Effect of Pharmacogenetics-Based Decision Support Tools in Improving Depression Outcomes: A Systematic Review

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Background

Pharmacogenetic (PGX) testing has shown promise addressing inadequate response to antidepressants. There are plenty of PGX tests available in the market; however, for the most part, there is limited supportive evidence of their clinical utility. Although previous systematic reviews (SRs) of the published literature have been conducted, variable outcomes in relation to PGX testing efficacy and safety were reported. In view of more recent randomized controlled trials (RCTs) published, an updated SR is called upon.

Study Objectives

- To summarize, update, and assess the quality of the available evidence regarding antidepressant-related PGX testing.
- To estimate the impact of using PGX-based decision support tools in depression clinical outcomes, including the Middle East and North Africa (MENA) region.

Methods

- **Inclusion criteria**: SRs and RCTs that assess the safety and efficacy of PGX testing in patients with depression.
- **Exclusion criteria:** Meta-analysis only, narrative reviews, RCTs included in eligible SRs, and animal studies.
- **Databases:** PubMed, EMBASE, SCOPUS
- **Search limits:** Human studies**,** from inception until June 30, 2020.
- **Study selection:** Titles and abstracts were screened, and based on full text review, eligible studies were selected for inclusion.
- **Data extraction:** Relevant data were extracted from individual studies using a standardized sheet.
- **Quality assessment:** Crowe Critical Appraisal Tool (CCAT).
- **Protocol:** Registered in the International Prospective Register of Systematic Reviews (PROSPERO) database with registration ID: CRD42020182936.

Results

- Results of SRs have provided weak evidence on the efficacy of PGX testing especially in patients with moderate-severe depression.
- There is a lack of evidence on safety outcomes reported in SRs.
- GeneSight was the most commonly studied test.
- RCTs with better methodologies showed clinical promise regarding efficacy.
- There is no available evidence regarding PGX testing in the MENA region.

