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Implementing PGx testing in the Veterans Health Administration

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Agenda

01 Veterans Health Administration (VHA) Overview

02 Pharmacogenomics (PGx) Access

03 PGx Implementation and Education

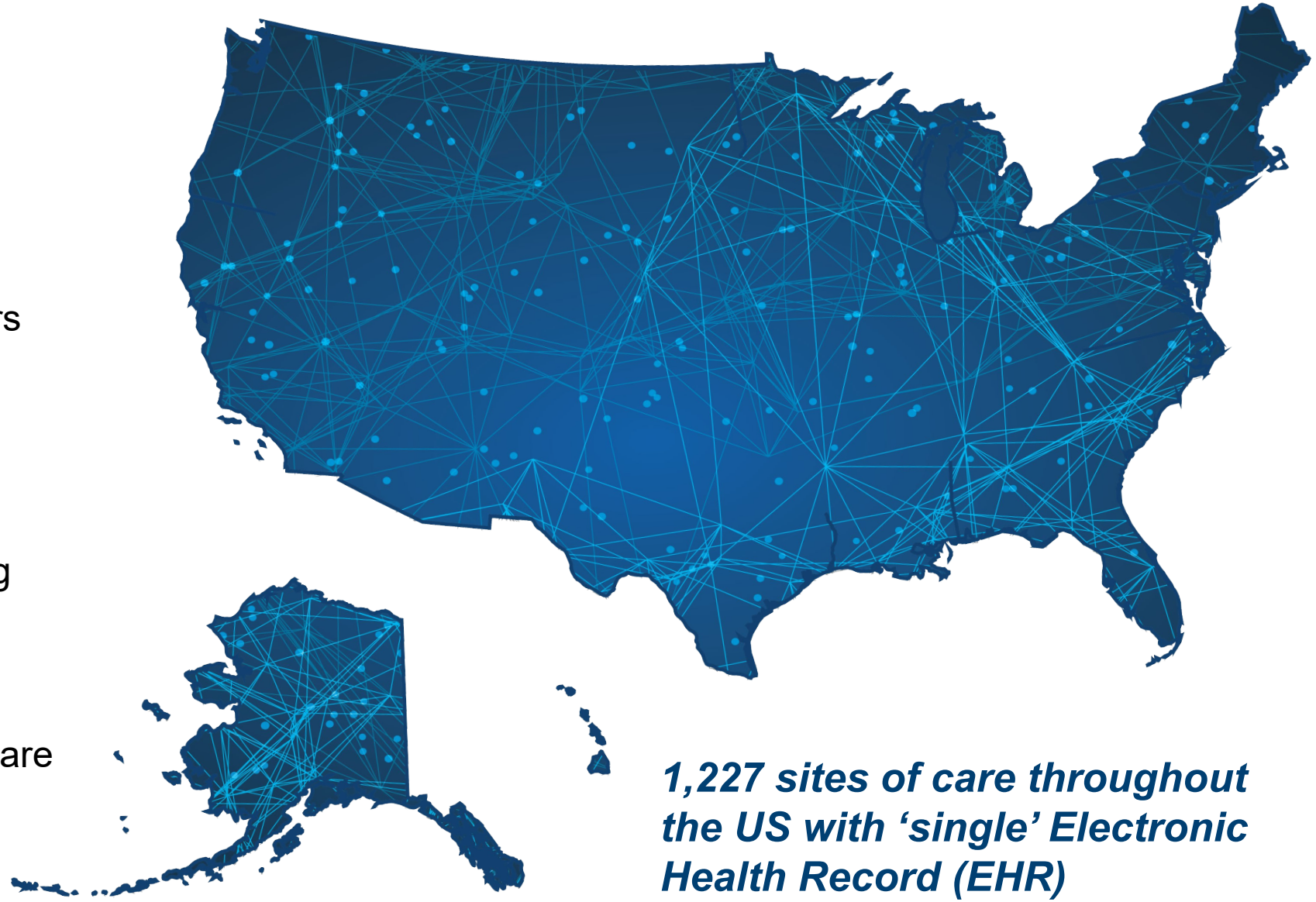
04 PGx Population Health Management

05 PGx Data Warehouse

06 Summary and Future Direction

VHA Overview

- **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 Sites of Care
- **>9 Million** Veterans receive care
- **~7 Million** using pharmacy benefits



1,227 sites of care throughout the US with 'single' Electronic Health Record (EHR)

Why does VA need a dedicated program to implement PGx?

VA began piloting pre-emptive, panel-based PGx testing in 2019, catalyzed by a donation from Sanford Health to bring PGx to 40 pilot sites (2019-2024).

Goals

- **Increase the value of PGx testing**
- **Reduce the barriers to using PGx testing**

Lessons Learned

- PGx implementation is a 'team-sport'
- Prescribers from all disciplines are our number one customers
- Pharmacists are necessary force-multipliers in implementing PGx
- Pre-emptive PGx testing requires a different delivery model than traditional lab-testing
- Implementation science is needed to design, evaluate, and improve PGx implementation
- PGx testing funding and clinical decision support (CDS) are necessary but not sufficient to support widespread adoption

Build ‘end-to-end’ provider support for implementing PGx at any facility

Access to panel-based PGx testing for more than 40 medications

Learning community of practice

Educational materials to review testing and interpretation

Remote pharmacist support for direct patient care and population health management

