Implementation of a pharmacist-led pharmacogenomics service for the Program of All-Inclusive Care for the Elderly (PHARM-GENOME-PACE)

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Abstract

Objectives: To determine the feasibility of implementing a pharmacist-led pharmacogenomics (PGx) service for the Program of All-Inclusive Care for the Elderly (PACE).

Setting: A national centralized pharmacy providing PGx services to community-based PACE centers.

Practice description: Individuals 55 years of age and older enrolled in PACE who underwent PGx testing as part of their medical care ($n=296$).

Practice innovation: Pharmacist-led PGx testing, interpreting, and consulting.

Evaluation: Implementation processes and roles were ascertained by reviewing policies and procedures for the PGx service and documented observations made by pharmacists providing the service. Genetic variants and drug-gene interactions (DGIs) were determined by interpretations of PGx test results. Types of recommendations provided by pharmacists were ascertained from PGx consultations. Prescribers' acceptance of recommendations were ascertained by documented responses or drug changes made after PGx consultations.

Results: Challenges to implementation included lack of systems interoperability, limited access to medical electronic health records, determining prescribers' responses, and knowledge and competency gaps in PGx. Pharmacist roles most essential to overcoming challenges were interpreting and applying PGx data, determining how to disseminate those data to prescribers, advocating for appropriate PGx testing, and educating about the application of test results to clinical practice. Participants frequently used drugs posing DGI risks, with the majority (73.6%) reporting more than 1 interaction. The overwhelming majority (89.0%) of pharmacists' recommendations to mitigate risks were accepted by referring prescribers.

Conclusion: Implementing a pharmacist-led PGx service for PACE is feasible. Implementation of this service highlights the leadership role of pharmacists in moving PGx from research to practice.

Disclosures: The authors performed this work as employees of Tabula Rasa HealthCare, doing business as CareKinesis, and they have stock options in the company. There was no direct cost for pharmacogenomics testing for Program of All-Inclusive Care for the Elderly participants.

Previous presentation: Preliminary results of this study were presented in part at the 2015 Federation Internationale Pharmaceutique (FIP) World Congress, Düsseldorf, Germany; 2016 FIP World Congress, Buenos Aires, Argentina; and 2016 National PACE Association Annual Conference, San Francisco, California.

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It is well known that different individuals respond in different ways to the same drug. Moreover, it is increasingly being appreciated that genetics plays an important role in interindividual variability in drug response. Having information about an individual's genetics before and during use of a drug, and especially during the use of multiple concomitant drugs, has obvious clinical implications. For example, having information about genetic variants in a patient's cytochrome P450 (CYP450) system allows a clinician to identify a drug-gene interaction (DGI) involving a drug and a gene coding for a CYP450 isoenzyme or other protein. This information also lets a clinician identify a drug-drug-gene interaction (DDGI), which involves a complex interaction resulting from
The ability to analyze and interpret PGx testing results and make clinical decisions based on those results may be a vital service for improving drug responses and patient outcomes. Indeed, services that incorporate PGx testing into patient care are emerging in primary care practices and community pharmacies. To determine if PGx services can become a component of everyday practice in these settings, feasibility assessments are needed. The present study sought to determine the feasibility of implementing a pharmacist-led PGx service for the Program of All-Inclusive Care for the Elderly (PACE). In the United States, PACE is a Medicare/Medicaid program that provides comprehensive medical and supportive services to individuals 55 years of age and older who are certified by their state to need nursing home care but are able to live safely in the community, through assistance by PACE organizations, as an alternative to institutionalization. The aim of PACE is to improve overall quality of life in 4 domains (physical, psychological, social, and spiritual) by means of a multidisciplinary approach. The vast majority of PACE organizations work with 1 pharmacy to dispense drugs, in addition to other pharmacy services, for their population of patients, which are typically referred to as participants. PACE organizations function under a per-member-per-month (PMPM) capitated payment model for all services.

Our primary objective was to describe the processes involved in implementing this service and the process-related challenges and solutions associated with implementation. Our secondary objectives were to describe pharmacists’ roles in implementation and to report the results of PGx consulting, including pharmacists’ recommendations and prescribers’ acceptance of these recommendations. In addition, we briefly summarize the results of PGx testing.

