GENETIC TESTING BRINGS BIG CHANGES TO THE HEALTH CARE SYSTEM
OptumRx® has been actively working to apply the recent advances in genetic testing to promote greater value for our pharmacy care services clients and consumers, as well as for the health care system at large. So we are pleased to present this report from Harvard Business Review Analytic Services.

As the following report makes clear, the genetics revolution in health care is not in the future anymore; it’s here, now. By helping predict how individuals will react to a particular drug, pharmacogenomic testing can help physicians choose the right medication, and dosage, for each individual.

Crucially, this paper emphasizes the key role pharmacy benefit managers (PBMs) and pharmacists will play in broadly distributing the benefits of pharmacogenomic testing. While some physician specialties, such as oncology, have vast experience in genetic treatments, this is not always the case. In contrast, genetics have been a standard part of the pharmacist educational curriculum for years. And OptumRx can call on a wide range of highly experienced pharmacists—one of our core strengths.

OptumRx is moving quickly to bring the power of pharmacogenomic testing to drive improved health care outcomes and the more efficient use of costly new medicines. OptumRx pharmacists deploy their genetics expertise on a daily basis, translating test results for providers and members.

Our existing prior authorization program includes some 100 biomarkers to help determine drug coverage where testing is supported by FDA-approved drug labeling. The work OptumRx pharmacists do to consult with physicians is critical to turning pharmacogenomic testing results into clinically relevant and actionable interventions.

The next challenge lies in creating new mechanisms to test further application of pharmacogenomic tests in order to improve outcomes and lower the total cost of care. What’s missing is a reliable way to demonstrate its cost-effectiveness. The only way to do that is to deploy evidenced-based testing in the real world—at scale. OptumRx is building a deep database of real-world experience that can demonstrate clinical utility, while also broadly distributing the benefits of pharmacogenomic testing.

The actions we are taking today place OptumRx at the forefront of pharmacogenomic testing. The future promises to be even more exciting as we unlock the full value of precision medicine to deliver improved outcomes and a lower total cost of care.

OptumRx is a leading pharmacy care services provider.
Learn more at OptumRx.com.
GENETIC TESTING BRINGS BIG CHANGES TO THE HEALTH CARE SYSTEM

Powerful new technologies like genetic sequencing are rapidly expanding physicians’ and pharmacists’ abilities to better calculate disease risk, understand how diseases develop in patients, and target improved diagnosis and individual treatment strategies.

Pharmacogenomics (PGx) is one of the most important components of this new, highly personalized approach to health care. PGx studies the inherited genetic makeup of patients and how that influences drug response and determines drug behavior. By helping predict how individuals will react to a particular drug—including the expected benefits and side effects—PGx allows physicians to choose the right medication, and dosage, for each individual.

Before the advent of PGx, the pharmaceutical industry worked on the assumption that drugs work for most everyone in the same way. But the one-size-fits-all approach turns out to be flawed. In reality, a great deal of trial and error is required to find the right treatment and dosage. In the process, patients can suffer toxic side effects and the frustration—and fear—that the treatments aren’t going to work.

“Trial-and-error prescribing is not really sustainable,” says Philip Empey, an associate professor at the University of Pittsburgh School of Pharmacy and associate director of the Institute of Precision Medicine at the university’s medical center (PITT/UPMC). “Prescription prices are going up and adverse drug reactions are a significant cause of mortality and morbidity.”

Because inherited genetic traits can influence how a drug responds, the effectiveness of certain drugs can be highly variable. Reactions to treatments can range from nontoxic and providing no benefit to highly beneficial but too toxic. Figure 1: As a result, each year, some 1.5 million serious and preventable medication errors occur, and these errors sap $170 billion of health care resources that could be put to much better use.1

Despite the enormous potential of PGx and precision medicine, however, health care providers and payers are not leveraging the technology as much as they could. Though PGx is evolving into the mainstream of clinical practice, the industry has yet to solidify the foundation for PGx implementation to accelerate its use.

