Introduction

Genetic testing is done to see if there are changes in chromosomes, genes, or the proteins made by genes. There are many reasons to do a genetic test, such as to confirm or rule out a genetic condition, to determine the chance of developing or passing on a genetic disorder, or to see if a person has an increased risk of having health problems. When it comes to mental health, genetic tests generally try to determine if a person is at risk for a condition such as schizophrenia. Other mental health genetic tests try to find out a person’s response to a certain drug or which dose to use for medications that might treat a mental health condition. To date, the medical studies on genetic testing for mental health or for managing drug dosing do not show that information from the test will change treatment or lead to better outcomes.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
Testing | Investigational
--- | ---
Genetic testing for mental health conditions | Genetic testing for variants associated with mental health disorders is considered investigational in all situations, including but not limited to the following:
- To confirm a diagnosis of a mental health disorder in an affected individual.
- To predict future risk of a mental health disorder in an asymptomatic individual.
- To choose a medication or decide on its dose in order to treat mental health disorders in an affected individual.

Genetic panels for selecting medications or doses of medication | Genetic testing panels, including but not limited to the following tests, are considered investigational for selecting medications or doses of medications for the treatment of psychiatric or mental health symptoms or disorders:
- Ally Diagnostics Genetic Testing Panel
- Alpha Genomics Psychiatry/ADHD Panel
- Frontier PGx Pharmacogenomic Testing
- Genecept Assay
- GeneSight Psychotropic Panel
- Genetic Technological Innovations Pharmacogenetic Testing
- Luminex xTAG CYP2C19 assay
- Luminex xTAG CYP2D6 assay
- Mental Health Insight DNA
- Millennium Pharmacogenetic Testing
- Molecular Testing Labs Psychotropic Medication Panel
- PersonaGene
- PGXL Multi-Drug Panel
- PharmaRisk Basic
- PharmaRisk Psychiatric Panel
- Physicians Choice Laboratory Services (PCLS) Pharmacogenetic Testing
- Primex Expanded Pharmacogenomics Panel
- Progenity Informed PGx Pharmacogenetic Testing
- Proove Drug Metabolism Panel
- Proove Opioid Risk assay
- STA2R SureGene
- YouScript Panel
### Coding

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<tr>
<th>Code</th>
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<tr>
<td><strong>CPT</strong></td>
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<tr>
<td>0015U</td>
<td>Drug metabolism (adverse drug reactions), DNA, 22 drug metabolism and transporter genes, real-time PCR, blood or buccal swab, genotype and metabolizer status for therapeutic decision support (code terminated 1/1/18)</td>
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<tr>
<td>81479</td>
<td>Unlisted molecular pathology procedure</td>
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### Related Information

**Genes Relevant to Mental Health Disorders**

Mental disorders encompass a wide range of conditions: the DSM-5 includes more than 300 different disorders. However, currently available genetic testing for mental health disorders is primarily related to several clinical situations:
1. Risk stratifying patients for one of several mental health conditions, including schizophrenia and related psychotic disorders, bipolar and related disorders, depressive disorders, obsessive-compulsive and related disorders, and substance-related and addictive disorders.

2. Predicting patients' response to, dose requirement for, or adverse effects from one of several medications (or classes of medications) used to treat mental health conditions, including: typical and atypical antipsychotic agents, serotonin and serotonin/norepinephrine reuptake inhibitors (SSRIs), and medications used to treat addiction, such as disulfiram.

Panels of genetic tests have been developed and have been proposed for use in the management of mental health disorders.

**Commercially Available Genetic Tests**

Several test labs market either panels of tests or individual tests designed as being relevant for mental health disorders. The following list includes many examples, but not necessarily all, of the available tests.

**The Genecept™ Assay** (Genomind, LLC, Chalfont, PA) is a genetic panel test that includes a range of genetic mutations and/or polymorphisms that have been associated with psychiatric disorders and/or response to psychotropic medication. The test consists of a group of individual genes, and the results are reported separately for each gene. There is no summary score or aggregate results derived from this test. The intent of the test is as a decision aid for treatment interventions, particularly in the choice and dosing of medications. However, guidance on specific actions that should be taken following specific results of the test is vague. Interpretation of the results and any management changes as a result of the test are left to the judgment of the treating clinician.

**The STA2R** (SureGene Test for Antipsychotic and Antidepressant Response, SureGene, LLC, Louisville, KY) is another genetic panel that provides information about medication response, adverse event likelihood, and drug metabolism. According to the manufacturer’s website, the test is recommended for initial medication selection, for patients who have poor efficacy, tolerability, or satisfaction with existing medications, and in cases of severe treatment failure. Specific mutations included in the panel were not easily identified from the manufacturer’s website.

