Original Article

The effect of medication reconciliation on generating an accurate medication list in a pharmacogenomics practice

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Contributions: (I) Conception and design: All authors; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Background: Medication reconciliation is recognized as a critically important medication safety element and a key initiative by multiple organizations. Within our precision medicine program, accurate medication lists are essential to our ability to make specific medication recommendations based on pharmacogenetic results. Our study aimed to identify discrepancies within the patient's medication list to improve medication management via genetic factors through a pharmacy team-based approach.

Methods: A dedicated team of pharmacists and trained student pharmacists conducted telephone interviews to complete medication reconciliation for individuals enrolled in our precision medicine preemptive screening program. Medication list discrepancies were tracked as well as if pharmacogenetic consults were altered by findings during the telephone interviews.

Results: Medication reconciliation was completed on 465 participants who had recently received or were awaiting pharmacogenetic testing. We found similar results to previously described rates of medication list discrepancies with an average of 4.9 medication discrepancies per patient as well as greater than 90% of individuals having at least one medication discrepancy. Pharmacogenetic recommendations for 20 individuals (4.3%) required adjustment following medication reconciliation.

Conclusions: This pilot program supports the value of a dedicated team for medication reconciliation and the importance of accurate medication lists to optimize precision medicine programs.

Keywords: Medication reconciliation; pharmacogenomics (PGx); patient care; medication safety; patient safety

Submitted Oct 11, 2022. Accepted for publication Oct 31, 2022.
doi: 10.21037/atm-2022-63
View this article at: https://dx.doi.org/10.21037/atm-2022-63

Introduction

Healthcare organizations across the world are striving to become highly reliable organizations. Highly reliable healthcare organizations are striving for continuous process improvement and aiming for zero preventable patient harm through use of patient and medication safety initiatives in addition to other processes. One seemingly simple process—an accurate and complete medication list—forms the foundation of all subsequent medication safety efforts. However, healthcare providers have found the methodology to obtain and maintain an accurate medication list is a challenging and complex process. Penm and colleagues outlined the need for a universal definition for medication reconciliation and key concepts to facilitate better understanding of resources needed to integrate into routine practice (1). The term "medication reconciliation" can be defined as the process of compiling the most accurate medication list by means of comparing which medications

a patient is taking against a list of prescribed medications, resolving discrepancies, and lastly communicating with healthcare teams (2).

Patient safety organizations, such as the World Health Organization (WHO), the Commonwealth Fund, The Joint Commission (TJC), and Institute for Healthcare Improvement, have endorsed or often require medication reconciliation (2-8). While the Joint Commission International does not have a specific standard to address medication reconciliation, the combination of two standards—"improve effective communication" and "improve the safety of high-alert medications"—encompass critical components of maintaining and communicating an up-to-date medication list with healthcare personnel (9). A study conducted in 2019 revealed nearly 41% of hospital discharge patients had at least one medication discrepancy resulting in a potential for an adverse drug events (ADEs) (10). The potential for medication discrepancies occurs at all points of contact with healthcare personnel due to the risk of communication barriers and breakdowns.

The importance of accurate medication lists is known to be critical to patient care; however, due to the complexities and volume of resources needed, implementation of medication reconciliation standards varies widely amongst healthcare facilities. The American Society of Health-System Pharmacists (11) and WHO propose the integration of pharmacists within the medication reconciliation arena due to medication expertise (12). Additionally, numerous studies have cited inclusion of pharmacists or trained pharmacy personnel to be the gold standard when obtaining an accurate medication list (13-15).

