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ARTICLE

Toward an integrated resource for pharmacogenomics (PGx): Survey findings from the genomic medicine communities

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ABSTRACT

Purpose: Pharmacogenomics (PGx) is a critical component of precision health care that aims to improve drug efficacy and reduce adverse events. Terminologies and standards have not always aligned between PGx and broader genomic medicine communities, which is a barrier to PGx implementation. An updated assessment of community barriers, needs, and perspectives is critical to enable more standardized terminologies and interpretation frameworks.
Methods: The Clinical Genome Resource's PGx Interpretation Committee (PGxIC, formerly referred to as the PGx Working Group, PGxWG) conducted 2 surveys targeting the PGx and genomic medicine communities ($n = 508$) to evaluate perspectives on PGx clinical validity and actionability frameworks, as well as other barriers to PGx implementation. Surveys were tailored toward self-reported familiarity with PGx. Data primarily consisted of free text, which were analyzed using qualitative content analysis methods.
Results: Survey responses indicated conflation of terminology across disciplines, including confusion around differing definitions of terms in PGx and non-PGx contexts. Data also indicated broad support for leveraging existing PGx guidelines and framework structures alongside the standardization of approaches and centralization of resources.
Conclusion: These novel survey results demonstrate broad consensus on the importance of integrating PGx into clinical practice, including support for development of gene-drug response clinical validity and actionability frameworks aligned with Clinical Genome Resource's frameworks for gene-disease relationships.

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Introduction

Pharmacogenomics (PGx) is a field at the intersection of pharmacology and genetics, studying how an individual's genetic makeup influences their response to medications. The application of PGx in clinical practice can be used to optimize drug therapy, thereby improving efficacy and reducing incidence and severity of adverse effects to ultimately improve patient outcomes and reduce health care costs. Over the last 3 decades, the body of PGx knowledge has greatly expanded: hundreds of drugs now have genetic evidence reported in peer-reviewed literature and several international consortia have been established to create clinical drug prescribing guidelines based on genotype information.

PGx has some unique features that distinguish it from clinical genomics, one of which is the star allele system used to describe haplotypes (combination of variants) in pharmacogenes. Star alleles use symbols and numbers, such as **1*, **2*, and so on, to denote variation across the gene. The same variant may be present in multiple star alleles that can have different function assignments due to the additive effects of all variants in the haplotype. For example, the NM_000106.6:c.100C>T p.(Pro34Ser)(rs1065852) variant is the functional variant in *CYP2D6*10* (PVID: PV00435),[1] an allele of *CYP2D6* (HGNC:2625) that has decreased function. (*CYP2D6*) c.100C>T is also found in different combinations with other variants in star alleles which have no function (eg, *CYP2D6*47*, PVID: PV00471).[1,2] As such, function assignment is required at the star allele level to account for the overall impact of gene variation.

PharmVar (Pharmacogene Variation Consortium) is a repository for pharmacogene variations that curates submitted allele sequences and assigns star allele nomenclature (eg, *CYP2D6*10*) using a standardized, rule-based system.[1] Clinical Pharmacogenetics Implementation Consortium (CPIC),[3] is a US-based international consortium that develops peer-reviewed, evidence-based guidelines for using PGx information in clinical practice. As part of the clinical prescribing recommendations. CPIC gene expert panels assess and assign star allele function (eg, decreased function, no function) using a combination of experimental data, clinical studies, and computational predictions.[4] This system enables precise metabolizer phenotype classification (eg, normal metabolizer, intermediate metabolizer, and poor metabolizer), critical for PGx implementation.

PharmGKB (Pharmacogenomics Knowledgebase)[5] is a comprehensive resource that collects, organizes, and disseminates a broad spectrum of knowledge about the impact of genetic variation on drug response. It provides detailed annotations of pharmacogenes and variants from peer-reviewed literature, drug labels, and clinical guidelines. PharmGKB incorporates and facilitates use of information from CPIC, PharmVar, and other key PGx knowledge resources, including the Dutch Pharmacogenetics Working Group (DPWG)[6] and the US Food and Drug Administration (FDA). DPWG was established by the Royal Dutch Pharmacist's Association to develop pharmacogenetics-based dosing recommendations.

The FDA has published a Table of Pharmacogenetic Associations (https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations), and PGx information is slowly being incorporated into the drug product labels from regulatory agencies from the United States and worldwide (https://www.pharmgkb.org/labelAnnotations) to inform prescribing using PGx. PharmGKB annotates information from these sources, integrates it with PGx literature, and presents it in searchable, browsable, and computational formats, enabling ease of access, retrieval of guidance by star alleles, and cross-comparison of guidance across sources.

