


Assessing the knowledge, perceptions, and practices of primary care clinicians toward pharmacogenetics

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Abstract

Introduction: Pharmacogenetics (PGx) testing is becoming increasingly available to patients and clinicians, but investigations of PGx testing in primary care and the pharmacist's role in educating clinicians have been limited.

Objectives: The objectives of this study were to: (a) determine the utilization of PGx testing in primary care clinics, (b) identify how clinicians document and act on PGx test results, and (c) determine clinician interest in PGx education or consultation from pharmacists.

Methods: A 16-item survey was distributed via email. Eligible participants included physicians, physician assistants, nurse practitioners, and pharmacists who work in family medicine, general medicine, geriatric, or pediatric primary care clinics at one academic medical center. Descriptive statistics were used to characterize the frequency of PGx tests ordered in primary care clinics, provider comfort with PGx test interpretation, documentation practices, and interest in PGx education or consultation from pharmacists.

Results: The overall survey response rate was 15.8% ($n = 55$). Most respondents were physicians (84%). Nearly 40% of respondents reported having a patient bring PGx test results to a visit, while only 9% reported ordering a PGx test. Documentation practices were variable, and response to PGx results was most commonly no change in therapy (52%). Only two (3.6%) respondents agreed with the statement, "I feel confident in my ability to interpret PGx test results," and the majority reported interest in PGx education. Eighty percent of respondents reported they would be likely or very likely to consult a PGx-trained pharmacist for help interpreting PGx results.

Discussion: Clinicians in this survey were more likely to have patients bring in results than to order PGx tests, did not feel confident in result interpretation, and expressed interest in working with pharmacists for PGx test interpretation. This research can help guide the development of PGx-focused pharmacy services and education for clinicians who are encountering PGx testing in their practice.

KEYWORDS

pharmacists, pharmacogenetics, precision medicine, primary health care

Pharmacogenetics (PGx) is the relationship between a person's genes and how they metabolize or respond to drugs. Pharmacogenetic testing has gained popularity over the past two decades, allowing patients and providers access to information regarding potential increased or decreased efficacy of certain medications or propensity for adverse effects secondary to drug-gene interactions.¹ Most well-established PGx considerations have impacted specialty disciplines, such as oncology and infectious diseases, however there is increasing attention for PGx associations for medications commonly prescribed in primary care.²⁻⁵ Implementation of PGx in the primary care setting has lagged behind the original predictions of its widespread use.^{2,6} There are several proposed barriers to widespread use of PGx testing in primary care patients. These include a lack of clinical trial evidence to support the utility of applying PGx, workflow barriers to routine integration, clinician lack of comfort with test ordering and interpretation, and concerns about testing costs.^{2,6-14}

With the approval of direct-to-consumer PGx test kits,¹⁵ the availability of PGx test results is likely to increase in the future. Interested patients may bring results to their primary care clinicians for interpretation. An observational study of people who received results from direct-to-consumer PGx testing found that 44% shared the results with their primary care physician.¹⁶ Though previous studies described primary care clinician perspectives on PGx testing, some were conducted nearly a decade ago when PGx testing was less common and fewer PGx resources were available. In general, these studies found that primary care clinicians see value in utilizing PGx testing, but identify barriers such as lack of clinician training on PGx concepts, unclear cost burden of testing, and lack of evidence for making clinical decisions based on PGx test results.^{7,8,11} More recent studies have been completed with similar findings, however they did not assess the types and quantities of PGx tests that clinicians were ordering.^{9,10,12} Additionally, previous studies have not investigated documentation practices of PGx results in patient's medical charts, which is important for ensuring all members of a patient's health care team have access to this information for therapeutic decision making.

At the time of this study, our institution had recently established a pharmacogenetics consult service, which is managed by two PGx specialty pharmacists. This service is freely available to all clinicians within the institution, however initial efforts for advertising the service were focused in psychiatry, as this clinical specialty was routinely using pharmacogenetic testing. Additional education regarding the availability of the service was provided to ambulatory care pharmacists. To our knowledge, no other PGx-focused education is provided to primary care providers at our institution, and any methods for obtaining, interpreting, or reporting PGx testing is at the discretion of the clinician.