HIGHLIGHTS

- Pharmacogenomics (PGx) studies the inherited genetic makeup of patients and how that influences drug response and determines drug behavior.
- PGx can increase the likelihood that patients will take their medications and feel confident that they won’t experience negative side effects.
- Thoroughly implementing PGx in clinical practice will need a finely tuned ecosystem including payers, physicians, pharmacists, patients, and pharmacy benefit managers.
PGx can increase the likelihood that patients will take their medications and feel confident that they won’t experience negative side effects. “When patients believe in the effectiveness of what they have been prescribed, they are much more likely to take their medications,” says Mark Dunnenberger, director of personalized medicine at NorthShore University Health System in the Chicago area. “And confidence goes up even if medications don’t have to be changed.”

FIGURE 2
Some clinical specialties and PBMs are already turning to pharmacogenomic testing and demonstrating its value. Oncology is a prime example; PGx testing to determine the best treatment options has become standard clinical practice in cancer treatment centers. And PBMs have introduced genotyping for anti-cancer medications like Tamoxifen, which treats breast cancer.2

In the early 2000s, pharmacy benefit management companies began applying PGx tests to patients who were prescribed warfarin to prevent strokes. One PBM worked with the Mayo Clinic, says Russell Teagarden, a veteran pharmacy practitioner, executive, and educator, who was a PBM executive at that time. Together, they examined claims data for patients who had received PGx tests—and where results suggested that an alternative treatment would drive better outcomes. The partners found a 30% drop in hospitalizations among patients after switching treatments based on the PGx results.

Medications for mental health—such as antidepressants, which address chemical imbalances that can cause anxiety and depression—are another case in point. The successful use of these treatments relies heavily on trial and error. Since there are no tests that can determine the precise imbalances, finding the right drugs and dosages has been a lengthy process often involving multiple drugs, taken separately or in combination with others. The trial-and-error process can be arduous for patients who continue to suffer until the right treatment
and dosage are found. Moreover, as the University of Minnesota’s Bishop points out, treatment for mental health conditions often lasts several years and can become quite costly with constant trial and error.

PITT/UPMC is also helping demonstrate the value of PGx. The initial focus is the blood thinner clopidogrel. “If a patient receives a heart stent, a medication is typically prescribed to help keep the stent open to avert secondary events like another heart attack or stroke,” says the University of Pittsburgh’s Empey. “Clopidogrel is the most commonly prescribed medication but doesn’t work in everyone.” To test the value of PGx, PITT/UPMC made it a standard part of care in the catheterization lab at its UPMC Presbyterian Hospital.

“We have tested nearly 3,000 patients so far,” says Empey. “We combine the test results with other clinical factors to guide prescribing and track the outcomes. From there, we can attach dollar figures to the outcomes and determine the value of PGx testing.” In addition, says Empey, PITT/UPMC found that patients who changed therapies because of the test had much better overall heart-related outcomes than those who didn’t change medications.

Overall, PGx can dramatically truncate the trial-and-error process, and its potential is driving high levels of commercial and research activity. At the 2018 Pharmacogenomics Conference, hosted by the University of Minnesota’s College of Pharmacy, keynote speaker Pamala Jacobson, a pharmacology professor at the school, told attendees that the number of PGx research projects is mounting quickly. In 2000, a few hundred peer-reviewed studies were published. By 2018, the number jumped to more than 2,000 studies.

The pharmaceutical industry has taken note of PGx’s potential. Some 40% of drugs in the pipeline are based on specific genetic markers that increase the odds of a drug working for the greatest number of patients. The number of commercially available tests has ballooned—by some estimates more than 75,000 different tests were on the market in 2017—showing that PGx availability is growing exponentially.

**Speed Bumps Along the Way**

Despite the promise of PGx, there are some significant roadblocks standing in the way of its full implementation. One major challenge is that physicians are not trained in genetics; PGx test results often consist of several pages

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**FIGURE 2**

**PGx TESTS DRIVE PATIENT CONFIDENCE**

Patients are much more likely to take their medications in conjunction with PGx tests.

