Penn Medicine

Building a pharmacogenomics program from the ground up: balancing research and clinical care

Sony Tuteja, PharmD, MS, BCPS, FAHA
Research Assistant Professor of Medicine
Division of Translational Medicine and Human Genetics
Assistant Director, Pharmacogenomics
Penn Center for Precision Medicine
University of Pennsylvania
Corporal Michael J. Crescenz VA Medical Center
Philadelphia, PA

Perelman School of Medicine University of Pennsylvania

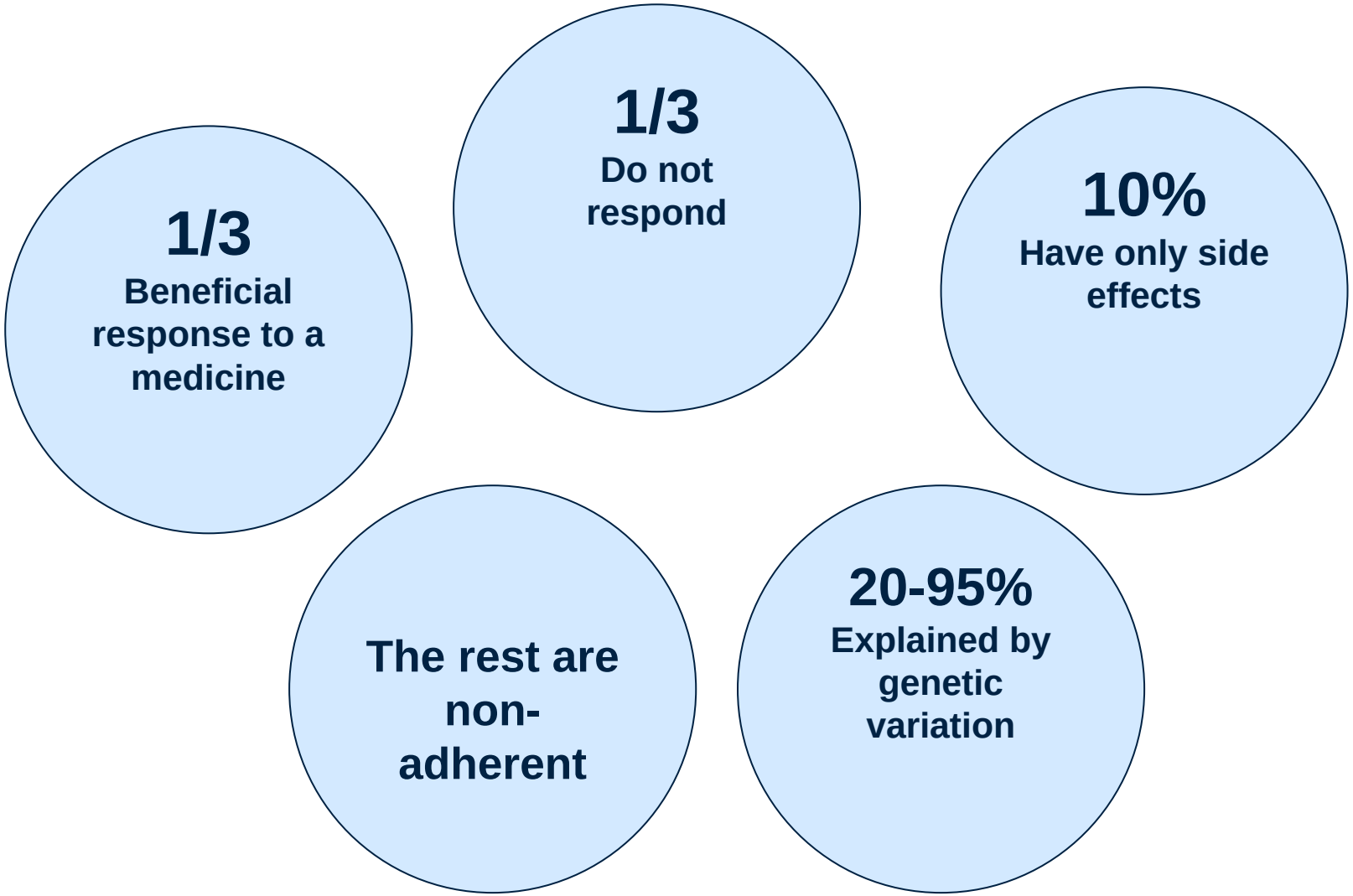
VA U.S. Department of Veterans Affairs

CPIC meeting October 5, 2023

Outline

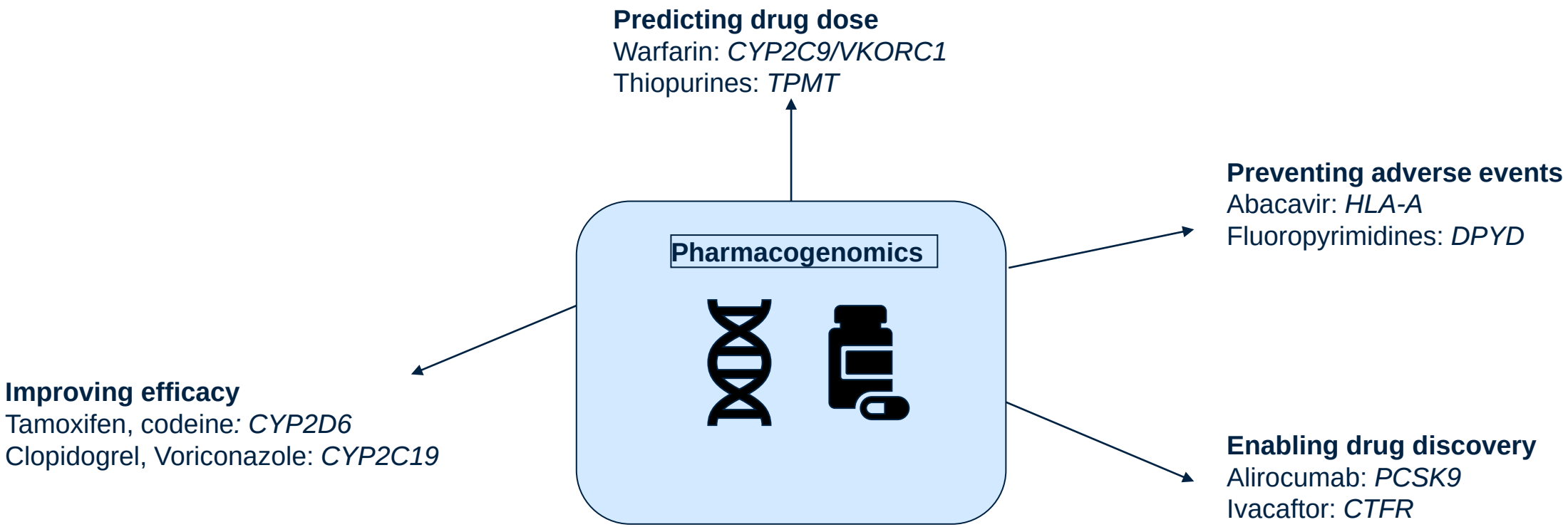
- Provide an overview of the PGx implementation strategy at Penn Medicine
- Describe current PGx implementation studies
- Discuss the outcomes of the PGx clinic

Variability in drug response



[1] Maitland-van der Zee. European J Pharmacology 2000; 410: 121-30
[2] Roden DM. Circulation 2011;123:1661-1670

Application of pharmacogenomics to clinical care and drug discovery



Primohamed M. Nature reviews genetics 2023

What is the impact of pharmacogenomics?

JAMA Network Open

Original Investigation | Genetics and Genomics

Projected Prevalence of Actionable Pharmacogenetic Variants and Level A Drugs Prescribed Among US Veterans Health Administration Pharmacy Users

Catherine Chanfreau-Coffinier, PhD; Leland E. Hull, MD, MPH; Julie A. Lynch, RN, PhD; Scott L. DuVall, PhD; Scott M. Damrauer, MD; Francesca E. Cunningham, PharmD; Benjamin F. Voight, PhD; Michael E. Matheny, MD, MPH; David W. Oslin, MD; Michael S. Icardi, MD; Sony Tuteja, PharmD

JAMA Network Open. 2019;2(6):e195345. doi:10.1001/jamanetworkopen.2019.5345 June 7, 2019

Out of 7.7 million veterans[1]:

99% have at least 1 level A variant

37% receive at least 1 level A drug

25% receive at least 2 level A drug

At Penn Medicine (3.3 million patients)[2]:

98% have at least 1 level A variant

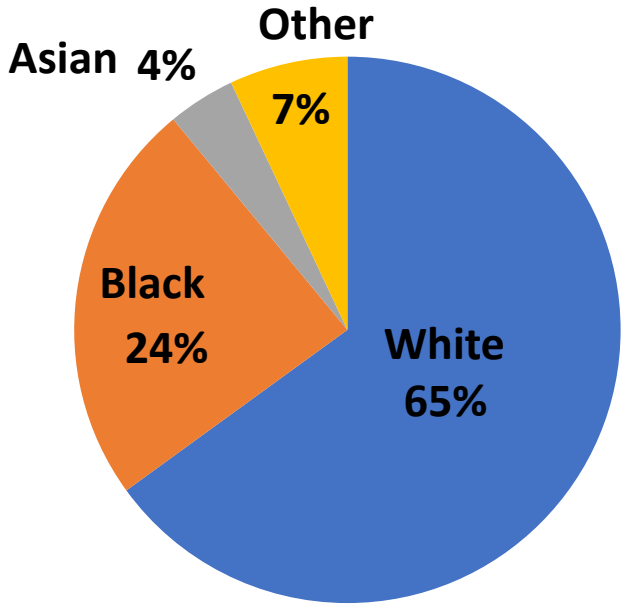
21% receive at least 1 level A drug

[1] JAMA Network Open. PMID: 31173123
[2] J Transl Med. PMID: 36443877

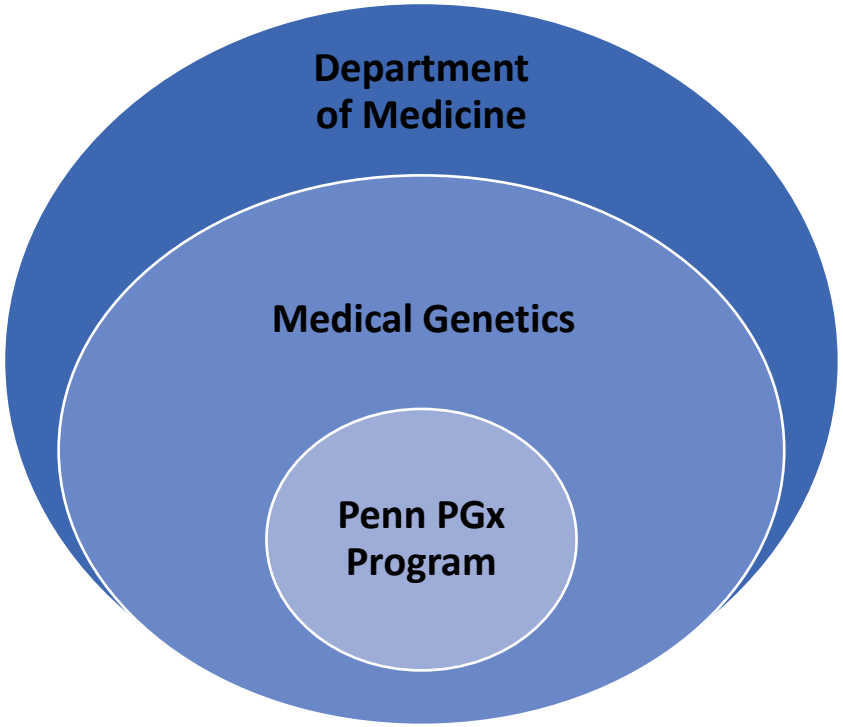
Elements needed to get PGx into clinical practice

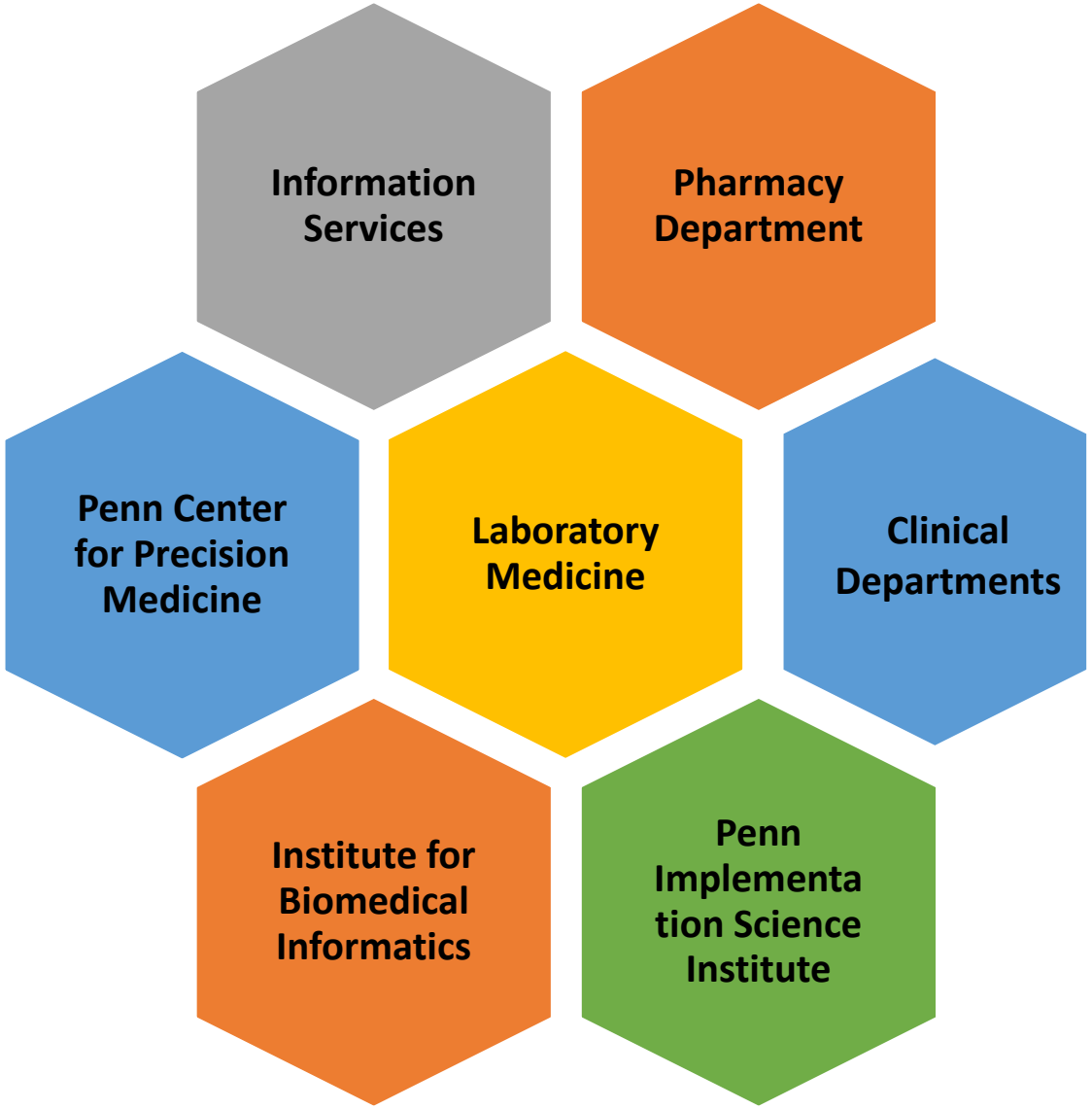
- Evidence for gene-drug pairs ✓
- Guidelines for translating results into prescribing decisions ✓
- Access to testing ✓
- Reimbursement for testing ✓
- Informatics infrastructure to incorporate user friendly clinical decision support tools ✓
- Provider knowledge regarding interpretation and application of PGx
- Incentives for clinicians to order tests

Penn Medicine



6.5 million	Outpatient visits
337,000	ED visits
129,000	Adult admissions
7,478	Physicians
47,000	Employees


