



Is the secret to treating depression hidden in your genes?

CLINICAL QUESTION

Can genetic testing improve the efficacy and safety of antidepressants?

BOTTOM LINE

Pharmacogenomics testing to guide treatment in patients with depression might increase response and remission rates at 8 weeks by about 5% (example response rate 29% with pharmacogenomics versus 25% usual care), with no clear effects on tolerability. Studies have significant limitations. Cost (up to > \$2000) and genes tested vary widely.

EVIDENCE

- Results statistically significant unless indicated.
- Thirteen systematic reviews of randomized controlled trials (RCTs), past 5 years.¹⁻¹³ Focusing on the most comprehensive [15 RCTs, 51-1944 participants, different tests used, mostly cytochrome P450 metabolism (example: CYP2D6)]:
 - 6213 participants (often with treatment-resistant depression) randomized to pharmacogenomics-guided therapy or usual care.¹³ At ~8 weeks:
 - Response rate: 29% (pharmacogenomics-guided) versus 25% (usual care). Number Needed to Treat (NNT)=25.

- Remission rate: 20% (pharmacogenomics-guided) versus 15% (usual care), NNT=20.
 - Discontinuation rates, adverse events: no difference.
 - Limitations: RCTs partially/fully industry funded; different populations, outcome definitions and pharmacogenomic tests used; high dropout rates (example: 21% in the largest RCT); Clinicians usually not blinded and might have been influenced by the results.
- Largest RCT, publicly funded: 1944 veterans with moderate-severe depression, 59% with post-traumatic stress disorder. At 24 weeks:¹⁴
 - Response rates: 32% (pharmacogenomics-guided) versus 28% (usual care), NNT=25.
 - Remission rates: No difference.
 - Adverse events: Not reported.
 - More participants in the pharmacogenomics group prescribed an antidepressant in the first 30 days (75% versus 69%).
- Recent publicly funded RCT (655 participants), not included in systematic reviews: Similar results but also suggested a reduction in adverse drug reactions (insomnia 2% versus 6%; hypersomnia 7% versus 12%; abnormal liver function 2% versus 5%; loss of appetite 11% versus 15%).¹⁵

CONTEXT

- Different pharmacogenomics tests are available, most without RCT evidence.¹⁶
- Tests usually evaluate cytochrome P450's and some pharmacodynamic variants (examples: genes that encode a serotonin receptor or proteins involved in transporting).^{16,17} Results include guidance regarding expected effect on efficacy and safety.
- Canadian depression guidelines do not recommend routine use of pharmacogenomics testing.¹⁷
- 2021 evaluation by the Canadian Agency for Drugs and Technologies in Health: unclear effects.¹⁸
- Cost¹⁶ between \$200-2300.

REFERENCES

1. Wang X, Wang C, Zhang Y *et al.* BMC Psychiatry. 2023; 23(1) : 334.
2. Arnone D, Omar O, Arora T *et al.* Neurosci Biobehav Rev. 2023 Jan;144:104965.
3. Bunka M, Wong G, Kim D *et al.* Psychiatry Res. 2023 Mar;321:115102.
4. Skryabin V, Rozochkin I, Zastrozhin M *et al.* Pharmacogenomics J. 2023 May;23(2-3):45-49.
5. Cheng Y, Liu H, Yuan R *et al.* Gen Psychiatr. 2023 Dec 26;36(6):e101050.
6. Baum ML, Widge AS, Carpenter LL *et al.* American Psychiatric Association (APA) Workgroup on Biomarkers and Novel Treatments. Am J Psychiatry. 2024 Jul 1;181(7):591-607.
7. Brown LC, Stanton JD, Bharthi K *et al.* Clin Pharmacol Ther. 2022 Dec;112(6):1303-1317.

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8. European College of Neuropsychopharmacology (ECNP) Pharmacogenomics & Transcriptomics Network. *Eur Neuropsychopharmacol*. 2022 Jun;59:68-81.
9. Brown L, Vranjkovic O, Li J *et al*. *Pharmacogenomics*. 2020 Jun;21(8):559-569.
10. Aboelbaha S, Zolezzi M, Elewa H. *Neuropsychiatr Dis Treat*. 2021 Jul 21;17:2397-2419.
11. Ontario Health (Quality). Multi-gene Pharmacogenomic Testing That Includes Decision-Support Tools to Guide Medication Selection for Major Depression: A Health Technology Assessment. *Ont Health Technol Assess Ser*. 2021 Aug 12;21(13):1-214.
12. Tesfamicael KG, Zhao L, Fernández-Rodríguez R *et al*. *Front Psychiatry*. 2024 Jul 11;15:1276410.
13. Milosavljević F, Molden PE, Ingelman-Sundberg PM *et al*. *Eur Neuropsychopharmacol*. 2024 Apr;81:43-52.
14. Oslin DW, Lynch KG, Shih MC *et al*. *JAMA*. 2022; 328(2):151-161.
15. Xu L, Li L, Wang Q *et al*. *Affect Disord*. 2024 Aug 15;359:117-124.
16. Maruf AA, Fan M, Arnold PD *et al*. *Can J Psychiatry*. 2020 Aug;65(8):521-530.
17. Lam RW, Kennedy SH, Adams C *et al*. *Can J Psychiatry*. 2024 Sep;69(9):641-687.
18. Darvesh N, Horton J, Lê ML. Pharmacogenomic Testing in Depression: A 2021 Update: CADTH Health Technology Review [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2022 Jan.

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