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Approaches and hurdles of implementing pharmacogenetic testing in the psychiatric clinic

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Abstract

Pharmacogenetic (PGx) testing has emerged as a tool for predicting a person's ability to process and react to drugs. Despite the growing evidence-base, enthusiasm, and successful efforts to implement PGx testing in psychiatry, a consensus on how best to implement PGx testing into practice has not been established and numerous hurdles to widespread adoption remain to be overcome. In this article, we summarize the most used approaches and commonly encountered hurdles when implementing PGx testing into routine psychiatric care. We also highlight effective strategies that have been used to overcome hurdles. These strategies include the development of user-friendly clinical workflows for test ordering, use, and communication of results, establishment of test standardization and reimbursement policies, and development of tailored curriculums for educating health-care providers and the public. Although knowledge and awareness of these approaches and strategies to overcome hurdles alone may not be sufficient for successful implementation, they are necessary to ensure the effective spread, scale, and sustainability of PGx testing in psychiatry and other areas of medicine.

KEYWORDS

implementation, mental health, pharmacogenetics, precision medicine, psychiatry

INTRODUCTION

The treatment of moderate to severe mental health conditions involves the use of psychotropic drugs (e.g., antidepressants, antipsychotics, mood stabilizers, anxiolytics/hypnotics, or stimulants) either alone or in combination with psychosocial therapy (e.g., cognitive behavioral therapy). Currently, more than 200 drugs are available to treat psychiatric disorders. At the population level, these drugs are typically regarded as efficacious and tolerable when used as indicated. At the individual level, however, the efficacy and

tolerability of these drugs can vary tremendously. This variability can make finding an appropriate drug and dose for an individual challenging, a process often referred to as "trial-and-error."

To combat the trial-and-error process, personalized prescribing strategies, such as hepatic and renal function testing, therapeutic drug monitoring, and adhering to clinical practice guidelines, have been used for decades. Yet still many individuals endure the trial-and-error process. For example, 30%–50% of patients with major depressive disorder (MDD) do not respond to the first antidepressant prescribed[1] and in the United States alone there are 25,000 emergency visits per year due to antidepressant-induced adverse events.[2] As such, additional personalized prescribing strategies that can complement current strategies are needed.

One such strategy is pharmacogenetic (PGx) testing. PGx testing utilizes genetic variation as a surrogate marker of a person's ability to process and react to drugs. This genetic variation is typically split into three groups: pharmacokinetic, pharmacodynamic and immune-related. Pharmacokinetic genetic variants are linked to genes that encode proteins involved in the absorption, distribution, metabolism, or elimination of drugs. Pharmacodynamic genetic variants are linked to genes that encode proteins involved in a drug's physiological effects, such as receptors, ion channels, and signaling pathways, while immune-related genetic variants are in genes that encode proteins associated with the human leukocyte antigen (HLA) system. All three groups of genetic variation have the potential to improve psychotropic drug prescribing but only pharmacokinetic (*CYP2C19*, *CYP2D6*, *CYP2C9*) and immune-related (*HLA-A*, *HLA-B*) genes have published guidelines with actionable PGx-based psychotropic drug selection and dosing recommendations.[3–7]

PGx-based guidelines are developed by expert groups, such as the Canadian Pharmacogenomics Network for Drug Safety (CPNDS),[8] French National Network of Pharmacogenetics (RNPGx),[9] Dutch Pharmacogenetics Working Group (DPWG),[10] and Clinical Pharmacogenetics Implementation Consortium (CPIC),[11] the latter two being the most utilized guidelines globally. CPIC guidelines have been endorsed by several professional organizations, such as the American Society of Health-System Pharmacists (AHSP)[12] and the American Society of Clinical Pharmacology and Toxicology (ASCPT).[13] To date, these expert groups have collectively developed guidelines for 24 psychotropic drugs and an additional nine psychotropic drugs contain actionable pharmacogenetic information on their FDA-approved labels (Table 1). These guidelines and drug labels have, in part, facilitated global recognition and clinical acceptability of PGx testing. This is exemplified by numerous medical centers and health systems across North America, Europe, and Asia that have implemented PGx testing[14] and an exponential growth in commercial pharmacogenetic testing options.[15,16] There are also examples of PGx testing being adopted at the national level via PGx identification card systems (e.g., Thailand and Taiwan)[17] and electronic drug prescribing and dispensing systems (e.g., Netherlands).[18] Notably, the National Health Service Improvement and Genomics England recently announced plans to implement pharmacogenetic testing by 2025.[19] Moreover, members of the International Society of Psychiatric Genetics have published a consensus supporting PGx testing for specific antidepressants, antipsychotics, mood stabilizers and ADHD medications,[20] reflecting the increasingly favorable attitudes toward PGx testing among health-care providers,[21,22] patients,[23] and the public.[24]

