Genomind Clinical Dossier

May 2023

genomind
The Science Behind Better

Contents

Table 1.

Summary of Dossier	
Analytic Validity	• CLIA/CAP/NYSDOH Certified
Clinical Validity	• PharmGKB/CPIC Gene-Drug Associations Scores[1,2] • FDA Table of Biomarkers/Associations[3,4]
Clinical Utility	• Healthcare Utilization study showing Genomind PGx testing associated with decreased costs, hospitalizations and ER visits compared to matched controls[5] • Randomized controlled trial post hoc showing increased depression remission rates when clinicians adhered to PGx test recommendations[6] • Open-label study showing high rates of actionability by providers who used PGx testing and improvements in patient's clinical symptoms[7]

Executive Summary

It is well known that differences in patient medication response patterns may be partially explained by underlying genetic and biochemical disparities.[8] The science of assessing how a patient's genetics affect drug efficacy and safety is termed pharmacogenomics (also known as pharmacogenetics [PGx]).[9] Utilizing PGx information may provide an important tool in diminishing the trial-and-error process in medication management. Genomind®, a unique personalized medicine platform that brings innovation to healthcare around the world, has designed a suite of products aimed to incorporate PGx into clinical decision-making when prescribing medications across multiple conditions. Genomind testing is conducted via a simple buccal swab and provides clinicians with insights regarding a patient's likelihood for drug response and tolerability to particular drugs and combinations of drugs.

Our product line includes:

1) **The Genomind Pharmacogenetic (PGx) Report:**
   a. Genomind Express Report: A concise report of 6 pharmacodynamic and 11 pharmacokinetic genes that impact medications across multiple disease states and specialties including psychiatry, primary care, cardiology, pain management, and geriatrics.
   b. Genomind NeuroPsych PGx Report: A comprehensive report that includes 15 pharmacodynamic and 11 pharmacokinetic genes that impact dosing, sensitivity or response to many medications used in the treatment of mental health.

2) **GenMedPro™:** an interactive clinical decision support software that identifies drug-drug interactions (DDI) and drug-gene interactions (DGI) for over 1,000 medications. The software provides published PGx treatment guidelines as well as an alternative medication feature.

The impact of PGx testing has been demonstrated in numerous peer-reviewed publications highlighting both the clinical and economic benefits of testing. Current data reflect the significant impact of PGx testing on medication changes or optimization, improved clinical outcomes, decreases in adverse drug reactions, and decreases in healthcare costs and utilization.[10–13] More specifically, the impact of Genomind's PGx platform has been highlighted in multiple peer-reviewed publications, including a propensity score matching case-control conducted in the database of the one of the nation's largest private health insurers, which found 40% fewer all-cause emergency room visits, 58% fewer inpatient all-cause visits, and a $1,948 reduction in healthcare costs in the 6 month period following the use of Genomind PGx testing in patients with mood disorders.[14] An additional naturalistic study found that 87% of patients with mood and anxiety disorders whose treatment was guided by Genomind PGx testing had clinically measurable mental health improvements.[15]

In addition to these data, the following professional organizations and societies have published guidelines, recommendations, and acknowledgements of the relevance of PGx testing in medication management and patient care: United States Food and Drug Administration (FDA), Clinical Pharmacogenetics Implementation Consortium (CPIC), the Dutch Pharmacogenetic Working Group (DPWG), the American Psychiatric Association (APA), the American Society of Health System Pharmacists (ASHP), the Association for Molecular Pathology (AMP), the International Society of Psychiatric Genetics (ISPG), and the Royal College of Physicians (UK).

Evidence

Analytic Validity

Our two, cross-validated state-of-the art genomics laboratories receive and process all Genomind tests. This ensures complete oversight of every aspect of quality, testing, informatics security, and privacy.

Laboratory results we report and procedures we follow meet or exceed the highest federal regulatory standards for quality, accuracy, reliability, and timeliness. Our laboratories are fully certified and accredited by:

- College of American Pathologists (CAP) – the international leader in laboratory quality assurance. CAP certification requires regular inspections and use of the most scientifically rigorous methods and principles.
- Clinical Laboratory Improvement Amendments (CLIA) – established by the United States Centers for Medicare and Medicaid Services (CMS). This certification allows our laboratories to perform highly complex testing.
- Our King of Prussia laboratory is also New York State Department of Health certified, which exceeds the highest level of federal standards.