To address these gaps in previous PGx survey research, and to gain a better understanding of the current use and gaps within our institution, we aimed to describe how often primary care clinicians order PGx tests as compared with how often patients bring outside test results to their attention, while also characterizing the type of tests and how they are documented. Additionally, we queried clinicians to determine how comfortable they feel interpreting PGx

results, and what interventions are made in response to those results. Importantly, our study also identifies the perceptions of clinicians towards various types of educational opportunities and consultation from pharmacists to assist with PGx test interpretation. We believe this research can help to inform the development of future pharmacist opportunities for education and training of primary care clinicians who are interested in utilizing PGx testing in their practice.

1 | METHODS

A 16-item Qualtrics questionnaire informed by prior genetics and PGx-focused surveys was developed including Likert scale agreement, multiple choice, and yes-no questions.^{7,8,10} Survey questions (provided in the Supporting Information) were grouped into the following domains: baseline knowledge and perception of PGx testing, prior exposure to PGx testing, documentation and interventions made in response to PGx testing, interest in future educational opportunities, and demographics. A pilot test was administered to three volunteers from different provider types to gain feedback on the survey (one physician, physician assistant, and pharmacist). The survey was modified to clarify questions based on this feedback. This study was granted an exemption by the local Institutional Review Board.

Eligible participants included physicians, physician assistants, nurse practitioners, and pharmacists who work in family medicine, general medicine, geriatric, or pediatric primary care clinics at one academic medical center. Eligible participants were identified via internal email lists. Participants were contacted via email with the link to the survey on two occasions and had 6 weeks to respond, from November 1, 2019 through December 13, 2019. Likert responses were dichotomized into strongly agree/agree and strongly disagree/disagree/indifferent. Descriptive statistics were used.

2 | RESULTS

2.1 | Demographics

The survey was distributed to 349 clinicians: 305 physicians, 13 physician assistants, 16 nurse practitioners, and 15 ambulatory pharmacists. A total of 55 respondents completed the survey, a 15.8% overall response rate. The majority of survey respondents were physicians ($n = 46$, response rate 15.1%), although proportionally, pharmacists had the highest response rate ($n = 5$, 33.3%) while nurse practitioners had the lowest response rate ($n = 2$, 12.5%). Eighty-four percent of survey respondents worked in the general medicine or family medicine clinics (Table 1).

2.2 | Knowledge and perception of PGx testing

Clinicians had divided opinions on the perceived utility of PGx tests (Table 2). More clinicians agreed with the statement "I believe that

TABLE 1 Demographics of survey respondents (n = 55)

	Number (%)
<i>Clinic type</i>	
General Medicine	26 (47.4%)
Family Medicine	20 (36.4%)
Pediatrics	6 (10.9%)
Geriatrics	3 (5.5%)
<i>Clinician type</i>	
Physician	46 (83.6%)
Nurse Practitioner	2 (3.6%)
Physician Assistant	2 (3.6%)
Pharmacist	5 (9.1%)

TABLE 2 Use of pharmacogenetics in respondents' clinics (n = 55)

Statement	Agree (n, %)	Disagree/ indifferent (n, %)
I believe that pharmacogenetic testing is useful for predicting the risk of adverse events in my clinic.	19 (34.5%)	36 (65.5%)
I believe that pharmacogenetic testing is useful for predicting the likelihood of drug effectiveness in my clinic.	26 (47.3%)	29 (52.7%)
I feel confident in my ability to interpret pharmacogenetic test results for my patients.	2 (3.6%)	53 (96.4%)

pharmacogenetic testing is useful for predicting the likelihood of drug effectiveness in my clinic" (47.3%) compared with the statement "I believe that pharmacogenetic testing is useful for predicting the risk of adverse events in my clinic" (34.5%). The difference in rates of agreement between these two statements reflects that 45% of physicians agreed with the efficacy statement while only 30% of physicians agreed with the adverse event statement. Non-physicians responded similarly to both statements, with 55.6% (n = 5) of respondents agreeing to both the efficacy and adverse event statements. In terms of PGx interpretation, the majority of respondents (96.4%) did not feel confident in their ability to interpret PGx test results. Of the two providers who did report feeling confident in result interpretation, one was a physician and one was a pharmacist.