Despite the growing evidence-base, enthusiasm, and successful efforts to implement PGx testing, a consensus on how best to implement PGx testing into practice has not been established and numerous hurdles to widespread adoption remain to be overcome. Herein, we review the current approaches and hurdles to implementing PGx testing into routine psychiatric care. When available, we also highlight effective strategies that have been used to overcome hurdles to further facilitate the spread, scale, and sustainability of PGx testing in psychiatry.

APPROACHES

The point at which PGx testing is offered and by whom along the clinical care continuum varies significantly as does the type of testing that is offered. In this section, we summarize the most used PGx testing approaches with the acknowledgement that the approaches discussed are not mutually exclusive nor inclusive of all the approaches that are currently being implemented.

Timing of PGx testing

PGx testing is offered using three main approaches: reactive, point-of-care, and preemptive (Figure 1). The *reactive approach* is the most used in psychiatry.[25] Users of this approach offer PGx testing after an individual experiences an inadequate response or intolerable side-effects to a psychotropic drug. The notion being that individuals who experience inadequate response or intolerable side-effects may be more likely to carry genetic variants that predispose them to unfavorable drug outcomes and that PGx testing could prevent future unfavorable drug outcomes. In the *point-of-care approach*, PGx testing is offered during or after the initial prescribing decision, but prior to an individual experiencing an inadequate response or intolerable side-effect. Although this approach does not inform immediate drug selection and dosing, it does provide an opportunity to adjust the drug regimen upon receipt of the test results and in theory, reduces unfavorable drug outcomes. The effectiveness and appropriateness of this approach is reliant on the time required to generate the test results, which can range from several days to weeks depending on the test provider. In contrast, the *preemptive approach* is less reliant on testing turnaround time because testing is offered, and results are available prior to the initiation of drug selection and dosing decisions. As a result, health-care providers can use an individual's PGx testing results to inform prescribing decisions without delay. Despite the obvious advantages, few health services have implemented the preemptive approach[26] primarily due to the paucity of clinical trials evaluating this approach and reimbursement

TABLE 1 List of drug–gene pairs with actionable recommendations and their PharmGKB evidence level

							PharmGKB clinical annotations	
Mental health medications	**Genes(s)**	**CPIC**	**DPWG**	**FDA**	**CPNDS**	**RNPGx**	**Level**	**Phenotype category**
Antidepressants								
Amitriptyline	*CYP2D6*	●		●		●	1A	Metabolism/PK, toxicity
Amoxapine	*CYP2D6*			●			-	-
Desipramine	*CYP2D6*	●		●		●	1A	Metabolism/PK, toxicity
Doxepin	*CYP2D6*	●	●	●		●	1A	Metabolism/PK
Clomipramine	*CYP2D6*	●	●	●		●	1A	Metabolism/PK, toxicity
	CYP2C19							Metabolism/PK
Imipramine	*CYP2D6*	●	●	●		●	1A	Metabolism/PK, toxicity, dosage
	CYP2C19							Metabolism/PK
Nortriptyline	*CYP2D6*	●	●	●		●	1A	Metabolism/PK, toxicity
Protriptyline	*CYP2D6*			●			-	-
Trimipramine	*CYP2D6*	●	●	●		●	1A	Metabolism/PK
	CYP2C19							Metabolism/PK
Fluvoxamine	*CYP2D6*	●		●			1A	Metabolism/PK
Citalopram	*CYP2C19*	●	●	●			1A	Metabolism/PK, toxicity
Escitalopram	*CYP2C19*	●	●	●			1A	Metabolism/PK, toxicity
Paroxetine	*CYP2D6*	●	●				1A	Metabolism/PK
Sertraline	*CYP2C19*	●	●				1A	Metabolism/PK
Venlafaxine	*CYP2D6*	●	●	●			1A	Metabolism/PK, toxicity
Vortioxetine	*CYP2D6*			●			3	Metabolism/PK
Antipsychotics								
Aripiprazole	*CYP2D6*		●	●			1A	Metabolism/PK
Brexpiprazole	*CYP2D6*		●	●			-	-
Clozapine	*CYP2D6*			●			-	-
Haloperidol	*CYP2D6*		●				1A	Metabolism/PK
Iloperidone	*CYP2D6*			●			3	Toxicity
Perphenazine	*CYP2D6*			●			-	-
Pimozide	*CYP2D6*		●	●			-	-
Quetiapine	*CYP3A4*		●				1A	Metabolism/PK
Risperidone	*CYP2D6*		●				1A	Metabolism/PK
Thioridazine	*CYP2D6*			●			3	Other
Zuclopenthixol	*CYP2D6*		●				1A	Metabolism/PK
ADHD medication								
Atomoxetine	*CYP2D6*	●	●	●			1A	Metabolism/PK, toxicity
Anticonvulsants/mood stabilizers								
Carbamazepine	*HLA-A*	●		●	●		1A	Toxicity
	HLA-B							
Fosphenytoin	*CYP2C9*	●	●	●			1A	Metabolism/PK, toxicity
	HLA-B							Toxicity