Precision medicine has been identified as another tool in the medication safety toolbox (16). Utilization of genetic results to customize healthcare treatments, more specifically medication regimens, has been identified as the initial steps towards precision medicine (17,18). Numerous studies have indicated genetic testing may improve medication outcomes by decreasing ADEs and/or therapeutic failures (19-22). For instance, individuals with dihydropyrimidine dehydrogenase (DPD) deficiency have an increased risk of toxicity when treated with fluoropyrimidines (23). Copious amounts of literature are available linking genetic variation in the *DPYD* gene with decreased DPD activity with 236 current publications listed in the Pharmacogenetics Knowledge Base (PharmGKB) related to *DPYD*. A recent analysis confirmed that carriers of decreased function or no function alleles for *DPYD* were at significantly increased risk of both severe toxicity and treatment modifications with fluoropyrimidine therapy compared to non-carriers (24). Wigle and colleagues reported outcomes comparing genotype-guided dosing of fluoropyrimidine therapy and noted the individuals prescribed guideline-based dose reductions experienced similar rates of serious adverse events as wild type individuals prescribed standard dosages (25). This drug-gene association yields sufficient data to warrant clinical guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Royal Dutch Association for the Advancement of Pharmacy-Pharmacogenetics Working Group (DPWG). More significantly, there are more than one hundred other drug-gene interactions with data supporting clinical pharmacogenomics (PGx) guidelines. Examples such as these highlight novel mechanisms to improve patient care is through the use of precision medicine. However, medication reconciliation remains the core component of effective medication therapy management as personal history must be taken into consideration along with other clinical and laboratory factors.

Sanford Imagenetics was established in 2014 as a pre-emptive genetic screening program and has successfully genotyped over 20,000 individuals to date (26,27). Sanford Imagenetics is a department within Sanford Health, which is the largest rural healthcare institution within the United States. The primary test offered at Sanford Imagenetics is the Sanford Chip, which is a preemptive screening array comprised of PGx testing as well as an optional medically actionable predisposition portion. The PGx portion of the Sanford Chip was initially comprised of 8 genes (*CYP2C19*, *CYP2C9*, *CYP2D6*, *CYP3A5*, *DPYD*, *SLCO1B1*, *TMPT*, and *VKORC1*) and the current test is comprised of 11 genes (addition of *CYP2C* cluster, *CYP4F2* and *IFNL3*). Clinical decision support (CDS) utilizes the discrete pharmacogenetic information within the electronic medical record (EMR) (Epic Systems, Verona, WI, USA) to provide real-time alerts to prescribers to avoid potential drug-gene interactions. Furthermore, all PGx results yield a comprehensive review by a clinical pharmacist which may be inclusive of alternative therapies if warranted based on individual's genetic results and medication history. In the event a medication was omitted from the medication list, the clinical PGx review and CDS alerts within the EMR cease to function appropriately. Therefore, the aim of this study was to identify discrepancies within the patient's medication list as an additional point of contact to improve medication management via genetic factors through a pharmacy team-based approach including:

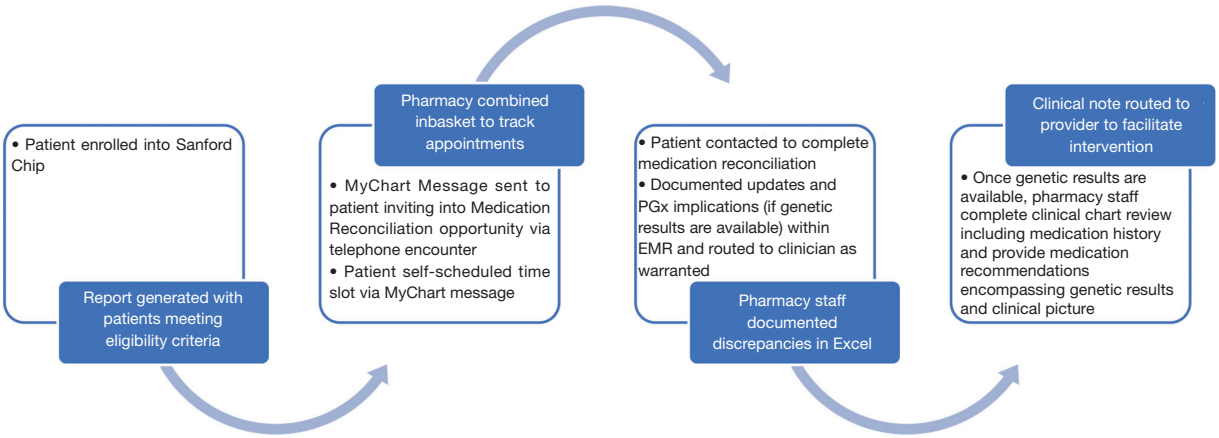

Figure 1 Medication reconciliation workflow in a pharmacogenomic practice. PGx, pharmacogenomic; EMR, electronic medical record.

