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Differences in Medicare Quality Measures among Nursing Homes after Pharmacogenetic Testing

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Abstract

Aim: Medical providers increasingly refer patients for pharmacogenetic testing. However, there is a dearth of data regarding the benefits of testing residents in long-term care facilities. The researchers conducted a retrospective population-level analysis to assess the usefulness of pharmacogenetic testing in nursing homes.

Methods: A subset of publicly available data of nursing home quality measures was identified as being possibly associated with medication-related problems and pharmacogenetic variability. The overall quality measures for nursing homes that had initiated pharmacogenetic testing for residents via the YouScript® Personalized Prescribing System, pharmacogenetic testing (PGxT) were compared to measures from control nursing homes that had not initiated testing YouScript®, PGxT testing.

Results: There was a 5.4% reduction in self-reported, moderate-to-severe pain in the residents of the PGxT nursing home compared to control homes that did not initiate testing YouScript®, PGxT testing (p=0.001). There was also a tendency towards a reduction in falls resulting in major injury in the YouScript®, PGxT nursing homes when compared against the national average.

Conclusion: The present study demonstrated a small reduction in the percent of residents reporting moderate-to-severe pain after results of pharmacogenetic testing were made available to the providers. Further studies will need to be done to assess if pharmacogenetic testing, using a Personalized Prescribing System, might reduce the use of potentially inappropriate medications and have a positive impact on the quality of life measures in the elderly.

Keywords: Medication-Related Problems; Pain; Pharmacogenetic Testing; Polypharmacy; Potentially Inappropriate Medications

Introduction

The number of medications prescribed to nursing home residents exceeds that taken by patients in any other medical setting largely because of the wide variety and severity of chronic comorbid conditions [1]. On average, nursing home residents take 8.8 medications and about a third take >9 medications per day, which increases the chances of drug interactions and medication-related problems (MRPs). A MRP is as an event or circumstance involving treatment that actually or potentially interferes with optimal medical care [2]. Nursing home residents are often frail and vulnerable, and hence are more susceptible to MRPs [3]. In a study of more than 13,000 nursing home residents in the U.S., the prevalence of polypharmacy (n ≥ 9 medications) was estimated to be 40% [4]. However, in a geriatric patient with multiple co-morbidities, polypharmacy may be unavoidable. Hence, an area of emphasis now is to try to minimize the use of potentially inappropriate medications (PIMs) in older adults [5-9]. Routinely prescribed psychiatric medications that are a common cause of adverse drug event (ADE)-driven emergency room visits, are also a substantial financial burden for the patient, the health care system, and the society as a whole [10-12].

Genetic variability in a patient's ability to metabolize many drugs can increase the risk of ADE and impact treatment effectiveness [13-15]. ADEs are a major healthcare burden with an estimated cost of $289 billion per year in added health care costs [14]. Ten to 17% of hospitalizations of older patients are directly related to ADEs [15]. Upon discharge, 50% of patients with ADEs experienced a decline in one or more activities of daily living, compared to 24% of patients without ADEs [16]. An estimated 35% of older persons experience ADEs and almost half of these are preventable [17-18]. Controlling risk of ADEs is complex because more than 85% of patients have significant genetic variation in the cytochrome p450 genes that metabolize the majority of the most commonly prescribed medicines [19-22]. Providers who suspect MRP in patients can refer the patient for pharmacogenetic testing (PGxT). PGxT may help identify the following MRPs: Improper drug selection, sub-therapeutic dosage, overdose, drug interactions, and adverse drug reactions.

Currently, electronic healthcare software systems do not incorporate individual pharmacogenetic data that could be easily understood and conveniently navigated by the healthcare providers. However, clinical decision support tools (CDST) have been developed that are being successfully used in conjunction with pharmacogentic

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testing to assist providers in making decisions regarding the most optimal and safe medication(s) for the individual based on their genetic profile. In a recently published retrospective study of more than 22,000 individuals, a CDST, You Script® Personalized Prescribing System was utilized to identify polymorphisms related to five cytochrome P-450 (CYP) genes commonly involved in drug metabolism. The results from this large study revealed that 93% of the subjects were not normal metabolizers of the CYP proteins suggesting that there is an increased likelihood of potentially serious adverse drug reactions especially in the elderly with a greater prevalence of polypharmacy [20]. In our present study, the researchers conducted a retrospective analysis to compare medication-related Medicare quality measure outcomes between nursing homes that had implemented PGxT using YouScript® Personalized Prescribing System as part of standard of care for their residents versus those nursing homes that did not utilize the PGxT, You Script testing.

