How Pharmacogenomic Testing May Help Clinicians Treat Certain Psychiatric Conditions

Fact Sheet

Mental Health is a Major Crisis in the U.S.

- About one in six Americans develop major depressive disorder (MDD) in their lifetime.[1]
- An estimated 17.3 million U.S. adults had at least one major depressive episode in 2017.[2]
- About 60 percent of people who die by suicide have had a mood disorder like MDD.[3]
- Approximately 18% of U.S. adults (or 40 million) suffer from anxiety disorders each year, making them the most common mental illness in the U.S. Only 36.9% of those suffering from anxiety disorders receive treatment.[4]
- Adults with ADHD are approximately three times more likely to have MDD than those without the disorder.[5]
- In a large study, fewer than 40% of patients achieved remission with their first antidepressant medication.[6]

Trial-and-Error Treatment Is Frustrating

Healthcare providers evaluate different factors when selecting medication and dosage to treat depression, anxiety and ADHD, including family history, symptoms, drug/drug interactions, food/drug interactions, and environmental factors such as lifestyle. They may prescribe an antidepressant or other medication based on their own previous experience in prescribing the medication.

This medication may or may not work for the patient. According to a large study, less than 40% achieved remission with their first depression medication. Healthcare providers may prescribe a different medication; however, only 31% of people became symptom-free with their second medication trial. Among those who had a third medication trial, only 14% became symptom-free.[6]

During this process, a patient may experience side effects (e.g., weight gain, insomnia, headaches, joint and muscle pain, digestive issues and/or diminished sexual interest). A healthcare provider may wait four to eight weeks to assess response to each medication – leading to months or even years of trying different medications. This trial-and-error process can cause frustration, wasted time, wasted money, and wasted medication.

How Can Pharmacogenomics Help Mental Health Treatment?

Pharmacogenomics uses information about a person's genetic makeup to help inform healthcare providers' medication selection and dosage by looking at two types of genes:

- **Pharmacokinetic genes** may affect how quickly a patient's body breaks down (metabolizes) medicine. Variation in these genes may cause a patient to break down some medications more slowly or more quickly than normal.
- **Pharmacodynamic genes** can provide information on how the medication is expected to work on the body. Variations in these genes may impact a person's likelihood of response or risk of side effects with certain medications.

Pharmacogenomic tests, like the GeneSight Psychotropic test, provide genetic information that is unique to each patient. Research indicates that up to 42% of variance in therapy response for major depressive disorder can be explained by genetic variation.[7]

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[1] Kessler RC, et al. "Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication." *AMA Archives of General Psychiatry*. 2005;62(6):593–602. doi:10.1001/archpsyc.62.6.593
[2] The National Institute of Mental Health Information Resource Center
[3] U.S. Department of Health & Human Services
[4] Anxiety and Depression Association of America
[5] Kessler, et al, Am J Psychiatry. 2006 Apr; 163(4): 716–723
[6] Rush, et al, *The American Journal of Psychiatry*. 2006 Nov; 163(11):1905-17
[7] Tansey, et al, *Biological Psychiatry*. 2013 Apr; 73(7):679-82

The GeneSight Psychotropic Test Study Results

The clinical validity, clinical utility and economic utility of the GeneSight Psychotropic test have been evaluated in eight clinical studies published in peer-reviewed journals. In fact, it's the only neuropsychiatric pharmacogenomic test backed by such extensive research.

PRIME Care Study

Major Depressive Disorder (MDD) remission rates were significantly improved when clinicians had access to GeneSight Psychotropic test results, according to a nationwide study of nearly 2,000 veterans conducted by the U.S. Department of Veterans Affairs (VA).

The PRIME Care (Precision Medicine in Mental Health Care) study is the largest pharmacogenomic (PGx) randomized controlled trial (RCT) ever conducted in mental health. Results of the study were published in the July 2022 issue of the *Journal of the American Medical Association (JAMA)*. The VA independently conducted and funded the study. Myriad Genetics provided the GeneSight tests for the study.

The PRIME Care Study showed:

- Over 24 weeks, the pharmacogenomic guided group had a 28% greater likelihood (odds ratio = 1.28, 95% confidence interval 1.05-1.57, p=0.02) of achieving remission from MDD symptoms (defined as a score of five or less on the PHQ-9 depression symptom questionnaire). There were no identified harms from receiving GeneSight testing in the study.
- Patients in the usual care group were approximately two times more likely (odds ratio = 2.08, 95% confidence interval 1.52-2.84, p=0.005) to be prescribed medications with substantial predicted gene-drug interactions compared to the pharmacogenomic guided group in the first 30 days after randomization.

GUIDED Study

The GUIDED Study was published in the *Journal of Psychiatric Research.* The 24-week landmark study included 1,167 patients with moderate-to-severe depression who had failed at least one psychotropic medication included on the GeneSight Psychotropic report.

The GUIDED Study showed:

- While there was more symptom improvement in the GeneSight group compared to the treatment as usual group at week 8, this difference in the primary endpoint trended toward but did not achieve statistical significance.[8] Symptom improvement is any change in the HAM-D17 score[9] and is based on the group average.
- There was a significant difference in the secondary endpoint of response. Patients who received the GeneSight Psychotropic test experienced a 30% relative increase in response rates at week 8 compared to treatment as usual.[8] Response is defined as a greater than or equal to 50% decrease in HAM-D17 score (i.e., 22 to 11).
- There was also a significant difference in the secondary endpoint of remission. Patients who received the GeneSight Psychotropic test experienced a 50% relative improvement in remission rates at week 8 compared to treatment as usual.[8] Remission is defined as having a score of 7 or below on the HAM-D17 depression rating scale.
- When depressed patients on medications with significant gene-drug interactions were moved to medications with no or moderate gene-drug interactions (as identified by the GeneSight test) by week 8, there was a 59% relative improvement in symptoms, a 71% relative improvement in response rates, and a 153% relative improvement in remission rates versus patients who remained on medications with significant gene-drug interactions.[8] These results are from a post-hoc analysis of 213 patients who entered the study on medications with significant gene-drug interactions.

[8] Greden, et al, *Journal of Psychiatric Research*, Volume 111, April 2019, Pages 59-67

[9] Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry* 1960; 23:56–62

Other clinical studies:

- The Medco Study showed that patients who received GeneSight testing saved, on average, $1,035.60 in total annual medication costs compared to patients who received treatment as usual.[10]
    - Further, patients who received the GeneSight test had a reduction in polypharmacy. One in five patients in the GeneSight group were on fewer medications by the end of the study (significantly greater than the treatment as usual group, $p < 0.0001$).[10]
- The Union Health Service Economic Study showed that when patients were taking medications with significant gene-drug interactions, their total healthcare utilization costs were $5,188 higher per patient per year than patients on medications with no or moderate gene-drug interactions.[11]

Read more at https://genesight.com/for-clinicians/clinical-studies/.

Important Note:
The GeneSight test must be ordered by and used only in consultation with a healthcare provider who can prescribe medications. As with all genetic tests, the GeneSight test results have limitations and do not constitute medical advice. The test results are one element of a clinician's decision-making process, which must be tailored to the specific circumstances of each patient. Do not make any changes to your current medications or dosing without consulting your doctor. Not all patients who receive the GeneSight test will experience improved outcomes and/or cost savings.

[10] Winner, et al, *Current Medical Research and Opinion*. 2015;31(9):1633-43

[11] Winner, et al, *Translational Psychiatry*. 2013 Mar; 3(3): e242