PHARMACOGENETICS:

Is Personalized Medicine in Your Plan’s Future?

By revealing how genetic makeup influences a patient’s response to a medication, pharmacogenetic testing may have the potential to help health plan sponsors control costs while improving health outcomes for plan members.

by | Jennifer K. Fuhrmann-Berger, Pharm.D.
Prescribing medication can be a trial-and-error process: Doctors prescribe medications that are indicated to treat their patients’ ailments. The medications often work, but sometimes they don’t.

Patients who don’t feel any relief or are made sicker by the medication go back to their physician, who prescribes a different medication. This routine continues, requiring patients to pay additional copays while their health care plan pays its share of the costs accumulated until, somewhere along the line, at last, the patient finds the right medication.

Pharmaceuticals are treated as if they are a one-size-fits-all therapy and, generally speaking, they are. But the relatively new field of pharmacogenetics provides a greater understanding of why some medications may work better than others for an individual. This information has the potential to improve health outcomes for patients and create savings for benefit plan sponsors by reducing ineffective or inappropriate spending on medications.

What Is Pharmacogenetics?

Pharmacogenetics (PGx) is the study of how a person’s genetic makeup influences his or her response to medication, considering differences in genes, metabolism and environment. A component of precision medicine, pharmacogenetics enables treatment to be tailored to the individual, delivering the right medication and the right dosage at the right time. It can eliminate the waste and frustration of the typical trial-and-error approach to finding an effective medication.

The metabolic pathway of a medication impacts the point at which enzymes in the body break down that medication, activate the therapy and then move it through to excretion. The rate at which an individual’s metabolism enables the enzymes to break down a medication can be too quick or too slow, and the medication may not offer the expected therapeutic effects. In some cases, the consequences go unnoticed, and the medication simply does not help. In others, the medication can be toxic to the individual.

Grapefruit juice is a good environmental example of how this process works. It is commonly understood that cholesterol and statin medications should not be taken with grapefruit juice. The acidity of grapefruit juice is considered an inducer because it speeds up (expedites) the breakdown of the medication in the stomach and reduces the effectiveness of the medication. Other substances—called inhibitors—slow the process or make a condition worse.

While many might think pharmacogenetics only applies to complex medications such as biologics, pharmacogenetic data can guide the prescribing of a wide range of medications, including those that treat common conditions such as high cholesterol and diabetes. The data also can be used in the prescribing of opioids, anesthetics, pain medications and cancer drugs, in addition to expensive specialty medications.

Personalized medicine, which is an approach that tailors treatment to an individual, also stands to benefit greatly from pharmacogenetic testing. According to a recent report from the Personalized Medicine Coalition, the number of U.S. Food and Drug Administration (FDA)–approved medications with personalized medicine requirements has increased from five drugs in 2008 to 132 drugs in 2016, and many more are in the pipeline. This means that the research and development process for these medications defined the genetic pathways in which the medications were most or least effective. Pharmacogenetic testing reveals those pathways.

Medications with personalized medicine requirements include drugs that carry black box warnings, which are safety warnings that help prescribers identify patients most at risk when using these medications. For example, the well-known antiplatelet medication Plavix® carries a black box warning that patients who possess a particular genetic variation—discoverable through pharmacogenetics testing—are unable to properly metabolize the medication, leaving them at risk for stroke, heart attack and associated complications.

How Testing Is Conducted

Testing is conducted with an oral (buccal) cheek swab of saliva. The saliva, which includes some skin cells from the cheek,
is mailed to a highly advanced diagnostic laboratory that specializes in performing genetic tests. The report generated from the results indicates whether the member is a good metabolizer or poor metabolizer for up to 150 medications, depending on the test, provider or lab. Because genetic makeup doesn't change, the report can be used not only for current health conditions and medications but also can help to determine the most effective drugs for conditions the individual may develop later in life.

A fully comprehensive test is not necessary in all cases. Patients and providers may be able to select from a specific therapeutic class of pharmacogenetic tests based on individual need and cost considerations. For instance, a patient diagnosed with diabetes can be referred for pharmacogenetic testing specific to diabetes, which can then help inform treatment decisions.

**Benefits of Pharmacogenetics**

By understanding how a member will metabolize medication, prescribers can make informed decisions and prescribe effective medications at accurate doses the first time the member visits them looking for help with a condition. This improves health outcomes and reduces costs.

Pharmacogenetics data can also be integrated as part of standard point-of-sale drug utilization review. This enables the pharmacy benefit manager’s (PBM) system to alert the dispensing pharmacist at a retail pharmacy when a medication is contraindicated because the patient cannot metabolize the medication—before the pharmacy dispenses the drug. This simple check can reduce waste, increase quality of care and deliver plan savings.

The clinical applications of the large amounts of data that genetic testing provides can vary significantly. Pharmacogenetic testing is less common than genetic testing applied in specialties such as oncology, which include screening for the BRCA1 or BRCA2 gene. The adoption rate for pharmacogenetic testing in the health care industry as a whole is slow due to several factors, including scarcity of physician education and insurance reimbursements.

Pharmacogenetics was first recommended in clinical guidance by the FDA in the 2000s, but many physicians have not had the ability to study this approach to treatment. As a result, they may not be sure how to apply their patients’ pharmacogenetic reports to their prescribing decisions. Many plan providers have yet to adopt pharmacogenetic testing as a standard part of their business models. This increases the difficulty in making effective use of pharmacogenetic data to improve patient outcomes and decrease overall cost.

Because of the large amount of information that pharmacogenetic testing delivers, the provider or PBM must have the ability to efficiently incorporate the data into the claim processing systems, as well as other clinical processes and protocols. By creating an automated system whereby pharmacists are alerted when pharmacogenetic test results contraindicate a given medication, providers and PBMs can work with patients and prescribers to find a better treatment option.

