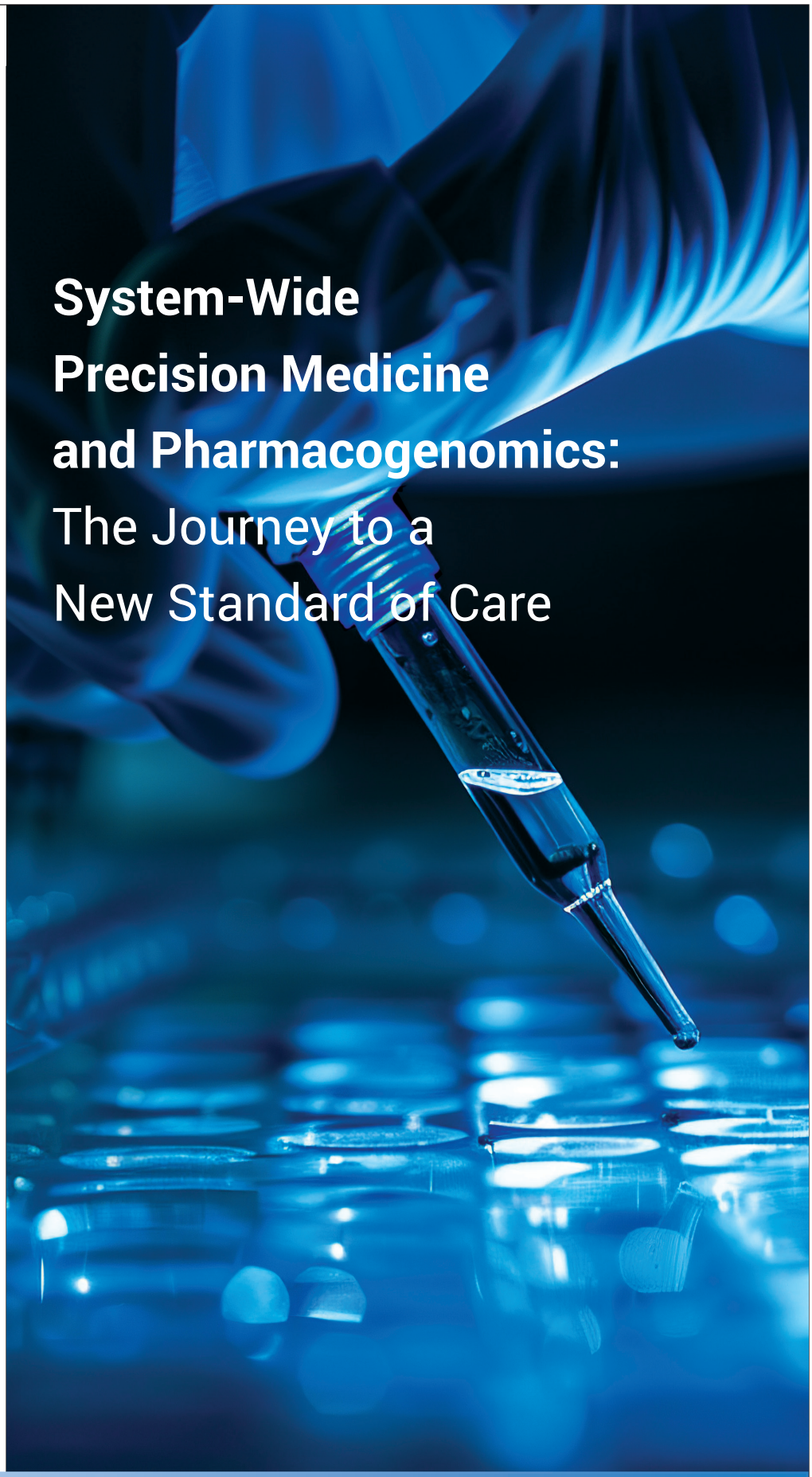
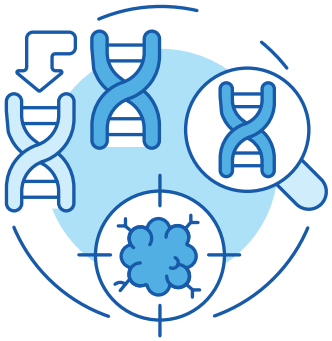
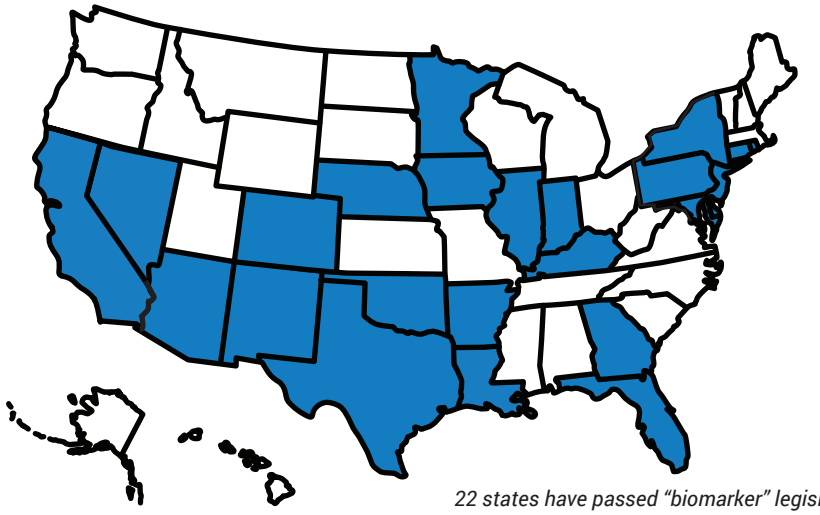


