

# The Power and the Promise: Integrating Pharmacogenomics into Clinical Practice

## Designing a PGx Program That Works

By Bernard Esquivel, Chief Medical Officer, GenXys Health Care Systems

### Introduction

Given the growing awareness of Adverse Drug Events (ADEs) for patients, new clinical tools are being offered to address a critical medical need for personalized health care (see **Figure 1**). Pharmacogenetics (PGx) is expanding the ability of physicians and pharmacists to provide highly personalized patient care,<sup>1</sup> especially through

decision support tools that predict if a patient will experience an adverse event, require a certain dosage, or benefit more from a different medication because of how they are likely to metabolize a drug. Because of this service, the patient may be more willing to take their medications as prescribed and have fewer concerns about unwanted side effects.<sup>1</sup> Though PGx is coming into the mainstream of

clinical practice, the industry has yet to solidify foundational practices for PGx implementation, which would accelerate its adoption by removing barriers to its use.

One of the most frequent questions we at GenXys get from health organization leaders looking to include PGx into their practice is: *How do I get started?*



**Figure 1: The Impact of Adverse Drug Reactions**

As stated by CDC and Watanabe and colleagues, adverse drug reactions result in 1.3 million emergency department visits, 350,000 hospitalization and \$528 billion spent on non-optimized medications per year.

In this paper, we lay down a decision-making framework for healthcare leaders to build a successful PGx program that aligns with their organizational goals. Once all parties are on board with establishing this program, the next step is to identify the people and populations who will benefit most from having pharmacogenetic (PGx) tests. Equally important is to have beforehand a strategy for what to do once tests have been run, especially if a patient comes in with pre-existing test results. At this stage, the important question is how a clinician or health system administrator should think about using the information to intervene on treatment options. In the final section of this paper, we will introduce an important tool for delivering a robust PGx program.

### A) Getting Started with Pharmacogenomics Programs

Because the value of using pharmacogenomics data and tools to improve patient outcomes has become increasingly clearer, it is time to understand how to get started. As noted above, one of the first steps is to identify which patients to test.

#### I) Who to test: How to identify the right people for PGx testing?

There are three distinct approaches to identifying the best candidates for PGx testing.

- Genes:** Those likely to have genetic variants. The genetic variants associated with clinically significant drug-gene interactions are common and largely unpredictable without a test.
  - 96.8% of samples from a cohort study in six primary care settings had at least

one actionable genotype for medication included in the medication decision support software.<sup>2</sup>

- Risk of Adverse Drug Reaction:** Those people who, due to a multitude of factors, have a higher risk of having an adverse drug reaction (ADR).
  - Adverse drug events (ADEs) result in 1.3 million emergency department visits, 350,000 hospitalization and \$528 billion spent on non-optimized medications in a year.<sup>3</sup>
  - Some studies estimate that 6.7% of hospitalized patients are admitted due to a serious ADR, with a fatality rate of 0.32%.<sup>4,5</sup>
- Drugs:** Those likely to be prescribed drugs that have clinically significant drug-gene interactions.

#### II) When to intervene: How to use PGx information to help patients find the right medications

There are two types of situations where PGx information will be used to intervene treatment decisions:

- Health Care Professionals:** When prescribers make prescription decisions and when a patient's medications are reviewed, most frequently by a pharmacist.
- Health Care Organization:** when healthcare executives offer pharmacogenetic testing and services at a population level in their organizations. These services often manifest at a health care professional level, but the decisions about who will be offered testing are made at an organizational level.

#### III) The Patient: Four sets of information to determine safe and effective drug options for an individual

What patient-specific information do healthcare providers need to consider when making medication decisions?

- Current Condition(s) for potential diagnosis**
  - Do they have condition X?
  - Are they at high risk of condition X based on clinical or genomic markers?
- Clinical Biophysical (Examples)**
  - Liver Impairment<sup>6</sup>: 10-20% prevalence<sup>7,8</sup>
  - Renal Impairment<sup>9</sup>: ~10% prevalence<sup>10,11</sup>
  - Potassium Abnormality<sup>12</sup>: ~10% prevalence<sup>13</sup>
  - QT Prolongation: 7% prevalence in people with Diabetes<sup>14</sup>
- Prescribed Drug Regimen**
  - What drugs are they already taking – are there potential drug-drug interactions?
  - What drugs have they taken before?
  - How many drugs are they currently taking—what is the level of polypharmacy?
- Pharmacogenetic information**
  - Do they have any genetic variants that may affect the dosage of potential drugs for this condition?

