

VA National Pharmacogenomics Program

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U.S. Department
of Veterans Affairs

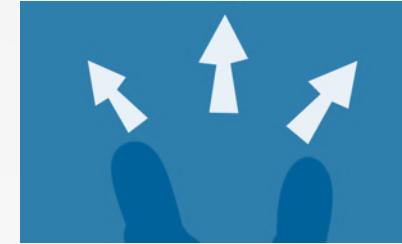
Overview



VA PHASER program

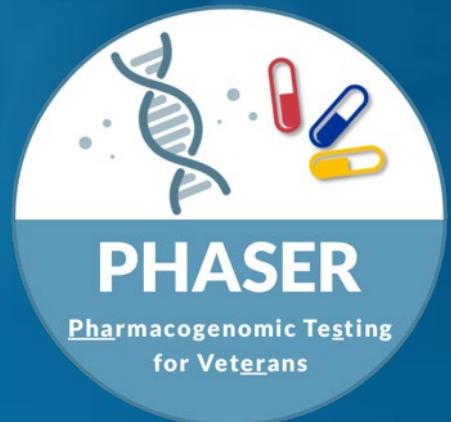


VA National Pharmacogenomics Program



PGx Learning Health System

VA Pharmacogenomics Testing for Veterans (PHASER) Program

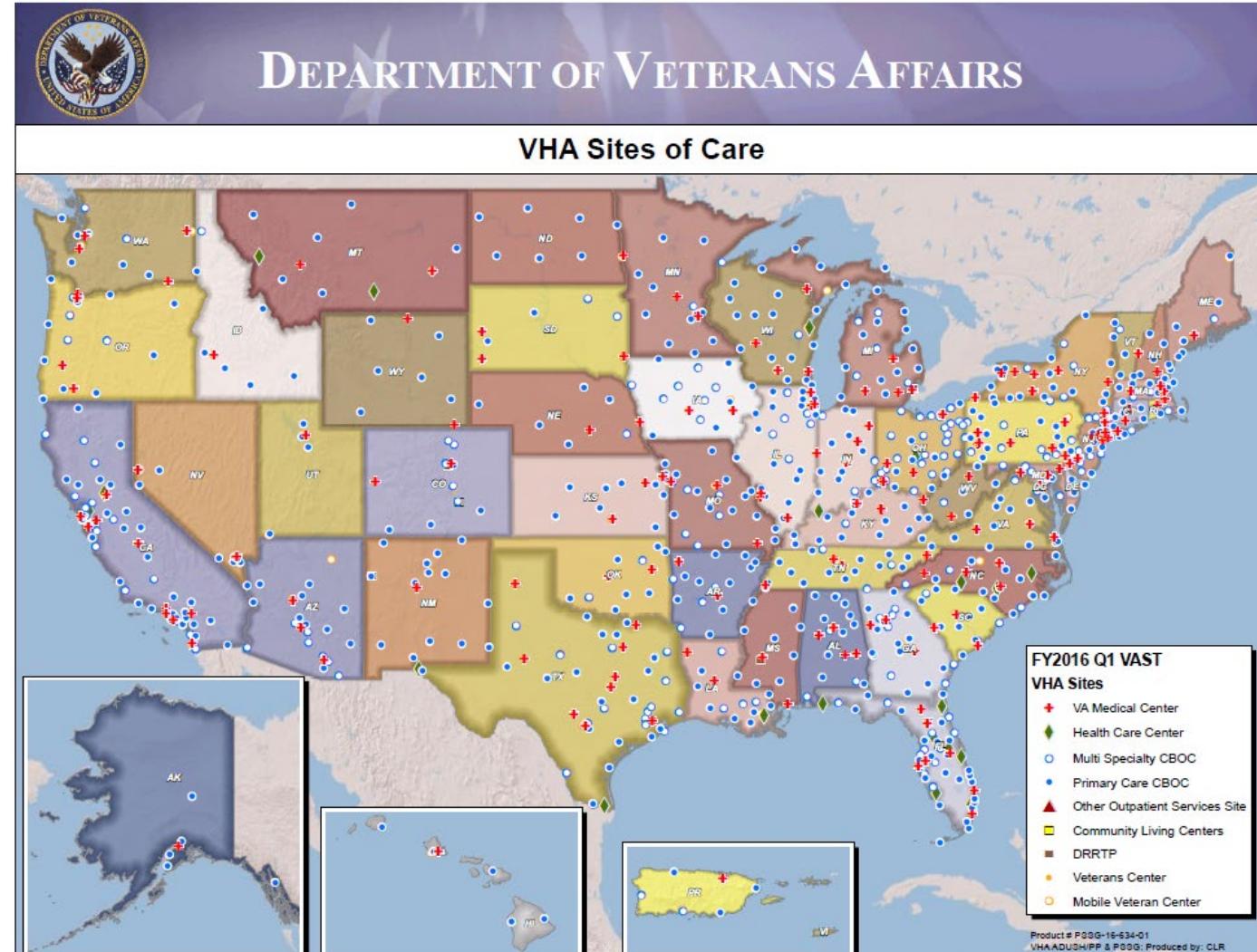


1,227 Sites of care throughout the U.S.

- 168 Medical Centers
- 1,047 Outpatient Clinics
- 135 Community Living Centers
- 113 Domiciliary Rehabilitation Treatment Programs
- 60 Mobile Sites of Care
- 300 Readjustment Counseling (Vet) Centers
- 80 Mobile Vet Centers

• **NOTE: The number of sites of care is NOT a total of the categories listed below, as several of the sites are also listed in multiple categories (e.g., there are 135 CLCs within the 168 medical centers)

• Source: VSSC QES 1st Qtr FY16

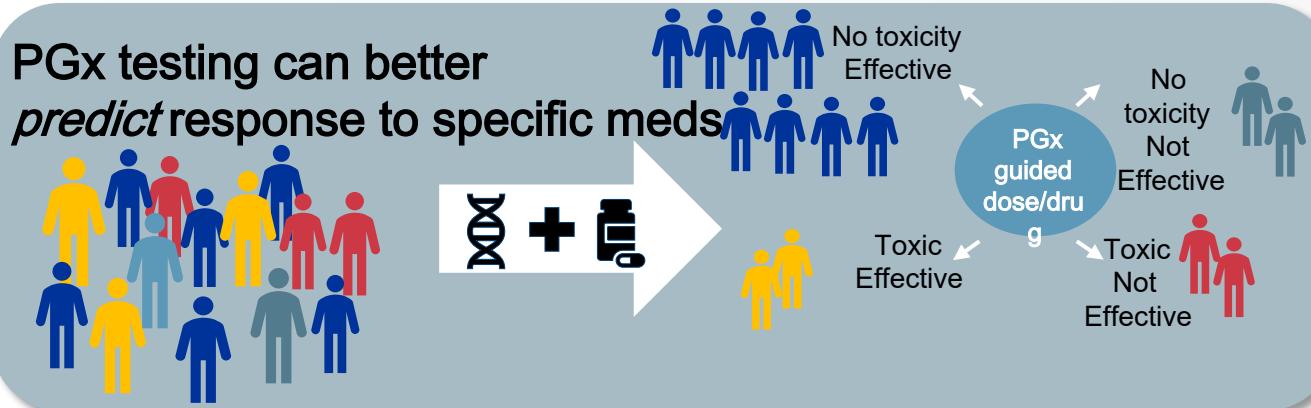
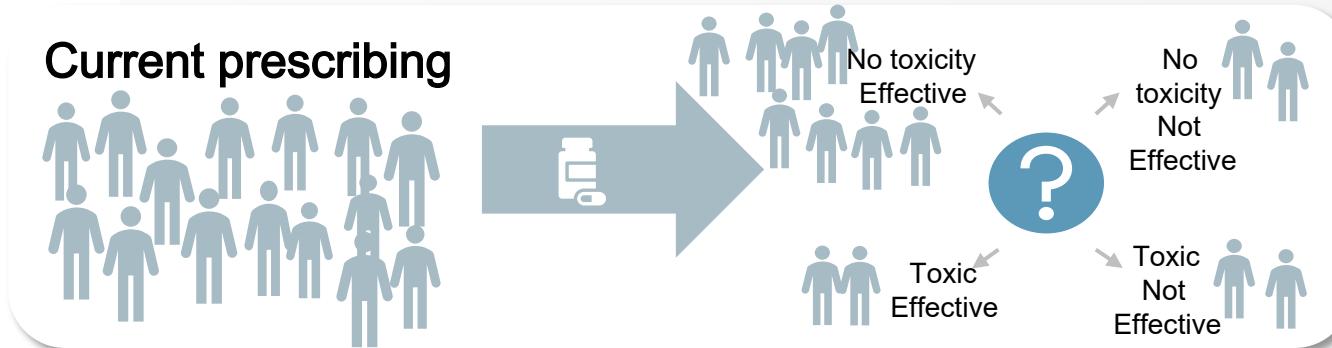


