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Pharmacogenetic testing in Italy: results of a nationwide survey by the Joint Working Group for the pharmacogenetics implementation in Italy

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Pharmacogenetics enables personalization of drug therapy based on an individual's genetic profile. Despite clinical relevance, implementation of pharmacogenetics remains limited. In Italy, integration is fragmented, with heterogeneous practices and a lack of national coordination. A comprehensive assessment of the current landscape is essential. A nationwide survey was conducted between January and October 2025 to map laboratories providing pharmacogenetic testing. A structured questionnaire collected data on institutional characteristics, testing workflows, pharmacogene panels, analytical methodologies, interpretation procedures, and reimbursement. Forty-nine laboratories participated (response rate: 65%). Most were part of public institutions (82%), primarily general or research hospitals. Testing was predominantly performed in medical genetics units (39%) and focused on oncology, specifically *DPYD* (94%) and *UGT1A1* (84%) for fluoropyrimidine and irinotecan therapies. Adherence to national (SIF/AIOM) and international (CPIC/DPWG) guidelines was generally high; compliance with AMP Tier 1 analytical standards varied substantially. Pharmacological counseling was provided by only 29% of laboratories, mainly by clinical pharmacology units. Considerable heterogeneity emerged in testing platforms, bioinformatics tools, and the use of CE-IVD-certified kits. Marked geographical disparities were evident, with pharmacogenetic activity concentrated in Northern Italy. This survey provides the first national overview of pharmacogenetics implementation in Italy, revealing variability in laboratory practices, interpretation standards, and clinical integration. While oncology-related testing is widely adopted and guideline adherence is increasing, the lack of a coordinated national framework restricts consistency and equitable access. Establishing a coordinated network of pharmacogenetic laboratories with harmonized standards for testing, reporting, and education is crucial for evidence-based pharmacogenetic care.

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INTRODUCTION

Pharmacogenetics examines the influence of genetic variability on drug response, providing the opportunity to tailor pharmacological treatments, thereby enhancing efficacy and reducing the risk of adverse drug reactions [1]. In recent years, multiple drivers, including decreasing sequencing costs, the availability of large-scale genomic resources, and substantial evidence from clinical trials, have accelerated the integration of pharmacogenetics into healthcare systems [2–4]. These advances are reflected in the growing number of international guidelines developed by scientific societies and expert consortia, which provide dosing recommendations for a wide range of clinically relevant gene–drug pairs [5,6].

However, despite this favorable scenario, the implementation of pharmacogenetics remains fragmented in several countries, including Italy. Although pharmacogenetic information is increasingly available on drug labels and national guidelines have been issued for selected gene–drug pairs, its translation into clinical practice remains inconsistent [7]. Furthermore, the language used in regulatory documents is not always sufficiently explicit to guide healthcare professionals on *when* and *how* to apply pharmacogenetic testing [8,9].

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A recent nationwide assessment of laboratories offering pharmacogenetic services (from the point of view of an external quality provider), documented a marked increase in the uptake of *DPYD* and *UGT1A1* testing over the past five years in Italy, together with improved adherence to guidelines and greater accuracy in clinical interpretation [10,11]. Nonetheless, considerable heterogeneity remains in terms of the panels used, timing of testing, the format in which results are communicated, and whether or not genetic counseling and pharmacological recommendations are provided alongside the results.

Overall, these findings converge on a critical issue: Italy lacks a standardized national framework for pharmacogenetic testing. Practices differ widely in terms of which tests are performed, when they are requested, who is responsible for them, turnaround times, and whether reports should be accompanied by clinical interpretation or pharmacological consultation [10].

This fragmentation underscores the need for a structured approach to harmonization. As a first and fundamental task, we prioritized conducting a national survey to map laboratories offering pharmacogenetic testing across Italy. This initiative aims to provide a systematic overview of existing services, promote networking among laboratories, and generate the evidence base required to inform national recommendations. Building on these premises, the objectives of the present work are to: (i) conduct a comprehensive nationwide survey of pharmacogenetic services in Italy; (ii) establish a multidisciplinary network of professionals in pharmacogenetics; (iii) promote integration of pharmacogenetics into clinical practice; (iv) harmonize infrastructure development across the country; (v) raise awareness among Italian stakeholders regarding pharmacogenetics implementation and regulation; (vi) increase international visibility for Italian pharmacogenetics initiatives; and (vii) create a collaborative network to foster the exchange of pharmacological, genetic, and clinical expertise.

METHODS

Survey design

A structured questionnaire was developed to systematically collect information on the organization and delivery of pharmacogenetic testing in Italy (Supplementary Material). The survey was designed to capture: (i) the range of pharmacogenetic tests offered; (ii) clinical contexts in which testing is requested; (iii) healthcare professionals responsible for ordering, signing the pharmacogenetic report and interpreting results; (iv) turnaround times; and (v) whether reports were accompanied by a clinical interpretation or pharmacological consultation. The design was based on by previous national experiences of implementing pharmacogenetic testing [12].

Identification of laboratories

A comprehensive list of laboratories potentially offering pharmacogenetic services was established from multiple sources, including institutional and hospital websites, national and regional registries, published reports, original articles and professional networks- complemented by targeted online search aimed at identifying germline pharmacogenetic laboratories operating in Italy. Both public and private laboratories were deemed eligible for inclusion.