**GeneSight® Psychotropic** (Assurex Health, Mason, OH) is a genetic panel that provides information about genes that may affect a patient’s response to antidepressant and antipsychotic pharmacotherapy. According to the manufacturer’s website, following testing the treating provider receives a report with the most common medications for the patient’s
diagnosed condition categorized by cautionary level, along with a report of the patient’s genetic variants. Details are not provided about the algorithm used by the manufacturer to generate risk levels.

**The Proove Opioid Risk Panel** (Proove Biosciences, Irvine, CA) is a panel to evaluate genes involved in the development of substance abuse or dependence and in response to medical therapy for substance abuse or dependence.

**Pathway Genomics** (San Diego, CA) offers the Mental Health DNA Insight™ panel, which is a single nucleotide polymorphism-based array test which evaluates a number of genes associated with the metabolism and efficacy of psychiatric medications.

**AltheaDx** (San Diego, CA) offers a number of IDgenetix-branded tests, which include several panels focusing on polymorphisms that affect medication pharmacokinetics for a variety of disorders, including psychiatric disorders. Specific mutations included in the panel were not easily identified from the manufacturer’s website.

**The Ally Diagnostics Genetic Testing Panel** (Ally Clinical Diagnostics, Farmers Branch, Texas) is a panel to evaluate genes that may affect a patient’s response to medications for the treatment of psychiatric or mental health symptoms or disorders. The panel includes three CYP450 tests, vitamin K epoxide reductase, and a non-specific molecular pathology procedure.

**Molecular Testing Labs Psychotropic Medication Panel** (Molecular Testing Labs, Vancouver, WA) offers a genetic testing panel which their website describes as identifying “five different categories of patients by the way they metabolize specific drugs”. The only specific gene mentioned is CYP2D6.

**The PharmaRisk Basic Panel** is described by OptimumMeds as a test that “analyzes the genes that metabolize many commonly prescribed medications used in all clinical practices including: internal medicine, cardiology, geriatrics, psychiatry and chronic pain management.” The test analyzes 55 genetic markers across 4 genes – CYP2C19, CYP2C9, CYP2D6 and VKORC1.

**The PharmaRisk Psychiatric Panel** includes CYP2D6, OPRM1, CYP2C9, COMT, DRD2, CYP2B6, CYP2C19, CYP1A2, UGT2B15.

**The PGXL Multi-Drug Panel** includes CYP2D6, CYP2C9, CYP2C190, CYP1A2, CYP3A4, CYP3A5, SLC6A4, OPRM1, VKORC1, SLCO1B1, SULT24A1, Factor II, Factor V, MTHFR and COM.

**The Alpha Genomix Psychiatry/ADHD Panel** includes CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A, ADRA2A, and COMT.

**Genetic Technological Innovations** (DBA Vantari Genetics) offers genetic testing for drug metabolism, preconception and pregnancy, inherited conditions and inherited cancer. Their pharmacogenetic panel for drug metabolism includes CYP2C19, CYP2D6, MTHFR and CYP3A4.
The PersonaGene panel uses next generation sequencing to test for metabolism of common drugs for pain management, cardiology, psychiatry and urology. Although this large panel encompassing four specialties, all of the mutations tested are within the CYP450 family.

Luminex offers a genotyping assay which can aid clinicians in determining therapeutic strategy for drugs metabolized by cytochrome P450.

There are three Progenity Informed PGx genetic testing panels – ADHD (4 mutations), Depression (7 mutations) and Psychotropic (7 mutations) - and each panel tests a variety of CYP450 genes, MTHFR, etc. In addition to the available panel tests, several labs offer genetic testing for individual genes, including MTFHR, CYP450 genes, and SULT4A1.

Evidence Review

Description

Several commercially available testing panels include genes related to neurotransmitter function and pharmacokinetics of psychiatric drugs. They are intended to be an aid in clinical decision making regarding interventions for psychiatric conditions.

Background

Psychiatric disorders cover a wide range of clinical phenotypes and are generally classified by symptomatology in systems such as the classification outlined in the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). In addition to counseling and other forms of behavioral treatment, treatment commonly involves one or more psychotropic medications that are aimed at alleviating symptoms of the disorder. Although there are a wide variety of effective medications, treatment of psychiatric disease is characterized by relatively high rates of inadequate response. This often necessitates numerous trials of individual agents and combinations of medications in order to achieve optimal response.

Knowledge of the physiologic and genetic underpinnings of psychiatric disorders is advancing rapidly and may substantially alter the way in which these disorders are classified and treated. Genetic testing could potentially be used in several ways including stratifying patients’ risks of developing a particular disorder, aiding diagnosis, targeting medication therapy, and optimally
dosing medication. Better understanding of these factors may lead to an improved ability to target medications to the specific underlying abnormalities, with potential improvement in the efficiency and efficacy of treatment.

Summary of Evidence

Panels of multiple genetic tests have been developed to aid in the diagnosis and treatment of mental health disorders. Genes included in the panels have shown some association with psychiatric disorders or with the pharmacokinetics of psychotropic medications.