Department of Medicine
Medical Genetics
Penn PGx Program

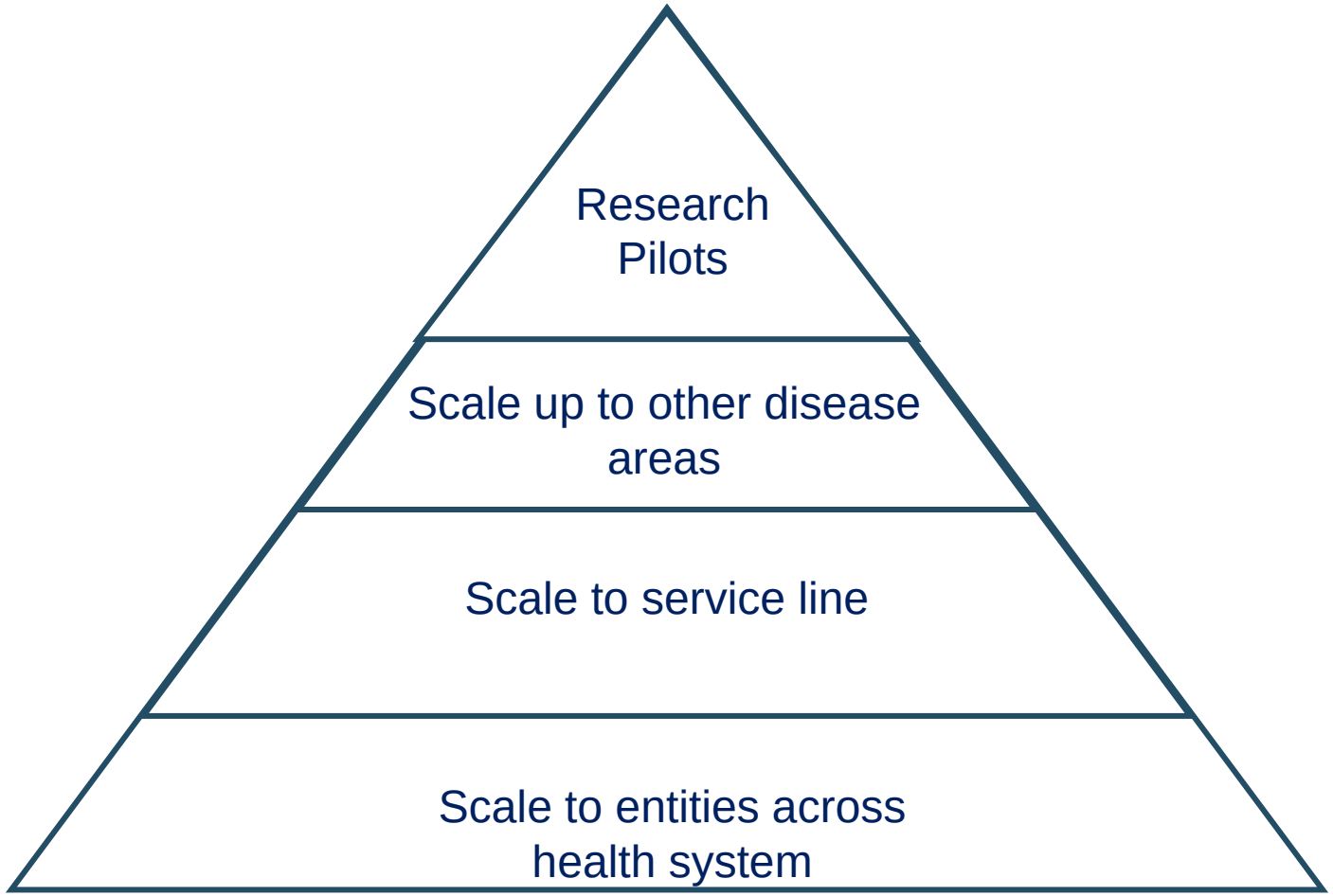

Information Services
Pharmacy Department
Penn Center for Precision Medicine
Laboratory Medicine
Clinical Departments
Institute for Biomedical Informatics
Penn Implementation Science Institute

Tackling roadblocks on the path to implementation

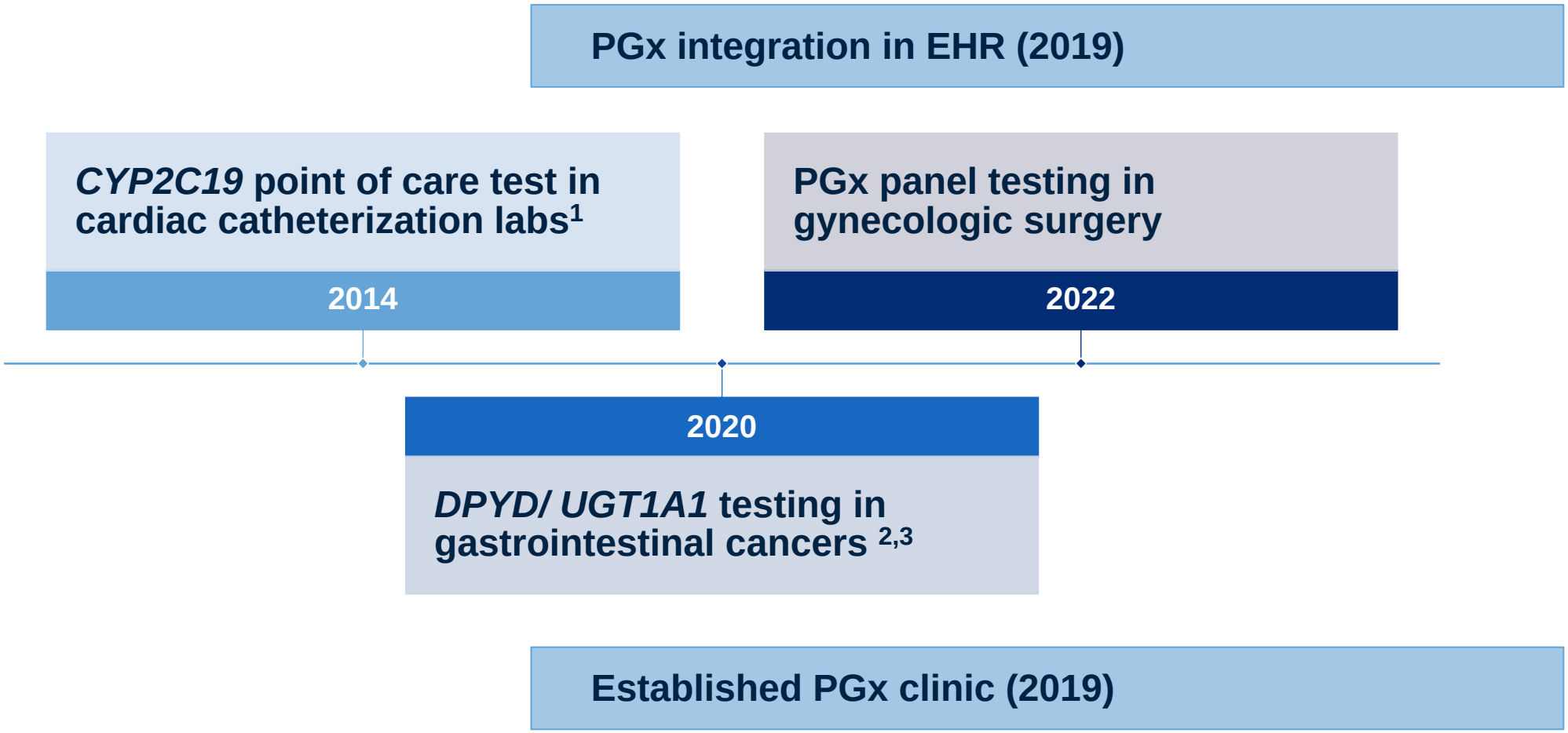
Barriers

- Clinician skepticism
- Lack of clinician knowledge about PGx
- Lack of endorsement of PGx by medical organizations
- Lack of genotyped guided RCTs
- Laboratory support
- EHR infrastructure for returning PGx results

Stepwise strategy for PGx implementation: a campaign of “wins”