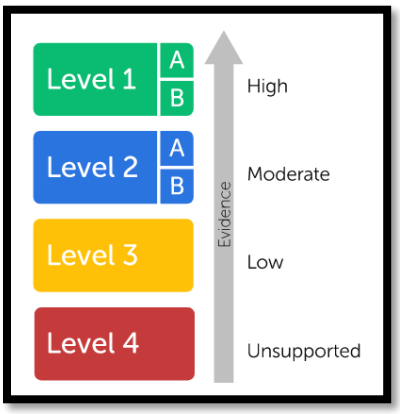
Genomind is fully compliant with HIPAA, HITECH, and GINA regulations. We are licensed in all states where required.

Our PGx reports and services are generated by 6 principle assays: OpenArray (OA), Copy Number Variation of CYP2D6 (CNV), SLC6A4 Real-time PCR (SERT), Rare SNP Multiplexing (MP), HLA-A*31:01 Detection (HLA), and Statins (Stat). Validation studies have been performed to assess accuracy, precision, limit of detection, reproducibility, temperature stressed samples, and interfering substances for each assay. Full validation protocols are available upon request.

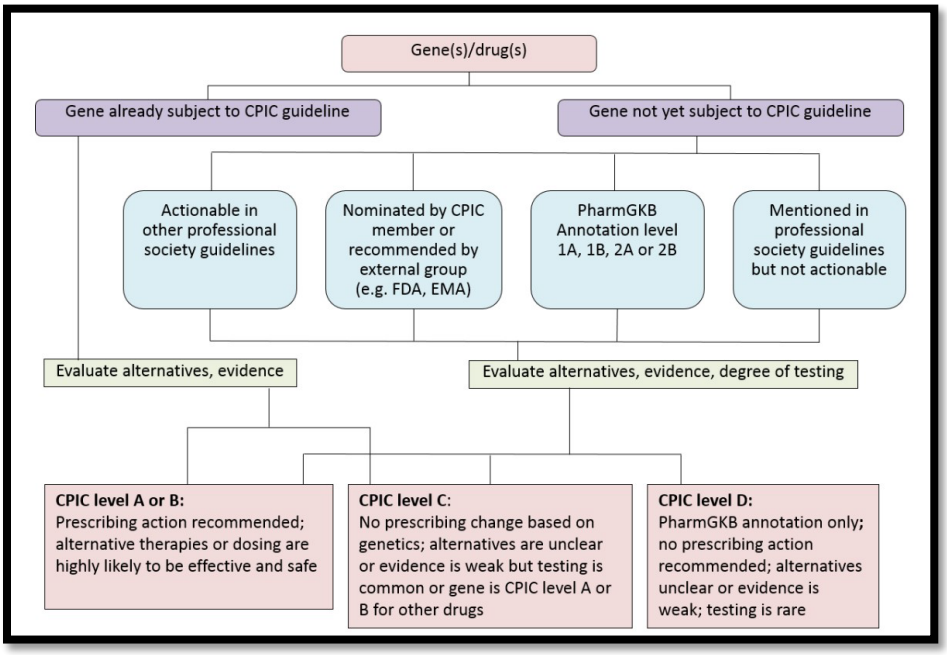
Clinical Validity

The clinical validity of gene-drug pair associations can be described by evidence levels defined by PharmGKB, an NIH/NHGRI/NICHD/NIDA funded pharmacogenomics knowledge resource, and CPIC, an international consortium focused on facilitating the use of pharmacogenetic testing for patient care. These evidence levels are generated based on the availability of clinical guidelines, drug label information, and robustness of evidence supporting gene-drug associations. The following graphics serve as an overview of these specific evidence levels:

PharmGKB Clinical Levels of Evidence[2]



CPIC Clinical Levels of Evidence[1]



The evidence level of any gene-drug pair denoted by Genomind pharmacogenomic testing can be readily assessed by utilizing the PharmGKB database at: https://www.pharmgkb.org/. In addition, gene-drug associations in our PGx reports (Neuropsych and Express) and our Clinical Decision Support Software (GenMedPro) have their respective level of evidence scores conspicuously posted.

