The GeneSight® Test

A Fact Sheet for Healthcare Providers

The GeneSight Psychotropic test from Myriad Genetics, Inc. (NASDAQ: MYGN), a leader in genetic testing and precision medicine, is the category-leading neuropsychiatric pharmacogenomic test, and has been ordered by tens of thousands of clinicians for more than two million patients.

The GeneSight test analyzes clinically important genetic variations in a patient's DNA and provides information about gene-drug interactions that may impact how patients metabolize or respond to certain medications commonly used to treat depression and other psychiatric conditions.

Research indicates that up to 42% of variance in therapy response for major depressive disorder can be explained by genetic variation.[1]

The GeneSight Test

- The GeneSight Psychotropic test identifies an individual's genetic variations that may impact how they metabolize or respond to certain medications commonly prescribed to treat depression, anxiety, ADHD and other psychiatric conditions. The GeneSight report:
    - Shows whether there are gene-drug interactions for more than 60 FDA-approved medications including antidepressants, anxiolytics, hypnotics, antipsychotics, stimulants and non-stimulants; to see a list of medications, visit genesight.com/product
    - Includes information on how a patient's smoking status may impact their body's metabolism of certain medications
    - Details the individual's genotypes and phenotypes for five pharmacodynamic genes and nine pharmacokinetic genes. COMT has been included for informational purposes
    - Shows which pharmacokinetic pathways each medication on the report uses and whether that pathway is compromised within the gene-drug interaction chart
- The GeneSight MTHFR test analyzes whether an individual has variation in MTHFR, which may limit their ability to create l-methylfolate

Challenges in Trial-and-Error Prescribing

Trial-and-error prescribing can result in frustration – as well as wasted time, money, and medication – for clinicians and patients:

- Less than 40% of patients achieve remission with initial drug treatment. With each medication trial, the chance of remission decreases, while treatment intolerance increases, according to a large study[2]
- 30% of patients discontinue treatment due to intolerable side effects
- Up to 70% of patients receiving prescriptions for antidepressants are non-adherent – adverse side effects is the most common reason

From Sample Collection to Results in Days

The process is simple:

- Orders are placed on MyGeneSight.com (our secure ordering and report portal)
- Buccal swabs are used to collect a sample of a patient's DNA
- You or the patient sends the sample to our CLIA- and CAP-certified lab in a prepaid FedEx envelope
- About two days after we receive the sample, you can access a patient's personalized report on MyGeneSight.com

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[1] Tansey, et al, *Biological Psychiatry*. 2013 Apr; 73(7):679-82

[2] Rush, et al, *The American Journal of Psychiatry*. 2006 Nov; 163(11):1905-17

GeneSight At Home

With GeneSight at Home, no in-person visit is needed for sample collection. Patients will be informed throughout the process via GeneSight at Home Patient Engagement. The process is simple:
1. Enter a new order at myGeneSight.com and select Yes to ship a kit to your patient.
2. You authorize the order
3. The kit is sent to the patient.
4. The patient collects and returns their samples to the GeneSight lab.
5. You view your patient's results at myGeneSight.com.

GeneSight at Home is efficient – ordering the test is simple, and results are available quickly. With GeneSight at Home, nothing changes with how samples are processed, just how the samples are collected.

Backed by Multiple Clinical Studies

The clinical validity, clinical utility and economic utility of the GeneSight Psychotropic test have been evaluated in more peer-reviewed publications than any other test in its category.

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 results of 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.[3] Symptom improvement is any change in the HAM-D17 score[4] 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.[3] Response is defined as a greater than or equal to 50% decrease in HAM-D17 score (i.e., 22 to 11).

[3] Greden, et al, *Journal of Psychiatric Research*, Volume 111, April 2019, Pages 59-67
[4] Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry* 1960; 23:56–62

- There was 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.[3] 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.[3] These results are from a post-hoc analysis of 213 patients who entered the study on medications with significant gene-drug interactions.

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, $p < 0.0001$).[5]
- 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.[6]

To read more about our clinical studies, please visit https://genesight.com/for-clinicians/clinical-studies/.

Scientific Advisory Board

- **Boadie Dunlop,** MD, MSCR, director and associate professor, Mood and Anxiety Disorders Program, Emory University
- **James L. Kennedy,** MD, FRCP(C), FRSC, head, Tanenbaum Centre for Pharmacogenetics, Centre for Addiction and Mental Health (CAMH)
- **Lawrence Lesko**, PhD, FCP, founding director, Center for Pharmacometrics and Systems Pharmacology, University of Florida
- **Erika L. Nurmi,** MD, PhD, medical director, Obsessive-Compulsive Disorder Intensive Outpatient Program, and associate director, Psychiatry Residency Track, University of California – Los Angeles
- **Andrew Nierenberg**, MD, endowed chair in psychiatry, Massachusetts General Hospital
- **Cathryn Lewis**, PhD, head of department, Social, Genetic and Developmental Psychiatry Centre, King's College, London

Resources Available

Our team of PharmDs, PhDs, and MDs is available to answer any questions healthcare providers may have and can be reached at medinfo@myriad.com, or phone 855.891.9415. To order the GeneSight test, contact our sales team through genesight.com/take-the-next-step.

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

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