Recruitment and data collection

Each identified laboratory was contacted by email and invited to participate in the survey. The invitation included a cover letter outlining the project's objectives and providing a secure link to the online questionnaire. Data collection was conducted between January and October 2025.

To maximize participation, a structured follow-up strategy was applied. Non-responding laboratories received up to two reminder emails at two-week intervals. If no response was obtained, telephone calls were made to ensure that the invitation reached the appropriate contact person within the institution.

Data handling and analysis

Survey responses were collected electronically and stored in a secure database. Data were analyzed descriptively to summarize the distribution of pharmacogenetic testing practices across institutions. Results are reported in aggregate to ensure the confidentiality of participating laboratories.

RESULTS

Survey respondent demographics

A total of 75 laboratories were contacted, of which 49 participated in the nationwide survey (response rate = 65%) (Fig. 1A). General hospitals were the most represented institutions ($n = 20$, 41%), followed by national research hospitals (IRCCS) ($n = 16$; 33%) and university hospitals ($n = 10$; 20%). Private laboratories ($n = 2$; 4%) and other institutions ($n = 1$; 2%) were only marginally represented (Fig. 1B). The majority of responders were public institutions ($n = 40$; 82%), while a smaller proportion were private facilities ($n = 9$; 18%) (Fig. 1C). Among private facilities, 67% ($n = 6$) were located in the Lombardy region.

Laboratory characteristics

Medical Genetics laboratories accounted for the largest proportion of pharmacogenetic testing ($n = 19$; 39%), followed by Clinical Pathology and Biochemistry units ($n = 9$; 18%) and Clinical Pharmacology departments ($n = 6$; 12%), together representing about two-thirds of all testing activities. Pathology units accounted for only 4% ($n = 2$), while 27% ($n = 13$) of responses were classified as "other" (Supplementary Table 1).

The training background of laboratory directors was diverse but mainly represented by geneticists ($n = 23$; 47%), followed by clinical pathologists/biochemists ($n = 9$; 18%) and pharmacologists ($n = 5$; 10%). Smaller proportions were pathologists ($n = 2$; 4%), hematologists ($n = 2$; 4%), and oncologists ($n = 1$; 2%), while 14% ($n = 7$) reported other specialties (Fig. 2A).

Pharmacogenetic testing was performed across multiple care settings: 90% ($n = 44$) of laboratories tested outpatients, 86% ($n = 42$) inpatients, and 45% ($n = 22$) private-care patients. Most laboratories ($n = 31$; 63%) processed both internal and external to the hospital requests, while 27% ($n = 13$) handled only internal requests and 10% ($n = 5$) only external ones, mainly from private providers (Supplementary Table 1).

Pharmacogenetic testing is primarily provided to support anticancer therapy. As shown in Fig. 2B The vast majority of laboratories tested patients to receive either fluoropyrimidines ($n = 46$; 94%) or irinotecan ($n = 41$; 84%), reflecting the widespread adoption of *DPYD* and *UGT1A1* testing. Thiopurines ($n = 16$; 33%), clopidogrel ($n = 8$; 16%), antidepressants ($n = 4$; 8%), and siponimod ($n = 13$; 27%) followed, while abacavir ($n = 9$; 18%), opioids ($n = 6$; 12%), voriconazole ($n = 3$; 6%) tamoxifen ($n = 2$; 4%), and a small number of other drugs including atazanavir, antiemetics, proton pump inhibitors, isoniazid, and tacrolimus ($n = 1$; 2% each) were less common. As shown in Fig. 2C, the implementation of pharmacogenetic testing among the laboratories participating in the survey was predominantly focused on oncology. Specifically, *DPYD* (fluoropyrimidine-related) and *UGT1A1* (irinotecan-related) genotyping represented 59% of the tests offered as diagnostic service.

Accordingly, requests originated predominantly from oncologists ($n = 46$; 94%), with smaller proportions from infectious diseases specialists and surgeons ($n = 5$; 10% each), neurologists ($n = 4$; 8%), cardiologists and radiotherapists ($n = 3$; 6% each), and a few from rheumatologists, geneticists, psychiatrists, and general practitioners (Supplementary Table 1).

Testing strategies

The selection of variant panels for each tested gene was evaluated in comparison with the recently published AMP (Association for Molecular Pathology) guidelines Tier 1 panels with variable results across pharmacogenes. *TPMT* showed the highest alignment (91%), followed by *CYP2C19* (63%). *CYP2C9* (17%) and *CYP2D6*

