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The Pharmacogenomics Global Research Network Implementation Working Group: global collaboration to advance pharmacogenetic implementation

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Conflicts of interest

J.N.P. is a consultant for VieCure and Clarified Precision Medicine. C.B. is founder of Sequence2Script Inc. J.R.B. is a consultant for OptumRx. N.K.T. is a member of the Association of Pathology Chairs (APC) Advocacy Working Group, Chair-elect of the Critical and Point-of-Care Testing Division, Association for Diagnostics and Laboratory Medicine (ADLM). J.D.A. is a consultant to Nurture Genomics and Precision Genetics. For the remaining authors, there are no conflicts of interest.

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Abstract

Pharmacogenetics promises to optimize treatment-related outcomes by informing optimal drug selection and dosing based on an individual's genotype in conjunction with other important clinical factors. Despite significant evidence of genetic associations with drug response, pharmacogenetic testing has not been widely implemented into clinical practice. Among the barriers to broad implementation are limited guidance for how to successfully integrate testing into clinical workflows and limited data on outcomes with pharmacogenetic implementation in clinical practice. The Pharmacogenomics Global Research Network Implementation Working

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Group seeks to engage institutions globally that have implemented pharmacogenetic testing into clinical practice or are in the process or planning stages of implementing testing to collectively disseminate data on implementation strategies, metrics, and health-related outcomes with the use of genotype-guided drug therapy to ultimately help advance pharmacogenetic implementation. This paper describes the goals, structure, and initial projects of the group in addition to implementation priorities across sites and future collaborative opportunities.

Keywords

implementation; outcomes; pharmacogenetics; strategies

Introduction

There is a wealth of evidence on genetic contributions to the inter-patient variability in drug response. Genetic information is now included in numerous drug labels approved by regulatory bodies around the world, and guidelines are available for interpretation of pharmacogenetic test results and application of results to drug prescribing [1–3]. Moreover, a number of commercial reference laboratories now offer pharmacogenetic testing [4]. Yet, even with well-recognized genetic associations with drug response and resources available to facilitate the clinical use of test results, pharmacogenetic-guided prescribing has not been widely implemented into clinical practice.

The Pharmacogenomics Global Research Network (PGRN) Implementation Working Group includes clinicians, researchers, and others from institutions worldwide who have an interest in clinical implementation of pharmacogenetic testing. The group strives to address common implementation challenges, including the limited data on strategies for successful testing integration into clinical workflow. Herein, we describe the goals, structure, and initial projects of the PGRN Implementation Working Group as well as implementation priorities across sites and opportunities provided through this global collaboration.

Pharmacogenomics Global Research Network Implementation Working Group

The PGRN aims to catalyze and lead discovery and translational research in the field of precision medicine [1]. The PGRN membership includes researchers, clinicians, laboratory professionals, and trainees from academic institutions, industry, government, and nonprofit organizations around the world who are interested in pharmacogenetic research, education, and practice. The Implementation Working Group within the PGRN was formed in September 2023 to broadly engage PGRN members interested in pharmacogenetic implementation to share and collectively disseminate information on implementation priorities, strategies, metrics, and health-related outcomes with the use of pharmacogenetic information for clinical care to ultimately advance testing globally. The working group is modeled after the Implementing GeNomics In pracTicE (IGNITE) Network Pharmacogenetics Working Group, and welcomes three types of PGRN members: (1) those who have implemented pharmacogenetic testing in practice (i.e. experienced

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implementers), (2) those in the process of implementing testing, and (3) those with an interest in implementation [5]. The expectation is that those in the early or planning stages of testing and those beginning to consider implementation will learn from experienced implementers.

The working group is led by a chair and cochair who are appointed for up to 3-year terms by the PGRN leadership. Members meet twice-monthly through teleconference calls and in-person at the annual PGRN meeting. Teleconferences are scheduled to occur between 11 a.m. and 12 p.m. U.S. Eastern Time in an effort to accommodate as many participants as possible. Recognizing that this time is most inconvenient for those in Asia, Australia, and other countries in that area, we are exploring having a quarterly conference call at a time more conducive for these participants. Distribution of meeting summaries, surveys, and other communication occurs through email so that those unable to join teleconferences may still participate. Additional more focused teleconferences are scheduled to move individual projects forward. Working group projects may be proposed by any member of the group, with a polling strategy used to assess interest across the group. A project leader(s) and writing team members are selected among volunteers for each project. Prior to participation in a project, each member signs a collaborative agreement, adapted from the International Warfarin Pharmacogenetics Consortium, which outlines member responsibilities, requirements for data access and sharing, and authorship guidance [6]. The agreement is available through the PGRN website [1]. Work by the group is done on a volunteer basis.