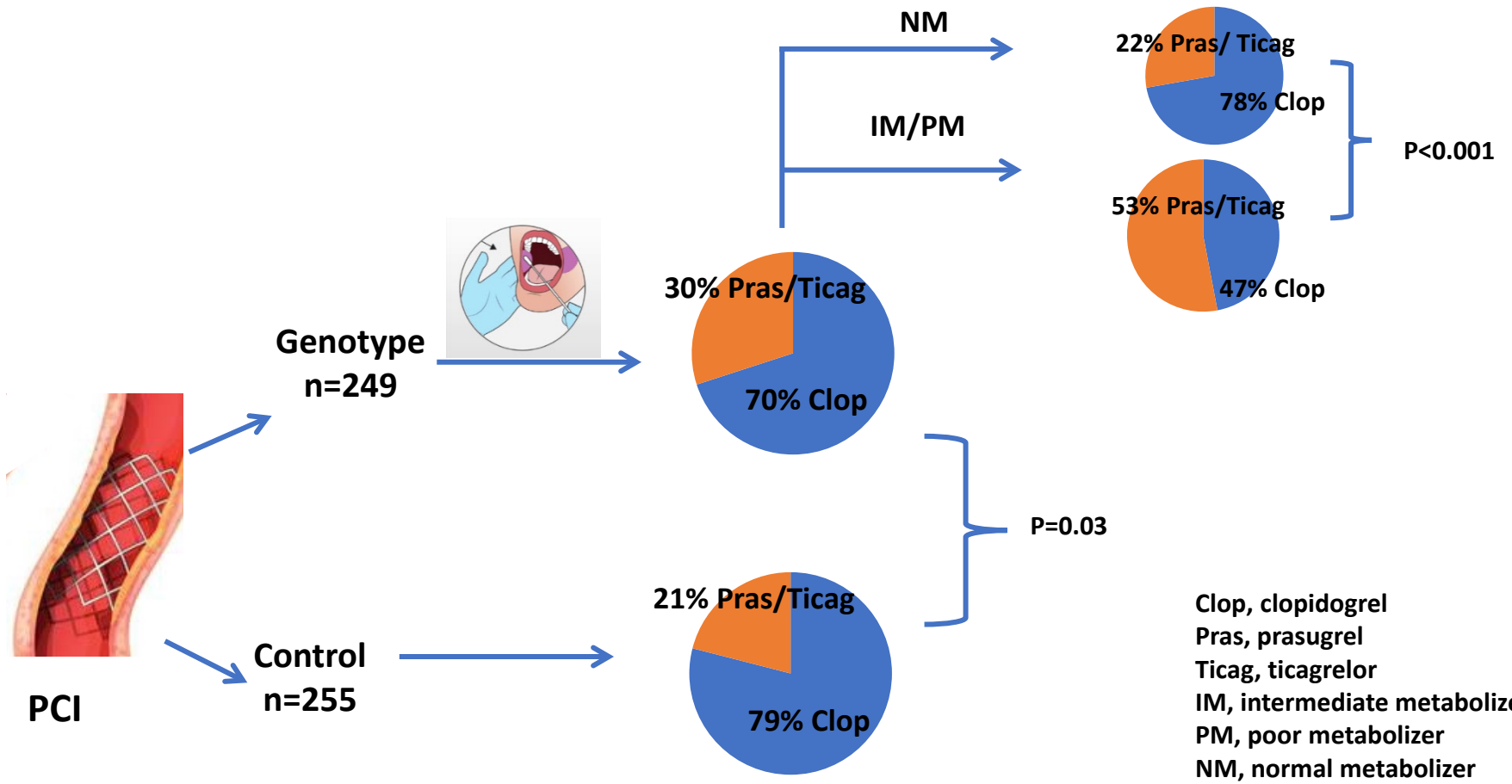


Timeline of PGx research and clinical testing at Penn Medicine



[1] PMID: 31928229
[2,3] PMID: 34996412, PMID: 35865463

CYP2C19- clopidogrel

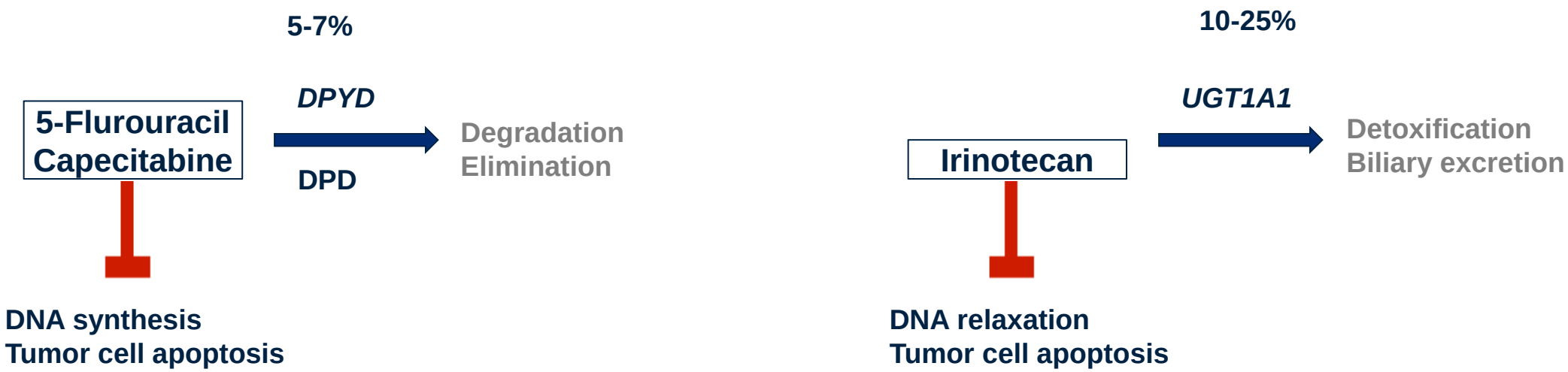


Tuteja S. Circulation Genomic and Precision Medicine 2020. PMID: 31928229
PMID: 34881641, PMID: 34984913

Benefits from the *CYP2C19* study

- Level of clinician engagement required for successful uptake of PGx
- Identified achievable intermediate outcomes to enable a “win” for PGx testing
- Established a workflow for returning PGx results to the EHR with CDS
- Helped facilitate transition to clinical use

DPYD/ UGT1A1- GI cancer therapies

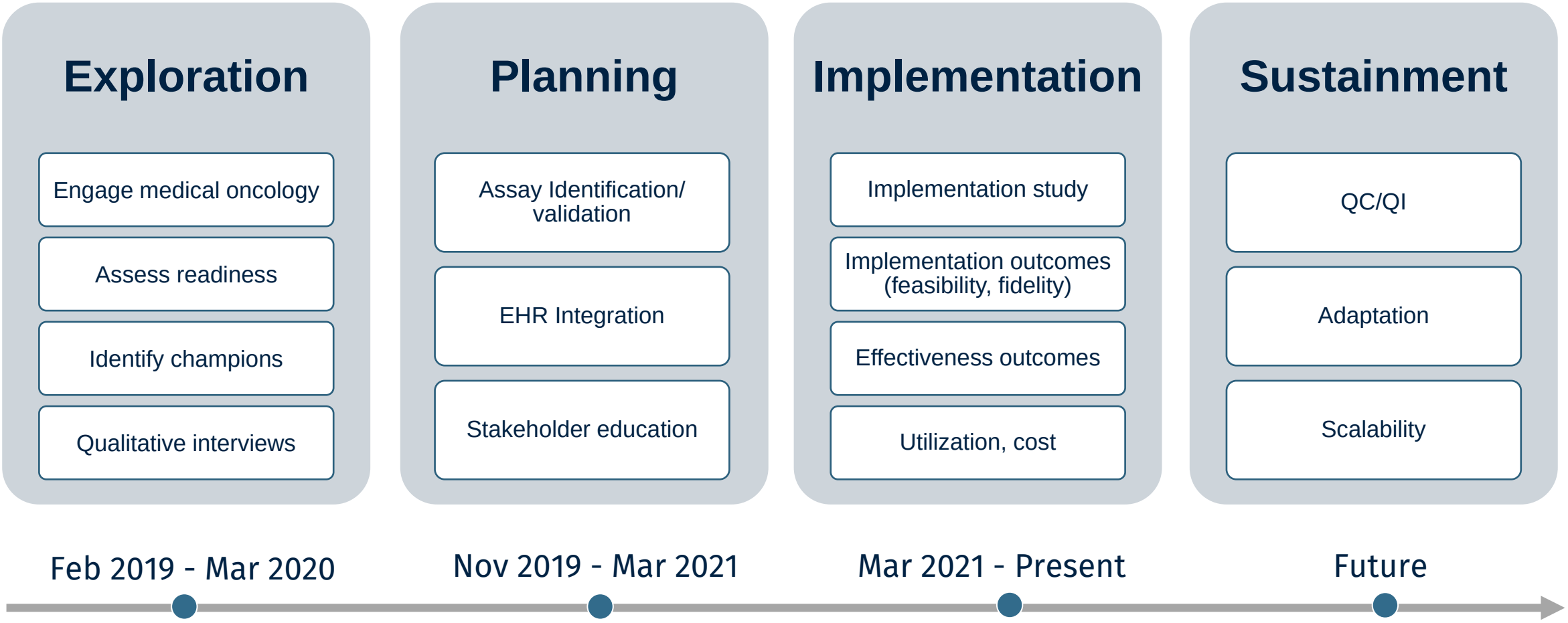


DPYD variant carriers have greater dose-related toxicities

- Hematologic
- Gastrointestinal

Varughese LA, et al. *Pharmacotherapy* 2020. PMID: 32985005

Implementation Science framework provides a roadmap



Aarons GA. *Adm. Policy Ment. Health 2011*

Qualitative study helped identify workflow barriers for *PGx* testing in cancer care

1-on-1 semi-structured interviews with 25 oncology specialists

Barrier	Strategy
Long turnaround time (send-out)	Developed test with local partners
Difficulty accessing results	Discrete reporting in genomics module in Epic
Unclear dosing recommendations	Clinical decision support Train oncology pharmacists on PGx dosing
Limited evidence base	Educational initiatives on current guidance
Test costs	Testing covered by research funds

Kelsey Lau-Min, MD

Lau-Min KS. BMC Cancer 2022; PMID: 34996412

IMPACT GI: ImpleMenting PhArmacogenetiC Testing in Gastrointestinal Cancers

- Pragmatic, non-randomized, open-label study across three Penn Medicine sites
- Goal: evaluate the feasibility of *DPYD/UGT1A1* testing in patients treated with fluoropyrimidines or irinotecan.

Implementation (primary)	Clinical effectiveness (secondary)
1. Determine feasibility, rate of PGx results returned prior to first dose of chemotherapy	1. Determine if providing PGx test results will decrease number of patients experiencing ≥Grade 3 toxicity over first 6 cycles
2. Determine fidelity, level of acceptance by prescribers with genotype-based dosing guidelines	2. Determine if providing PGx test results will improve patient reported outcomes (PROs)
3. Determine penetrance, rates of testing among eligible patients	

Lisa Varughese, PharmD

Target enrollment: 300 patients

NCT04736472

PhaRmacogEnetic-guided ChoIce of post-SurgEry analgesics (PRECISE)

- Randomized, controlled, study across two gynecology clinics (general and gyn-onc)
- Goal: Evaluate the feasibility of performing a multi-gene PGx panel test to provide tailored pain medication recommendations in patients undergoing major gynecologic surgery