(Continues)

TABLE 1 (Continued)

Mental health medications	Genes(s)	CPIC	DPWG	FDA	CPNDS	RNPGx	PharmGKB clinical annotations Level	PharmGKB clinical annotations Phenotype category
Oxcarbamazepine	*HLA-B*	●		●			1A	Toxicity
Phenytoin	*CYP2C9*	●	●	●			1A	Metabolism/PK, toxicity
	HLA-B							Toxicity
Anxiolytics/hypnotics								
Clobazam	*CYP2C19*			●			3	Metabolism/PK, toxicity, efficacy
Diazepam	*CYP2C19*			●			3	Metabolism/PK

Note: Level 1A/B = high, 2A/B = moderate, 3 = low, 4 = unsupported. Detailed PharmGKB level of evidence definitions can be found here: https://www.pharmgkb.org/page/clinAnnLevels.

Abbreviations: CPNDS, Canadian Pharmacogenomics Network for Drug Safety; CPIC, Clinical Pharmacogenetics Implementation Consortium; DPWG, Dutch Pharmacogenetics Working Group; FDA, US Food and Drug Administration; PK, pharmacokinetics, RNPGx, French National Network of Pharmacogenetics.

FIGURE 1 Pharmacogenomics implementation approaches.

policies that favor reactive approaches.[27] However, PGx testing results produced using a reactive or point-of-care approach are often used preemptively, when appropriate, for future drug selection and dosing decisions. Conversely, individuals who undergo preemptive PGx testing for only a select number of genes may need additional testing (reactive or point-of-care testing) if they require a drug that has associated genetic information that was not available through the preemptive testing.[26]

PGx testing providers

PGx testing is offered by commercial and noncommercial entities, although most testing in psychiatry is being performed by commercial laboratories. In the United States alone, 76 commercial laboratories offer PGx testing[16] and testing in about 50 medical centers or health systems worldwide,[14] including approximately 18 Children's Hospitals in the United States,[25] includes a mix of commercial and noncommercial testing. Both commercial and noncommercial PGx testing are mostly performed in an accredited clinical laboratory (e.g., College of American Pathologists/Clinical Laboratory Improvement Amendments [CAP/CLIA]; International Organization of Standardization [ISO] 15189; Canadian Association For Laboratory Accreditation [CALA]). However, commercial and noncommercial PGx testing often differ in the model used to offer the testing.

There are two types of models: direct-to-consumer and gatekeeper. The *direct-to-consumer* model does not require the involvement of a health-care provider in the ordering process, whereas the *gatekeeper model* requires a referral from a health-care professional (e.g., physicians, pharmacists) prior to commencing the PGx test. Commercial laboratories have adopted both models, but medical health centers exclusively employ the gatekeeper model. In the direct-to-consumer model, individuals will directly receive their PGx testing results from the laboratory and sometimes include a free consultation with a health-care provider. In contrast, tests within the gatekeeper model are typically interpreted by physicians, pharmacists, genetic counsellors, or nurse practitioners, individually or as part of a team-based approach.[28] Although there is debate on which of these models or variations of them are optimal for use in psychiatry, there is a consensus that a health-care provider, preferably a provider who knows the patient's history, should be involved in the test ordering and interpretation of results.[29]