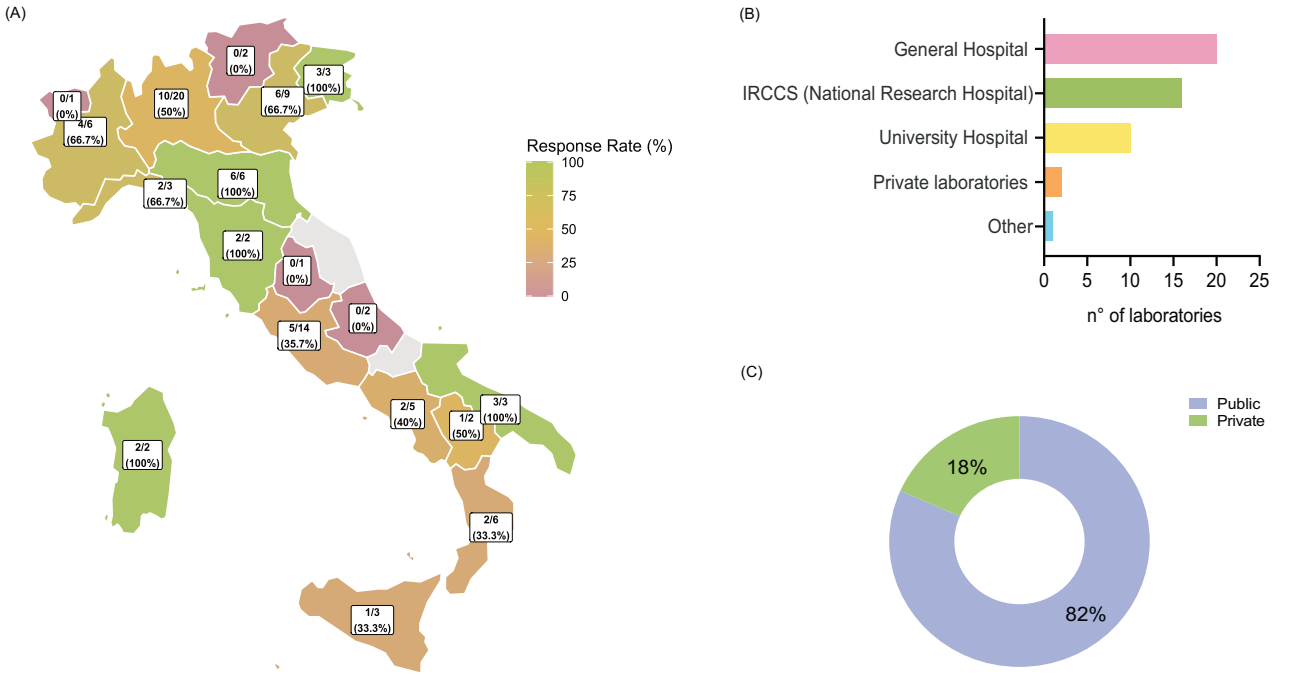

Fig. 1 Geographic distribution and institutional characteristics of participating laboratories. A Map showing survey response rate by region. **B** Distribution of participating laboratories by institution type. **C** Distribution by institutional setting: public vs. private.

(20%) showed lower concordance. No laboratory adopted the AMP Tier 1 panel for *DPYD*, but instead, the selection of variants was largely consistent with the national SIF–AIOM panel (81%). For *UGT1A1*, alignment with the SIF–AIOM panel was 32%, whereas agreement with DPWG recommended variants reached 59%. Even when alignment with the AMP Tier 1 panel was low for *CYP2C19* and *CYP2C9*, the laboratories showed higher concordance rates to other panels, at 63% and 67%, respectively. Notably, *CYP2D6* exhibited marked variability in the selection of testing panels across laboratories (Table 1).

Considering the current availability of Italian pharmacogenetic guidelines for *DPYD*/ fluoropyrimidines and *UGT1A1*/ irinotecan, we evaluated their consistency with the variant panels recommended by various scientific societies/consortia (i.e., AMP, CPIC, DPWG, and RNPGx) for these two gene/drug interactions (Supplementary Table 2). For *DPYD*, a high degree of concordance was observed between the different panels adopted, with the *DPYD**2 A, *DPYD**13, c.1236 G > A (or c.1129-5923 C > G), and c.2846 A > T included in all except RNPGx, which does not include any HapB3 marker polymorphisms. The SIF-AIOM panel also includes the *DPYD**6 variant (to be tested in a post-toxicity context), while the AMP Tier 1 panel is the most comprehensive of all. For *UGT1A1*, all panels include *UGT1A1**28/*36/*37 and *UGT1A1**6, except for the SIF-AIOM panel, which only includes *UGT1A1**28 and *UGT1A1**6 and RNPGx, which does not include *UGT1A1**6. Currently, there are no CPIC guidelines available for *UGT1A1*/ irinotecan.

Testing was almost universally provided pre-treatment for *DPYD* (100%) and *UGT1A1* (97%), while semi-preemptive strategies were reported for *CYP2C19* (53%) and *HLA-B* (50%). A reactive testing strategy is the least frequent overall, though it appears quite common for *CYP2D6* (39%), which is frequently tested in response to drug-related adverse events or for therapy adjustments.

qPCR was the most commonly used method (38–90% depending on the gene), while targeted next-generation sequencing (NGS) was mainly applied to *HLA-B* (40%). International CPIC and DPWG guideline adherence for result interpretation was highest for *CYP2C19* (88%), *CYP2D6* (80%), and *CYP2C9* (83%), and lower for *DPYD* and *UGT1A1*, reflecting a major reliance on national SIF–AIOM recommendations.

Adoption of CE-IVD–certified kits varied widely across pharmacogenes (Supplementary Table 3). The highest level of implementation was reported for *DPYD* (38 centers, 11 different kits) and *UGT1A1* (31 centers, 7 kits), confirming their established role in oncology. In contrast, CE-IVD use was limited for *CYP2C19* (3 out of 13 centers) and *CYP2C9* (2 out of 13 centers), each employing two distinct kits. *TPMT* and *HLA-B* were tested with certified assays in only two centers, while a single-center use was reported for *ABCB1*, *CYP2D6*, and *HLA*. *F5L* and *NAT2* were analyzed exclusively with non-certified methods. Overall, CE-IVD implementation predominated for *DPYD* and *UGT1A1* but remained fragmented for other pharmacogenes. Only one laboratory reported using whole-exome sequencing (WES) for pharmacogenetic testing.