Characteristics and implementation priorities of member institutions

A survey was distributed via email to PGRN Implementation Working Group members from 54 institutions in early 2024 to assess institutional characteristics, current and planned pharmacogenetic implementations, use of single versus multigene testing, and pharmacogenetic guidance used in implementation. The survey specifically asked about implementation of 52 gene–drug pairs and 7 phenotype–drug pairs (Fig. 1). The survey was approved as exempt by the University of Florida Institutional Review Board. Surveys were returned from 39 of the 54 institutions (72% of total institutions); 31 of the 39 institutions responding (79%) were from the USA (U.S.), and 8 (21%) were from other countries (Fig. 2, Table 1). Of these institutions, 28 (72%) reported being academic, and 20 (51%) reported serving patients of all ages (Fig. 3a and b). Most (74%, 29 of 39) responded that they do not serve a specific specialty, while 26% of institutions (10 of 39) reported a focus on particular specialties (e.g. hematology/oncology, cardiology, psychiatry, burn treatment) or populations (e.g. patients with Alzheimer’s disease or autism). Overall, 35 of the 39 sites responding (90%) have clinically implemented pharmacogenetic testing. Of these, 46% (16 of 35) use both single and multigene testing, 40% (14 of 35) use only multigene testing, and 14% (5 of 35) use only single gene testing (Fig. 3c); 69% (24 of 35) reported using multigene testing as the primary means of genotyping, and 17% (6 of 35) use it in some cases. The initial implementation strategy reported at each site illustrated a shift from single gene to multigene testing in recent years (Fig. 4).

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Figure 1 portrays the percentage of sites that have implemented different gene–drug and phenotype–drug pairs, with *CYP2C19*-clopidogrel (83%) being the most common, followed by *TPMT/NUDT15*-thiopurines, *CYP2C19/CYP2D6*-antidepressants, *CYP2D6*-opioids, *CYP2C19*-voriconazole, and *CYP3A5*-tacrolimus. Twelve sites reported implementation of a gene–drug pair that was not listed on the survey; these are summarized in Supplementary Table 1, Supplemental digital content 1, http://links.lww.com/FPC/B503. A similar analysis was conducted for gene–drug pairs that sites plan to implement in the future (Supplementary Figure 1, Supplemental digital content 1, http://links.lww.com/FPC/B503), with *ABCG2*-rosuvastatin, *DPYD* genotyping-fluoropyrimidines, *CYP2C19*-voriconazole, *CYP2C19*-proton pump inhibitors, and *SLCO1B1*-statins being the most common. Almost all sites (92%) reported using Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines to inform which gene–drug pairs to include for implementation; 79% used guidance by the U.S. Food and Drug Administration (FDA), 68% used Association of Molecular Pathology guidance, 58% used Dutch Pharmacogenetics Working Group (DPWG) guidelines, and 13% used clinical practice guidelines from medical societies.

Initial projects

Landscape of pharmacogenetic testing project

While widespread adoption of pharmacogenetic testing is not yet ubiquitous, there has been significant progress across various domains, including quality of evidence, insurance coverage, and standardization [7,8]. A number of early implementation initiatives have been described [9–16]. Efforts to implement pharmacogenetic into practice are shaped by institution-specific factors and available resources (e.g. personnel, equipment), which generate variable program designs and approaches as described above. Therefore, the PGRN Implementation Working Group is conducting a more detailed landscape survey to assess implementation practices and gather a global characterization of pharmacogenetic programs.

An electronic survey will be distributed to the PGRN membership. Participants are eligible to complete the survey if they have implemented pharmacogenetic into practice or plan to implement pharmacogenetic at their site. The survey will comprehensively cover nine domains related to pharmacogenetic implementations: program characteristics; program infrastructure; pharmacogenetic test characteristics; patient population; electronic health record (EHR) integration; clinical services; funding and billing; ethical, legal and social issues (ELSI); and educational efforts. These domains were selected to identify specific program designs and approaches and the contexts in which they function. Program characteristics will capture descriptions of the health system or clinic associated with the pharmacogenetic program, in addition to the start date of the program, implementation start date, and stage of the implementation. The program infrastructure will identify the primary governance for the program (e.g. precision medicine department, pathology department, pharmacy & therapeutics committee) and the personnel involved in the program. In addition to collecting the types of personnel involved in the program (e.g. pharmacogenetic pharmacist, physician, genetic counselor), the survey will collect personnel effort and whether the pharmacogenetic program explicitly funds various positions. The pharmacogenetic test characteristics will describe the patient setting in which the test is

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offered (e.g. inpatient, outpatient), the testing setting (e.g. internal, external), test type (e.g. single gene, multigene), test methodology, genes tested, and a summary of tests performed. The patient population domain will further identify the medical specialties that order testing and the approach to testing (e.g. fully preemptive, testing based on medication response or diagnosis). EHR integration will identify the type of EHR system used, the location and structure of genetic data in the EHR, and describe available clinical decision support (CDS). The clinical services domain will capture available clinical services related to pharmacogenetic implementation, including workflows for referrals and testing, personnel involved, and the launch date of services. The funding and billing domain will address the funding for the program itself in addition to the reimbursement approach for pharmacogenetic tests and clinical services related to care. Information on healthcare payment models will also be collected to inform potential future projects examining how differing models may influence implementation approaches. The ELSI domain will characterize practices related to patient informed consent and biobanks. The final domain investigates methods, timing, and intended audiences for education initiatives.

The data obtained will be the most extensive characterization of implemented programs worldwide and serve as a diverse framework for implementing pharmacogenetic into clinical practice. Results from this survey will help institutions identify trends and considerations when designing or redesigning their pharmacogenetic program.