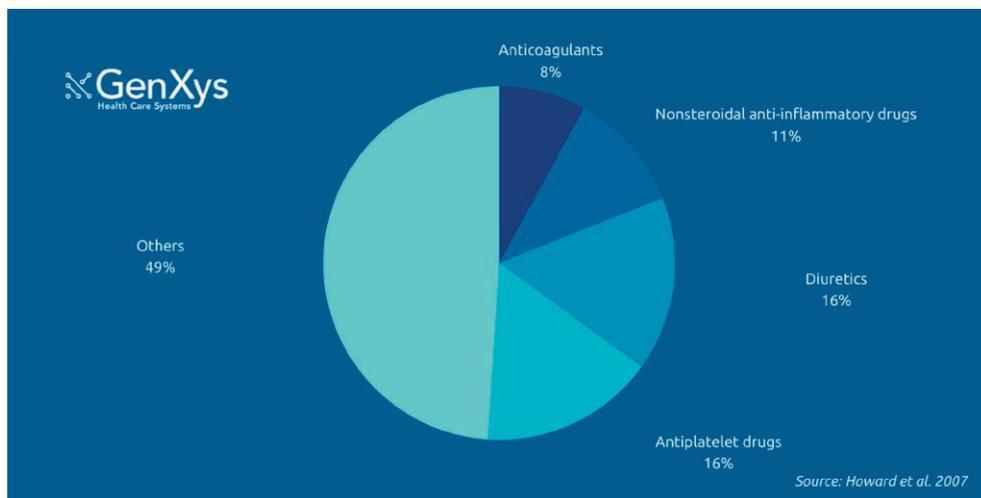
Pharmacogenetics is only one variable that might affect how someone reacts to a drug. As noted in points above, other factors include kidney and liver function, comorbidities, and other medications that a patient is taking. For instance, drugs used to treat depression might interact with the medications used for diabetes or arthritis, and the doses of these drugs might have to be adjusted according to the presence of kidney or liver disease in the patient. The ability to automatically combine these variables with PGx data is necessary to increase PGx adoption.

The specific drugs which most often cause ADRs vary by populations in the region or country under observation, but there are some commonalities. In a review of multiple countries,<sup>16</sup> the majority (51%) of preventable drug-related admissions involved (see also **Figure 2**):

- Antiplatelet drugs (16%)
- Diuretics (16%)
- Nonsteroidal anti-inflammatory drugs (11%)
- Anticoagulants (8%)

Two main factors determine which drugs cause the most problems:

- What is being prescribed:** In different countries, physicians use different drugs. ➤



**Figure 2: The Medication: Which drugs cause the most problems?**

The specific drugs which most often cause ADRs is variable by the region or country under observation, but there are some commonalities. The majority (51%) of preventable ADRs preventable drug-related admissions involved either, Antiplatelet drugs (16%), Diuretics (16%), Nonsteroidal anti-inflammatory drugs (11%) or Anticoagulants (8%).

The first-line drugs for a condition may vary from country to country.<sup>12,16</sup>

2. **How the Adverse Drug Reaction (ADR) is recorded:** For example, bleeding is a common reason for admission related to an adverse drug event. If the patient is on more than one drug that can cause bleeding, the coding of this reaction may not reflect which drug or combination of drugs caused the reaction.<sup>17</sup>

## B) Strategizing the right PGx program for your health organization: 3-Step Guide

**Step 1: Define clinical targets with a staged approach to PGx testing and intervention: Various ways to identify who to test**

Some populations who might be useful to test are: people likely to receive one of the 269 drugs with Drug-Gene Interactions (DGIs)<sup>18</sup>; people with a condition where PGx is likely to be beneficial; and people who meet a combination of these criteria – for example, a patient with depression who is failing to respond to a first-line therapy, or who is on multiple drugs with known drug-gene interactions.