VA PHASER Program Overview

- **Public-private partnership** between VA and Sanford Health Care in Sioux Falls, SD
- PHASER can provide panel-based, pre-emptive pharmacogenomic testing to up to **60 VA healthcare systems**
- PHASER positions VA to be a **leader in the field of precision medicine**
- The largest, most effective, and integrated PGx program in the US



Pharmacogenomic Testing Can Reduce Toxicity, Improve Efficacy



Pharmacogenomic Testing Can Reduce Toxicity, Improve Efficacy



Medications impacted by PGx are commonly prescribed

*Approximately 1 in 2
Veterans prescribed a
medication informed
by PGx pane¹*



This could impact over
3 million Veterans

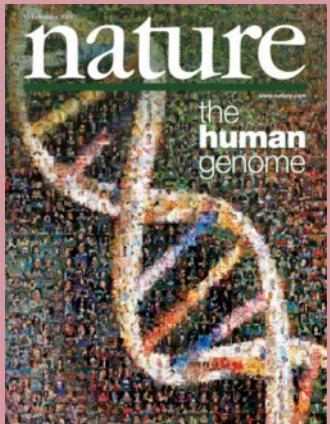
*Approximately 1 in 10
will have a prescription
modified by test*



This could impact over
600,000 Veterans

How do we connect the dots from PGx research into practice?

Slide adapted from Geoffrey Ginsburg, MD, PhD



Human
Genome
Project



Clinical Trials



Personalized &
Improved
Health

Realizing the Promise of Genomic Medicine

Just some of the questions a provider may have when thinking about using PGx clinically....

- How do I identify which of my patients need PGx testing?
- How do I know if my patient has already had PGx testing?
- What test do I order?
- How do I learn to interpret test results and apply them to patient care? What if I forget?
- How do I adjust (or not) medications based on PGx test results?
- How do I communicate with my patient PGx test results and their implications?
- Where do I go for help when integrating PGx into clinical care?

PHASER provides an ‘end-to-end’ solution for implementing PGx in any VA health system



Provider-friendly summary of PGx test results in VistA Imaging



Return of results to patients is handled by the PHASER program



Educational materials (TMS modules and written materials) to review testing and interpretation



Pharmacogenomics trained pharmacist for post-testing consultation



EHR Templates to facilitate documentation/ordering



Automated clinical decision support tools for point-of-prescribing alerts for drug gene interactions



Learning community of practice with a PHASER listserv and monthly case conference

What type of genetic testing does PHASER offer?

DNA testing for common,
actionable, genetic variants in
11 well-described
“Pharmacogenes”

Drug metabolizing
enzymes (i.e.,
cytochrome P450)

Drug transporters

Drug targets



Testing performed on single
EDTA blood sample



No testing beyond these genes
(e.g., no testing for cancer
or
cardiovascular risk)



Sample destroyed once results
returned to VA



CPIC Level A:
Preponderance of evidence in
favor of changing prescribing
based on PGx (A)

Medications Impacted by the PHASER Panel

Category	Drug Class	Medication
Oncology	Fluoropyrimidines	Capecitabine; Fluorouracil
Autoimmune	Thiopurines	Azathioprine; Mercaptopurine; Thioguanine
Cardiovascular	Anticoagulants	Warfarin
	Antiplatelets	Clopidogrel
	Statins	Simvastatin; Atorvastatin; Fluvastatin, Rosuvastatin, Pitavastatin
Gastrointestinal	Antiemetics	Ondansetron
	Proton Pump Inhibitors	Dexlansoprazole; Lansoprazole; Omeprazole; Pantoprazole
Infectious diseases	Antifungals	Voriconazole
	Interferons	Peginterferon alfa-2a; Peginterferon alfa-2b
Pain	NSAIDs	Celecoxib; Flurbiprofen; Ibuprofen; Meloxicam; Piroxicam
	Opioids	Codeine; Tramadol
Psychotropic	Anti-ADHD Agents	Atomoxetine
	Anticonvulsants	Fosphenytoin; Phenytoin
	Antidepressants	Amitriptyline; Citalopram; Clomipramine; Desipramine; Doxepin; Escitalopram; Fluvoxamine; Imipramine; Nortriptyline; Paroxetine; Sertraline; Trimipramine
Transplant	Immunosuppressants	Tacrolimus

PGx Education is Foundational for Effective Implementation of PGx

Asynchronous Learning

Patient education



Provider education



Synchronous Learning

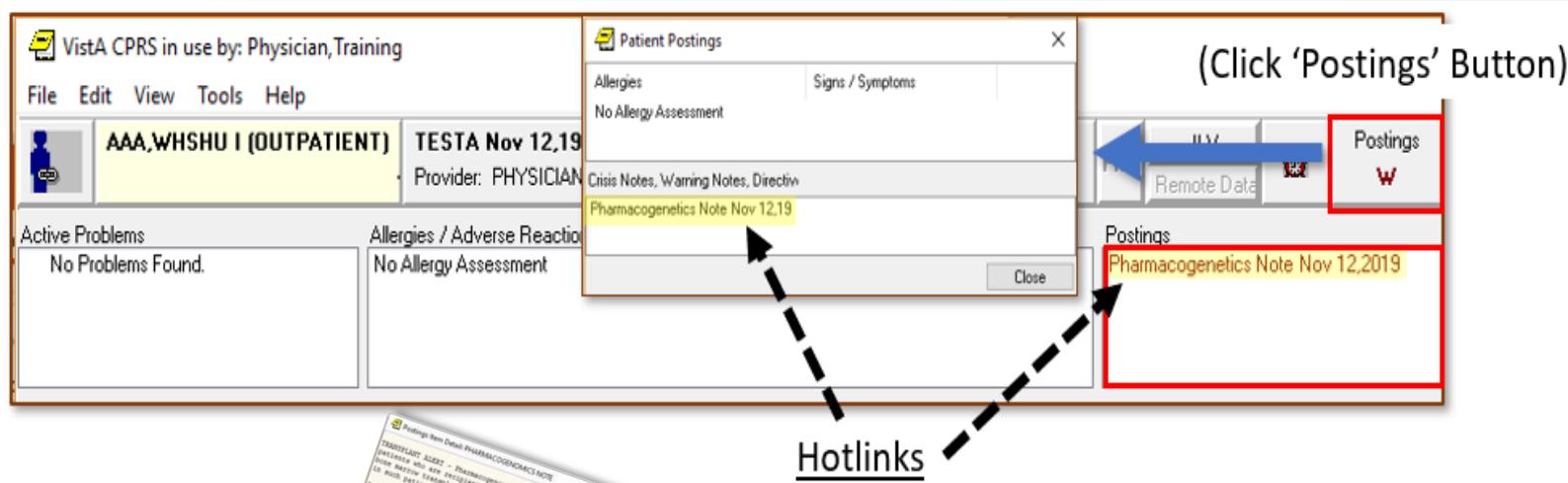


Train the trainer

coming soon



Clinical “Postings” alert all providers of existing PGx test results.