- What types of discrepancies are identified when a pharmacist and/or pharmacy student conduct medication reconciliation via telephone encounters?
- How does medication reconciliation impact PGx recommendations?

Methods

The project was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Sanford institutional review board (No. STUDY00001624) and informed consent was not required from all individual participants per IRB as was determined as not human research. A team of pharmacists and trained pharmacy students conducted medication reconciliation via telephone encounter during an 8-month pilot (July 2019–February 2020). Four pharmacists were responsible for conducting medication reconciliations and served as the supervising pharmacists for 17 student pharmacists. Student pharmacists conducted medication reconciliation while on their 5-week advanced learning experience PGx elective. Additionally, a PGY1 pharmacy resident completed a PGx rotation and performed patient interviews during the 4-week block.

Student pharmacists' instruction was provided by one pharmacist to ensure consistency and continuity in training based on Sanford Health's standardized medication reconciliation policies and procedures. Educational efforts consisted of didactic learning (presentation) paired with hands on experience via competencies. Successful completion of a written competency was required prior to any patient contact. The written competency is 20 questions and includes short answer and true/false format. Many of the short answer questions include a short scenario followed by short answer questions such as "How would you enter this?" or "How would you update this?" or "What other questions would you want to ask?". The standardized consistent process included scripting for students to use while initiating the telephone call and cues utilized to tailor conversations to yield the most meaningful information. Scripting included how to introduce themselves, reason for the call, steps to obtain what medications the patient is taking, and next steps related to receiving genetic results. To acquire the best possible medication history (BPMH) health care providers should incorporate two components into curation of the medication list: a structured interview process to review all medications with the patient and a process to verify information obtained from the patient (14). In every effort to maintain the BPMH, students were educated on interview tactics and utilization of additional reliable resources such as pharmacy medication dispensing histories via internal and external records when available, medical records, and patient communication via the EMR patient portal (MyChart®, Epic Systems Inc., Verona, WI, USA) to send pictures of medication bottles or medication lists. Additionally, each medication review was documented within the EMR highlighting any changes made to the medication list and overseen by a supervising pharmacist. Upon review of the documentation, student pharmacists were provided feedback and if any additional clarification was warranted the patient was contacted for clarification. *Figure 1* depicts the flow from patients opting into the preemptive genetic screening to receipt of genetic results to be included in the pharmacist's PGx clinical review.

Inclusion and exclusion criteria

A report designed to identify patients enrolled in the Sanford Chip was further refined to identify patients meeting certain criteria with a focus on targeting patients most likely to be impacted by medications with drug-gene interactions as per CPIC guidelines. Patients were included if they had enrolled in the Sanford Chip and met one or more of the following criteria: patients with 10 or more medications; patients on high alert medications as defined per the Institute for Safe Medication Practices and TJC; patients with dyslipidemia; patients with cardiovascular disease; or patients with depression as identified per the problem list. The identified patients were sent a MyChart® message inviting them to arrange a time for a telephone consult to review medications with a pharmacy team member. Included individuals also had to be 18 years of age or older, have a MyChart® account, and be English speaking.

The pharmacy team utilized comments within the shared inbasket to track appointment times. Within the EMR, telephone encounters were used to update medication list within the medication reconciliation navigator (home medication list) and to write a chart note with documented changes. If actionable drug-gene interactions or significant changes were identified, the encounter was routed to the primary care provider for awareness and/or intervention.

