



# Personalized Health Solutions, LLC

The future is  
Personalized Medicine.

<p><b>What is Pharmacogenomics (PGx)?</b></p>	<p>Many commonly prescribed medications used to treat everyday ailments can be metabolized differently based on an individual's inherited genetic variants. Pharmacogenomic testing is an important component of Personalized Medicine blending the study of drugs with the study of genetic mapping and DNA sequencing. Testing helps physicians select effective, safe medications and doses that are tailored to an individual's specific genetic makeup.</p> <p>There are several common genetic variations that substantially reduce or increase the functionality of enzymes involved in metabolizing frequently prescribed drugs. If a patient's genetic profile contains one or more of these variants, it may significantly affect their ability to break down and absorb many commonly prescribed medications. PGx testing analyzes how the genetic makeup of an individual affects his/her response to drugs in order to avoid reduced efficacy of the medication or increased risk of adverse drug reactions.</p>
<p><b>Pharmacogenomics and Personalized Medicine</b></p>	<p>Pharmacogenomic testing looks at the genes that metabolize many of the medications we take, and can often predict response in an individual. Many of the medications that are often used to treat hypertension are metabolized by the genes that are studied. (Note that some medications are not metabolized, but are eliminated unchanged.)</p> <p>Research funded by the National Institutes of Health suggests that Pharmacogenomic testing will improve patient trust in the medication that has been prescribed for them. Confidence in the safety and efficacy of a drug, stemming from knowledge that the drug and dose are personalized to the patient, will lead to a greater likelihood that patients will adhere to a treatment plan.</p>
<p><b>Patient Adherence</b></p>	<p>Patients have varied reasons for poor adherence to prescribed therapies, but their failure to take their medications as prescribed has been identified by the World Health Organization as "the primary cause of unsatisfactory control of blood pressure". Anxiety about a possible adverse event and distrust of medications have been cited by patients as some of the reasons that they do not follow advice.</p>

<p><b>Is testing the right choice?</b></p>	<p>Adverse Drug Events (ADEs) are responsible for over 700,000 visits to the emergency room each year<sup>1</sup>. Additionally, over 128,000 deaths in the US are directly attributable to ADEs, ranking as one of the top five causes of death in the US each year<sup>2</sup>. Up to ten per cent of the population aged 65 years and older suffers an ADE each year despite the proper administration of medications. Genetic variations affecting how drugs are metabolized are present in 75% of the population. Testing reduces the risk of ADEs caused by a dose that is too high, improves efficacy when a dose is too low, and enables selection of the right drug for the patient.</p> <p>PGx testing, as a component of medication therapy management, can reduce risk by predicting drugresponse and alerting prescribers to potential for toxicity or drug-drug interactions. Additionally, testing can address patient non-compliance with prescribed medication therapy by reducing the potential for side effects and increasing the patient confidence that the drug will perform as indicated.</p>
<p><b>Utilization</b></p>	<p>Members of the Psychiatry profession have been among the first to routinely offer testing to their patients. Across all specialties, adoption varies regionally. Often, providers affiliated with academic medical centers are among the first healthcare providers to begin testing in cities including Boston, Washington, DC, Tallahassee, Philadelphia, Rochester, MN.</p> <p>Fortunately, because specimens are collected through buccal swabs and are stable, close proximity to a lab is not necessary and tests can be performed all across the country. Samples can be shipped to the lab through postal delivery services and results are delivered through a web portal or via fax.</p>
<p><b>Reimbursement</b></p>	<p>Medicare will typically cover pharmacogenomic testing for specific genes, namely the CYP2C19, CYP2D6, CYP2C19 and VKORC1. Testing for these genes can predict patient response when prescribing Plavix, SSRIs such as Elavil, Pamelor, and Warfarin.</p>

<sup>1</sup> US Department of Health and Human Services, Office of Disease Prevention and Health Promotion

