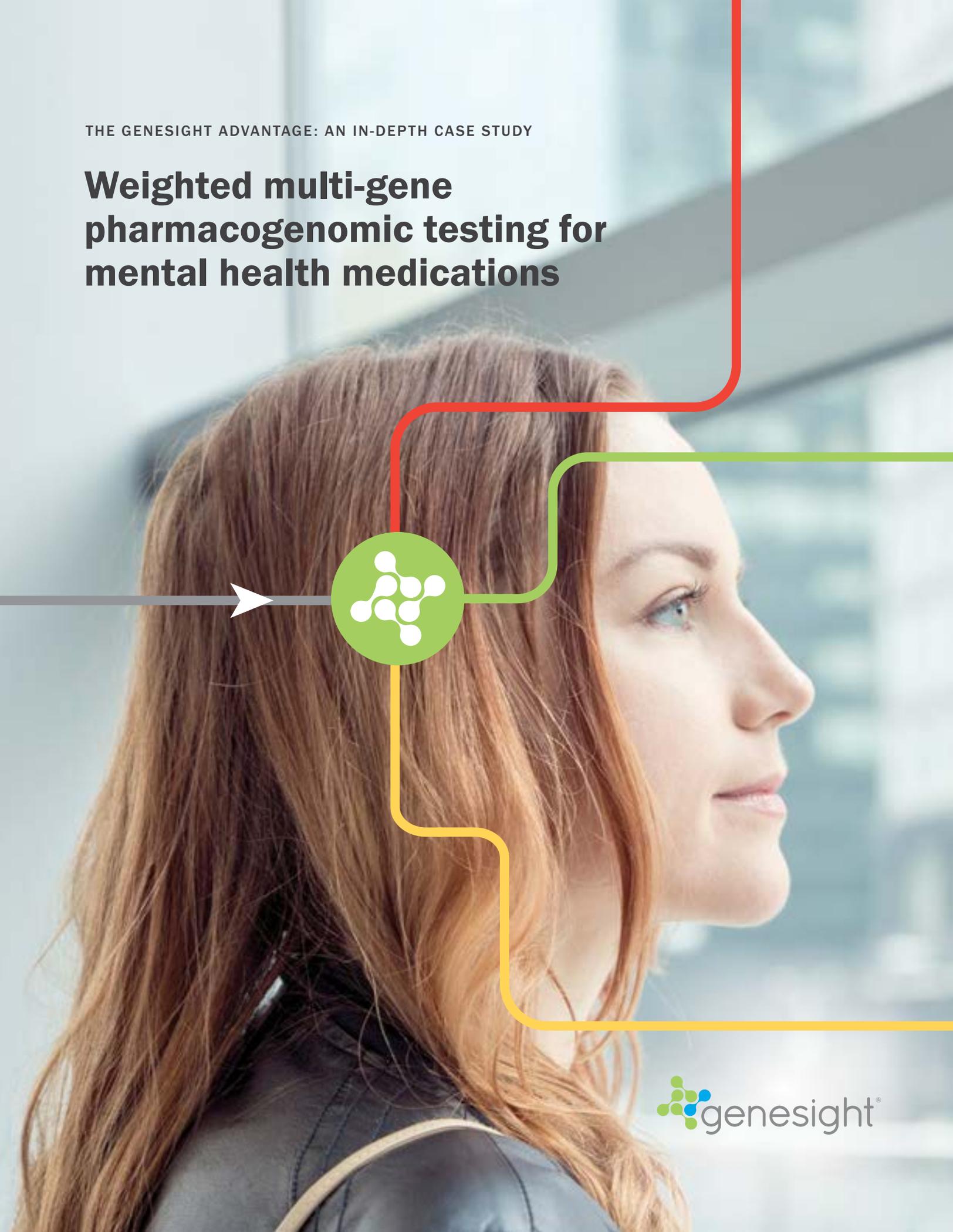


THE GENESIGHT ADVANTAGE: AN IN-DEPTH CASE STUDY

# Weighted multi-gene pharmacogenomic testing for mental health medications



# What is weighted multi-gene pharmacogenomic testing?

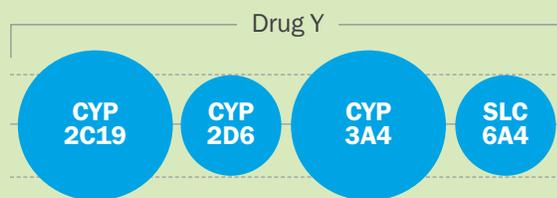
## The approach behind more actionable insights with the GeneSight® test

The goal of pharmacogenomic testing is to better understand how clinically important genetic variations may impact the ways a patient metabolizes or responds to certain medications. Given that most medications are processed through multiple genetic pathways, a **weighted multi-gene approach**, which measures different genomic variants and

evaluates the holistic impact, is critical to obtaining the most actionable insights. The GeneSight test uses a weighted multi-gene approach to provide comprehensive information about how an individual's genetic variation may impact treatment outcomes with certain medications.