A comparable heterogeneity emerged in the use of bioinformatics tools (Supplementary Table 4). Overall, 18 different software programs were reported, with the most significant variability observed for *DPYD* and *UGT1A1*, analyzed by 31 and 28 centers, respectively, using approximately ten distinct software solutions each. These findings underscore the lack of standardization in data interpretation across laboratories.

Interpretation and reporting

The personnel responsible for signing pharmacogenetic reports are most frequently geneticists by training, accounting for nearly two-thirds of cases ($n = 32$; 65%). Clinical pathologists and biochemists represented the second most common group ($n = 15$; 31%), followed by pharmacologists ($n = 6$; 12%), while 8% ($n = 4$) of laboratories reported other training backgrounds for the personnel allowed to sign pharmacogenetic reports.

Nearly all laboratories ($n = 44$; 90%) usually provide a written clinical interpretation of the results embedded in the pharmacogenetic report. These comments most frequently include an indication of the presence of a risk phenotype for toxicity or lack of efficacy ($n = 36$; 73%), followed by the interpretation of the predicted phenotype based on the genotype ($n = 23$; 47%). Only about one quarter ($n = 12$; 24%) of laboratories include specific dosing or therapeutic recommendations (pharmacological counseling), and 31% ($n = 15$) reported including a reference to relevant clinical guidelines or redirecting the patient to a specialist (Supplementary Table 1).

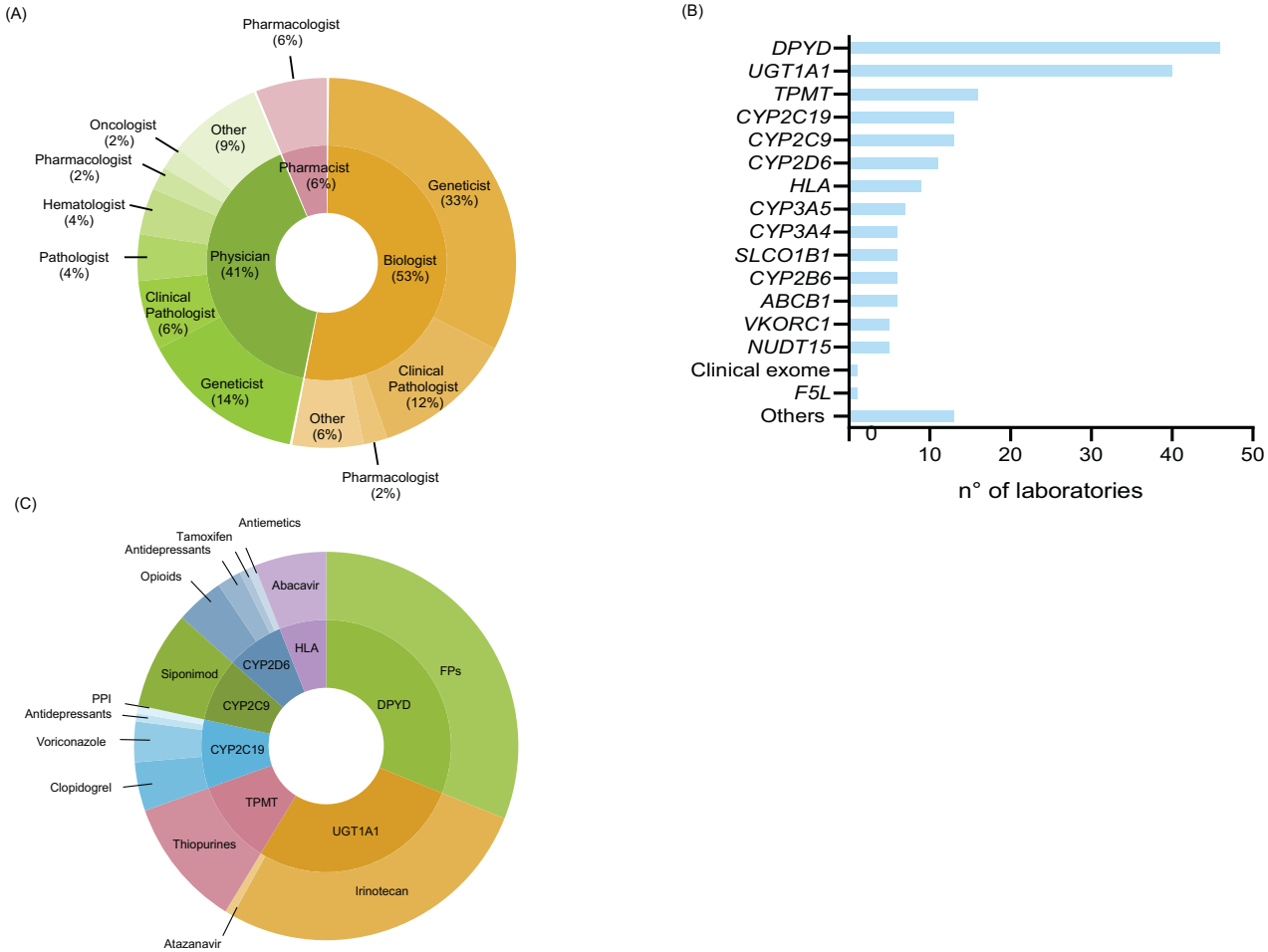

Fig. 2 Professional background of laboratory directors and pharmacogenetic testing characteristics. A Double donut chart showing the training background (inner ring) and clinical specialty (outer ring) of directors of laboratories performing pharmacogenetic testing. **B** List of genes analyzed by laboratories. **C** Double donut chart illustrating the genes genotyped by the laboratories (inner ring) and the corresponding drugs for which the pharmacogenetic testing is performed (outer ring).