PharmGKB, CPIC, and PharmVar use PharmVar allele nomenclature and display CPIC-assigned allele function to ensure consistency across these resources. Together, these efforts facilitate the translation of genetic information into actionable prescribing decisions by providing comprehensive catalogs of gene-variant-drug relationships and consensus clinical practice guidelines based on standards[4] to support the integration of PGx into clinical care.

Additionally, the Clinical Genome Resource (ClinGen) is a National Institutes of Health (NIH)-funded initiative aimed at building a centralized resource to define the clinical relevance of genes and variants for use in precision medicine and research.[7] ClinGen has developed systematic, transparent frameworks for gene-disease validity, actionability, dosage sensitivity, and variant pathogenicity.[8-11]

For the past 20 years, the major PGx resources and ClinGen have worked on creating and implementing standards and terminologies that do not always align because they were developed independently. Historically, ClinGen has focused on inherited disease genes and provides links to PGx resources (PharmGKB and CPIC), which focus on gene-drug relationships for pharmacogenes. Given the importance of PGx for precision medicine, the Pharmacogenomics Interpretation Committee (PGxIC: https://clinicalgenome.org/working-groups/pharmacogenomics/, formerly known as the Pharmacogenomics Working Group) was re-established in 2022 after an 8-year hiatus with the mission to develop shared frameworks between ClinGen and the PGx resources of tiered standard terminology and definitions that reflect clinical significance for germline genomic variants implicated in drug response variability (efficacy, dosing, and adverse event risk).[12]

Toward these aims, ClinGen's PGxIC conducted 2 surveys to gather input from professionals in the PGx and broader genomic medicine communities regarding criteria and terminology for PGx clinical validity and actionability and to assess community needs. The results of these 2 surveys and subsequent recommendations will help refine foundational frameworks for PGx clinical validity and actionability using ClinGen-aligned terminology alongside the development of a single integrated resource, ClinPGx (https://clinpgx.org/).

Materials and Methods

Study design and distribution

The PGxIC conducted 2 similarly constructed surveys: the PGx Community Survey and the Genomic Medicine Community Survey (see Supplemental Survey Questions for the text of both surveys along with branching logic). The first survey was conducted in February and March 2023 for 42 days, and targeted the PGx community, including PGx experts and clinical practitioners (pharmacists, physicians, pharmacologists, etc). This focus on those involved in PGx implementation programs, laboratorians, and PGx trainees was achieved by survey distribution through PharmGKB blog posts, PGx community mailing lists (including CPIC, the Pharmacogenomics Global Research Network, the American Society of Health-System Pharmacists, and several additional European PGx community mailing lists), social media (eg, Twitter, LinkedIn), web banners, outreach to PGx programs, and via word of mouth. The second survey was conducted in March through July of 2023 for 112 days and released in advance of American College of Medical Genetics and Genomics (ACMG)'s annual meeting. The second survey targeted the broader genomic medicine community, including clinicians, geneticists, genetic counselors, laboratorians, genetics and medical students, and others who may not have in-depth PGx knowledge and experience.

Additional distribution methods for the second survey included targeting clinical genetics association mailing lists (eg, ClinGen, genetic counseling associations) and through conference posters and discussion at ACMG. Respondents were asked not to participate in the second survey if they had already completed the first. Both surveys were designed and deployed using Qualtrics.

The PGx Community Survey was designed with 2 blocks of questions (Supplemental Survey Questions). The first block sought to gather demographic information about the respondent, including up to 11 questions depending on their answers (eg, questions about clinical specialty were only included if the respondent identified themselves as a clinician). The second block consisted of free-text responses to questions about definitions for terms such as clinical actionability and clinical validity of gene-drug-phenotype relationships, whether existing criteria could be leveraged for these definitions (and if so, how or why not), and the respondent's perspectives on the necessity or lack thereof of standardization. This second block also included several questions about familiarity with the existing criteria mentioned, including CPIC allele functional status terms and other PGx nomenclatures.

The Genomic Medicine Community Survey included 2 additional demographic questions. The first was a branch question to determine the respondent's self-reported level of PGx familiarity, and the second allowed them to specify province if they stated they resided in Canada. Because it was targeted to nonexperts, the Genomic Medicine Community Survey included an additional block and branching logic that altered the presentation of the second block from the first survey. Users who responded to the branch question with 1 of 6 answers that indicated lower levels of PGx familiarity (Supplemental Survey Questions) were given a tailored second block that removed all 4 questions about CPIC allele functional status terms and other PGx nomenclatures and displayed slightly tailored introductory text. Those with lower PGx familiarity ($n = 124$) were presented with an additional block of questions immediately after the demographics portion of the survey. This additional block included a basic explanation of PGx followed by questions around their level of interaction with PGx-relevant contexts, as well as their perceptions of institutional attitudes toward PGx, drivers of PGx implementation, PGx standardization, and potential value of PGx. For respondents that indicated clinical experience, this block also asked whether they had been asked to interpret PGx or other precision medicine genetic testing reports.