Hotlinks

Passive Clinical Decision Support via PDF interpretation based on CPIC guidelines

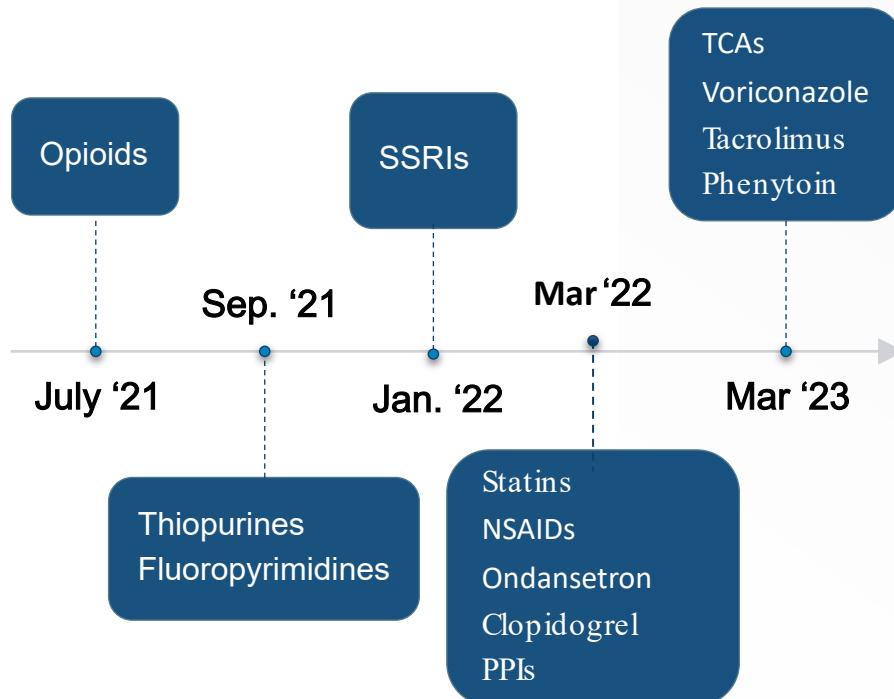
Potentially Impacted Medications			
CATEGORY	DRUG CLASS	NO ALTERNATIVES NEEDED BASED ON GENETICS; CONTINUE WITH STANDARD DOSING PER YOUR PROVIDER	YOUR PROVIDER MAY CONTACT YOU TO DISCUSS ALTERNATIVES AFTER CONSIDERING OTHER FACTORS
Anticancer Agents	Fluoropyrimidines	Capecitabine (Xeloda®) Fluorouracil (Adrucil® (IV); Carac® (topical); Efudex® (topical))	
	Thiopurines	Azathioprine (Azasan®, Imuran®) Mercaptopurine (Purinethol®, Purixan®) Thioguanine (Tabloid®)	
Cardiovascular	Anticoagulants	Warfarin (Coumadin®)	
	Antiplatelets		Clopidogrel (Plavix®)
	Statins	Simvastatin (Zocor®)	
Gastrointestinal	Antiemetics	Ondansetron (Zofran®, Zuplenz®)	
	Proton Pump Inhibitors		Dexlansoprazole (Dexilant®, Kapidex®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®)
	Antifungals		Voriconazole (Vfend®)
Infections	Interferons		Peginterferon alfa-2a (Pegasys®) Peginterferon alfa-2b (Pegintron®, Sylatron®)

 **Clopidogrel**
Plavix®

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer)

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Interruptive Clinical Decision Support (i.e., drug-gene pop-ups)



Order Checking

(2 of 2) Pharmacogenomics Warning - Platelet Inhibitors

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AFFECTED MEDS: Clopidogrel

ACTION: Consider removing clopidogrel order. Patient at risk for stent thrombosis or recurrent cardiovascular events on clopidogrel based on pharmacogenomics (PGx) results. For medicines that are currently prescribed, adjustment is only indicated if the patient is not appropriately responding to therapy.

ALTERNATIVES:

- * Consider prasugrel in those:
 - Age < 75 years
 - Body weight > 60 kg
 - No history of stroke or TIA
- * Consider ticagrelor for those with no prior history of ICH
- * Close monitoring for safety concerns is strongly recommended

ADJUSTMENT: Dose adjustments are not sufficient based on PGx results. Consider disease specific alternatives based on provider preference.

RATIONALE: Patient has reduced sensitivity to clopidogrel (i.e., intermediate metabolizer of CYP2C19). Far fewer active metabolites form than expected resulting in lower platelet inhibition, and higher risk for stent thrombosis and recurrent cardiovascular events.

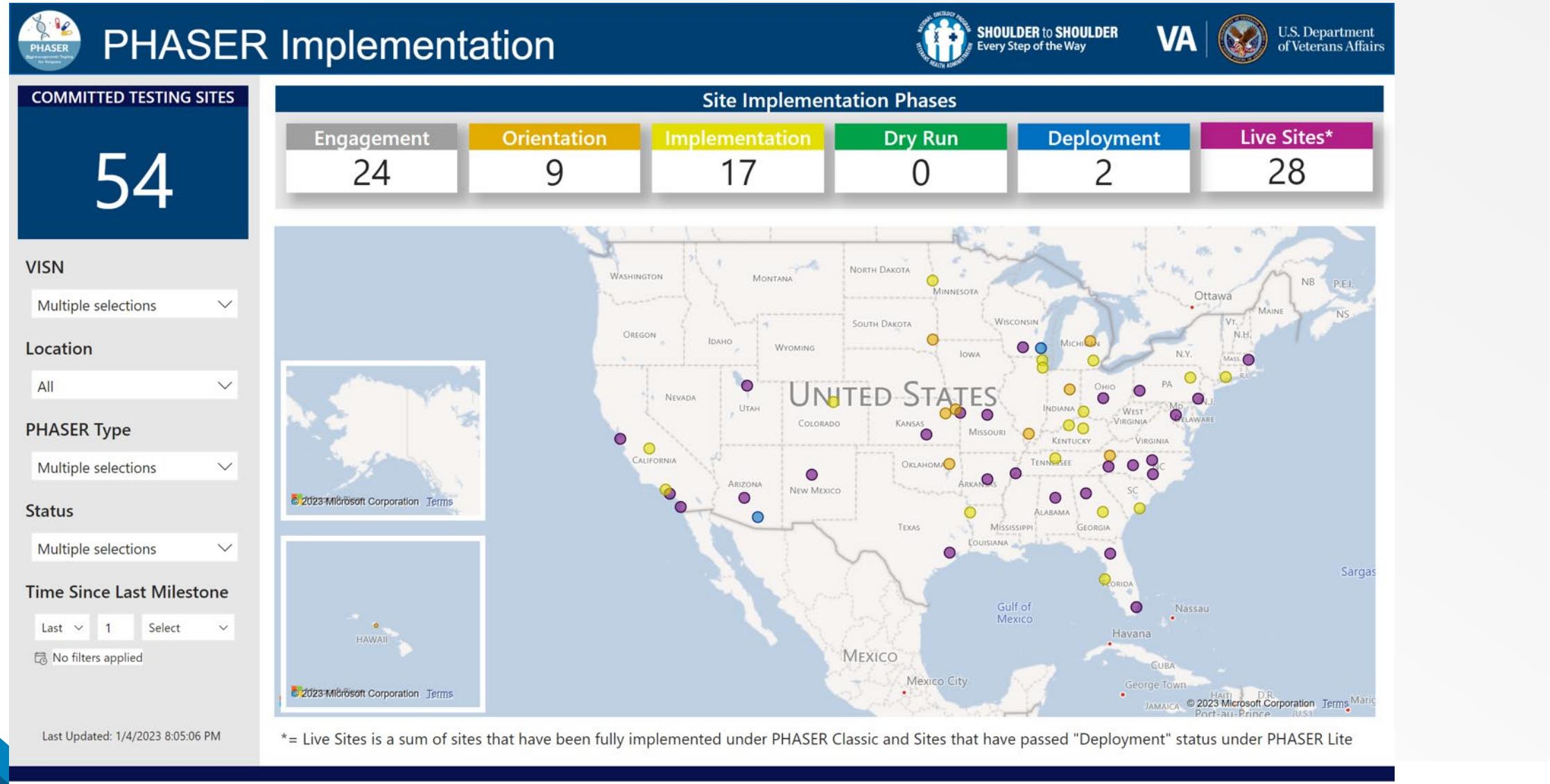
RESOURCES:

- * Clinical assistance: order local or interfacility pharmacogenomics consult
- * Non-clinical support: IM or email PHASERtechsupport@va.gov
- * Information on testing: go to <https://bit.ly/PHASERhome>
- * Feedback on this alert: email PHASER-CROC@va.gov

=====

Accept Order **Cancel Order** **Drug Interaction Monograph**

PHASER program status



PGx Orders: Cumulative Volume & Provider Count



PHASER National Report

22093

Cumulative Orders

4/1/2019

First Order Date

1/3/2023

Most Recent Order Date

Count of PHASER Orders
Placed in Last 30 days

1041

Compared to Previous 30-day
Period

Ratio of PHASER Orders Placed
per Provider in Last 30 days

2.80

Compared to Previous 30-day
Period

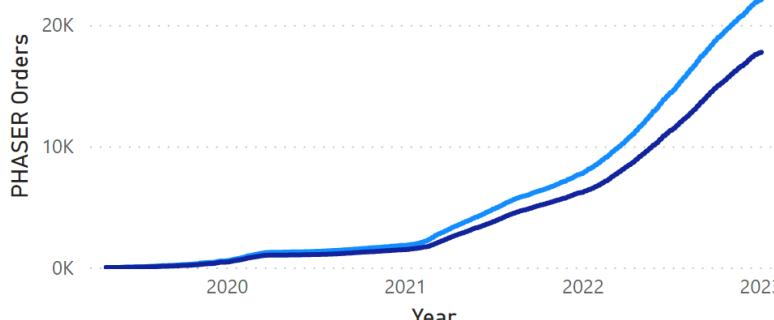
Count of Unique Ordering
Providers in Last 30 days

401

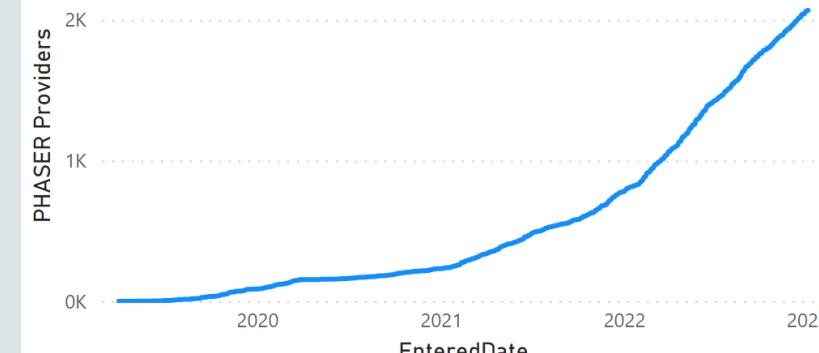
Compared to Previous 30-day
Period

Cumulative Order/Sample Count

● RunningTotal of Orders ● RunningTotal of SampleCount



Cumulative Provider Count



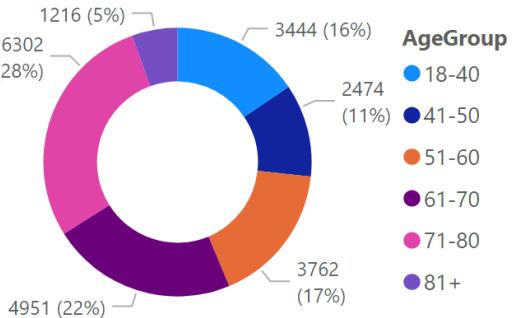
1/4/2023
Refresh Date

Patient and provider characteristics

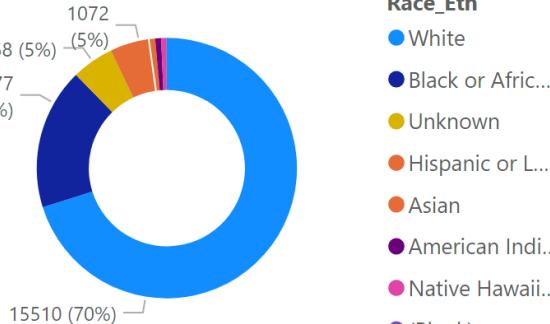


PHASER Patient Demographics and Provider Specialties

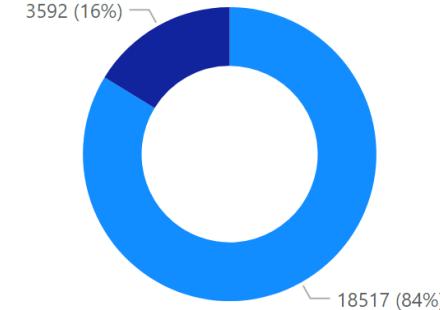
Patient Age Group



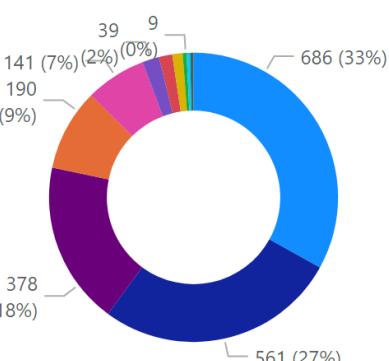
Patient Race/Ethnicity



Patient Gender



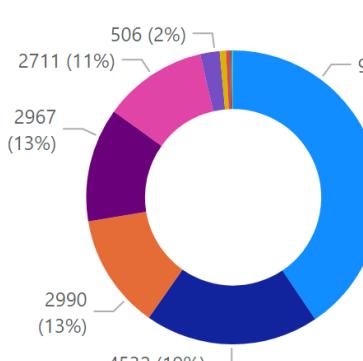
Provider Specialty (Count of Provider)



department

- Primary care/m...
- Mental health
- Other
- Pharmacy
- Oncology/he...
- Cardiology
- Surgery
- Pulmonary me...
- ANESTHESIOL...

Provider Specialty (Count of Orders)



department

- Primary care/m...
- Mental health
- Pharmacy
- Other
- Oncology/hem...
- Cardiology
- Pulmonary me...
- Surgery
- GASTROENTER...



Frequency and Impact of interruptive clinical decision support



CROC Occurrences at Ordering of PHASER Medications

Total Alerts

4983

Unique Patients

1858

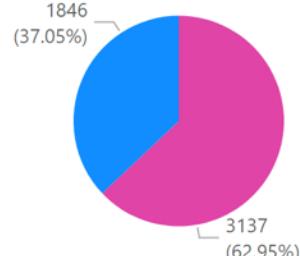
% Of Patient Tested

10.99%

Total Providers

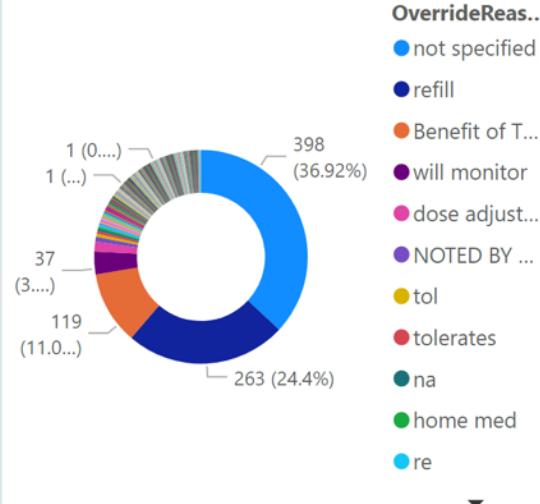
1506

Orders by Order Status



ORDER_FLAG
● CANCELLED
● ORDERED

Distribution of Override Reasons (required for High Severity only)