2.3 | Experience with PGx testing

Overall, less than half of responding clinicians (40%, n = 22) had interacted with PGx results in their clinic. Thirty-eight percent of respondents reported that a patient had brought them a PGx test to interpret (n = 21). Sixteen clinicians, all general or family medicine physicians, indicated that this situation had occurred in the past 6 months. Only 9.1% reported having ordered a PGx test (n = 5). Four family medicine physicians ordered PGx panel tests for psychotropic prescribing, while

TABLE 3 Documentation and interventions made in response to pharmacogenetics results

Total respondents who have interacted with PGX results	22
Location of documentation	Number (%)
Respondents could select more than one option	
PDF document upload	18 (81.8%)
Visit progress note	11 (50%)
Other	4 (18.2%)
Did not add to medical record	2 (9.1%)
<i>Interventions</i>	
No change	11 (50%)
Switched medication	9 (40.9%)
Stopped medication	1 (4.5%)
Reduced dose	1 (4.5%)
Other	2 (9.1%)

Abbreviations: PDF, portable document format; PGX, pharmacogenetics.

one general medicine physician ordered *HLA-B*58:01* testing to determine the risk of adverse effects to allopurinol.

2.4 | Documentation and interventions

Of the clinicians who reported interacting with PGx test results in their practice, many indicated they are documenting the results in more than one place within the electronic health record (Table 3). Most commonly, the results are scanned into a document upload in PDF format and/or added to the visit progress note. A very small number of respondents (n = 2) reported that they did not document the PGx results in the health record. Half of respondents who had interacted with PGx test results reported making no change to the patient's treatment based on the test result (Table 3). For those who did make a change, the most common intervention was to switch to a different medication.

2.5 | Further education and opportunities for pharmacists

When asked about interest in specific educational activities to increase knowledge and confidence in PGx test interpretation, 92.7% of respondents indicated they were interested in additional PGx education. Seventy percent indicated they were specifically interested in live educational activities, such as clinic meetings or grand rounds. The second most frequent education strategy of interest was online learning activities, with 60% reporting interest. Additional suggestions for PGx education included real-time resources such as a pocket PGx reference card or inclusion of PGx recommendations in the formulary that could be easily accessible to clinicians.

Clinicians were also asked their preferences on consulting a PGx-trained pharmacist prior to clinician-patient PGx conversations. Over half of respondents (60%) reported they were likely to refer a patient with PGx testing for a scheduled visit with a PGx pharmacist. Approximately 80% of primary care clinicians reported they were likely to directly consult a pharmacist to discuss a PGx result prior to their meeting with the patient. All physician assistant, nurse practitioner, and pharmacist respondents indicated they would be likely to consult a PGx-trained pharmacist compared with 80% of physicians.

3 | DISCUSSION

This survey of primary care clinicians revealed the current attitudes and interest of this population towards PGx, experience with PGx testing, and likelihood of a clinician to consult a PGx-trained pharmacist about test results in this setting. The knowledge and perception questions of the survey revealed that less than half of responding clinicians perceived PGx testing as important for predicting adverse effects or efficacy in their clinics, which is lower than reported in previous surveys.^{7,17,18} A recent survey of clinicians in Europe reported 84% of respondents found PGx relevant to their practice; however, this was a population of clinicians whose clinic sites had previously been chosen to implement a PGx educational program.¹⁷ Similarly, a survey of Japanese and American pediatricians reported that greater than 80% of respondents found PGx valuable for improving the safety and efficacy of medications, though less than 10% of this population rated themselves as familiar with PGx.¹⁸ More consistent with our survey results, in a cohort of Canadian family medicine physicians, 43% agreed that learning about implications of genetic testing was relevant to patient care in their clinics.¹⁴

