screening at 0.70% (4/1,145).
The mean response time (MRT)—measured from request to report release—ranged between 1 and 176 days. The overall MRT was 8.36 days, and 7.01 days for tests processed via the OpenArray® platform. The MRT for HLA B57:01 was 15.75 days. Results for RYR1.(text truncated).



a) b)

Figure 3. (a) Total count of PGx assays performed during the study timeframe, number of requests concerning patients for whom therapy modification could be relevant, and distribution of genotype-driven

treatment changes by gene. (b) Percentage of results for each gene that resulted in phenotype-guided therapeutic adjustments.

The outcomes of the pharmacogenetic evaluations for DPYD, UGT1A1, CYP2C19, CYP3A5, and HLA-B57:01 showed the following:

3.86% (15/388) of DPYD analyses and 11.01% (37/336) of UGT1A1 tests required modification of 5-Fluorouracil/Capecitabine and Irinotecan dosing, respectively. For CYP2C19, 13.15% (5/38) of genotyping results prompted the use of an alternative therapy to voriconazole. Concerning CYP3A5, 25.64% (10/39) of tests resulted in adjusted tacrolimus starting doses in eligible renal transplant patients. Among TPMT/NUDT15, 13.63% (9/66) led to dose alterations of Azathioprine or 6-Mercaptopurine. Only 3 of 14 CYP2C9 genotypes necessitated changes in siponimod dosing.

Outside the OpenArray-based assays, HLA-B57:01 results showed that 11.32% (6/53) of tested individuals were at increased risk for abacavir hypersensitivity, requiring a switch to an alternative HAART regimen **(Figure 3b)**. Regarding RYR1, 50% (2/4) of those evaluated carried at least one clinically meaningful variant. All malignant hyperthermia–related tests were requested only after a compatible perioperative adverse reaction, meaning none were conducted proactively. One detected alteration, NM_000540.2 (RYR1):c.15014C>T (p.Thr5005Met), was categorized as a variant of uncertain significance, indicating that additional work-up would be needed to assess its relevance to malignant hyperthermia risk. The second variant, NM_000540.2 (RYR1):c.14545G>A p.(Val4849Ile), was identified as pathogenic.

Table 1. provides the full list of genotype frequencies and their corresponding proportions.

Gene / Phenotype	Diplotype / Genotype	Absolute number (n)	Percentage (%)
DPYD activity score	2 (normal)	373	96.13
	1.5 (intermediate)	12	3.09
	1 (poor)	3	0.77
UGT1A1	*1/*1	162	48.21
	*1/*28	136	40.48
	*28/*28	36	10.71
	*1/*37	1	0.30
	*28/*37	1	0.30
CYP2C19	*1/*1	23	60.53
	*1/*2	7	18.42
	*2/*3	1	2.63
	*1/*17	3	7.89
	*2/*17	1	2.63
	*1/*8	1	2.63
	*17/*17	2	5.26
CYP2C9	*1/*1	6	42.86
	*1/*2	5	35.71
	*1/*3	1	7.14
	*2/*3	2	14.29
CYP3A5	*1/*1	1	2.56
	*1/*3	9	23.08
	*3/*3	28	71.79
	*3/*7	1	2.56
MTHFR c.677C>T (rs1801133)	GG (wild-type)	26	40.00

	GA (heterozygous)	26	40.00
	AA (homozygous mutant)	13	20.00
TPMT	*1/*1	95	93.14
	*1/*3A or *3B/*3C	7	6.86
NUDT15	*1/*1	100	98.04
	*1/*3 (*1/*2)	2	1.96
HLA-B*57:01	Negative	47	88.68
	Positive	6	11.32
RYR1 (malignant hyperthermia)	Pathological variant present	2	50.00
	Non-pathological	2	50.00
CACNA1S (malignant hyperthermia)	Pathological variant present	0	0.00
	Non-pathological	4	100.00
Total pharmacogenetic tests performed		**1,145**	

The impact of preemptive PGx testing in optimizing therapy selection and substantially limiting adverse drug reactions has been consistently demonstrated in the literature [5, 24]. Here, we present a detailed review of the performance and operational patterns of our Clinical Pharmacogenetics Unit based on one year of activity. This evaluation includes trends in test demand, the resulting outcomes, and obstacles encountered by the Unit. To illustrate progress, we directly compared our real-world findings with data previously reported from the same Unit across earlier time intervals. This comparison highlights key advancements, identifies operational gaps, and outlines opportunities that may strengthen the integration of precision medicine.

