



Improving Patient Outcomes Through the Integration of Pharmacogenomic Testing into Comprehensive Medication Management Care Models

By Jennifer M. Bingham,¹² Veronique Michaud,^{3,4} Kristin Wiisanen,⁵ Jill Bates,^{6,7} Anthony P. Morreale,⁸ Philip E. Empey,⁹ Rustin D. Crutchley,¹⁰ Ghada Elnashar,¹¹ Jane Gilbert,¹² and Jacques Turgeon^{3,4*} writing on behalf of the Get the Medications Right Institute

Abstract:

The role of pharmacogenomics in the clinical setting is shifting from a reactive testing approach toward a preemptive model. Since many clinicians have embraced comprehensive medication management (CMM), the goal of this white paper is to educate healthcare professionals on the value of precision medicine and pharmacogenomic testing services in CMM care models. We will also explore methods for implementation, reimbursement opportunities, and present evidence to support its role in mitigating polypharmacy and optimizing medication regimens, patient outcomes, and cost savings.

1. Introduction

Adverse drug events (ADEs) have been categorized as a leading cause of preventable death according to the Centers for Disease Control and Prevention.^{1,2} One contributing factor to the use of potentially inappropriate medications is polypharmacy.³ Poorly managed medications are associated with ADEs, which in turn, can lead to increased cost, medication related morbidity, and poor patient outcomes.^{4,5} Furthermore, medication risk scores that assess appropriateness of drug regimens have been independently associated with an increased risk of mortality.⁶⁻⁸ It must be realized that risk factors known to worsen patient outcomes are improved through the appropriate selection and combination of medications in a regimen. As such, improvement does not require the use of expensive technologies or invasive procedures. Instead, healthcare experts can mitigate these risks and optimize medication use through comprehensive medication management (CMM) in practice with evidence-based guidance.

Comprehensive medication management (CMM)

Comprehensive medication management (CMM) enables clinical pharmacists and physicians to use “a systematic approach to medications 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.”⁹ Previous white papers from the American College of Clinical Pharmacy (ACCP) define CMM in team-based care.¹⁰ CMM, as a patient-centered approach to medication management, is shown to reduce healthcare costs and improve the patient

care experience, provider wellbeing, and overall care.⁹ Studies have shown improved medication adherence,¹¹ patient experience, healthcare costs, and provider well-being following CMM reviews.^{1,2}

Pharmacogenomics and CMM

Pharmacogenomics has utility as a multifactorial process that assesses the genome and explores its association with medication optimization.¹³ Genetically guided selection of medications has improved cost avoidance¹⁴ and clinical utility,¹⁵ especially in treating patients with multimorbidity (e.g., depression, cardiovascular diseases) and polypharmacy.¹⁶ Interprofessional CMM models that consider genetic variants are shown to mitigate medication-related problems (MRPs) and improve medication safety.¹⁷ It is also shown that improved disease management and prevention is achieved through precision medicine using pharmacogenomic testing.¹⁶ Tools that integrate genotypic information, predict phenotypes, and identify potential phenoconversion are proven to be advantageous in patients with polypharmacy and chronic diseases.¹⁷⁻²²

Overall, pharmacogenomic testing as part of a more personalized and precise medicine strategy steers away from the one size fits all model and could significantly improve the utility and value of CMM. We intend this paper to be a resource and reference to educate healthcare professionals on the value of precision medicine and pharmacogenomic testing services in CMM care models.

2. Operationalizing Pharmacogenomics into the Delivery of CMM

Key elements should be considered before integrating pharmacogenomic services into an existing CMM care model. A well-defined workflow process to optimize interactions within the healthcare team is vital to the success of any CMM program.²³ In 2003, Hood *et al.* predicted that pharmacogenomics would lead to novel approaches in drug discovery, including an individualized application of drug therapy and new insights into disease prevention.²⁴ *Scientific knowledge* has evolved significantly since then; however, the translation of this information into *clinical practice* has been challenged by the hurdles raised by the systematic approaches for success²⁵ and the continued need for stakeholder and management support.

2.1. An iterative model

The integration of pharmacogenomics into CMM care models is a process that employs several concepts that must be mastered by the clinician to ensure safe, effective, and optimized medication use across various systems. For example, variant

Table 1: Examples of pharmacogenomic information on drug labels

Genomic biomarkers
Drug exposure and clinical response variability
Risk for adverse events
Genotype specific dosing
Mechanisms of drug action
Polymorphic drug target and disposition genes
Trial design features

alleles may impact either the pharmacokinetic (e.g., drug metabolizing enzymes or transporters) or pharmacodynamic (e.g., drug receptor or intra/extracellular enzymatic systems) properties of a drug in an individual, thus dictating considerations for dosing changes or therapeutic alternatives for the patient.

Pharmacogenomic considerations are not, however, included in usual evidence-based guidelines for the management of chronic diseases, especially given the notion that national consensus treatment guidelines formulate their recommendations using generalizable evidence from large populations enrolled in randomized clinical trials rather than information from selected individuals.²⁶⁻²⁸ Once the use of pharmacogenomic information becomes part of the clinical decision procedure, a constant and reiterative effort must be implemented to refine the process. See **Figure 1** for a graphic depiction of the combined model.

2.2 Walk before you run

Currently, more than 300 therapeutic products recognized by the United States Food and Drug Administration (FDA) include pharmacogenomic information in their drug labeling (see **Table 1** for type of information).²⁹

CMM programs may find it particularly challenging to launch broad pharmacogenomics programs that aim to test all therapeutic classes of medications and their various indications. It is highly advisable to focus on a series of drugs (either from a drug class or a particular indication or those impacted by gene variants tested by a particular assay on a selected gene), then make interventions only for those drugs or those genes. One ideal way to initiate such services and gain confidence is to follow clinically actionable gene-drug pairs described by the Clinical Pharmacogenetics Implementation Consortium (CPIC) in their consensus guidelines.³⁰

For instance, as a first step to establishing a pharmacogenomics program foundation, one could apply pharmacogenomic knowledge related

to CYP2C19 for clopidogrel, CYP2C9 for warfarin, or CYP2D6 for some antidepressants. As a second step, one could review additional drugs that share similar metabolic pathways involving CYP2C19, such as proton pump inhibitors, or CYP2C9, such as nonsteroidal anti-inflammatory drugs, and finally on CYP2D6, such as opioids. As a final step, one may want to consider drugs impacted by more than one genetic polymorphism, such as antidepressants being metabolized by CYP2D6 and CYP2C19, or warfarin being metabolized by CYP2C9 and interacting with the vitamin K epoxide reductase complex encoded by VKORC1, and then the role of CYP4F2 and CYP2C cluster.

2.3 Initiate your combined pharmacogenomic-CMM program by targeting a special population

At the initiation of a pharmacogenomic program, it is advisable to start the person-centered CMM activities by targeting patients who are treated for one specific disease. Select patients with diseases that are relevant based on your clinical activities and expertise. For instance, one could start by focusing on patients who are treated with azathioprine for rheumatoid arthritis. In this case, it would be important to recognize the major enzymatic systems involved in the activation of the prodrug to its active metabolites (i.e., thioguanine nucleotides).