Surveys were designed and piloted by PGxIC members. Both surveys were consented through use of a preamble (Supplemental Survey Questions). Responses were anonymous unless the respondent chose to share their email address for follow-up surveys.

Inclusion and exclusion criteria

Responses were included for analysis if the participant answered at least 1 question outside of the demographic question block (Supplemental Survey Questions). A total of 247 responses met the inclusion criteria in the PGx Community Survey, whereas 261 responses met the inclusion criteria in the Genomic Medicine Community Survey, for a total of 508 responses across both surveys.

Analysis methods

Given the goal of these 2 surveys was to collect useful feedback on criteria for evaluation of PGx clinical validity and actionability among both PGx and broader genetics communities, the bulk of nondemographic response data collected was free text. As such, these data were analyzed qualitatively using content analysis methods.[13] Demographic data are reported using descriptive statistics.

Qualtrics was used for analysis of demographic data, whereas free-text responses were exported from Qualtrics to Microsoft Excel for coding. Codes were developed inductively (Supplemental Data Code Tables) and were manually applied in columns to each included response. Responses were not confined to one code—each response was scored with all applicable codes.

Two sets of overarching coding topics were used: codes that pertained to clinical implementation and codes that pertained to aspects of gene-drug validity and actionability. Codes are detailed in a supplement table (Supplemental

Data Code Tables). The "Evidence Base" and "Access" categories were used in both contexts due to relevance across the board.

Responses that indicated uncertainty, confusion, or self-described lack of sufficient expertise to answer the corresponding question were also given a unique code. Responses that were nonanswers, entirely off-topic, or did not meet any other code criteria were given a unique code and were not included for the bulk of analysis, although they contributed to each question's total response count.

Survey questions are included in Supplemental Survey Questions, and the response data are available upon reasonable request. The COUNTIF function was used to tally response counts for each code for both surveys. Free-text questions were given an n = responses that met inclusion criteria that responded to that question.

Results

Respondents from both surveys were predominantly in the United States (70%, 66%, including 31 and 34 states, respectively) but included a range of countries globally (27, 40 additional countries, respectively) (see Supplemental Geographic Data). Education varied as expected between surveys, with the PGx Community Survey having more respondents with a PharmD degree (47% compared with 26%), and the largest portion of Genomic Medicine Community Survey respondents had PhDs (44%). Respondent occupation varied, but both surveys leaned predominantly toward nonprofit hospitals and universities over for-profit workplaces, with the majority of PGx Community Survey respondents describing themselves as PGx implementers, researchers, and pharmacists and the greatest proportion of Genomic Medicine Community Survey respondents describing themselves as researchers and clinicians.

Demographics mostly varied in terms of familiarity with PGx and involvement in PGx initiatives (Table 1). The largest single response group in the PGx Community Survey reported devoting >75% of their time to PGx (33%), with a similar combined amount devoting anywhere under 25% of their time. Nearly all respondents to this survey reported an understanding of whether their institution implemented PGx testing (98%) and reported familiarity with and involvement in institutional PGx initiatives (94%). PGx Community Survey respondents had greater familiarity with PGx resources such as CPIC and DPWG guidelines, the PharmGKB, and PharmVar compared with Genomic Medicine Community Survey respondents, who more frequently reported a lack of awareness that these resources existed.

A total of 124 respondents (48%) in the Genomic Medicine Community Survey were branched because of lower reported familiarity with PGx, which is consistent with reported percentage of professional time respondents devoted to PGx: 64% devoted a combined <25% of their time to PGx, and only 16% dedicated >75% of their time to PGx. A greater proportion of Genomic Medicine Community Survey respondents (17%) reported a lack of familiarity with whether their institution implemented PGx testing. Similarly, 35% of Genomic Medicine Community Survey respondents reported a personal lack of involvement with PGx initiatives. Reported percentage of professional time spent on PGx was consistent with self-described comfort engaging with PGx for Genomic Medicine Community Survey respondents.

Overall, respondents to both surveys placed the greatest emphasis on PGx education when asked "What do you feel could help lead to greater uptake and clinical use of pharmacogenomics." Respondents also provided concerns regarding cost and development of infrastructure, standardization, and guidelines as potential facilitators of clinical adoption, followed by research (including general and domain-specific) (Figure 1). Education was also a key focus of responses when asked "What would help drive implementation of pharmacogenomics at your primary institution?" in the Genomic Medicine Community Survey, but infrastructure was predominant in responses to that question (Figure 2).