The provision of pharmacological counseling varied considerably depending on the type of unit providing the test. All pharmacology units ($n = 6$; 100%) reported offering counseling services, whereas this activity was less common among other units: 16% ($n = 3$) of medical genetics units, 11% ($n = 1$) of clinical pathology units, and 25% ($n = 2$) of laboratories classified as "other" reported providing counseling. No pathology units declared offering this service (Fig. 3A).

Separate pharmacological consultation reports are produced by a minority of laboratories ($n = 9$; 18%), while 57% ($n = 28$) do not provide them. Furthermore, only 12% ($n = 6$) of laboratories offer pharmacological consultation services for pharmacogenetic reports issued by external laboratories (Supplementary Table 1).

Most laboratories ($n = 36$; 73%) reported obtaining informed consent before performing pharmacogenetic testing. Among these, 12 laboratories used a consent form specifically designed for pharmacogenetic testing, while the remaining laboratories reported using a general consent form for germline analysis. The vast majority of laboratories ($n = 44$; 90%) indicated that pharmacogenetic incidental findings (e.g., those obtained through clinical exome sequencing) are not communicated to patients (Supplementary table 1).

Feedback and annotations

Nineteen responders (40%) provided suggestions for improving pharmacogenetics implementation in Italy, selecting from various proposed items. The most frequent item was "Collaboration and networking" (14%), emphasizing the importance of stronger inter-laboratory connections, sample-sharing initiatives, and organization of regional or national meetings. "Clinical practice and guidelines" (10%) included requests for harmonized recommendations and standardized reporting. "Education and training" (8%) emphasize the need for structured courses and workshops, while policy and healthcare system integration (8%) focused on reimbursement and more explicit regulatory guidance. "Communication and dissemination" (6%) highlighted the need for newsletters and updates, whereas "Research and innovation" (6%) pointed to an interest in participating in joint projects and exome-based pharmacogenetic research (Fig. 3B).

Impact and economic considerations

Sixty-nine percent of laboratories performed pharmacogenetic testing for more than 200 patients in the previous year, 19% for 100–200, 4% for 50–100, and 8% for fewer than 50 patients. Testing capacity was unevenly distributed across Italy, with the North hosting the most high-volume centers (23 laboratories with more than 200 tests/year), followed by the Center [4] and South & Islands [6] (Fig. 4). The median turnaround time for *DPYD* testing was 6.5 days (IQR 5–9.25).

Most laboratories (73%) reported full reimbursement of pharmacogenetic testing by the National Health System, 22% reported partial reimbursement, and 4% no reimbursement. However, reimbursement policies vary across regions, reflecting

Table 1. Compliance of tested variant panels and clinical interpretation with different pharmacogenetic guidelines, and testing approaches for key pharmacogenes.

Gene	Panel AMP Tier 1 compliance	Validated panel compliance*	SIF-AIOM panel compliance§	Testing setting				Methodology mainly utilized	Guidelines for interpretation	
				Pre-emptive	Semi-preemptive	Pre-treatment	Reactive		SIF-AIOM	CPIC/DPWG
DPYD	0%	93%	81%	0%	2%	100%	19%	qPCR (90%)	90%	5%
UGT1A1	-	59%	32%	0%	3%	97%	8%	qPCR (65%)	65%	27%
TPMT	91%	91%	–	9%	0%	91%	0%	qPCR (50%)	-	91%
CYP2C19	63%	63%	–	13%	0%	75%	38%	qPCR (38%)	-	88%
CYP2C9	17%	67%	–	17%	0%	83%	17%	qPCR (67%)	-	83%
CYP2D6	20%	20%	–	20%	0%	20%	60%	qPCR (60%)	-	80%
HLA-B	–	80%	–	20%	20%	60%	0%	Targeted NGS (40%)	-	60%

For each gene, the table summarizes AMP Tier 1 compliance, adherence to panels proposed by different pharmacogenetic guidelines (SIF–AIOM, CPIC, DPWG), predominant testing settings (pre-emptive, semi-preemptive, pre-treatment, reactive), most commonly used methodology, and pharmacogenetic guideline adherence for the results interpretation.
*Validated according to either CPIC, DPWG, or SIF–AIOM guidelines.
§ Only for *DPYD* and *UGT1A1*.

the decentralized structure of the Italian National Health System. Within the Italian reimbursement system, (pharmaco)genetic testing is reimbursed according to procedural codes (e.g., single-gene tests, gene panels, or NGS tests), rather than on an individual gene-by-gene basis. Several laboratories also reported the absence of dedicated reimbursement codes specific to pharmacogenetic testing, which may contribute to heterogeneous administrative and reimbursement practices across institutions.