<table>
<thead>
<tr>
<th>STRONGLY AGREE</th>
<th>SOMewhat AGREE</th>
<th>NEITHER AGREE NOR DISAGREE</th>
<th>SOMewhat DISAGREE</th>
<th>STRONGLY DISAGREE</th>
</tr>
</thead>
<tbody>
<tr>
<td>43%</td>
<td>30%</td>
<td>13%</td>
<td>11%</td>
<td>4%</td>
</tr>
</tbody>
</table>

I feel more confident that medication(s) prescribed to me will not cause side effects and/or will help my condition, compared with past prescriptions I’ve received without testing.

| 29% | 29% | 32% | 9% | 2% |

I am more likely to take medications prescribed by my health care provider.

Note: Due to rounding, figures may not add up to exactly 100%

SOURCE: PRESENTATION BY MARK DUNNENBERGER, PHARMACOGENOMICS CONVENTION, 2018
“When patients believe in the effectiveness of what they have been prescribed, they are much more likely to take their medications,” says Mark Dunnenberger, director of personalized medicine at NorthShore University Health System.

of detailed technical information and require a level of understanding on the part of the clinician. “If all a clinician gets back is a genetic result, then you have a sizeable problem,” says NorthShore’s Dunnenberger. “Doctors haven’t been trained in this type of information, so it creates a barrier that can slow down or even halt progress in the near term.”

Physician uncertainty about PGx landed on the front page of The Wall Street Journal in October 2019. In an article titled “Doctors Limit What to Tell Patients About Their DNA Test,” the newspaper reported that many physicians are reluctant to talk about genetic tests even if the patient has ordered them. Currently, the test results are too difficult to digest to drive a meaningful conversation with a patient.4

Given knowledge gaps and time constraints on the part of physicians, Dunnenberger has found that doctors need PGx results succinctly expressed in 20 words or less—or possibly even two or three with a graphic. Moreover, the information needs to be provided in real time, ideally at the point when the prescriber is writing the prescription.

The complexity of the test results also means that not just doctors but consumers, too, need to know more about PGx. “Consumers need to understand what PGx offers,” says Bishop. “We need consumer education efforts that focus on what the tests can tell people and what they can’t.”

PBMs can also play a major role in disseminating PGx knowledge to physicians and consumers. One PBM, for example, contacted patients who had been prescribed warfarin and told them to discuss PGx testing with their doctors. “PBMs have a very large role to play here,” says Bryan Dechairo, executive vice president of development at Myriad Genetics, a molecular diagnostic company. “They can identify patients who can benefit from PGx at the right time, who actually need the intervention and will benefit from that intervention.”

Beyond the lack of physician expertise, there are compounding challenges, including an explosion in the sheer number of PGx tests and significant regulatory uncertainties. Several testing companies that provide PGx tests also offer guidance on interpreting the results, suggesting that a given drug might not be appropriate for the person being tested. The FDA believes that these tests should fall under the FDA’s jurisdiction in the same way that it now verifies that therapeutic drugs provide the benefits that drug companies claim they do.

But PGx test companies argue that the tests should instead fall under different government regulations that monitor and approve only the accuracy of lab tests. Complicating matters further, says Dr. Marc Williams, director of the Genomic Medicine Institute at Geisinger Health System, doctors see PGx tests as part of medical practice, which is not within the FDA’s regulatory scope.

“It is an evolving and dynamic process,” Dunnenberger says. “In addition to the FDA giving guidance on what a testing company cannot do, it would be helpful if it provided guidance on ‘here is what you can do and how to do it.’”

In the meantime, PBMs are also tackling the challenge through FDA product labeling. “In some cases, the FDA evaluates PGx tests designed for a new treatment at the time of its launch,” says Robert Epstein, a board member for Veracyte, a genomic
PHARMACISTS HAVE THE TRAINING TO PLAY A KEY ROLE IN HELPING PRESCRIBERS INTERPRET PGX TESTING TO INFLUENCE THERAPEUTIC OPPORTUNITIES SUCH AS STOPPING, ADJUSTING, OR SWITCHING DRUGS.
GIVEN THEIR GROWING INTEREST IN GENETIC DATA, PATIENTS WILL INCREASINGLY ASK PHYSICIANS TO ORDER TESTS OR EVEN ORDER THE TESTS THEMSELVES.
In addition to pharmacists’ knowledge of genetics, their PBM ranks also have significant infrastructure that can be vital for the advancement of PGx. “PBMs are used to having call centers and informatics to guide prescriptions,” says Empey. He adds that they are well-positioned to play a central role, and that they “may also have access to medical claims data that can demonstrate the impact of PGx.”