Types of PGx testing

There are three types of PGx tests: single gene tests, multi-gene tests, and combinatorial tests. *Single gene tests* include one or multiple genetic variants (also known as alleles) in a single gene that is associated with efficacy or tolerability of a drug or group of drugs. For example, *CYP2C19* for escitalopram, *CYP2D6* for risperidone, or *HLA-B*15:02* for carbamazepine. The second type of test is a *multi-gene test* (also known as a "panel test") where a laboratory tests genetic variants in multiple genes. Multi-gene tests are sometimes organized by therapeutic area (e.g., mental health, cardiovascular, or pain management) in which genes most relevant to the drugs used in

that area are included. Both commercial and noncommercial laboratories typically offer this type of testing. Finally, *combinatorial tests* are a special type of multi-gene panel test that uses proprietary algorithms to translate test results into prescribing recommendations. Although some of these combinatorial PGx tests have positive clinical findings,[30,31] the drug selection and dosing recommendations may differ when compared to recommendations based on published PGx-based prescribing guidelines (e.g., CPIC, DPWG) or PGx information on drug labels (e.g., FDA).[32–34]

HURDLES

When implementing any innovative solution, there are hurdles (Figure 2) that must be overcome along the path toward full adoption. Although PGx testing in psychiatry faces many such hurdles, none are unsurmountable. In this section, we will summarize the most consistently reported hurdles in the literature[29,35–40] and offer potential strategies to overcome them.

Uncertainty about clinical efficacy and cost-effectiveness

The credibility and reliability of scientific evidence regarding the efficacy of PGx testing is one of the main hurdles for implementation into clinical practice. Although there is robust evidence for several gene–drug associations relevant to psychiatry (Table 1), most of the evidence is from retrospective cohorts or pragmatic trials.[20,41–44] A lack of high-quality randomized controlled trials (RCTs) has contributed to the low confidence in the clinical efficacy of PGx testing in psychiatry. The RCTs that have evaluated PGx-guided versus unguided (standard) prescribing in psychiatry have been sponsored by commercial laboratories and most have utilized proprietary combinatorial testing, raising concerns about conflicts of interest and transparency, respectively.[38] A meta-analysis of five RCTs showed that adults with MDD that received PGx-guided prescribing ($n = 887$) were 71% more likely to achieve symptom remission compared to those that received unguided prescribing ($n = 850$).[45] In children, one RCT with 176 adolescents diagnosed with MDD has been conducted and found that combinatorial PGx-guided treatment had no effect on symptom improvement, side-effect burden, or patient satisfaction.[46] Although RCTs are typically seen as the gold standard in evidence-based medicine, this approach is not always necessary, practical, or possible for evaluation of PGx-guided treatment.[47] Pragmatic studies are more generalizable, less costly, and more efficient to conduct compared to RCTs; however, they are prone to selection bias and confounding.[42] High-quality pragmatic trials could provide us necessary real-world evidence to facilitate the implementation of PGx testing as a companion tool to further refine prescribing decisions in psychiatry practice. Supporting this notion, several pragmatic preemptive and reactive PGx implementation trials are underway, such as the Implementing GeNomics In pracTicE (IGNITE) and the Ubiquitous Pharmacogenomics Consortium's PREemptive Pharmacogenomic Testing for Preventing Adverse Drug REactions (PREPARE) study.[42]

Accompanying uncertainty related to the clinical efficacy is uncertain evidence related to the cost-effectiveness of PGx testing