Materials and Methods

The Quorum Review IRB based in Seattle, WA, reviewed and approved this retrospective study. Data on quality measures were collected and analyzed from two separate groups; one group of nursing homes that had instituted PGxT using You Script versus a control group of nursing homes that did not test residents [23-24]. For the remainder of this document, PGxT refers to genetic testing complemented by software that describes drug-drug, drug-gene, and drug-drug-gene interactions and additionally provides prescribing recommendations from the pharmacist for the physician (YouScript® Personalized Prescribing System).

PGxT nursing homes

Each PGxT nursing home 1) referred residents experiencing MRPs for PGxT based on the clinical judgment of the provider(s), 2) referred its first long-term care resident for PGxT via the You Script system on or before June 30, 2014, 3) referred at least 5% of beds during the quarter in which the home referred its first resident, and 4) had data available in Medicare's online database for two consecutive quarters preceding (Pre-PGxT period) and for two consecutive quarters following the quarter during which the home referred its first resident for testing (Post-PGxT period). A total of 14 homes referred 1 or more residents for testing in 2012 and 2013. Of these, 4 homes (3 in New York State and 1 in Washington State) referred ≥5% of residents up through March 31, 2014. The number of referrals made by each home ranged between 23 and 91 residents. For each resident referred, providers sent a specimen to the Genelex Corporation laboratory for testing along with documentation of the clinical indication for testing, the tests to be conducted, and a list of current medications. Genelex used PCR based assays to detect the following alleles, including common and most rare variants (frequency >1%) with known clinical significance at analytical sensitivity and specificity >99%: CYP2C19 (*2 - *10, *12, *17), CYP2D6 (*2, *2A, *3 - *12, *14, *15, *17, *19, *20, *29, *36, *41; gene deletion and duplications) CYP2C9 (*2 - *6, *8, *11, *13, *15), and VKORC1 (c.-1639G>A). A total of 65 residents were tested for all of the above alleles except for one resident who did not get tested for CYP2C19.

The results report relayed to the provider for each resident tested included the patient's phenotype for each gene tested (Normal/Intermediate/Poor/Ultra Rapid metabolizer; High/Intermediate/Low Sensitivity to warfarin), the genotype for each gene tested, the medications the resident was taking, the type of interaction (e.g., drug/gene, drug/drug/gene, drug/drug), interpretation of the results, and the prescribing suggestions (including change medication or dose, consider changing a medication or dose, or monitor patient for side effects and/or effectiveness). The nursing home residents were also provided with their phenotype results. Adjustment of a resident's medications in response to test results was left up to the provider's discretion; however, data regarding medication changes was not available to the researchers for this study.

Control nursing homes

Each control nursing home 1) was located in the same county as at least one of the PGxT homes, 2) did not refer any residents for testing via the You Script® Personalized Prescribing System and, 3) reported quality outcome data to Medicare, including one or more of the quality measures of interest during the same quarters as the PGxT homes (data regarding every measure was not available for every control home). Depending on the quality outcome measure, the number of control homes available for the analysis ranged from 177 to 228 homes.

Data management and statistical analysis

Publicly available data on five Medicare quality measures possibly associated with medication-related problems and pharmacogenetic variability as deemed by a team of pharmacists was downloaded for both the PGxT and control homes during the respective quarter (for 2012 and 2013) [23-24]. Data were obtained for 168 homes in New York State (3 PGxT and 165 control homes) and 64 homes in Washington State (1 PGxT and 63 control homes). The downloaded data consisted of a percentage value per nursing home in each calendar quarter. For each Medicare quality outcome, the quarterly values included the two quarters preceding the initiation of PGxT (Q3 & Q4 of 2012 for NY state and Q4 of 2012 & Q1 of 2013 for WA state) and the two quarters immediately after the initiation of PGxT testing (Q2 & Q3 of 2013 for NY state and Q3 & Q4 of 2013 for WA state). The two values in the pre-PGxT period and the two values in the post-PGxT period were averaged to give a single value for each nursing home.