**Methods**

**Setting and practice description**

This study was approved by the Biomedical Research Alliance of New York Institutional Review Board and is registered with clinicaltrials.gov (NCT03257605). The practice setting was a centralized pharmacy (CareKinesis, Moorestown, NJ) that serves 15%-20% of PACE participants in 21 states. The dispensing of all drugs for PACE participants, including OTC products and drugs obtained by on-site fulfillment (i.e., automated dispensing machines) and local procurement (i.e., community pharmacy networks), is managed by CareKinesis and documented in their electronic pharmacy record. In addition to dispensing drugs, the pharmacy provides medication therapy management (MTM) services, including comprehensive and targeted medication safety reviews, which consider competitive drug interactions to optimize drug selection and time-of-day dosing. The pharmacy is also a training site for introductory and advanced pharmacy practice experience students and postgraduate year 1 and 2 pharmacy residents.

In May 2014, as part of its comprehensive pharmacy services, CareKinesis began offering PGx testing, pursuant to an order by a PACE prescriber, and providing PGx interpretations and consultations led by pharmacists. Two senior pharmacists (K.B., J.T.) with expertise in the fields of MTM,
geriatric pharmacotherapy, and PGx and a pharmacy resident (E.S.) with focused training in PGx primarily led the services. Pharmacy services, including PGx coordination, interpretation and consultation, also are compensated via the aforementioned PMPM model. PGx testing, however, is charged to PACE organizations as a separate fee.

**Participant selection and data collection**

Participants 55 years of age and older enrolled in PACE who underwent PGx testing as part of their medical care from May 2014 to June 2016 and consented to the use of their deidentified data for research purposes were included; those not meeting these criteria were excluded. Prescribers selected participants for PGx testing based on their medical decisions. These decisions typically involved one of the following scenarios: (a) participant not responding to drug or drugs as intended (i.e., ineffectiveness, intolerability) despite clinical-guided adjustments; (b) participant expected to be prescribed a new drug or drugs for which actionable PGx-based recommendations exist; or (c) participant coming up for assessment of reenrollment in PACE, whereby a comprehensive medication review is needed. Pharmacists aided PACE prescribers in medical decision making and with selecting participants for PGx testing by educating prescribers about the roles of genes in drug metabolism and response and by identifying participants with potentially actionable drug-gene pairs. Education was performed both a priori, in the form of multiple PGx-based webinars to audiences of PACE prescribers, and at the point of care on a per-prescriber basis. Similarly, identification was performed both a priori, in the form of pharmacy reports, and at the point of care on a per-participant basis.
The following data were collected from CareKinesis pharmacy records and stored in a secure database for deidentified population-level review: participant date of birth, sex, and race or ethnicity (when available); ordering and referring prescriber (typically a physician or nurse practitioner); baseline drug regimen; date of specimen collection; date PGx test results received; date of pharmacist consultation; genotypes and phenotypes; causative gene (the “perpetrator” of the interaction); “victim” drug (the drug affected by the interaction); pharmacist recommendation for each DGI; and postconsultation drug regimen.

**Pharmacogenomic testing and consulting**

Eleven genes associated with the metabolism, transport, and target of numerous drugs were included in the PGx test panel: CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, CYP4F2, VKORC1, SLC01B1, TPMT, ATM, and F5. The processes involved in implementing the PGx service are depicted in Figure 1a. Prescribers ordered PGx tests for consenting participants based on their clinical judgment, as previously described. With the use of the Coriell Life Sciences (CLS, Camden, NJ) PGx testing kit, buccal swab samples for DNA extraction were collected from participants during their scheduled visits to the PACE centers where they received medical care. Testing was provided at no cost to PACE participants; as previously described, a separate fee was billed to PACE organizations by the pharmacy.

After DNA collection, the samples were directly sent to a Clinical Laboratory Improvement Amendments–certified laboratory (e.g., Genetrait Laboratories, Columbia, MO) for testing. CLS received the test results from the laboratory and interpreted the reference single-nucleotide polymorphism numbers to genotypes and phenotypes. These results were sent to CareKinesis via secure file-transfer protocol (SFTP). Subsequently, CareKinesis pharmacists accessed PGx test results via SFTP and performed consultations for prescribers. Pharmacist-performed consultations were aided by multidrug interaction screening performed by our Web-based clinical decision support system (CDSS; Medication Risk Mitigation™ Matrix), an evidence-based software that identifies DDI, DGI, and DDGI risks.18

