admera health | A GENEWIZ COMPANY

Lowering Healthcare Costs with Personalized Medicine

Pharmacogenomics Testing Reduces the Healthcare Burden of Individual Genetic Variability

The notion of individual genetic variability has long been accepted and promoted within both the scientific community and the healthcare industry. Advances in molecular testing, and completion of the mapping of the human genome in particular, give credence to the fact that patients respond differently to medications based on their individual genetic makeup. Such advancements brought about the concept of personalized medicine, the practice of using an individual's genetic profile to guide decisions for the prevention, treatment, and diagnosis of disease. Correspondingly, a major problem in the managed care industry is the variability of drug efficacy from patient to patient. While some patients complain about lack of effectiveness, other patients suffer from adverse drug events (ADEs).[1] Personalized medicine has the ability to alleviate the burden of individual genetic variability and the resulting varied drug responses across different patient populations.

In the United States, ADEs incur up to $100 billion in costs annually, as well as hundreds of thousands of deaths every year. Accordingly, ADEs have been described as the fourth leading cause of death in the United States, only surpassed by heart disease, cancer, and strokes.[3] Studies attribute 6.5% of hospital admissions to ADEs, with the average hospital stay estimated at four days.[3] On average, ADEs extend patient hospital visits up to four days, which result in additional fees estimated up to $6000; so, for a 700-bed hospital, managed care costs associated with ADEs are approximately $5.6 million annually.[3,4] Addressing the health and cost implications of ADEs, personalized medicine facilitates cost containment while improving patient care and quality of life.

Aside from the resulting financial burden, ADEs significantly impact health outcomes; patients report decreased quality of life, which often results in more testing to identify the cause of their symptoms.[5] An often overlooked consequence of ADEs is the impact on patient adherence. Patients neglect to follow prescription guidelines due to their lack of faith in drug efficacy or the belief that they are prone to side effects from their medications.[6] A solution to ADEs and lack of medication efficacy is pharmacogenomics, which helps to predict how patients will respond to drugs based on individual molecular and biological characteristics. Pharmacogenomics testing reviews individual genetic makeup to:

- Identify the likelihood of ADEs, thereby reducing occurrences among the patient population;[1]
- Increase drug efficacy;[2]
- Increase adherence through patients' first-hand positive experiences, encouraging treatment continuity;[7,8] and
- Reduce healthcare costs incurred from ADEs, poor efficacy, and lack of patient adherence.[9]

Admera Health's Solution to the Healthcare Burden of Individual Genetic Variability

Admera Health has developed an innovative pharmacogenomics test that addresses major healthcare issues resulting from individual genetic variability. PGxOne™, Admera Health's pharmacogenomics test, analyzes 13 well-established genes involved in drug absorption, metabolism, and activity. The test utilizes next generation sequencing technology and provides information for individual patient responses to 76 FDA-approved drugs.[10]* All drugs covered by PGxOne™ have been endorsed by the FDA (Food and Drug Administration), EMA (European Marketing Authority), and/or the CPIC (Clinical Pharmacogenetics Implementation Consortium), an organization that provides clinical guidelines and recommendations on pharmacogenomics.