DISCUSSION

The application of pharmacogenetics to pharmacological treatment management has seen a significant advancement in the last few years; however, its clinical implementation appears to be still challenged by a poor harmonization of clinical and laboratory procedures as well as a still deficient regulatory framework in the field [7,8,10].This nationwide survey provides the first comprehensive overview of pharmacogenetic testing practices in Italy. The results reveal a substantial heterogeneity in service organization, testing procedures, and clinical integration across different institutions as well as a high plethora of educational and harmonization needs expressed by professionals in the field.

Pharmacogenetic testing emerged as predominantly applied in the oncology therapeutic area, particularly for *DPYD* and *UGT1A1* in support of fluoropyrimidine and irinotecan treatment. Regulatory initiatives have played a central role in promoting clinical implementation in this context. In 2020, the European Medicines Agency (EMA) recommended pre-treatment *DPYD* testing [13], and the Italian Medicines Agency (AIFA) adopted this guidance [14], formally recognizing the clinical utility of both *DPYD* and *UGT1A1* testing. These developments have been facilitated by the availability of national guidelines jointly issued by SIF and AIOM, which promote standardized genotyping and dosing strategies, with a well established clinical utility supported by recent studies [15].

However, national pharmacogenetic guidance remains limited outside the oncological field. Expanding national recommendations to other gene–drug pairs could help define testing priorities and support broader implementation. Moreover, the involvement of medical professional societies, as done for the *DPYD/ UGT1A1* national guidelines, developed in a collaboration between pharmacologists and oncologists, can boost the awareness of the value of pharmacogenetics among medical practitioners, thereby facilitating the translation of pharmacogenetic guidelines into improved clinical practices. Continued collaboration among national professional societies, along with the alignment to international frameworks like CPIC and DPWG, will be essential to advance pharmacogenetics integration across therapeutic areas.

Compared with similar surveys conducted in other European countries [4,12,16,17], the Italian pharmacogenetic ecosystem appears less standardized and more fragmented, particularly regarding testing panels, software tools, and result interpretation. The marked heterogeneity in testing platforms and interpretation software further highlights the absence of harmonized technical standards. The use of 18 different bioinformatics tools, along with the coexistence of numerous CE-IVD and non-certified kits, may lead to variability in genotyping accuracy and phenotype prediction. Developing consensus on validated assays, reference variant lists, and interpretation pipelines would therefore represent a critical step toward improving reproducibility and clinical reliability across sites. Moreover, while most laboratories primarily rely on targeted panels, an increasing number of groups are shifting toward broader approaches such as NGS, which enable a more comprehensive assessment of individual pharmacogenetic profiles. This evolution may facilitate the detection of rare or previously untested variants, thereby expanding the clinical scope of pharmacogenetics, an approach that has already shown

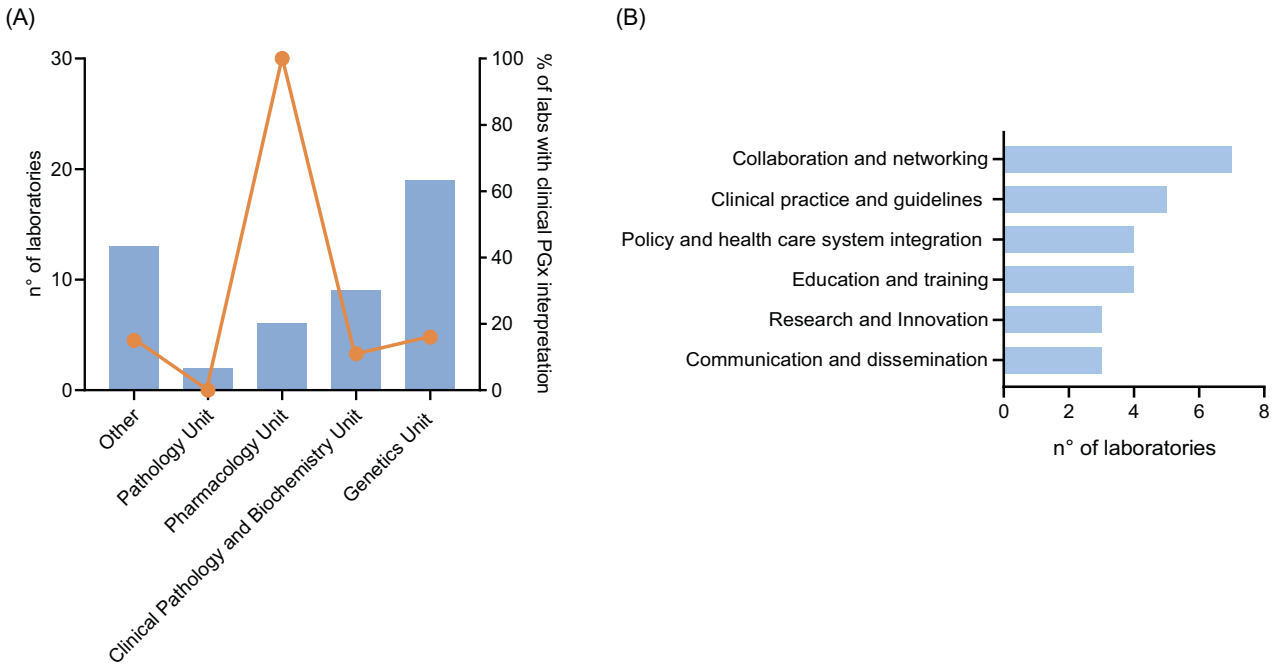

Fig. 3 Characteristics of laboratories performing pharmacogenetic testing and overview of survey feedback. A Type of unit performing pharmacogenetic testing. Bars indicate the number of laboratories per unit type; the line shows the percentage of laboratories providing pharmacological counseling within each type of unit. **B** Overview of feedback and annotations submitted by laboratories participating in the survey, grouped by thematic area.