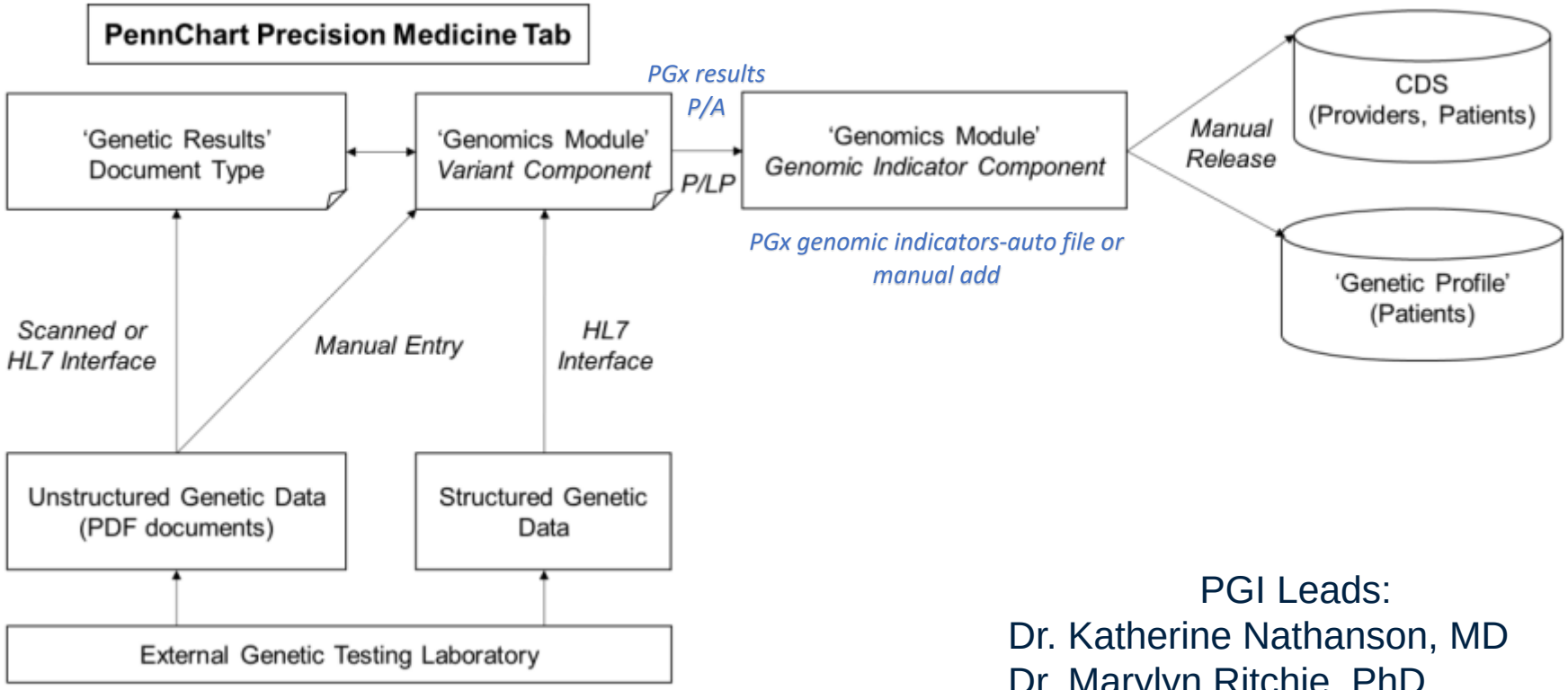
Implementation (primary)	Clinical effectiveness (secondary)
1. Determine feasibility of integrating PGx panel test in the EHR with a pharmacist PGx e-consult 2. Determine the fidelity to genotype-guided pharmacotherapy recommendations	▪ Determine if PGx testing will: • Improve patient self-reported numeric pain scores • Reduce total MME • Decrease ADRs

Target enrollment: 200 patients

Glenda Hoffecker, PharmD

NCT05548660

PennChart Genomics Initiative (PGI)

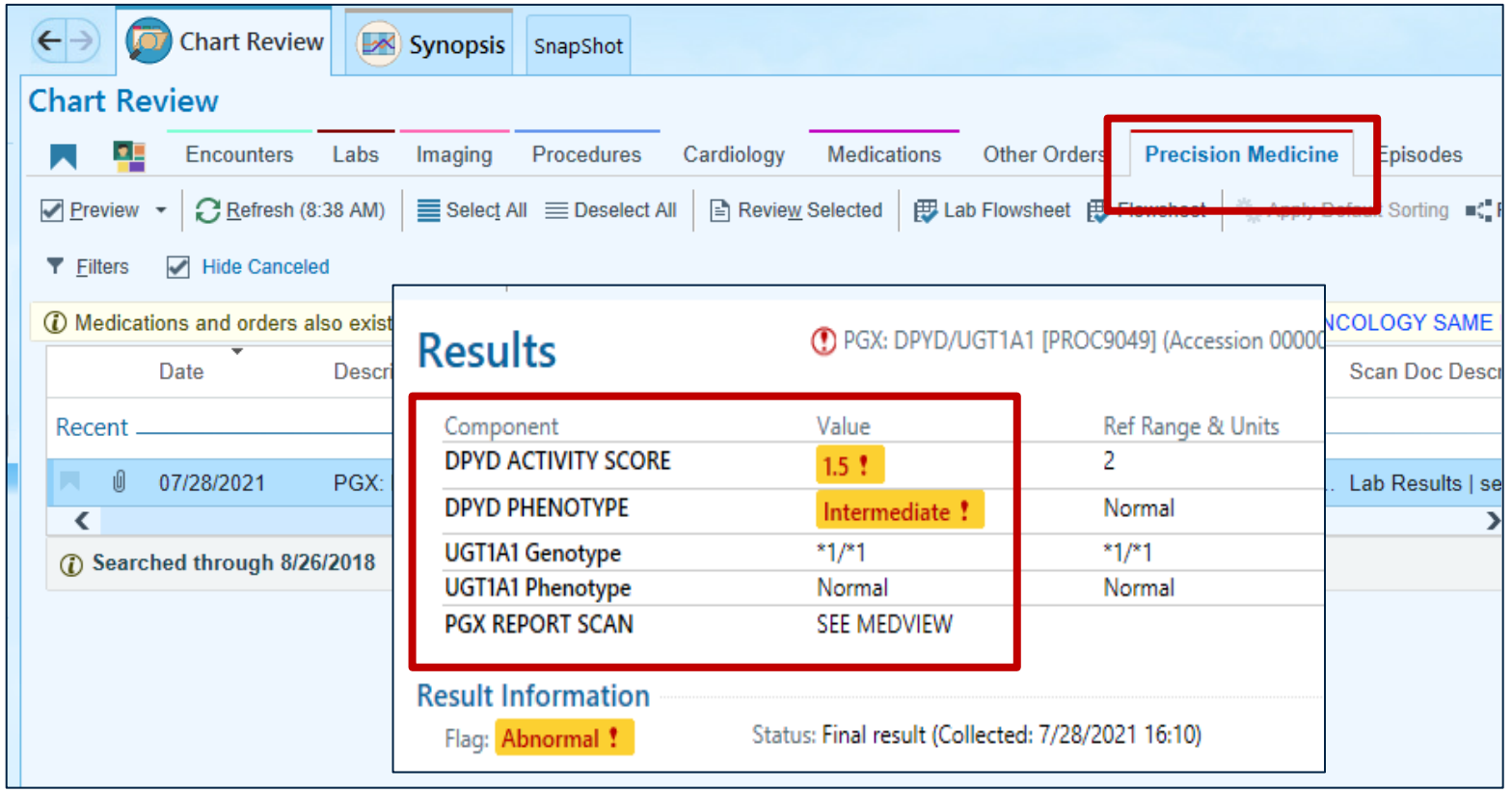


P/LP- pathogenic/ likely pathogenic
P/A- present/absent

PGI Leads:
Dr. Katherine Nathanson, MD
Dr. Marylyn Ritchie, PhD

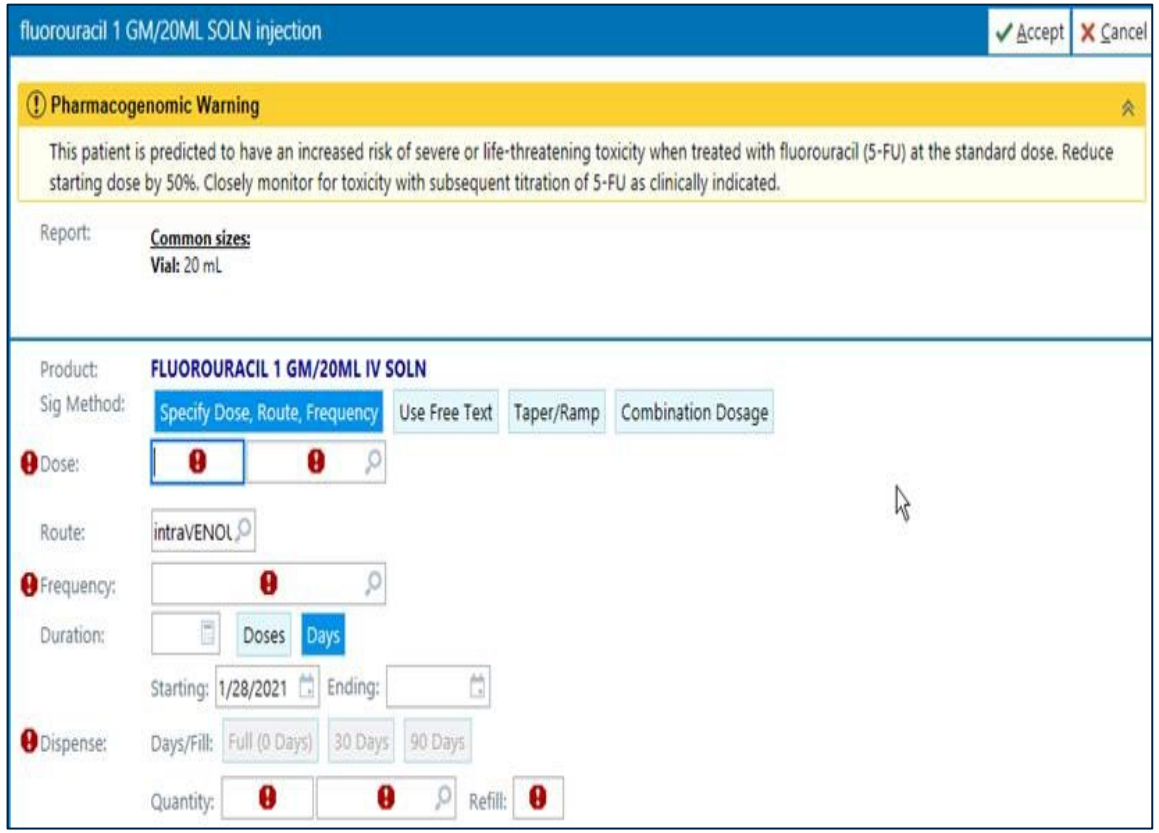
Lau-Min KS. Genetics in Medicine 2021 PMID: 33299147