Other questions to ask to identify who to test: Who would benefit most? Who is more at risk? When deciding who to test as a health care organization, one can use an ADE strategy, a disease strategy, or a combination of the two. As well, if a healthcare professional is considering doing a renal function or liver function test to assess drug dose, they might consider a PGx test as well.

## Step 2: Sort population by risk cohorts: Putting It All Together: What patient characteristics identify a patient at risk?

Two groups, Evans *et al.* (2005)<sup>19</sup> and Onder *et al.* (2010),<sup>20</sup> have put together the risk factors of patient-specific variables, with similar results in both studies. Each variable is labelled with a range of numbers that shows how much it could increase the risk of an adverse drug reaction. When putting it all the variables together, an ADR risk score is calculated. This score allows us to identify patients who are at higher or lower risk of an ADR (list below and Figure 3).

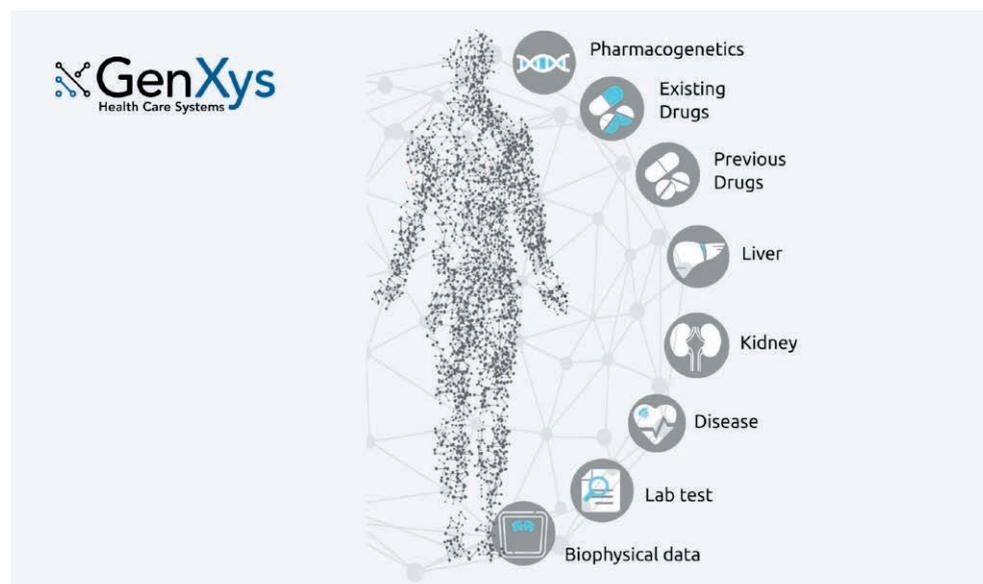
- Gender (1.5-1.7)
- Age (0.7-0.9)
- Weight (1.2-1.4)
- Creatinine clearance (0.8-4.7)
- Number of comorbidities (1.1-12.6)
- Drug administration dosage (1.2-3.7)
- Administration route (1.4-149.9)
- Number of concomitant drugs (1.2-2.4)
- Diagnosis-related group (1.5-5.7)

If you take these factors and put them together, what is the actual impact?

In Evans *et al.* (2005) and Onder *et al.* (2010), we see that the number of conditions could increase the risk of an adverse drug reaction by 10% (1.1) to 120% (12.6). The number of comorbidities increases your risk of an adverse drug reaction (see Figure 4), as does the number of drugs being taken. A crucial factor is whether drugs are given intravenously as opposed to orally; intravenous drugs are associated with a substantial number of adverse drug reactions compared those taken orally.

## Pre-emptive PGx testing?

Decision-makers can pre-emptively select a certain population for PGx tests who will be likely to make use of this information in the future as a preventive measure. For example, in long-term care populations such as the elderly, PGx testing is an appropriate measure. When a pharmacist performs a medication review, they can include PGx information with the other variables being considered. As well, it is worth considering: If a patient's condition got worse, what would be the next best medication option?



**Figure 3: Putting It All Together: What patient characteristics identify a patient at risk?**

Here are some of the patient-specific variables that can affect the risk of adverse drug reactions.