OverrideReasons
● not specified
● refill
● Benefit of T...
● will monitor
● dose adjust...
● NOTED BY ...
● tol
● tolerates
● na
● home med
● re



Total Stations

22

First Occurrence Date

7/23/2021

Last Occurrence Date

1/4/2023

1/4/2023

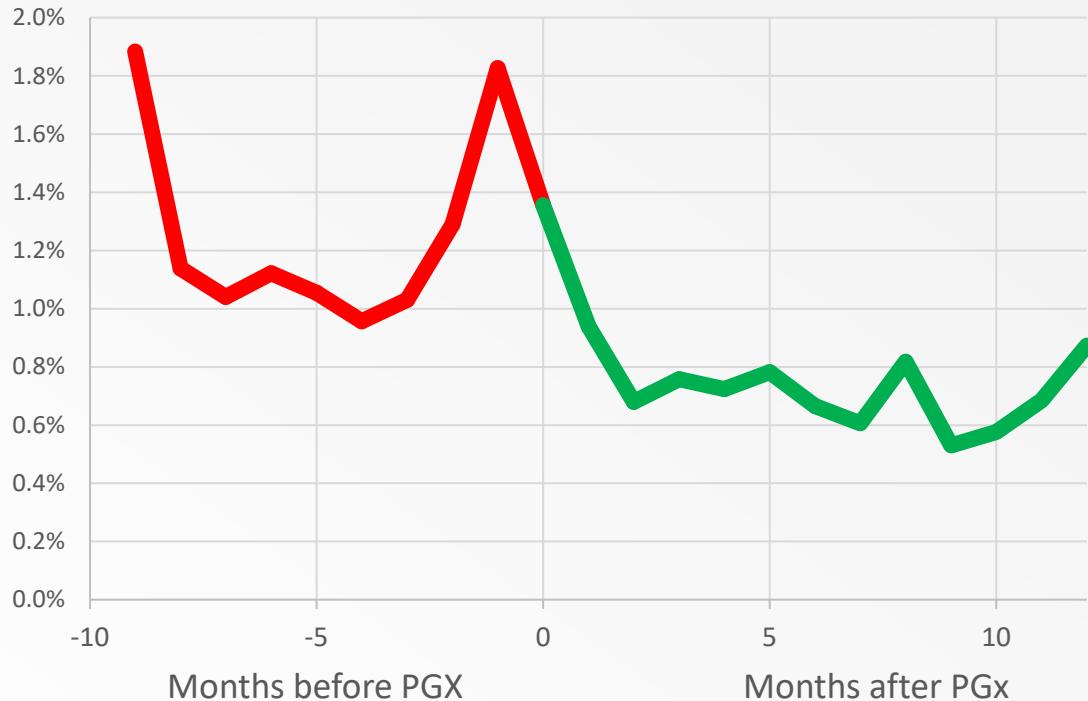
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Potential Value of PGx Testing



12,773 of
12,860 patients
with actionable
PGx result

Frequency of drug-gene mismatches before and after PGx testing



*Data for these metrics are drawn down once each month so lag behind the # resulted

*Data are unadjusted for any confounders (e.g., temporal trends)

PHASER program summary



PGx can optimize the prescription of nearly 40 medications that are prescribed to 1 in 2 Veterans



PHASER provides an end-to-end solution for integrating PGx testing into clinical practice

- EHR toolkit
- Access to panel-based PGx testing at no cost
- Evidence based interpretation of PGx results
- Access to PGx trained pharmacists for e-consultation



Key users of PGx testing are primary care, mental health, cardiology, oncology, among others