Discrete PGx results in Precision Medicine tab



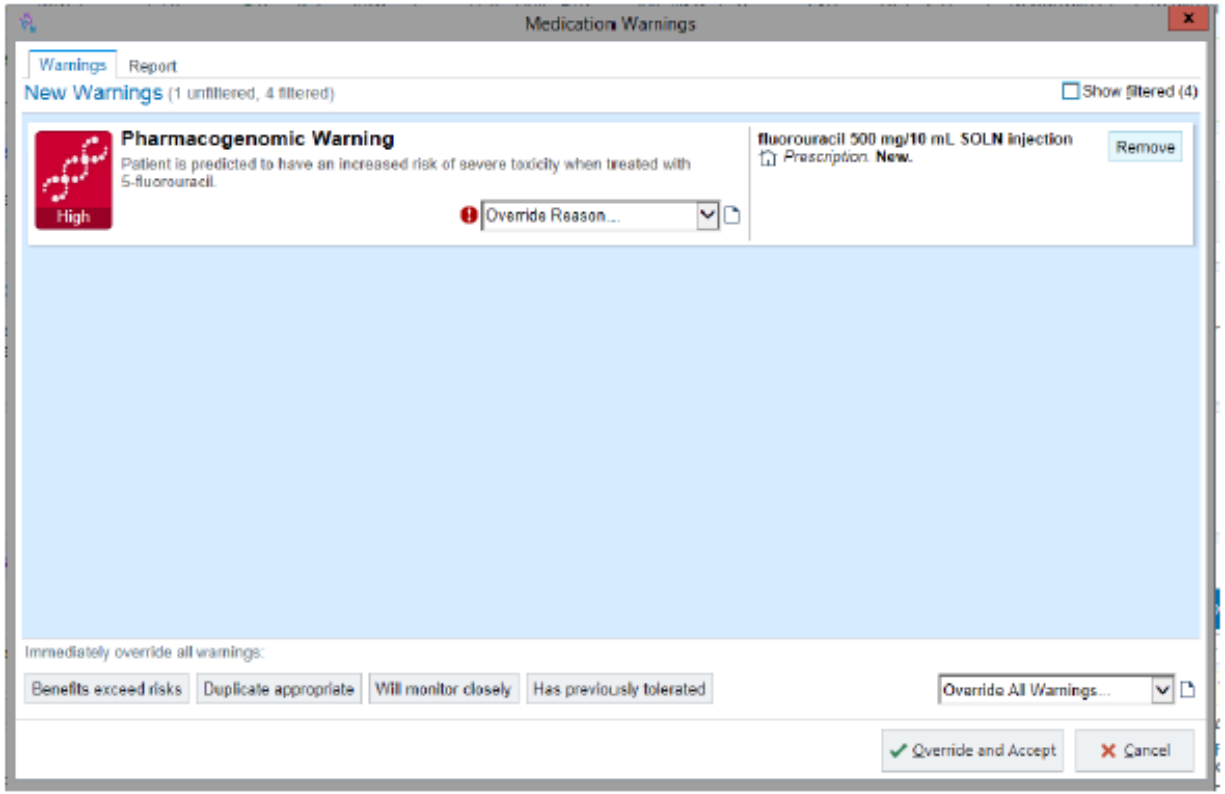
PGx warnings at time of order entry

In-line warnings for patients with actionable results



DPYD-High risk medication alert

Pop up Med Warning (priority set to high):



PGx infrastructure build in the EHR

- 50 Genomic Indicators for 13 genes
  - *DPYD (3)*
  - *UGT1A1 (3)*
  - *CYP2B6 (5)*
  - *CYP2C9 (5)*
  - *CYP2C19 (5)* → Poor metabolizer, intermediate metabolizer, normal metabolizer, Rapid metabolizer, ultrarapid metabolizer
  - *CYP2D6 (5)*
  - *CYP3A5 (3)*
  - *HLA-A *31:01 (2)*
  - *HLA-B *15:02, *57:01, *58:01 (6)*
  - *IFNL4 (2)*
  - *NUDT15 (4)*
  - *SLCO1B1 (3)*
  - *TPMT (4)*
  - In progress (*VKORC1, CYP4F2, CYP2C* cluster)

- Clinical decision support
  - 83 inline warnings with pharmacotherapy recommendations created for 31 CPIC Level A or B medications

Hoffecker et al. Genetics in Medicine Open. March 08, 2023. DOI:https://doi.org/10.1016/j.gimo.2023.100779

Perelman School of Medicine University of Pennsylvania

PennChart Genomics Initiative

Optimizing the EHR for Use in Genomic Medicine

Home | Videos | Resources | Personnel | Publications | Feedback

Home

Welcome to the PennChart Genomics Initiative (PGI) at the University of Pennsylvania. PGI is a multidisciplinary collaborative that aims to optimize the electronic health record (EHR). The PGI team has successfully developed the EHR infrastructure supporting genomic medicine and is now among the most advanced in the nation. In response to repeated requests from other institutions for details about how to optimize their respective EHR platforms to easily order genetic testing directly through the EHR, as well as receive and store genetic test results in a standardized way, we have developed this website to facilitate the sharing of this information, making it accessible to other institutions globally.

On this website, you will find:

https://www.med.upenn.edu/pgi/

Videos

- ***Optimizing Genomic Medicine in the Electronic Health Record*** - In this video, Katherine Nathanson, MD depicts the integration of genomics into the electronic health record at Penn Medicine via the PennChart Genomics Initiative. She covers the importance of optimizing genetics in the EHR, barriers to implementation of genomic medicine, and how to set up a genomic medicine friendly EHR.

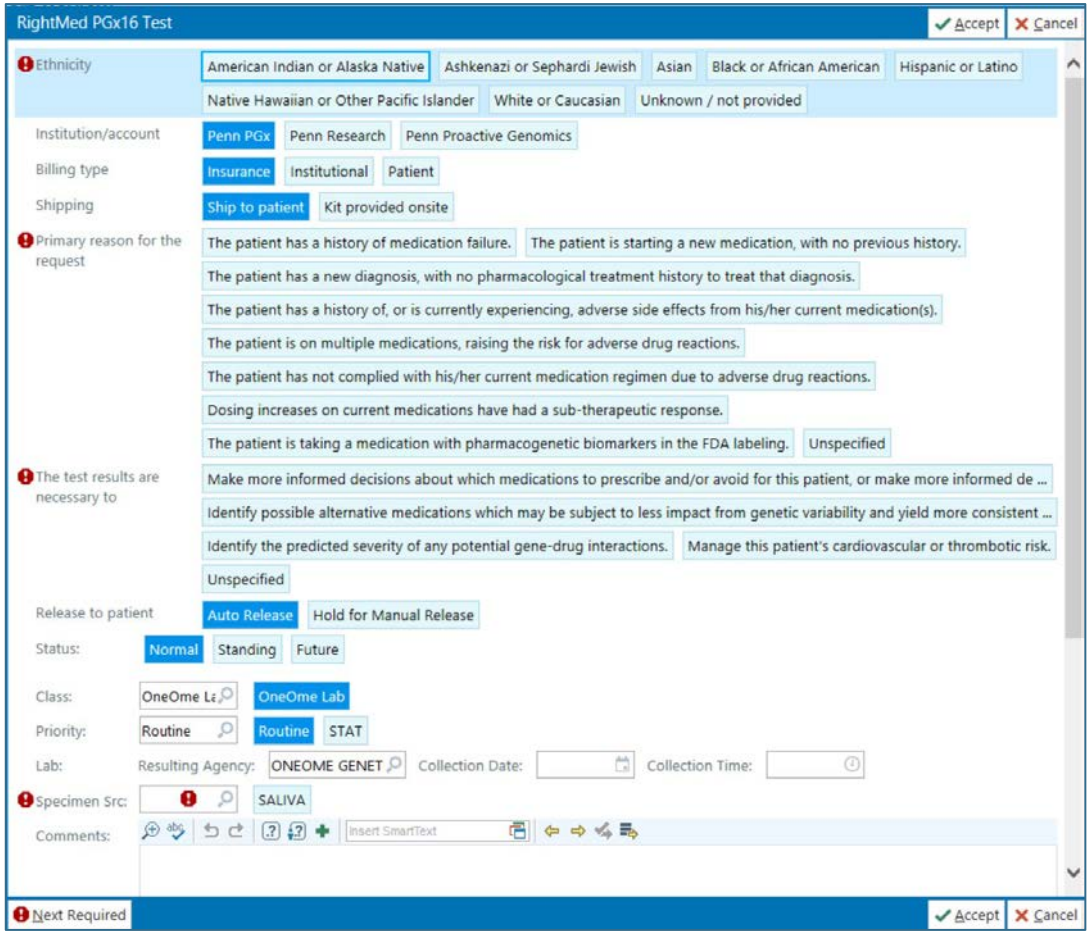
- ***Customizing the Electronic Health Record for Delivery of Pharmacogenetics*** - Sony Tuteja, PharmD, MS, BCPS, FAHA discusses pharmacogenetic variants that impact medical care for patients, specifically the types of medications they are prescribed. She describes how pharmacogenetic implementation was tested and implemented at Penn Medicine, including setting up an infrastructure that facilitates standardization and the inclusion of clinical decision support aids for clinicians.