The US Food and Drug Administration (FDA) also maintains a Table of Pharmacogenetic Biomarkers in Drug Labeling and a Table of Pharmacogenetic Associations.[3,4] These tables identify gene-drug pairs that influence drug serum levels, require dosage changes or increased monitoring, or qualify as a contraindication. Our PGx reports and software highlight these associations and link a clinician to these FDA databases when relevant genes are present.

Clinical Utility

The practice of medicine has historically followed a "one size fits all" approach that may not meet the more personalized or specific needs of individual patients and has the potential to lead to the negative effects of medication usage, either in the form of adverse drug reactions (ADRs) or medication inefficacy.[8,16] In fact, it is estimated that, for the top ten grossing medications in the United States, 3 to 24 patients do not show a response for every one patient that does benefit.[8] Additionally, according to data from the American Society of Pharmacovigilance, ADRs account for 1 million emergency department visits, 2.2 million hospital admissions, and $126 billion in U.S. healthcare costs on an annual basis.[17] While genetic variations do not account for all differences in drug response and tolerability, the addition of PGx to clinical decision-making aims to provide a more personalized, patient-centric approach to patient care and medication management.[8]

PGx testing is increasingly being incorporated into clinical practice, particularly in certain disciplines such as oncology, psychiatry, and cardiovascular medicine. The incorporation of PGx into clinical practice has shown great promise and has been associated with improved clinical outcomes and decreases in health care resource utilization and hospitalizations in various settings.[10–13] The following excerpts serve as an overview of key evidence behind the use of PGx testing:

An Analysis of Pharmacogenomic-Guided Pathways and Their Effect on Medication Changes and Hospital Admissions: A Systematic Review and Meta-Analysis
https://pubmed.ncbi.nlm.nih.gov/34394187/

"A meta-analysis was undertaken on all the studies that report the number of PGx tested patients that had medication change(s) and the number of PGx tested patients that were hospitalized, compared to participants that received TAU (treatment as usual). The search strategy identified 5 hospitalization themed studies and 5 medication change themed studies for analysis…The analysis shows that PGx testing can produce substantial benefits in patient populations, by substantially increasing the number of medication changes that could potentially result in a reduction in serious adverse events as measured by hospital admission. Hospital admissions were halved across the interventions included in this study. These findings contribute to the evidence for the clinical utility of PGx testing which is often lacking in literature and altogether provide strong proof-of-concept for the clinical utility of PGx testing in guiding medication changes that results in clinical improvements and that PGx testing can potentially reduce hospitalization."[10]

A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomized crossover implementation study
https://pubmed.ncbi.nlm.nih.gov/36739136/

"We conducted an open-label, multicentre, controlled, cluster-randomised, crossover implementation study of a 12-gene pharmacogenetic panel in 18 hospitals, nine community health centres, and 28 community pharmacies in seven European countries (Austria, Greece, Italy, the Netherlands, Slovenia, Spain, and the UK). Patients aged 18 years or older receiving a first prescription for a drug clinically recommended in the guidelines of the Dutch Pharmacogenetics Working Group (i.e., the index drug) as part of routine care were eligible for inclusion…In patients with an actionable test result for the index drug (n=1558), a clinically relevant adverse drug reaction occurred in 152 (21·0%) of 725 patients in the study group and 231 (27·7%) of 833 patients in the control group (odds ratio [OR] 0·70 [95% CI 0·54-0·91]; p=0·0075), whereas for all patients, the incidence was 628 (21·5%) of 2923 patients in the study group and 934 (28·6%) of 3270 patients in the control group (OR 0·70 [95% CI 0·61-0·79]; p <0·0001)… Genotype-guided treatment using a 12-gene pharmacogenetic panel significantly reduced the incidence of clinically relevant adverse drug reactions and was feasible across diverse European health-care system organisations and settings. Large-scale implementation could help to make drug therapy increasingly safe."[11]