On receipt of participants’ PGx test results and interpretations, genotype and phenotype data were automatically uploaded into our CDSS. Potential drug interactions identified by the CDSS were interpreted by CareKinesis pharmacists who formulated evidence-based and patient-centered recommendations for monitoring, continuing, or changing participants’ drug regimens. As depicted in Figure 1b, evidence-based recommendations were based on clinical practice guidelines from the CPIC, Dutch Pharmacogenetics Working Group (DPWG), or Canadian Pharmacogenomics Network for Drug Safety (CPNDS).19 Patient-centered recommendations were based on participants’ drug regimens and categorized into 1 of 4 suggestions: (1) normal response expected, continue drug; (2) decreased response expected, increase drug dose and monitor; (3) increased response expected, decrease drug dose and monitor; or (4) poor or no response expected, consider alternative drug.

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**Figure 1.** continued
Results and outcomes

Implementation processes were ascertained by reviewing the pharmacy’s policies and procedures for the PGx service as well as observations documented by the pharmacists providing the service. Prevalence of genetic variants was determined by pharmacists’ interpretations of PGx test results, and prevalence of DGIs was determined by the CDSS’s detections of drug interactions. Types of pharmacists’ recommendations were ascertained from consultations and categorized descriptively as monitoring of clinical signs, symptoms, or laboratory tests; change in the timing of administration of the drug; modification of the drug dose; or substitution or complete discontinuation of the drug. Finally, rates of prescribers’ acceptances were ascertained from consultations whenever feasible, as well as determined by extrapolation from drug profiles. In the case of the former, prescribers could directly respond to pharmacists’ recommendations, either verbally or transcriptionally. The responses were recorded by pharmacists and documented in the consultations that were stored in our pharmacy records. We ascertained those responses from the consultations. In the case of the latter, when prescribers did not directly respond to pharmacists, we examined participant’s drug profiles before and after consultations. As a proxy for prescribers’ responses, we used 3 cutoff points (7 days, 30 days, and 90 days) to determine whether or not drug changes were made after pharmacist-conducted PGx consultations. We extrapolated that drug changes implementing pharmacists’ PGx-based recommendations and occurring within 90 days of the consultations implied prescriber acceptance.

Results

Enrolling

Table 1 describes the characteristics of PACE participants referred to our PGx service. During the study period, a total of 296 participants met inclusion criteria and underwent PGx testing. The mean age of participants was 74.5 ± 10.0 years, and 70.3% were female. Participants were prescribed 14.5 ± 6.0 medications at the time that PGx test results were

Table 1
Demographic and drug use data on study participants (n = 296)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>74.5 ± 10.0 (55–99)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>74.0 (67–82)</td>
</tr>
<tr>
<td>Female</td>
<td>208 (70.3)</td>
</tr>
<tr>
<td>Male</td>
<td>88 (29.7)</td>
</tr>
<tr>
<td>Race or ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>244 (82.4)</td>
</tr>
<tr>
<td>Not specified</td>
<td>36 (12.2)</td>
</tr>
<tr>
<td>African American</td>
<td>13 (4.4)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>Drugs, number per participant</td>
<td>14.5 ± 6.0 (2.0–35.0)</td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>14.0 (10.8–18.0)</td>
</tr>
</tbody>
</table>

Abbreviations used: IQR, interquartile range; SD standard deviation.

we used from drug regimen lists at the time that pharmacogenomic test results were available to pharmacists for consultation. Drug regimen lists included nonprescription drugs, vitamins, and supplements in addition to prescription drugs. These data were always available to both pharmacists providing consultations and prescribers ordering pharmacogenomic tests and requesting consultations.

The final reports, which consisted of pharmacists’ consultations and PGx test results, were sent to the referring prescriber via secure e-mail exchange and with file protection as well as uploaded to participants’ pharmacy records, which were accessible to referring prescribers via secure Web access. In addition, prescribers could verbally consult with pharmacists, and this method of collaboration was encouraged. Because consultations were provided from pharmacists to prescribers, PACE participants were not contacted by pharmacists.