Most (76%) respondents across both surveys (n = 331) considered the development of a framework of tiered standard terminologies and definitions for genomic variants implicated in drug response variability (similar to ACMG's pathogenic to benign terminology for germline disease variants) necessary. Many respondents who did not indicate agreement did not dispute the utility of developing a framework; however, they added that the ACMG framework required additional considerations for PGx (eg, incorporation of clinical actionability). This is evidenced by responses to the question "What criteria should be used to define clinically actionable pharmacogenes?" (Figure 3), which heavily themed around concepts uniquely PGx (eg, medication efficacy and toxicity) alongside other themes common to ACMG criteria (eg, risk likelihood and impact).

Similar to alignment with ACMG, both survey groups broadly supported leveraging existing PGx guidance. 83% of PGx Community Survey respondents (n = 241) and 72% of Genomic Medicine Community Survey respondents (n = 225) supported utilizing CPIC criteria for development of frameworks for PGx clinical validity and actionability.

Both surveys showed overwhelming support for the idea that the genomic medicine community would benefit from a centralized resource for pharmacogene and variant classification (Figure 4). The vast majority of respondents across both surveys indicated agreement that they felt the genomic community would benefit from a centralized resource (n = 300 / 316, 95%). Only a small percentage of respondents indicated concerns: 3% responded "maybe," whereas 1% indicated that they were not sure or unclear on whether there would be benefits, and 1% stated "no." Survey respondents widely supported the effort to increase

Table 1 Demographic data (total respondents = 364; 487[a])

Category (n PGx; Genomic Medicine)	Demographic	PGx Community	Genomic Medicine Community
Respondents	Respondents who met inclusion criteria	247[a]	261[a]
Geography	US-Based Participants	70%	66%
n = 149; 250	Number of US States represented	31	34
	Number of Countries represented	28	41
Education	MD or DO	20%	18%
n = 245; 257	PharmD	47%	26%
	PhD	40%	44%
	RN or NP	1%	2%
	MS or MPH or MSPH	16%	24%
	BS or BA	2%	4%
Occupation (could select multiple)	Researcher	48%	36%
n = 246; 260	Clinician or health care professional	35%	34%
	Pharmacist	39%	23%
	Student	5%	3%
	Patient, or family, caregiver, or friend of patient	3%	3%
	PGx implementer	48%	23%
	Laboratorian	8%	19%
	Other	6%	10%
Workplace setting n = 246; 260	Non-profit or academic hospital or clinic	48%	51%
	For-profit hospital or clinic	9%	6%
	Reference or clinical laboratory	11%	14%
	Educational or research resource	7%	7%
	University	31%	19%
	Research or clinical institute	13%	9%
	Laboratory test interpretation service	10%	7%
	Other	12%	11%
PGx familiarity n = 168; 193	Over 75% of time spent on PGx	33%	16%
	Less than or equal to 25% of time spent on PGx	33%	64%
n = 245; 258	Unfamiliar with whether their institution implements PGx testing	2%	17%
n = 185; 258	Uninvolved with PGx initiatives	6%	35%
n = 260 (Genomic Medicine Community Only)	Uncomfortable engaging or unfamiliar with PGx	N/A	25%

BA, Bachelor of Arts; *BS*, Bachelor of Science; *DO*, Doctor of Osteopathic Medicine; *MD*, Doctor of Medicine; *MPH*, Master of Public Health; *MS*, Master of Science; *MSPH*, Master of Science in Public Health; *NP*, Nurse Practitioner; *PGx*, Pharmacogenomics; *PharmD*, Doctor of Pharmacy; *PhD*, Doctor of Philosophy; *RN*, Registered Nurse.

[a]Respondents could choose to skip questions. Total *n* for each question is listed in the left column of the table.

standardization of terminology and gene-drug validity and actionability curation (253, 76% across both surveys, $n = 331$), including commentary pointing to it as a potential way to mitigate existing confusion around PGx relationships in the broader genomic medicine community.

Discussion

Overall, these 2 surveys demonstrate a broad consensus on both the importance of PGx and the necessity placed on its continued integration into clinical practice. Despite increased understanding of the effect of germline genetic variation on drug response, broad adoption of PGx clinically is not currently routine. One major obstacle is the limited knowledge and training among clinicians regarding PGx. Many healthcare providers are unsure how to use genetic information to guide drug prescribing, and the gap in knowledge is compounded by the rapid advancements in the field and fragmented resources, making it difficult for implementers to stay current with the latest evidence and recommendations.[14,15] Other challenges hindering PGx adoption include high test costs and inconsistent reimbursement, alongside challenges in the integration of PGx data into electronic health records and clinical decision support systems.[16,17] PGx also uses a unique nomenclature