DPYD/UGT1A1 implementation strategies project

Germline pharmacogenetic testing has emerged into the care of patients diagnosed with cancer to guide fluoropyrimidine and irinotecan therapy [17,18]. Fluoropyrimidines, consisting of 5-fluorouracil, capecitabine, and tegafur, are used to treat numerous cancer types including gastrointestinal, breast, and head and neck cancers. Dihydropyrimidine dehydrogenase (DPD) is the rate-limiting step in fluoropyrimidine catabolism [19]. Certain variants in *DPYD*, the gene that encodes for DPD, result in reduced DPD activity, elevated systemic fluoropyrimidine exposure, and increased risk for potentially life-threatening toxicity [20–22]. Both CPIC and DPWG provide evidence-based guidelines for adjusting fluoropyrimidine therapy based on *DPYD* genotype results [23,24]. Studies have also shown that *DPYD*-guided dosing can improve patient safety without negatively affecting overall survival [25,26].

European countries have been early adopters of testing, due in part to the European Medicines Agency (EMA) recommending *DPYD* genotyping or phenotyping prior to initiation of a fluoropyrimidine [27,28]. In contrast, the FDA does not recommend testing. However, in response to a citizen's petition requesting that fluoropyrimidine drug labels recommend *DPYD* testing, and as part of the FDA's Project Renewal, the FDA recently revised the patient counseling section to recommend prescribers discuss toxicity risks and *DPYD* test availability with their patients, and also added to the label that *DPYD* testing should be considered [29,30]. The National Comprehensive Cancer Network guidelines either do not mention *DPYD* genotyping for fluoropyrimidine therapy (e.g. pancreatic guideline) or state uncertainty about *DPYD* testing due to concerns about reduced treatment effectiveness in those who would receive dose reductions (e.g. colorectal guideline) [30,31].

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Nevertheless, many cancer centers and other academic institutions have proceeded with implementing *DPYD* testing into patient care [32]. Nearly 60% of the working group sites surveyed have implemented *DPYD* testing (Fig. 1) and a number of other sites are planning to implement *DPYD* testing in the future (Supplementary Figure 1, Supplemental digital content 1, http://links.lww.com/FPC/B503).

Irinotecan is used to treat numerous cancer types, particularly gastrointestinal cancers in combination with a fluoropyrimidine. *UGT1A1* encodes for the uridine diphosphate glucuronosyltransferase (UGT) 1A1 enzyme that has a role in elimination of the active metabolite of irinotecan, SN-38, via glucuronidation [33]. Variants in *UGT1A1* can increase the risk of irinotecan-induced toxicity due to increased exposure to SN-38 [33]. There are evidence-based guidelines describing how to adjust irinotecan dosage based on *UGT1A1* genotype results to mitigate toxicities [34]. Similar to *DPYD*, adoption of *UGT1A1* genotyping has been hampered due to limited guidelines recommending *UGT1A1* testing prior to irinotecan therapy [33,35]. Other anti-cancer drugs that may be impacted by *UGT1A1* variants include sacituzumab govitecan-hziy and belinostat [33].

To better understand the global landscape of *DPYD* and *UGT1A1* genotyping adoption, the Implementation Working Group has developed a survey focused on *DPYD* and *UGT1A1* implementation that will be distributed to group members. This effort aims to better understand successful strategies for integrating *DPYD* and *UGT1A1* genotyping into patient care. PGRN sites that have implemented such testing or are in the planning stage for implementation, will be asked to complete the survey to determine commonalties among sites that have successfully integrated testing into patient care. Comparisons and contrasts will be explored between different regions globally, particularly between regions where testing is recommended versus those where testing is not recommended. Findings may help to further inform successful strategies for *DPYD* and *UGT1A1* implementation to mitigate drug-induced toxicities.

Other planned projects

Several projects are in the planning stage, with project leaders and writing group members identified. These include a plan to examine implementation strategies for *CYP3A5*-guided tacrolimus dosing in transplant patients and *CYP2C19*-guided clopidogrel use for neurovascular indications. An additional project will examine how direct-to-consumer pharmacogenetic test results are used in clinical practice. For each project relevant to pediatric patients, a smaller group of pediatric-focused implementers will review the surveys and results to ensure that the data are applicable to the pediatric population. When appropriate, pediatric-focused analyses will be performed and disseminated.

Future collaborative research opportunities

The PGRN Implementation Working Group provides a rich environment in which to explore collaborative research opportunities around the globe. Members of this group represent different types of healthcare institutions (e.g. academic, community, nonprofit, private) across several countries and regions, which have different payer systems and regulatory bodies. These differences can be leveraged to evaluate barriers to and facilitators

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of pharmacogenetic testing, including the evolving landscape for test reimbursement and clinical implementation in diverse populations worldwide. Evidence of clinical utility is often cited as a major barrier to implementation of genomic medicine [36–38]. The working group offers an unparalleled opportunity to assess real-world clinical and implementation outcomes, thereby enriching the pharmacogenetic evidence base and advancing research in genetically diverse populations [39,40]. The working group also provides the opportunity to compare implementation strategies and the adoption of clinical pharmacogenetic testing and guidelines in a myriad of settings. For example, implementation strategies and adoption can be evaluated in the context of international differences in clinical standards of care, prescribing patterns, access to pharmacogenetic testing, provider education and knowledge, cultural attitudes, and health disparities. Other potential areas of future research include how varied workforce capacities, infrastructure capabilities, and information technology resources (e.g. EHRs and CDS tools) influence pharmacogenetic implementation globally. Lastly, the working group can leverage its international representation to assess the real-world cost-effectiveness of genotype-guided therapy, particularly in the setting of different funding models, resources, and local and national health priorities.