Table 2
Challenges and solutions associated with implementing a PGx service for PACE

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health care system—related challenges</td>
<td>Our pharmacists communicated PGx test results and consultations with prescribers directly by transmitting documents through secure HIPAA-compliant servers (i.e., encrypted e-mails) and indirectly by uploading documents to participants’ pharmacy records, which were readily accessible to prescribers.</td>
</tr>
<tr>
<td>We encountered a lack of systems interoperability for HIE.</td>
<td>Our CDSS automatically uploaded PGx data to promote appropriate interpretation and utilization of test results. These data were accessible to prescribers at the point of prescribing and to pharmacists during medication reviews and PGx consultations.</td>
</tr>
<tr>
<td>Pharmacists had limited access to participants' medical EHR.</td>
<td>Our pharmacists based their recommendations primarily on available pharmacy data, which always included participants’ complete drug regimens, PGx test results, and drug-related allergies. When medical data (e.g., height and weight, serum creatinine) were available, pharmacists used these additional data to inform their recommendations.</td>
</tr>
<tr>
<td>We did not require a response from prescribers to pharmacists’ consultations.</td>
<td>We manually curated prescribers’ responses, mostly through review of pharmacy records after consultations.</td>
</tr>
<tr>
<td>We experienced knowledge and competency gaps among health professionals, particularly prescribers.</td>
<td>As an organization, we provided educational sessions (e.g., webinars) to prescribers on various topics in the field of PGx. As a service, we used a select group of pharmacists with extensive education and training in PGx, and pharmacists were readily available to prescribers for one-on-one telephone consultations.</td>
</tr>
</tbody>
</table>

Abbreviations used: CDSS, clinical decision support system; EHR, electronic health record; HIE, health information exchange; HIPAA, Health Insurance Portability and Accountability Act; PACE, Program of All-Inclusive Care for the Elderly; PGx, pharmacogenomics.
returned to the pharmacy and just before pharmacists’ consultations.

Implementing

Experiences

Table 2 summarizes the challenges we experienced with implementing this PGx service for PACE. The compilation described in the table entails health care system— and health professional—related challenges, all of which would need to be considered by anyone interested in implementing a similar service. The table also summarizes the solutions we used to mitigate these challenges.

The biggest challenge we experienced was a lack of systems interoperability for health information exchange. Although our operating system, supported by the CDSS, allowed PGx test results and consultations to be documented in the pharmacy record, documenting this information in the PACE medical electronic health record (EHR) proved to be a challenge.

Pharmacist roles

The roles of pharmacists in implementing this PGx service are listed in Table 3. Operationally, pharmacists played an essential role in forming processes for ordering (of tests), conducting (of consultations), communicating (of test results and consultations), and documenting (of test results and consultations). Clinically, pharmacists were involved in all aspects of providing the PGx service, including development of algorithms and rules for the interpretation and application of PGx-specific data through our CDSS. Finally, from an educational perspective, our pharmacists helped to advocate for appropriate PGx testing and participated in educating the PACE community about the applications of PGx in clinical practice.

Testing

Overall, nearly every participant (n = 295; 99.7%) had at least 1 genetic variant, and more than one-third (n = 106; 35.8%) had 4 or more. Participants frequently used drugs posing DGI risks, with the majority (73.6%) having at least 1 reported interaction: 29.1% had 1 interaction, 24.3% had 2 interactions, 10.5% had 3 interactions, and 9.8% had 4 or more interactions. Supplemental Table 1 provides an overview of the drugs and drug classes most commonly involved in a DGI. A total of 446 DGIs were detected, and in many cases (n = 228; 51.1%), potential interaction threats were determined by pharmacists to be severe enough to warrant consideration or implementation of a drug-dose adjustment or drug-regimen change (Table 4).

Consulting

As presented in Table 4, the overwhelming majority (89.0%) of pharmacists’ recommendations were accepted by referring prescribers. The percentage of recommendations to “consider” a change in drug regimen was 34.4%, and these types of recommendations were always (100%) accepted by referring prescribers. The percentage of recommendations to “implement” a change in drug regimen was 17.9%, and these types of recommendations were accepted roughly one-third of the time.

Discussion

Although other researchers have recently begun to assess feasibility of implementing PGx services in community-based practice settings,7–12 to the best of our knowledge, this is the first study to report on feasibility within the PACE model of health care. We showed that implementing a pharmacist-led PGx service for PACE is feasible, demonstrating that pharmacists and prescribers can collaborate to integrate PGx information into participants’ care. The major PGx finding of our study is that, in a sample of participants enrolled in PACE who underwent testing, there was a high prevalence of interaction...
risk—associated genetic variants, with almost 3 out of 4 participants having at least 1 DGI.