Despite the lower perception of importance of PGx testing on clinical outcomes in our study, a high percentage of clinicians were interested in receiving PGx education. This dichotomy and the prior European survey findings, indicate that a lack of PGx knowledge may contribute to the lack of perceived utility. It is also possible that the perceived PGx utility in this survey population was lower due to a lack of experience in ordering and interpreting these tests.¹⁷ As mentioned by a respondent who suggested creating PGx pocket guides for clinicians, one important role for pharmacists is to educate clinicians not only on general PGx knowledge but also on how to use PGx resources. Pharmacists should focus on teaching clinicians how to utilize many of the free online PGx resources, such as the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines and the PharmGKB database, to improve physician confidence in interpretation.^{19,20} A survey of pediatricians in the United States found that less than 10% had heard of CPIC.¹⁸ Pharmacists could also educate other clinicians about more advanced PGx training opportunities, such as PGx certificates that are offered by multiple pharmacist organizations. Educational opportunities for primary care clinicians could improve the perception of PGx utility. Multiple groups have investigated the impact of PGx educational activities on pharmacists, trainees, and physicians.^{17,21-23} For example, when surveyed after a

semester-long PGx course, pharmacy students were more likely to agree that PGx is relevant to patient care and reported increased confidence in PGx test interpretation compared with before the course.²¹ A survey of pharmacists and pharmacy students who were provided 11 online genetics modules found a post-intervention increase in self-perceived competency surrounding counseling patients on the ethical, psychological, and cultural implications of pursuing PGx testing.²² Following a grand rounds presentation on PGx implications for several cardiovascular medications, physician attendees were more likely to indicate a willingness to recommend PGx testing for patients on these medications.²³ Types of interventions used for training these populations include live lectures, online modules, and grand rounds-style presentations presented by pharmacists.²¹⁻²³ Studies of prescriber PGx educational strategies have previously demonstrated that live presentations are more popular and can reach a larger number of people, while online formats are less popular and not as likely to be completed.^{17,24}

Respondents in the current study reported low confidence in their ability to interpret PGx test results similar to prior surveys of primary care physicians nearly a decade ago.^{7,8} Despite their low confidence, this study reveals that clinicians are being asked by their patients to respond to PGx results, more often for tests they did not personally order, a clinical scenario that has not been previously described for primary care clinicians. A recently published report aimed at implementing PGx in primary care suggests starting with identifying appropriate patients for PGx testing.²⁵ While this proposed algorithm provides important practical guidance on ordering and interpreting PGx tests, it is necessary to consider scenarios where patients self-initiate PGx testing. With an increasing number of PGx testing companies advertising their products to the general public, or receiving approval for direct-to-consumer sales, PGx testing is becoming a more patient-driven process.¹⁵ Clinicians need to be prepared to interpret and apply PGx results to patient care decisions even if they choose not to order PGx testing themselves. It is also critical that clinicians understand the broader implications of the PGx results. For example, a clinician that orders or interprets a psychotropic PGx panel that includes a CYP2C19 phenotype should understand that this result has implications for antidepressants and cardiovascular medications. The identified gap in primary care clinician knowledge and confidence in PGx test interpretation creates an opportunity for pharmacists trained in PGx to provide additional services with primary care clinicians.