For example, clinicians should be cognizant of the effects of thiopurine methyltransferase (TPMT) and nudix hydrolase (NUD15) enzymes, as both exhibit genetic polymorphisms associated with reduced enzyme activities (e.g., *TPMP*2*, *TPMP*3A*, *TPMP*3C*, *NUDT15 C415T rs11685232*). These polymorphisms have the potential to impact azathioprine's dosage and administration, as well as the patient's risk of toxicity and myelosuppression associated with higher levels of thioguanine. Clinicians should consider guidelines from CPIC and the Dutch Pharmacogenetics Working Group (DPWG) when determining appropriate doses for individuals with low or deficient enzyme activity.³¹⁻³⁴

As a second example, one could consider the role of the hepatic solute carrier organic anion transporter family member 1B1 (SLCO1B1) on the efficacy and toxicity of simvastatin in patients treated for hypercholesterolemia, and even consider other factors in a research environment, such as the role of the monocarboxylate transporter 1 (MCT1) on drug accumulation in muscle cells and toxicity that may be not currently part of the guidelines.^{35,36}

Once a practitioner masters most of these skills, pharmacogenomic testing could target patients who are unable to reach therapeutic goals or experience ADEs in the context of a more

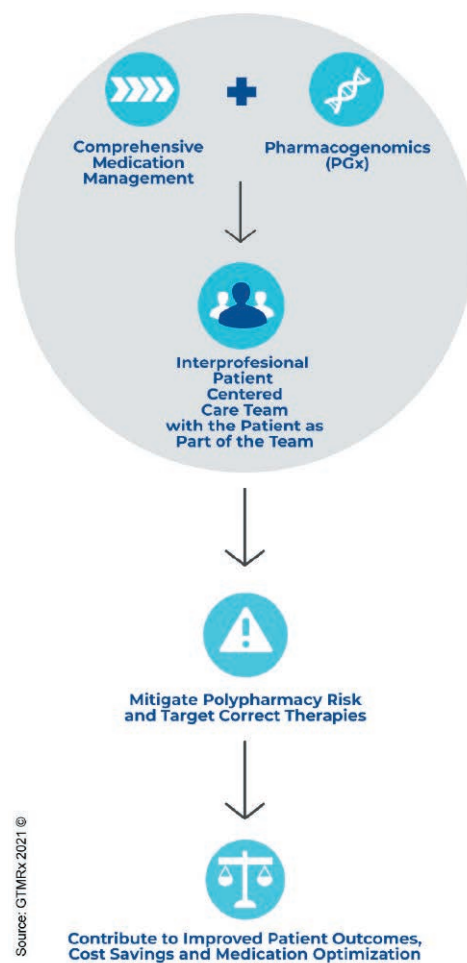


Figure 1: A comprehensive medication management and pharmacogenomic testing model.

comprehensive strategy that defines a person-centered CMM approach.¹⁰ This could include patients with multimorbidity, with polypharmacy, or who can benefit from preventative therapy.¹⁰ Yet, this approach would require one to understand the patient's medication history, comorbidities, preferences, and beliefs.⁹

It is important to note that patients with polypharmacy often need more extensive pharmacogenomic interpretation, as they are more likely to have multiple drug-gene and drug-drug gene pair interactions. Medication therapy should be evaluated using a person-centered approach that identifies environmental factors (e.g., smoking tobacco) and actual use patterns of all medications, including over-the-counter, bioactive supplements, recreational drugs, and prescriptions. Risk stratification strategies can be useful in identifying patient cohorts suitable for these services.^{4,37} Thus, the complementary outcomes associated with pharmacogenomics and CMM care

models have the potential to optimize medication safety, effectiveness, and appropriateness.

2.4 Phenoconversion

Interpretation of a genetic test result and translation of the genetic code into a predicted phenotype of a person is faced with obstacles. One must question:

- i. what is the reproducibility and precision of the test used?
- ii. were the appropriate single nucleotide polymorphisms, alleles, and haplotypes tested?
- iii. how were the results validated? and
- iv. were the results predictive of a phenotype?

For example, one cannot ascertain the “predicted phenotype” from a report if only five different alleles are tested for *CYP2D6*, as we know that more than 100 different alleles exist, leading to various haplotypes and phenotypes.²⁵ Expert tools have been developed to assist practitioners, but they require routine updates and should be reflective of the demographic population being tested.³⁸ One proposed solution is the use of therapeutic drug monitoring, if available, to predict accuracy of phenotypes.

Next, one should consider other confounding variables that could modify the predicted phenotype into the clinically “observed phenotype.” The modulation of phenotypic traits is called phenoconversion.

For instance, a genetic test using DNA sequencing could establish that a patient is *CYP2D6 *1/*1*, also known as a normal metabolizer of *CYP2D6* as the predicted phenotype. Based on this result, one would expect the patient to “normally” metabolize *CYP2D6* substrates, such as beta blockers (e.g., propranolol, metoprolol, nebivolol, carvedilol),³⁹⁻⁴³ antidepressants (e.g., amitriptyline, venlafaxine),⁴⁴⁻⁴⁷ antihistamines (i.e., diphenhydramine), and to be able to activate opioid prodrugs into their active metabolites (e.g., codeine into morphine or oxycodone into oxymorphone, respectively).⁴⁷ However, coadministration of medications that are potent inhibitors of *CYP2D6*, (e.g., quinidine, terbinafine, or paroxetine) or higher affinity substrates (e.g., bupropion) would decrease *CYP2D6* activity and impair the metabolism of other medications, thus, potentially phenoconverting a “normal metabolizer” into either an “intermediate metabolizer” or a “poor metabolizer.”¹⁹

Diseases such as type 2 diabetes and chronic inflammatory status can also modulate *CYP450* activities associated with phenoconversion.^{48,49} Under these conditions, the risk of toxicity would be increased for active products, and a lack of efficacy would be expected for the prodrugs.



The benefit of combining pharmacogenomic testing with a CMM approach is the ability to consider all covariables (normal or phenoconverted) that may impact, the predictive appreciation and estimation of the individual's ability to metabolize drugs and expected efficacy or toxicity.

2.5 Obtain access to Advanced Clinical Decision Support Systems (CDSS)

As patients continue to present with more complex drug regimens, clinicians need access to comprehensive tools. Use of advanced CDSS guides healthcare members and improves the quantity of clinically relevant recommendations⁵⁰ while considering the most appropriate medication given unique patient characteristics. Advanced CDSS also help to personalize drug regimens that are in alignment with national consensus treatment guidelines, but otherwise not optimal given patient-specific drug-drug interactions and genetic predispositions. Interprofessional team-based care with a clinical pharmacist working in collaborative practice with a physician is one way that healthcare workers can practice synergistically, with all their competencies supported by CDSS to take into consideration pharmacokinetic/pharmacodynamic drug properties, drug-drug interactions, pharmacogenetics, and efficacy and toxicity of each active drug ingredient.⁵¹

At minimum, clinicians should be preemptively alerted by the CDSS to the potential of a gene-drug

interaction. Most clinicians are only exposed to interruptive alerting; in the ideal case, clinicians should also have access to advanced CDSS that go beyond traditional drug-drug interaction databases and software systems. The advanced CDSS should provide meaningful and actionable clinical insights by considering every element of a medication regimen.^{4,52,53} Furthermore, the provision of computer-based decision support and clinical recommendations employed by CDSS is known to improve clinical practice.⁵⁴

2.6 Work as a team

Clinical pharmacists should work in tandem with other clinicians to assess the patient, evaluate medication therapy, and develop an action plan.¹⁰ Clinical pharmacists also play a key role in the assessment of a drug regimen for medication appropriateness, effectiveness, safety, and adherence – while collaborating with others to help the patient achieve clinical goals for each therapy.⁹ It is also critical that such assessments take into account not only the pharmacogenomics, but also the pharmacodynamic and patient demographic variables that influence medication effectiveness.