The mean±SE of the outcome in the Pre-PGxT period, in the Post-PGxT period, and their difference (Post-PGxT minus Pre-PGxT) were calculated separately for each nursing home. The data were analyzed for both states (NY&WA) combined and for each individual state. We also compared the temporal changes (Post-PGxT minus Pre-PGxT) in the outcomes between the PGxT and the control nursing homes. The comparison included an unadjusted comparison and a comparison adjusted for state and the Pre-PGxT period (baseline) value. The two-sample t-test was used for the unadjusted analysis and linear regression was used for the adjusted analysis. In the linear regression, the difference (Post-PGxT minus Pre-PGxT) was regressed on the group (PGxT vs. control), the state (New York vs. Washington) and the Pre-PGxT value. The presented results from the two-sample t-test and linear regression procedures are the estimated unadjusted and adjusted differences (PGxT minus control), their 95% confidence intervals and p-values. In addition to the estimated absolute differences between PGxT and control homes, the corresponding relative differences are presented as well. All statistical analyses were carried out in R (Vienna, Austria), version 3.1.0. A p-value <0.05 was considered statistically significant [25]. Tests were not adjusted for multiple comparisons.

Results

Across the four PGxT nursing homes, a total of 66 residents were referred for testing (12 patients from the WA home in Q2 2013 and 54 from the NY homes in Q1 2013). Of these residents, medication lists were provided for all (100%). Residents referred for testing had been prescribed an average of 14.3 medications (range 3-32). The focus of this study was not to compare individual subjects but rather the change in the Medicare quality outcome measures in nursing homes before and after PGxT.

Among the quality outcomes measured, the change in the percentage of long-stay residents who self-reported moderate-to-severe pain was the only outcome that was statistically significant between the PGxT homes and control homes (Table 1A, Figure 1). While the unadjusted difference in the pain outcome was not statistically significant (difference = -7.7%, p=0.2) it was statistically significant once we adjusted for state and the pre-PGxT value (difference = -5.4%, p=0.001). Specifically, in NY state, the mean±SE percentage of those who self-reported moderate to severe pain decreased substantially from 11.3±6.3% to 3.1±0.9% (-8.3±6.2% change) among the three PGxT homes while it decreased only slightly from 3.5±0.3% to 3.2±0.3% (-0.2±0.2% change) among the 159 control homes (Table 1B). Similarly, in Washington state, the percentage of those who self-reported moderate-to-severe pain decreased substantially from 16.0% to 8.6% (-7.4% change) for the single PGxT home while the mean±SE percentage decreased from 10.2±0.9% to 9.6±0.9% (-0.6±0.7% change) among the 55 control homes (Table 1B). The estimated adjusted differences for this outcome and for the remaining four outcomes (expressed as relative changes) are shown in Figure 1. No statistically significant differences between PGxT and control nursing homes were found in antipsychotic use, depressive symptoms, falls and bladder or bowel incontinence.

Discussion

The primary objective of this retrospective study was to evaluate whether the results of PGxT conducted in nursing homes as part of standard care resulted in any improvements in quality measures for nursing home residents. Guides that list potentially inappropriate medications (PIMs), such as the Beers criteria list, have been helpful for providers taking care of the elderly, but may not provide insight into drug-drug, drug-gene, or cumulative interactions. Pharmacogenetic testing in our study identified several medications in addition to those already listed as PIMs on the Beers Criteria list (Figures 2A-2B).

A significant major finding of this study was the reduction in the perception of pain among nursing home residents' post-PGxT vs the control homes (Table 1A, 1B, Figure 1). Recent studies of nursing homes residents have shown that verbally communicative elderly with even mild and moderate cognitive impairment are able to report their pain symptoms and pain intensity [26]. The quality measure we used was the self-report of moderate-to-severe pain by the residents, which is considered the gold standard for pain evaluation in long-term care settings. The prevalence of pain in nursing home residents is reported to be as high as 84% [27]. Many reasons exist for the high prevalence of pain in the elderly, including degenerative musculoskeletal diseases, inflammation and arthritic pain, peripheral neuropathies, and side effects secondary to medications [28-34]. Persistent or moderately severe pain could have serious negative implications for the health of the older individuals. Some common sequelae of pain include depression, anxiety, impaired mobility, falls, abdominal discomfort, reduced appetite, constipation, poor sleep, dys regulation of the immune-stress response, and delayed healing [26, 31]. Activation of the sympathetic system during pain can also increase the blood pressure and even produce myocardial ischemia [28-33]. Hence pain brings with it a myriad of other co-morbid conditions that impair the quality of life of the elderly subjects and often require medications for the management of additional symptoms [28-34]. With treatment of each additional condition, the chances of polypharmacy, drug-drug interactions, drug-gene interactions and adverse drug effects get magnified [3-5].