Evidence on the clinical validity of genetic testing for mental health disorders consists primarily of genome-wide association studies (GWAS) that correlate specific genetic polymorphisms with clinical factors, and case-control studies that examine the odds ratio for genetic variants in individuals with a clinical disorder compared with individuals without the disorder. In general, cross-sectional and case-control studies cannot be used to generate diagnostic characteristics such as sensitivity and specificity or clinically relevant risk prediction.

Studies suggest that there may be a number of genetic variants associated with increased risk of mental health disorders and/or response to specific treatment, although estimates of the magnitude of the increased risk and findings of significance are variable across studies. For the individual tests, results from GWAS and case control studies are insufficient to determine clinical utility. To determine clinical utility, evidence is needed that testing for variants in these genes leads to changes in clinical management that improve outcomes.

No clinically valid studies were identified that evaluated defined groups of patients (eg, patients with schizophrenia) and reported the sensitivity and specificity of the panel results for those patients. Therefore it is not possible to estimate the clinical sensitivity and specificity of the tests as a diagnostic tool for specific patient groups.

Practice Guidelines and Position Statements

None identified.
Regulatory Status

The Genecept Assay, STA2R test, the GeneSight Psychotropic panel and the GeneSight MTFHR tests are laboratory-developed tests that are not subject to U.S. Food and Drug Administration (FDA) approval. Clinical laboratories may develop and validate tests in-house (“home-brew”) and market them as a laboratory service; such tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). Other examples of these tests are YouScript (Genelex), Proove Drug Metabolism (PROOVEBio), Mental Health Insight DNA (Pathway Genomics), Millennium Pharmacogenetic Testing (Millennium Health), Primex Expanded Pharmacogenomics Panel (PrimexLab) and DNA Test Assay Pain Management Panel (Ally Clinical Diagnostics).

Tests include three CYP450 tests, vitamin K epoxide reductase, and a non-specific molecular pathology procedure.

References


64. de Leon J. The crucial role of the therapeutic window in understanding the clinical relevance of the poor versus the ultrarapid metabolizer phenotypes in subjects taking drugs metabolized by CYP2D6 or CYP2C19. J Clin Psychopharmacol. Jun 2007;27(3):241-245. PMID 17502769


71. Macaluso M, Preskorn SH. CYP 2D6 PM status and antidepressant response to nortriptyline and venlafaxine: is it more than just drug metabolism? J Clin Psychopharmacol. Apr 2011; 31(2):143-145. PMID 21346604


### History

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<td>12/09/13</td>
<td>New Policy. New policy developed with literature review through September 30, 2013. The Genecept™ assay is investigational for all indications.</td>
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<td>05/23/14</td>
<td>Update Related Policies. Add 12.04.509 and removed 12.04.82 as it was deleted.</td>
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<tr>
<td>08/11/14</td>
<td>Annual Review. Policy updated with literature review through April 14, 2014. Policy expanded to include other genetic testing panels for mental health disorders; title of policy changed to “Genetic Testing Panels for Mental Health Conditions.” Rationale extensively revised. References 1, 2, 7-11, 19-26, 28-8 added. Policy statement changed to indicate that individual genetic tests (as mutations or genetic variations) and genetic testing panels for mental health disorders are investigational.</td>
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<td>Minor update. New test added to Policy Statement for genetic testing panels: Primex Expanded Pharmacogenomics Panel.</td>
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<td>07/14/15</td>
<td>Annual Review. Policy number changed from 12.04.110 to 12.04.515 due to the addition of several local plan tests to the Policy Statement, Description and Reference section. In this revision, PersonaGene, Progenity PGx Informed and two Luminex panel tests added. Policy updated with literature review through April 21, 2015. Numerous references added. Policy statements changed to clarify which categories of genetic testing the policy addresses; intent of policy statements unchanged.</td>
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<td>05/01/16</td>
<td>Annual Review, approved April 12, 2016. Added rationale and references for CYP450 for use in review of mental health conditions/medications. References 51-93 added. No change in policy statements.</td>
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<td>10/07/16</td>
<td>Coding update. Reference codes removed from Description section; these were informational only. CPT codes 81355 and 81479 added to the Coding section.</td>
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<td>02/14/17</td>
<td>Policy moved into new format; no change to policy statements. References missing in error adding to Reference section.</td>
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<td>08/01/17</td>
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<td>10/01/17</td>
<td>Coding update. Added new CPT code 0015U (effective 8/1/17).</td>
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<td>01/23/18</td>
<td>Coding update. Added new CPT code 81328 (new code effective 1/1/18).</td>
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<td>01/30/18</td>
<td>Coding update, added note that CPT code 0015U was terminated 1/1/18.</td>
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U.S. Department of Health and Human Services
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