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

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OBJECTIVE

- Here, we present the results of a meta-analysis of prospective, two-arm studies examining the clinical utility of using the combinatorial pharmacogenomic test, GeneSight Psychotropic®, 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 one prior medication failure***.
- 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 (RR) of response and remission were calculated using a random effects model.
- Sub-analyses were performed according to study type.

RESULTS

- Overall, 1,556 patients were included from four studies (two open-label studies and two randomized controlled trials (RCT)).
- 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).
- When the analysis was restricted to RCTs, all endpoints remained significant.
  - Symptom Improvement: 10.08, [1.67, 18.50], 0.019
  - Response RR: 1.40, [1.17, 1.67], <0.001
  - Remission RR: 1.49, [1.17, 1.89], 0.001

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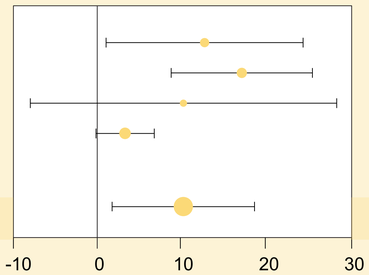
Forest plot of random-effects meta-analysis of four prospective, two-arm studies that examined the clinical utility of GeneSight Psychotropic in guiding treatment decisions for patients with MDD.

(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.

A. Symptom Improvement

Study	Guided-Care	Unguided-Care	Difference	Δ	95% CI	p-value	Weight
Hall-Flavin et al. 2012	22	22		12.60	[0.95, 24.25]	0.034	22.1%
Hall-Flavin et al. 2013	72	93		17.00	[8.65, 25.35]	<0.001	27.9%
Winner et al. 2013	25	24		10.10	[-8.01, 28.21]	0.274	13.8%
Greden et al. 2019	621	677		3.20	[-0.24, 6.65]	0.069	36.1%
Random effects model	**740**	**816**		**10.08**	**[1.67, 18.50]**	**0.019**	**100.0%**

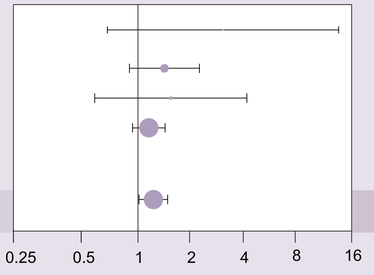
Heterogeneity: Q=10.62, I^2=71.75, p=0.014



B. Response

Study	Guided-Care	Unguided-Care	Risk Ratio	RR	95% CI	p-value	Weight
Hall-Flavin et al. 2012	22	22		3.50	[0.82, 14.97]	0.091	1.5%
Hall-Flavin et al. 2013	72	93		1.60	[1.04, 2.46]	0.032	16.8%
Winner et al. 2013	25	24		1.73	[0.68, 4.41]	0.251	3.6%
Greden et al. 2019	621	677		1.32	[1.08, 1.61]	0.006	78.2%
Random effects model	**740**	**816**		**1.40**	**[1.17, 1.67]**	**<0.001**	**100.0%**

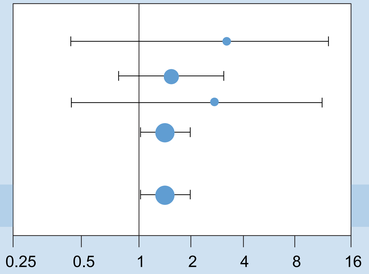
Heterogeneity: Q=2.43, I^2=0.00, p=0.489



C. Remission

Study	Guided-Care	Unguided-Care	Risk Ratio	RR	95% CI	p-value	Weight
Hall-Flavin et al. 2012	22	22		2.00	[0.41, 9.79]	0.392	2.2%
Hall-Flavin et al. 2013	72	93		1.42	[0.84, 2.40]	0.189	20.6%
Winner et al. 2013	25	24		2.40	[0.51, 11.25]	0.267	2.4%
Greden et al. 2019	621	677		1.47	[1.12, 1.93]	0.006	74.8%
Random effects model	**740**	**816**		**1.49**	**[1.17, 1.89]**	**0.001**	**100.0%**

Heterogeneity: Q=0.54, I^2=0.00, p=0.910



CONCLUSION

- In a meta-analysis of 4 independent studies, all outcomes were significantly improved for patients in the GeneSight Psychotropic® guided-care arm vs TAU.
- This meta-analysis adds to the body of evidence supporting the clinical utility of using GeneSight Psychotropic® to guide medication selection for patients with MDD that have experienceed at least one medication failure.