In our study, a number of drugs associated with a drug-drug, drug-gene or drug-drug-gene interaction were identified in the nursing homes that could have resulted in significant ADEs in the elderly (Figures. 2A-2B and Table 2). These included centrally acting drugs such as antipsychotics that have the potential to produce a Parkinsonian syndrome and exacerbate pain. The elderly are also more susceptible to drug interactions because of decreased drug elimination rates due to a reduction in metabolism of most of the cytochrome p450 enzymes [6,10,20]. This frequently exacerbates ADEs in the older population [8-16].

Persistent or moderately severe pain could have serious negative implications for the health of older individuals. Over-medication for pain with opioids or centrally acting drugs can result in falls and fall-related injuries, often requiring emergency room visits or hospitalizations [33-35]. The three most commonly prescribed pain medications in the PGxT nursing homes were acetaminophen, oxycodone, and tramadol (Table 2). When all the prescribed drugs were evaluated, the highest number of interaction warnings were observed with metoprolol, quetiapine, and simvastatin for all interactions and

Medicare nursing home quality measure	Mean Pre-PGxT, all	Control NH, means			PGxT NH, means			Unadjusted Difference (PGxT- ontrols) ‡		Adjusted Difference (PGxT- ontrols) ‡	
		Pre-PGxT	Post-PGxT	Diff. (%) †	Pre-PGxT	Post-PGxT	Diff. (%)†	Est. (%)	p	Est. (%)	p
% of residents who self-report moderate to severe pain	5.3	5.2	4.9	-0.3 (-6%)	12.5	4.4	-8.0 (-151%)	-7.7 (-144%)	0.2	-5.4 (-101%)	0.001 *
% of residents who lose control of their bowel or bladder	35.0	35.1	37.4	2.4 (7%)	31.4	34.6	3.2 (9%)	0.8 (2%)	0.7	0.5 (1%)	0.9
% of residents who have depressive symptoms	16.8	16.6	15.3	-1.2 (-7%)	27.8	32.1	4.3 (26%)	5.6 (33%)	0.10	7.5 (45%)	0.14
% of residents experiencing one or more falls with major injury	2.0	1.9	1.9	-0.1 (-3%)	2.0	1.9	-0.1 (-7%)	-0.1 (-3%)	0.8	0.0 (-1%)	1.0
% of residents who received an antipsychotic medication	22.4	22.1	20.8	-1.3 (-6%)	38.7	37.9	-0.8 (-4%)	0.5 (2%)	0.9	2.0 (9%)	0.4

PGxT= pharmacogenetic testing; "PGxT NH" = nursing homes that used pharmacogenetic testing with Pre-PGxT, being the period before actual pharmacogenetic testing and Post-PGxT, the period after testing. "Control NH" = control nursing homes that did not have pharmacogenetic testing, with Pre-PGxT and post PGxT being the matching time periods for the PGxT-NH that underwent actual pharmacogenetic testing.

†diff = difference, after PGxT testing minus before PGxT testing; ‡ difference of differences (PGxT difference minus control difference). (%) = the percentage values in the parentheses are the difference expressed in relative terms as % of the mean before testing (all nursing homes). Est. = estimated difference. The adjusted difference was the difference adjusted for region and baseline value. The two-sample t-test was used for the unadjusted analysis and linear regression was used for the adjusted analysis. *p <0.05.

Table 1a: Changes in Medicare nursing home quality measures before and after PGxT in PGxT nursing homes versus control.