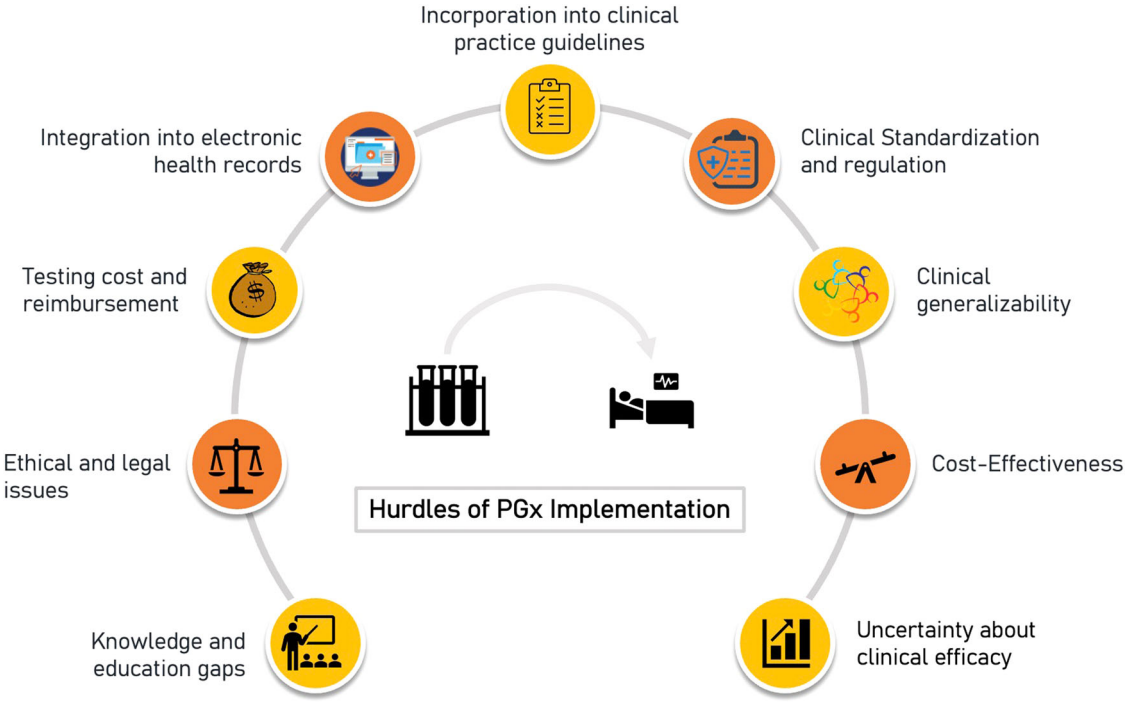

FIGURE 2 Hurdles of implementing pharmacogenetic (PGx) testing in psychiatry.

compared to standard care. Although most economic analyses have shown PGx testing to be a cost-effective or cost-saving strategy,[48] few studies have been conducted in the mental health-care context. The economic studies that have been conducted in mental health have evaluated commercial PGx tests. One such study found significant reductions in health-care utilization (e.g., emergency room visits, hospitalizations)[49] and three other studies showed overall per patient cost savings that ranged from $5962 to $7112 USD per year.[50–52] Despite the supportive evidence, methodological limitations are present (e.g., absent of quality-of-life or willingness-to-pay thresholds, focus on the US health-care system, small samples, or data derived from non-RCTs). Willingness-to-pay thresholds are particularly important as they play a key but not necessarily determining role in whether PGx testing is covered by a health-care system. Notably, willingness-to-pay thresholds are defined on a national level and vary by country. For example, the United Kingdom has a threshold of £20,000, whereas a value between $50,000 and $70,000 is considered cost-effective in the United States.[48] Additional economic evaluations addressing this and other limitations will be needed before firm conclusions about the cost-effectiveness of PGx testing in psychiatry can be made.

Clinical generalizability

The generalizability of PGx testing results poses another hurdle in the implementation effort. For example, almost all prospective PGx studies in psychiatry have included patients with MDD who have failed one medication trial or developed adverse drug reactions. This raises the issue of the utility of the evidence for initial drug selection and/or dosing decisions. Moreover, some panel-based tests do not detect all genetic variants that are applicable to all ethnic groups. This can result in inaccurate prediction of metabolizer phenotype and potentially erroneous medication selection and dosing recommendations. For example, using 1000 Genomics Project Phase III data, Wright and colleagues[53] found that most of the variation (>90% of variants) within 120 pharmacogenes were rare, with allele frequencies less than 0.5%, and that the frequency of many rare variants differ by ancestry. As such, PGx testing based on European population data may lack generalizability to non-European populations and create challenges for universal applicability. To ensure PGx testing is equally useful across different populations, concerted efforts to include individuals from non-European populations in PGx research are required and should be a priority for the field.