Clinical decision support systems

Local PGx trained Pharmacist to lead the change in practice behavior

PGx trained pharmacist for post-testing consultation

Return of results to patients

Provider-friendly summary of PGx test results in EHR

Data warehouse

Build ‘end-to-end’ provider support for implementing PGx at any facility: Access

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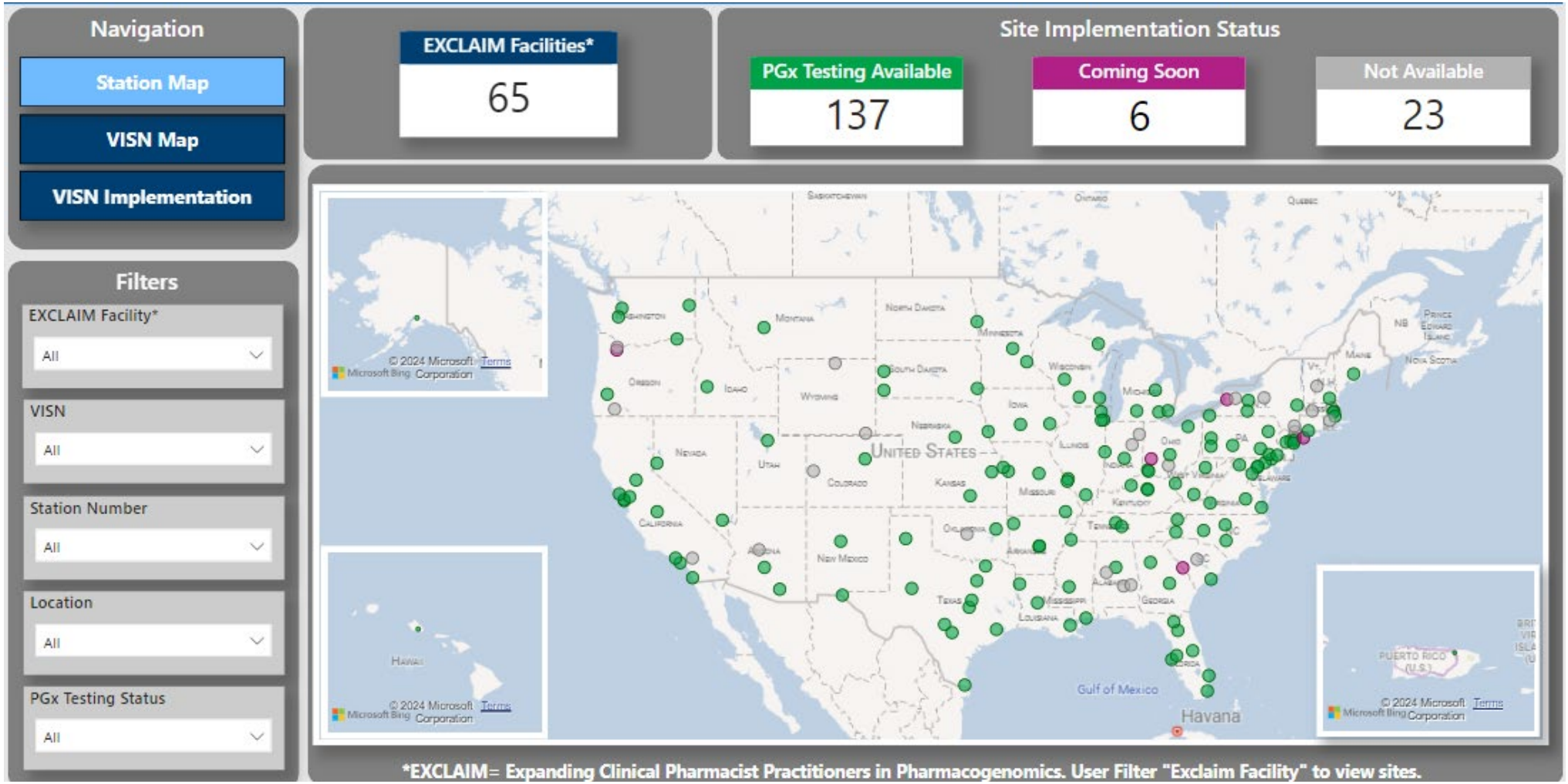
Primary PGx Panel

Medications Informed by Panel‡			
Abacavir	Amitriptyline	Aripiprazole	Atazanavir
Atomoxetine	Atorvastatin	Azathioprine	Belinostat
Brexpiprazole	Capecitabine	Celecoxib	Citalopram
Clobazam	Clomipramine	Clopidogrel	Codeine
Dapsone	Desipramine	Deutetrabenzine	Dexlansoprazole
Doxepin	Efavirenz	Eliglustat	Escitalopram
Fluorouracil	Flurbiprofen	Fluvastatin	Fluvoxamine
Fosphenytoin	Ibuprofen	Iloperidone	Imipramine
Lansoprazole	Lovastatin	Meloxicam	Mercaptopurine
Methylene Blue	Metoclopramine	Nitrofurantoin	Nortriptyline
Omeprazole	Ondansetron	Pantoprazole	Paroxetine
Pegloticase	Phenytoin	Pimozide	Piroxicam
Pitavastatin	Pitolisant	Pravastatin	Primaquine
Rasburicase	Rosuvastatin	Sertraline	Simvastatin
Siponimod	Tacrolimus	Tafenoquine	Tetrabenazine
Thioguanine	Tramadol	Trimipramine	Valbenazine
Venlafaxine	Voriconazole	Vortioxetine	Warfarin

Genes	Alleles Tested†
ABCG2	c.421C (p.GLN141)
CYP2B6	*5, *6, *7, *18, *22
CYP2C cluster	g.96405502G
CYP2C19	*2, *3, *4, *5, *6, *7, *8, *9, *10, *16, *17, *22, *24, *25, *26, *35
CYP2C9	*2, *3, *4, *5, *6, *8, *11, *12, *13, *15, *16
CYP2D6	*2, *3, *4, *5, *6, *7, *8, *9, *10, *12, *14, *15, *17, *21, *29, *39, *41, *42, *49, *56, *59, *114, allele duplication
CYP3A5	*3, *6, *7
CYP4F2	*3
DPYD (NM_000110.4)	c.299_302del, c.557A>G (p.Y186C), c.703C>T (p.R235W), c.1129-5923C>G, c.1236G>A, c.1156G>T (p.E386*), c.1679T>G (p.I560S), c.1898del (p.P633Qfs), c.1905+1G>A, c.2846A>T (p.D949V), c.2983G>T (p.V995F)
G6PD	B, A, Asahi, Canton, Chatham, Cosenza, Mediterranean, Coimbra-Shunde, Vancouver, Kaiping, A-202A_376G, A-968C_376G
HLA-B*57:01 screen	positive
NUDT15	*2, *3, *4, *5, *6, *7, *8, *9
SLCO1B1	*5, *14, *15, *37
TPMT	*2, *3A, *3B, *3C, *4, *11, *14, *15, *23, *29, *41
UGT1A1	*6, *27, *28, *36, *37
VKORC1 (NM_024006.5)	c.-1639G>A

