Editorial

Medication reconciliation to support pharmacogenomics implementation

Scott A. Mosley[1], Joshua M. Pevnick[2]

[1]Department of Clinical Pharmacy, University of Southern California (USC) School of Pharmacy, Los Angeles, CA, USA; [2]Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Correspondence to: Scott A. Mosley. Department of Clinical Pharmacy, University of Southern California (USC) School of Pharmacy, Los Angeles, CA, USA. Email: samosley@usc.edu.

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Petry *et al.* (1) reported on the first large-scale study quantifying and classifying the impact of using medication reconciliation (med rec) to support the implementation of pharmacogenomics (PGx) test results into clinical care within a health care system. Over an 8-month period, a 21-member team of pharmacists and pharmacy trainees with advanced PGx training contacted 465 patients by telephone to identify 2,311 medication discrepancies and classified them based on their implications for patient safety. PGx results were reviewed to assess for gene-drug interactions and phenoconversion due to drug-drug interactions. Subsequently, patients' primary care providers were alerted if there were opportunities to improve medication use. The authors found that 93% of patients had at least 1 medication discrepancy and that on average, each patient had at least one medication with a gene-drug interaction, but the exact proportion was not reported. Furthermore, 4.3% of patients required interventions to align their medication regimen with existing PGx guidelines (2). Finally, this study reports pharmacy staff spending an average review time of 15.8 minutes per patient, much of which was provided by pharmacy trainees (1).

PGx involves testing for patient-specific genetic variation to predict drug response based on changes in pharmacokinetic or pharmacodynamic relationships between a gene and a drug. Clinicians and patients can use PGx to guide therapeutic decisions, potentially reducing the risk of adverse drug reactions and therapeutic failure. There are two general approaches by which PGx can be implemented, reactive or pre-emptive, but successful mixed models have also been reported (3). Currently, most PGx testing is still performed reactively, meaning it is ordered for select patients to guide a specific drug therapy or to explain undesirable responses to a drug after adverse events, intolerable side effects, or therapeutic failure. Increasingly, more institutions are taking a pre-emptive approach to PGx testing, so results are available at the time of prescribing (3). The pre-emptive approach offers several potential advantages, but this practice is largely confined to academic institutions and early adopters of PGx implementation, like members of the Implementing GeNomics In pracTicE (IGNITE) Network PGx Working Group (4).

For new prescriptions, clinical decision support (CDS) embedded within the electronic health record (EHR) can help guide medication and dosing choices. Storing PGx results as discrete data, as Petry *et al.* (1) describe in their study, is also recognized as a critical component to support this CDS (3,5). Although we believe CDS to be one important aspect of implementing PGx, we also recognize that more research is needed to determine its role in improving patient outcomes (6). To address these situations, PGx test results can be analyzed by pharmacy staff or other providers with PGx expertise in conjunction with medication regimens as they are recorded in the EHR. Realistically, we know that these regimens are frequently inaccurate (7). In fact, these regimen inaccuracies prevent CDS from providing optimal recommendations for new prescriptions. Med rec, or understanding what medications

patients have been prescribed and are taking, is the logical solution to improving the accuracy of medication regimens contained in the EHR. These more accurate regimens can be used to support the use of PGx results in medication management, whether this is predominantly driven by CDS or pharmacy staff recommendations.

Several prior studies have used PGx as part of larger medication therapy management (MTM) plans targeted to high-risk patients (8-10). Even though some studies have reported improved outcomes and reduced costs, no clear consensus has emerged on the benefit of enhancing MTM with PGx (9,11). We believe this may be, at least in part, due to the pharmacy staff resources needed for MTM. While med rec has been reported to take between 15–70 minutes per patient (12), with Petry *et al.* (1) sharing methods to target the lower end, MTM can require upwards of 90 minutes and requires pharmacists or other clinicians to conduct them (13). Additionally, we appreciate that multiple patient specific factors, including PGx results, influence variation in drug response. Therefore, other clinical services, such as PGx consultation, MTM, or CMM aim to collect and interpret a wider range of patient specific factors to optimize drug therapy, but at the cost of more time and expertise. The experience of Petry *et al.* (1), then, is significant for detailing to what extent med rec alone can be used to implement PGx and may be more generalizable to those with limited time and resources.

Med rec is a key foundational step for nearly everything that pharmacists do [e.g., order verification, MTM, comprehensive medication management (CMM)] since an accurate medication list is a prerequisite for any medication management. This is especially true for outpatient medication management because patients administer their own medications and supplements and because prescribing and dispensing are not necessarily reviewed by any central provider. Despite this excellent face validity for med rec, there is also potential for it to consume enormous amounts of time. Thus, there are always questions surrounding its clinical and economical value: who should receive priority? How much time will it take? How much benefit will be realized?

