The Clinical Utility of Combinatorial Pharmacogenomic Testing for Patients with Depression: A Meta-Analysis

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BACKGROUND

- Pharmacogenomic testing has emerged as a possible approach to make data-driven treatment decisions for patients with Major Depressive Disorder (MDD).
- However, there is mixed evidence for the utility of pharmacogenomic testing due to differences in tests used, populations studied, and outcomes evaluated.
- Meta-analyses provide a high level of evidence and can be useful in evaluating the overall utility of a testing approach for clinical use.
- Given the meaningful differences between tests, all tests need to be evaluated separately and meta-analyses should be performed for each individual pharmacogenomic test.

OBJECTIVE

We present the results of a meta-analysis of prospective, two-arm studies examining the clinical utility of using a combinatorial pharmacogenomic test to inform treatment decisions for patients with MDD who had at least one prior medication failure.

METHODS

- The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines were utilized for this meta-analysis.
- A systematic search was performed, and all identified reports were screened to identify two-arm, prospective studies evaluating the clinical utility of this specific test that included patients ≥18 years of age diagnosed with MDD who had at least 1 prior medication failure.
- Overall, 1,556 patients were included from 4 studies [2 open-label studies and 2 randomized controlled trials (RCTs)].
- All included studies assessed symptom improvement, response, and remission using the 17-item Hamilton Depression Rating Scale (HAM-D17).
- The pooled mean effect of symptom improvement and pooled relative risk ratio of response and remission were calculated using a random effects model.
- Sub-analyses were performed according to study type.

REFERENCES:

1. Brown, L. et al., 2020., *Pharmacogenomics*. doi: 10.2217/pgs-2019-0157

RESULTS

- Patient outcomes were significantly improved for patients with MDD whose care was guided by the specific combinatorial pharmacogenomic test results compared to unguided-care (Figure 1).
- Heterogeneity in effect size across studies was significant, but moderate, for symptom improvement, but was not significant for response and remission.
- When the open-label studies were assessed separately, symptom improvement and response were significantly improved in the combinatorial pharmacogenomic guided-care group versus unguided-care group (Figure 2).
- When the analysis was restricted to RCTs, all 3 evaluated outcomes were significantly improved in the combinatorial pharmacogenomic guided-care group versus unguided-care group (Figure 2).

Figure 1. Meta-analysis of 4 prospective clinical utility studies of the combinatorial pharmacogenomic test

Forest plot of random-effects meta-analysis of 4 prospective, two-arm studies that examined the clinical utility of the combinatorial pharmacogenomic test in guiding treatment decisions for patients with MDD. (a) Average difference in symptom improvement (b) relative risk ratio for response, and (c) relative risk ratio for remission between guided- and unguided-care. Circle size indicates weight in overall analysis.

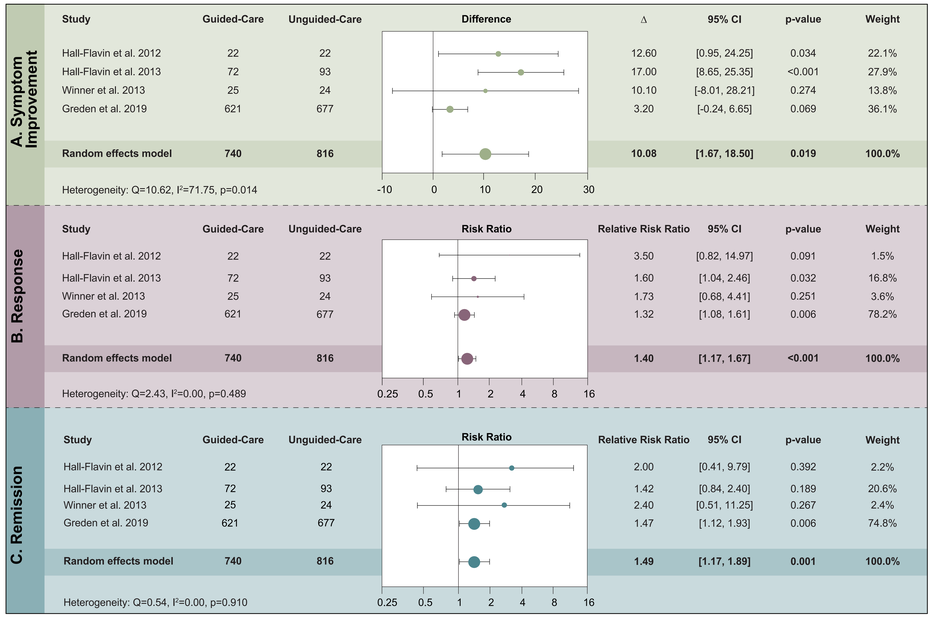
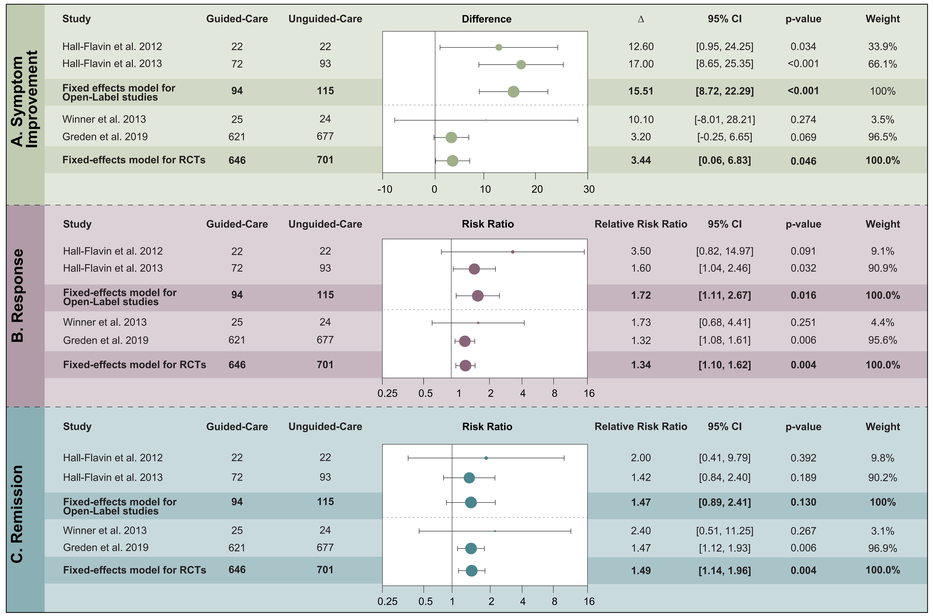


Figure 2. Sub-analysis of open-label and randomized controlled trials of the combinatorial pharmacogenomic test

Forest plot of fixed-effects meta-analysis for the open-label and RCTs. (a) Average difference in symptom improvement (b) relative risk ratio for response, and (c) relative risk ratio for remission between guided-and unguided-care. Circle size indicates weight in overall analysis.



CONCLUSIONS

- In a meta-analysis of 4 independent studies of the combinatorial pharmacogenomic test, all outcomes were significantly improved for patients in the guided-care arm versus unguided-care.
- This meta-analysis adds to the body of evidence supporting the clinical utility of using this combinatorial pharmacogenomic test to inform medication selection for patients with MDD who have failed at least 1 medication.[1]

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