Access to PGx testing

As of June 13, 2024

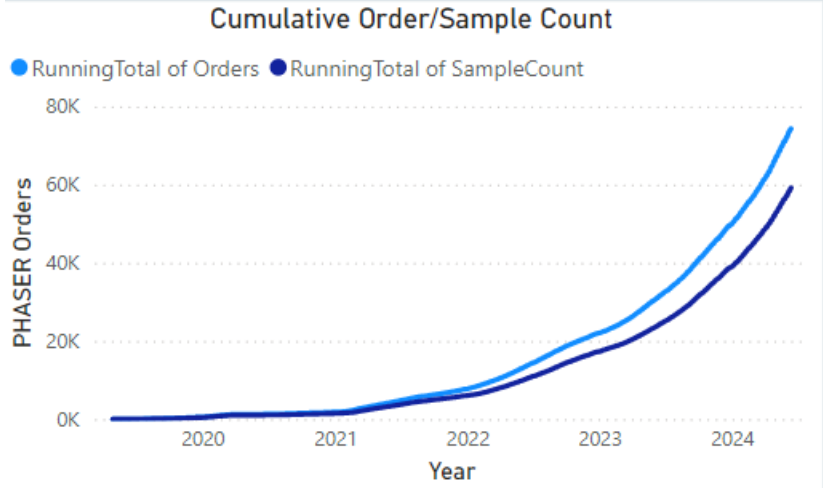


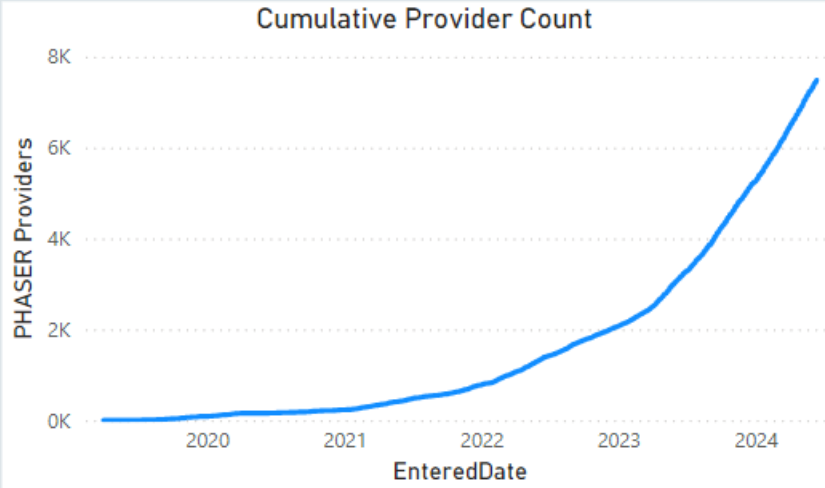
PGx Orders: Cumulative Volume & Provider Count

as of June 13, 2024

74340	4/1/2019	6/12/2024
Cumulative Orders	First Order Date	Most Recent Order Date

Count of PHASER Orders Placed in Last 30 days	Ratio of PHASER Orders Placed per Provider in Last 30 days	Count of Unique Ordering Providers in Last 30 days
5860	3.20	1934
Compared to Previous 30-day Period	Compared to Previous 30-day Period	Compared to Previous 30-day Period