Across this period, 1,000 PGx tests were specifically ordered for patients who might benefit from genotype-guided treatment alterations. Among these, 7.60% (76/1,000) produced results that led to actual therapeutic adjustments. Only limited literature exists documenting aggregate PGx variant prevalence in comparable populations for direct comparison [25].

Although fluoropyrimidines and immunosuppressant-related PGx assessments are currently the most frequently ordered tests, they accounted for only 2.7% and 6.7% of overall laboratory testing in our earlier report [6]. This shift reflects substantial growth in both oncology-related testing and in the Unit's overall activity—patterns that align with trends observed in other European centers [26].

Our observed DPYD decreased-activity allele prevalence (3.86%) differed from that documented in larger European cohorts, which describe higher frequencies [27], as well as from the estimates reported by the EMA [28]. No definitive reason could be established, though variations in population characteristics, ethnic composition, and sample size may account for these discrepancies.

In contrast, our findings for CYP2C19 and CYP3A5 demonstrate a greater frequency of relevant variants than what has been documented in predominantly Caucasian or broader European cohorts [29, 30]. These regional genetic patterns may partly account for the prevalence differences observed across studies. Collectively, the data strongly support the adoption of preemptive testing for both genes and underscore the substantial genotype variability across European subpopulations. Proportionally, the largest rate of therapy modification occurred with tacrolimus in kidney transplant recipients, where 25.64% of genotyped individuals required an adjusted starting dose—closely resembling reports from East Asian populations and suggesting shifts in the demographic landscape of those treated [31].

In absolute numbers, DPYD and UGT1A1 screening resulted in the greatest number of therapy changes, identifying 15 and 37 individuals, respectively, who needed altered treatment regimens. These observations highlight the practical value of routine PGx use and reinforce the benefits of individualized therapeutic strategies.

A comparison with similar work conducted in a different clinical environment over a longer time horizon is particularly instructive. In the study by Zhang *et al*., which evaluated fewer genes (CYP2C19, CYP2C9, MTHFR, VKORC1, ALDH), CYP2C19 constituted 50.2% of all test requests [32]. In our dataset, the same test represented only 3.31% of total PGx orders. Moreover, Zhang *et al*. reported that Cardiology and Critical Care accounted for 55% of their PGx requests, whereas Oncology contributed only 0.6%. The authors did not detail the availability

of DPYD or UGT1A1 testing in their institution, which may explain these marked differences [32]. Although these disparities could also be shaped by recommendations issued by the Chinese regulatory authority, no relevant information regarding this factor was identified during our review.

Earlier data published by Borobia *et al*. examined the activity of the LPUH PGx laboratory from January 2014 to December 2016, reporting 2,539 tests overall (2,287 excluding IL28B, which is now obsolete due to advances in antiviral therapy) [33]. Relative to our current figures, this indicates an approximate 35% increase in testing volume across six years. While the test panel has been updated over time to include newer pharmacogenetic insights, rising demand has likely been driven by regulatory recommendations and increased clinician awareness.

When comparing specific test patterns, several substantial shifts become apparent. One striking change is the steep reduction in HLA-B57:01 requests—formerly the most commonly ordered test—which have declined by about 91% per year, representing a drop of 506 requests compared with earlier activity. This pattern clearly reflects evolving HIV management, with abacavir now used later in treatment sequences than in earlier HAART strategies [34].

Among the remaining available tests, TPMT was the second most frequently requested assay in the Borobia *et al*. analysis, a finding that differs considerably from our results. In our study, medical oncology emerged as the predominant source of PGx requests, largely due to the high number of colorectal cancer patients evaluated. This aligns with the average age distribution in our cohort and with the two most frequently performed assays. This trend can be partly attributed to the incorporation of DPYD testing into the SmPC for capecitabine and 5-FU, and to safety alerts issued by the Spanish regulatory authority [35], even though its benefit had been established in prior years [36]. Similar increases in activity have been reported in other European laboratories [26]. Likewise, UGT1A1 assessment is required before initiating irinotecan [37]. Considering the substantial clinical burden of colorectal cancer and the therapeutic implications of DPYD and UGT1A1, it is unsurprising that oncology generated the highest volume of PGx requests in this study. Overall, this expansion in testing reflects the influential role of regulatory bodies in promoting the broader uptake of pharmacogenetic screening and encouraging the shift toward preemptive genotyping models.