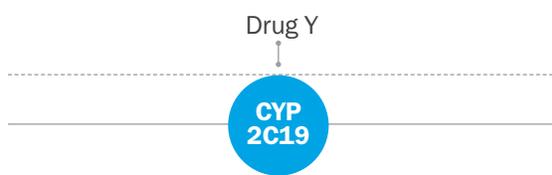
### The GeneSight test:

The **weighted multi-gene approach** measures multiple genomic variants for each individual and evaluates the holistic impact.

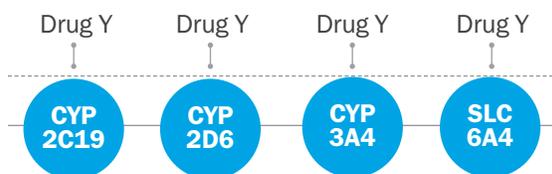


### Other pharmacogenomic approaches:

**Single-gene tests** evaluate only one gene and associate that single result with medication metabolism or mechanism of action.



**Multi-gene tests** evaluate multiple genes independently and provide an output for each gene-drug pair separately.



# The GeneSight advantage: Genetic insights to help improve outcomes for your mental health patients

Only the GeneSight test is backed by  
7 peer-reviewed studies that support  
its effectiveness

Multiple studies have compared the ability of the GeneSight weighted multi-gene approach to predict medication blood levels and patient outcomes compared to single-gene analysis.

Based on their findings, the GeneSight test was shown to:

- Better predict medication blood levels<sup>1-3</sup>
- Better predict depressive clinical outcomes<sup>2</sup>
- Identify more patients with actionable gene-drug interactions for sertraline and citalopram indicative of decreased metabolism<sup>1,3</sup>



IN AN ANALYSIS OF OVER  
1 MILLION PATIENTS

**More than 3x as many patients** were identified as having actionable information related to a significant gene-drug interaction with reduced metabolism of citalopram when using the GeneSight test compared to CYP2C19 single-gene testing and guidance.



Patient case study:

# Major depressive disorder

## Patient Information

**Age:** 29  
**Race:** White  
**Sex:** Female  
**Past medical history:** N/A  
**Social history:** Recreational alcohol use  
**Family history:** Maternal uncle: bipolar, schizophrenia  
Mom, dad, maternal uncle: alcohol and drug abuse  
**Smoking status:** Non-smoker



## Clinical Presentation

**Primary target psychiatric symptoms:** Depressed mood, fatigue, anxiety, poor sleep, irritability, anhedonia, inconsistent appetite, low libido, hopelessness

**Primary psychiatric diagnosis:** Major depressive disorder

**Other psychiatric diagnoses:** Generalized anxiety, borderline personality disorder

## Treatment History

### Previous medication trials:

sertraline (Zoloft®)  
paroxetine (Paxil®)  
bupropion (Wellbutrin®)  
venlafaxine (Effexor®)  
escitalopram (Lexapro®)  
oxcarbazepine (Trileptal®)  
duloxetine (Cymbalta®)

### Medication list at the time of pharmacogenomic testing:

escitalopram (Lexapro®) 15 mg (10 mg + 5 mg) daily  
propranolol (Inderal®) 20 mg daily

### Treatment changes being considered prior to pharmacogenomic testing:

citalopram (Celexa®)

# Comparing testing methods' recommended use of citalopram based on the case study patient's genetic results

## Gene                      Phenotype                      Recommended use of citalopram

**Single-gene testing:** Single treatment recommendation based on one gene

CYP2C19                      Intermediate Metabolizer                      → Initiate therapy at recommended starting dose

**Multi-gene testing:** Conflicting treatment recommendations based on multiple genes\*

CYP2C19                      Intermediate Metabolizer                      → Consider using the recommended starting dose

CYP2D6                      Poor Metabolizer                      → Consider initiating therapy at a lower dose

CYP3A4                      Extensive (Normal) Metabolizer                      → Consider using the recommended starting dose

SLC6A4                      Normal Response                      → The patient is predicted to have a normal response to selective serotonin reuptake inhibitors



### Single treatment recommendation based on the weighted impact of multiple genes

CYP2C19                      Intermediate Metabolizer

CYP2D6                      Poor Metabolizer

CYP3A4                      Extensive (Normal) Metabolizer

SLC6A4                      Normal Response

→ Serum levels may be too high, lower doses may be required. Use of this drug may increase risk of side effects

\*Multi-gene testing may not always produce conflicting treatment recommendations.