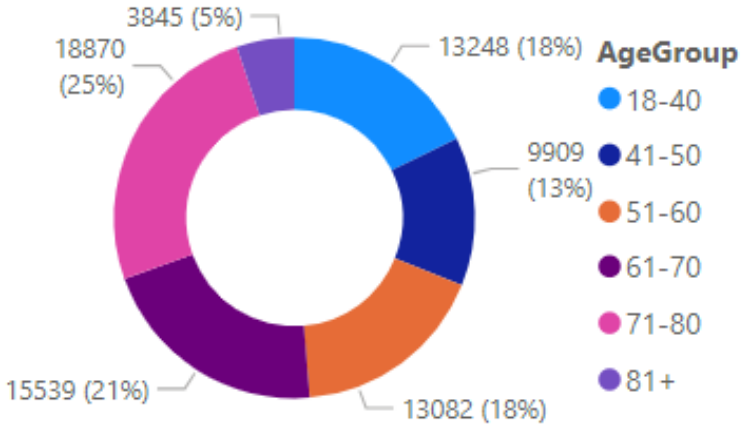




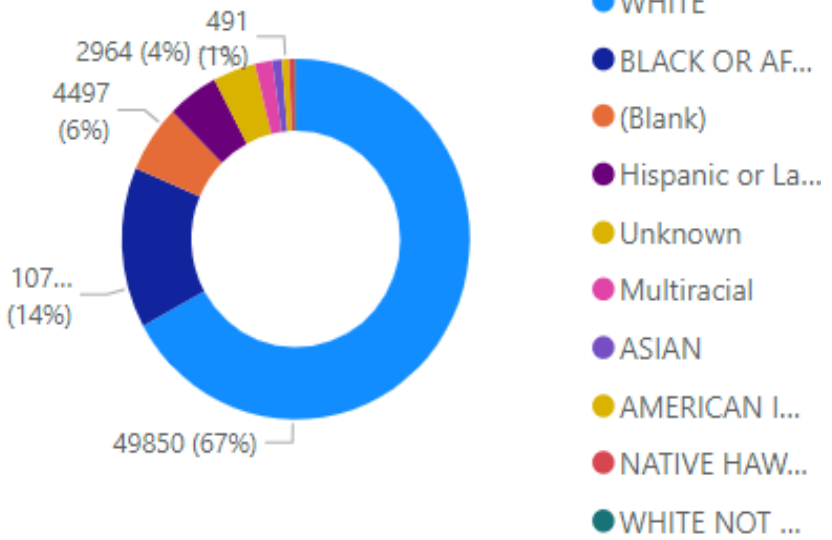
PGx Orders: Patient Demographics

as of June 13, 2024

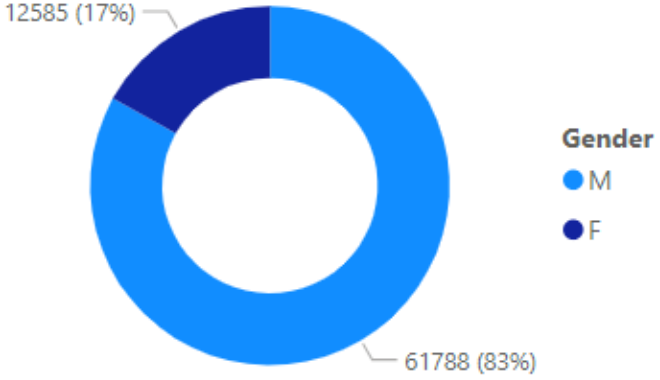
Patient Age Group



Patient Race/Ethnicity



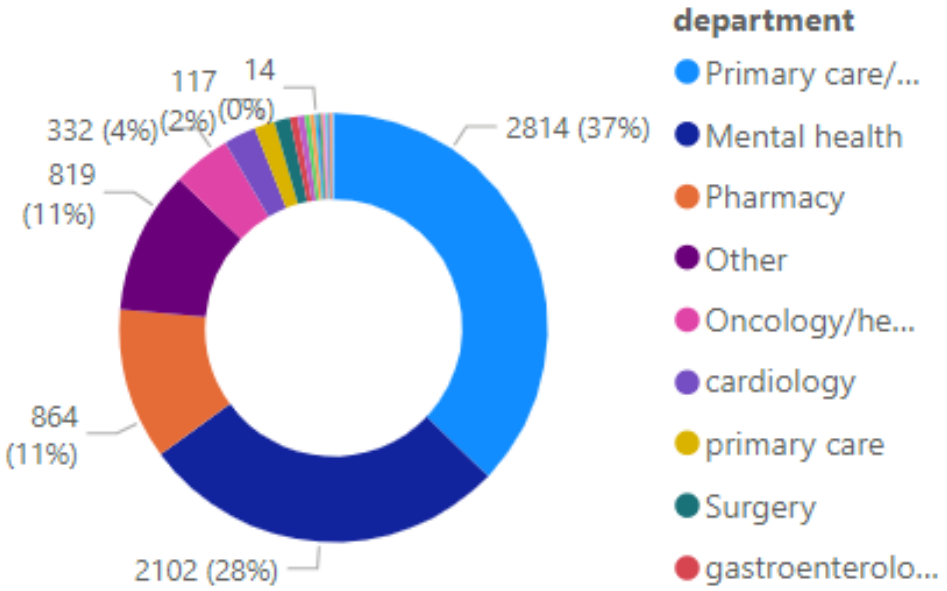
Patient Gender



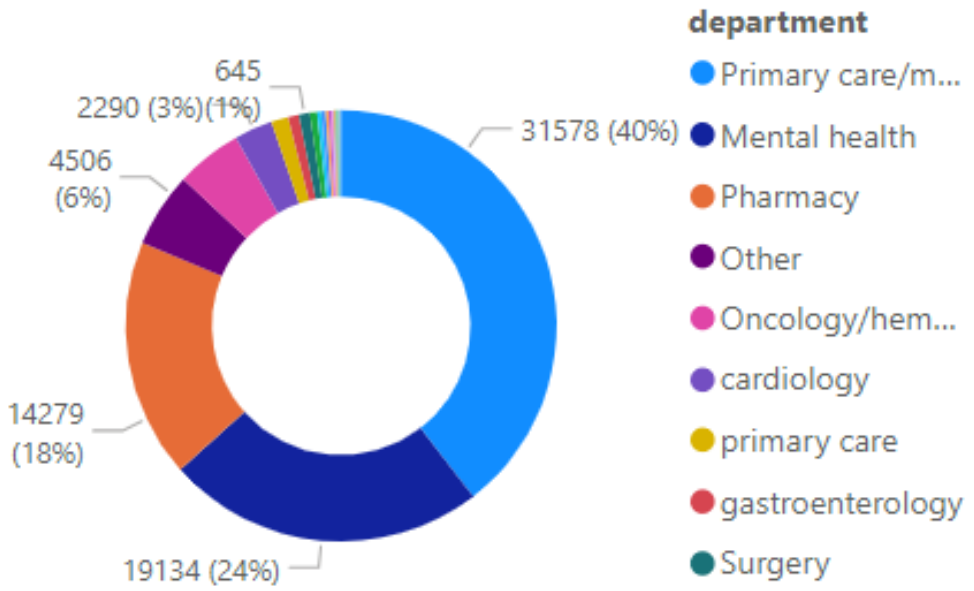
PGx Orders: Provider Specialties

as of June 13, 2024

Provider Specialty (Count of Provider)



Provider Specialty (Count of Orders)



Factors associated with uptake in PGx testing

Factors Associated with Obtaining a PGx Test Order: (n=24,073 cases and matched controls)

	OR	95% LL	95% UL	p-value
<---Patient Characteristics--->				
Sex				
Female vs Male	1.00	0.95	1.05	NS
Age (years)				
18-39 vs 70+	1.65	1.53	1.78	***
40-49 vs 70+	1.39	1.30	1.49	***
50-59 vs 70+	1.22	1.15	1.30	***
60-69 vs 70+	1.07	1.01	1.12	*
Race/Ethnicity				
nH Black vs nH White	1.46	1.38	1.55	***
Hispanic vs nH White	1.52	1.39	1.67	***
Other vs nH White	1.18	1.08	1.27	***
Married				
Yes vs No	1.10	1.06	1.14	***
Area Deprivation Index Quarter[a]				
4 vs 1	1.04	0.98	1.10	NS
3 vs 1	1.05	1.00	1.11	NS
2 vs 1	1.06	1.00	1.13	*
missing vs 1	1.34	1.19	1.51	***
Distance to VHA (miles)				
>45 vs <= 15	0.91	0.86	0.96	**
PHASER education mailer- Sent				
Yes vs No	1.09	1.00	1.18	*
Charlson Comorbidity Index				
1 vs 0	0.88	0.83	0.93	***
2 vs 0	0.92	0.86	0.98	*
3 vs 0	0.85	0.79	0.91	***
4+ v 0	0.87	0.81	0.92	***
Depression Diagnosis				
Yes vs No	1.22	1.17	1.28	***
PTSD Diagnosis				
Yes vs No	1.05	1.00	1.10	NS
Has PGx Drug Allergy				
Yes vs No	1.40	1.33	1.47	***
Unique PGx Prescriptions[b]				
2+ vs 0	1.18	1.11	1.24	***
<---Patient's Provider Characteristics--->				
Provider sex				
Female vs Male	1.15	1.11	1.20	***
Provider age (years)				
18-39 vs 60+	1.51	1.42	1.60	***
40-49 vs 60+	1.62	1.53	1.72	***
50-59 vs 60+	1.31	1.24	1.39	***
Provider type				
NP/PA vs Physician	1.08	1.05	1.12	***
Pharmacist vs Physician	1.45	1.39	1.50	***
Provider caseload (Tertile)[c]				
Middle vs Low	0.97	0.93	1.00	NS
High vs Low	0.91	0.87	0.95	***
PHASER Educational Mailer Opt In				
Yes vs No	2.74	2.58	2.90	***

Abigail Silva, Deepak Voora, Rebekah Ryanne Wu, Brian Bartle, Catherine Chanfreau-Coffinier, Allison Hung, Corrine I. Voils (unpublished)

Build ‘end-to-end’ provider support for implementing PGx at any facility: Implementation and Education

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Data Warehouse

Enhancing education and implementation through a PGx trained Clinical Pharmacist Practitioner (CPP)