Genes Assayed by PGxOne™ and Applicable Therapeutic Areas

CYP1A2 Psychiatry

CYP2C19 Cardiology
Gastroenterology
Neurology
Psychiatry
Rheumatology

CYP2C9 Cardiology
Rheumatology

CYP2D6 Anesthesiology
Cardiology
Psychiatry
Urology

DPYD Oncology

F5 Hematology
Women's Health

G6PD Endocrinology
Infectious Diseases
Oncology
Rheumatology

HLA-B Infectious Diseases;
Neurology

IFNL3 Infectious Diseases

SLCO1B1 Cardiology

TPMT Oncology
Rheumatology

UGT1A1 Oncology

VKORC1 Cardiology

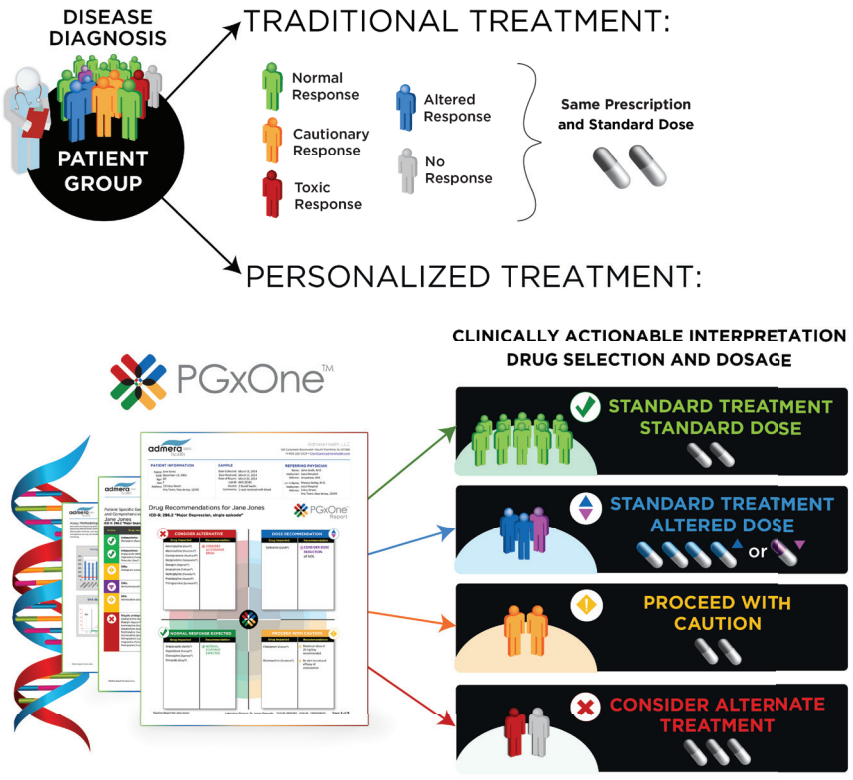

Figure 1: Traditional treatment involves prescribing the same medication at a standard dosage across the patient population. PGxOne™ allows personalized treatment for each patient.

PGxOne™ results provide physicians with concise, medically actionable information about a patient's genotype, thus allowing them to make effective treatment decisions. Because a patient's genotype remains constant, PGxOne™ results can be used to inform medical treatment throughout their lifetime. In 2015, Admera Health will release an expanded version of PGxOne™ that will provide information for additional drugs with proven pharmacogenomics indications.

By providing tailored treatment regimens for every patient, physicians will see a significant reduction of ADEs, as well as a marked increase in drug efficacy. Results from the PGxOne™ test are broken down into major therapeutic areas that impact large subsets of the patient population, including but not limited to cardiology, depression, oncology, and pain. Examples of therapeutic categories and drug classes covered by PGxOne™ are highlighted in the following noteworthy case studies.

*At the time of publication, PGxOne™ results inform dosing recommendations for 76 commercial drugs. The FDA, EMA, and/or CPIC update pharmacogenomic recommendations frequently. For the most up-to-date list, please refer to the list of pharmacogenomic drug labels.[10]

Case Study: Warfarin

Two genes tested by PGxOne™, CYP2C9 and VKORC1, are commonly used to predict a patient's response to warfarin. Warfarin is an oral anticoagulant drug prescribed for the treatment and prevention of thromboembolic events, such as pulmonary embolism or venous thrombosis. Warfarin has a narrow therapeutic window and significant variability in patient dosing, and is a leading cause of emergency room visits and drug-related deaths.[11] Clinical studies indicate that proactive pharmacogenomics testing could reduce hospitalization rates of warfarin patients by 30%, saving the healthcare industry at least $1800 for every new patient prescribed warfarin each year. These savings translate to $3.6 billion based on approximately two million new warfarin patients in the United States every year.[12]