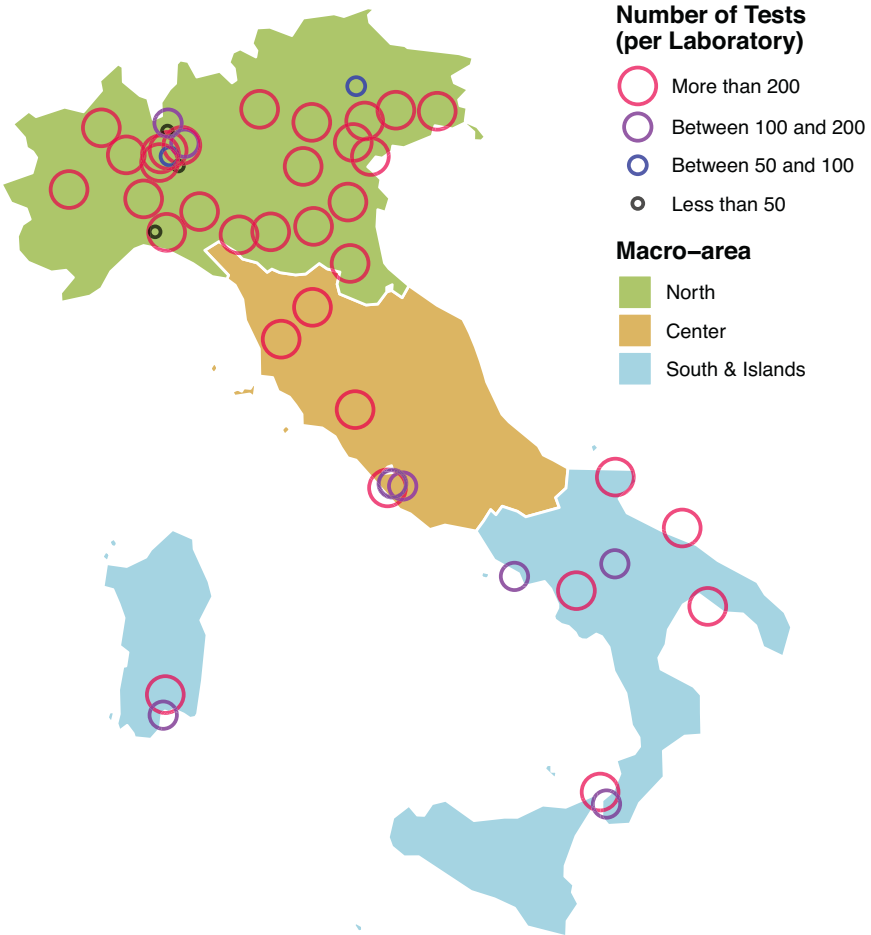

Fig. 4 Map of pharmacogenetic laboratories across Italy. Background colors represent geographic macro-areas, and circle size indicates the average number of pharmacogenetic tests performed per laboratory, per year.

potential clinical advantages [18–20]. However, the transition toward such technologies also underscores the need for enhanced bioinformatics infrastructures and more standardized analysis pipelines [21], as also highlighted by feedback collected in the survey. An opportunity in this context is offered in oncology, where repurposing NGS data on tumor tissue generated within Molecular Tumor Boards (MTBs) could represent a cost-effective opportunity. The germline component of tumor–normal sequencing is routinely produced but remains largely underutilized for pharmacogenetic purposes, despite its potential to support personalized treatment decisions [22].

At both national and international levels, several consortia have emerged to standardize and harmonize pharmacogenomics laboratory procedures, in order to ensure analytical consistency, clinical reliability, and cross-laboratory comparability. Among these, the AMP has developed comprehensive recommendations defining the minimum variant sets (Tier 1 panels) required for accurate genotype-to-phenotype translation. These panels were designed according to criteria such as allele frequency across multiple populations, evidence of functional impact, and clinical validity supported by peer-reviewed studies, thereby promoting the inclusion of variants across diverse ethnic groups [23–26].

In parallel, international expert bodies such as the CPIC and the DPWG have focused on the clinical interpretation of pharmacogenetic results, providing evidence-based, gene–drug–specific recommendations for dose adjustment or therapeutic selection [27]. Together, these initiatives constitute a complementary framework: while AMP establishes the analytical foundation to ensure that pharmacogenetic assays capture clinically relevant variants, CPIC and DPWG translate these data into actionable clinical guidance.

A key finding concerns the inconsistency in the genetic content of pharmacogenetic panels used across laboratories. The present survey highlights that AMP compliance is achieved for some pharmacogenes (e.g., *TPMT*), but remains low or variable for others (*CYP2C9*, *CYP2D6*, *DPYD*), underscoring the need for consensus on variant selection and standardized analytical validation criteria, and highlighting once more how the availability of clinical guidelines mediated by the national societies remains the major reference for the laboratory activity.

Testing settings also showed important trends. Oncology-related genes such as *DPYD* and *UGT1A1* are almost exclusively tested pre-treatment, in line with recent studies and publications that support the positive impact of preemptive genotyping on treatment outcomes [2].