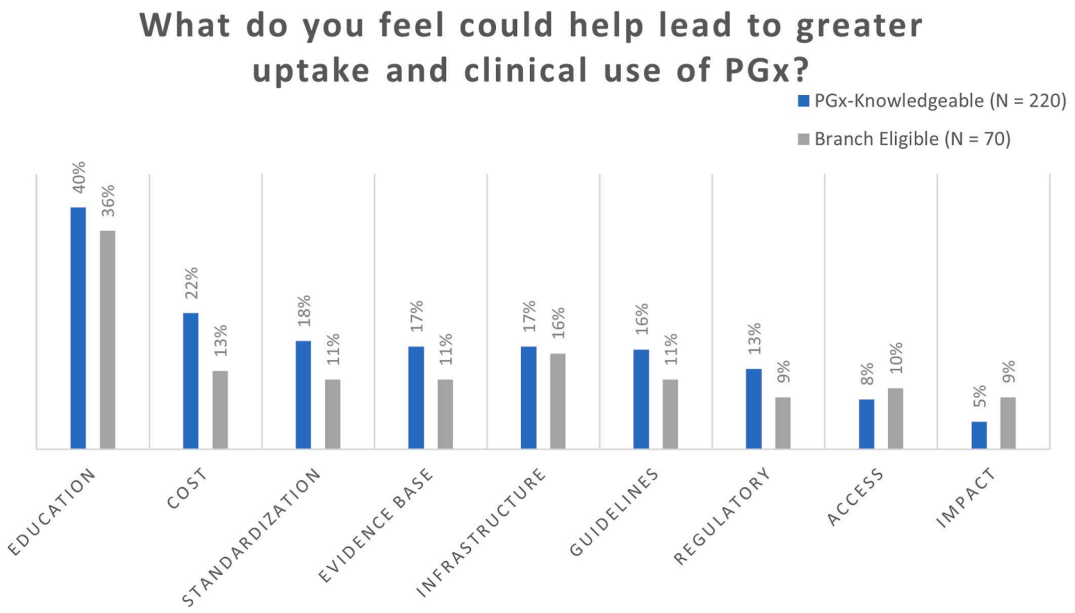

Figure 1 Content analysis results for the question "What do you feel could help lead to greater uptake and clinical use of pharmacogenomics?" across both surveys (see Supplemental Data Code Tables for coding structure). PGx-knowledgeable respondents include those who self-described as comfortable engaging with PGx and/or who regularly or primarily engage with PGx professionally in both surveys. PGx, pharmacogenomics.

system, the star (*) allele system,[1,18] which can be challenging even for trained genetic specialists because of the differences in terminologies and how variants and haplotypes impact clinical phenotypes. The vast array of alleles and continuous updates also present significant challenges for accurate interpretation and clinical