**Table 2. Variables Included in the Score<sup>a</sup>**

Variable	OR (95% CI)	Points
≥4 Comorbid conditions	1.31 (1.04-1.64)	1
Heart failure	1.79 (1.39-2.30)	1
Liver disease	1.36 (1.06-1.74)	1
No. of drugs		
≤5	1 [Reference]	0
5-7	1.90 (1.35-2.68)	1
≥8	4.07 (2.93-5.65)	4
Previous ADR	2.41 (1.79-3.23)	2
Renal failure <sup>b</sup>	1.21 (0.96-1.51)	1

Abbreviations: ADR, adverse drug reaction; CI, confidence interval; OR, odds ratio.

<sup>a</sup>The ORs and 95% CIs are derived from stepwise multivariate logistic regression. The variables were retained in the model when  $P \leq .10$ .

<sup>b</sup>Defined as a glomerular filtration rate of less than 60 mL/min.

**Figure 4: Variables Included in the Score**

Two groups, Evans *et al.* (2005)<sup>19</sup> and Onder *et al.* (2010)<sup>20</sup>, have put together the risk factors of patient-specific variables, with similar results in both studies. Each variable is labelled with a range of numbers that shows how much it could increase the risk of an adverse drug reaction. When putting it all the variables together, an ADR risk score is calculated.

### Step 3: Maintain synchronized EHR data to inform changes and provide clinicians with the tools they need to administer the program: *Proactive vs. Reactive PGx Interventions*

It might be difficult for healthcare leaders to decide whether a proactive or a reactive program is best for them. Proactive programs aim to identify those who will benefit from PGx, even if they have not yet had issues with their medications or even are on any medications. This is often based on risk stratification using patient characteristics at a population level to predict where testing efforts might be most useful. Reactive programs can alert clinicians about how PGx could be used for individual patients, even where no testing has been done: for example, if a high-risk patient is about to be prescribed a medication that has significant drug-gene interactions, their clinician might be alerted to this. Reactive programs also involve providing treatment information based on existing PGx data. Here are some of the characteristics of each type of program:

#### Proactive Programs:

- Risk-based population stratification
- Synchronized EHR data
- Patient outreach & testing
- Ongoing medication management

#### Reactive Programs:

- PGx results in the EHR
- Alert clinicians in the EHR prior to inappropriate prescriptions
- Suggest a consult, test, or the use of PGx clinical decision support systems (CDSS)
- Generate awareness of PGx use to prevent ADRs

What enhances the use of PGx information in both cases? *Giving the healthcare providers the right tools: medication decision support software with real-time actionable alerts.* The ongoing use of precision medication management tools makes sure that the right information is always available to identify people who are great PGx candidates and help clinicians understand where and when to use those results.

### C) Common Barriers to PGx Use Complexity

Pharmacogenetics is not easy to understand for many health care providers. One type of resource is evidence about the utility of pharmacogenetic tests in certain conditions, which has been assembled by two international consortiums: one in Europe called the Dutch Pharmacogenetics Working Group (DPWG)<sup>21</sup>, and another group in USA called the Clinical Pharmacogenetics Implementation Consortium (CPIC)<sup>18</sup>. CPIC has developed guidelines on important genetic variants and how this information can be used. A companion database, PharmGKB,<sup>22</sup> gives detailed information about the gene-drug associations that inform these guidelines. The Food and Drug Administration (FDA) also evaluates the evidence of pharmacogenetic associations and maintains a table<sup>23</sup> that tracks if this evidence indicates that clinicians could use this information to intervene in treatment.

Guidelines and evidence databases are both useful to clinicians and also serve to demonstrate the complexity of translating pharmacogenetic information for clinical care. To add to the complexity, many variables need to be considered