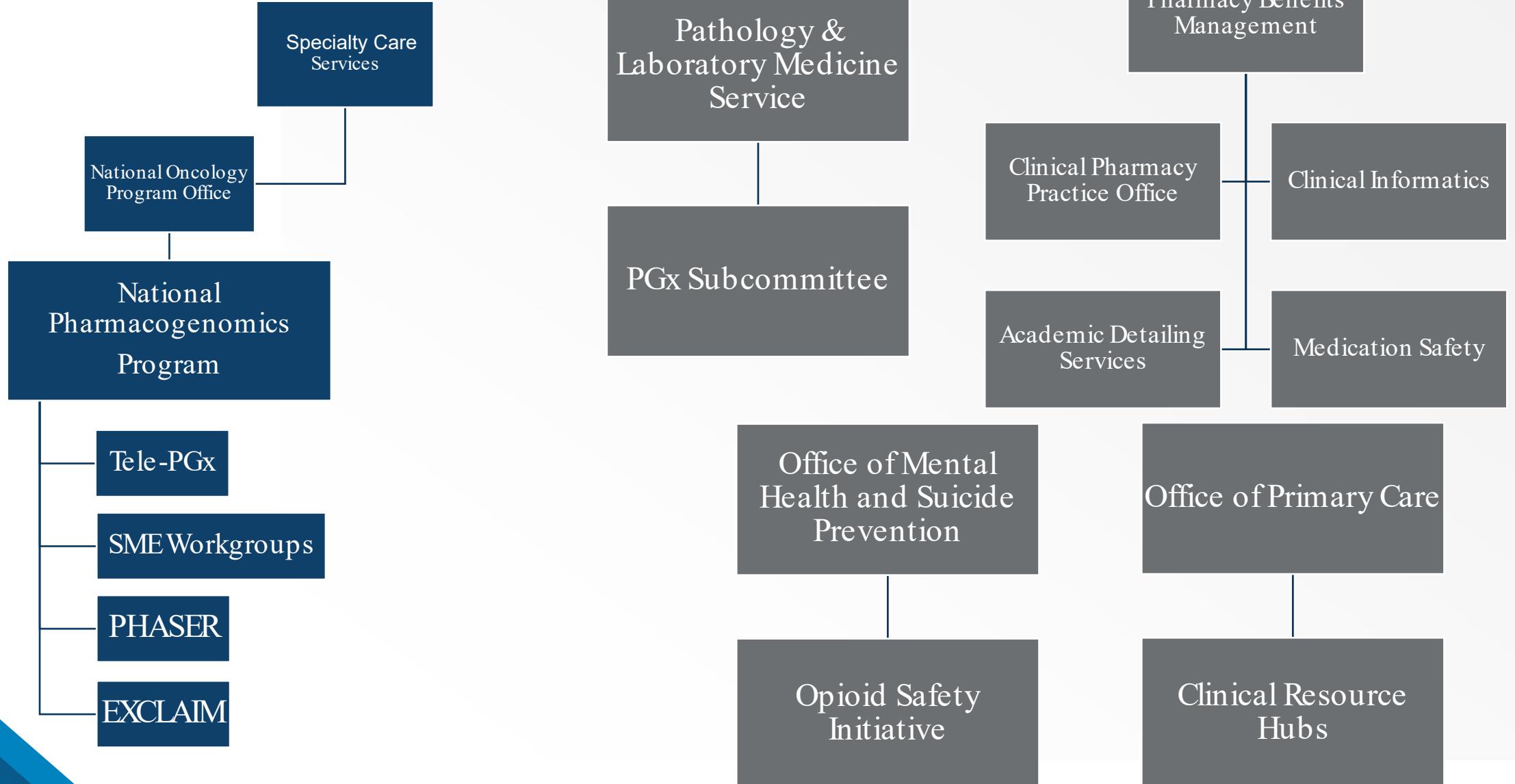
VA National Pharmacogenomics Program

VA

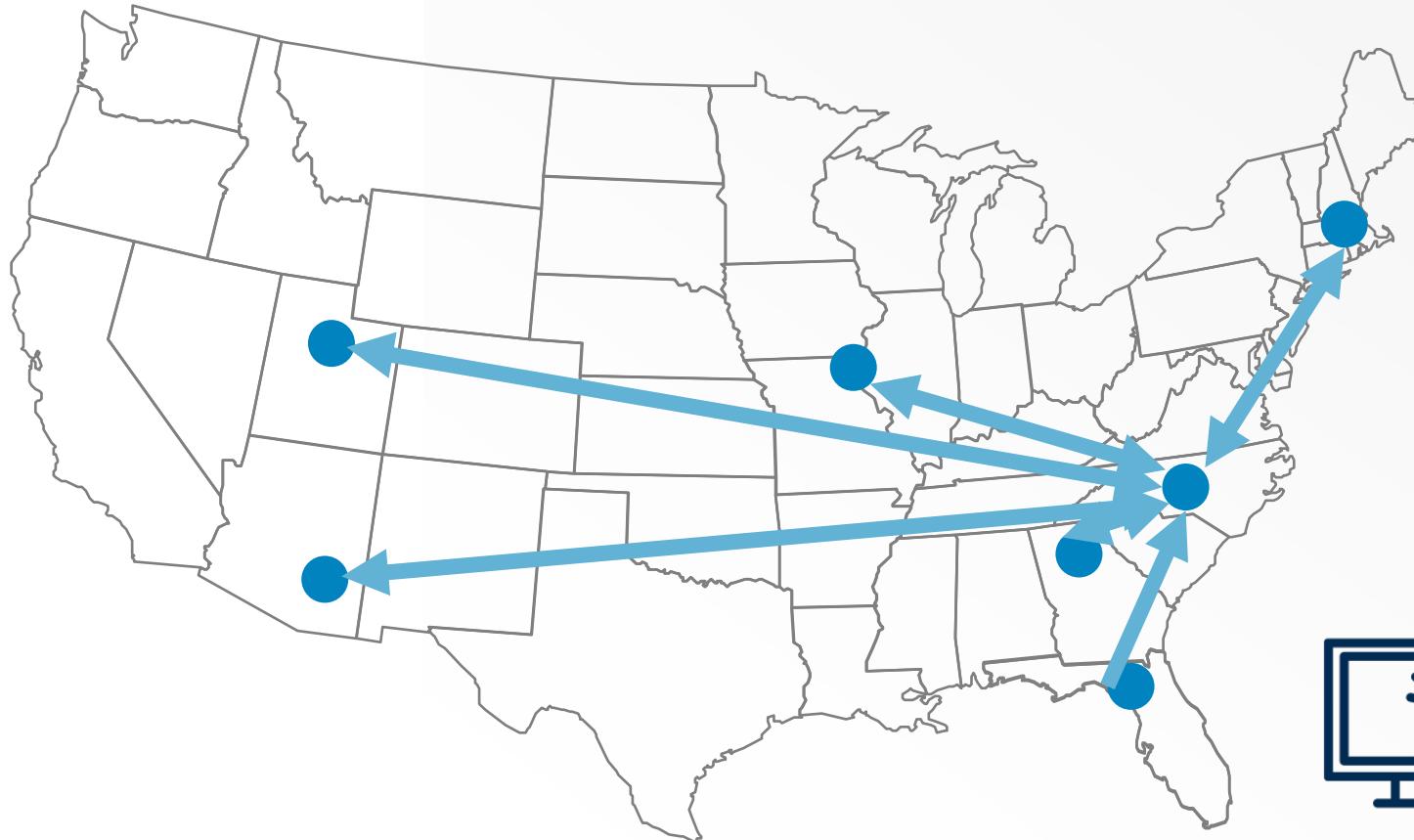


U.S. Department
of Veterans Affairs

Organization and Stakeholders



National Tele-PGx service for additional patient and provider support.



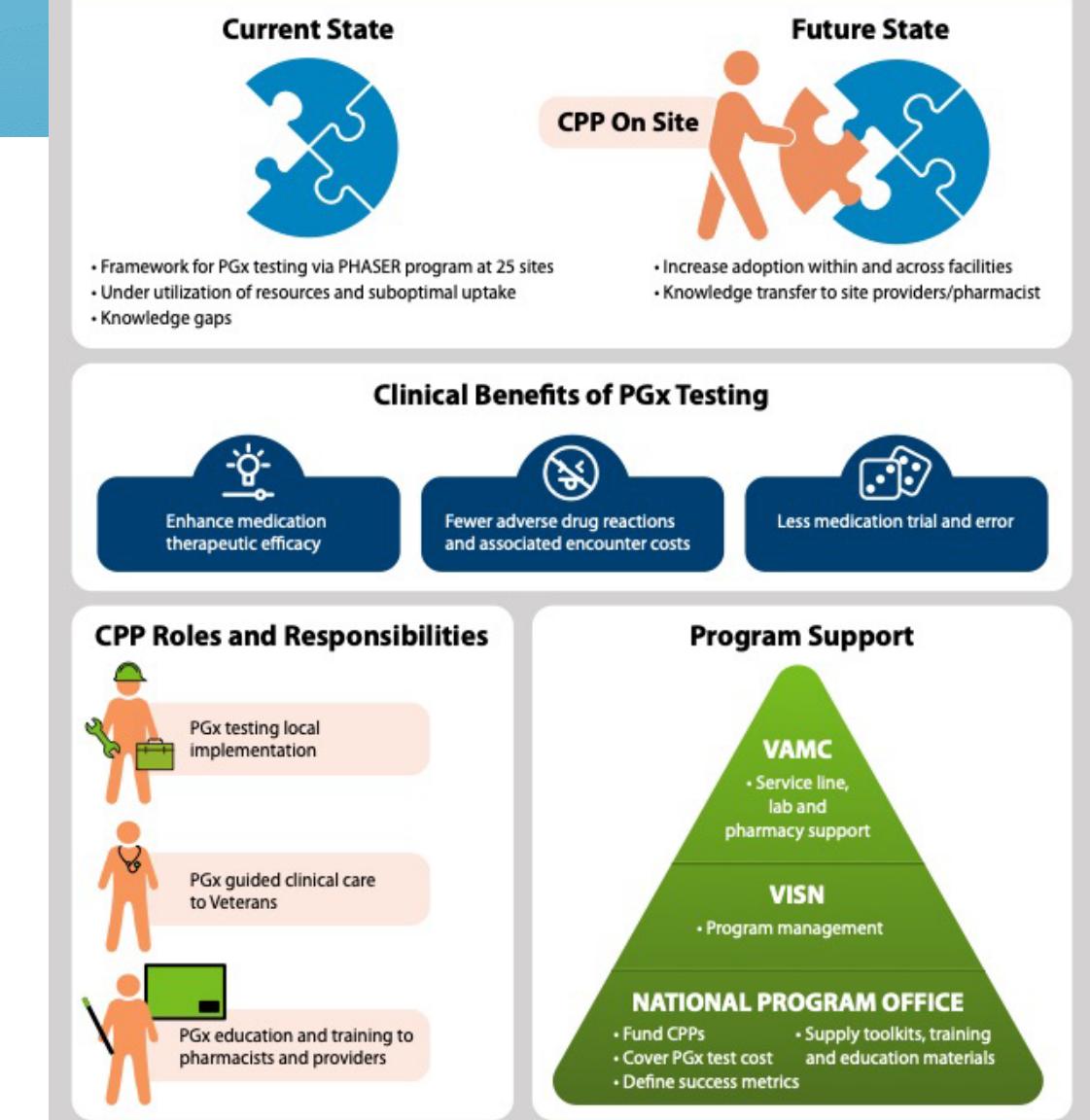
- Provider-provider e-consultation
- Direct-to-Veteran telePGx services
- Population health management



PGx CPP expansion model

- The VA is funding the addition of **120 full time pharmacist equivalents** by FY24 who will specialize in diffusion of PGx practice
- These pharmacists will use an **implementation facilitation model** to deploy provider education, access to PGx testing, and PGx clinical care throughout their VISN