Discussion

Evidence supporting the clinical utility of pharmacogenetic testing is accumulating [41]. For example, the large, multi-center, European PREemptive Pharmacogenomic testing for preventing Adverse drug REactions (PREPARE) trial recently demonstrated a 30% reduction in adverse reactions with pharmacogenetic testing [42]. A recent PREPARE substudy of participants with schizophrenia, major depressive disorder, or bipolar disorder, showed a similar reduction in adverse drug effects in addition to fewer hospitalizations and reduced treatment cost with pharmacogenetic testing [43]. A U.S.-based study found implementing pharmacogenetic-enriched comprehensive medication management reduced direct medical charges by approximately $7000 per participant [44]. Professional organizations such as CPIC, DPWG, and the Canadian Pharmacogenomics Network for Drug Safety synthesize available data to produce evidence-based guidelines designed for clinicians to translate genetic test results into actionable prescribing decisions [2,3,45]. As of mid-2024, CPIC has published 26 guidelines that each focus on a unique drug or drug class for which a significant pharmacogenetic interaction has been demonstrated [2]. Regulatory agencies like the FDA and EMA have also recognized the importance of pharmacogenetics and have amended hundreds of drug labels to include information on pharmacogenetic interactions, albeit few include recommendations for testing [46,47]. Moreover, organizations such as Standardizing Laboratory Practices in Pharmacogenomics (STRIPE) and the Association of Molecular Pathology are working to harmonize pharmacogenetic testing standards, practices, and resources [48,49].

There is variable guidance for pharmacogenetic testing across countries. For example, the EMA recommends testing for DPD deficiency prior to initiating fluoropyrimidine therapy whereas the National Comprehensive Cancer Network does not [50,51]. The decision by working group members to implement testing in the absence of national organization clinical practice or regulatory guidance was based on a number of factors. There is general consensus among working group members that genetic information,

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much like renal function or consideration of drug interactions, can inform more optimal therapy for individual patients, and, similar to renal function or consideration of drug–drug interactions, does not require clinical trial evidence of its utility prior to implementation, particularly when genetic test results are already available. CPIC and DPWG share this perspective, which is reflected in their evidence-based prescribing recommendations (e.g. select alternative drug or dose) for various gene–drug pairs. Other factors considered in implementation decisions include the severity of outcomes associated with genetic variants; availability of CPIC, DPWG, or similar guidelines; testing as a mean of market differentiation; increased payer coverage for testing; and drug labeling changes, such as the recent addition of language to fluoropyrimidine labels about informing patients as to the availability of testing. Pharmacogenetic testing may also be a means to improve health equity, especially for populations that have a high frequency of variants that increase risk for adverse drug-related outcomes. In some cases, concerns about legal liability influenced decisions to implement, especially following lawsuits related to fluoropyrimidines and clopidogrel prescribing in the absence of genotyping [22,52]. A recent Hawaiian lawsuit further illustrates the risk for worsening health disparities by not offering testing [52]. We also note that while implementation provides the infrastructure for pharmacogenetic testing, this does not necessarily mean that pharmacogenetic testing is routinely done, and thus, is not inconsistent with professional guidelines in that regard.

While pharmacogenetic testing has been incorporated into some clinical practice settings, adoption is variable and depends on many factors; this can result in significant inequities in access to pharmacogenetic testing. Urban academic medical centers and well-resourced health systems were early adopters of pharmacogenetics in clinical care; however, many rural, community-based facilities with limited access to specialty care lag in implementation. Differing healthcare payment models (e.g. single-payer, public insurance, private insurance) can also influence the uptake of pharmacogenetic testing on a global scale. Some institutions rely on patient self-payment for testing, which has implications for widening healthcare disparities. Fragmented health systems create another challenge to implementation. Studies cite testing costs, antiquated infrastructure, and lack of provider awareness as barriers to implementation efforts, which are further exacerbated in rural and resource-limited settings [53–55]. Additionally, inadequate representation of minority and underserved populations in genomic research present challenges to the equitable implementation and understanding of the clinical utility of pharmacogenetic. To date, genomic research has disproportionally included populations of European ancestry and those living in urban areas with access to specialty care [56]. Many medications used in pediatric patients have pharmacogenetic studies performed only in adults, though the side effect profile and pharmacokinetics are often different in pediatric patients compared to adults [57]. The importance of this issue necessitates that policy makers, providers, and researchers concentrate their efforts to address these challenges and achieve equitable implementation. Recent legislation requiring insurers to cover biomarker testing may help in this regard [58].