The types of genetic variants and drugs implicated in DGIs in this study are similar to other samples of older adults who have had PGx testing, but it appears that the prevalence of DGIs in our sample is much higher than in other samples.27 In a sample of 1143 patients (mean age ± 60 ± 15 years; mean number of drugs 8.4 ± 5.7) with known CYP2C9, CYP2C19, and CYP2D6 genotypes, researchers reported a DGI prevalence of 12.0%.27 In a larger sample of 22,162 patients (mean age 60 years; mean number of drugs 9.1) referred for PGx testing of CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5 genes, researchers detected that 24.6% of all severe drug interactions were DGIs, although the overall prevalence of DGIs was not reported.2 Notwithstanding the differences, such results are clinically important because multiple drug use among older adults is common and increases the risk of DGIs.28

We attribute the feasibility of our program, in large part, to the systematic processes used and the roles of pharmacists involved in implementation. Yet it must be acknowledged that prescribers’ responses to genetic information are vital to the success of precision-medicine initiatives, such as our PGx service. Another major contributor to feasibility implementing our PGx service was the use of a sophisticated CDSS that aided pharmacists with interpreting PGx test results in the context of multidrug interactions. Use of a CDSS is critical to bridging the gap between the promise and realization of PGx in clinical practice.29-31

Challenges to implementing PGx services in PACE

It is well recognized that implementation of PGx services into clinical practice has been slower than anticipated,8 although it is not surprising. As with any new service in health care, some challenges with implementation are expected. These challenges will likely vary by practice setting.

Lack of systems interoperability

We encountered a lack of systems interoperability for health information exchange. We are not alone in encountering this challenge. Rather, the entire health care system is challenged with the uncertainty of how PGx testing results may be most effectively integrated into technology.9 This translates into clinical importance because the storage and portability of a patient’s PGx test results will affect the level of utilization.32 We were fortunate to work in a partially integrated health care system, whereby both prescribers and pharmacists had access to a centralized pharmacy system with an IT platform for integrating PGx test results into clinical practice. Access to these data by providers in other health care systems, however, may be limited or nonexistent.10,32,33

Limited access to the medical electronic health record

Understandably, pharmacist access to the medical EHR may have altered some of the recommendations made by our pharmacists. However, the bigger picture is that our experience contradicts the notion that implementing a PGx service is feasible only in institutions with an EHR system. To the contrary, like several other researchers,7-12,33 we demonstrated that implementing a PGx service is feasible in a community-based practice setting. Moreover, based on the high prevalence of DGIs detected by our pharmacists (73.6%) and similarly reported in other older adult populations,27 we surmise that enhancing MTM services with PGx not only is feasible, even with limited access to the medical EHR, but also allows pharmacists to identify additional medication-related problems—beyond those traditionally identified during MTM services—that should be addressed with patients’ prescribers.

Consideration of prescriber response to PGx consultations

Although we did not require prescribers to directly respond to our consultations, we were able to ascertain responses through extrapolation. Extrapolating prescribers’ responses to pharmacists’ consultations is a common method used in the evaluation of MTM services.34,35 For example, to evaluate Star ratings for pharmacy benefit managers providing MTM services, Centers for Medicare and Medicaid Services extrapolates Part D data to determine changes in prescription drug regimens following pharmacist-conducted comprehensive medication reviews. Using this methodology, we observed that PACE prescribers welcomed our pharmacists’ recommendations. No prescribers outright rejected our PGx-based recommendations.