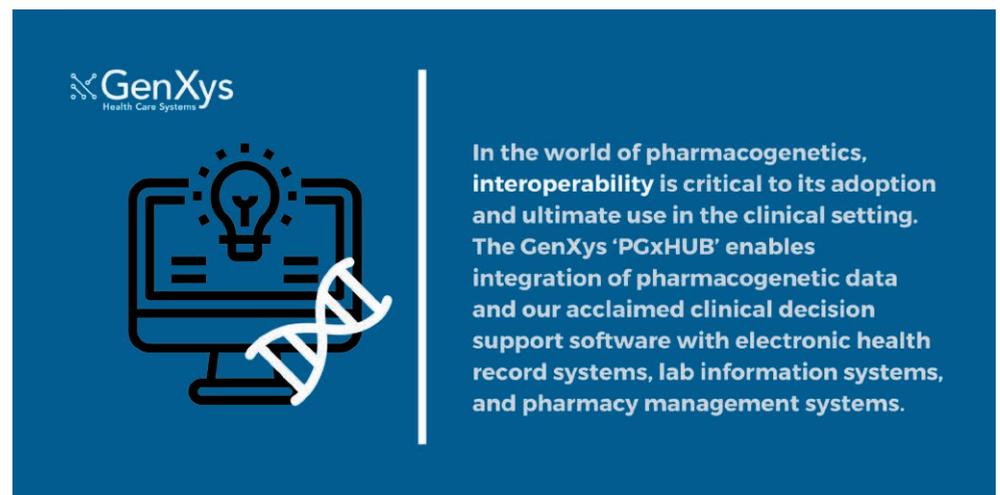
along with PGx information for optimal medication use.

GenXys uses these guidelines and the clinical knowledge of experienced healthcare professionals as a basis for our proprietary algorithms to ease the burden of this complexity on the provider.

### Static Reports and the Need to Keep Up to Date

Legacy PGx reports may be buried in electronic health records or even a paper charts, and are typically about 50 pages long. As well, if they are static and lack dynamic features, such as updates based on new evidence, they may lead to decisions that are not made with the latest industry guidance or every piece of evidence in mind.

Cloud based clinical decision support application solve this challenge and GenXys addresses this barrier by keeping up to date with the latest PGx evidence and integrating this evidence into our SaaS based software. This is essential because evidence is constantly being improved upon. As more and more studies are conducted investigating the relationship between genetic variation and how medications are metabolized, any newly generated evidence may bring about changes in the course of action that guidelines suggest for a gene-drug pair or the metabolizer status associated with the variant. As well, when new medications are created or have new indications, they may have interactions with certain genetic variants, and that information will need to be reflected in medication decisions. So, it is essential that medication decisions are based on up-to-date evidence and guidelines rather than out of date static reports. ▶



**Figure 5: Why Interoperability is Key to Widespread PGx Adoption?**

Caption: Interoperability is critical to the adoption of pharmacogenetics and its ultimate widespread use in the clinical setting. The clinical decision support component of a successful PGx implementation needs to be interoperable with electronic health records (EHRs), claims management systems, lab information systems and pharmacy management systems (PMS).

Similarly, PGx information is often not shared properly with the appropriate spectrum of healthcare professionals and patients.

### Testing Standardization

A common concern is whether DNA tests are rigorous and effective enough. There are good clinical pharmacogenetic test companies which provide accurate results. However, there are also genealogy-type tests which are not designed for clinical use, even if they are CAP approved. Because of this confusion, clinicians may not believe in the rigor of PGx test results. However, groups like the Standardizing Laboratory Practices in Pharmacogenomics Collaborative Community<sup>24</sup> are working towards standards, practices, and resources to improve this.

### D) Overcoming the PGx Adoption Barriers with the Right Solutions

#### PGx translation and inclusion at the point of care

In Summit 5 “Implementation” of the American Medical Association and ASHP’s Pharmacogenomics Virtual Summit Series,<sup>25</sup> one of the questions posed was “What changes would you like to see in the implementation of PGx over the next 5 years?” Reimbursement came up quickly, but many of the other answers were specific to the role of digital automation and the availability of ‘Commercial off-the-shelf’ software.

Requests included:

- Automatic inclusion of drug-to-drug interactions alongside PGx interactions,
- Pre-emptive inclusion of PGx to inform prescription changes,

- Structured PGx data transport from the lab to the clinician,
- Referential/stop alerts replaced with practice action alerts with optimized medication alternatives presented in the EHR workflow
- Interactive portals for patients and clinicians, and
- Full inclusion of non-PGx data for auto personalization and optimization of drug choices.

The good news is that these features are already available in existing software proven in the market with the capability to enhance PGx translation and reporting.

#### Pharmacist-centric to support physicians and nurses.

Prescribers are not the only health care professionals who can use PGx for their patients. Pharmacists are often well-equipped to take leadership roles in PGx implementation programs due to their expertise in pharmacology.