The PGRN Implementation Working Group presents a unique opportunity to address several challenges facing the global field of pharmacogenetic. For example, in recent years, economic evaluations have been conducted to assess the cost-effectiveness of pharmacogenetic testing [59]. However, with most economic evaluations taking place in

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the US, applying these results to other countries can be challenging [60]. Countries have different cost-effectiveness thresholds, different payment models for healthcare services, different costs for drugs and services, and different frequencies of the pharmacogenetic variants depending on race and ethnicity. Therefore, cost-effectiveness in one country may not directly translate to cost-effectiveness in another [61,62]. An additional challenge, specific to U.S. sites, relates to the FDA's final rule on laboratory developed tests as *in vitro* diagnostic products [63]. The PGRN Implementation Working Group offers a collaborative and diverse community that can evaluate the cost-effectiveness of implementing pharmacogenetic testing around the globe, the impact of the FDA rule on laboratory developed pharmacogenetic tests, and other challenges related to pharmacogenetic implementation.

The results of our survey provide a snapshot of implementation priorities across PGRN sites. Most sites reported using CPIC guidelines to inform implementation. CPIC guidelines for clopidogrel and thiopurines were the earliest ones published, reflecting the high degree of evidence supporting genotype-guided use of these medications, and thus, it is not surprising that these are among the most common examples of pharmacogenetic implementation [2]. A recent American Heart Association Scientific Statement in support of *CYP2C19* testing for clopidogrel may lead to broader implementation efforts in this area [64]. CPIC guidelines have been published for other commonly implemented gene–drug pairs, such as *CYP2D6*-opioids, *CYP2D6/CYP2C19*-antidepressants, *CYP3A5*-tacrolimus, and *SLCO1B1*-statins, for close to or over 10 years, likely influencing the high uptake of these implementations across sites surveyed. Notably, not all sites within the PGRN that have implemented pharmacogenetic testing into practice responded to our survey, and there are other sites not affiliated with the PGRN that have implemented (or are planning to implement) pharmacogenetic testing. Nonetheless, we believe that the implementation priorities captured herein likely reflect those of the broader population of implementers, especially for U.S. sites, which represented the majority of respondents. We recognize the low representation of non-U.S. sites, and especially those from Asian and South American countries, as a limitation. Given that infrastructure, funding models, and implementation approaches may differ by country, we are working with the PGRN Global PGx Committee to increase global engagement in PGRN Implementation Working Group to ensure global representation in our future projects.

For sites within the PGRN that are in the process of implementing pharmacogenetic testing or are interested in implementation, this collaboration will be extremely useful. It will provide a learning platform for these institutions where they can benefit from the experience of more established sites that have already implemented successfully. Implementation strategies that can be shared include genotyping techniques, timing of genotyping, clinician and patient education methods, CDS, return of results approaches, and billing information. In turn, sites that have not yet implemented testing can share specific barriers for going forward, which may inform projects by the group that could help address these barriers. In addition, it will open up avenues for collaboration, particularly addressing underrepresented populations, rare alleles, and rare outcomes where large cohorts are required. The PGRN Implementation Working Group will also offer experienced implementers valuable information, such as data on outcomes and cost-effectiveness from

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other sites that may have precluded them from implementing a specific gene–drug pair. Similar to previous work by the IGNITE Network, collaborative efforts across sites that have successfully implemented the same gene–drug pair will allow data sharing to create a patient population that is large enough to examine outcomes of pharmacogenetic implementation [65]. The PGRN effort will extend such work to a global scale. This may ultimately provide evidence to support testing reimbursement and broader implementation. Sites outside the PGRN are also expected to learn from the publications by this working group and will have opportunities for future collaborations.