Need for continuing education in PGx

Research suggests that prescribers are interested in integrating PGx into practice and applying PGx test results to improve drug decision making.36-41 However, research has also found disparities in knowledge and competency regarding PGx among prescribers.36-41 For example, a national survey completed by 10,303 U.S. physicians found that a high percentage of respondents (97.6%) agreed that genetic variants may influence drug response, but a comparatively small percentage (10.3%) felt sufficiently informed about PGx testing and its relevance in making drug regimen choices in their practice; only 29.0% of physicians overall had received any education in the field of PGx.38 Another challenge related to education is misperceptions of prescribers about a dearth of evidence to support the utility of PGx in practice. As an example, in a survey completed by 597 U.S. physicians, when deciding whether or not to order a PGx test to predict likelihood of an adverse drug response or determine likelihood of drug efficacy, the availability of clinical practice guidelines was considered to be an important factor by the majority (85.5%) of respondents, yet 79.6% indicated they had never ordered a PGx test.36 In a similar survey of 300 physicians, more than 80% of respondents indicated that they had not ordered a PGx test during the past year. When those who indicated that they had not ordered a PGx test in the past year were asked why they had not, 51.9% cited uncertainty about the clinical value of the test.31 This research suggests that a substantial proportion of prescribers are not aware, or are skeptical, of published clinical practice guidelines from the CPIC, DPWG, or CPNDS.
Research also suggests that there are gaps in pharmacists’ knowledge and competency on this subject. Most pharmacists report low knowledge and confidence in using PGx information for drug selection and management. To address these gaps, professional pharmacy organizations have called for the addition of PGx training into pharmacy curricula, and many colleges and schools of pharmacy have begun to respond.

Solutions to implementing PGx services in PACE

Although we encountered some challenges with implementation, we were able to circumvent many other challenges encountered by early clinician adopters and prospective implementers of PGx services, which have been described in more detail elsewhere. For example, we were fortunate to work in PACE, which is a partially integrated and fully capitated health care system, whereby pharmacists’ access to PGx tests and results and pharmacy reimbursement for PGx services, respectively, were not challenges that we experienced, unlike many others in community-based practice settings. In these settings, disparate access to PGx testing and lack of reimbursement are 2 of the most significant challenges to integrating PGx into MTM services. We attribute a large portion of the feasibility of implementing our PGx service to the extent to which our pharmacists are valued in PACE and to our pharmacists’ roles in providing this service. Having pharmacists with expertise in PGx lead this service, as in the present study, may further help to close the knowledge and competency gaps among prescribers, as has been suggested by experts in the field.

Study limitations

This study is subject to a few limitations. The first is that because it was a feasibility study, wherein we describe the processes involved in implementing our PGx service, we cannot report on outcomes. There are, however, myriad publications demonstrating the positive impact of integrating PGx into patient care on outcomes. Nevertheless, in the future, we plan to measure economic, clinical, and humanistic outcomes to demonstrate the value of our PGx services to PACE organizations and their participants. Secondly, pharmacists did not receive responses from prescribers on all of their consultations, and there was no incentive for either prescribers or pharmacists to directly respond to or follow up on responses, respectively. Therefore, we needed to review drug regimens before and after consultations, with the use of extrapolation methods to ascertain responses. Although extrapolating prescribers’ responses to pharmacists’ consultations is a common method used in the evaluation of MTM services, it is an imprecise method. During this implementation, we learned the importance of having a method for tracking both prescribers’ responses to pharmacists’ consultations and prescribers’ implementation of pharmacists’ recommendations and the potential need for encouraging this service. Although we are working on the former, the latter continues to be challenging; yet we believe that demonstrating the value of PGx services on outcomes will provide an incentive, at least partially, for improved collaboration between prescribers and pharmacists, which will improve response rates. Finally, during implementation of our PGx service, we used the standard phenotype terminology for drug-metabolizing enzymes: extensive, intermediate, poor, and ultrarapid metabolizers. Shortly after the completion of the study time period, the CPIC published a consensus paper for standardizing terms for PGx testing results, whereby extensive metabolizers are now referred to as normal metabolizers, and there is now a distinction between rapid and ultrarapid metabolizers. It is plausible that the addition of rapid metabolizer phenotype may have changed some of the pharmacists’ recommendations, but we think that the changes would have had clinically insignificant impact on the pharmacist’s recommendations for the majority of PACE participants. Since the CPIC publication, we have adopted the standardized terms in both our consultations and the CDSS.

Conclusion

Implementing a pharmacist-led PGx service for PACE is feasible. Implementation of this service highlights the leadership role that pharmacists can take in moving PGx from research to practice. Community-based pharmacists who desire to pursue this type of service in their practice should be encouraged by our solutions but must also consider the challenges associated with implementation. We have described some of those challenges to stimulate discussion concerning potential next steps.

Acknowledgments

The authors are grateful to the PACE prescribers and health professionals who collaborated with them to make the implementation of this pharmacogenomics (PGx) service a reality in clinical practice. They are also grateful to the PACE participants who agreed to allow their PGx data to be used for research purposes.