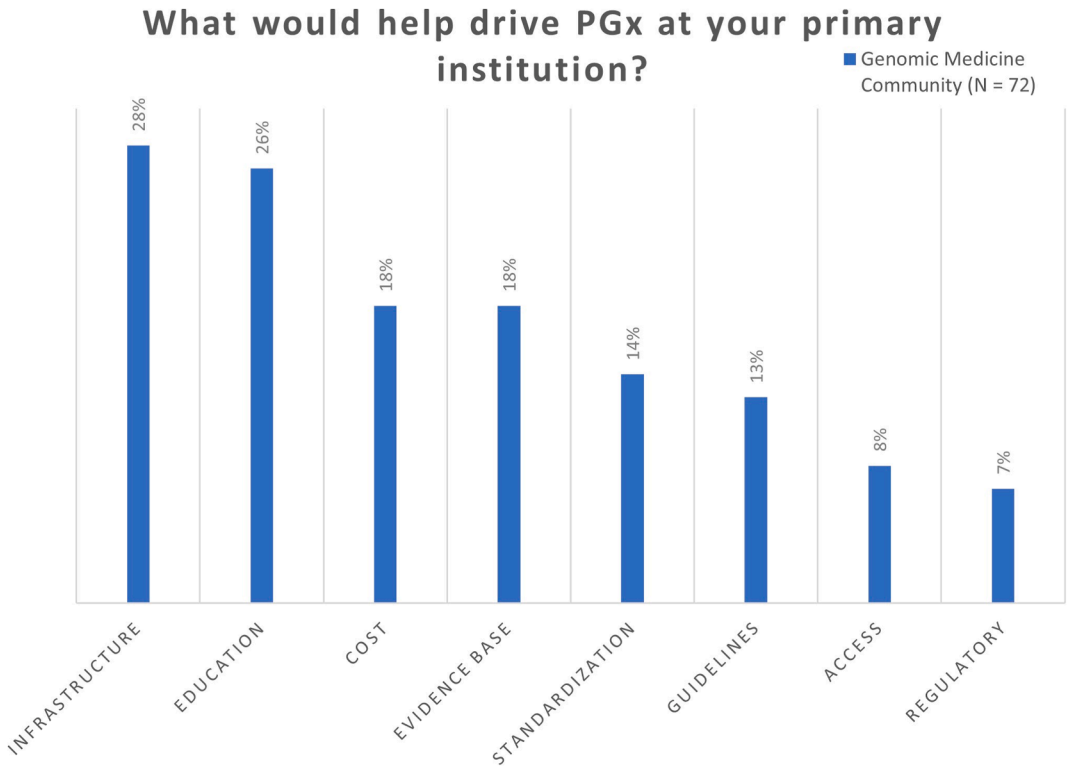

Figure 2 Content analysis results for the question "What would help drive implementation of pharmacogenomics at your primary institution?" (see Supplemental Data Code Tables for coding structure). This question was only asked of branch participants in the Genomic Medicine Community Survey. PGx, pharmacogenomics.

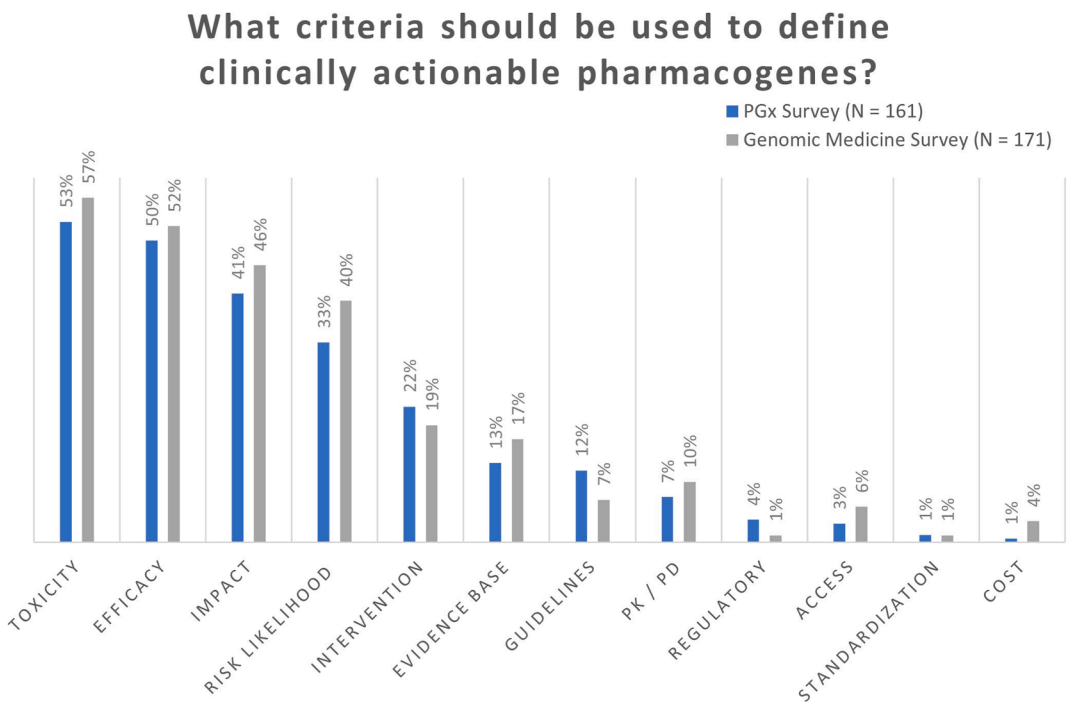

Figure 3 **Content analysis results from both surveys ($n = 332$) to the question "What criteria should be used to define clinically actionable pharmacogenes?"** PGx, pharmacogenomics.

implementation. On the other hand, developing standardized PGx result interpretation across genome resources, enhancing education and training for health care providers and patients, and using terminologies familiar to the medical genetics communities are frequently mentioned as facilitators for successful clinical implementation of PGx.[19,20]

Currently, standardized terms exist for genotype, phenotype, and strength of evidence for PGx gene-drug associations through CPIC (which has strength of recommendations) and PharmGKB (for clinical annotation levels of evidence). However, ACMG's terminology for variant classification does not apply to PGx because PGx variants