Standardization and regulation

The genes and alleles included in PGx testing panels vary significantly.[15,32–34,54] This lack of standardization across tests stems from loose regulations in most jurisdictions and the challenge of developing a consensus on which genes and alleles should or should not be included on a PGx panel. The variability in gene and allele content between these tests can ultimately lead to differences in prescribing decisions, as clinical recommendations are dependent on the genes and alleles tested.[32] To mitigate this issue, the Association for Molecular Pathology has created allele selection recommendations for *CYP2D6*,[55] *CYP2C19*,[56] and *CYP2C9*[57] and others have proposed a minimum gene and allele panel for psychiatry.[58] The Standardizing Laboratory Practices in Pharmacogenomics (STRIPE) forum was also recently formed to connect public and private sector members to achieve common objectives and leverage collective opportunities to accelerate the development of precision medicine practices as a standard of care.[59] The hope is that these initiatives will result in a more standardized approach to pharmacogenetic testing.

In addition to standardization of gene and allele content, it is also recognized that medication selection and dosing guidelines developed by the CPIC, DPWG, and FDA are not always concordant[60] because of differences in evidence review and genotype-to-phenotype translation procedures.[40,61] Recent efforts are currently underway to rectify the discordance in these procedures. For example, the genotype-to-phenotype translation procedure for *CYP2D6* was recently harmonized between the CPIC and DPWG to reduce interlaboratory discrepancies and differences in clinical recommendations.[62]

Incorporation into clinical practice guidelines

PGx-based prescribing guidelines help with how to interpret and use PGx information when it is available but provide minimal or no advice on when and who to test. PGx-based prescribing guidelines defer from clinical practice guidelines developed and endorsed by professional clinical associations, networks, or societies. Current clinical practice guidelines used in psychiatry are silent or provide minimal guidance on the use of PGx testing in practice. This in turn creates uncertainty among psychiatrists about when and for whom the testing should be performed. Notable exceptions include recommendations from the International Society of Psychiatric Genetics (ISPG) to conduct *HLA-A* and *HLA-B* testing prior to use of anticonvulsants (carbamazepine and oxcarbazepine), in alignment with drug regulatory agencies and expert groups.[63] The ISPG also recommends that "Genetic information for *CYP2C19* and *CYP2D6* would likely be most beneficial for individuals who have experienced an inadequate response or adverse reaction to a previous antidepressant or antipsychotic trial."[20,63] Future inclusion of similar recommendations in clinical practice guidelines developed by psychiatric associations, societies, and networks around the globe are needed to facilitate the implementation of PGx testing in mental health care.

Integration into electronic health records

To be clinically useful, PGx test results must be easy to access and update. Traditionally, PGx testing results are provided in paper-based

or static electronic (e.g., PDF) formats that are stored in a paper chart or scanned into an electronic health record (EHR). This type of integration into a patient health record presents challenges for longitudinal use of PGx testing results. In this situation, the ordering physician is often the only one aware that PGx testing has been performed, reducing the clinical utility of the testing. Fortunately, advancements have been made for the transition from paper-based reporting to PGx alerting systems integrated into the EHRs. For example, Vanderbilt University Medical Center successfully implemented a system that can generate summaries of drug–gene interactions, treatment recommendations and alerts, and can update genetic records when guidelines and/or clinical recommendations are updated.[64] Another successful example is the integration of a clinical decision support tool into the EHR at St Jude Children's Hospital.[64] However, the process is not seamless, and health-care professionals have raised concerns about the current processes of incorporating PGx results into the EHR, including delays in incorporating the results, how alert systems are being set up, and increases in consultation time.[65,66] The lack of a standardized process for reporting PGx test results from different laboratories makes their translation, interpretation, and integration into clinical workflows difficult.[36] To increase the uptake of PGx testing into clinical workflows, PGx reports need to be simplified and standardized (e.g., allele function and phenotype determination) across providers to improve interpretability by clinicians.[41]

Testing cost and reimbursement

The cost and lack of reimbursement of testing are commonly cited hurdles to PGx testing, given that for most patients testing is an out-of-pocket expense with few, if any, reimbursements available from third-party payors. Insurance support for reactive testing is gaining momentum in the United States, such as the recent approval of expanded coverage for Medicare patients through new Molecular Diagnostic Services local coverage determinations.[27] With the cost of PGx and genetic testing continuing to decline, it is expected that the monetary hurdle to testing will be largely mitigated in the future. In the short-term, we anticipate reimbursement for PGx testing to remain a hurdle to testing for many patients, resulting in equity concerns among those with lower incomes. The development of public programs to offset these disparities will be needed to ensure equitable access to PGx testing.