References


## Appendix

**Supplemental Table S1**

Top 5 drug classes and associated drugs involved in DGIs in study participants

<table>
<thead>
<tr>
<th>Drug class (&quot;victim&quot; drug)</th>
<th>Participants affected, $n$ (%)</th>
<th>Causative gene (&quot;perpetrator&quot;)$^b$</th>
<th>Evidence-based guideline available$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulants–Antiplatelets</td>
<td>101 (22.8%)</td>
<td>CYP2C19</td>
<td>CPIC, DPWG</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>54 (12.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>47 (10.7%)</td>
<td>CYP2C9, CYP3A4, VKORC1</td>
<td>CPIC, CPNDS</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>85 (19.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>22 (5.0%)</td>
<td>CYP2C19</td>
<td>CPIC, DPWG</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>14 (3.2%)</td>
<td>CYP2D6$^d$</td>
<td>DPWG</td>
</tr>
<tr>
<td>Sertraline</td>
<td>13 (3.0%)</td>
<td>CYP2C19</td>
<td>CPIC, DPWG</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>10 (2.3%)</td>
<td>CYP2C19</td>
<td>CPIC, DPWG</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>8 (1.8%)</td>
<td>CYP2C19, CYP2D6</td>
<td>DPWG</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>7 (1.6%)</td>
<td>CYP2D6, CYP3A4</td>
<td>DPWG</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>3 (0.7%)</td>
<td>CYP2D6</td>
<td>CPIC, DPWG</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>2 (0.5%)</td>
<td>CYP2D6</td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>1 (0.2%)</td>
<td>CYP2C19, CYP2D6</td>
<td>CPIC, DPWG</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>59 (13.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>33 (7.5%)</td>
<td>CYP2C19</td>
<td>DPWG</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>17 (3.9%)</td>
<td>CYP2C19, CYP3A4</td>
<td>DPWG</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>5 (1.1%)</td>
<td>CYP2C19, CYP3A4</td>
<td>DPWG</td>
</tr>
<tr>
<td>Dexlansoprazole</td>
<td>2 (0.5%)</td>
<td>CYP2C19</td>
<td></td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>1 (0.2%)</td>
<td>CYP2C19, CYP3A4</td>
<td>DPWG</td>
</tr>
<tr>
<td>Opioids</td>
<td>58 (13.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>21 (4.8%)</td>
<td>CYP2D6, CYP3A4</td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20 (4.5%)</td>
<td>CYP2D6, CYP3A4</td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>14 (3.2%)</td>
<td>CYP2D6</td>
<td>DPWG</td>
</tr>
<tr>
<td>Codeine</td>
<td>3 (0.7%)</td>
<td>CYP2D6, CYP3A4</td>
<td>CPIC, CPNDS, DPWG</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>1 (0.2%)</td>
<td>CYP3A4</td>
<td></td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>55 (12.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>40 (9.1%)</td>
<td>CYP2D6</td>
<td>DPWG</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>15 (3.4%)</td>
<td>CYP2D6</td>
<td>DPWG</td>
</tr>
</tbody>
</table>

Abbreviations used: CPIC, Clinical Pharmacogenetics Implementation Consortium; CPNDS, Canadian Pharmacogenomics Network for Drug Safety; CYP, cytochrome P450; DGI, drug-gene interaction; DPWG, Dutch Pharmacogenetics Working Group; VKORC1, vitamin K epoxide reductase complex subunit 1.

- $^a$ Participants with at least 1 detected DGI of any severity.
- $^b$ Genes encoding for isoenzymes responsible for at least 30% of the drug’s metabolism or activation of a prodrug to its active metabolite (e.g., codeine to morphine).
- $^c$ Despite the unavailability of an evidence-based guideline, the evidence indicates a clinically relevant drug-gene pair for the following: fluoxetine-CYP2D6$^{20,21}$, dexlansoprazole-CYP2C19$^{12,23}$, hydrocodone-CYP2D6 and -CYP3A4$^{20,24}$, and buprenorphine-CYP3A4$^{25,26}$.
- $^d$ Although the CYP1A2 gene encodes for the isoenzyme responsible for about 70% of duloxetine’s metabolism, it is not listed, because it was not included in the pharmacogenomic test panel.