The final component associated with a successful pharmacogenomic-integrated CMM care model is the development of a patient action plan that includes baseline health marker data and goals of therapy. To achieve desired clinical goals and outcomes, routine follow-up with patients is required to determine effects of changes,

reassess actual outcomes, and recommend further therapeutic changes.⁹ Watanabe *et al.* proposed that clinical pharmacists play a key role in the expansion of CMM programs, particularly through collaborative practice agreements (CPAs), and these programs should include pharmacogenomics-based practices.⁵⁵ Interprofessional collaborative practice (ICP) enables healthcare professionals to complement the expertise of one another to improve patient health outcomes.⁵⁶ Studies have documented that CPAs between clinical pharmacists and prescribers may have value in this arena and lends evidence to support that ICP improves patient health outcomes and reduced costs.⁵⁵

2.7 Favor pre-emptive testing

Conceptually, pharmacogenomic testing requires the collection and transfer of a sample to a specialized laboratory, sample processing for DNA isolation and analysis, data interpretation, return of results, and medication profile reevaluation. To date, the usual time encountered between sample collection and obtaining results is approximately 7-10 days.⁵⁶ This delay in turnaround time prohibits the prescriber from efficiently using the results from pharmacogenomic testing to initiate appropriate therapy. Pharmacogenomics is experiencing a shift from a reactive approach to a more proactive testing model.²⁵ With consented, preemptive testing, the prescriber and the clinical pharmacist ▶



In certain populations (e.g., Programs of All Inclusive Care for the Elderly, PACE), the cost-avoidance benefits of pharmacogenomic-integrated CMM care models have demonstrated promising results.¹⁴ One study by Bain *et al.* found a mean cost avoidance of \$1,983 per actionable drug-gene pair.¹⁴ Another study found that pharmacists using a pharmacogenomics tool designed to analyze cumulative drug-gene interaction helped predict the magnitude of drug-level changes and provided more meaningful recommendations to providers.⁶¹ As a result, multi-gene tests are superior to single gene tests, given their increased cost effectiveness.⁶⁹

In other cases, pharmacogenomic testing guides clinicians to reduce total medication costs and improve patient outcomes by reducing risks associated with unsafe medications.⁷⁰ In one study, pharmacogenomic testing decreased the probability of death from suicide compared to patients who received standard care for certain mental health conditions.⁶⁴ Thase *et al.* also found that provider education and patient satisfaction improved with pharmacogenomic testing.⁶⁴ Hence, the significance of testing is that it facilitates identification of MRPs and optimization of medication action plans used in CMM.⁶²

Finally, studies consistently show that nearly all patients carry at least one actionable pharmacogenomic variant,^{69,71} and that nearly one in five medications in the United States have a labeled pharmacogenomic recommendation based on those variants.⁷² For many years, pharmacogenomic testing has been valued and acclaimed in various settings – including CMM and PACE – towards the mitigation of polypharmacy, optimization of medication regimens and patient outcomes, and cost savings.¹⁴

As preemptive pharmacogenomic testing has been associated with reduced ADEs,⁷³ it is advisable to incorporate preemptive testing into CMM care models. Importantly, patients should not be excluded based on certain conditions, as there

Table 2: Recommended data to collect and monitor to facilitate reimbursement

Patient name/ID
Insurer
CD-10 code
Medications at time of test order and/or results
CPT code
Amount billed
Test successfully reimbursed (yes/no)
Amount reimbursed (e.g., full, partial)

have direct access to the results during the assessment and prescribing process. In the context of a CPA between the clinical pharmacist and providers, information can be readily available in real time, and pharmacogenomic results are better received in appropriate context.²² In addition, patient convenience is optimized using a CPA as it decreases the demand on the pharmacogenomic laboratory and offers more sufficient time for reporting and result interpretation.

2.8 Stakeholder acceptance

One key prerequisite for implementing an effective pharmacogenomic-integrated CMM care model is prescriber and patient acceptance. Another critical element is the need for management buy-in to support and maintain the pharmacogenomic-integrated CMM care model under their purview. Often, clinician resistance results from poor literacy in genomics.²⁵ Some studies have defined a need to supplement pharmacogenomic test results with educational materials and courses to support implementation.^{58,59} One survey by Peterson *et al.* found that educational course

participation better informed healthcare providers on the use of pharmacogenomics in their practice.⁶⁰ In addition, education may promote the integration of pharmacogenomic test results into the care plan and further mitigate medico-legal risks associated with clinical negligence.

Hence, it is advised that all pharmacogenomic-integrated CMM care models integrate educational courses. Education is crucial to effect change, so the next generation of prescribers can use pharmacogenomics as a tool to optimize treatment outcomes. In turn, prescribers are able to advise patients with knowledge about the process and purpose of preemptive testing.

3. Value of Pharmacogenomic-Integrated CMM Care Models

Pharmacogenomic integration into existing CMM care models is known to decrease cost⁶¹ and to improve provider education and patient satisfaction.^{61,62} In addition, the value of pharmacogenomic-integrated CMM care models improves patient access to healthcare,⁶² and clinical outcomes.^{62,64-68}

is a clear association between the potential for preemptive testing and improved patient outcomes for all patients.²⁵

4. Reimbursement Mechanisms for Pharmacogenomic CMM Services

Payer coverage for pharmacogenomic testing remains inconsistent in the United States, but it is improving. Current procedural terminology (CPT®) codes have been developed to facilitate billing and coverage of some single gene tests.⁷⁴ Certain large commercial payers have introduced new coverage policies for multigene panels, specifically for antidepressants and antipsychotics.⁷⁵ Similarly, significant new local coverage determinations (LCDs) that include both single and panel-based tests were promulgated for Medicare beneficiaries through the MoDx program.⁷⁶ Testing for more than 50 actionable gene/drug pairs included in CPIC guidelines and/or FDA labeling is covered for patients in the 28 states impacted.⁷⁶ However, the guidelines are vague regarding coverage in preemptive testing models, as the policies convey that testing is indicated when medications are being considered for use (or medications that have already been administered); particularly for those that are medically necessary, appropriate, and approved for use based on indication and known gene(s)-drug interactions.

Since reimbursement for pharmacogenomic testing remains inconsistent, the field faces multiple challenges in this area. Reimbursement is determined by the insurer based on their own analyses of available evidence supporting the clinical utility of testing. This inconsistency creates a lack of transparency that drives a cautious approach for many providers that are considering clinical billing for pharmacogenomic testing.

There is also significant variability among insurers, which creates apprehension and hesitancy among providers who are ordering the test. While CPT® codes are now available for pharmacogenomic testing, documentation of testing and results in medical records is inconsistent.⁷⁷

The major medical insurance industry has been largely resistant to advocacy and other efforts to standardize evidence evaluation, clinical utility determination, and documentation for pharmacogenomic testing. In addition, while pre-emptive pharmacogenomic testing is preferable to reactionary single-gene testing, many insurers remain hesitant to cover panel-based testing as compared with single-gene tests despite the clear benefit of panel-based testing.⁷⁸ Finally, because it is an emerging science, many clinicians are unfamiliar with the billing logistics for pharmacogenomic

testing and may have difficulties navigating this process.

Beyond the testing, scaling reimbursement for clinician services is also needed to establish CMM services that incorporate pharmacogenomics. Because testing is scientifically complex, results can affect numerous medications at the time the test is conducted and throughout the patient's lifetime and thereby create challenges for reimbursement in a CMM setting. Fewer patients may be eligible for pharmacogenomic testing coverage as compared to patients qualifying for CMM. This could decrease sustainability of pharmacogenomics as a CMM service and limit its growth.⁷⁹ Unlike many other routine clinical tests, pharmacogenomic testing may require pre- and post-test medication assessment and/or patient education. Therefore, it is not solely the test that must be reimbursed, but also the provider's time and efforts.⁸⁰ Until pharmacogenomics has established a history of clinical use, several patient visits may be required to allow for time for the test results to be returned and pre- and/or post-test counseling (i.e., two-visit care model). Taken together, these may complicate financial viability.

