CASE STUDY

Cost-Effectiveness of Multigene Pharmacogenomic Testing in a Medicare Population

What is Pharmacogenomics?

Pharmacogenomics (PGx) is the combination of pharmacology (the study of drugs) and genomics (the study of genes and their functions). This branch of precision medicine (an innovative approach to tailoring disease prevention and treatment that takes into account differences in people's genes, environments and lifestyles[1]) is backed by a significant body of evidence including professional guidelines and Food and Drug Administration (FDA)-approved drug labels. Studies from Mayo Clinic and Vanderbilt indicate that greater than 90% of people have at least one genetic variant that may affect the way they respond to medications, increasing the likelihood of side effects and/or treatment failure.[2,3]

Comprehensive medication management (CMM) focuses on patients who have not achieved clinical goals of therapy. It is a systematic approach where physicians and pharmacists ensure that medications (whether they are prescription, nonprescription, alternative, traditional, vitamins or nutritional supplements) are individually assessed to determine that each medication is appropriate for the patient, effective for the medical condition, safe given the comorbidities and other medications being taken and able to be taken by the patient as intended.[4] It is a patient-centered, team-based approach to optimizing medication use and improving patient health. The integration of PGx testing as an important tool—used in combination with CMM—allows health care providers to gain insight into how individual patients' genes may affect their response to certain medications. This allows providers to target correct therapies and mitigate harmful effects.

Success factors for both cost savings and utility

- Education of patients and health care professionals[5]
- Availability of multigene PGx panels[6,7]
- Reimbursement of PGx testing[8,9,10]
- Delivery of a service component through comprehensive medication management (CMM)[11,12,13]
- Shifting from reactive to preventative testing[2,3]

Potential of PGx + CMM

- Lower risk of adverse drug reactions[14,15]
- Improved medication efficacy[14,16,17]
- Increase in both patient and provider confidence[18]
- Improved patient adherence[19,20]
- Reduced clinic visits, ER visits and hospitalizations[6,18,21,22]
- Reduce total health care costs through more personalized prescribing[21,23,24]

How Can PGx Help?

PGx is a companion and complimentary diagnostic tool that, when combined with the delivery of CMM services, helps address the problems of non-optimized medication use including adverse drug reactions (ADRs) and lack of efficacy. ADRs are the fourth leading cause of death in the US and research suggests that many commonly used medications have a response rate between 50 to 70%.[14,25] It is estimated that more than $528 billion is spent annually in the US because of the morbidity and mortality from non-optimized medication therapy.[23] This is approximately 16% of US health care expenditures,[23] as total health care spending was 3.6 trillion in 2018.[23,26] PGx, used as a tool during the CMM process, has the potential to reduce medication related issues by tailoring the patient's medication regimen based on their genetic profile, often by selecting an alternative medication or dose. PGx is a clinical tool that providers can utilize to reduce the trial-and-error approach of traditional prescribing.

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Single Gene vs Multigene PGx Tests

Single gene testing is a type of PGx test that looks at only one gene. This is often done for reactive testing (testing at the time the drug is needed). A multigene panel can be used at the time the necessary (new) medication is needed and may also be used preemptively in the future for other medications in different therapeutic areas. This often is more cost effective as single gene tests can be similar in price.

Economic Use Cases in an Elderly Population

STUDY	METHODOLOGY	RESULTS	CONCLUSION
Cost-effectiveness of Multigene Pharmacogenetic Testing in Patients with Acute Coronary Syndrome After Percutaneous Coronary Intervention[23]	▪ Markov model ▪ Cohort of 300,000 Medicare beneficiaries post-percutaneous coronary intervention (PCI) for Acute Coronary Syndrome (ACS) was simulated and assigned to each intervention strategy. ▪ Intervention strategies included: Standard of care (SOC, no PGx testing) vs single PGx testing and multi-gene testing. ▪ 12 months, 24 months and lifetime cost was investigated.	▪ Cost per quality-adjusted life year gained: – Multigene testing vs SOC – 12 months: $59,876 – 24 months: $33,512 – Lifetime: $3,780 ▪ Multigene testing was superior in cost savings compared to single-gene testing at all time horizons.	▪ On the basis of projected simulations, the results suggest that multigene testing is a potentially cost-effective strategy that may help optimize medication selection for Medicare beneficiaries post-PCI for ACS.
The Effect of Pharma-Cogenetic Profiling with a Clinical Decision Support Tool on Healthcare Resource Utilization and Estimated Costs in the Elderly Exposed to Polypharmacy[26]	▪ Observational study ▪ Compared prospective cohort of patients ≥65 years subjected to pharmacogenetic testing (N=205) to a propensity score (PS) matched historical cohort of untested patients (N=820) in a claims database. ▪ Four-month outcomes examined included hospitalizations, emergency department (ED) and outpatient visits.	▪ Hospitalization rate was 9.8% in the tested group vs. 16.1% in the untested group. ▪ ED visit rate was 4.4% in the tested group vs.15.4% in the untested group. ▪ Outpatient visit rate was 71.7% in the tested group vs. 36.5% in the untested group. ▪ Potential cost savings were estimated at $218 (mean) in the tested group.	▪ Patients PGx tested and treated according to the personalized prescribing system had a significant decrease in hospitalizations and emergency room visits, resulting in potential cost savings.