Case Study: Antidepressants

Antidepressants are used by approximately 11% of the United States population, and are prescribed by primary care physicians and specialists on a regular basis. Moreover, antidepressants are classified as the third most common prescription drug type taken throughout the United States.[13] PGxOne™ assays several genes that inform patients' response to antidepressants including amitriptyline, clomipramine, and doxepin. Discontinuation of antidepressants due to side effects or drug intolerance is very common; 42.4% of patients discontinue therapy within the first thirty days of treatment.[7] In addition, two thirds of patients on antidepressants also take other prescription medications, which increases the risk of ADEs.[5] Proactive pharmacogenomics testing with PGxOne™ will enable physicians to prescribe the best medication for their patients, negating the typical trial and error that takes place during the process of antidepressant treatment. Furthermore, PGxOne™ testing will reduce ADEs and, importantly, reassure the patient that their physician is prescribing the most appropriate drug for him or her. Patient confidence facilitated by the results of pharmacogenomics testing encourages adherence, which will result in improved health outcomes.[6]

PGxOne™ & Improved Patient Adherence

Patient non-adherence to medications is a significant economic burden; the resulting estimated annual healthcare costs are close to $3 billion in the United States.[6] The benefits of pharmacogenomics testing to patient adherence are frequently overlooked. Patients fail to take their medications for a number of reasons, such as the general sense that the medications do not work, and anxieties related to the possible side effects listed within drug labels. For the non-adherent subset of the patient population, pharmacogenomics testing can serve as positive reinforcement and incentive for patients. Pharmacogenomics test results provide personalized, actionable facts for patients. Using the PGxOne™ report, physicians can visually demonstrate how patients will respond to different medications; explaining the benefits of adherence and involving patients in the medication selection process are likely to bring about improved adherence.[6] Likewise, studies have shown that pharmacogenomics testing improves adherence and clinical outcomes, with one study reporting a 72% improvement among diabetes patients.[8] Furthermore, studies reinforce that the simple act of pharmacogenomics testing could serve to alleviate patient anxieties and increase adherence.[6]

PGxOne™ Testing, Drug-drug Interactions and Health Outcomes

Polypharmacy patients, or patients on multiple prescription drugs, tend to be at the highest risk for ADEs. ADEs in polypharmacy patients are often due to drug-drug interactions (DDIs). Notably, ADEs often produce symptoms that result in patients being prescribed additional drugs, which produce DDIs, further complicating patient treatment.[5] DDIs in polypharmacy patients have serious implications for managed care, as they result in increased healthcare costs and can negatively affect patient health outcomes. Surveys conducted throughout the United States indicate that 7% of patients aged 18 years and older take five or more prescription drugs on a regular basis. When considering the patient population aged 65 years and older, this percentage increases significantly – 44% of men and 57% of women reported taking five or more medications daily, and 12% of both sexes reported taking ten or more prescriptions daily. One report estimated the costs associated with mismanaged polypharmacy patients at $1.3 billion in the United States in 2012.[14]

The elderly population in the United States continues to increase from 40 million in 2010 to an estimated 71 million by 2030, lending to an expected rise in polypharmacy; presumably, this rise will lead to increased likelihood of ADEs.[14] Proactive pharmacogenomics testing in the elderly population is likely to reduce the need for multiple medications, thus mitigating associated costs. Further study to observe and analyze the effects of PGxOne™ testing within an elderly population will illuminate the potential benefits of pharmacogenomics testing among this demographic. While some of the problems associated with polypharmacy cannot be addressed by pharmacogenomics testing, ensuring that all patients are taking the most appropriate medications will obviate the need for additional medications in many cases, thus reducing DDIs.