4.1 Research your patient and payer mix

Before beginning pharmacogenomic-integrated CMM care models, identify which of your patients are most likely to benefit and their primary insurer to identify existing pharmacogenomic testing coverage policies, indications, billing codes, and any documentation requirements. Some insurers provide guidance for documentation needed for test reimbursement. For example, the Centers for Medicare and Medicaid Services (CMS) LCD for pharmacogenomic testing states that among required elements, providers must have a record of drugs being considered for treatment and their indications to ensure test coverage.⁸⁰ It further specifies that pharmacogenomic testing is not considered reasonable and necessary solely based on a patient having a particular diagnosis.⁸⁰ Although not universally applicable, this type of guidance is increasingly available from insurers to inform best billing and documentation practices for pharmacogenomic testing. This step can also help clinicians identify if payers have any requirements for or restrictions on coverage of pre-emptive vs. single gene testing.

4.2 Document billing and reimbursement outcomes

Clinicians should consider adopting a continuous quality improvement approach to pharmacogenomic test reimbursement data. Ongoing monitoring of billing data metrics can inform needed changes in the

clinical service or workflow to optimize the likelihood of reimbursement. Documentation and dissemination of these data are also important in moving pharmacogenomic CMM models forward, as it provides clinicians who are considering implementing pharmacogenomics with objective information to guide their operational strategies. **Table 2** shows the data that is most recommended to collect and monitor on an ongoing basis.

4.3 Explore strategies to increase efficiencies and educational opportunities

Use of mechanisms to streamline pre- and post-test patient education, medication management, and clinician engagement can help increase sustainability of a new service. For example, choosing whether to adopt a two- vs. one-visit model, degree of reliance on telehealth or printed materials as compared with face-to-face education, and choice of documentation strategy can all influence the quality of care, as well as financial viability of a new service. Use of appropriate patient-facing clinical decision support (e.g., patient/provider education and return of results via secure web portal) for genomic data has been shown to be feasible, may enhance patient and provider understanding, and can help streamline the education process.⁸¹

4.4 Explore emerging practice models

Pharmacogenomics could be integrated into established CMM practices within employer health programs or chronic care management programs. One example reduced healthcare spending through a collaborative partnership between retirees, physicians, and pharmacists from a coalition.⁸² The pilot program's real time approach contributed to it as a scalable model for employers and other benefit managers.⁸² New clinics in community settings that incorporate creative multidisciplinary models involving clinical pharmacists, physicians, and genetic counselors have been deployed^{83,84} and can support billing through CPAs or established providers.

5. Conclusion

Integration of pharmacogenomic testing into CMM care models is fulfilling its promise to increase cost savings, improve patient outcomes, and ensure medication safety. To achieve this promise, healthcare teams should participate in educational courses to improve health literacy in genomics. As more healthcare providers become knowledgeable in pharmacogenomics, testing should be considered for all patients that receive CMM services, especially, those on multi-drug regimens who have:

- 1) a higher likelihood of positive correlations of the pharmacogenomic results to their medication outcomes;
- 2) an increased probability of phenoconversion, and

- 3) genotype-to-phenotype mismatches requiring results interpretation.

Finally, healthcare systems should adopt pharmacogenomic-integrated CMM care

models that use advanced clinical decision support systems to personalize care and mitigate the risk of medication safety related problems, adverse drug events, and medication related mortality. [JOPM](#)



Jennifer M. Bingham

Dr. Jenny Bingham, PharmD, BCACP serves as Director of Ambulatory Care Residency Programs & Research at Tabula Rasa HealthCare and is a Clinical Instructor in the Department of Pharmacy Practice and Science at the University of Arizona. Dr.

Bingham is a sought-after presenter, speaker, and author on telehealth. She has published more than 30 peer reviewed articles and presented her research at national and international venues. She received her doctor of pharmacy degree from the University of Arizona College of Pharmacy. Throughout her career, Dr. Bingham has held numerous leadership roles in interprofessional organizations and led pharmacogenomic and transitions of care programs. She has been recognized as the Next-Generation Pharmacist Technology Innovator of the Year by Pharmacy Times for her work on advancing patient care standards and business profitability. Dr. Bingham also received the Jack R. Cole PhD Distinguished Alumnus Award from the University of Arizona College of Pharmacy for her leadership and positive impact on the pharmacy profession.



Veronique Michaud

Veronique Michaud, BPharm, MSc, PhD, is the Chief Operating Officer of the Tabula Rasa HealthCare Precision Pharmacotherapy Research & Development Institute in Lake Nona. She was previously associate professor,

Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, associate professor, Faculty of Pharmacy, Université de Montréal and researcher at the University of Montreal Hospital Research Center (CRCHUM). She directed a pharmacokinetic and bioanalytic core facility at the CRCHUM. Dr. Michaud is currently an adjunct professor, Faculty of Pharmacy, Université de Montréal. Dr. Michaud is recognized for her unique expertise in pharmacokinetics, drug-metabolism, drug-drug interactions, pharmacogenomics and the study of intracellular drug-metabolism. Her research investigates the contribution of CYP450 drug-metabolizing enzymes in drug disposition, with a special attention to the role of disease states (focusing on type 2 diabetes), the role of pharmacogenomics and drug-drug interactions while attempting to better understand and predict variation in drug responses. She has earned more than \$22 million in research awards, published more than 62 peer-reviewed journal articles, and mentored graduate students and Pharm.D. residents. Dr. Michaud completed postdoctoral fellowships at Indiana University and McGill University and earned her PhD and MSc degrees from the Université de Montréal.



Kristin Wiisanen

Dr. Wiisanen is associate director of the University of Florida Health (UF Health) Precision Medicine Program, director of Continuing Pharmacy Education, director of the Graduate Program in Precision Medicine, and clinical professor in

the Department of Pharmacotherapy and Translational Research in the College of Pharmacy. Dr. Wiisanen leads clinical and educational efforts for pharmacogenomics in the UF Health Precision Medicine Program and serves as residency program director for an accredited postgraduate Clinical Pharmacogenetics Residency and Director of the Clinical Fellowship in Pharmacogenomics program. She is Editor-in-Chief of Pharmacy Today for the American Pharmacists Association (APhA), a fellow of APhA and the American College of Clinical Pharmacy, and a University of Florida Entrepreneurial Faculty Fellow. Dr. Kristin Wiisanen received her Pharm.D. from the University of Florida in 1998 and completed residency training at the Medical College of Virginia.



Jill Bates

Jill S. Bates is an experienced clinical pharmacist with a demonstrated history of working in the hospital and health care industry. Skilled in clinical research, oncology, hematology, pharmacy and health care, she currently serves as the

program manager for the PHASeR (Pharmacogenomics Action for Cancer Survivorship) initiative—a public-private partnership between the VA and Sanford Health, one of the largest health systems in the United States, which pledges to genetically test 250,000 veterans at 125 sites by 2022 – all at no cost to the veterans. Prior to entering the profession of pharmacy, Jill was a high school science teacher. As part of her professional service, Jill has been an active member of ASHP as well as HOPA. Jill's involvement with ASHP has included serving on the Council on Therapeutics as vice chair and chair. In addition, she served on the New Practitioner Education Advisory Group and as a member of the Educational Steering Committee and Clinical Leadership Section Advisory group for the Section of Clinical Specialists and Scientists. In 2012, Jill was elected chair of the Section of Clinical Scientists and Specialists and currently serves in this role. She holds a leadership position on the UNC Chemotherapy Policy Advisory group and participates in the Oncology Pharmacy and Therapeutics Committee, Oncology Patient Education Committee and the Interdisciplinary Triad Committee for Performance Improvement of Acute Care Hematology/Oncology Services. As part of her professional service, Jill is an active manuscript reviewer for various pharmacy journals. She received her doctor of pharmacy degree at the University of Illinois at Chicago and a research-based master of science in biochemistry and biophysics from Northern Illinois University. Jill completed an ASHP-accredited pharmacy practice (PGY1) and oncology (PGY2) residency at Duke University Medical Center, and she is board-certified in oncology pharmacy.