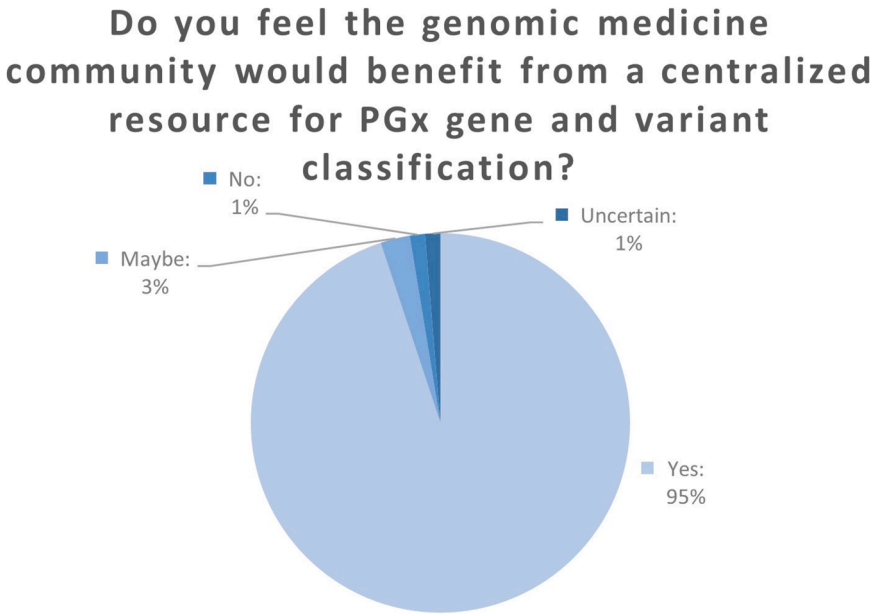

Figure 4 **Responses from both surveys ($n = 316$) to the question "Do you feel the genomic medicine community would benefit from a centralized resource for pharmacogenomics gene and variant classification?"** Free-text entry was permitted, and free-text responses were manually classified. PGx, pharmacogenomics.

do not appropriately map to terms such as "benign" and "pathogenic." As such, there is an unmet need for standardization in variant terminologies to describe clinical validity and actionability in variant-gene-drug phenotype relationships. Respondents to both surveys were broadly supportive of addressing this need and agreed on the need for standardization of PGx nomenclature, evidence evaluation approaches, and recommendations.

ClinGen PGxIC's development of standardized frameworks for gene-drug response clinical validity and actionability aims to align with ClinGen's structure and terminology while integrating existing PGx approaches and supplementing the standardization work already done by existing resources.[12] Survey responses broadly support this approach, including the leveraging of established PGx resources such as CPIC alongside ClinGen structure to accomplish this aim.

Emphasis is placed by respondents on the recognized need to address key differences between PGx and disease genetics throughout the framework development process.

Overall, our analysis of responses discussing barriers and facilitators points to (1) utilization of and respect for existing PGx resources alongside support for leveraging these; (2) an underlying need for a validated source of truth for gene-drug validity and actionability and variant classification that is acceptable to both the PGx community and the broader genomic medicine community; and (3) confidence in ClinGen's PGxIC's approach to leverage accepted frameworks and align standards and terminologies to bridge that gap.

Addressing barriers via framework standardization

Although standardization is one of several factors that can influence PGx implementation and uptake, it has unique potential to mitigate barriers described both in previous needs assessments and by respondents to both surveys.[4] Standardization of nomenclature alongside processes by which clinical validity and actionability are determined can greatly drive adoption and facilitate education, resulting in fewer potential sources of confusion, increased consistency in labeling, and consistent use of terminology. Utilizing a framework and nomenclature aligned with ClinGen can make implementation easier in multiple ways, including facilitating the creation of reporting templates that could be used as models by laboratories. Additionally, it has the potential to reduce confusion around results interpretation, which could potentially reduce test turnaround time and increase practicality of testing. Standardization also makes infrastructure development more efficient, effective, and less costly. Reduction in resources needed also has the power to increase stakeholder buy-in, and reduction in siloing of PGx resources will increase the availability and accessibility of PGx data, supporting more effective integration into electronic health record systems. Reduced siloing and more consistent evaluation of validity and actionability across PGx and the broader genomic medicine community are crucial pieces facilitating a common standard for research quality and will allow for better highlighting of gaps in knowledge and areas of need. A standardized framework utilizing a baseline structure that has buy-in within the broader genomic medicine community has the potential to increase the accessibility of PGx guidelines within that group. Moreover, standardization facilitates the development of internal policies: consistency in terminology and stronger infrastructure can better support the adoption and implementation of PGx testing standards and policies.

Clinical validity and actionability in pharmacogenomics

Although gene-disease validity and actionability are distinct concepts in ClinGen, gene-drug validity and actionability are intrinsically linked. Gene-drug validity refers to the evidence supporting a gene-drug interaction (eg, a drug is metabolized by a given enzyme), whereas gene-drug actionability refers to the potential for altering drug therapy based on genetic information (eg, CPIC or FDA label guidance). These concepts are closely intertwined in PGx because the validity of a gene-drug interaction directly informs its potential for clinical action, and gene-drug clinical validity must be established to consider evaluating the actionability of the gene-drug relationship. This complexity was also noted in survey responses: respondents with PGx expertise were more likely to comment on the intricacies of the relationship between definitions of PGx validity and actionability. The intertwined nature of these terms underscores the need for increased standardization of nomenclature and curation frameworks for gene-drug validity and actionability, and, as previously stated, survey results further support these efforts.

