Why doesn't the GeneSight® test analyze certain genetic variants?

Why does the GeneSight test only test for pharmacogenomic markers and not diagnostic markers?

While a great deal of groundbreaking research is being conducted on the genetic etiology of psychiatric illnesses, there are currently no genetic markers identified that are able to accurately diagnose any particular psychiatric illness. Psychiatric disease is multifactorial, and genes that have been identified often contribute only a small amount to the overall disease risk.[1,2] At this time, testing for these genetic markers is unlikely to provide clinically meaningful information.[3]

What do we mean by "clinically meaningful?"

Genes that are added to the GeneSight test must provide clinically meaningful information to a healthcare provider. The information provided by testing for a particular genetic variant has the potential to alter the treatment course for the patient. For example, a gene that predicts differential response between two commonly prescribed classes of medications that are both indicated for a particular condition (e.g. SSRIs vs. SNRIs) may be considered clinically meaningful. However, a genetic variant with inconsistent or conflicting data, or that has a low effect size (e.g. a 2 point drop in systolic blood pressure following antihypertensive treatment) is unlikely to be clinically meaningful.

By what criteria do we judge whether a genetic variant is clinically meaningful?

Any gene that is added to a GeneSight panel undergoes a rigorous review of published literature surrounding its impact on medication outcomes.

1. The gene must have a variant that appears at a high enough frequency to be clinically meaningful. Some alleles appear at a lower frequency than the technical error rate in a laboratory (e.g. below 0.01%). In these cases, it is difficult to determine whether a positive result is a true positive or due to laboratory error.

2. A well-designed study must be conducted that shows that the polymorphism has a statistically significant impact on outcomes with a particular medication or medication class.

3. A well-designed study must be conducted that shows that the polymorphism has a significant clinical impact on outcomes with a particular medication or medication class. In other words, the information gained from the knowledge of the patient's genotype should provide additive value to the healthcare provider's decision making process.

4. The variant must show consistent replication of the findings in multiple independent patient populations. In other words, a preponderance of studies must demonstrate a statistically and clinically significant impact. Variants with inconsistent or conflicting data require more study and will not be added to a GeneSight panel until its clinical utility has been demonstrated.

A particular variant must meet all four criteria to be added to a GeneSight panel. The GeneSight test only tests for genes that have been demonstrated to be clinically meaningful in multiple independent studies. The GeneSight test has been demonstrated to help improve clinical outcomes in multiple peer-reviewed publications.[4–8]

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