Results Cont'd

Figure 1. Flow Diagram of Selection Process

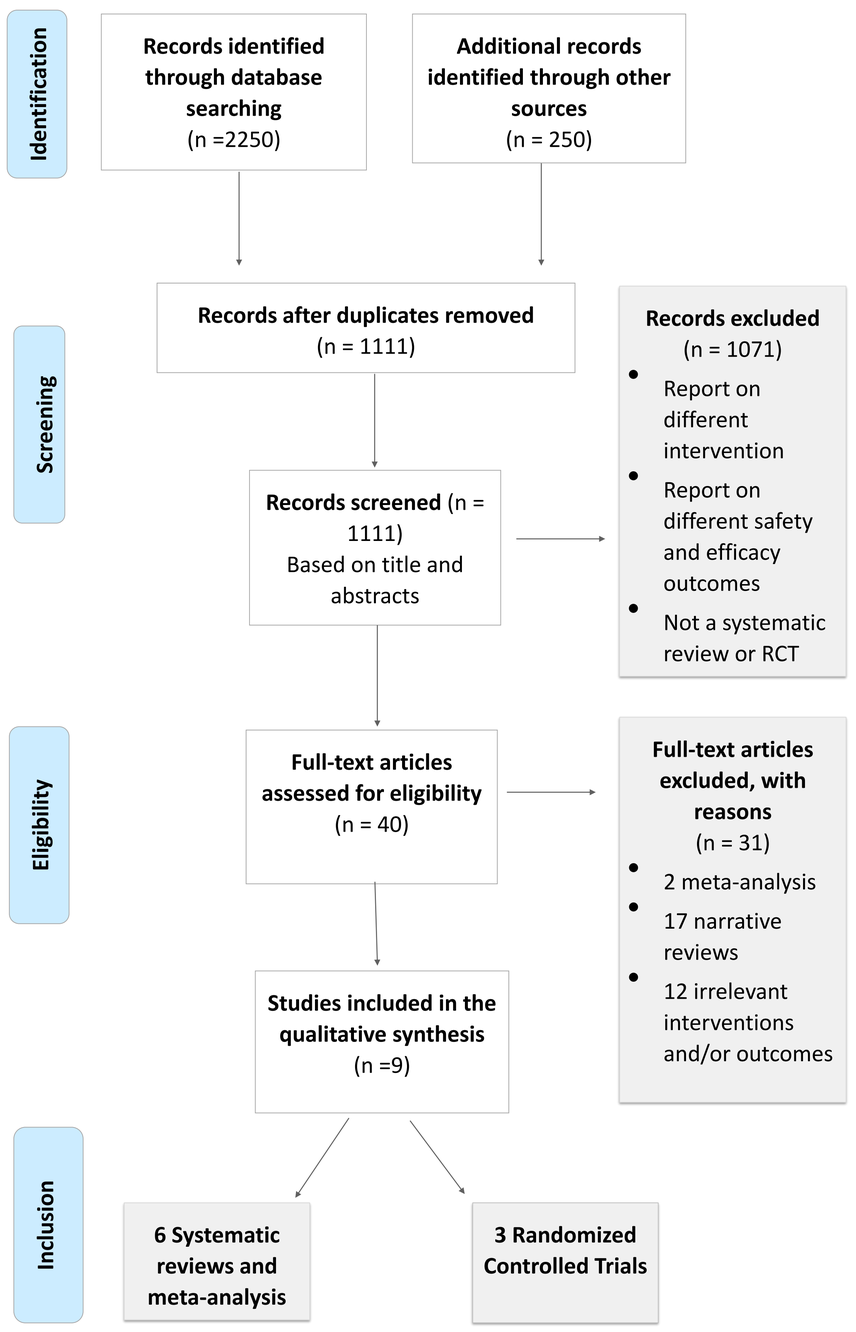


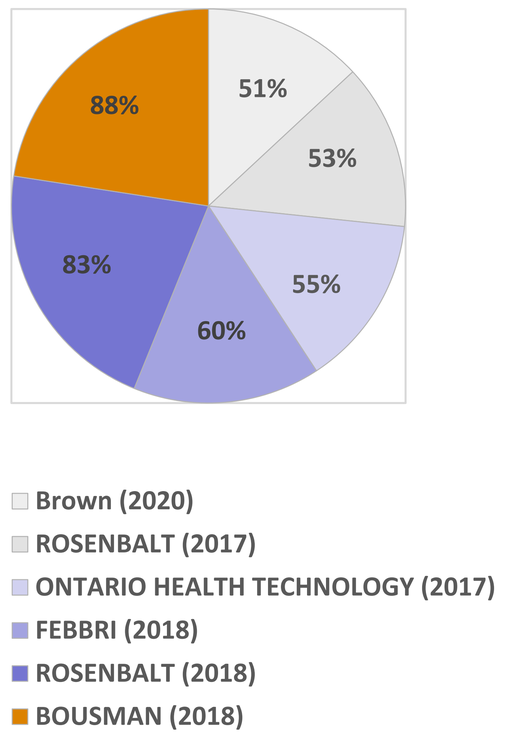
Table 1. Randomized Controlled Trials Findings

Study	Characteristics	Safety	Efficacy
Han et al.[1] (2018)	**Sample size:** 100 **Duration:** 8 weeks **Participants:** Koreans who failed previous anti-depressant **Tool:** Neuropharmagen	**Side effects Frequency** **Intensity** **Burden**	**Mean change in depression score** **Response** **Remission**
Greden et al.[2] (2019)	**Sample size**: 1398 **Duration:** 8 weeks **Participants:** Adults with uncontrolled depression **Tool:** GeneSight®	**Side effects n. n. of patients experienced side effects**	**Mean change in depression scores** **Response** **Remission**
Michael et al.[3] (October, 2019)	**Sample size:** 912 **Duration:** 8 weeks **Participants:** Adults with uncontrolled depression and gene drug-interaction **Tool:** GeneSight®	**N/A**	**Mean change in depression score** **Response rate** **Remission rate**

** Statistically significant for PGX guided treatment. All efficacy outcomes were measured using Hamilton Depression Rating Scale(HAM-D).

Results Cont'd

Figure 2. Quality Scores of Systematic Reviews



Poor (0-50%), moderate (51-74%), high (75-100%)

Conclusion

- This SR summarizes findings, provides updates on and assesses the quality of available SRs on the clinical utility of PGX testing in depression.
- Available SRs are of poor quality and have shown substantial variability on depression clinical outcomes when treatment is guided by PGX testing.
- Findings of this study have demonstrated that PGX-testing improves efficacy outcomes at 8 weeks.
- Further studies are warranted to assess PGX-testing impact on safety outcomes.

Future Studies

- Conducting pragmatic RCTs with large sample size for long duration to assess the impact of PGX testing on safety outcomes including adverse effects, tolerability, and suicide.
- Conducting pragmatic RCTs that compare between different PGX tests in patients with depression.
- Conducting studies that assesses the impact of PGX-testing in the MENA region.

References

1. Han C, Wang SM, Bahk WM, et al. A Pharmacogenomic-based Antidepressant Treatment for Patients with Major Depressive Disorder: Results from an 8-week, Randomized, Single-blinded Clinical Trial. *Clin Psychopharmacol Neurosci*. 2018;16(4):469-480. doi:10.9758/cpn.2018.16.4.469.
2. John F. Greden, at al. Impact of pharmacogenomics on clinical outcomes in major depressive disorder in the GUIDED trial: A large, patient- and rater-blinded, randomized, controlled study, Journal of Psychiatric Research, Volume 111, 2019, Pages 59-67, ISSN 0022-3956, https://doi.org/10.1016/j.jpsychires.2019.01.003.
3. Michael E. Thase, Sagar V. Parikh, et al. Impact of Pharmacogenomics on Clinical Outcomes for Patients Taking Medications with Gene-Drug Interactions in a Randomized Controlled Trial. J Clin Psychiatry. 2019 Oct 31; 80(6) Published online 2019 Oct 31. doi: 10.4088/JCP.19m12910.

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