System-Wide Precision Medicine and Pharmacogenomics: The Journey to a New Standard of Care



Precision medicine is in the process of becoming a standard of care. For example, the use of pharmacogenomics (PGx), which is part of precision medicine, is rapidly growing in many health systems and individual practices. The increased use is based on recent (and accumulating) data showing substantial improvements in patient outcomes and overall reduced healthcare costs.

Insurance coverage of pharmacogenomics and other genetic testing is continuing to expand. 22 states have passed "biomarker" legislation mandating that private insurance carriers and often Medicaid cover genetic tests such as pharmacogenomics – and many more are considering legislation. As an example, California recently passed a law that requires pharmacogenomic testing to be covered for Medi-Cal patients, the state's version of Medicaid. Typically PGx tests will be covered in line with clinical guidelines from CPIC and the FDA.



. *22 states have passed "biomarker" legislation*

Likewise, Medicare coverage for pharmacogenomics has continued to improve, and with the recent Medicare coverage expansion for the National Government Services (NGS) region, all 50 states now have local coverage designations (LCD) for expanded pharmacogenomics testing, aligned with CPIC A/B + FDA guidelines. All Medicare regions have also adopted a specific new CPT code for pharmacogenomics panels (81418). There are significant positive implications for Medicare patients: the 4 year exposure risk for Medicare aged patients to medications with known drug-genomic interactions exceeds 50%[1].

Furthermore, the American Society of Health-System Pharmacists (ASHP) recently released a statement on the strategic role pharmacists should play in clinical pharmacogenomics. They believe pharmacogenomic testing can improve medication-related outcomes for patients across all health system practice settings. These improvements in patient outcomes include decreased side effects, increased efficacy, lower cost of treatment, and better adherence among several other benefits.

It's becoming clear that organizations that take a system-wide approach to precision medicine will see benefits in terms of medication efficacy, fewer adverse drug reactions and re-admissions while establishing a major differentiator to attract new patients.

PGx Shown to Reduce Serious Adverse Reactions in a large, randomized study

In 2023, an international group completed a large controlled, randomized, 7,000 patient study where medications were matched to the patient using their genetics. The results published in Lancet[2], show a 30% reduction in serious medication adverse reactions for those patients who utilized pharmacogenomic testing compared to the control group who had no genetic testing. The 30% reduction represents a big impact when it comes to reducing serious medication adverse reactions. The study is yet another data point: when precision medicine is applied there can be a significant impact on patient outcomes.

Beyond Pharmacogenomics: Benefits of Screening for Common Actionable Hereditary Conditions

A recent study published in the Annals of Internal Medicine evaluated the cost-effectiveness of screening for 3 common, actionable, hereditary conditions. The conclusion: population genomic screening is likely to be cost-effective, even among adults under 40 years old. And given the relatively low cost of genetic screening, it will likely be cost effective to extend screening to additional actionable genetic conditions.

Cost Effectiveness of Clinical Decision Support

The Journal of Personalized Medicine recently evaluated the benefits of utilizing clinical decision support in combination with pharmacogenomics. The result: a reduction of close to $7,000 per patient in medical costs through a voluntary pharmacogenomics-based medication management program. They note that with a clinical decision support system combined with medication management the cost reduction trends are encouraging – and they support the idea that system wide adoption would be beneficial.

ROI at a Major U.S. Health System

A major US health system, who is an ActX customer, did an ROI (return on investment) pharmacogenomics study using selected employees. The health system is self-insured for all of its employee's healthcare and hence has a full view of medical claims and medication costs. To better understand the value of a pharmacogenomics (PGx) program, they offered PGX to a pilot group of employees.The study showed medical cost savings of $2,084 per patient in the first year. There were over a 1,000 medication therapy changes in the first year. The second year showed an ongoing reduction in costs of $436 per study patient per month. Total savings in the pilot have already totaled $2.2 million[3]

Building PGx into Regular EHR Workflow

As early programs develop and more data becomes available, it seems inevitable that pharmacogenomics will become a standard of care. When thinking through widespread PGX implementation, health systems must consider that the only practical way to deliver complex genetic knowledge without disrupting clinical workflow is through genomic decision support embedded in the electronic health record (EHR).

Clinical implementation of PGx into the electronic health record (EHR) at the point of care is critical for maximizing access and usage of PGx results. For example, at Nemours Children's Health their PGx program is fully integrated with the Epic EHR in all phases of inpatient and outpatient care[4].