Pharmacogenomic Testing and Depressive Symptom Remission: A Systematic Review and Meta-Analysis of Prospective, Controlled Clinical Trials

https://pubmed.ncbi.nlm.nih.gov/36111494/

"Thirteen trials comprising 4,767 patients were analyzed, including 10 randomized controlled trials, and three open label trials. Across all included trials, those that received PGx-guided antidepressant therapy (n = 2,395) were 1.41 (95% confidence interval (CI) = 1.15-1.74, P = 0.001) more likely to achieve remission compared with those that received unguided antidepressant therapy (n = 2,372). Pooled risk ratios for randomized controlled trials and open label trials were 1.46 (95% CI: 1.13-1.88) and 1.26 (95% CI = 0.84-1.88), respectively. These results suggest that PGx-guided antidepressant therapy is associated with a modest but significant increase in depressive symptom remission in adults with MDD."[12]

Real-World Impact of a Pharmacogenomics-Enriched Comprehensive Medication Management Program

https://pubmed.ncbi.nlm.nih.gov/35330421/

"The availability of clinical decision support systems (CDSS) and other methods for personalizing medicine now allows evaluation of their real-world impact on healthcare delivery. For example, addressing issues associated with polypharmacy in older patients using pharmacogenomics (PGx) and comprehensive medication management (CMM) is thought to hold great promise for meaningful improvements across the goals of the Quadruple Aim. However, few studies testing these tools at scale, using relevant system-wide metrics, and under real-world conditions, have been published to date. Here, we document a reduction of ~$7000 per patient in direct medical charges (a total of $37 million over 5288 enrollees compared to 22,357 non-enrolled) in Medicare Advantage patients (≥65 years) receiving benefits through a state retirement system over the first 32 months of a voluntary PGx-enriched CMM program. We also observe a positive shift in healthcare resource utilization (HRU) away from acute care services and toward more sustainable and cost-effective primary care options. Together with improvements in medication risk assessment, patient/provider communication via pharmacist-mediated medication action plans (MAP), and the sustained positive trends in HRU, we suggest these results validate the use of a CDSS to unify PGx and CMM to optimize care for this and similar patient populations."[13]

Genomind Platform

In addition to the above publications, the utility of our Genomind PGx solutions has been documented in multiple peer-reviewed papers to date. The following excerpts highlight data regarding improved clinical outcomes, decreases in healthcare utilization, and the potential for improved identification of drug-gene interactions seen with the use of Genomind products.[14–16,18]

A Naturalistic Study of the Effectiveness of Pharmacogenetic Testing to Guide Treatment in Psychiatric Patients with Mood and Anxiety Disorders

https://pubmed.ncbi.nlm.nih.gov/26445691/

This was a naturalistic, unblinded, prospective analysis of psychiatric patients and clinicians who utilized (Genomind PGx) between April and October of 2013. Data from 685 patients were collected. Approximately 70% and 29% of patients had primary diagnoses of either a mood or anxiety disorder, respectively. Clinician-reported data, as measured by the Clinical Global Impressions Improvement scale, indicated that 87% of patients showed clinically measurable improvement (rated as very much improved, much improved, or minimally improved), with 62% demonstrating clinically significant improvement. When analysis was restricted to the 69% of individuals with ≥ 2 prior treatment failures, 91% showed clinically measurable improvement. Patients also reported significant decreases in depression ($P < .001$), anxiety ($P < .001$), and medication side effects ($P < .001$) and increases in quality of life ($P<.001$).[15]

Pharmacogenetic testing among patients with mood and anxiety disorders is associated with decreased utilization and cost: a propensity-score matched study

https://pubmed.ncbi.nlm.nih.gov/29734486/

A propensity-score matched case-control analysis of longitudinal health claims data from a large US insurer was performed. Individuals with a mood or anxiety disorder diagnosis (N = 817) whose physician utilized Genomind PGx

were matched to 2,745 individuals who did not receive such testing. Outcomes included number of outpatient visits, inpatient hospitalizations, emergency room visits, and prescriptions, as well as associated costs over 6 months. On average, individuals who underwent testing experienced 40% fewer all-cause emergency room visits (mean difference 0.13 visits; $P < 0.0001$) and 58% fewer inpatient all-cause hospitalizations (mean difference 0.10 visits; $P < 0.0001$) than individuals in the control group. The Genomind PGx users consumed an estimated $1,948.00 less in health care resources than controls in the six-month period after testing. The two groups did not differ significantly in number of psychotropic medications prescribed or mood-disorder related hospitalizations.[14]