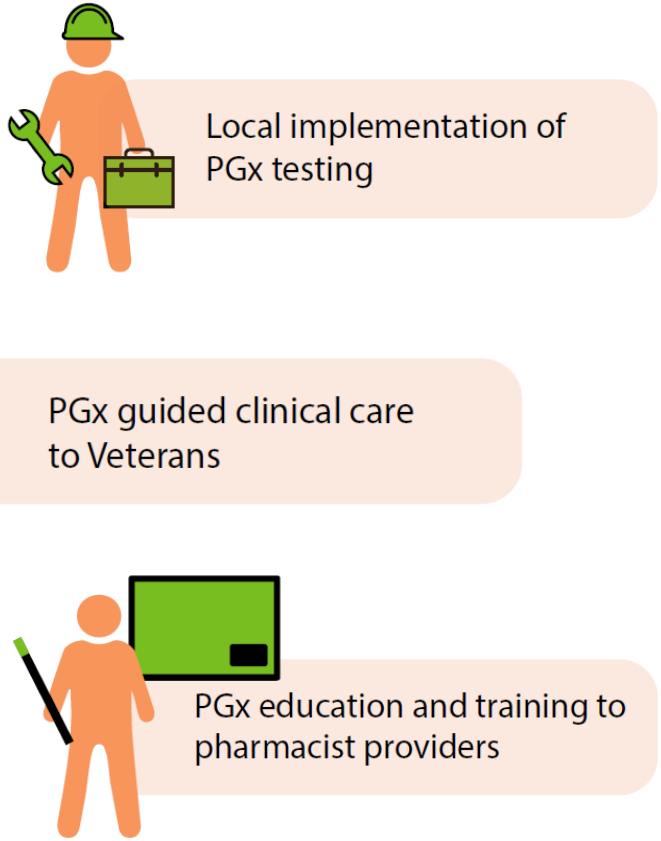
2019-2023

- Framework for PGx testing
- Limitations to educational outreach
- Lower than anticipated uptake
- **Main focus: Pre-emptive PGx testing**

2023 and Beyond

- Increase adoption within and across facilities
- Knowledge transfer to frontline providers/pharmacists
- **Main focus: Reactive PGx testing**

CPP Roles and Responsibilities



Clinical Workflows Overview

SMEs across clinical specialties:

- Identify ***specific patient subgroups*** who are more likely to ***benefit from PGx*** in the near term
- Collaborate on ***when and how to integrate PGx*** so that results are available when needed
- Guide clinical decision support tools:
  - Drug gene alerts
  - Population health management
  - Therapy and dosing recommendations

PGx clinical workflows include:

- Metrics to ***measure uptake and appropriate use*** of PGx testing
- Resources consisting of ***pre- and post-test dashboards, EMR clinical decision support tools, and educational material*** targeting prescribers

CPPs implement PGx clinical workflows:

- ***Utilize implementation resources*** including toolkit, PowerPoint presentation, fact sheet, and CPIC guidelines available in a single package online
- Apply PGx test results to ***support care coordination***

Implementation strategies are infused into the foundation of each clinical pathway:

- Increase demand and mandate change
- Train and educate providers and stakeholders
- Implementation facilitation
- Revise professional roles
- Audit-and-feedback
- Data warehousing
- Change record systems
- Prepare patients to be active participants
- Centralized technical assistance

Road to Implementation

Phase 1: Clinical Workflow Development

- SMEs identify patient population and draft clinical workflow
- Stakeholder buy-in from SMEs
- Assess operational and technical feasibility, clinical workflow metrics and dashboard feasibility

Phase 2: Implementation Planning

- Finalize implementation resources (implementation toolkit, implementation PowerPoint, flow map, in-service PowerPoint)
- SMEs test dashboard for functionality to ensure patients in need of testing and those with existing test results are identified
- EHR clinical decision support:
  - Pre-test
  - Post-test

Phase 3: Clinical Workflow Implementation

- Local leadership, provider, and pharmacist education
- In-services
- 1:1 education targeted at front line providers

Monitoring of Implementation

- Reports with metrics for percentage uptake and concordance at provider, facility, VISN, regional level

PGx Clinical Workflow Updates

P2Y12 'Escalation' and 'Descalation'

- Focus: Improve antiplatelet efficacy and safety following percutaneous coronary intervention
- Launch: February 2024
- Implementation: 34 systems

DPYD and Fluoropyrimidines

- Focus: Medication safety
- Launch: April 2024
- Implementation: 49 system

Resources supporting CPPs with workflow implementation:

- Implementation toolkit
- Implementation presentation, In-service presentation
- Data tracking
- Provider-Facing Fact sheets
- Third party PGx educational opportunities through University of Pittsburg Test2Lern

Current and Future Clinical Workflows

SME Workgroup	Clinical Pathway	Release Date or Anticipated Release Date
Cardiovascular	Cardiac Cath Lab	February 2024
Oncology	DPYD and Fluoropyrimidines	April 2024
Oncology	TPMT, NUDT15 and Mercaptopurine for Acute Lymphoblastic Leukemia (ALL)	June 2024
Mental Health	Interventional Psychiatry for Treatment of Depression	August 2024
Primary Care	Depression Management	October 2024
Neurology	Carbamazepine and HLA-B	December 2024
Rheumatology	Thiopurines	FY25
Transplant	Tacrolimus and CYP3A5	FY25
Chronic Pain	TBD	FY25
Acute Pain/Anesthesia	TBD	FY25
Infectious Disease	TBD	FY25
Oncology	Irinotecan/Irinotecan-liposomal and UGT1A1 homozygous/PM	FY25
Mental Health	Antipsychotics	FY25

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PGx Population Health Management