In this case, Petry *et al.* (1) is helping us to take the first steps towards answering these questions as they pertain to med rec in support of a PGx implementation. Prioritizing patients taking 10 or more medications, taking high-risk medications, or with cardiovascular disease, dyslipidemia, or depression seemed perhaps insufficiently focused in that only 4.3% of these patients required an adjustment to their therapy following med rec, based on their PGx results. Although the 15.8 minutes required for med rec seems manageable and compares quite favorably with med rec conducted in other settings (12,14), this would translate to over 6 hours of time spent conducting med rec for each change in therapy due to their PGx results (100/4.3 = 23.3 patients per actionable PGx result, 23.3 × 15.8 minutes = 367 minutes). Perhaps one reason for the high reported time commitment per actionable genotype is that the study design likely included patients who were active participants in their own healthcare. To their credit, the authors were transparent in their recruiting methods, which enrolled patients who previously participated in a genotyping study and communicated readily through an electronic patient portal. Therefore, there may not have been as many discrepancies for these patients compared to others who do not utilize healthcare resources as readily and as often as those included in the study. With this in mind, it is possible that the benefit captured is underestimating the true impact, and may serve as the lower bound of possible benefits this type of service can provide. Even so, the fact that Petry *et al.* (1) identified at least one medication discrepancy in 93% of patients, including 355 patients (77%) who had med rec documented within the past 6 months, further reinforces the importance of reviewing medication lists during each point of contact with patients, even among those who have frequent clinical encounters.

Beyond demonstrating the clinical utility of including PGx in the med rec process, Petry *et al.* (1) provides an excellent template for institutions with comparable resources to begin similar efforts. These authors and others who are advancing the utility of PGx and moving precision medicine into practice should be applauded and encouraged to continue candidly sharing their experiences, especially challenges, with implementation. They present methods and results which supports integrating PGx results in the EHR, but for many institutions throughout the USA, this workflow may still look like the distant future due to financial, technological, and educational challenges.

Currently, in considering the implementation of pre-emptive PGx testing, many provider organizations face several challenges. First, lack of reimbursement has been a major barrier for many institutions to act on exciting advancements in precision medicine. It is true that PGx testing has not routinely been covered by healthcare payers in the USA, and may have kept many provider organizations from entertaining the idea of incorporating PGx into their healthcare system (15). The good news is that payers,

including Medicare, are expanding coverage for PGx testing and include a wide range of patient conditions utilizing medication therapies with known gene-drug interactions (16).

Second, there are substantial information technology challenges. Major support at the health system level is usually needed to successfully launch and maintain CDS to guide PGx interpretation (5,17). The authors describe the impressive operation and infrastructure Sanford Health has built over years of investment which includes a pre-emptive genetic laboratory developed test (Sanford Chip) for patients, pharmacists trained in PGx interpretation with designated in-basket alerts, and PGx results integrated into the EHR with real-time CDS for prescribers.

Beyond these reimbursement and information technology issues, it is always a staffing challenge for pharmacy services to provide additional med rec. As previously noted, although the time per encounter may be short, the frequency of actionable results would need to be considered in supporting med rec for these patients versus others. Petry *et al.* (1) involved pharmacy trainees in the workflow. Since this is a great opportunity for teaching and helps to minimize costs, this is an excellent option. In settings without trainees, we agree with the authors that pharmacy technicians, who have proven capable and competent to conduct accurate med rec, may be a cost-effective option (14). Another patient-centered option worth exploring further is to encourage patient-led med-rec by making the process easy-to-use, accurate, and efficient. A recent randomized study by Ebbens *et al.* (18) reported that a patient-led med rec conducted using a patient portal was non-inferior to med rec by a pharmacy technician, in terms of medication discrepancies identified. Patients were satisfied with the portal and saved the pharmacy technician an average of 6.8 minutes per patient.

Another barrier may be specialized training in PGx. It is important to remember that all pharmacists are qualified to guide therapeutic decisions based on pharmacokinetic and pharmacodynamic considerations that affect drug response, and these are the parameters most often implicated by variation in PGx results. There are specialized education and training opportunities, both live and online, for pharmacists and other members of the healthcare team to gain experience and practice interpreting and applying clinical recommendations for PGx results. Many of the training opportunities provide learners with a certificate and are conducted by professional pharmacy organizations like the American Society of Health-System Pharmacists (ASHP) and the American College of Clinical Pharmacy (ACCP), and by academic leaders in PGx research and practice, but these programs are available to other professions (e.g., MD/DO, PA, NP/RN, etc.). Also, medical professional organizations like the American Society for Clinical Pharmacology and Therapeutics (ASCPT) and the American Society of Human Genetics (ASHG) often incorporate PGx into their conference content, continuing education, and publications. Because PGx evidence is rapidly evolving, it is important for all involved members of the healthcare team to maintain PGx education so that updated PGx guidelines can be optimally interpreted to improve patient care (19).

These data reported by Petry and colleagues may serve as a springboard for justifying frequent high quality med rec to guide the integration of PGx test results for patients with high impact disease states or those with high probability of having gene-drug interactions. While the service described has financial and technological barriers to widespread uptake, the clinical utility of PGx testing (as evidenced by the number and types of interventions identified) and the rate of patient engagement suggests there is patient demand and therapeutic benefit from providing this increased level of care to select patients. Since there will be an ever-increasing number of patients with an ever-increasing number of PGx results, and because an aging population will be taking an ever-increasing number of medications despite declining physiologic reserves, it is clear that the future of patient-centered care will demand clinician use of PGx results and other precision medicine approaches to optimize therapy for all patients. Yet, many institutions remain unprepared to serve their patients in this capacity. If anything, results like this should encourage pharmacy services to create an institution-specific action plan to meet the needs of patients who have these PGx results now or will in the future. The success and challenges shared by Petry *et al.* (1) and others on the forefront of successful PGx implementation efforts will continue to help shape future efforts to optimize the use of PGx in supporting high-quality medication management and patient care.

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Footnote

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