Randomized, controlled, participant- and rater-blind trial of pharmacogenomic test-guided treatment versus treatment as usual for major depressive disorder
https://pubmed.ncbi.nlm.nih.gov/32383277/
Eight-week multicenter RCT examined the impact of Genomind PGx testing (AGT; N=151) versus treatment-as-usual (TAU; N=153) among outpatients with major depressive disorder. Both participants and raters were blinded to treatment conditions for the primary outcome (Hamilton Depression Rating Scale; SIGH-D-17). For the primary outcome, no significant difference was detected between AGT and TAU at Week 8 ($p = .53$). Exploratory analyses suggested significantly fewer individuals experienced worsening of depressive symptoms following AGT, and that treatment concordant with assay results was associated with greater likelihood of remission (OR 2.23; 95% CI 1.17-2.83).[18]

Predicting drug-drug and drug-gene interactions in a community pharmacy population
https://pubmed.ncbi.nlm.nih.gov/36374614/
Drug-drug and drug-drug-gene interactions were assessed in a large community-based population utilizing the logic incorporated into GenMedPro, a commercially available digital gene-drug interaction software program that incorporates genetic variants to evaluate drug interactions (DDIs) and drug-gene interactions (DGIs). Based on prescription data only, the probability of a DDI of any impact (mild, moderate, or major) was 26% [95% CI: 0.248-0.272] in the population. This probability increased to 49.6% [95% CI: 0.484-0.507] when simulated genetic polymorphisms were additionally assessed. When assessing only major impact interactions, there was a 7.8% [95% CI: 0.070-0.085] probability of drug-drug interactions and 10.1% [95% CI: 0.095-0.108] probability with the addition of genetic contributions. The probability of drug-drug-gene interactions of any impact was correlated with the number of prescribed medications, with an approximate probability of 77%, 85%, and 94% in patients prescribed 5, 6, or 7+ medications, respectively. When stratified by specific drug class, antidepressants (19.5%), antiemetics (21.4%), analgesics (16%), antipsychotics (15.6%), and antiparasitics (49.7%) had the highest probability of major drug-drug-gene interaction. [16]

Guidelines and Statements from Professional Societies

A variety of professional organizations and societies have released guidelines, endorsements, and acknowledgements regarding the utility and impact of pharmacogenomic testing.

Guidelines

Genomind strongly relies on guideline and guidance information from the Food and Drug Administration (FDA), CPIC, and DPWG.[19,20] The FDA's Table of Pharmacogenetic Biomarkers in Drug Labeling and Table of Pharmacogenetic Associations provide pharmacogenetic precautions, warnings, and/or dosing guidance for over 300 approved medications.[3,4] DPWG is a Dutch-based multidisciplinary organization that develops PGx-based therapeutic recommendations and publishes guidance and recommendations for numerous medications. Genomind has actively incorporated the guidance from these leading organizations into our pharmacogenetic reports and GenMedPro software to allow for real-time interpretation and application of guidance.

Endorsements and Acknowledgements

American Psychiatric Association (APA)

In a letter, APA President Saul Levin to Noridian (a CMS Medicare administrative contractor) in 2019, the following statement regarding PGx testing was highlighted:

"In general, we view several indications as appropriate for pharmacogenetic testing. With some medications, pharmacogenetic testing prior to treatment is important to identify whether a patient is at heightened risk of developing a serious complication. In this context, knowledge of the patient's genetic status can contribute to a decision to avoid use of a specific medication when several possibilities are under consideration… With other medications, such as those metabolized through cytochrome P450 enzymes, pharmacogenetic testing may be less relevant to initial medication selection but may be important for optimizing medication doses to limit toxicity or enhance outcomes based on principles of pharmacokinetics and known metabolic pathways. In these contexts, pharmacogenetic testing may be indicated once a medication is selected for use or may be more relevant when doses are being adjusted after a patient is already taking a medication."