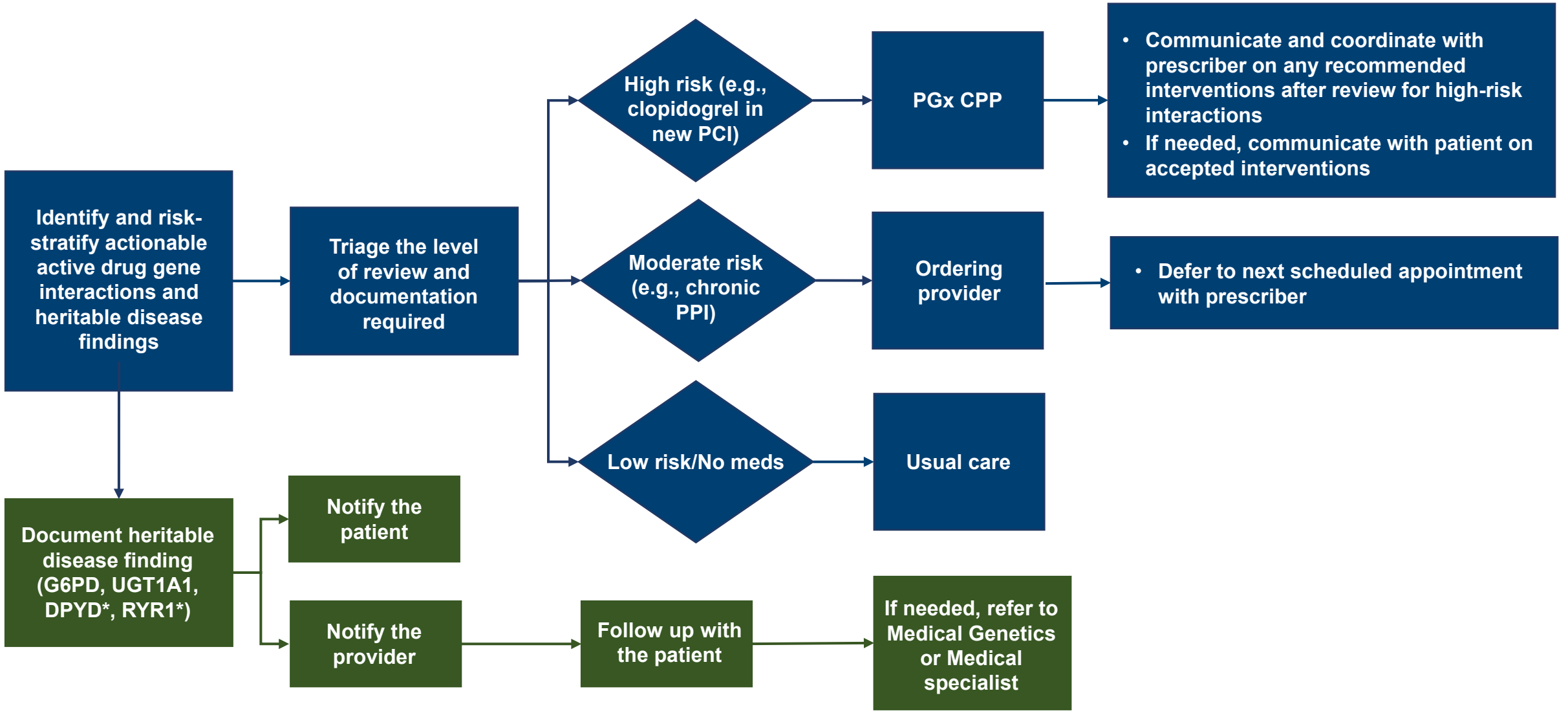
Need

- Incidental findings
  - Concomitant medications
  - Heritable conditions
- Surveillance for new, high-risk drug gene interactions despite CDS systems.

Enabling Features

- Pharmacovigilance is an established practice in VA medication safety
- Telehealth capabilities allow pharmacists to cross health systems and state lines
- PGx trained pharmacists at local, regional, and national levels
- Centralized PGx database of all PGx test results
- Dashboards that evaluate and resolve existing medications/PGx results for potential intervention

PGx Population Health Management Workflow



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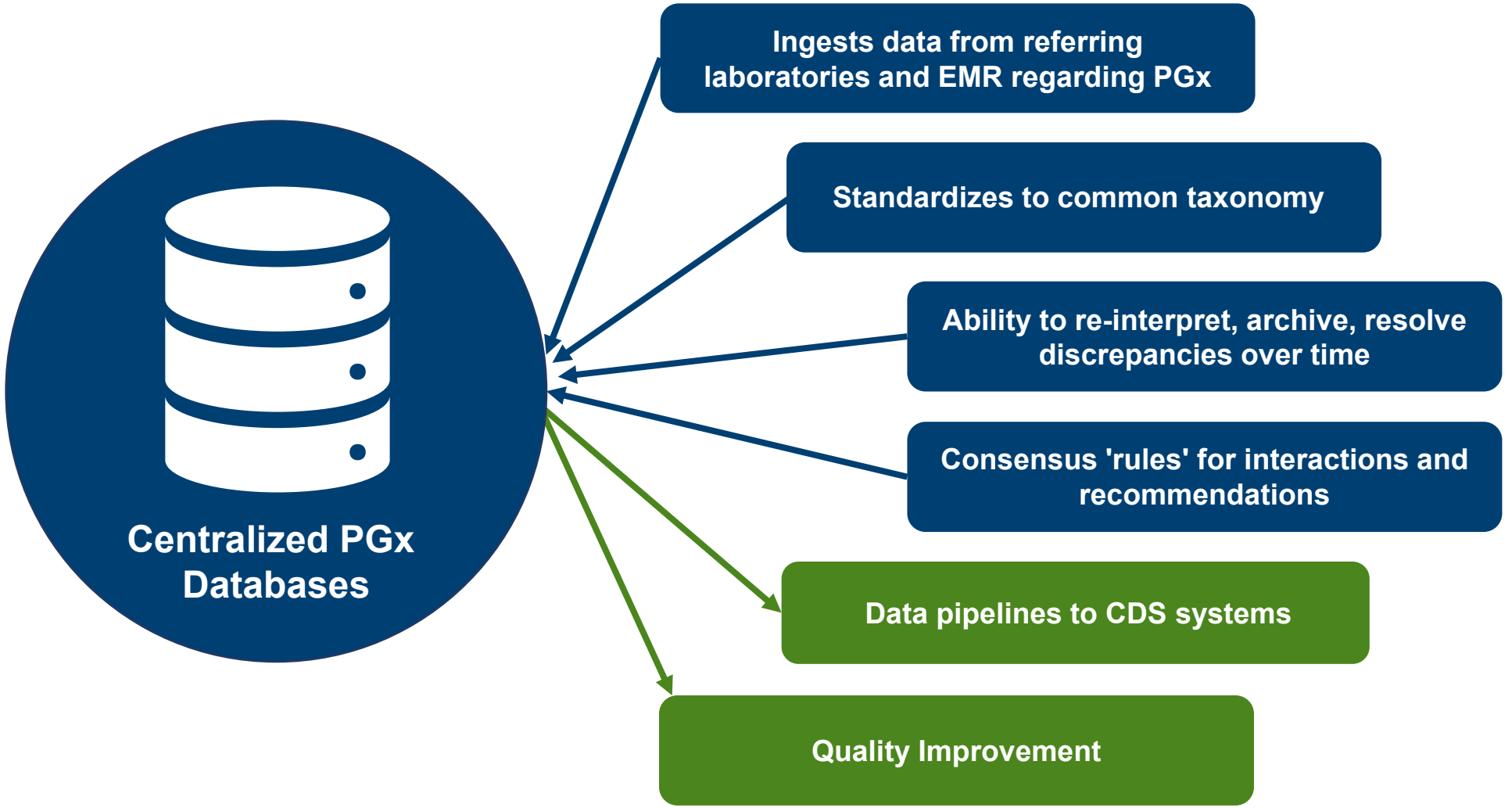
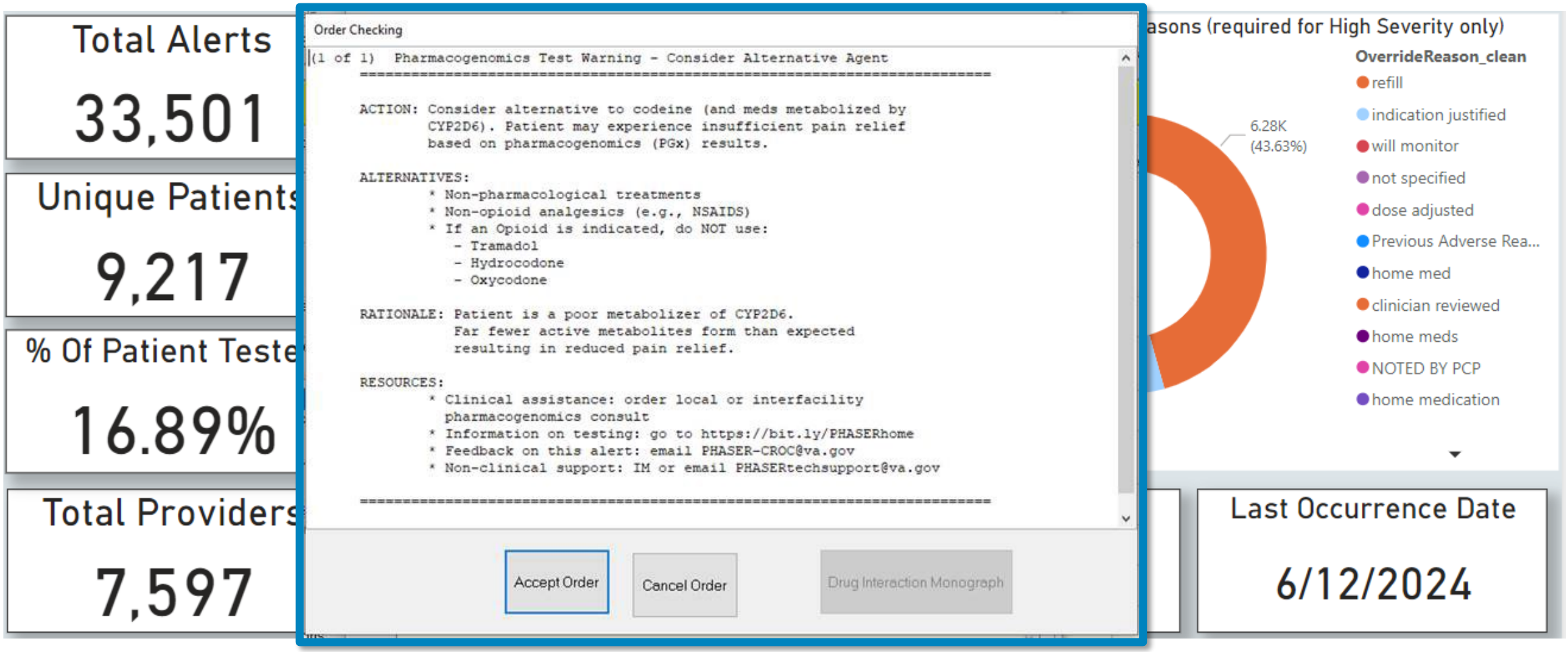
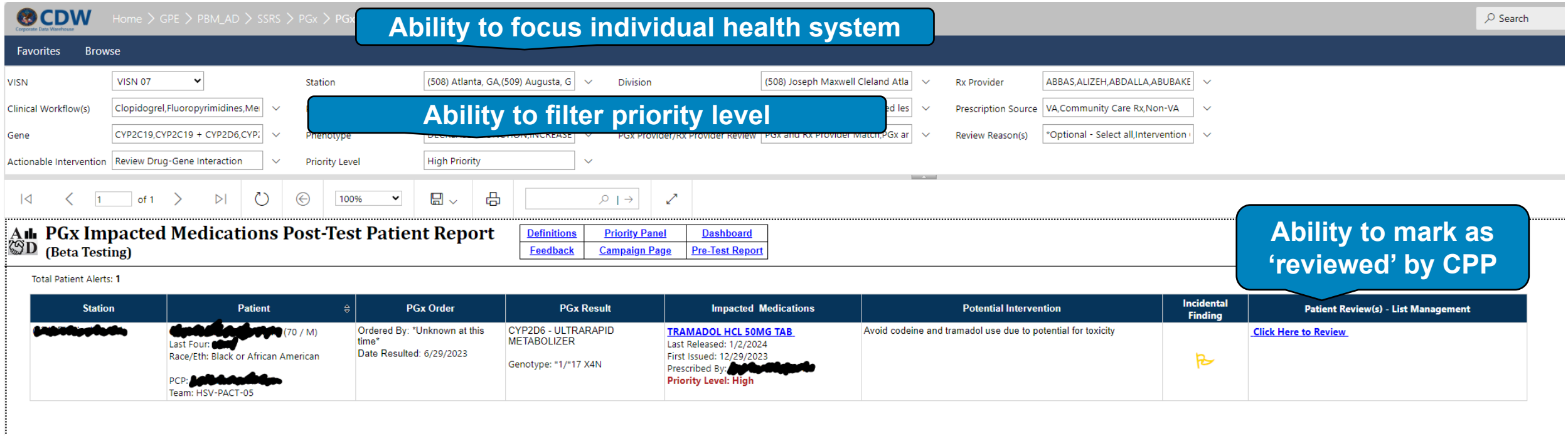
PGx Data Warehousing