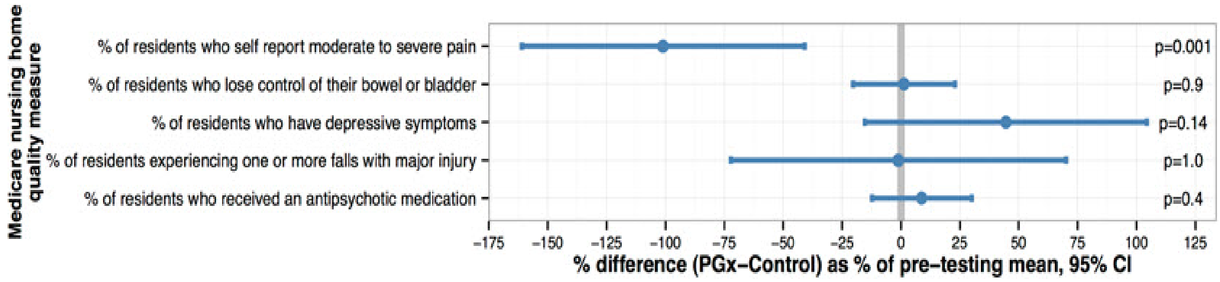


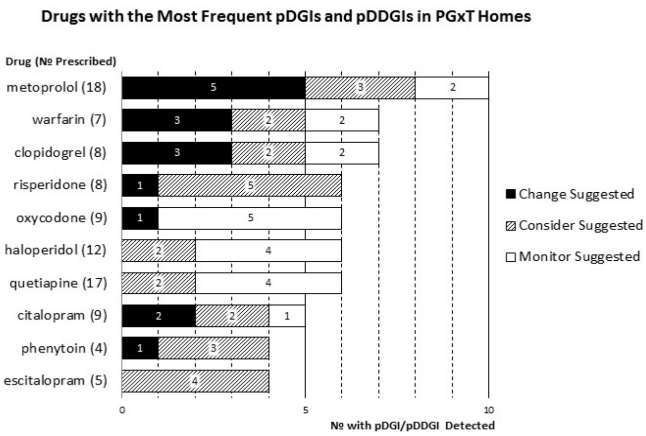
Figure 1: Difference in Medicare nursing home quality measures before and after testing between PGxT and control nursing homes, adjusted for state and baseline values. The difference is expressed as the % of the pre-PGxT mean among all nursing homes. The error bars around the estimates are the 95% confidence intervals. The 95% confidence intervals (CI) were calculated by linear regression.

State	Control NH, means†			PGxT NH, means ‡		
	NY	NY	NY	Pre-PGxT	Post-PGxT	Difference
NY	3.5 ± 0.3%	3.2 ± 0.3%	-0.2 ± 0.2%	11.3 ± 6.3%	3.1 ± 0.9%	-8.3 ± 6.2%
WA	10.2 ± 0.9%	9.6 ± 0.9%	-0.6 ± 0.7%	16.00%	8.60%	-7.40%

†Control homes: For NY state n=159 and for WA state n=55.

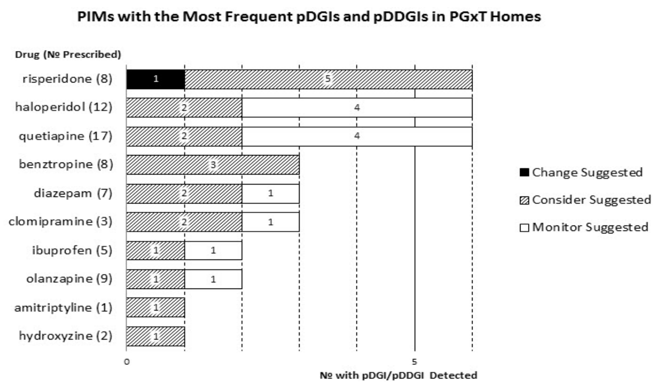
‡ PGxT homes: For NY state n=3; and for WA state n=1.

Table 1B: The percentage of self-reported moderate to severe pain in nursing homes in NY vs WA



This figure depicts drugs with all identified interactions that contained one of the following action recommendations given to the providers through using pharmacogenetic testing. "Change suggested" = change medication or dose. "Consider suggested" = consider dose adjustment or alternative drug; change may not be necessary based on current clinical situation; "Monitor suggested" = monitor patients for side effects and/or effectiveness. pDGI = potential drug-gene interactions, pDDGI = potential drug-drug-gene interactions. The x-axis denotes the actual number (no.) of pDGI/pDDGI interactions detected.