Expanding Clinical Pharmacy Practitioners in Pharmacogenomics (EXCLAIM)

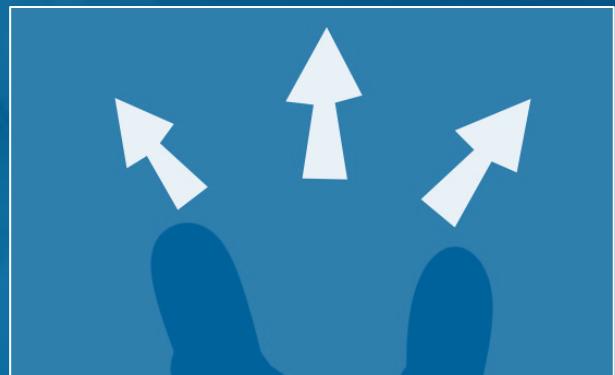


EXCLAIM “Core” PGx Clinical Workflows

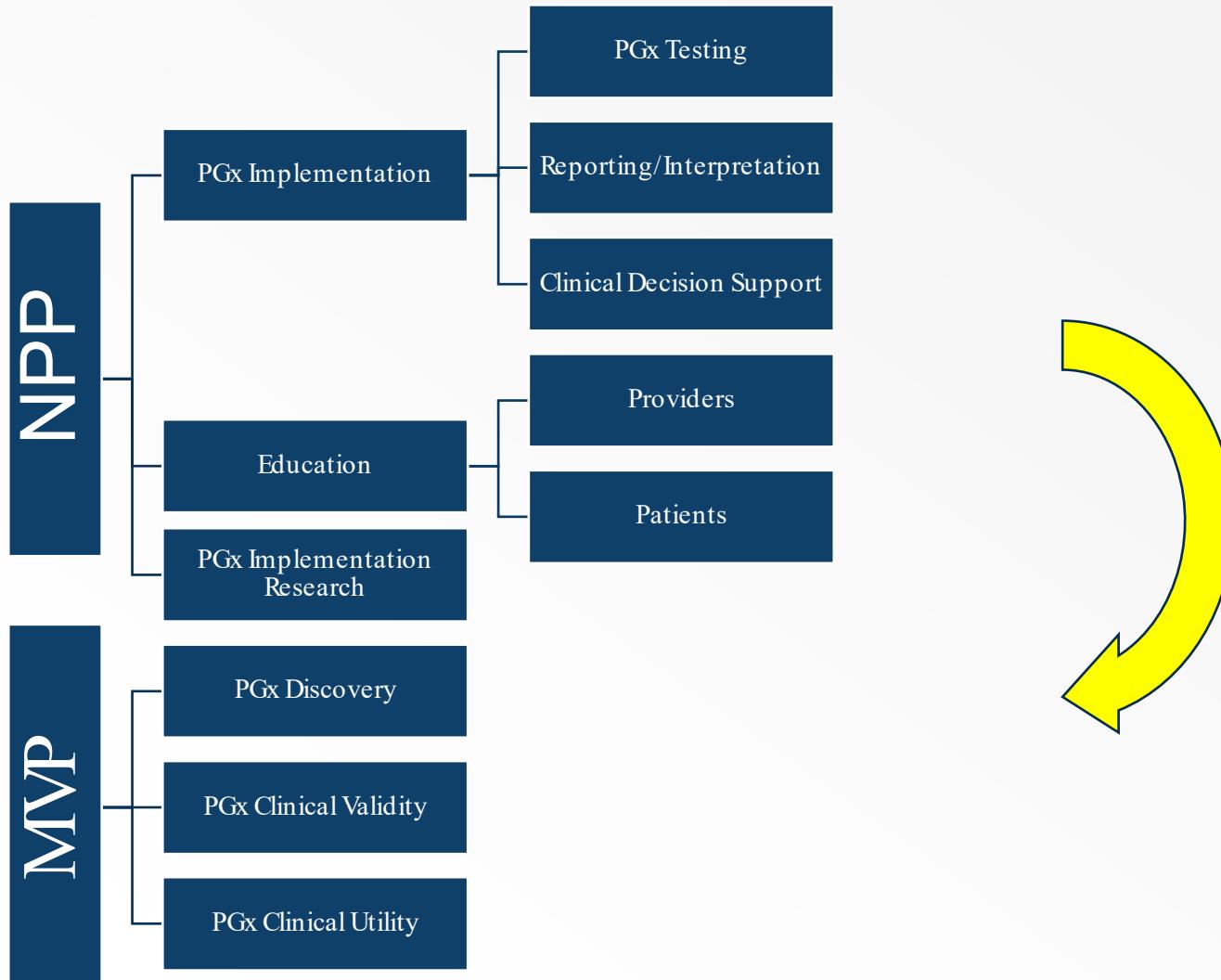
Workflow	Drug Class of Interest	Clinical Outcome of Interest	Clinical Utility Evidence	Cost-effectiveness Evidence
Cardiology	Antiplatelets	Prevent stent thrombosis or myocardial infarction, stroke, or death in patients undergoing coronary stenting	CPIC evidence level - 1 PHARMGKB evidence level - 1A FDA label - Actionable PGx 	Cost-effectiveness - Highest 
Mental Health	SSRIs	Improve depression symptoms, remission and persistence with therapy in patients with major depression	CPIC evidence level - 1 PHARMGKB evidence level - 1A FDA label - Actionable PGx 	Cost-effectiveness - High 
Oncology	Fluoropyrimidines Thiopurines	Reduce severe treatment related toxicities for patients with selected malignancies and autoimmune disorders	CPIC evidence level - 1 PHARMGKB evidence level - 1A FDA label - Testing recommended 	Cost-effectiveness - High 
PGx Care Coordination	Cardiology, Mental Health, Oncology, HLA-typing, Statins, Opioids, and TCAs	Identify incidental drug-gene interactions and communicate actionable findings to care team members	CPIC evidence level - 1 PHARMGKB evidence level - 1A FDA label - Actionable PGx 	Cost-effectiveness - High 
HLA Typing	Xanthine Oxidase Inhibitors Anticonvulsants Antivirals	Prevent severe cutaneous adverse drug reactions	CPIC evidence level - 1 PHARMGKB evidence level - 1A FDA label - Testing recommended required 	Cost-effectiveness – Highest*  *Contingent on ethnicity

Reference: [Clinical Pharmacogenetics Implementation Consortium](#) and [PharmGKB](#)

PGx Learning Health Care System



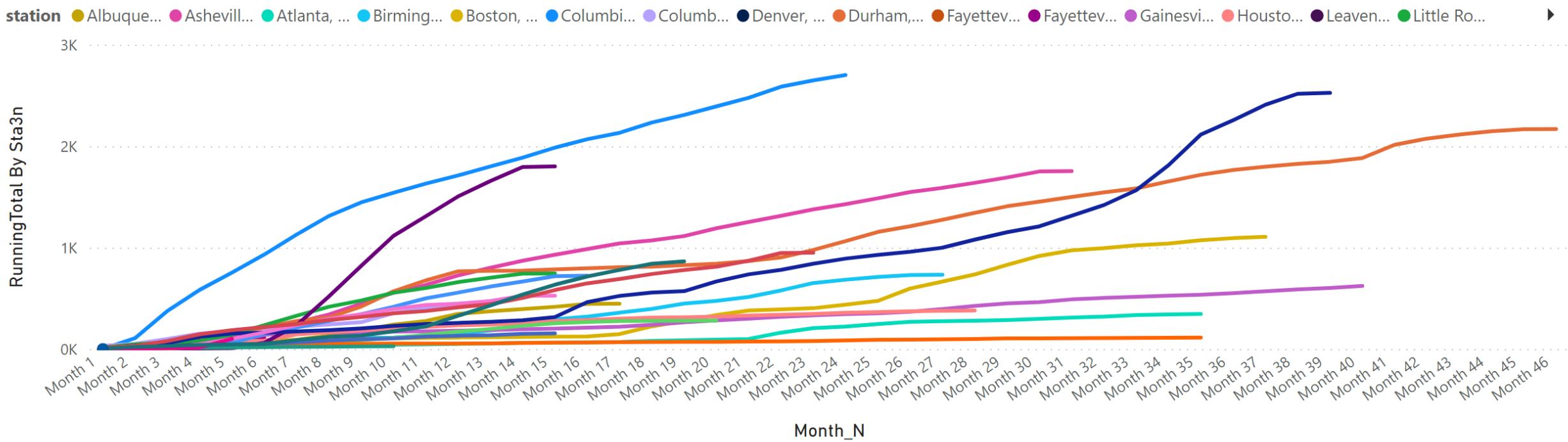
A PGx Learning Health System





PHASER Order Total by Station, normalized by "Go Live" month

RunningTotal By Sta3n by station



*Month N represent the start month of each station. For example, Month 1 for 558 is April, 2019, but for 521 is November, 2020.

