Impact of Combinatorial Pharmacogenomic Testing on Hospitalization Rates in a Real-World Dataset of Patients with Major Depressive Disorder

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Background

- Pharmacogenomic (PGx) testing analyzes genetic variations that may affect medication outcomes and can be a valuable tool to inform treatment decisions.
- Large randomized controlled trials have demonstrated that PGx-guided care significantly improves remission, response,[1,2] and symptoms[2] in patients with major depressive disorder (MDD) and at least one treatment failure.
  - Receiving medications congruent with the PGx testing result has been shown to be a critical factor in improving these MDD outcomes.[1]
- However, little is known about the impact of PGx testing in real-world settings.

OBJECTIVES

The current study used a large US administrative claims dataset to determine:

1. The proportion of MDD patients prescribed medications with significant gene-drug interactions pre- and post-PGx testing.
2. Hospitalizations pre- and post-PGx testing.

Method

STUDY COHORT

- A dataset was generated by linking patients who received combinatorial PGx testing (GeneSight®, Myriad Genetics, Inc.) to administrative claims from the Optum Labs Data Warehouse.
  - Before linkage, the datasets were tokenized and Expert Determination was employed to yield a de-identified dataset with low risk of re-identification.
- The study cohort was created from the linked dataset using the inclusion/exclusion criteria shown in **Figure 1**.

COMBINATORIAL PGx TESTING

- Medications prescribed 90 days pre- and post-PGx testing were organized by the GeneSight test report into the following categories: 1) no known gene-drug interactions, 2) moderate gene-drug interactions, or 3) significant gene-drug interactions.

CONGRUENCY GROUPS

- Medications with no or moderate gene-drug interactions were considered congruent. Medications with significant drug interactions were considered incongruent.
- Patients taking one or more incongruent medications were considered incongruent; otherwise, they were considered congruent.
- Patients were assigned to the following groups based on congruency of medications 90 days pre- and post-PGx testing: 1) congruent-to-incongruent, 2) incongruent-to-congruent, or 3) no change in congruency.

HOSPITALIZATIONS

- The number of patients with any, psychiatric, and non-psychiatric hospitalizations was statistically compared (McNemar's tests) between the 180 day pre- and post-PGx testing periods in the overall cohort and by congruency group.

Figure 1: Patient selection flow chart

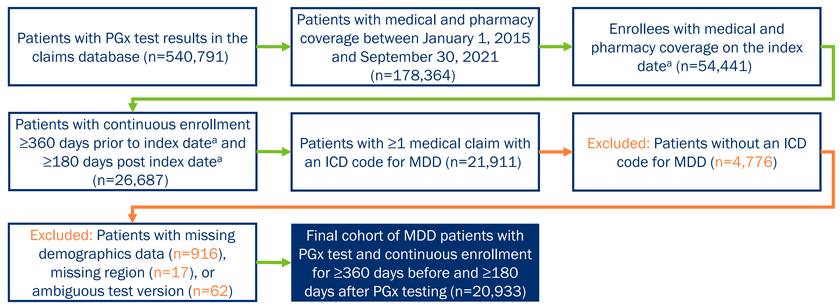

Fig. 1: Patient selection flowchart demonstrating how the total MDD cohort was derived following inclusion and exclusion criteria.
[a]The index date was defined as the date the PGx test result was reported to the healthcare provider.

Results

Table 1: Patient Demographics

	Statistic	Total Cohort	All patients with medications[a]	Incongruent to Congruent	No Change in Congruency	Congruent to Incongruent
Number of patients	n (%)	20,933 (100%)	16,965 (100%)	2,173 (100%)	14,352 (100%)	440 (100%)
Confirmatory MDD Diagnosis	n (%)	12,026 (57%)	10,239 (60%)	1,427 (66%)	8,523 (59%)	289 (66%)
GeneSight Medications Per Patient in the 360-Day Baseline						
	Mean ± SD	3.27 ± 2.31	3.74 ± 2.20	4.23 ± 2.40	3.66 ± 2.16	3.92 ± 2.09
Age	Mean ± SD	46.42 ± 18.97	47.54 ± 18.84	46.25 ± 18.87[b]	47.68 ± 18.81	49.1 ± 19.54
Gender						
Female	n (%)	14,698 (70%)	12,080 (71%)	1,543 (71%)	10,233 (71%)	304 (69%)
Male	n (%)	6,235 (30%)	4,885 (29%)	630 (29%)	4,119 (29%)	136 (31%)
Insurance Type						
Commercial	n (%)	14,559 (70%)	11,357 (67%)	1,526 (70%)	9,571 (67%)	260 (59%)
Medicare Advantage	n (%)	6,374 (30%)	5,608 (33%)	647 (30%)	4,781 (33%)	180 (41%)[c]
Quan Charlson Score[3]						
0	n (%)	13,525 (65%)	10,612 (63%)	1,385 (64%)	8,971 (63%)	256 (58%)
1-2	n (%)	5,158 (25%)	4,367 (26%)	553 (25%)	3,678 (26%)	136 (31%)
3-4	n (%)	1,512 (7%)	1,338 (8%)	162 (7%)	1,145 (8%)	31 (7%)
5+	n (%)	738 (4%)	648 (4%)	73 (3%)	558 (4%)	17 (4%)

High levels of psychiatric comorbidities were observed in the total MDD cohort during the 180-day baseline, with ~78% experiencing comorbid anxiety. These real-world results are representative of expected comorbidities in MDD patients.[4, 5]

[a] Includes patients with medications in the 90-day baseline and follow-up periods. These patients were further categorized based on the congruency of medications during the baseline and follow-up periods (incongruent to congruent, no change, or congruent to incongruent).
[b] Significantly different than the no change in congruency and congruent-to-incongruent categories ($p<0.05$, one-way ANOVA).
[c] Significantly different than the incongruent-to-congruent and no change in congruency categories ($p<0.05$, chi-squared test).
MDD: major depressive disorder; SD: standard deviation.