<sup>2</sup> Harvard University, Safrá Center for Ethics, 6/27/14

	<p>Commercial payers may cover the cost of FDA approved testing in cases where the test result can affect the course of treatment. For example, if a patient has undergone long term therapy without remission or has experienced adverse events, a provider may use testing to determine an alternate therapy.</p>
<p><b>Turnaround Time</b></p>	<p>Testing turnaround time varies among labs from a few days to several weeks. If testing is to be done preemptively, time may not be an issue. If testing is done to provide guidance for an acute issue, it is important to use a lab that can offer results within a short time frame.</p>
<p><b>Interpretation of Results</b></p>	<p>Because Pharmacogenomic Testing is not yet in widespread use, many clinicians have little experience with testing and have not received training in application of results. Providers will want to work with a lab that can offer support to ordering physicians.</p> <p>Support can take several forms. It could mean a detailed report that identifies genetic variants and recommendations for alternate therapies, or often, it is in the form of consultation with pathologists who are available to consult with providers.</p>
<p><b>Benefits to Incorporating PGx Testing into your Practice</b></p>	<p>PGx can improve outcomes and shorten time from diagnosis to resolution. For instance, patients struggling with Depression and Dysthemia will benefit if genetic variants that affect the metabolism of SSRIs are revealed. Often, patients have to try several medications or combinations of medications before finding relief.</p> <p>Physicians can rule out ineffective medications before the patient initiates treatment and avoid time spent using the wrong drug. Results from a Northwestern University study in conjunction with the eMERGE project indicated providers followed recommendations when receiving clinical response in 42% of cases.</p> <p>Under MACRA legislation, providers are eligible for adjustments in reimbursement based on multiple outcome measures. PGx testing may improve</p>

	<p>outcomes in several metrics, for example: Depression Resolution within 6 or 12 months, Unplanned Admissions for Patients with Heart Failure, Medication Reconciliation, Controlling Hypertension</p>
<b>Antidepressant Therapy</b>	<p>7.6% of Americans aged 12 and over are depressed. Numerous studies show the p-glycoprotein prevents most SSRIs from crossing the blood brain barrier. This explains why a patient may have a higher concentration of SSRIs in the plasma but will not respond to treatment <sup>3</sup></p> <p>PharmGKB, the Pharmacogenomics Knowledge Base, has declared that study of the CYP2D6 gene can reveal genotypes that require an increased or decreased dose of common SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine or sertraline).</p>
<b>Statin Therapy</b>	<p>The c.2155T&gt; C variant of the KIF6 gene was shown to influence physiological responses to treatment with simvastatin and atorvastatin.<sup>4</sup></p> <p>Detection of evidence of coronary atherosclerosis prior to an event allows aggressive and individualized preventive measures to be taken that have the potential to significantly reduce the probability of future coronary events in a primary prevention population.<sup>5</sup></p>
<b>Heart Disease</b>	<p>Researchers at the University of Alabama at Birmingham began testing patients requiring a stent to determine which anticoagulants would be most effective.</p> <p>In 30% of cases, patients were given something other than a combination of Plavix and aspirin. The research team found a 50% reduction in mortality rates after one year.<sup>6</sup></p>
<b>Getting Started</b>	<p>Providers will want to establish a relationship with a testing lab to obtain test kits and a login to the lab's online portal. Eventually, all patients will benefit from PGx testing, but given limits of reimbursement, certain</p>

<sup>3</sup> *Depression and Pharmacogenomics, Archives of Psychiatric Nursing 10.1016/j.apnu.2017.10.011*

<sup>4</sup> *KIF6 gene as a pharmacogenetic marker for lipid-lowering effect in statin treatment. Ruiz-Iruela C, et al. PLoS 2018*

<sup>5</sup> *Genetic Testing for Early Detection of Individuals at Risk of Coronary Heart Disease and Monitoring Response to Therapy: Challenges and Promises, Current Atherosclerosis Report, 2011 Oct; 13(5): 396–404.*

<sup>6</sup> *Pharmacogenomics as Predictor, Birmingham Medical News October 18 2018*

	<p>patients may present for whom testing is most appropriate.</p> <p>Currently, 44% of men and 57% of women older than age 65 take five or more medications per week; about 12% of both men and women take 10 or more medications per week.<sup>7</sup> These are often the patients who will benefit most from PGx testing. Additionally, patients with conditions such as heart disease, GERD, depression and others who are not reaching desired outcomes may be considered for testing. Once candidates have been identified, testing begins with a simple cheek swab.</p>
<p><b>Resources</b></p>	<p>National Center for Biotechnology Information  <a href="https://www.ncbi.nlm.nih.gov/">https://www.ncbi.nlm.nih.gov/</a></p> <p>Clinical Pharmacogenetics Information Consortium  <a href="https://cpicpgx.org">https://cpicpgx.org</a></p> <p>Pharmacogenomics Knowledge Base  <a href="https://www.pharmgkb.org">https://www.pharmgkb.org</a></p>
<p><b>Contact Us</b></p>	<p>Personalized Health Solutions, LLC        888-947-4748 / 251-706-2777  <a href="http://www.personalizedhealthsolutions.com">www.personalizedhealthsolutions.com</a></p>

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<sup>7</sup> A Survey on Polypharmacy and Use of Inappropriate Medications, *International Journal on Toxicology*. 2012 Jan-Apr; 19(1): 68–73.