Respondents indicated a general interest in the availability of PGx consults, either to the patient or provider, for assistance with PGx result interpretation. Previously reported strategies for integrating PGx into the clinic setting include several different approaches. In primary care clinics, one approach is making a PGx-trained pharmacist available to clinicians for consultation. A study comparing an in-house pharmacist to an on-call pharmacist found that the presence of an in-house pharmacist resulted in more PGx testing.²⁶ Another study of pharmacist-led PGx services implemented in a rural primary care clinic found that referrals to the service for patients outside the original study population increased after study completion, possibly because

of increased awareness of the pharmacist's role.²⁷ These findings suggest PGx may be an important area of training for ambulatory care pharmacists who are embedded in primary care clinics and community pharmacists.²⁸ The availability of pharmacists for PGx consultation has been described as key for facilitating the integration of PGx testing in physician workflows.²¹ Another approach that has been described is to create a standalone PGx clinic where providers can refer patients for PGx testing. This clinic included a medical geneticist, genetic counselor, pharmacist, and nurse practitioner and reported receiving the most referrals from psychiatry providers, followed by primary care, and then oncology.²⁹

Another important finding from our study was that PGx result documentation practices were variable. In some cases, clinicians reported no documentation of the PGx test, however the majority added results to their visit note or uploaded the results as a scanned PDF document. There are significant concerns with this lack of standardization. One concern with this current process is that the result may not be searchable within the electronic health record, potentially increasing the risk of missing critical results or performing duplicate testing. This issue is especially concerning when considering results that have significance across multiple disease states. Models for incorporating PGx results into the electronic medical record with clinical decision support have been published previously.^{30,31} However, a key step in establishing these models is developing a location for structured result storage, which can present a substantial informatics burden and is particularly challenging when addressing results from multiple laboratories. Although not addressed in our survey, an additional consideration is what information is being recorded by the clinician who is documenting the PGx test result. A clinician may document the laboratory interpretation or laboratory-derived treatment recommendations instead of the genetic result, which limits the application of this test result to other clinical areas. It is crucial to ensure standardization efforts include what data from the PGx test report is being documented, in addition to standardizing where the information is documented. This highlights the increasing need for the development of institutional policies and procedures around how to manage genetic test results so that appropriate clinical decision support can be developed. Again, pharmacists consulted for help with test interpretation could help to ensure documentation practices are standardized in a clinically meaningful format when PGx results are added to a patient's medical record.

There are several limitations to this study. The number of respondents was low, especially for non-physicians, and we used a non-validated survey. The number of non-physician respondents as well as the number of clinicians who practice in geriatric or pediatric clinics were too small to make meaningful conclusions about whether perceptions, or current practice, of PGx differed among these subgroups. Although an effort was made to define PGx testing to survey respondents and examples were given in the survey's opening statement, we acknowledge that some respondents who indicated that patients brought PGx results to their attention may have mistakenly reported genetic disease risk or ancestry results, which are more available to the general public. Generalizability is also limited as participants all

came from one academic medical center and could be biased by regional and institutional practices; however, there is variability in the size and patient populations of the clinics where respondents practice. Similar to other survey-based research, this survey is subject to respondent bias as those who chose to respond may have stronger baseline knowledge or opinions about PGx, leading them to take the survey. Recall bias is also a concern, as those who ordered tests more recently may have been more likely to remember specific encounter details. Some clinicians who responded to our survey may have known about the availability of a PGx consult service, however no PGx education is provided at an institutional level to these clinicians. Because the survey responses were deidentified, we were unable to determine if any respondents had interacted with the PGx consult service. Future research is warranted to determine best practices for PGx result documentation and outcomes of pharmacist-led PGx educational activities in primary care.

Ultimately, our survey confirmed that primary care clinicians continue to report low confidence in their ability to interpret PGx results, yet we discovered that over one-third are being asked to perform these interpretations by patients who bring in test results that they did not order. Documentation practices for recording PGx results were also not standardized, which could increase the risk that clinically relevant results are missed or that duplicate tests are ordered. Overall, our surveyed clinicians indicated they are interested in additional education and would consider consultation with pharmacists about PGx. Pharmacists are uniquely positioned to help address these current education gaps for primary care clinicians and can also play an active role in primary care clinics as PGx consultants or members of a multidisciplinary PGx team.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

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

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