Summary

The PGRN Implementation Working Group provides the infrastructure for global collaboration among individuals with a shared interest in pharmacogenetic implementation. Through on-going and future projects, the working group will collectively disseminate data on successful implementation strategies, lessons learned, and outcomes with pharmacogenetic testing in practice. Data provided through this collaboration are expected to help address common implementation challenges and inform broader implementation efforts worldwide.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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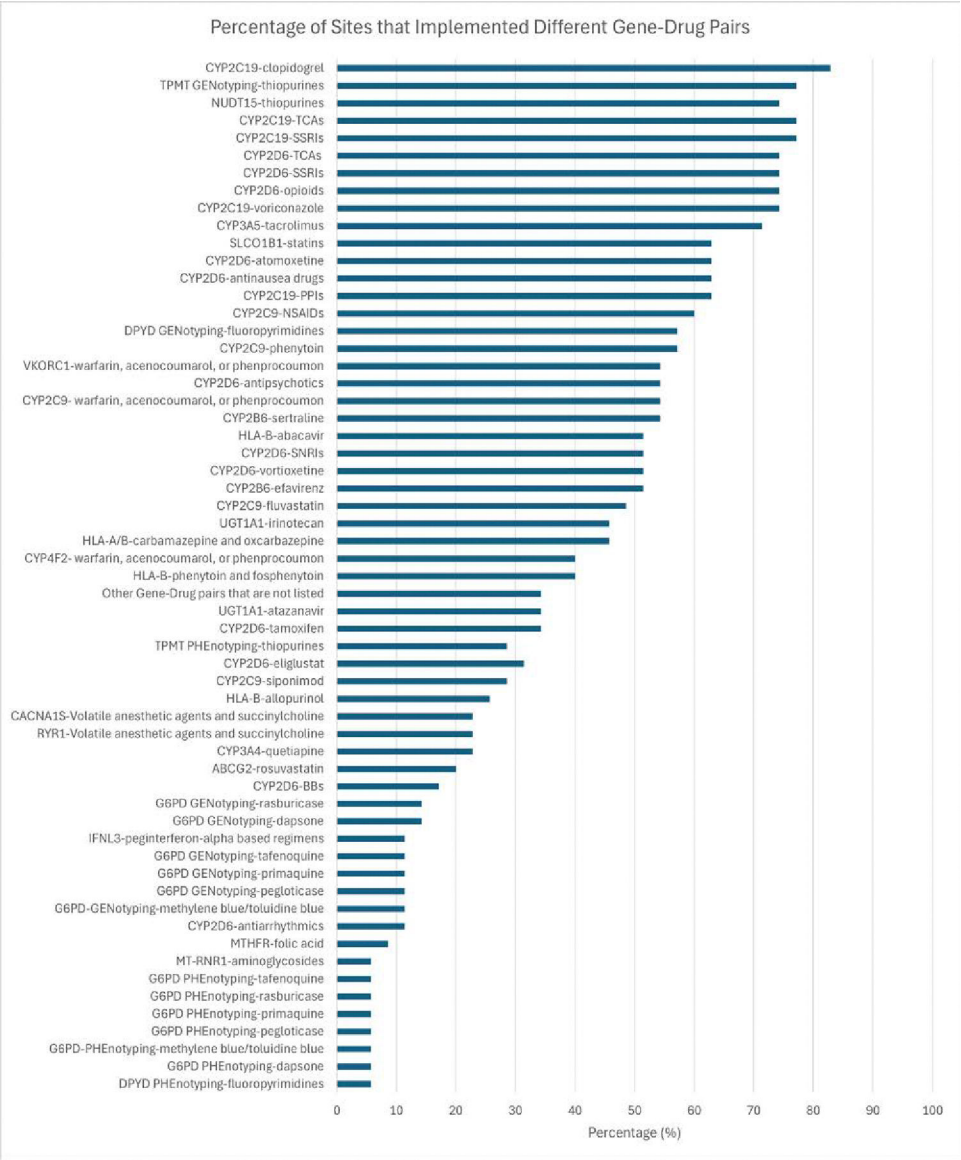

Fig. 1.

Summary of gene–drug and phenotype–drug pairs implemented across sites. The bar graph shows the percentage of the 35 sites that have implemented each gene–drug pair. Data are ranked in descending order. The most common *CYP2D6*-antipsychotic medications implemented were aripiprazole, brexpiprazole, haloperidol, and risperidone. The most common *CYP2D6*-SNRI medication implemented was venlafaxine. Twelve (34%) sites reported implementation of an ‘other gene-drug pair not listed’ in the survey, which are summarized in Supplementary Table 1, Supplemental digital content 1, http://links.lww.com/FPC/B503. BBs, beta-blockers; NSAIDs: nonsteroidal anti-inflammatory drugs; PPIs, proton pump inhibitors; SNRIs, serotonin and norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants

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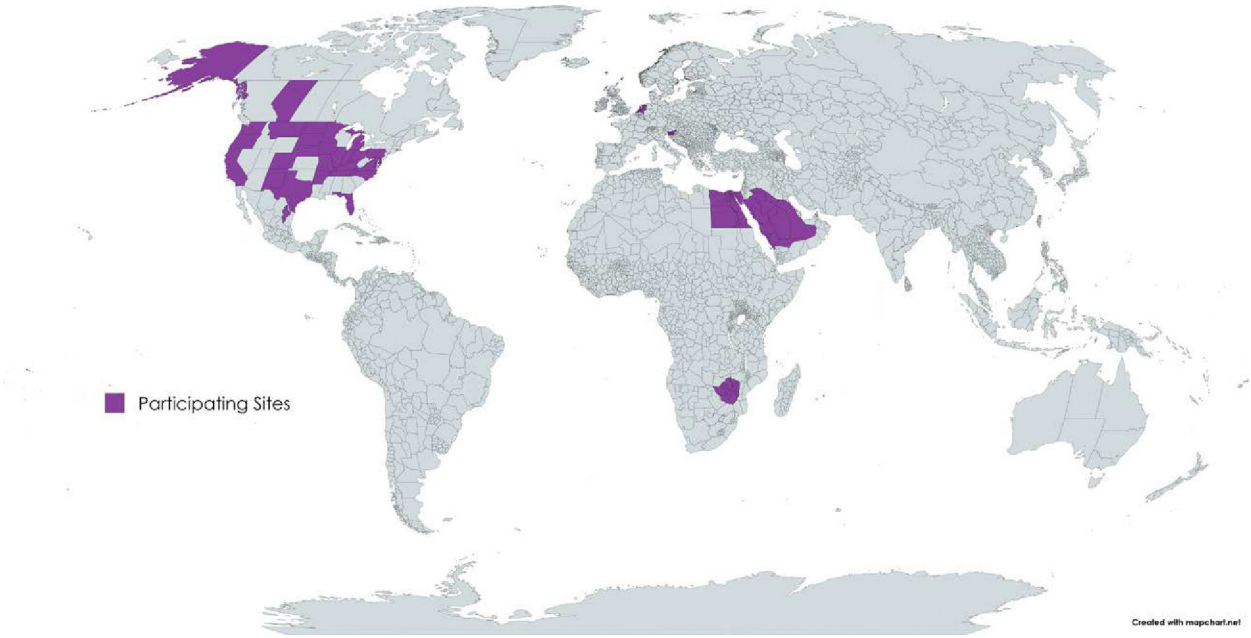

Fig. 2.