In contrast to disease genetics, PGx interactions require a relevant drug exposure to trigger the resulting phenotype. This is a distinguishing point for the use of the term "actionability" in the PGx sphere: actionability in the context of a gene-drug relationship refers to any future prescribing change that can be taken to reduce medication toxicity or increase medication efficacy based on the patient's genetics. PharmGKB defines FDA labels with "actionable PGx" information as those that discuss "a dose adjustment, contraindication or alternate drug recommendation, or other guidance for patients with a particular genotype or metabolizer phenotype, if known." In contrast, ClinGen defines actionability (in the context of a gene-disease relationship) as referring to "genes that, when significantly altered, confer a high risk of serious disease that could be prevented or mitigated if the risk is known."

Conflation of these 2 uses for the same term, alongside conflation of validity and actionability, is a source of confusion for both areas of focus and can make it difficult to distinguish between the different meanings of the same word.

ACMG nomenclature for variant classification does not translate directly to PGx variants for similar reasons. PGx variants and haplotypes are not considered in terms of whether they are "pathogenic" or "benign" because they typically cause no clinical phenotype in the absence of treatment with a relevant drug.

Support for a unified resource for pharmacogenomics

Historically, various resources in the United States for PGx data, knowledge, and nomenclatures have been funded separately by the NIH and operated independently, with data stored in disparate databases.[1,3,5,21] This presents significant hurdles for researchers and clinicians seeking comprehensive information to access, interpret, and apply PGx insights effectively in clinical settings. Additionally, maintaining these separately funded resources and ensuring synchronization is challenging and costly, especially with the rapidly evolving evidence base and changes to preferred nomenclature.

A centralized, global resource would streamline access to PGx information and facilitate the discovery and use of these data by researchers and clinicians. Furthermore, centralization can increase and support stakeholder buy-in (eg, clinical, laboratory, and insurance) alongside overall confidence in the science behind PGx testing, thus increasing the utility of existing resources. An initiative to centralize will foster greater collaboration, enhance data integration, improve accessibility, and ultimately facilitate the integration of PGx into clinical decision-making processes for more effective patient care.

Limitations

Although, to our knowledge, this was the largest PGx survey conducted across the PGx and genomic medicine communities to date, some limitations must be acknowledged. First, the convenience (snowball) sampling approach may produce incomplete sampling and may not be representative data of the communities that were intended to sample. Similarly, respondents were primarily based in the United States and were English speaking; therefore, responses may not wholly encompass the perspectives of non-US PGx expertise (including experts who primarily or only speak languages other than English) and may signal a significant limitation of our dissemination approach.

Second, the relatively high proportion of free-text response questions limited the ability to analyze these questions quantitatively. The thematic coding process was manual and thus subject to interpretation biases, as well as human error. The relatively high proportion of free-text response questions may have also contributed toward survey fatigue, which potentially influenced response bias. However, the availability of free text is valuable in surveys because it removes potential surveyor bias stemming from use of predetermined answers, and this broadened the scope of narratives that could be captured, including those that would otherwise have been missed.

Finally, all demographics were self-reported, which includes time spent on PGx, as well as PGx expertise. Although both categories overlap as expected, it is entirely possible that certain respondents are miscategorized because of an inflated sense of personal expertise. This potential limitation was discussed during the design process, and the committee determined that other methods of assigning PGx expertise would be subject to researcher biases.

Conclusion

PGx is increasingly being considered standard of care with other genomic medicine and disease risk assessments. As such, it is crucial to evaluate the barriers and facilitators to effective, accurate, and practical clinical implementation of PGx. Harmonizing tiered standard terminology and definitions of existing resources toward a framework that reflects gene validity and clinical significance of genomic variants implicated in drug response variability is a necessity. A central resource accessible to the broader genomic medicine community is critical for ensuring laboratories have access to up-to-date and validated evidence as they develop and validate PGx tests. Based on our results, there is a well-defined need for a validated and accepted source of truth for PGx. Our survey data provide evidence of broad support for the development of ClinPGx (www.clinpgx.org), as an affiliated resource to ClinGen that unifies major PGx resources and aligns with the genomic medicine communities to eliminate the historical professional silos in clinical genomics.

Data Availability

Response data are available upon request. To request data access, please contact the coordinator of the ClinGen PGxIC (https://clinicalgenome.org/working-groups/pharmacogenomics/).

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Ethics Declaration

The needs assessment study described in this article does not include human subjects research. Participation in this study was voluntary, and informed consent was implied by completion of the anonymous online survey. Information regarding purpose and use of data collection was included in the survey preamble (Supplemental Survey Questions).

Conflict of Interest

The authors declare no conflicts of interest.

Additional Information

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