Ethical and legal issues

The use of testing without concrete clinical evidence (e.g., RCT evidence), nonapplicability, or nongeneralizability of testing results, informed consent, incidental findings, misuse of data, accessibility, cost/affordability, and reimbursement are some of the fundamental ethical issues regarding PGx testing. The fear of misuse of genetic data, that is, genetic discrimination, is a major hurdle of implementation. A survey of health-care professionals reported genetic discrimination could affect health-care systems in several ways, including the cost of insurance premiums, the use of confidential medical information, patient access to therapy, and the impact of physician and/or patient preferences in selecting treatment choices.[67] Legislation to prevent genetic discrimination in insurance determination, including life insurance, has been enacted in many countries. The US Congress passed the *Genetic Information Non-discrimination Act (GINA)* in 2008 to protect Americans from genetic discrimination. A similar law, *Bill S-201*, in Canada prohibits and prevents genetic discrimination, which also amends the *Canadian Human Rights Act* to prohibit discrimination on the ground of genetic characteristics. The purpose of these laws is to prohibit private health insurance companies from using an individual's health status, including genetic information, in deciding whether to issue or modify an insurance policy.[68] The fear of misuse is also linked with data privacy, which is justified with many cases of unauthorized access (e.g., hacking) of health data. The nontransparency of the future use of data also adds to the fear of data privacy. In the case of data privacy, legislation is in place to protect consumers, and testing providers need to be compliant with these regulations, for example, *Health Insurance Portability and Accountability Act* (HIPAA), USA; *The Personal Information Protection and Electronic Documents Act* (PIPEDA), Bill 6, Canada; and *General Data Protection Regulation* (GDPR), Europe.[69]

Legal liability associated with the use (or failure to use) PGx information when available could also be seen as both a hurdle and motivation of implementation of PGx testing in psychiatry practice. To reduce litigation risk, it has been recommended that physicians should become familiar with PGx guidelines for medications they most frequently prescribe, document the use of (or decision not to use) test results, and seek expert consultation when needed.[29] Moreover, physicians should discuss PGx test results with their patients and set realistic expectations about how the results can be reasonably used.[70]

Upon receipt of PGx test results, secondary or incidental findings are typically low, but there are examples where some PGx test results may have implications for an individual's health status or disease risk.[71] In addition, PGx testing might reveal information that would be relevant to family members, which raises fundamental questions about how “informed consent” for testing is obtained and how test results should be communicated to patients. This is a major concern as there are no standard guidelines regarding this issue. Patient and provider education regarding these issues will both increase knowledge and reduce adverse responses related to secondary findings.[71]

Knowledge and education gaps

The most consistent hurdles to PGx testing identified by numerous studies[29,35–38,72,73] are knowledge and education gaps among physicians, pharmacists, genetic counsellors, nurse practitioners,

and the public. Studies to date suggest that 80%–90% of health-care professionals agree about the value of PGx testing in drug selection and dose optimization; however, only 10%–20% are properly trained or confident enough to routinely use PGx testing in their practice.[23,73–75] The lack of training stems from the fact that most medical schools have not integrated pharmacogenomics into their curriculum.[76] In 2016, the Center for the Advancement of Pharmacy Education recommended "pharmacogenomics" to be incorporated into the clinical realm of pharmacy education. This led to the addition of PGx education in pharmacy curriculum in almost all pharmacy schools in North America.[76] Continuing professional educational programs with online delivery are showing signs of success in educating practicing health-care professionals.[37] Proper education, training, and awareness among all stakeholder groups, including next-generation health-care trainees, will help to reduce the gap and ultimately help the implementation process.

CONCLUSION

Despite the many hurdles, PGx testing has great promise to optimize medication selection and dosing in psychiatry practice. While the clinical evidence-base is growing, a collaborative multi-stakeholder approach can overcome hurdles discussed in this review. The development of user-friendly systems for test ordering, guidelines for use and communication of results, reimbursement policies, and strategies for effectively educating health-care providers and the public will facilitate the successful implementation of PGx testing into the psychiatric clinic.

CONFLICTS OF INTEREST

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PATIENT CONSENT STATEMENT

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CLINICAL TRAIL REGISTRATION

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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