*Highlight the legend on the top left to see individual station

*Uncheck 1 to remove COVID Period

1/4/2023

Refresh Date

QUERI Partnered Evaluation Initiative (Year 2 of 3)

- **Aim 1:** Identify factors that promote **facility adoption** of PGx testing by comparing organizational facilitators and barriers to adoption and implementation strategies between (low versus high volume) participating sites.
- **Aim 2:** Identify factors associated with individual **provider adoption** of PGx testing by examining the relationship between the extent of ordering and provider characteristics.
- **Aim 3:** Identify factors associated with patient adoption and effectiveness of PGx testing by characterizing patient factors associated with **testing participation and medication adherence**.

Corrine Voils,
PhD (PI)

Learning Health System

Clinic
Cons
and C

Craig R. Le
Charles Mi
Jean-Sébast
Julie A. Joh

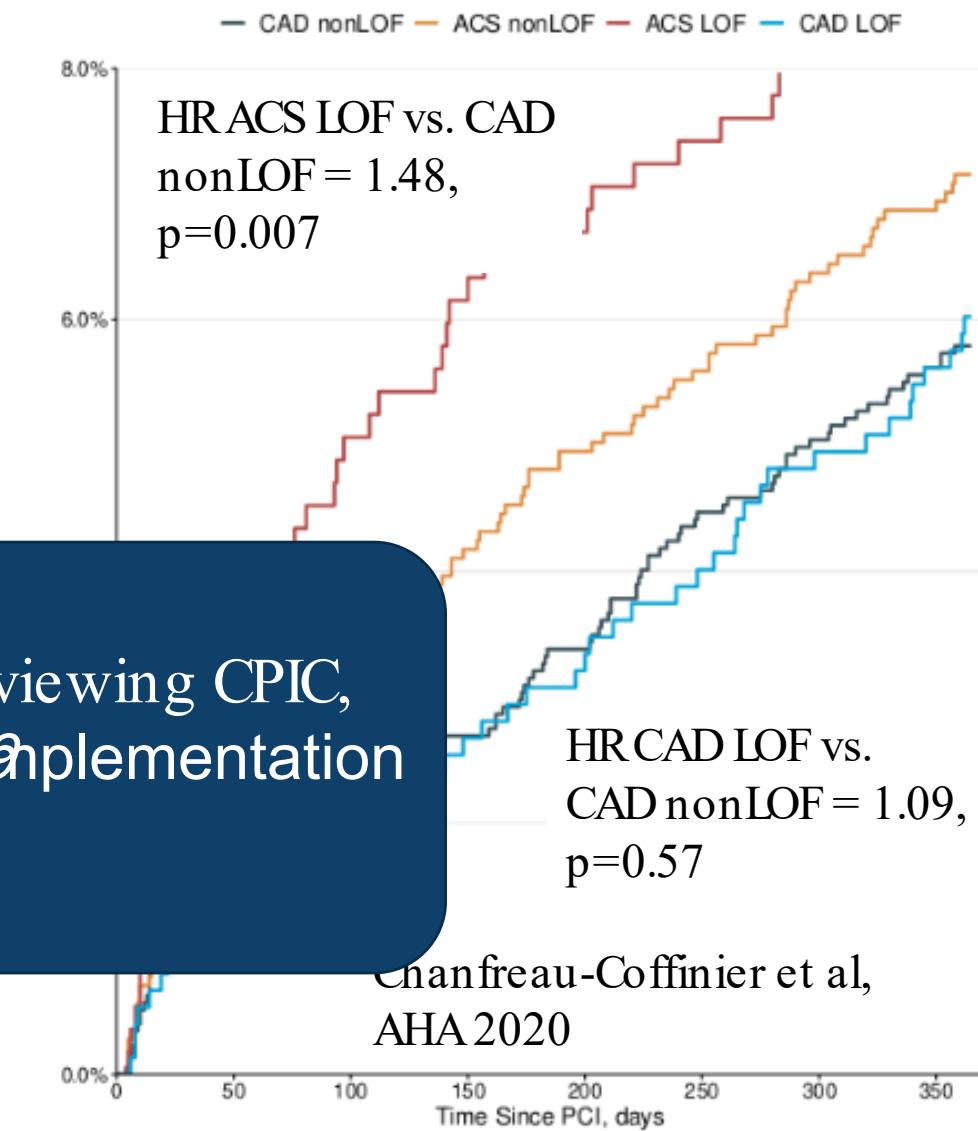
CPIC UPDATE

Table 2 Antiplatelet therapy recommendations based on CYP2C19 phenotype when considering clopidogrel for cardiovascular indications

CYP2C19 phenotype ^a	Implications for phenotypic measures	Therapeutic recommendation	Classification of recommendation ^b - ACS and/or PCI ^c	Classification ACS, non-PC
CYP2C19 ultrarapid metabolizer	Increased clopidogrel active metabolite formation; lower on-treatment platelet reactivity; no association with higher bleeding risk	If considering clopidogrel, use at standard dose (75 mg/day)	Strong	No
CYP2C19 rapid metabolizer	Normal or increased clopidogrel	If considering clopidogrel, use at	Strong	No
CYP2C19 normal metabolizer				
CYP2C19 likely intermediate metabolizer				
CYP2C19 intermediate metabolizer				

Subject matter expert workgroup reviewing CPIC,
MVP, other data to guide VA CYP2C19 implementation
in PCI

6



	No. at risk								
CAD nonLOF	1745	1721	1711	1698	1685	1665	1653	1640	
ACS nonLOF	1415	1375	1365	1353	1341	1332	1317	1306	
ACS LOF	553	531	524	518	515	511	505	496	
CAD LOF	748	737	732	727	723	717	709	703	

Summary

- The VA PHASER program is the first, scalable implementation of panel-based PGx testing available to any VA health care system.
- The VA National Pharmacogenomics Program (NPP) will build off PHASER to expanding access to PGx testing and enhance its use enterprise-wide.
- A PGx Learning Health System is critical to ensuring PGx is a high-value intervention within VA.

Acknowledgements

PHASER operational team

- Jennifer Chapman
- Jill Bates, PharmD
- Caroline Wyrosdick Webb
- Catherine Chanfreau PhD
- Adrienne Simmons
- Jesse Williamson
- John Barker
- Lindsey Wyatt
- Sal Rivas, PharmD
- Michael Naglich (ret)
- Hope McFarland (ret)
- Susan Rozelle
- Russell Jacobitz
- Wandalyn Belt
- Jack Lichy, MD
- Elaine Tomas
- Xai Lor
- Gary Stack, MD

- Elan Easter
- Haley Sirota
- Jahnae Bagley
- Jasmine Crosby
- Maikel McCaskill
- Nicholas Kypraios
- Reagan Woo
- Shanetta Williams
- Shawn Dalton, PharmD

PHASER Site Champions and Site Coordinators

PHASER Evaluation team

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- Nina Sperber, PhD
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Thank you!

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