FDA

Through the establishment of their Table of Pharmacogenetic Associations and Table of Pharmacogenetic Biomarkers in Drug Labeling, the FDA states

"Pharmacogenetic tests, along with other information about patients and their disease or condition, can play an important role in drug therapy. When a health care provider is considering prescribing a drug, knowledge of a patient's genotype may be used to aid in determining a therapeutic strategy, determining an appropriate dosage, or assessing the likelihood of benefit or toxicity."

"Pharmacogenomics can play an important role in identifying responders and non-responders to medications, avoiding adverse events, and optimizing drug dose. Drug labeling may contain information on genomic biomarkers and can describe:

- *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"*

American Society of Health System Pharmacists (ASHP)

"The American Society of Health System Pharmacists (ASHP) believes pharmacogenomic testing can improve medication-related outcomes across the continuum of care in all health system practice settings. These improvements include improved clinical outcomes, decreased side effects, lower cost of treatment, increased medication adherence, more appropriate selection of therapeutic agents, decreased length of treatment, and enhanced patient safety."

Association for Molecular Pathology (AMP)
"To build upon these guideline-development and evidence-curation efforts, a working group of AMP leaders examined the current environment of pharmacogenomic testing and determined that clinically meaningful pharmacogenomic tests can improve patient care and professional practice, provided certain conditions are met."

International Society of Psychiatric Genetics (ISPG)
"Pharmacogenetic testing should be viewed as a decision-support tool to assist in thoughtful implementation of good clinical care. We recommend HLA-A and HLA-B testing prior to use of carbamazepine and oxcarbazepine, in alignment with regulatory agencies and expert groups. Evidence to support widespread use of other pharmacogenetic tests at this time is still inconclusive, but when pharmacogenetic testing results are already available, providers are encouraged to integrate this information into their medication selection and dosing decisions. Genetic information for CYP2C19 and CYP2D6 would likely be most beneficial for individuals who have experienced an inadequate response or adverse reaction to a previous antidepressant or antipsychotic trial."

Royal College of Physicians (UK)
"There is increasing scientific evidence that natural variation in particular genes influences how well a medicine works for an individual, and whether they will experience side effects. The study of this area is called pharmacogenomics. Pharmacogenomic testing can be used to discover which variants of genes an individual carries, and whether they impact on the response to medicines they are given. This information can be used to guide the choice of medicine and dose, increasing the likelihood that each person receives the most effective medicine for them, at the best dose, the first time they are treated. Pharmacogenomic testing is already benefiting NHS…. The ultimate goal is to make pharmacogenomic-based prescribing a reality for all in the UK NHS. This will empower healthcare professionals to deliver better, more personalised care, and in turn improve outcomes for patients and reduce costs to the NHS. Although we focus on the UK, many of the issues discussed in the report are also relevant to other global healthcare systems and learning from each other will be important in optimising medicines use around the world."

Conclusion

Genomind offers a unique and comprehensive precision medication management platform aimed at providing clinicians with the necessary tools and support to incorporate PGx into their clinical care. Genomind's PGx offerings and the use of PGx in general have been associated with improved patient clinical outcomes, reductions in ADRs, and decreases in the monetary burden to the healthcare system. Genomind believes the time for PGx testing to become a standard of care is now and views the broad implementation as beneficial to patients, providers and payers alike.

Contact Genomind:
www.genomind.com
877-895-8658
2200 Renaissance Blvd, Suite #100
King of Prussia, PA 19406

David Krause, MD, Chief Medical Officer - dkrause@genomind.com
Rob Dublin, Chief Administrative Officer - rdublin@genomind.com