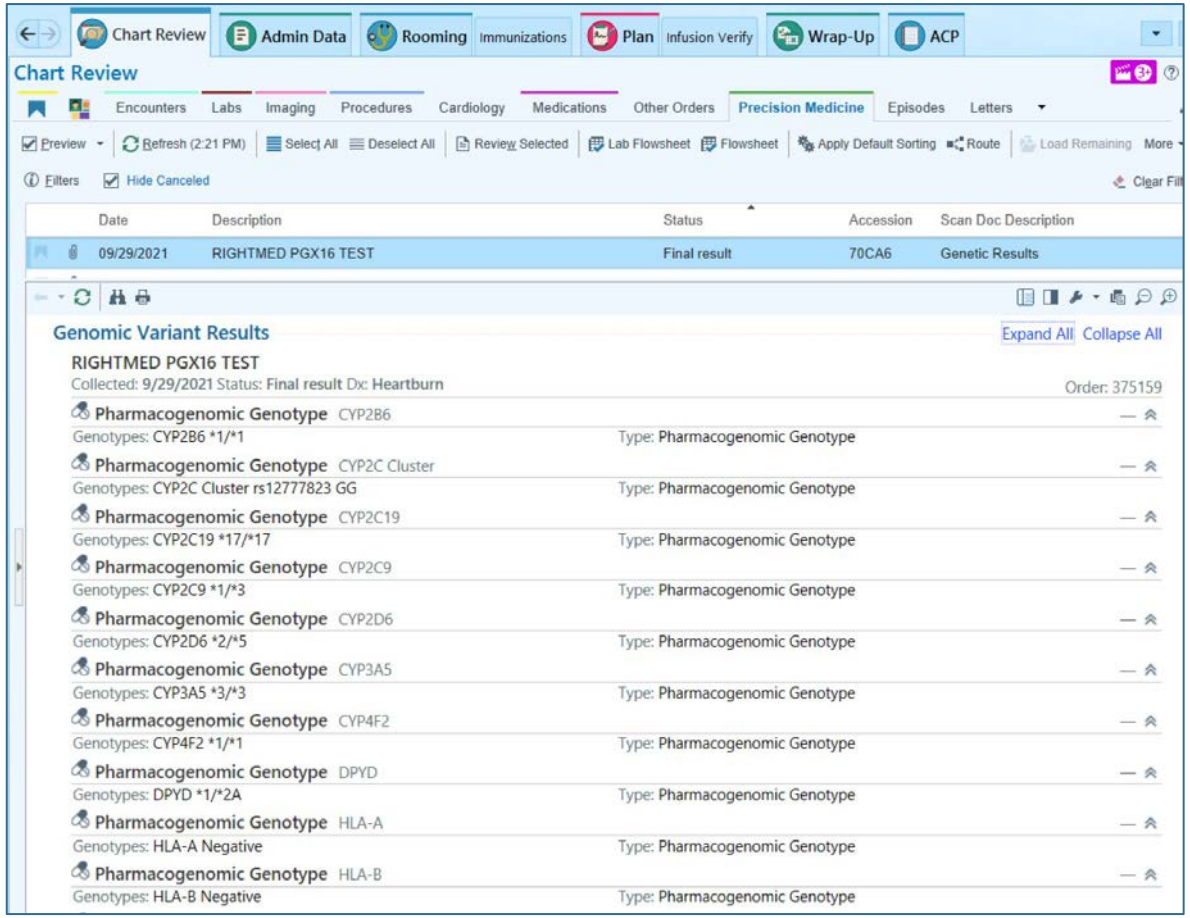
Resources

You will be required to use your Epic login to access resources.

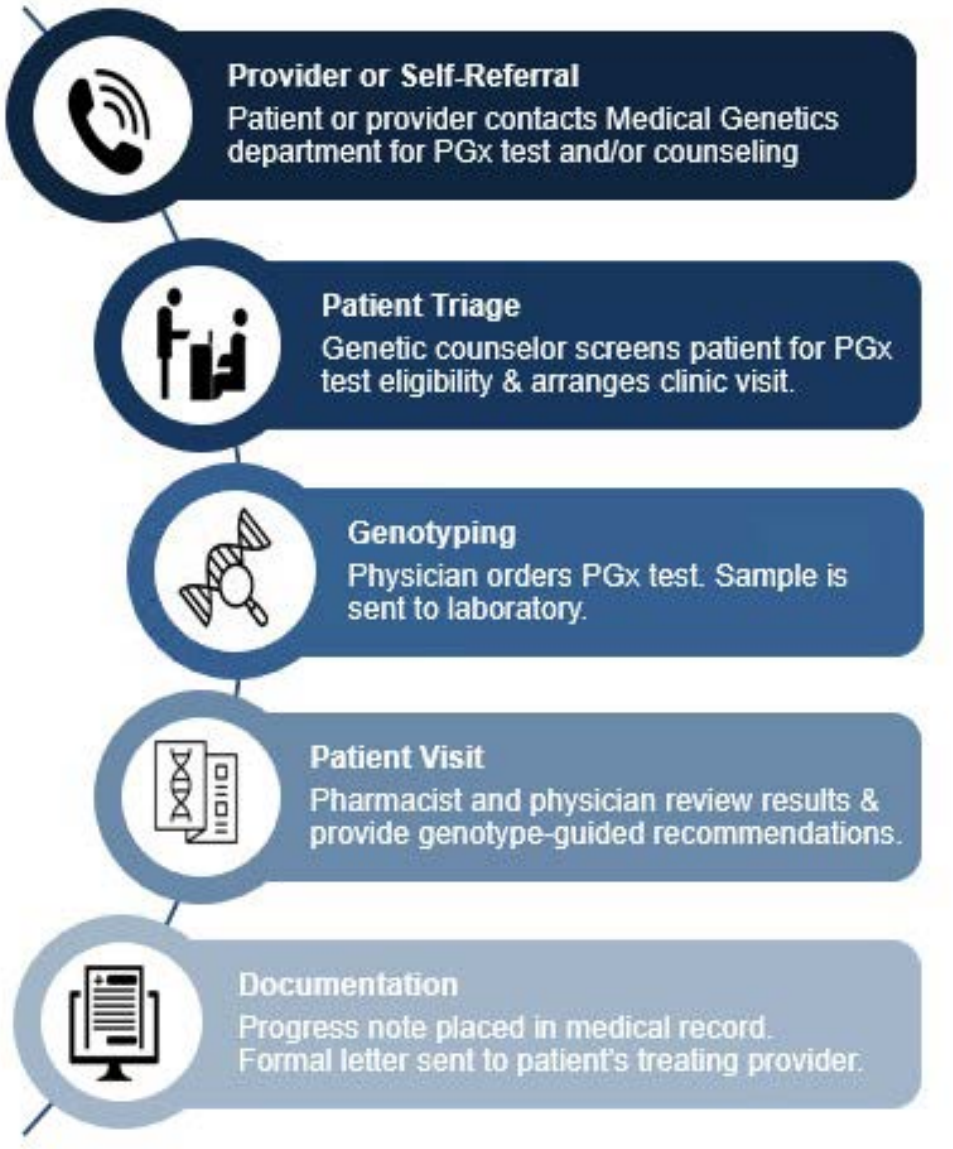
- ***Penn Overview Tutorials*** - these videos will depict:

Electronic integration with external PGx lab

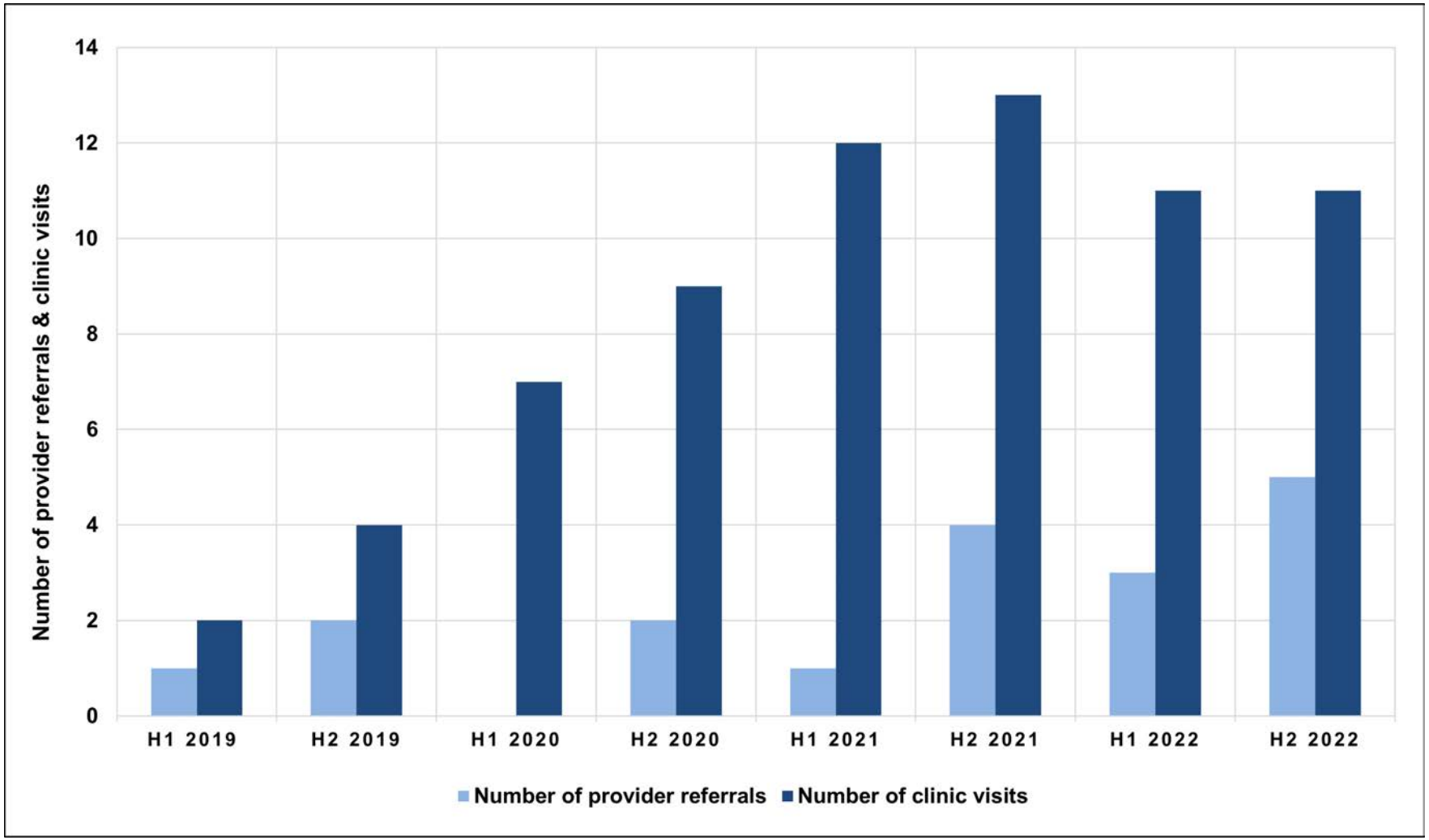




Establishment of a multi-disciplinary PGx clinic



Growth of clinic volume and referrals



Patient demographics

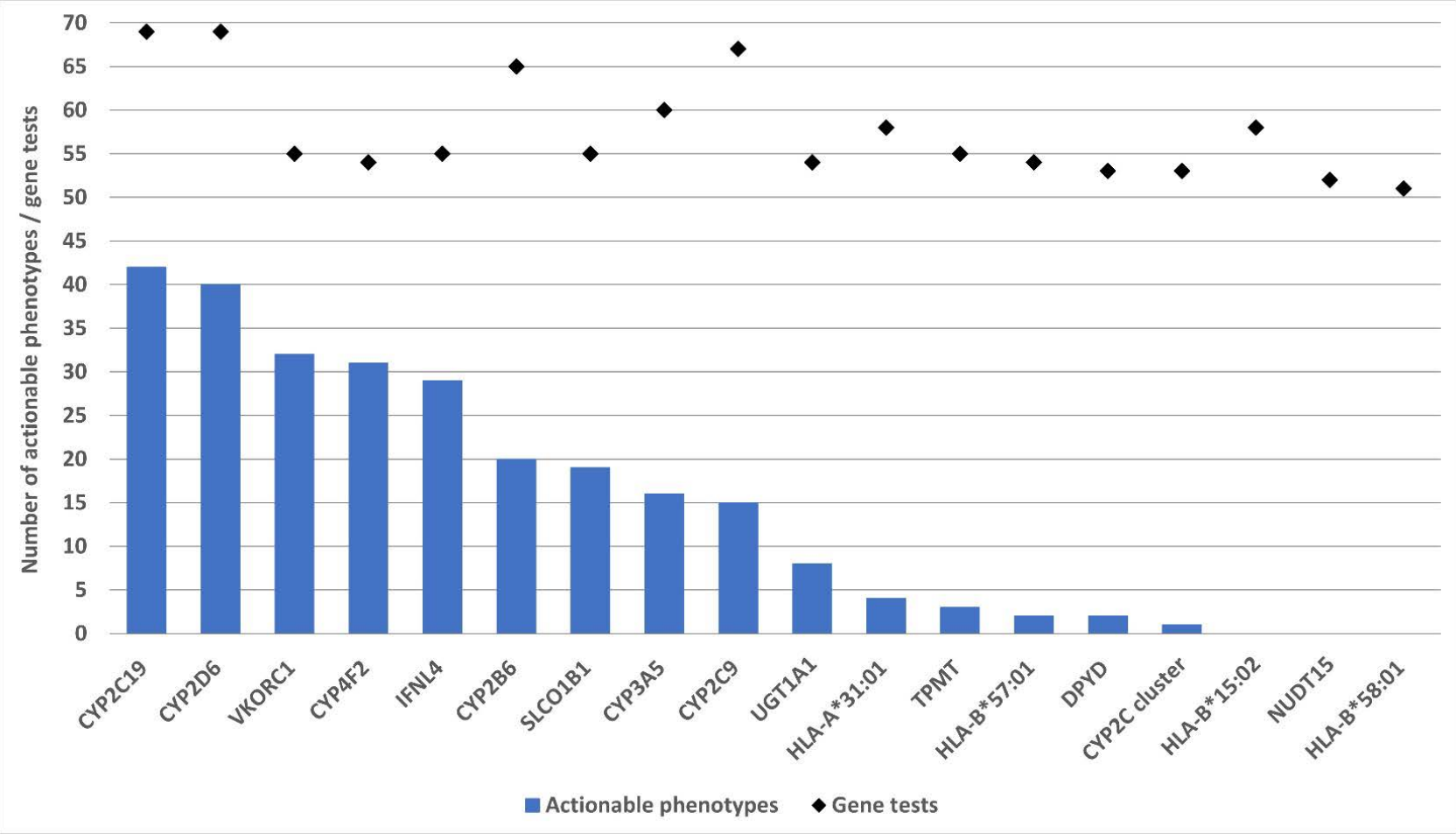
	N=69
Age, years	48 ± 16
Female sex, n (%)	40 (58%)
Ethnicity, n (%) White Other Unknown	 58 (84%) 6 (9%) 5 (7%)
Referral Method, n (%) Self-referred Preventative genomics screening program Psychiatrist Primary care	 32 (46%) 20 (29%) 7 (10%) 6 (9%)
Reason for consult, n (%) Current or historical ADRs Preventative genomic screening History of medication nonresponse	 26 (38%) 20 (29%) 11 (16%)

Clinical Impact of PGx testing

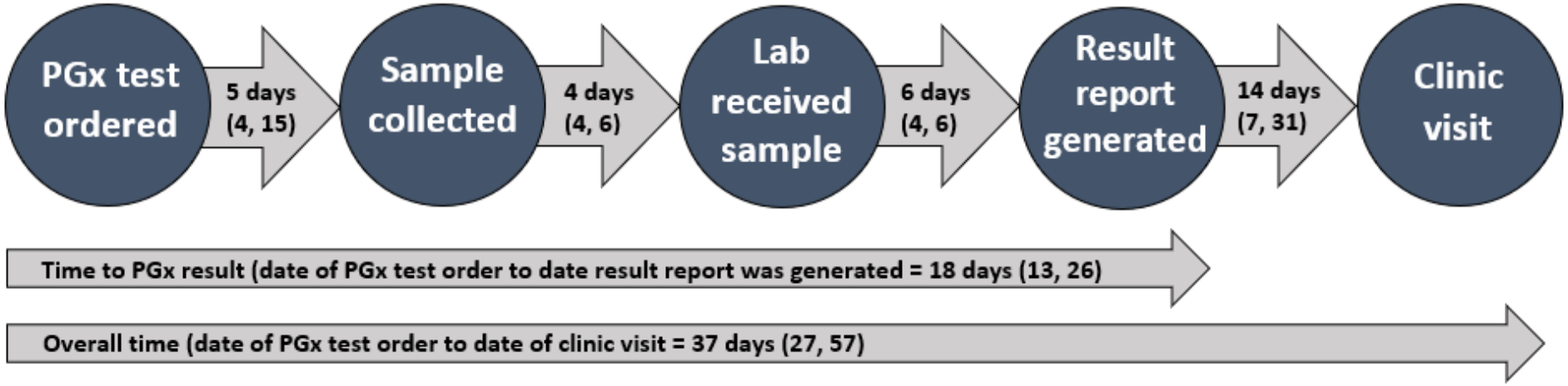
All patients had at least one actionable PGx allele

Actionable alleles	
Average per patient, mean ± SD	4 ± 1.8
≥ 3 actionable alleles	51 (74%)
Drug-gene interactions	
current medication	17 (25%)
historical medication	12 (17%)
CYP2C19/CYP2D6- SSRI	8
CYP2D6- opioids	4
CYP2C19/CYP2D6-TCAs	4
CYP2C19 – proton pump inhibitor	3
SLCO1B1- statins	3
CYP2C9- NSAIDS	2
Other	4

Most common PGx alleles identified



Timeframe for testing and clinic visits



Next Steps for PGx clinic

- PGx e-consult services
- Advertise the clinic internally to Penn providers to increase referrals
- New PGx pharmacist

Summary

- Implementation science provided a roadmap for PGx implementation and provides a set of process outcomes that can help demonstrate early “wins”
- Investment in EHR infrastructure was critical
- Patient needs/demands was the impetus for the PGx clinic
- Strategy of wins will help scale PGx across the health system

Acknowledgements

Penn PGx Program

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Daniel Rader, MD

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Cardiology

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Laboratory Partners

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OneOme

Questions?