Anthony P. Morreale

Anthony Morreale has served as the Associate Chief Consultant for Clinical Pharmacy and Policy for the Department of Veterans Affairs Pharmacy Benefits Management in VA Central Office since 2018. For the previous 8 years he served as the Assistant Chief Consultant for Clinical Pharmacy Services and Healthcare Services Research. Morreale has led multiple initiatives focused on organizing,

standardizing and expanding the scope of clinical pharmacy practice throughout the VA. His major responsibilities are focused on identifying and resolving gaps in patient care in which clinical pharmacists have demonstrated positive outcomes and to establish new roles in complex medication management environments where clinical pharmacists can use their knowledge and training to improve patient care. His long career as a clinical pharmacist, married with his interest in pharmacoconomics, formulary management and clinical pharmacy health services research, resulted in the creation and implementation of numerous innovative practices for clinical pharmacists. Some of Morreale's groundbreaking accomplishments include creating the first VA pharmacogenomics and pharmacogenomics pharmacist positions, serving as a founding member of VA's national formulary and PBM outcomes research group, establishment of the first accredited oncology, pharmacoconomics, pharmacogenomics, nephrology and clinical informatics residency programs in VA, and establishment of the national VA PBM Clinical Pharmacy Practice Office, which led to the development of comprehensive programs involving integration of clinical pharmacy specialists (CPS) into Patient Aligned Care Teams (PACT), mental health, pain management, antimicrobial stewardship, hepatitis C, Substance Use Disorders and rural health. Morreale is board certified in pharmacotherapy and has been the recipient of numerous professional recognitions and awards including being recognized as a Fellow of the American and California Society of Health Systems Pharmacists for his many contributions to the profession. He has also been recognized as an honorary member of the United States Public Health Service for his dedication to public health initiatives. He is a past recipient of the ASHP Best Practice Award, ASHP Literature Award for innovation, VA Under-Secretary's Innovation Award, JMCP Quality Reviewer Award for Accuracy and Thoroughness, San Diego Society Pharmacist of the year, Pharmacy Foundation of California Michelotti Public Health Prize, and most recently the AMCP Steven G. Avey Award and the APhA Distinguished Federal Pharmacist award, which recognizes sustained, exemplary and distinguished service to the profession. Morreale has authored or co-authored more than 60 peer reviewed articles, has served on editorial boards, and as reviewer on a number of journals and has been actively involved in leadership roles within many pharmacy organizations, both nationally and internationally.



Philip E. Empey

Dr. Philip Empey is the associate director for Pharmacogenomics of the Pitt/UPMC Institute for Precision Medicine and leads the PreCISE-Rx and Test2Learn teams to implement pharmacogenomics clinical, research and educational

initiatives. He also directs the University of Pittsburgh – Thermo Fisher Scientific Pharmacogenomics Center of Excellence which is deploying population scale preemptive pharmacogenomics testing (to >150,000 patients) in western Pennsylvania. As a clinician-scientist in the Department of Pharmacy and Therapeutics, Dr. Empey conducts NIH-funded clinical and translational research aimed at understanding the mechanisms of the variability in drug response to improve medication-related outcomes in critically-ill patients. He received

his Pharm.D. from the University of Rhode Island and completed PGY1 and PGY2 residencies in Pharmacy Practice and Critical Care at the University of Kentucky. He earned a Ph.D. in Clinical Pharmaceutical Sciences at the University of Kentucky before completing postdoctoral research training at the University of Pittsburgh.



Rustin D. Crutchley

Dr. Rustin Crutchley is an Associate Professor in the Department of Pharmacotherapy in the College of Pharmacy and Pharmaceutical Sciences at Washington State University (WSU). He actively teaches different courses in

pharmacogenomics, including a HIV/Precision Medicine advanced pharmacy practice experience (APPE) rotation he established in South Africa. Dr. Crutchley is a certified American Academy of HIV Medicine Pharmacist (AAHIVP). He currently works as a clinical pharmacist/pharmacogenomics consultant at Comprehensive Healthcare. Prior to WSU he served as a faculty member at the University of Houston, also working as a HIV Clinical Pharmacist in both adult and pediatric populations. In this position he was a residency director and preceptor for a new PGY-2 HIV Ambulatory Care/Clinical Pharmacogenetics residency he created. Dr. Crutchley received his Pharm.D. from University of North Carolina at Chapel Hill. He received his PGY-1 Pharmacy Practice Residency at the University of Texas at Tyler and his PGY-2 HIV Specialty Residency at State University of New York at Buffalo. He also completed a STAR Health Disparities Fellowship at the University of North Texas Health Science Center at Fort Worth, TX.



Ghada Elnashar

Dr. Ghada Elnashar is the medical science liaison at OneOme.

There, she educates and informs key opinion leaders, providers, and other healthcare professionals on pharmacogenomics. She leads in bringing the benefits of precision medicine so as to help improve healthcare outcomes and reduce healthcare costs. Dr. Elnashar completed her residency training in Managed Care at HealthPartners clinics and health plan. She earned her M.S. in Biotechnology from The Johns Hopkins University and her Pharm.D. from the University of Minnesota. Throughout her proliferative career, she helped patients on both the individual and population level.



Jane Gilbert

Jane Cheshire Gilbert is the director of retiree health care for the Teachers' Retirement System of the State of Kentucky (TRS) and has served TRS retirees since April 2002. She manages two retiree health plans covering 48,000

retirees. She also serves as a leader in the areas of health insurance cost containment, project management, risk management and federal health care solutions. Gilbert served in management and directorship positions for a Louisville Kentucky law firm and cost containment company, The Rawlings Company, from 1989 through 2002. Prior to that, she worked as an accountant for a national CPA firm. Gilbert earned a bachelor's degree in accounting from Bellarmine University in Louisville, Kentucky and is a certified public accountant and a certified government benefits administrator. She currently serves on the board of the State and Local Government Benefits Association and is a member of the Public Sector Healthcare Roundtable.



Jacques Turgeon

Jacques Turgeon, BPharm, PhD, is the Chief Scientific Officer at Tabula Rasa HealthCare in Moorestown, N.J., and CEO of the company's Precision Pharmacotherapy Research and Development Institute in Lake Nona. He was previously associate

dean of the Lake Nona campus at the University of Florida (UF) College of Pharmacy and professor in the Department of Pharmaceutics. Before joining UF, Dr. Turgeon held several leadership positions at the University of Montreal, as vice-rector for research, dean of the School of Pharmacy, chief executive officer of the university hospital, and director of the hospital's research center. He also taught pharmacology at the University of Pennsylvania Perelman School of Medicine. Dr. Turgeon is a known expert on pharmacogenetics and drug-drug interactions, particularly among treatments for cardiovascular disease. Through his research, he has worked to implement clinical decision support systems and optimize patient care. In 2010, Dr. Turgeon received the Prix Louis-Hébert Award for career excellence from the Ordre des pharmaciens du Québec. For his contributions to pharmacology education and training he took home the Prix d'excellence en enseignement from the Université Laval twice, in 2011 and 2013. He is a fellow of the Canadian Academy of Health Sciences and Académie Nationale de Médecine, France. Dr. Turgeon began his pharmacy studies at the Université Laval in Québec, Canada, earning his BSc, MSc, and PhD from the École de Pharmacie. In 1998, he moved to Nashville, Tenn., to pursue a postdoctoral fellowship in the Department of Clinical Pharmacology at Vanderbilt University. He has supervised and mentored more than 100 undergraduate and graduate students and belongs to numerous societies, including the American Heart Association, the International Society for the Study of Xenobiotics, and the Canadian Society of Pharmacology and Therapeutics. Dr. Turgeon is the newest member of the American Society for Clinical Pharmacology and Therapeutics (ASCPT) board of directors and began his appointment as treasurer in March 2019.