One example of a PGx program in which pharmacists take a crucial role is has been established in a pharmacy coalition in Kentucky.<sup>26</sup> In this program, pharmacists can communicate pharmacogenetics-based concerns with the prescribing physician to reduce ADRs and other side effects. A key factor to the success of this program is the established trust between the pharmacists and the patients and physicians.

The pharmacology expertise of pharmacists also means they are well placed to become PGx consultants. As they are often well-versed in the science and logistics, they can go into physicians’ offices and help patients understand PGx reports

and how the results might be used to change their medications.<sup>27</sup> Consulting pharmacists also help communicate these decisions with the physician.

#### Advanced PGx decision support for pharmacists and primary care physicians and nurses

During a focus group with healthcare professionals, there was a consensus that PGx data should be integrated into the software they use.<sup>28</sup> One comment was that “it would be essential to have it included into a software that can help us not miss some information” (Pharmacist, group 2). GenXys’ mission is to equip physicians and pharmacists with tools that allow them to make effective decisions quickly and easily through workflow-specific tools to drive efficiency and outcomes.

Physicians should generally think with a condition-first mindset to match their diagnosis workflow when it comes to PGx for reasons that include: first, more evidence has shown that PGx is a useful tool for some conditions than for others. This means that when deciding who to test, the population with these conditions can be a good place to start. As well, prescribers need to be able to have all essential information to treat the condition, along with the PGx information. Finally, when a patient is taking more than one medication (common for patients with comorbidities or in the elderly), the decision must also factor the possible interactions between the existing medications and the proposed addition to their regimen. Decision support tools can automate this process. The addition of PGx can further eliminate options that might be unsafe or ineffective.

On the other hand, pharmacists should first think about the patient’s current medication. During medication reviews, pharmacists need to see patients’ current medications and other patient-specific information that may affect their medications and dosage. They can interpret PGx data on top of all that information to identify medication safety and appropriateness issues. Any automation for this process would need to show medication-related warnings and adjustments, as well as deprescribing opportunities. Overall, PGx decision support needs to enable pharmacists to make recommendations, provide optimized medication alternatives and produce comprehensive medication management reports to share with physicians efficiently.

#### Benefit of EHR-interoperability: Better communication between the healthcare team for greater productivity, and fewer errors or gaps in patient care

A study from the GTMRx Institute<sup>29</sup> about issues

**The new wave of empowered patients will drive interoperability in healthcare.**

*“Patients are getting much more involved in their care. I think patients are going to require an interoperable system because they are not satisfied with the current state of healthcare.”*

Source: Precision Insights Podcast with Dave Wolfe

**Figure 6: Benefits of EHR-Interoperability: Improved Patient Care and Enhanced Patient Experience**

In one of GenXys’ Precision Insights podcasts, a health information system expert, Dave Wolfe of FusionRx, mentioned that as patients are getting much more involved in their care, they will become more aware of the need for an interoperable system because they are not satisfied with the current state of healthcare.

that healthcare leaders see in the healthcare industry shows that one of the most significant barriers to effective medication management is a lack of communication between physicians and pharmacists.

Interoperability is a key component to making sure that physicians and pharmacists have access to the same information about a patient (refer to **Figure 5**). If prescribers and pharmacists are using the same EHR-integrated tools, they can work together more effectively to manage patients' health outcomes and medications.

### *Benefit of EHR-interoperability: Improved Patient Care and Enhanced Patient Experience*

In a time where we can order and pay for groceries from our watches, patients sometimes expect that all their providers would, (let alone should), have access to their electronic health record. Meanwhile, the failure of healthcare data to follow patients to every care setting can lead to delays or inaccuracies. This is a barrier on both the patient and provider sides which manifests as a significant social and economic cost burden.

In one of GenXys' Precision Insights podcasts,<sup>30</sup> a health information system expert, Dave Wolfe of FusionRx, mentioned that as patients are getting much more involved in their care, they will become

more aware of the need for an interoperable system because they are not satisfied with the current state of healthcare (as highlighted in **Figure 6**).

### **Conclusion**

Building a successful PGx program is challenging, however, data has shown the benefits far outweigh any initial teething pains. Interoperable software can make PGx program development and deployment easier and ensure that the point-of-care use of PGx is efficient and accurate. This feeds into a virtuous cycle that leads to significant adoption for the benefit of all.