Data collection

Data obtained prior to telephone call included patient name, when pharmacogenetic test was drawn/collected, provider, clinic/department, next primary care provider appointment, if patient met criteria for 10 or more medications or high alert medications or hyperlipidemia or cardiovascular disease or depression, and when the patient message was sent to schedule a call. Data collection during/after the phone call included documenting in spreadsheet columns the number of discrepancies related to column heading. Discrepancies were defined by any variance between the patient reported medication regimen and documentation within the EMR. Discrepancies were classified into the following dependent variable categories: missing/wrong dose, wrong frequency, wrong medication (defined as wrong medication formulation such as immediate release as opposed to extended release or look-alike, sound-alike medications), medication discontinued, duplicate medications, medication omissions, and added "prn" reason. Additional data points were collected to assist in demonstrating proper interval for medication lists to be considered accurate and complete such as patient taking medication differently, patient not taking medication, medication reconciliation <30 days, medication reconciliation >30 days but <6 months, medication reconciliation >6 months. Furthermore, components specific to PGx were collected if the medication reconciliation was completed after the PGx review, number of medications with drug-gene relationships per CPIC, if revisions were warranted to the PGx note, and a column to document medication name (used to determine if phenoconversion was applicable). Phenoconversion, or when an otherwise normal phenotype is converted to a poor metabolizer status, has been described as the Achilles heel of PGx guided medication utilization (28).

Statistical analysis

Interview metrics and identified dependent variable discrepancies were tracked and quantified in a custom spreadsheet in Microsoft Excel. Descriptive statistics—number, mean, frequency—were calculated for dependent variables (such as discrepancy classification). Independent variables in this study included pharmacists, students, and PGx results. A power analysis was not conducted as this was a pilot study.

Results

We identified 989 patients who met criteria for medication reconciliation with some meeting criteria in more than one category. MyChart® messages were sent to these 989 patients with 465 (47%) having a medication reconciliation interview completed by the pharmacy team. The average review time was 15.8 minutes per patient encounter. The total number of identified discrepancies was 2,311. The average number of discrepancies per patient was 4.9, and at least 1 medication discrepancy was identified on 93% of patients. EMR discrepancy dependent variables are represented in *Figure 2* and potential consequences and implications included in *Table 1*. The most frequent types of discrepancies were omissions and deletions. *Table 2* provides a full list of patient demographics with the majority of the patient population represented as elderly Caucasian females. Over half of the patient population was identified as having hyperlipidemia and approximately one third were on 10 or more medications and high alert medications. *Table 3* references the last time medication reconciliation was done for the patient.

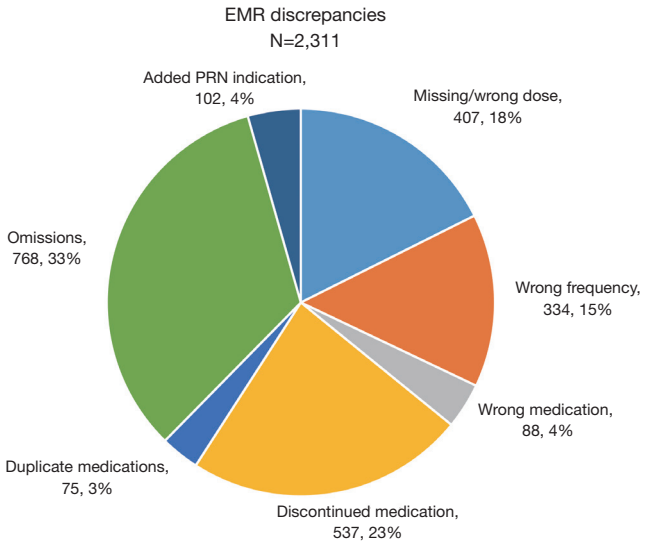

Figure 2 EMR discrepancies by percentage. EMR, electronic medical record; PRN, pro re nata.