Figure 2a: Drugs with the Most Frequent pDGIs and pDDGIs in PGxT Homes.



This figure depicts medications identified as potentially inappropriate medications (PIMs) that also had pharmacogenetic interactions that contained one of the following action recommendations given to the providers through using pharmacogenetic testing. "Change suggested" = change medication or dose. "Consider suggested" = consider dose adjustment or alternative medication; change may not be necessary based on current clinical situation, "Monitor suggested" = monitor patients for side effects and/or effectiveness. *Potentially inappropriate medications were identified using American Geriatrics Society Beers Criteria. pDGI = potential drug-gene interactions, pDDGI = potential drug-drug-gene interactions. The x-axis denotes the actual number (no.) of pDGI/pDDGI interactions detected.

Figure 2b: Potentially inappropriate medications (PIMs) with the Most Frequent pDGIs and pDDGIs in PGxT Homes.

with metoprolol, warfarin, and clopidogrel for pharmacogenetic interactions (Figure 2A). When pain medications were evaluated, the highest number of interaction warnings were observed with oxycodone, tramadol, and acetaminophen/hydrocodone for all interactions as well as pharmacogenetic interactions (Table 2). Among 80.3% of patients, PGxT resulted in one or more recommendations to change a medication or dose, consider a change, or monitor for adverse effects and/or decreased effectiveness.

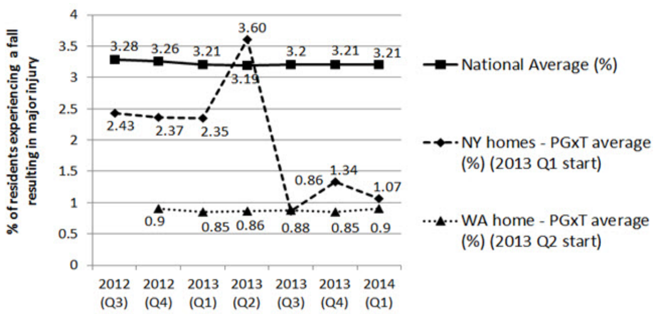
Relationship between pain management and falls & fall-related injuries

In a recent study of older adults in the United States, the prevalence of recurrent falls in the past year (≥2 falls) was 19.5% in participants with pain and 7.4% in those without pain [36]. An important and often overlooked cause of falls in the elderly is pain. If PGxT using the You Script® Personalized Prescribing System reduced the absolute risk of unmanaged pain by 5.4% (Table 1A), and the same ratios applied, fall risk could be reduced by 1.1% per year in the elderly ambulatory population. Although this may seem insignificant, falls are a major cause of morbidity in the elderly and on average the hospitalization cost for a fall-related injury is $34,294 (in 2012 dollars) [37]. For the three New York homes that initiated PGxT, the average percentage of falls resulting in major injury was 2.43% six months pre-PGxT and 0.86% six months post-PGxT (64.52% relative risk reduction, 1.57% absolute

Drug Name	**CYP metabolic pathways†**	**Frequency**	**pDGI/pDDGIs ‡**		
			Change	Consider	Monitor
acetaminophen	none	43	0	0	0
oxycodone	2D6 Minor, 3A4/3A5 Major	9	1	0	5
tramadol	2D6 Major	7	0	1	2
acetaminophen/ hydrocodone	3A4 Major, 2D6 Minor	5	0	1	3
aspirin	2C9 Minor	5	0	1	0
clonidine	2D6 Major	5	0	0	1
ibuprofen	2C9 Major	4	0	1	1
morphine	none	4	0	0	0
acetaminophen/ oxycodone	3A4/3A5 Major, 2D6 Minor	2	0	0	2
hydrocodone	3A4 Major, 2D6 Minor	2	0	0	0
hydromorphone	none	1	0	0	0
naproxen	2C9 Minor	1	0	0	0
phenazopyridine	none	1	0	0	0

This table shows how often each pain drug was prescribed in the nursing home population, as well as which CYP pathway(s) each drug is metabolized through and pDGIs/pDDGIs detected. CYP = cytochrome p450. † CYP2D6, CYP2C19, CYP2C9, CYP3A4, and/or CYP3A5 pathways only; path size definitions - Minor: < 30%, Major: 30-90%, Exclusive: 100%. ‡ pDGI = potential drug-gene interactions, pDDGI = potential drug-drug-gene interactions. Counts reflect highest rated pDGI/pDDGI triggered by the drug for each patient; multiple interactions on a single patient count as 1. “Change” = change drug or dose; “Consider” = consider dose adjustment or alternative drug; change may not be necessary based on current clinical situation; “Monitor” = monitor patients for side effects and/or effectiveness.