Interruptive CDS systems for over 50 medications



Bringing PGx data to PGx Clinical Pharmacists



Dashboards to allow audit-feedback and targeted provider education

Drill down to individual health systems

Benchmarking to regional peers and national metrics

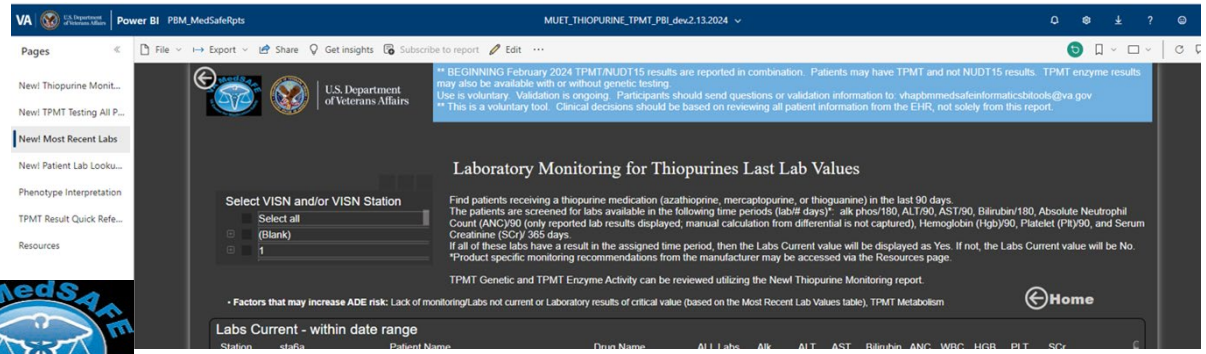
Provider lists to target education.