Table 1 Potential safety implications for incorrect medication list

Discrepancy classification	Potential consequence for PGx	Potential implication for patient safety
Missing/wrong dose	Some PGx guidelines/package labeling contain specific dosing recommendations	Dosing outside of prescribed dosage could result in either under or overdosing, each of which could affect safety/efficacy
Wrong frequency	–	Altered frequency dosage could result in either under or overdosing, each of which could affect safety/efficacy
Wrong medication	PGx recommendations may be missed, or incorrect recommendations may be made, implications if wrong medication is a strong inhibitor	Taking alternative medications unbeknownst to the treatment team could result in significant drug-drug interactions or could trigger an adverse event thought to be a new symptom thus triggering the prescribing cascade
Discontinued medication	Incorrect recommendations may be made; implications if discontinued medication is a strong inhibitor	Not taking medications that the healthcare team believes are being taken can result in less effective alternative medications being used
Duplicate medications	–	Can result in prescriber and healthcare team confusion with cluttered medication lists
Omissions	PGx recommendations may be missed, implications if added medication is a strong inhibitor	Taking alternative medications unbeknownst to the treatment team could result in significant drug-drug interactions or could trigger an adverse event thought to be a new symptom thus triggering the prescribing cascade
Added PRN indication	–	Joint Commission requirement; clarifies patient taking medication for correct reason

PGx, pharmacogenomic; PRN, pro re nata.

Approximately two-thirds of patients in this pilot had medication reconciliation done within the last 6 months.

A number of problems related to PGx were also identified. Issues related to phenoconversion (strong inhibitors) were identified in 11 patients. Identified issues included addition of strong inhibitor medications to the medication list that were previously missing; addition of medications affected by strong inhibitors already on medication list; and discontinuation of phenoconverting medications. Phenoconversion related items that had the potential to occur included both the possibility

Table 2 Demographics of completed medication reconciliation patients

Characteristics	Value
Age (years)	Average: 61
Sex	
Female	288 (62%)
Male	177 (38%)
Race	
Caucasian	456 (98%)
African American	2 (<1%)
American Indian/Alaska Native	1 (<1%)
Asian	1 (<1%)
Pacific Islander	1 (<1%)
Declined	3 (<1%)
Unknown	1 (<1%)
10 or more medications[†]	150 (32%)
High alert medications[†]	164 (35%)
Hyperlipidemia[†]	261 (56%)
Cardiovascular disease[†]	64 (14%)
Depression[†]	76 (16%)

[†], patients may have met more than one criterion.

Table 3 Time of last medication reconciliation prior to PGx medication reconciliation

Time	Value
Medication reconciliation done <30 days	195 (42.11%)
Medication reconciliation done >30 days but <6 months	160 (34.56%)
Medication reconciliation done >6 months	47 (10.15%)
Last medication reconciliation not documented	61 (13.17%)

PGx, pharmacogenomic.

of genetic result misinterpretation as well as medication changes based on PGx results influencing the metabolism of concurrent medications. For example, a medication adjustment from sertraline to fluoxetine in an otherwise normal CYP2D6 metabolizer is expected to decrease the analgesic effects of their tramadol (due to phenoconversion to CYP2D6 poor metabolizer).

On average each patient had at least one medication with genetic guidance per CPIC guidelines on their medication list. Nearly two-thirds of patients underwent medication reconciliation after PGx consultation was completed. A portion of the study population (4.3%) required revisions to PGx recommendations post medication reconciliation. Medications previously omitted from home regimens which were subsequently added during the medication reconciliation process with CPIC and/or phenoconversion implications most commonly included antidepressants (amitriptyline, fluoxetine ×3, bupropion ×2, citalopram, sertraline ×2) and proton pump inhibitors (PPIs) (omeprazole ×3, and pantoprazole). Other medications added to the medication list with PGx-associated guideline recommendations included clopidogrel, ondansetron, tramadol ×2, simvastatin, and warfarin. St. John's Wort, an over-the-counter (OTC) herbal product that is a CYP2C19 and CYP3A4 inducer, was added to one patient's medication list. Medications removed from medication list with CPIC implications included sertraline and citalopram.