Lowering the Cost of Healthcare through PGxOne™ Pharmacogenomics Testing

Admera Health's PGxOne™ test has the ability to inform physicians' treatment decisions, and thus ensure patients receive the right medication at the right dose throughout the course of their lifetime. Utilization of PGxOne™ by physicians and healthcare providers will drive the reduction of patient ADEs, while concurrently increasing drug efficacy and patient adherence. As such, adoption of pharmacogenomics testing and proactive testing with PGxOne™, will lower healthcare costs and improve patient quality of life.

References

1 Kitzmiller, J. P., Groen, D. K., Phelps, M. A. & Sadee, W. Pharmacogenomic testing: relevance in medical practice: why drugs work in some patients but not in others. *Cleveland Clinic journal of medicine* 78, 243-257, doi:10.3949/ccjm.78a.10145 (2011).
2 Samer, C. F., Lorenzini, K. I., Rollason, V., Daali, Y. & Desmeules, J. A. Applications of CYP450 testing in the clinical setting. *Molecular diagnosis & therapy* 17, 165-184, doi:10.1007/s40291-013-0028-5 (2013).
3 Alomar, M. J. Factors affecting the development of adverse drug reactions (Review article). *Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society* 22, 83-94, doi:10.1016/j.jsps.2013.02.003 (2014).
4 Bates, D. W., Spell, N., Cullen, D. J. & et al. The costs of adverse drug events in hospitalized patients. *Jama* 277, 307-311, doi:10.1001/jama.1997.03540280045032 (1997).
5 Preskorn, S. H. How Drug-Drug Interactions Can Impact Managed Care. The *American journal of managed care* 10, S186-S198 (2004).
6 Haga, S. B. & LaPointe, N. M. A. The potential impact of pharmacogenetic testing on medication adherence. *The pharmacogenomics journal* 13, 481-483, doi:10.1038/tpj.2013.33 (2013).
7 Olfson, M., Marcus, S. C., Tedeschi, M. & Wan, G. J. Continuity of antidepressant treatment for adults with depression in the United States. *The American journal of psychiatry* 163, 101-108, doi:10.1176/appi.ajp.163.1.101 (2006).
8 Grant, R. W. et al. The clinical application of genetic testing in type 2 diabetes: a patient and physician survey. *Diabetologia* 52, 2299-2305, doi:10.1007/s00125-009-1512-7 (2009).
9 Phillips, K. A., Veenstra, D. L., Ramsey, S. D., Van Bebber, S. L. & Sakowski, J. Genetic testing and pharmacogenomics: issues for determining the impact to healthcare delivery and costs. *The American journal of managed care* 10, 425-432 (2004).
10 PharmGKB. Drug Labels with Pharmacogenomics Information. *https://www.pharmgkb.org/view/drug-labels.do*
11 Epstein, R. S. et al. Warfarin genotyping reduces hospitalization rates results from the MM-WES (Medco-Mayo Warfarin Effectiveness study). *Journal of the American college of cardiology* 55, 2804-2812, doi:10.1016/j.jacc.2010.03.009 (2010).
12 McWilliam, A., Lutter, R. & Nardinelli, C. Healthcare impact of personalized medicine using genetic testing: an exploratory analysis for warfarin. *Personalized Medicine* 5, 279-284, doi:10.2217/17410541.5.3.279 (2008).
13 Pratt, L. A., Brody, D.J., Gu, Q. Antidepressant Use in Persons Aged 12 and Over: United States, 2005–2008. *NCHS Data Brief. US Department of Health and Human Services, Centers for Disease Prevention and Control* (2011).
14 Aitken, M., and Valkova, S. Avoidable Costs in US Healthcare: The $200 Billion Opportunity From Using Medicines More Responsibly. *IMS Institute for Healthcare Informatics* (2013).

angsana Molecular & Diagnostics

Angsana Molecular & Diagnostics Laboratory Pte Ltd
(A subsidiary of Parkway Pantai)
No. 1 Science Park Road, #04-10, The Capricorn
Science Park II, Singapore 117528
T +65 6873 9959 | **F** +65 6873 9860
E sg.info.angsana@parkwaypantai.com

admera health | A GENEWIZ COMPANY