Worldwide map of participating sites. The map highlights the countries and US states that have participating sites (shaded in purple).

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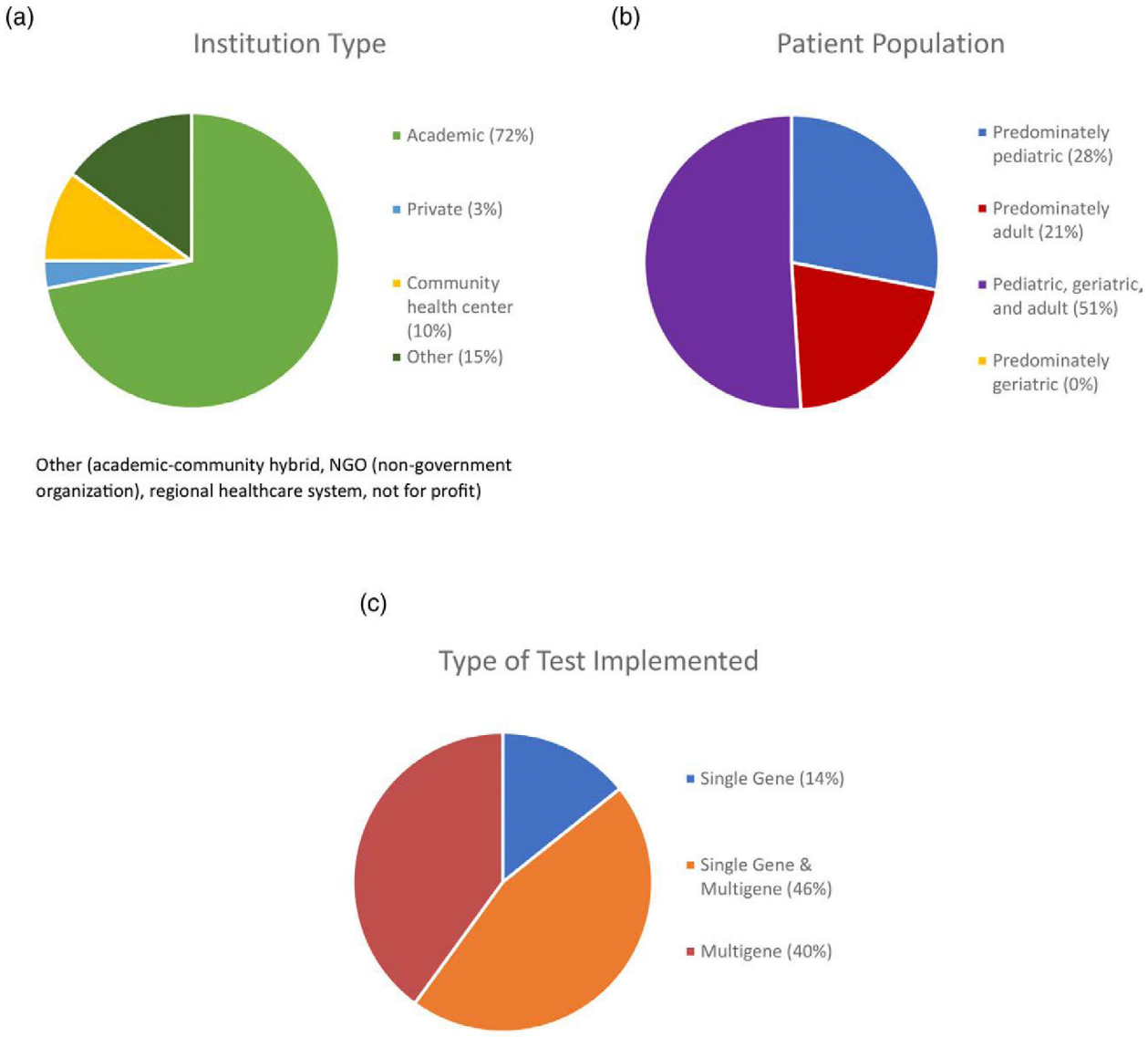

Fig. 3.

Summary of participating site characteristics. (a) The type of institution of the 39 institutions that responded to the survey. (b) The patient population(s) served of the 39 institutions that responded to the survey. (c) The type of pharmacogenetic test implemented among the 35 sites reporting implementation of testing.

