Poster ID # P43

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

Holly L. Johnson;[1] Andria L. Del Tredici;[1] Devika Chawla;[1] Brady DeHart;[2] Alexander Gutin;[1] Pamela Morin;[2] Laura Becker;[2] Julia Certa;[2] Katie Johansen Taber;[1] Andrew A. Nierenberg[3]

1. Myriad Genetics, Salt Lake City, UT 2. Optum, Eden Prairie, MN 3. Massachusetts General Hospital, Harvard Medical School, Boston, MA

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 helping to improve these MDD outcomes.[1]

However, little is known about the impact of PGx testing in real-world settings.

OBJECTIVE: The current study used a large US de-identified administrative claims dataset to determine:

- The proportion of MDD patients who filled medication prescriptions with significant gene-drug interactions pre- and post-PGx testing.
- Hospitalizations pre- and post-PGx testing.

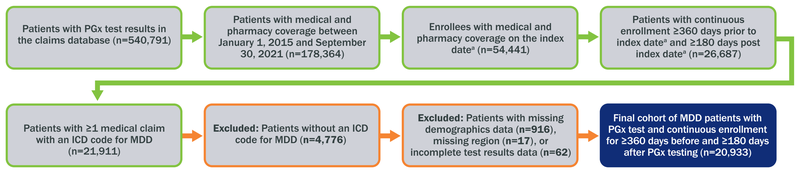
Methods

Study Cohort: A de-identified dataset was generated by linking patients who received weighted multi-gene PGx testing (GeneSight®, Myriad Genetics, Inc.) with administrative claims.

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** in patients ≥18 years of age.

Figure 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.

Weighted Multi-Gene PGx Testing: Medications prescribed and filled 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 gene-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.

Patient Demographics

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]

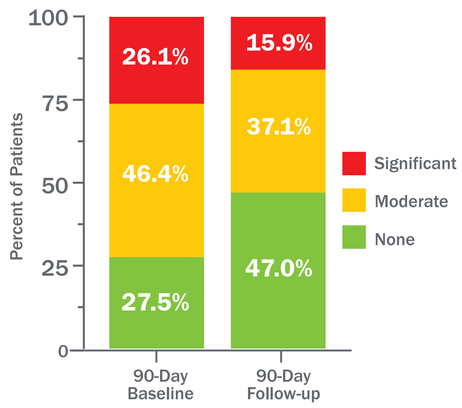
Table 1. Patient demographics

	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%)
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[b]	Mean ± SD	46.42 ± 18.97	47.54 ± 18.84	46.25 ± 18.87	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[c]	n (%)	6,374 (30%)	5,608 (33%)	647 (30%)	4,781 (33%)	180 (41%)
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%)

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. Significant differences were observed between medication congruency groups by one-way ANOVA ($p<0.05$).
c. Significant differences were observed between medication congruency groups by chi-squared testing ($p<0.05$).
MDD: major depressive disorder; SD: standard deviation.

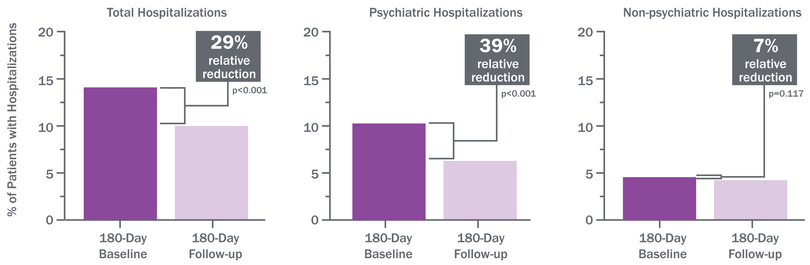
Outcomes in Patients with Medications at Baseline and Follow-Up

Figure 2. Gene-drug interactions in patients with medications at baseline and follow-up



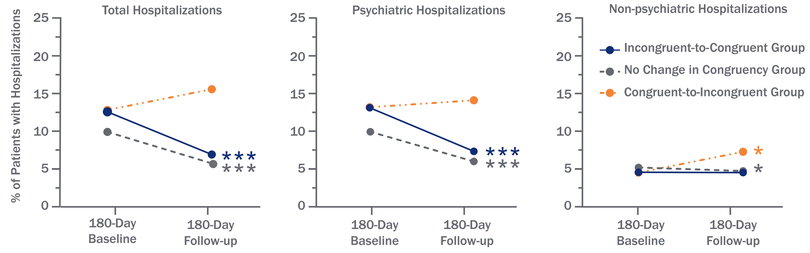
Following PGx testing, there was a 39% relative reduction in the proportion of patients who filled medication prescriptions with significant gene-drug interactions **in all patients with medications** (n=16,965). This suggests that, in a real-world setting, PGx test results are being used for medication decisions similar to that observed in randomized clinical trials[1,2] **(Figure 2)**.

Figure 3. Hospitalizations in patients with medications at baseline and follow-up



Following PGx testing, the percent of patients with hospitalizations was significantly reduced in all patients with medications (n=16,965). 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 3)**.

Figure 4. Hospitalizations by congruency groups in patients with medications at baseline and follow-up



*p<0.05, ***p<0.001

Post PGx testing, there was a significant reduction in the percentage of patients with any type of hospitalization or psychiatric-related hospitalizations in the **incongruent-to-congruent** (n=2,173) and **no change in congruency** (n=14,352) groups. The **congruent-to-incongruent** (n=440) group showed a non-significant increase in the percentage of patients with any type of hospitalization and psychiatric hospitalizations. 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] **(Figure 4)**.

Conclusion

Post-PGx testing, fewer patients filled medication prescriptions with significant gene-drug interactions and the percentage of patients with psychiatric hospitalizations was significantly reduced compared to pre-PGx testing. The percentage of patients with hospitalizations was not reduced in patients who were switched to medications with significant gene-drug interactions. 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]

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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.

Email for questions: holly.johnson@myriad.com