For Nemours one of the important considerations for selecting a genomic decision support vendor was ensuring results are supported for any chosen PGx testing laboratory. A vendor who can integrate internal and external test results was a requirement for Nemours to support an in-house array while allowing for future flexibility for expansion to an external laboratory.

Another key consideration for Nemours was for PGx results to be integrated into the EHR in a method that is easily accessible for the clinician. Many PGx laboratory reports are imported as a PDF or image making results difficult to locate over the course of a patient's care. Many vendor programs require providers to access an external portal with a unique login to view results which is often disruptive to workflows.

CASE STUDY: NorthShore

At NorthShore, medication orders and prescriptions entered within the normal Epic order workflow are automatically checked against the patient's genomics. Clinicians get an alert if an issue is detected with medication efficacy, dosing, or adverse reactions. That is due to technology which specializes in integrating real-time genomic clinical-decision support into EHR workflows.

The program is helping advance precision medicine at NorthShore, whose DNA-10K program has already found favor among clinicians. In that program ninety-nine percent of eligible physicians have already ordered tests for their patients. Of those more than half said the program has already provided a direct clinical benefit.

Nearly all (99.8%) of tested patients had at least one actionable finding detected through pharmacogenomic efforts in the NorthShore study. A long-term benefit is provided as the need for new medications arises.

The Pitfalls of "DIY" Pharmacogenomics

Some health systems consider integrating genomics into their EHR via an internally developed project. While internal projects can demonstrate the potential of

genomic decision support, they face serious scaling and maintenance challenges. EHR's either have nowhere to store genetic data or are able to store only a small number of variants per patient (the average individual has 6 million variants). Genomics can be very complex and existing EHR decision support configurable rule systems lack the ability to cover all the cases.

Examples of challenges include:

- Writing, maintaining, and testing hundreds or thousands of logically complex alerts. Maintenance is driven by new rapidly changing knowledge and can be very challenging.
- Creating alert content which provides all guidance in clinician-friendly language built into normal workflow
- Storing and analyzing patient genetic data sets which can be as large as 6M variants per patient
- Human capital costs: an internal project can require thousands of hours from team members and consultants including IT personnel, project managers, physicians, geneticists, PharmDs, and more
- Scalability: new alerts or changes to existing alerts need to be developed continuously as our knowledge advances. Computer resources can be strained as the genetic data on file grows and complex algorithms execute
- Finding a vendor that can work with both internal system and external labs

Where to begin

For health systems to deliver on the promise of precision medicine a turnkey, scalable solution is needed. Health System executives should start with the big picture – by understanding just how much genetic testing is occurring in their institution. And then diving deeper, understanding how many of those genetic results are ending up as PDFs – likely providing minimal value for time-strained clinicians.

Consultations with internal departments such as oncology, behavioral health/psychiatry, cardiology, primary care, and pharmacy leadership can shed more light on where the needs are opportunities lie. Consideration should also be given to the system laboratory and whether it's feasible to conduct genetic testing onsite. Review resources like CPIC to better understand the guidelines, challenges and opportunities with pharmacogenomics.

When exploring pharmacogenomics vendors health systems should also keep in mind IT and informatics it's not just about finding the right labs, but also considering how will you handle the data inside your EHR.

When all these considerations are taken and a system-wide effort is applied the results are often worth the effort. A pharmacogenomics project done right can provide real world value for patients, providers and help to differentiate a health system as a world-class leader in the space.

Citations

1. PLOS One 2016 11 (10) e0164972, Samwald et al.
2. A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover impleme tation study. Swen, Jesse JBuunk, Annemarie et al. The Lancet, Volume 401, Issue 10374, 347 - 356 *** need date
3. *Results based on unpublished data, available on request
4. Cook, K.J., Duong, B.Q., Seligson, N.D., Arn, P., Funanage, V.L., Gripp, K.W., Ki win, S.M., Lawless, S.T., Lee, M.M., Robbins, K.M., West, D. and Blake, K.V. (2021), Key Considerations for Selecting a Genomic Decision Support Pla form for Implementing Pharmacogenomics. Clin Pharmacol Ther, 110: 555 558. https://doi.org/10.1002/cpt.2328
5. David SP, Dunnenberger HM, Choi S, DePersia A, Ilbawi N, Ward C, Wake DT, Khandekar JD, Shannon Y, Hughes K, Miller N, Mangold KA, Sabatini LM, Helseth DL, Xu J, Sanders A, Kaul KL, Hulick PJ. Personalized medicine in a community health system: the NorthShore experience. Front Genet. 2023 Nov 28;14:1308738. doi: 10.3389/fgene.2023.1308738. PMID: 38090148; PMCID: PMC10713750.
6. Cook, K.J., Duong, B.Q., Seligson, N.D., Arn, P., Funanage, V.L., Gripp, K.W., Ki win, S.M., Lawless, S.T., Lee, M.M., Robbins, K.M., West, D. and Blake, K.V. (2021), Key Considerations for Selecting a Genomic Decision Support Pla form for Implementing Pharmacogenomics. Clin Pharmacol Ther, 110: 555 558. https://doi.org/10.1002/cpt.2328