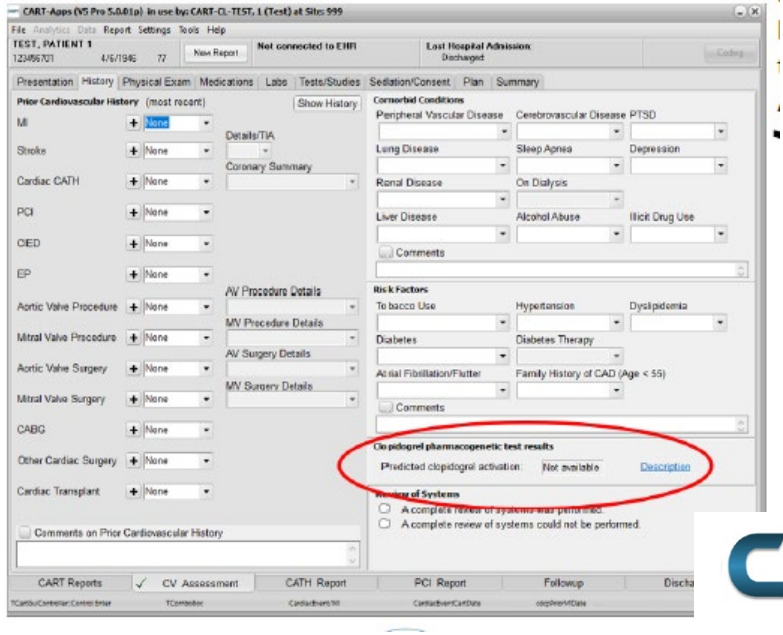
Quality Indicator		Workflow	Preferred Di	PGx Testing Completed	Nat. Avg	May Need PGx Actionable Staff /
Oncology						
% of patients on Fluoropyrimidines + PGx ordered		Oncology - Fluoropyrimidines				
	Station Name	Oncology - Fluoropyrimidines	↑	7.7	20.0	12
	Station Name	Oncology - Fluoropyrimidines	↑	33.3	20.0	2
	Station Name	Oncology - Fluoropyrimidines	↑	100.0	20.0	
	Station Name	Oncology - Fluoropyrimidines	↑	38.5	20.0	
	Station Name	Oncology - Fluoropyrimidines	↑	0.0	20.0	
	Station Name	Oncology - Fluoropyrimidines	↑	0.0	20.0	12
% of patients on Fluoropyrimidines + PGx results		Oncology - Fluoropyrimidines	↑	20.0	20.0	484
	Station Name	Oncology - Fluoropyrimidines	↑	7.7	20.0	12
	Station Name	Oncology - Fluoropyrimidines	↑	33.3	20.0	2
	Station Name	Oncology - Fluoropyrimidines	↑	100.0	20.0	0
	Station Name	Oncology - Fluoropyrimidines	↑	38.5	20.0	8
	Station Name	Oncology - Fluoropyrimidines	↑	0.0	20.0	2
	Station Name	Oncology - Fluoropyrimidines	↑	0.0	20.0	12

Bringing PGx data to Prescriber specific clinical dashboards

STORM Patient Detail Report
Stratification Tool for Opioid Risk Mitigation

- Stratifies risk of overdose
- Identifies modifiable risk factors
- Displays PGx results for codeine/tramadol users

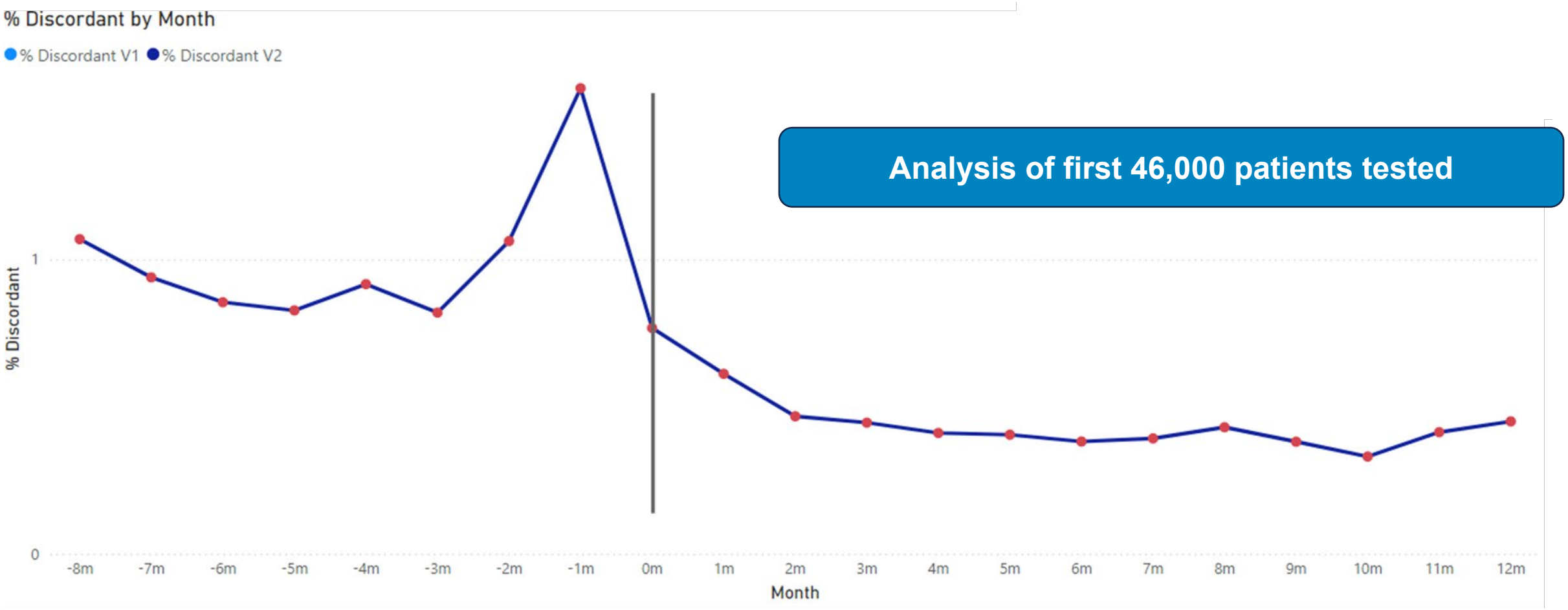




CART

Discordant Medication Orders: Pre-Post Comparison

as of June 14, 2024



Analysis of first 46,000 patients tested

Summary

- VA has the evidence to demonstrate that PGx can improve health outcomes
- Implementation barriers exist beyond access/cost of PGx testing
- Investments are needed to shift the balance of *perceived* value vs. barrier of PGx
- PGx is as much a behavioral intervention as it is a medical one
- Existing front line health care providers like pharmacists can be upskilled and enabled to drive practice change

Future Directions

- Expand access to PGx testing
- Reduce variation across geographic location, pharmacist investment model, and EHR
- Perform cost analyses from payer perspective
- Conduct clinical outcomes analysis

Questions

If you have any additional questions, please contact deepak.voora@va.gov.

THANK YOU