Illustrative PGx Patient Case

Meet Sandra Paulsen

Sandra Paulsen is a 68-year-old female with a history of hypertension and coronary artery disease status post ST-elevation myocardial infarction (STEMI) and placement of multiple drug-eluting stents in 2018. She is currently presenting to her primary care provider (PCP) and pharmacist with new-onset major depressive disorder (MDD), wanting her care team to assess her current medication regimen and recommend treatment for her mood. At the time of her STEMI, Sandra received PGx testing on a multigene panel, which included CYP2C19, so that her medical team could use the results to inform her antiplatelet therapy as part of a comprehensive medication management approach. The upfront cost of the panel was paid for by the institution, which later received reimbursement by Medicare through diagnosis-related group (DRG) payment.

Genotype	Phenotype	Expected Activity/ Function of Protein
CYP2C19 *2/*2	Poor Metabolizer	None
CYP2D6 *1/*41	Normal Metabolizer	Fully functional
CYP2C9 *2/*3	Poor Metabolizer	None
CYP3A5 *3/*3	Non-Expresser	None
SLCO1B1 *1/*1	Normal Function	Fully functional
TPMT *1/*1	Normal Metabolizer	Fully functional
NUDT15 *1/*1	Normal Metabolizer	Fully functional
DPYD *1/*1	Normal Metabolizer	Fully functional
VKORC1 A/A	Results for these genes, in combination with CYP2C9 and clinical factors, may be used to predict initial warfarin dose.	
CYP4F2 *1/*1		
CYP2C Cluster G/G (rs12777823)		

Multigene PGx Test Results

Prior to Sandra's discharge from the hospital for her STEMI, her PGx test results returned from the laboratory (shown above), revealing that she is a CYP2C19 poor metabolizer, a result found in about 2% of the European population.[27] This result indicates that she lacks CYP2C19 activity and is therefore unable to activate the common antiplatelet agent clopidogrel to its active form via CYP2C19, placing her at increased risk of stroke, myocardial infarction and death upon stent placement and treatment with clopidogrel. Based on these results and other clinical factors considered, her medical team placed her on ticagrelor and aspirin.

Current Applications of PGx Test Results to Drug Therapy

Two years after her STEMI, Sandra reports to her PCP that she has been experiencing feelings of worthlessness, indecisiveness, lack of energy, diminished interest in most of her activities and depressed mood for the past two months. She tells her PCP that "it's all just getting to be too much—first the heart attack, then all of these medications—I'm tired all the time."

While in Sandra's chart, her PCP noticed the prior PGx test results, and asked the ambulatory care pharmacist on site for a recommendation for an antidepressant. Selective serotonin reuptake inhibitors (SSRIs) are a first line treatment for MDD. Escitalopram and citalopram are two SSRIs inactivated by the CYP2C19 enzyme. Sandra's poor metabolizer CYP2C19 phenotype is associated with increased plasma concentrations and a higher risk of adverse effects with these SSRIs.[28]

PGx + CMM-Guided Drug Therapy Recommendations

Considering the patient's CYP2C19 and CYP2D6 test results and her fatigue, the ambulatory care pharmacist recommended that Sandra's PCP start the patient on venlafaxine 37.5 mg once daily, acknowledging that any of the following would also be appropriate: Avoid sertraline, escitalopram and citalopram or decrease dose by 50% if use is warranted; consider a non-CYP2C19 SSRI (i.e., paroxetine, fluoxetine, or fluvoxamine) as alternative because of patient's normal CYP2D6 metabolizer status; or consider a non-SSRI antidepressant (e.g., duloxetine, bupropion, venlafaxine).

The pharmacist explained that these PGx test results could be used to guide numerous potential future medication regimens as well, including certain opioids (e.g., tramadol) for pain, tamoxifen for breast cancer and warfarin for anticoagulation. Having these PGx results available at the point of prescribing holds the promise to improve patient outcomes while being cost-effective.[6]

DEVELOPED BY THE GTMRX PHARMACOGENOMICS PAYMENT AND POLICY TASKFORCE:

Brian Litten, JD, *Chief Strategic Growth Officer, Tabula Rasa HealthCare*

Tom Kraus, JD, MHS, *Vice President, Government Relations, American Society of Health-System Pharmacists*

Meghan Arwood, Pharm.D., MS, BCPS, *Clinical Research Scientist, Tabula Rasa HealthCare*

Julie Ceno-England, MD, *Medical Director, Medical Affairs, OneOme*

Malavika Deodhar, BPharm, Ph.D., *Clinical Research Scientist, Tabula Rasa HealthCare*

Michael Greenhalgh, *Strategic Growth Analyst, Tabula Rasa HealthCare*

Doug Huynh, JD, *Director, Federal Legislative Affairs, American Society of Health-System Pharmacists*

Bayli Larson, Pharm.D., MS, BCPS, *Strategic Initiatives Associate, Office of the Chief Operating Officer and Senior Vice President, American Society of Health-System Pharmacists*

Nicole Scovis, Pharm.D., BCPS, BCACP, *Strategic Growth Director, Tabula Rasa HealthCare*

Jennifer Taggart, MBA, *Strategic Growth Senior Director, Tabula Rasa HealthCare*

ENDNOTES

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