Table 2: Pain medications by number prescribed (frequency), CYP pathway (N = 66), and pDGI/pDDGIs.



PGxT = pharmacogenetic testing.

Q1-4 = quarters 1-4

Figure 3: Percentage of residents experiencing a fall resulting in major injuries in PGxT homes compared to the average percentage of falls resulting in major injuries nationally in nursing homes. Note that there was a sharp reduction in falls-related major injuries in the nursing homes in New York (NY) after institution of PGxT.

risk reduction) compared to the national average of 3.28% in the same quarter as pre-PGxT and 3.20% (2.44% relative risk reduction, 0.08% absolute risk reduction) in the same quarter as post-PGxT nursing homes. For the Washington home that initiated PGxT the following quarter, the percentage of falls was 0.90% six months pre-PGxT and 0.85% six months post-PGxT (5.56% relative risk reduction and 0.05% absolute risk reduction) compared to the national average of 3.26% before and 3.21% (1.53% relative risk reduction and 0.05% absolute risk reduction after. Although the reduction in falls associated with major injuries was not found to be statistically significant in the county comparison, a larger reduction was shown in all four homes after PGxT compared to the national average trend (Figure 3).

Although the data on falls is not statistically significant, the tendency towards a reduced rate of falls in the PGxT group and the correlation between fall risk and unmanaged pain indicates the need for additional studies on the potential impact that PGxT could have on both pain management and falls in a larger population, including both ambulatory and long-term care patients. The study suffers from a number of limitations which includes its retrospective ecological nature which could determine associations only, not causality. In addition, the researchers cannot rule out the possibility that the control nursing homes referred residents for PGxT elsewhere. It is possible the providers referred those residents for pharmacogenetic testing who appeared more vulnerable during that time period. Another drawback is that post-PGxT data was not available and hence, it is unclear which proportion of the recommendations was actually implemented by the healthcare providers. Lastly, due to the nature of how Medicare outcomes are reported in a nursing home, Medicare outcomes were assessed for the PGxT home as a whole, not just for PGxT subset population. Therefore, a direct correlation between the magnitudes of the effect of PGxT on Medicare outcomes cannot be made.

In spite of the limitations, it is notable that this is the first study in nursing home long-term care residents that demonstrated a significant difference in the perception of moderate-to-severe pain in the elderly after implementation of PGxT and presentation of actionable results to the providers. This study also suggests a tendency towards a reduced rate of falls after PGxT, but the data need to be interpreted with caution because of the small number of PGxT nursing homes compared against the national average. Nevertheless, if these results can be validated and reproduced in large prospective trials, they could have far reaching implications for reducing potentially inappropriate medication use and improving the quality of life of nursing home residents. A recent observational study of 205 elderly subjects that had undergone pharmacogenetic testing demonstrated a 39% reduction in hospitalization and a 71% reduction in emergency department visits versus propensity score matched subjects from a registry who had not been tested [13, 21]. In this particular study, more than 95% of the providers found the results of the pharmacogenetic tests helpful and more than half the providers implemented the changes suggested by the clinical decision support tools [21]. Finally, we also need to be aware of healthcare policy issues and ethical implications of pharmacogenomics. Privacy concerns of individuals and coverage of genetic tests by private health insurers and public programs will require careful evaluation to ensure that the cost of personalized medicine does not result in an increase in healthcare disparity. In addition, the selected pharmacogenetic tests will need to demonstrate significant clinical utility with a clear benefit versus risk ratio, especially in vulnerable populations. Hence, in spite of the excitement behind the research and the potential value of pharmacogenomics, the clinical value of pharmacogenetic testing will require further prospective studies.

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