References

- Centers for Disease Control and Prevention. Available online: <https://www.cdc.gov/nchs/products/databriefs/db328.htm> (accessed 2 June 2020)
- American Society of Pharmacovigilance. Available online: <http://fourthcause.org/> (accessed 5 May 2021)
- Reis, C.M.; Dos Santos, A.G.; de Jesus Souza, P.; Reis, A.M.M. Factors associated with the use of potentially inappropriate medications by older adults with cancer. *J Geriatr Oncol* 2017,8(4),303-307.
- Banks, D.; Jin, H.; Fimmel, S.; Michaud, V.; Knowlton, C.; Turgeon, J.; Stein, A. Association of a Novel Medication Risk Score with Adverse Drug Events and Other Pertinent Outcomes Among Participants of the Programs of All-Inclusive Care for the Elderly. *Pharmacy* 2020, 8(2), 87.
- Lown Institute. Available online: <https://lowninstitute.org/projects/medication-overload-how-the-drive-to-prescribe-is-harming-older-americans> (accessed 5 May 2021)
- Ratigan, A.; Michaud, V.; Turgeon, J.; Bikmetov, R.; Gaona, G.; Anderson, H.; Pulver, G.; Pace, W. Longitudinal Association of a Medication Risk Score With Mortality Among Ambulatory Patients Acquired Through Electronic Health Record Data. *J Pat Safety* 2021 [Epub ahead of print].
- Häppölä, P.; Havulinna, A.S.; Tasa, T.; Mars, N.J.; Perola, M.; Kallela, M.; Milani, L.; et al. A data-driven medication score predicts 10-year mortality among aging adults. *Sci Rep* 2020 Sep 25, 10(1), 15760.
- Radomski, T.R.; Zhao, X.; Hanlon, J.T.; Thorpe, J.M.; Thorpe, C.T.; Naples, J.G.; et al. Use of a medication-based risk adjustment index to predict mortality among veterans dually-enrolled in VA and Medicare. *Health (Amst)* 2019, 7(4), S2213-0764(18)30230-
- Patient-Centered Care Primary Care Collaborative. Available online: <https://www.pccpc.org/sites/default/files/media/medmanagement.pdf> (accessed 6 May 2021).
- American College of Clinical Pharmacy. Available online: <https://www.accp.com/docs/positions/misc/CMM%20Brief.pdf> (accessed 23 October 2020)
- Brummel, A.; Carlson, A.M. Comprehensive Medication Management and Medication Adherence for Chronic Conditions. *J Manag Care Spec Pharm* 2016,22(1),56-62.
- McFarland, M.S.; Buck, M.L.; Crannage, E.; Armistead, L.T.; Ourth, H.; Finks, S.W.; et al. Assessing the Impact of Comprehensive Medication Management on Achievement of the Quadruple Aim. *Am J Med* 2021,134(4),456-461.
- Malsagova, K.A.; Butkova, T.V.; Kopylov, A.T.; Izotov, A.A.; Potoldykova, N.V.; Enikeev, D.V.; et al. Pharmacogenetic Testing: A Tool for Personalized Drug Therapy Optimization. *Pharmaceutics* 2020,12(12),1240.
- Bain, K.T.; Knowlton, C.H.; Matos, A. Cost avoidance related to a pharmacist-led pharmacogenomics service for the Program of All-inclusive Care for the Elderly. *Pharmacogenomics* 2020,21(10),651-661.
- Bain, K.T.; Matos, A.; Knowlton, C.H.; McGain, D. Genetic variants and interactions from a pharmacist-led pharmacogenomics service for PACE. *Pharmacogenomics* 2019,20(10),709-718.
- Leopold, J.A.; Loscalzo, J. Emerging Role of Precision Medicine in Cardiovascular Disease. *Circ Res* 2018,122(9),1302-1315.
- Schwartz, E.J.; Turgeon, J.; Patel, J.; Patel, P.; Shah, H.; Issa, A.M.; et al. Implementation of a Standardized Medication Therapy Management Plus Approach within Primary Care. *J Am Board Fam Med* 2017,30(6),701-714.
- Bain, K.T.; McGain, D.; Cicali, E.J.; Knowlton, C.H.; Michaud, V.; Turgeon, J. Precision medication: An illustrative case series guiding the clinical application of multi-drug interactions and pharmacogenomics. *Clin Case Rep* 2019:1-8.
- Deodhar, M.; Dow, P.; Rihani S.B.; Turgeon, J.; Michaud, V. An illustrative case of phenoconversion due to multi-drug interactions. *Clin Case Rep* 2020,1(3),1-6.
- Shoojat, S.; Bardolia, C.; Turgeon, J.; Amin, N. Medication-Related Problems in Older Adults and the Importance of Comprehensive Medication. *Clin Case Reports* 2020,10(8).
- Ballinghoff, T.; Bain, K.T.; Matos, A.; Bardolia, C.; Turgeon, J.; Amin, N.S. Opioid response in an individual with altered cytochrome P450 2D6 activity: implications of a pharmacogenomics case. *Clin Case Rep J* 2020,1(6),1-4.
- Bain, K.T.; Schwartz, E.J.; Knowlton, O.V.; Knowlton, C.H.; Turgeon, J. Implementation of a pharmacist-led pharmacogenomics service for the Program of All-Inclusive Care for the Elderly (PHARM-GENOME-PACE). *J Am Pharm Assoc* (2003) 2018,58(3),281-289.e1.
- Pestka, D.; Frail, C.; Sorge, L.; Funk, K.; Roth, M.; Sorensen, T. The practice management components needed to support comprehensive medication management in primary care clinics. *J Am Coll Clin Pharm* 2020,3(2),438-447.
- Hood E. Pharmacogenomics: the promise of personalized medicine. *Environ Health Perspect* 2003,111(11),A581-9.
- Krebs, K.; Milani, L. Translating pharmacogenomics into clinical decisions: do not let the perfect be the enemy of the good. *Hum Genomics* 2019,13,39.
- Ackley, B. J.; Swan, B. A.; Ladwig, G.; Tucker, S. (2008). Evidence-based nursing care guidelines: Medical-surgical interventions. (p. 7). St. Louis, MO: Mosby Elsevier.
- Nebraska Methodist College. Available online: <https://libguides.methodistcollege.edu/c.php?g=498278> (accessed 5 May 2021).
- Burns, P.B.; Rohrich, R.J.; Chung, K.C. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg* 2011,128(1),305-310.
- Food and Drug Administration. Available online: <https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling> (accessed 5 May 2021)
- Clinical Pharmacogenomics Implementation Consortium. Available online: <https://cpicpgx.org/guidelines/> (accessed 5 May 2021).