Figure 2: Gene-Drug Interactions in Patients Prescribed Medications at Baseline and Follow-up (n=16,965)

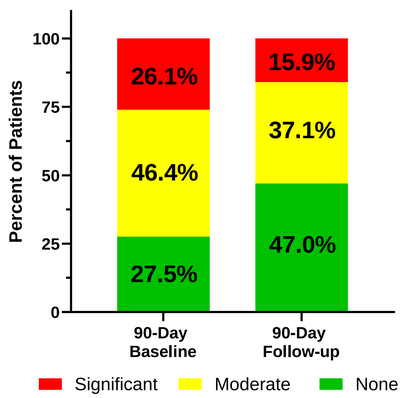

Fig. 2 Following PGx testing, **the proportion of patients prescribed medications with significant gene-drug interactions decreased.** This suggests that, in a real-world setting, PGx test results are being used for medication decisions similar to findings in randomized controlled trials.[1,2]

Figure 3: Hospitalizations in Patients Prescribed Medications at Baseline and Follow-up (n=16,965)

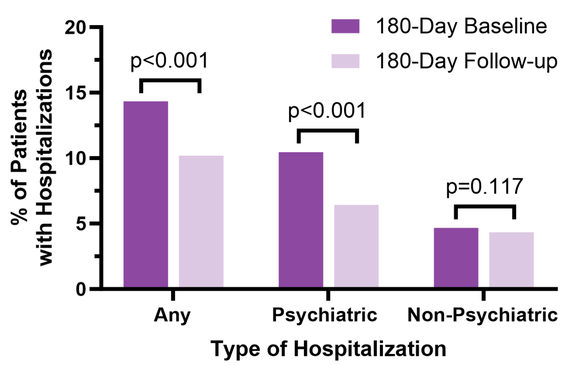

Fig. 3: Following PGx testing, **the percent of patients with hospitalizations was significantly reduced in all patients with medications.** The percent of patients with **any** hospitalization and **psychiatric** hospitalizations were significantly reduced by 29% and 39%, respectively. No significant differences were observed in non-psychiatric hospitalizations.

Figure 4: Hospitalizations by Congruency Group in Patients Prescribed Medications at Baseline and Follow-up (n=16,965)

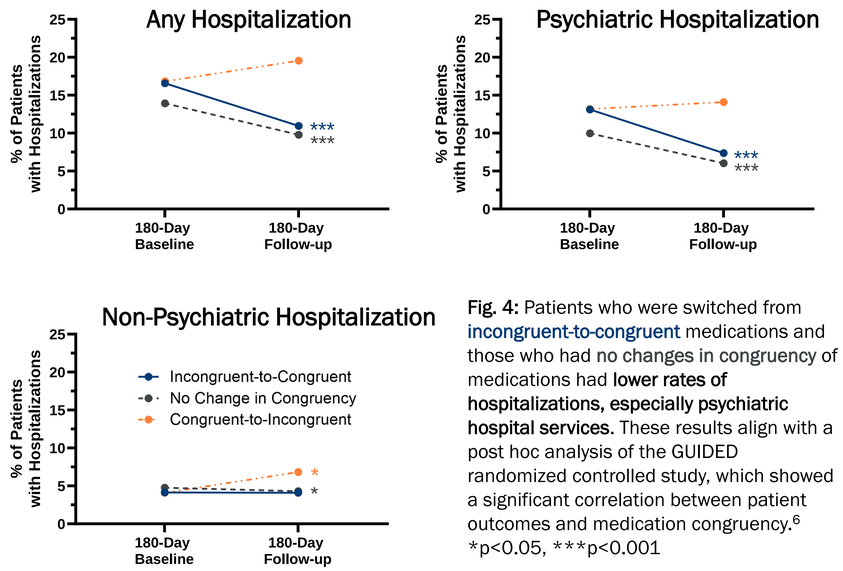

Fig. 4: Patients who were switched from incongruent-to-congruent medications and those who had no changes in congruency of medications had **lower rates of hospitalizations, especially psychiatric hospital services.** These results align with a post hoc analysis of the GUIDED randomized controlled study, which showed a significant correlation between patient outcomes and medication congruency.[6]
*$p<0.05$, ***$p<0.001$

Conclusions

Post-PGx testing, fewer patients were prescribed medications with significant gene-drug interactions and hospitalizations were reduced compared to pre-PGx testing. These real-world results are consistent with multiple prospective studies demonstrating the utility of PGx-guided treatment for improving response and remission rates in MDD.[e.g., 1, 2] Future directions include investigating the impact of post-PGx medication selection on healthcare costs.

References: 1. Greden et al. (2019) *J Psychiatr Res*. 2. Oslin et al. (2022) *JAMA*. 3. Quan et al. (2011) *Am J Epidemiol*. 4. Marx et al. (2023) *Nat Rev Dis Primers*. 5. Saha et al. (2021) *Depress Anxiety*. 6. Rothschild et al. (2021) *Psychiatry Res*.

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