Conversely, semi-preemptive strategies are emerging for *CYP2C19* and *HLA-B*, indicating a gradual shift toward broader clinical implementation. This higher prevalence of semi-preemptive testing for *CYP2C19* and *HLA-B* may be due to their frequent inclusion in broader pharmacogenetic panels, which are often performed independently of an immediate therapeutic decision but can still provide clinical benefit later. However, reactive testing—performed only after an adverse event or treatment failure—remains prevalent for genes like *CYP2D6*, suggesting that routine pre-emptive or panel-based approaches are not yet integrated into Italian clinical workflows.

The predominance of genetics and clinical pathology units in performing pharmacogenetic tests likely reflects the historical evolution of molecular diagnostics within the Italian healthcare system. However, the limited involvement of pharmacology units —despite their expertise in dose adjustment and therapy optimization—suggests a need to strengthen interdisciplinary collaboration. The relatively low proportion of laboratories providing explicit pharmacological counseling (24%) underscores this gap. Notably, pharmacological counseling is most often provided by pharmacology units, which, however, are limited in number and unevenly distributed across the country. This highlights the potential value of establishing a national network of specialized laboratories and experts to provide pharmacological support in the interpretation of pharmacogenetic data. Furthermore, concentrating pharmacogenetic analyses in accredited genetic laboratories could ensure high-quality, standardized testing while enabling hub pharmacological centers to support spoke healthcare facilities with comprehensive pharmacological consultations.

A direct consequence of this fragmented landscape is the considerable variability observed across the different regions of the country. Testing activity was indeed found to be concentrated in the northern regions, with marked geographical disparities in availability and volume, as well as variable access to pharmacological counseling and reimbursement mechanisms. At the system level, the uneven distribution of pharmacogenetic services in the territory, with the majority of high-volume laboratories located in Northern Italy, raises concerns about equitable access to testing nationwide. Similarly, while most laboratories report full or partial reimbursement by the National Health Service, differences in coverage across regions contribute to inconsistent integration of pharmacogenetics into routine care. This clearly reflects the organization of the Italian health care system, which delegates to individual regions the responsibility for defining many aspects of the healthcare delivery, including the allocation of resources, laboratory accreditation, and reimbursement mechanisms. While this regional autonomy can promote flexibility and innovation, it also results in marked heterogeneity in the implementation of pharmacogenetic testing and in patient access to these services. A coordinated national framework is urgently needed to address these disparities, by defining minimum testing requirements, accreditation criteria, and pathways for sustainable reimbursement.

The high rate of responders providing feedback on the needs to advance pharmacogenetics implementation in Italy demonstrates strong interest and motivation among professionals in the field. All the feedback received from the laboratories participating in the survey can be summarized as highlighting the need for structured training and networking opportunities to support the implementation of pharmacogenetics in clinical practice. This clearly underscores the urgent need for dedicated training and education programs in pharmacogenetics. Consistent with other surveys, the lack of specific pharmacogenetic training is recognized as one of the significant barriers to its widespread clinical implementation [4,12,16,17]. To address this gap, ongoing initiatives promoting pharmacogenetics in Italy should be actively supported and coordinated by scientific organizations such as the Italian Society of Pharmacology (SIF) and the Italian Society of Human Genetics (SIGU) to foster education, standardization, and interdisciplinary collaboration across clinical and research settings.

Overall, the insights gained from this survey provide a foundation for the activities of the *Joint Working Group for the Implementation of Pharmacogenetics in Italy*. The next steps should include the establishment of a permanent national network of laboratories, the harmonization of testing and reporting standards, and the promotion of education and awareness initiatives for clinicians and healthcare stakeholders. Enhanced collaboration between geneticists, pharmacologists, and clinicians will be essential to embed pharmacogenetic testing into patient-centered therapeutic strategies, to align Italy with international best practices.

The main strengths of this study lie in its nationwide coverage and high response rate, providing a representative picture of pharmacogenetic laboratory activity across Italy. Limitations include its self-reported design and the possibility of participation bias, as laboratories with more structured pharmacogenetic programs may have been more inclined to respond.

In conclusion, this survey establishes the first national map of pharmacogenetic services in Italy. It highlights key challenges—heterogeneity, fragmentation, and regional disparities—but also substantial potential and motivation for integration, improvement, and potential development of appropriate health care pathways.

Building on these findings, a coordinated national strategy could foster the harmonization of practices, strengthen the link between genotyping and clinical decision-making, and ultimately enhance patient outcomes through personalized therapy.

DATA AVAILABILITY

Data supporting the findings of this study are available within the article. Additional information is available from the corresponding author upon reasonable request.

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AUTHOR CONTRIBUTIONS

RR, MF and EC conceptualized and designed the study. RR, MF, SP, MG, EZ and EC carried out interpretation of data. RR, MF, SP, MG, EZ and EC designed the questionnaire and wrote the manuscript. SP, MGa, EZ, MRM, AS, SA, PB, MGe, GN, VC, AF, GS, MF and EC edited and revised the questionnaire and the manuscript. All authors read and approved the final manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

ETHICAL APPROVAL AND INFORMED CONSENT

In accordance with national and institutional guidelines, ethical approval was not required for this study, as it did not involve human participants, patients, clinical data, or identifiable personal information. The survey collected only laboratory-level organizational data from laboratory directors.

ADDITIONAL INFORMATION

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