31. Relling, M.V.; Schwab, M.; Whirl-Carrillo, M.; Suarez-Kurtz, G.; Pui, C.H.; Stein, C.M.; et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. *Clin Pharmacol Ther* 2019, 105(5), 1095–1105.
32. Royal Dutch Pharmacists Association (KNMP). Available online: <https://www.knmp.nl/patientenzorg/medicatiebewaking/farmacogenetica/pharmacogenetics-1>. (accessed 6 May 2021).
33. Royal Dutch Pharmacists Association (KNMP). Available online: <https://www.knmp.nl/patientenzorg/medicatiebewaking/farmacogenetica/pharmacogenetics-1>. (accessed 6 May 2021).
34. Dean, L. Azathioprine Therapy and TPMT and NUDT15 Genotype. 2012 Sep 20 [updated 2020 Aug 5]. In: Pratt VM, Scott SA, Pirmohamed M, Esquivel B, Kane MS, Kattman BL, Malheiro AJ, editors. *Medical Genetics Summaries* [Internet]. Bethesda (MD): National Center for Biotechnology Information (US).
35. Vooora, D.; Shah, S.H.; Spasojevic, I.; et al. The SLC01B1*5 genetic variant is associated with statin-induced side effects. *J Am Coll Cardiol* 2009, 54(17), 1609–1616.
36. Leung, Y.H.; Turgeon, J.; Michaud, V. Study of Statin- and Lorazepam-Induced Muscle Pain Mechanisms Using Human Skeletal Muscle Cells. *Pharmaceutics* 2017, 9(4), 42.
37. Cicali, B.; Michaud, V.; Knowlton, C.; Turgeon, J. Application of a Novel Medication-Related Risk Stratification Strategy to a Self-Funded Employer Population. *Benefits Quarterly* 2018, 34, 49–55.
38. Pharmacogene Variation Consortium. Available online: <https://www.pharmvar.org/> (accessed 5 May 2021).
39. Sawinski, K.M.; Burlew, B.S. Impact of CYP2D6 poor metabolizer phenotype on propranolol pharmacokinetics and response. *Pharmacother* 1997, 17(6), 1305–10.
40. Rau, T.; Heide, R.; Bergmann, K.; Wuttke, H.; Werner, U.; Feifel, N.; Eschenhagen, T. Effect of the CYP2D6 genotype on metoprolol metabolism persists during long-term treatment. *Pharmacogenetics* 2002, 12(6), 465–72.
41. McGourty, J.C.; Silas, J.H.; Lennard, M.S.; Tucker, G.T.; Woods, H.F. Metoprolol metabolism and debrisoquine oxidation polymorphism—population and family studies. *Br J Clin Pharmacol* 1985, 20(6), 555–66.
42. Zakrzewski-Jakubiak, M.; de Denus, S.; Leblanc, M.H.; White, M.; Turgeon, J. Enantioselective quantification of carvedilol in human plasma by HPLC in heavily medicated heart failure patients. *J Pharm Biomed Anal* 2010, 52(4), 636–41.
43. Lefebvre, J.; Poirier, L.; Poirier, P.; Turgeon, J.; Lacourciere, Y. The influence of CYP2D6 phenotype on the clinical response of nebivolol in patients with essential hypertension. *Br J Clin Pharmacol* 2007, 63(5), 575–82.
44. Bertilsson, L.; Dahl, M.L.; Sjöqvist, F.; Aberg-Wistedt, A.; Humble, M.; Johansson, I.; et al. Molecular basis for rational megaprescribing in ultrarapid hydroxylators of debrisoquine. *Lancet* 1993, 341(8836), 63.
45. Lessard, E.; Yessine, M.A.; Hamelin, B.A.; O'Hara, G.; LeBlanc, J.; Turgeon, J. Influence of CYP2D6 activity on the disposition and cardiovascular toxicity of the antidepressant agent venlafaxine in humans. *Pharmacogenetics* 1999, 9(4), 435–43.
46. Hamelin, B.A.; Turgeon, J.; Vallée, F.; Bélanger, P.M.; Paquet, F.; LeBel, M. The disposition of fluoxetine but not sertraline is altered in poor metabolizers of debrisoquin. *Clin Pharmacol Ther* 1996, 60(5), 512–21.
47. Hamelin, B.A.; Bouayad, A.; Méthot, J.; Jobin, J.; Desgagnés, P.; Poirier, P.; et al. Significant interaction between the nonprescription antihistamine diphenhydramine and the CYP2D6 substrate metoprolol in healthy men with high or low CYP2D6 activity. *Clin Pharmacol Ther* 2000, 67(5), 466–77.
48. Gravel, S.; Chiasson, J.L.; Turgeon, J.; Grangeon, A.; Michaud, V. Modulation of CYP450 Activities in Patients With Type 2 Diabetes. *Clin Pharmacol Ther* 2019, 106(6), 1280–1289.
49. Darakjian, L.; Deodhar, M.; Turgeon, J.; Michaud, V. Chronic Inflammatory Status Observed in Patients with Type 2 Diabetes Induces Modulation of Cytochrome P450 Expression and Activity. *Int. J. Mol. Sci.* 2021, 22, 4967.
50. Bingham, J.M.; Michaud, V.; Turgeon, J.; Axon, D.R. Effectiveness of an Advanced Clinical Decision Support System on Clinical Decision-Making Skills in a Call Center Medication Therapy Management Pharmacy Setting: A Pilot Study. *Pharmacy* 2020, 8, 228.
51. Turgeon, J.; Michaud, V. Clinical Decision Support Systems: Great Promises for Better Management of Patients' Drug Therapy. *Exp Opin Drug Metab Toxicol* 2016, 12(9), 993–995.
52. Cicali, B.; Badaea, G.; Bain, K.T.; Knowlton, C.H.; Turgeon, J. Visualization technique for FAERS-based adverse event prediction. *Clin Pharmacol Ther* 2017, 101, S25.
53. US Trademark Registrations. Available online: <https://uspto.report/TM/88768328> (accessed 6 May 2021).
54. Kawamoto, K.; Houlihan, C.A.; Balas, E.A.; Lobach, D.F. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. *BMJ* 2005, 330(7494), 765.
55. Watanabe, J.H.; McInnis, T.; Hirsch, J.D. Cost of Prescription Drug-Related Morbidity and Mortality. *Ann Pharmacother* 2018, 52(9), 829–837.
56. Lee, J.K.; McCutcheon, L.R.M.; Fazel, M.T.; Cooley, J.H.; Slack, M.K. Assessment of Interprofessional Collaborative Practices and Outcomes in Adults With Diabetes and Hypertension in Primary Care: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2021, 4(2), e2036725.
57. Moyer, A.; Rohrer Vitek, C.R.; Giri, J.; Caraballo, P.J. Challenges in Ordering and Interpreting Pharmacogenomic Tests in Clinical Practice. *Am J Med* 2017, 130(12), 1342–1344.
58. Bank, P.C.; Swen JJ, Guchelaar HJ. A nationwide survey of pharmacists' perception of pharmacogenetics in the context of a clinical decision support system containing pharmacogenetics dosing recommendations. *Pharmacogenomics* 2017, 18(3), 215–25.
59. de Denus, S.; Letarte, N.; Hurlimann, T.; Lambert, J.P.; Lavoie, A.; Robb, L.; et al. An evaluation of pharmacists' expectations towards pharmacogenomics. *Pharmacogenomics* 2013, 14(2), 165–75.
60. Peterson, J.F.; Field, J.R.; Shi, Y.; Schildcrout, J.S.; Denny, J.C.; McGregor, T.L.; et al. Attitudes of clinicians following large-scale pharmacogenomics implementation. *Pharmacogenomics* 2016, 16(4), 393–8.
61. Brixxner, D.; Biltaji, E.; Bress, A.; Unni, S.; Ye, X.; Mamiya, T.; et al. The effect of pharmacogenetic profiling with a clinical decision support tool on healthcare resource utilization and estimated costs in the elderly exposed to polypharmacy. *J Med Econ* 2016, 19(3), 213–228.
62. Rodríguez-Escudero, I.; Cedeño, J.A.; Rodríguez-Nazario, I.; Reynaldo-Fernández, G.; Rodríguez-Vera, I.; Morales, N.; et al. Assessment of the clinical utility of pharmacogenetic guidance in a comprehensive medication management service. *J Am Clin Coll Pharm* 2020, 3, 1028–1037.
63. Haga, S.B.; Moaddab, J.; Mills, R.; Patel, M.; Kraus, W.; Allen LaPointe, N.M. Incorporation of pharmacogenetic testing into medication therapy management. *Pharmacogenomics* 2015, 16(17), 1931–41.
64. Groessl, E.J.; Tally, S.R.; Hillery, N.; Maciel, A.; Garces, J.A. Cost-Effectiveness of a Pharmacogenetic Test to Guide Treatment for Major Depressive Disorder. *J Manag Care Spec Pharm* 2018, 24(8), 726–734.
65. Thase, M.E.; Parikh, S.V.; Rothschild, A.J.; Dunlop, B.W.; DeBattista, C.; Conway, C.R.; et al. Impact of Pharmacogenomics on Clinical Outcomes for Patients Taking Medications with Gene-Drug Interactions in a Randomized Controlled Trial. *J Clin Psychiatry* 2019, 80(6), 19m12910.
66. Elliott, L.S.; Henderson, J.C.; Neradilek, M.B.; Moyer, N.A.; Ashcraft, K.C.; Thirumaran, R.K. Clinical impact of pharmacogenetic profiling with a clinical decision support tool in polypharmacy home health patients: A prospective pilot randomized controlled trial. *PLoS ONE* 2017, 12(2), e0170905.
67. Bradley, P.; Shiekh, M.; Mehra, V.; Vrbrick, K.; Layle, S.; Olson, M.C.; Maciel, A.; et al. Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: A randomized clinical trial demonstrating clinical utility. *J Psychiatr Res* 2018, 96, 100–107.
68. Greden, J.F.; Parikh, S.V.; Rothschild, A.J.; Thase, M.E.; Dunlop, B.W.; DeBattista, C.; et al. Impact of pharmacogenomics on clinical outcomes in major depressive disorder in the GUIDED trial: A large, patient- and rater-blinded, randomized, controlled study. *J Psychiatr Res* 2019, 111, 59–67.
69. Van Driest, S.L.; Shi, Y.; Bowton, E.A.; Schildcrout, J.S.; Peterson, J.F.; Pulley, J.; et al. Clinically actionable genotypes among 10,000 patients with preemptive pharmacogenomic testing. *Clin Pharmacol Ther* 2014, 95(4), 423–31.
70. Winner, J.G.; Carhart, J.M.; Altar, C.A.; Goldfarb, S.; Allen, J.D.; Lavezzari, G.; et al. Combinatorial pharmacogenomic guidance for psychiatric medications reduces overall pharmacy costs in a 1-year prospective evaluation. *Curr Med Res Opin* 2015, 31(9), 1633–1643.
71. Roden, D.M.; Van Driest, S.L.; Mosley, J.D.; Wells, Q.S.; Robinson, J.R.; Denny, J.C.; Peterson, J.F. Benefit of preemptive pharmacogenetic information on clinical outcome. *Clin Pharmacol Ther* 2018, 103(5), 787–94.
72. Relling, M.V.; Evans, W.E. Pharmacogenomics in the clinic. *Nature* 2015, 526(7573), 343–50.
73. Deenen, M.J.; Meulendijks, D.; Cats, A.; Sechterberger, M.K.; Severens, J.L.; Boot, H.; et al. Upfront genotyping of DPYD*2A to individualize fluoropyrimidine therapy: a safety and cost analysis. *J Clin Oncol* 2016, 34(3), 227–34.
74. Hefti E, Blanco JG. Documenting Pharmacogenomic Testing with CPT Codes. *J AHIMA*. 2016 Jan;87(1):56-9.
75. Anon. UnitedHealthcare to Cover Genetic Testing for Precision Medicine in Depression, Anxiety. *Clinical OMIcs*. August 2, 2019. <https://www.clinicalomics.com/topics/molecular-dx-topic/unitedhealthcare-to-cover-genetic-testing-for-precision-medicine-in-depression-anxiety/>. Accessed May 5, 2021.
76. Empey, P.E.; Pratt, V.M.; Hoffman, J.M.; Caudle, K.E.; Klein, T.E. Expanding evidence leads to new pharmacogenomics payer coverage. *Genet Med* 2021, Epub ahead of print.
77. Anderson, H.D.; Crooks, K.R.; Kao, D.P.; Aquilante, C.L. The landscape of pharmacogenetic testing in a US managed care population. *Genet Med* 2020, 22(7), 1247–1253.
78. Weitzel, K.W.; Cavallari, L.H.; Lesko, L.J. Preemptive Panel-Based Pharmacogenetic Testing: The Time is Now. *Pharm Res* 2017, 34(8), 1551–1555.
79. Heise, C.W.; Gallo, T.; Curry, S.C.; Woosley, R.L. Identification of populations likely to benefit from pharmacogenomic testing. *Pharmacogenet Genomics*. 2020, 30(5), 91–95.
80. Centers for Medicare and Medicaid Services. Available online: <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=38294&ver=16> (accessed 6 May 2021).
81. Williams, J.L.; Rahm, A.K.; Zallen, D.T.; Stuckey, H.; Fultz, K.; Fan, A.L.; et al. Impact of a Patient-Facing Enhanced Genomic Results Report to Improve Understanding, Engagement, and Communication. *J Genet Couns* 2018, 27(2), 358–369.
82. GTMRx. Available online: <https://16bv1028dn7zhgp35k7rzh5c-wpengine.netdna-ssl.com/wp-content/uploads/2019/09/GTMR-Sept-18-2019-PGX.pdf> (accessed 6 May 2021).
83. Dunnenberger, H.M.; Biszewski, M.; Bell, G.C.; Sereika, A.; May, H.; Johnson, S.G.; et al. Implementation of a multidisciplinary pharmacogenomics clinic in a community health system. *Am J Health Syst Pharm* 2016, 73(23), 1956–1966.
84. Dressler, L.G.; Bell, G.C.; Abernathy, P.M.; Ruch, K.; Denslow, S. Implementing pharmacogenetic testing in rural primary care practices: a pilot feasibility study. *Pharmacogenomics* 2019, 20(6), 433–446.