Discussion

Criteria for identifying medication reconciliation patients was used to ascertain patients most likely to have possible PGx actionable recommendations based on medications such as high alert medications, patients on ≥10 medications, or specific disease states with medications known to have drug-gene evidence-based guidelines (hyperlipidemia, cardiovascular disease, or depression). Data was specifically collected on high alert medications and individuals with ten or more medications on the current medication list for multiple reasons. High alert medications, medications which bear an increased risk for causing harm if used incorrectly (9,29), pose a specific risk for medication list inaccuracies. Secondarily, many high alert medications also have CPIC guidelines (anticoagulants, opioids, chemotherapeutic agents) making accurate lists increasingly useful from a safety and efficacy standpoint in our PGx reviews. Additionally, polypharmacy may contribute to development of ADEs, hospitalizations and healthcare utilization and therefore, these individuals were prioritized as they may see the most benefit from medication reconciliation (30-34). Despite over three-quarters of patients having medication reconciliation completed within the last 6 months, a large majority of patients had at least one discrepancy highlighting the importance of complete and thorough medication reconciliation at every visit. A study by Rangachari and colleagues identified two main concepts for inaccuracies

within medication lists, the first being lack of ownership and accountability amongst healthcare providers and the second is due to complexities related to transitions of care (35). An accurate medication list is valuable to all aspects of healthcare regardless of the ordering medication specialty as discrepancies pose a significant risk for patient harm.

Despite the abundance of literature surrounding medication reconciliation, to the best of our knowledge there are no studies to highlight the PGx implications. In addition, the classification of medication discrepancies is not universal (36). The majority of medication reconciliation data stems from inpatient settings; however, one study reported 90% of outpatient medication lists contain medication discrepancies (37). Similarly, 93% of our patient population had at least 1 medication discrepancy. An article by Cornish and colleagues cited medication discrepancies have been linked to potential ADEs in 38% of cases (38). A telephone-based medication reconciliation study conducted in an ambulatory clinic identified at least one medication discrepancy per patient in 84.7% of patients as well as 3.2 medication discrepancies per patient with an average review time of 15 minutes (39). Our findings found a considerably higher number of discrepancies at 4.9 discrepancies per patient; however, our approach provides more granularity to the type of discrepancies such as outlining if an indication was omitted from an as needed medication. Omissions from the medication lists was the most common type of discrepancy encountered within this study, which corresponds to existing literature on medication reconciliation discrepancies (38,40,41). A study by Nassaralla and colleagues identified the addition or removal of medications from medication lists and patient misreporting of medications to be common discrepancies as also noticed within our findings. Additionally, Nassaralla and colleagues described absence of route of administration and frequencies to be common discrepancies (42). While our study did not specifically track changes to route of administration each medication entry included the route of administration upon completion of the medication reconciliation process.

As noted, obtaining accurate medication histories is a challenging task and often inaccuracies in lists occur. OTC medications create a specific challenge for ensuring accurate medication histories given the ability for individuals to purchase these products either at the advice of a prescriber or unbeknownst to the clinical team. Given the recently published CPIC guidelines on the use of nonsteroidal anti-inflammatory medications and PPIs, the importance of accurate OTC medication lists is imperative for clinical PGx reviews (43,44).

A study by Sutherland and colleagues recently assessed the accuracy of patient medication lists using quantitative methods. In this study, the investigators used liquid chromatography-tandem mass spectrometry methods to determine presence of 263 OTC and prescription medications and compared these results against the medication list (45,46). Not surprisingly, there were higher rates of OTC medications detected that were not on the medication list than prescription medications with percentages as high as 84% with naproxen and 82% with ibuprofen being detected but not on the medication list (44). The detection of PPIs without evidence of prescription, such as pantoprazole and omeprazole, were lower at 30% and 20% respectively, however, this may still be clinically significant if the individual has variation in their *CYP2C19* metabolizer status (44).