Specifically, advanced medication decision support tools with embedded PGx that are EHR-integrated are the key to delivering a successful PGx program for your organization. This software needs to be workflow-specific because both pharmacists and prescribers play a vital role in making sure that the patients are getting the best medication options to treat their conditions. Since members of each profession may care about subtly different information, these medication support tools need to be able to reflect that difference.

Overall, decisions about who to test and when to intervene with PGx information should be based on organizational goals related to the patients' conditions and medication needs. The decision-making frameworks laid out in this article should be a great resource to help you get started. [i-PM](#)



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Bernard Esquivel is a practicing physician-scientist, senior executive, and international leader with in-depth expertise developing new markets, devising compelling value propositions, go-to-market strategies, and launching programs to fulfill organizational goals and objectives in the healthcare space. With training as a Clinical Immunologist, Allergies, and Medical Genetics specialist he also has 10+ years experience in materializing biotech and health sciences ideas and concepts into clinically actionable solutions. Dr. Esquivel mobilized the local healthcare community to engage them in the practice of precision medicine by founding and presiding over the Latin American Association of Personalized Medicine (ALAMP). This organization now includes >500 members from 9 countries in Latin America, holds symposiums, provider workshops, and other educational outreach per year. Serving as Chief Medical Officer for several well-renowned global organizations, he has demonstrated his passion and advocacy for bringing precision medicine closer to patients.