Author Affiliations

1. Tabula Rasa HealthCare, Office of Translational Research and Residency Programs; jbingham@trhc.com
2. Department of Pharmacy Practice & Science, University of Arizona College of Pharmacy; jbingham@trhc.com
3. Tabula Rasa HealthCare, Precision Pharmacotherapy Research & Development Institute; VMichaud@trhc.com; JTurgeon@trhc.com
4. Faculty of Pharmacy, Université de Montréal; VMichaud@trhc.com; JTurgeon@trhc.com
5. Department of Pharmacotherapy and Translational Research, University of Florida College of Pharmacy; Kwisananen@cop.ufl.edu
6. Durham Veterans' Affairs Health Care System; Jill.Bates@va.gov
7. Department of Clinical Education, University of North Carolina Eshelman School of Pharmacy; Jill.Bates@va.gov
8. Clinical Pharmacy Services & Policy, Veterans Affairs Central Office; Anthony.Morreale@va.gov
9. Department of Pharmacy and Therapeutics, University of Pittsburgh School of Pharmacy; Pempey@pitt.edu
10. Department of Pharmacotherapy, Washington State University College of Pharmacy and Pharmaceutical Sciences; Rustin.crutchley@wsu.edu
11. OneOme; Ghadaelnashar@oneome.com
12. Teacher's Retirement System of Kentucky; jane.gilbert@trs.ky.gov

* Correspondence:

Jacques Turgeon, BPharm, PhD, Chief Scientific Officer, Tabula Rasa HealthCare, Precision Pharmacotherapy Research & Development Institute, 13485 Veterans Way, Suite 410, Orlando, Florida, 32827, USA

Conflict of Interest Disclosures

JB, VM, and JT are shareholders and employees of Tabula Rasa HealthCare. GE is currently a full-time employee of OneOme. PE has received grant funding from on Implementing Genomics in Practice (IGNITE) project grant (U01 HG010245) and has provided consultative services for CIPHEROME. The other authors did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors for this study.

Acknowledgments

This article was written on behalf of the GTMRx Institute™. The authors would like to acknowledge Katherine H. Capps and M. Isabella Serji MPH for their contributions.

Keywords

pharmacogenomics; comprehensive medication management; clinical decision support systems; cost savings; polypharmacy; reimbursement