Creating a Finely Tuned PGx Machine

Despite the enormous potential of PGx to boost health care outcomes while making measurable reductions in drug spending, the widespread use of these tests is still in the early stages. Despite a sizable number of devotees across the health care spectrum, thoroughly implementing PGx in clinical practice will need a finely tuned ecosystem including payers, physicians, pharmacists, patients, and PBMs to make PGx a reality.

Physicians will always be a central node in the operation since they have the broadest knowledge of the patient’s medical history and ultimately determine treatment plans. They also must authorize these tests if payers are to cover them.

The process also includes consumers. Given their growing interest in genetic data, patients will increasingly ask physicians to order tests or even order the tests themselves. If consumers are to advocate for the tests, PGx knowledge needs to be more widespread than it currently is.

Although the stakeholders needed to implement PGx are disparate, PBMs have the inherent motivation and expertise that makes them likely to emerge as the catalysts who can drive the process and education of PGx.

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Pharmacists, with their PGx expertise, are also deeply embedded within the PBM organizations. According to the Academy of Managed Care Pharmacy, thousands of pharmacists and other health care professionals work in the managed care industry, which includes PBMs. They have been working for years, building intimate connections between and among clinicians, patients, laboratories, and payers.

That deep connectedness can also help bring payers on board more quickly, which is important because they hold the purse strings. PBMs matter here, as they serve payers and benefit plan sponsors and are charged with promoting high-quality health care while controlling the costs. As genomic knowledge grows, PBMs are in a prime position to advocate for the use of the tests as payers seek to control their costs. “How do you really explain to the providers, the prescribers, and the patients the value of why you’re doing [PGx], and how do you use the results?” asks Myriad Genetics’ Dechairo. “Obviously, PBMs have the pharmacy expertise.”

Conclusion

Medical treatment tailored to a specific patient’s needs and the ability to head off illnesses are no longer futuristic visions. In particular, technological advances in genetics have opened the door for personalized medicine.

As genetic research gains speed, doctors will be able to assess the risks of patients developing certain diseases and the effectiveness of preventative
AS GENETIC RESEARCH GAINS SPEED, DOCTORS WILL BE ABLE TO ASSESS THE RISKS OF PATIENTS DEVELOPING CERTAIN DISEASES AND THE EFFECTIVENESS OF PREVENTIVE MEASURES.

measures. PGx, for instance, is already well-integrated into oncology, as tests help predict the likelihood of breast cancer recurring. These tests can also significantly cut back the trial-and-error process of treatment, boosting success in what is often a race against time.

PGx offers enormous prospects. However, in a fractured health care industry, obstacles to build the required infrastructure for PGx—one that involves and leverages all relevant stakeholders to ensure the effective use of the tests—remain. PGx knowledge needs to be more widely distributed, and regulatory discrepancies need to be settled.

But the tide is changing and PGx champions are emerging in all areas. Physicians, pharmacists, and PBMs are at the fulcrum of demonstrating the clinical and economic impacts, as well as the value, of PGx. As these professionals spur PGx usage and compile clinical practice data that clearly defines its economic value, genetic testing will continue to charge ahead. “We have a lot of information on genetic markers that inform drug response,” says Deepak Voora, associate professor of medicine at Duke University and executive team member of the Duke Center of Applied Genomics and Medicine. “Now we are seeing more research on the clinical value. In the next five years, we should see more and more institutions using PGx once we have a clearer understanding of the clinical and economic value.”

Endnotes
1 The National Academies of Sciences, Engineering and Medicine, "Preventing Medication Errors," 2006.
5 “What Is Managed Care Pharmacy?,” Academy of Managed Care Pharmacy (AMCP) webinar, presented September 18, 2018.