PCSK9 inhibitors offer a good example of how pharmacogenetics can be applied. Proprotein convertase subtilisin/kexin type 9, referred to as PCSK9, interferes with the liver’s ability to remove cholesterol from the blood. A PCSK9 inhibitor can reduce low-density lipoprotein (LDL or "bad") cholesterol by 61% compared with the standard treatment using statins (e.g., Lipitor®, Zocor®). This can lead to reduced risk of heart disease. However, PCSK9 inhibitors cost about $15,000 annually, while the cost of standard statin therapy can be as low as $200 per year.

In the United States, 28% of the population takes a statin. If every one of these people switched from the standard statin therapy to a PCSK9 inhibitor, most plans would take a significant financial hit. Some plans probably did take a hit in 2015 when the first PCSK9 inhibitor was introduced, depending on the clinical programs that may have been in place. Making the finances even harder to swallow is the fact that pharmacogenetics data has shown that only one in five users of PCSK9 inhibitors metabolizes the medication effectively.

While many providers have addressed the concerns regarding PCSK9 inhibitors through step therapy and management protocols, pharmacogenetic testing can save time in determining the right medication, dosage or combination of drug therapy. Step therapy requires the prescriber and patient to check off boxes on a list until they find the right solution. Pharmacogenetics testing can tell the prescriber which boxes could and should be skipped entirely because of how the patient would metabolize the product. Patients who cannot metabolize PCSK9 inhibitors need not waste time and money on ineffectual treatment or raise their risk factors by spending several weeks on a medication that does little or nothing to reduce their LDL numbers.

Medical errors, which include the
use of inappropriate medication, are the third leading cause of death in the U.S. behind heart disease and cancer, according to researchers at Johns Hopkins University. This equates to approximately 700 deaths a day, or 9.5% of deaths annually. By applying pharmacogenetic data to the health care delivery process, members could avoid taking medications that may be harmful to them. This can reduce errors in prescribing and reduce fatalities or other harm.

Offering Pharmacogenetic Testing

Pharmacogenetic testing can cost hundreds of dollars per test, so it is likely not feasible to offer testing to all plan participants. Furthermore, pharmacogenetic tests are only applicable to specific medications and conditions at this time. Conducting tests of all plan participants is both impractical and unnecessary. Plan sponsors might instead consider offering tests only to plan members with complex health conditions or others who are most likely to receive significant benefit from the investment.

According to the Agency for Healthcare Research and Quality, 1% of people account for more than 28% of total health care expenditures. By helping these patients find better solutions to their health care needs through pharmacogenetics, providers can reduce these expenditures, saving money and reducing waste at all levels of health care.

When reviewing how best to implement pharmacogenetic testing as a plan provider, one possible strategy is to focus on members who rely on medications that have a significant impact on long-term disease such as hepatitis C, cancer, cardiovascular disease and diabetes. Plan sponsors might also focus on members who are taking a high number of different medications or members with higher levels of drug spending in an effort to help reduce their expenses. It is incumbent upon the plan provider to determine how pharmacogenetic testing rules should be applied, but members should always have the option to decline the tests.

The challenge with offering testing only to certain members is that other members may perceive this as an added benefit and question why it isn’t offered by the plan sponsor to everyone. Plan sponsors should be prepared for this reaction and can address this concern by providing information to members that explains the nature and current applications and limitations of pharmacogenetic testing.

Once the test is conducted, the member can take the resulting report to their prescribers to keep on file. The PBM should be able to apply the data to its claim processing system and integrate it with point-of-sale drug utilization reviews. The data could also be used with clinical programs such as prior authorizations and step therapy.

If pharmacogenetics data indicates a member will receive the greatest benefit from a drug not typically prescribed first, or listed as a step 2 medication, for instance, that member can be flagged to bypass other, less effective or step 1 medications, saving time and money. PBMs should use pharmacogenetic data to double-check the effectiveness of prescriptions for members before anything is dispensed at the pharmacy.

While additional factors such as the patient’s age and sex can impact the efficacy and appropriateness of a medication, many prescribers and providers already have systems in place to take these common factors into account. Pharmacogenetic data can be used in conjunction with data on other influencers of drug response to identify the best course of treatment for an individual.

There are many strategies plan sponsors can use to pay for testing. Testing could simply be covered by the health care plan, or the plan could charge a copayment or coinsurance to share the cost with members. The expectation is that the up-front cost of the test will eventually be offset with more effective...
care, which reduces office visits and the costs associated with trying several different medications before finding the right one.

What About Privacy Concerns?

The discussion of pharmacogenetic testing often includes a question of member privacy. It is important to understand that this testing looks at genetic factors that affect metabolism and not the deeper details of genetic makeup or DNA. This is not the same type of genetic testing conducted to decipher genotype or the likelihood to develop cancer based on genetic and hereditary considerations. Another common, yet incorrect, leap when people hear the term genetic testing is the type of personal genetic testing offered by companies such as 23andMe, which looks at DNA chromosome breakdowns to provide information such as ancestry details, traits and genetic health risks. Pharmacogenetic testing is different. It looks only at the specific genes known to affect an individual's metabolism.

Pharmacogenetic testing is, however, personal and, along with all genetic data, is protected by the Genetic Information Nondiscrimination Act of 2008 (GINA), the federal law that protects individuals from discrimination based on genetic information by both health insurance providers and employers.

Conclusion

Pharmacogenetic testing is a relatively new concept in the world of health care and is not yet a standard offering from PBMs or health insurers. However, as drug costs continue to increase and research in the field advances, plan sponsors may wish to consider it as a viable cost-control option.

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