References

1. CPIC Level of Evidence Scoring. Accessed May 4, 2023. CPIC Level of Evidence Scoring
2. PharmGKB. PharmGKB Level of Evidence Scoring. Accessed May 4, 2023. https://www.pharmgkb.org/page/clinAnnLevels
3. FDA. Table of Pharmacogenomic Biomarkers in Drug Labeling. FDA Table of Pharmacogenomic Biomarkers in Drug Labeling. Published August 11, 2022. Accessed May 1, 2023. https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
4. US Food and Drug Administration. FDA Table of Pharmacogenetic Associations. Published October 26, 2022. Accessed May 1, 2023. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations
5. Perlis RH, Mehta R, Edwards AM, Tiwari A, Imbens GW. Pharmacogenetic testing among patients with mood and anxiety disorders is associated with decreased utilization and cost: A propensity-score matched study. *Depress Anxiety*. 2018;35(10):946-952. doi:10.1002/da.22742
6. Perlis RH, Dowd D, Fava M, Lencz T, Krause DS. Randomized, controlled, participant- and rater-blind trial of pharmacogenomic test-guided treatment versus treatment as usual for major depressive disorder. *Depress Anxiety*. 2020;37(9):834-841. doi:10.1002/da.23029
7. Brennan FX, Gardner KR, Lombard J, et al. A naturalistic study of the effectiveness of pharmacogenetic testing to guide treatment in psychiatric patients with mood and anxiety disorders. *Prim Care Companion J Clin Psychiatry*. 2015;17(2). doi:10.4088/PCC.14m01717
8. Pirmohamed M. Pharmacogenomics: current status and future perspectives. *Nat Rev Genet*. Published online 2023. doi:10.1038/s41576-022-00572-8
9. Nih S. *What Is Pharmacogenomics? How Is Pharmacogenomics Affecting Drug Design, Development, and Prescribing Guidelines?* https://www.nigms.nih.gov.
10. David V, Fylan B, Bryant E, Smith H, Sagoo GS, Rattray M. An Analysis of Pharmacogenomic-Guided Pathways and Their Effect on Medication Changes and Hospital Admissions: A Systematic Review and Meta-Analysis. *Front Genet*. 2021;12. doi:10.3389/fgene.2021.698148
11. Swen JJ, van der Wouden CH, Manson LE, et al. A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. *The Lancet*. 2023;401(10374):347-356. doi:10.1016/S0140-6736(22)01841-4
12. Brown LC, Stanton JD, Bharthi K, Maruf A Al, Müller DJ, Bousman CA. Pharmacogenomic Testing and Depressive Symptom Remission: A Systematic Review and Meta-Analysis of Prospective, Controlled Clinical Trials. *Clin Pharmacol Ther*. 2022;112(6):1303-1317. doi:10.1002/cpt.2748
13. Jarvis JP, Peter AP, Keogh M, et al. Real-World Impact of a Pharmacogenomics-Enriched Comprehensive Medication Management Program. *J Pers Med*. 2022;12(3). doi:10.3390/jpm12030421

14. Perlis RH, Mehta R, Edwards AM, Tiwari A, Imbens GW. Pharmacogenetic testing among patients with mood and anxiety disorders is associated with decreased utilization and cost: A propensity-score matched study. *Depress Anxiety*. 2018;35(10):946-952. doi:10.1002/da.22742

15. Brennan FX, Gardner KR, Lombard J, et al. A naturalistic study of the effectiveness of pharmacogenetic testing to guide treatment in psychiatric patients with mood and anxiety disorders. *Prim Care Companion J Clin Psychiatry*. 2015;17(2). doi:10.4088/PCC.14m01717

16. Dowd D, Williams G, Vandorn D, et al. Predicting Drug-Drug and Drug-Gene Interactions in a Community Pharmacy Population. *Am J Manag Care*. 2022;28(11):200-205. doi:10.37765/ajmc.2022.89259

17. ASP. American Society of Pharmacovigilance. Accessed May 1, 2023. https://www.stopadr.org/

18. Perlis RH, Dowd D, Fava M, Lencz T, Krause DS. Randomized, controlled, participant- and rater-blind trial of pharmacogenomic test-guided treatment versus treatment as usual for major depressive disorder. *Depress Anxiety*. 2020;37(9):834-841. doi:10.1002/DA.23029

19. CPIC. CPIC Guidelines. CPIC Guidelines . Published 2022. Accessed May 1, 2023. https://cpicpgx.org/

20. DPWG. DPWG: Dutch Pharmacogenetics Working Group. DPWG: PharmGKB Entry. Published 2022. Accessed May 1, 2023. https://www.pharmgkb.org/page/dpwg