# Patient case study: Selected results from the GeneSight® test

**GeneSight® Psychotropic**  
Pharmacogenomic Test

**Patient, Sample**  
Date of Birth: MM/DD/YYYY  
Clinician: Sample Clinician

Order Number: 000000  
Report Date: MM/DD/YYYY  
Reference: 000000

Questions about report interpretation?  
Contact our Medical Information team:  
855.891.9415 | [medinfo@genesight.com](mailto:medinfo@genesight.com)

## Antidepressants

**Non-Smokers** Smoking is defined as the daily inhalation of burning plant material (cigarettes, marijuana), and **excludes** vaping and e-cigarettes. This is used to determine medication results.

Use as Directed	Moderate Gene-drug Interaction	Significant Gene-drug Interaction
desvenlafaxine (Pristiq®)	selegiline (Eamasm®) 1	citalopram (Celexa®) 1,6
levomilnacipran (Fetzima®)	sertraline (Zoloft®) 1	escitalopram (Lexapro®) 1,6
	trazodone (Desyre®) 1	fluoxetine (Prozac®) 1,6
	vilazodone (Viibryd®) 1	mirtazapine (Remeron®) 1,6
	bupropion (Wellbutrin®) 1,6	venlafaxine (Effexor®) 1,6
		amitriptyline (Elavil®) 1,6,8
		clomipramine (Anafranil®) 1,6,8
		desipramine (Norpramin®) 1,6,8
		doxepin (Sinequan®) 1,6,8
		duloxetine (Cymbalta®) 1,6,8
		fluvoxamine (Luvox®) 1,6,8
		imipramine (Tofranil®) 1,6,8
		nortriptyline (Pamelor®) 1,6,8
		paroxetine (Paxil®) 1,6,8
		vortioxetine (Trintellix®) 1,6,8



### Clinical Considerations

- 1: Serum level may be too high, lower doses may be required.
- 6: Use of this drug may increase risk of side effects.
- 8: FDA label identifies a potential gene-drug interaction for this medication.

Treatment recommendations based on the weighted multi-gene approach of the GeneSight test.

**GeneSight® Psychotropic**  
Pharmacogenomic Test

**Patient, Sample**  
Date of Birth: MM/DD/YYYY  
Clinician: Sample Clinician

Order Number: 000000  
Report Date: MM/DD/YYYY  
Reference: 000000

Questions about report interpretation?  
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## Anxiolytics and Hypnotics

**Non-Smokers** Smoking is defined as the daily inhalation of burning plant material (cigarettes, marijuana), and **excludes** vaping and e-cigarettes. This is used to determine medication results.

Use as Directed	Moderate Gene-drug Interaction	Significant Gene-drug Interaction
alprazolam (Xanax®)		propranolol (Inderal®) 1,6,8
bupirone (BuSpar®)		
chlordiazepoxide (Librium®)		
clonazepam (Klonopin®)		
clorazepate (Tranxene®)		
diazepam (Valium®)		
eszopiclone (Lunesta®)		
lemborexant (Dayvigo®)		
lorazepam (ativan®)		
oxazepam (Serax®)		
suvorexant (Belsomra®)		
temazepam (Restoril®)		
zolpidem (Ambien®)		

**Clinical Considerations**

- 1: Serum level may be too high, lower doses may be required.
- 6: Use of this drug may increase risk of side effects.
- 8: FDA label identifies a potential gene-drug interaction for this medication.

Patient case study:

## Treatment decisions and outcomes

1

Prior to pharmacogenetic testing, the patient's clinician had been considering citalopram as the next treatment option for the patient's depression.

2

The patient's GeneSight test results indicated that the patient may have an elevated serum level of citalopram and lower doses may be required, and citalopram may increase the patient's risk of side effects. Therefore, the clinician decided to prescribe an alternative antidepressant.

3

After starting the new treatment plan, the patient participated in more social activities, began looking for new employment, and expressed interest in returning to school.

**Have questions about the GeneSight weighted multi-gene approach?** Get in touch with a member of the medical affairs team. Scan the QR code or visit [genesight.com/for-clinicians/medical-affairs](https://genesight.com/for-clinicians/medical-affairs) today.



**References:** **1.** Shelton RC, Parikh SV, Law RA, et al. Combinatorial Pharmacogenomic Algorithm is Predictive of Citalopram and Escitalopram Metabolism in Patients with Major Depressive Disorder. *Psychiatry Research*. 2020;290:113017. doi:<https://doi.org/10.1016/j.psychres.2020.113017>. **2.** Rothschild AJ, Parikh SV, Hain D, et al. Clinical validation of combinatorial pharmacogenomic testing and single-gene guidelines in predicting psychotropic medication blood levels and clinical outcomes in patients with depression. *Psychiatry Research*. 2021;296:113649. doi:<https://doi.org/10.1016/j.psychres.2020.113649>. **3.** Parikh SV, Law RA, Hain DT, et al. Combinatorial pharmacogenomic algorithm is predictive of sertraline metabolism in patients with major depressive disorder. *Psychiatry Research*. 2022;308:114354. doi:<https://doi.org/10.1016/j.psychres.2021.114354>.

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