### **References**

- Harvard Business Review Analytic Services. Genetic Testing Brings Big Changes to the Health Care System. <https://www.optum.com/content/dam/optum3/optum/en/resources/PDFs/3149445-21672-hbr-wp-optum-march2020.pdf>. Accessed July 30, 2021.
- Dawes, Martin & Aloise, Martin & Ang, J. & Cullis, Pieter & Dawes, Diana & Fraser, Robert & Likhaitzky, Gideon & Paterson, Andrea & Stanley, Paul & Suarez-Gonzalez, Adriana & Katzov-Eckert, Hagit. (2016). Introducing pharmacogenetic testing with clinical decision support into primary care: a feasibility study. *CMAJ Open*. 4. E528-E534. 10.9778/cmajo.20150070.
- Medication safety basics. Centers for Disease Control and Prevention. <https://www.cdc.gov/medicationsafety/basics.html>. Published September 28, 2010. Accessed July 30, 2021.
- Lazarou J, Pomeranz B, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. *JAMA* 1998;279:1200-1205.
- Gurwitz JH, Field TS, Avorn J, McCormick D, Jain S, Eckler M, et al. Incidence and preventability of adverse drug events in nursing homes. *Am J Med* 2000;109(2):87-94.
- Naranjo CA, Busto U, Maldones R. Adverse drug reactions in liver cirrhosis. *European Journal of Clinical Pharmacology*. 1978;13(6):429-434. doi:10.1007/bf00566321
- Moon AM, Singal AG, Tapper EB. Contemporary epidemiology of chronic liver disease and cirrhosis. *Clinical Gastroenterology and Hepatology*. 2020;18(12):2650-2666. doi:10.1016/j.cgh.2019.07.060
- Liver Disease in Canada. Canadian Liver Foundation. <https://www.liver.ca/wp-content/uploads/2017/09/Liver-Disease-in-Canada-E-3.pdf>. Published September 2017. Accessed July 30, 2021.
- Villain C, Metzger M, Combe C, et al. Prevalence of atheromatous and non-atheromatous cardiovascular disease by age in chronic kidney disease. *Nephrology Dialysis Transplantation*. 2018;35(5):827-836. doi:10.1093/ndt/gfy277
- Arora P, Vasa P, Brenner D, et al. Prevalence estimates of chronic kidney disease in CANADA: Results of a nationally representative survey. *Canadian Medical Association Journal*. 2013;185(9). doi:10.1503/cmaj.120833
- Chronic kidney disease in the United States, 2021. Centers for Disease Control and Prevention. <https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html>. Published March 4, 2021. Accessed July 30, 2021.
- Kongkaew C, Hann M, Mandal J, et al. Risk factors for hospital admissions associated with adverse drug events. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2013;33(8):827-837. doi:10.1002/phar.1287
- Nilsson E, Gasparini A, Årnlöv J, et al. Incidence and determinants of hyperkalemia and hypokalemia in a large healthcare system. *International Journal of Cardiology*. 2017;245:277-284. doi:10.1016/j.ijcard.2017.07.035
- Veglio M, Bruno G, Borra M, et al. Prevalence of increased QT Interval duration and dispersion in type 2 diabetic patients and its relationship with coronary heart disease: A POPULATION-BASED cohort. *Journal of Internal Medicine*. 2002;251(4):317-324. doi:10.1046/j.1365-2796.2002.00955.x
- Howard RL, Avey AJ, Slavenburg S, et al. Which drugs cause preventable admissions to hospital? A systematic review. *British Journal of Clinical Pharmacology*. 2007;63(2):136-147. doi:10.1111/j.1365-2125.2006.02698.x
- Gandhi TK, Weingart SN, Borus J, et al. Adverse drug events in ambulatory care. *New England Journal of Medicine*. 2003;348(16):1556-1564. doi:10.1056/nejms020703
- Oka, Y., Okamoto, K., Kawashita, N., Shirakuni, Y. & Takagi, T. Meta-analysis of the Risk of Upper Gastrointestinal Hemorrhage with Combination Therapy of Selective Serotonin Reuptake Inhibitors and Non-steroidal Anti-inflammatory Drugs. *Biological Pharm Bulletin* 37, 947-953 (2014)
- Genes-drugs. CPIC. <https://cpicpgx.org/genes-drugs/>. Accessed July 30, 2021.
- Evans, R. S., Lloyd, J. F., Stoddard, G. J., Nebeker, J. R. & Samore, M. H. Risk Factors for Adverse Drug Events: A 10-Year Analysis. *Ann Pharmacother* 39, 1161-1168 (2005)
- Onder G, Petrovic M, Tangisuran B, et al. Development and validation of a score to assess risk of adverse drug reactions Among In-hospital patients 65 years or older. *Archives of Internal Medicine*. 2010;170(13). doi:10.1001/archintermed.2010.153
- Dutch Pharmacogenetics Working Group. PharmGKB. <https://www.pharmgkb.org/page/dpwg>. Accessed July 30, 2021.
- PharmGKB. <https://www.pharmgkb.org/>. Accessed July 30, 2021.
- Table of Pharmacogenetic Associations. FDA. <https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations>. Accessed July 30, 2021.
- STRIP Collaborative Community. American Society of Pharmacovigilance. <https://www.stopadr.org/strip>. Accessed July 30, 2021.
- Pharmacogenetics Virtual Summit 5: Implementation. AMA. <https://www.ama-assn.org/delivering-care/precision-medicine/pharmacogenomics-virtual-summit-5-implementation>. Accessed July 30, 2021.
- The pharmacist's role in implementing pharmacogenomics [podcast]. GenXys. <https://www.genxys.com/content/the-pharmacists-role-in-implementing-pharmacogenomics/>. Published September 30, 2020. Accessed July 30, 2021.
- How can pharmacogenetics be helpful to doctors? [podcast]. GenXys. <https://www.genxys.com/content/how-can-pharmacogenetics-be-helpful-to-doctors/>. Published January 29, 2020. Accessed July 30, 2021.
- Frigon M-P, Blackburn M-E, Dubois-Bouchard C, Gagnon A-L, Tardif S, Tremblay K. Pharmacogenetic testing in primary care practice: Opinions of physicians, pharmacists and patients. *Pharmacogenomics*. 2019;20(8):589-598. doi:10.2217/pgs-2019-0004
- Press release: Nearly one in four people say their medications are not Routinely reviewed and evaluated by their medical team. Get The Medications Right. <https://gtmr.org/press-release-nearly-one-in-four-people-say-their-medications-are-not-routinely-reviewed-and-evaluated-by-their-medical-team/>. Published July 14, 2021. Accessed July 30, 2021.
- Interoperability in Healthcare: Is it living up to the Hype? [Podcast]. GenXys. <https://www.genxys.com/content/interoperability-in-healthcare/>. Published July 8, 2020. Accessed July 30, 2021.