Study limitations

This study provides valuable insight into medication reconciliation and impact on PGx, however, does have some limitations. One limitation is the lack of formalized methodology for patients to schedule a telephone appointment, therefore, relying on patients to respond to messages within MyChart®. The inability to arrange patients on a formalized schedule may have resulted in a more targeted patient population who are more likely to be active participants in their own healthcare. Second, while the objective of this study was to provide medication reconciliation services prior to reviewing genetic results, unfortunately due to the patient facilitated scheduling effort, not all medication reconciliation telephone encounters were conducted prior to result review. Another limitation was the total number of CPIC medications was not tracked pre- and post-med reconciliation. Additionally, the array of pharmacists and student pharmacists conducting the medication reconciliation telephone encounters could create variables in classification of discrepancies and interview tactics. In effort to mitigate any variances between interview styles and classification of discrepancies, all staff involved received training by one pharmacist. Utilization of telephone encounters to conduct BPMH limits the availability to view medication bottles, however, healthcare institutions may develop creative technology solutions to overcome this limitation as described by Heyworth and colleagues at Veterans Affairs in Boston (47). Through the use of a patient portal within the EMR, patients may upload

pictures of medication bottles or medication lists in every effort to obtain an accurate medication list. While patients do not always provide medication bottles during face-to-face visits to discuss medications, utilizing telephone encounters provided patients the opportunity to have direct access to medications stored in various locations of their residence. While this study was conducted at one institution within the United States, the implications of medication reconciliation are universal to all healthcare facilities across the globe.

Implications for practice and future research

This pilot project provided valuable insight for future related initiatives. Using lessons learned, we plan to develop a process to streamline contacting patients. MyChart® correspondence is inefficient, but creating a schedule within the EMR to manage telephone consultations will likely increase efficiency. Leveraging technology in the form of video visits may allow for more patient interaction and accurate medication lists in lieu of physical medication bottles and provide an added safety feature compared to obtaining medication information via telephone. Due to workloads, it is unrealistic to efficiently call and provide medication reconciliation for all patients in our program; thus, another future direction includes identifying at-risk patient populations who would gain the most benefit from telephone consultations. Medication reconciliation is one piece of a complex health care puzzle. We are in the process of developing a PGx clinic to meet with patients with the goal to narrow the gap of communication while increasing clinical care. In this clinic, medication reconciliation can be completed at the visit in addition to educating patients on genetic results and the implications to patients' medications. It also is worth exploring the role of other well-trained qualified individuals (e.g., nurses, pharmacy technicians) to complete medication reconciliation to allow pharmacists to use their time to complete other tasks.

Conclusions

Accurate up-to-date medication lists are imperative to provide highly reliable safe healthcare services. All healthcare personnel should strive for collecting and maintaining the BPMH to ensure exceptional medical care is delivered. PGx is another tool in the safety toolkit; however, it is necessary to have an accurate and complete medication list to facilitate precision medicine.

Acknowledgments

The authors express their gratitude to April Schultz, PharmD; Madison Croomes; Hannah Moran. Manuscript expands upon data presented as a poster at the American Society of Health-Systems Pharmacists Mid-Year Meeting, December 2020.

Funding: This work was funded by a generous gift from T. Denny Sanford creating the Imagenetics initiative (merging Internal Medicine and Genetics).

Footnote

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-2022-63/dss

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-2022-63/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-2022-63/coif). NJP and JFB are co-investigators on RFA-HG-17-008: A Depression and Opioid Pragmatic Trial (ADOPT-PGx) which is separate and unrelated to this work. NJP and JFB received honorariums also unrelated to this work. JVH and AM have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The project was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Sanford institutional review board (No. STUDY00001624) and informed consent was not required from all individual participants per IRB as was determined as not human research.

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Cite this article as: Petry NJ, Van Heukelom J, Baye JF, Massmann A. The effect of medication reconciliation on generating an accurate medication list in a pharmacogenomics practice. Ann Transl Med 2022;10(23):1259. doi: 10.21037/atm-2022-63