The rise in requests for DPYD and UGT1A1 analyses, together with the broader patterns reported here, highlights the growing clinical value of genotype-informed prescribing for improving therapeutic response and overall patient care. These trends also reflect how embedding preemptive testing into clinical protocols and SmPCs facilitates the routine use of PGx tools in practice.

Even with these encouraging developments, several obstacles continue to illustrate why achieving widespread PGx adoption is still difficult. One recurrent issue involves interpreting results generated at external laboratories, which may use different methodologies—an increasingly common scenario as more patients receive care across multiple regions or countries.

Another challenge relates to the limited familiarity or training of test requesters. This occasionally resulted in repeated submissions of the same PGx assay (duplicates, which were not included in our dataset) or tests ordered in situations where they were not clinically justified. A clear example is the ordering of TPMT genotyping for a patient who had received an orthotopic liver transplant, where the donor genotype, rather than the recipient's own, may determine susceptibility to toxicity [38].

Similarly, we repeatedly observed PGx petitions—such as CYP3A5—for kidney transplant recipients who were already being dosed based on trough concentration monitoring. In these cases, genotype information offers minimal additional value because therapeutic adjustments rely directly on blood-level measurements [39].

To address such problems, our institution has established an internal tracking system that flags prior PGx evaluations and alerts clinicians to possible duplicates or unnecessary test orders. For individuals already undergoing therapeutic drug monitoring, manual review of electronic health records by the clinician handling the request helps identify redundant petitions and prioritize cases that require expedited PGx results.

Altogether, these experiences emphasize that genetic data are inherently complex, and turning them into meaningful recommendations requires clear guidance and harmonized reporting standards. The structure of our Clinical Pharmacogenetics Unit helps mitigate these barriers by combining clinical pharmacologists and specialist geneticists into a single team capable of interpreting multilayered genetic information in the context of comorbidities, therapeutic aims, and concurrent medications.

The interpretation of this work must also consider several limitations. Although the Unit has been operational for 10 years, the dataset was influenced by multiple transitions in information-management systems as LPUH modernized its IT infrastructure and electronic medical records. These changes prevented the inclusion of a longer

historical period, as only a portion of earlier information was retrievable. Moreover, the COVID-19 pandemic significantly affected activity: operations stopped entirely during the lockdown, and subsequent financial reallocations within the SNHS diverted resources from units—such as ours—that provide individualized patient support but were not deemed essential during the crisis [40]. The lack of strong cost-effectiveness evidence to justify public spending on PGx services similar to ours further exacerbated the situation. Nonetheless, several promising investigations are currently in progress, including research from our own group, which may help clarify the contribution of pharmacogenetics to SNHS sustainability [41].

Conclusion

This study offers important insights, representing, to our knowledge, the first detailed evaluation of the functioning of a Clinical Pharmacogenetics Unit across two distinct time windows within the same institution. By doing so, it provides an in-depth perspective on how PGx is being applied in a real-world clinical environment, with its accompanying obstacles and successes. Our results demonstrate a clear uptick in PGx utilization, reflecting increased recognition among healthcare providers of its role in tailoring therapies to patient-specific genetic characteristics. This trend marks ongoing movement toward precision medicine, with the overarching goal of delivering treatments that are both safer and more effective for each individual.

The real-world findings presented here add to the expanding evidence base supporting the adoption of PGx testing in everyday clinical care, enabling personalized therapeutic strategies that strengthen patient management. Implementing PGx programs that involve both a geneticist and a clinical pharmacologist can substantially improve how healthcare resources are deployed and bring clinical practice closer to genuinely individualized care. By enhancing treatment efficiency and reducing adverse drug events, pharmacogenetics may also promote a more sustainable healthcare framework. Further research is needed to fully characterize and confirm these potential advantages and to integrate PGx and economic assessments in a robust and generalizable manner.

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Ethics Statement: None

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