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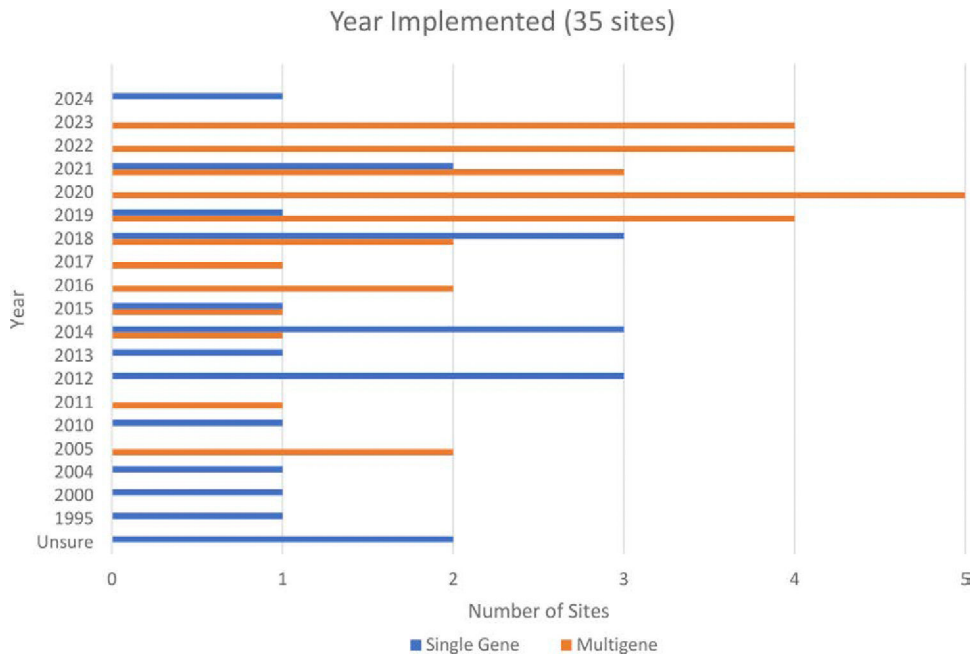

Fig. 4.

Summary of the initial year of pharmacogenetic implementation among participating sites. The bar graph shows the number of sites by calendar year that initiated clinical implementation at their institution using single gene testing or a multigene panel. Sixteen sites reported implementation of both single gene and multigene testing. The initial calendar year for both the single gene and multigene implementation at each of these sites are included in the figure.

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Table 1

Name and location of the 39 participating sites

Institution	Location
African Institute of Biomedical Science & Technology AND University of Zimbabwe, Dept. of Oncology	Harare, Zimbabwe, Africa
Allegheny Health Network	Pittsburgh, PA, USA
Ann & Robert H. Lurie Children's Hospital of Chicago	Chicago, IL, USA
Arkansas Children's Hospital	Little Rock, AR, USA
Atrium Health (part of Advocate Health)	Charlotte, NC, USA
Children's Cancer Hospital, Egypt 57357	Cairo, Egypt
Children's Hospital Los Angeles	Los Angeles, CA, USA
Children's Mercy Kansas City	Kansas City, MO, USA
Children's Minnesota	Minneapolis, MN, USA
Cincinnati Children's Hospital Medical Center	Cincinnati, OH, USA
Erasmus MC	Rotterdam, The Netherlands
Indiana University	Indianapolis, IN, USA
Johns Hopkins Medicine	Baltimore, MD, USA
King Faisal Specialist Hospital and Research Center	Riyadh, Saudi Arabia
L.S. Skaggs Institute for Health Innovation, University of Montana	Missoula, MT, USA
Lifespan	Providence, RI, USA
MedStar Health	Multi-state health system, USA (DC, MD, VA)
Moffitt Cancer Center	Tampa, FL, USA
Nemours Children's Health, (Florida)	Jacksonville, FL, USA
Nemours Children's Health, Delaware Valley	Wilmington, DE, USA
Providence Health	Multi-state health system, USA (AK, CA, OR, WA, MT, NM, TX)
Roudebush Veterans Affairs Medical Center	Indianapolis, IN, USA
Sanford Health	Multi-state health system, USA (IA, MN, MT, ND, NE, SD)
St. Elizabeth Healthcare	Multi-state health system, USA (KY, IN)
St. Jude Children's Research Hospital	Memphis, TN, USA
Tecnologico de Monterrey	Monterrey Nuevo Leon, Mexico
University of Calgary	Calgary, Alberta, Canada
University of California, Davis	Davis, CA, USA
University of Colorado/UCHealth	Boulder, CO, USA
University of Florida	Gainesville, FL, USA
University Medical Centre Groningen/University of Groningen	Groningen, The Netherlands
University of Illinois, Chicago	Chicago, IL, USA
University of Ljubljana	Ljubljana, Slovenia
University of Maryland, Baltimore	Baltimore, MD, USA
University of Michigan	Ann Arbor, MI, USA
University of Minnesota/M Health Fairview	Minneapolis MN, USA
University of North Carolina at Chapel Hill	Chapel Hill, NC, USA
University of Pennsylvania/Penn Medicine	Philadelphia, PA, USA

Institution	Location
University of Virginia	Charlottesville, VA, USA

AK, Alaska; AR, Arkansas; CA, California; CO, Colorado; DC, District of Columbia; DE, Delaware; FL, Florida; IA, Iowa; IL, Illinois; IN, Indiana; KY, Kentucky; MD, Maryland; MI, Michigan; MN, Minnesota; MO, Missouri; MT, Montana; NC, North Carolina; ND, North Dakota; NE, Nebraska; NM, New Mexico; OH, Ohio; OR, Oregon; PA, Pennsylvania; RI, Rhode Island; SD, South Dakota; TN, Tennessee; TX, Texas; VA, Virginia; WA, Washington.

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