



Demonstrating the Value of Clinical Laboratory Medicine: Impact of Pharmacogenetic Panel Testing on a Health Plan

Andrew Fletcher, MD, MBA, CPE, CHCQM, FCAP

Medical Director, Consultative Services

Learning Objectives

Describe the premise of pharmacogenetic testing and cite specific basic examples of drug-gene interactions

Explain strategies for laboratory and pharmacy to implement a pharmacogenetic panel testing to address quality and cost metrics within a health plan

Understand the potential challenges of implementing a pharmacogenetic screening program

Discuss the potential impact of pharmacogenetic testing to both patients and the health plan.

13 Billion

laboratory tests
performed annually
in the U.S.

70%

of medical decisions are
influenced by laboratory data

3%

of U.S. healthcare
expenditures spent on
laboratory services

Downstream Impact



- Pharmacy

PEW charitable trust

Figure 1

U.S. Prescription Drug Spending Estimates and Projections by Source, 2010-20



Note: Figures in the billions of dollars.

\$300 bil

Prescription drug
\$300 billion a year. ¹

700k

Adverse drug events
account for nearly
700,000 emergency. ³

**3.8 &
3.3 mil**

Medication errors
occur in 3.8 million
inpatient and 3.3
million outpatient. ²

~275k

~275,000 deaths a
year attributable to
medication errors. ⁴

1. "A Look at Drug Spending in the U.S.," Pew Charitable Trust, 28 Aug. 2018. <https://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2018/02/a-look-at-drug-spending-in-the-us>. Accessed 18 Feb 2020.
2. "Preventing Medication Errors: A \$21 Billion Opportunity," Network for Excellence in Health Innovation, 2011. https://www.nehi.net/bendthecurve/aup/documents/Medication_Errors_%20Brief.pdf. Accessed 18 Feb 2020.
3. "Medication Errors and Adverse Drug Events," US Health and Human Services, Sept 2019. <https://psnet.alrq.gov/primer/medication-errors-and-adverse-drug-events>. Accessed 18 Feb 2020.
4. Watanabe J, et al, "Cost of Prescription Drug-Related Morbidity and Mortality," Ann Pharmacother. 2018 Sep;52(9):829-837



\$14,800

The total cost of health care, including premiums and out-of-pocket costs for employees and dependents, is estimated to average \$14,800 per employee in 2019.

- Society human resource management

85%

Of employers, pharmacy pricing was their predominant concern.

-National Business Group on Health (NBGH)

18.5%

Average total drug spending per hospital admission between FY2015 and FY2017

28.7%

Outpatient drug spending per hospital admission

AHA



How can laboratory medicine play a role in reducing drug spend and increase quality in partnership with Pharmacy?

Pharmacogenetics

The branch of pharmacology concerned with the effect of genetic factors on reactions to drugs



Adherence



Appropriateness



Adversity

Pharmacogenetics Coagulation

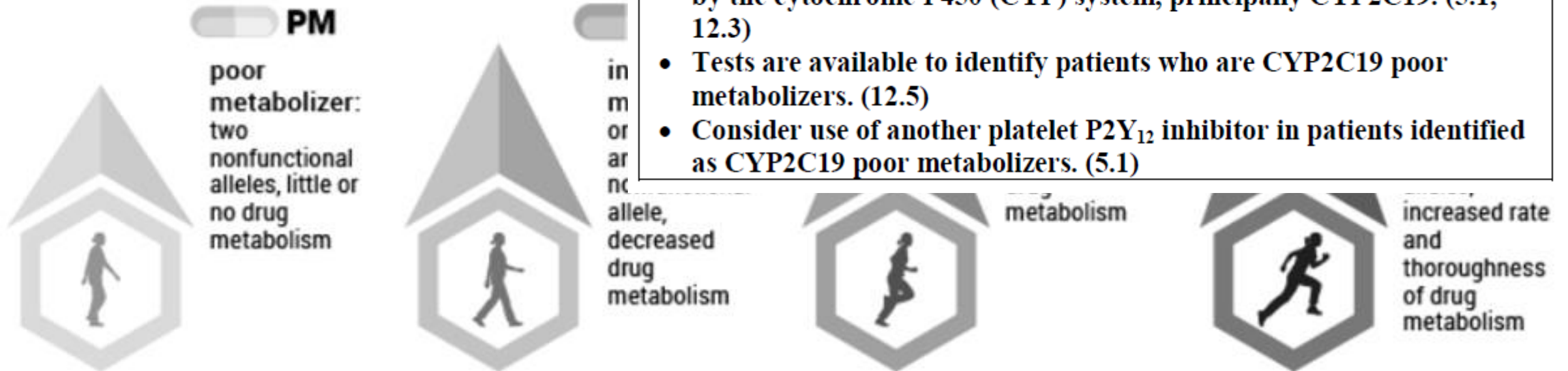
Clopidogrel (Plavix)

- *CYP2C19*

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE CYP2C19 GENE

See full prescribing information for complete boxed warning.

- Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1, 12.3)
- Tests are available to identify patients who are CYP2C19 poor metabolizers. (12.5)
- Consider use of another platelet P2Y₁₂ inhibitor in patients identified as CYP2C19 poor metabolizers. (5.1)



Pharmacogenetics reimbursement



PALMETTO GBA®
A CELERIAN GROUP COMPANY

# (N=377)	GENE (UNIQUE = 127)	DRUG (UNIQUE = 240)	GUIDELINE	CPIC LEVEL	PHARMGKB LEVEL OF EVIDENCE	PGX ON FDA LABEL	CPIC PUBLICATIONS (PMID)
1	HLA-B	abacavir	Guideline	A	1A	Testing required	<ul style="list-style-type: none"> • 24561393 • 22378157
2	HLA-B	allopurinol	Guideline	A	1A		<ul style="list-style-type: none"> • 23232549 • 26094938
3	CYP2D6	amitriptyline	Guideline	A	1A	Actionable PGx	<ul style="list-style-type: none"> • 23486447 • 27997040
4	CYP2C19	amitriptyline	Guideline	A	1A		<ul style="list-style-type: none"> • 23486447 • 27997040
5	UGT1A1	atazanavir	Guideline	A	1A		<ul style="list-style-type: none"> • 26417955
6	CYP2D6	atomoxetine	Guideline	A	1A	Actionable PGx	<ul style="list-style-type: none"> • 30801677
7	TPMT	azathioprine	Guideline	A	1A	Testing recommended	<ul style="list-style-type: none"> • 21270794 • 23422873 • 30447069
8	NUDT15	azathioprine	Guideline	A	1A	Testing recommended	<ul style="list-style-type: none"> • 21270794 • 23422873



<https://cpicpgx.org/genes-drugs/>

COVID-19 Medication Safety Pharmacogenomics Report

Coriell Life Sciences
4747 S. Broad St., Suite 222 • Philadelphia, PA
Phone: (856) 699-8069
Laboratory Director: N/A
CLIA ID Number: SAMPLE
<https://www.coriell.com/>

CORIELL
LIFE SCIENCES

Patient: Doe, Jane Date of Birth: Jan 01, 1945 Gender: Female Patient ID: 3284903892084024	Physician: Dr Example Practice: Example Healthcare	Date Collected: Jul 27, 2020 Date Accessioned: Jul 27, 2020 Specimen type: Buccal swab Sample ID: cls101
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About this Test:

This patient has been tested for genetic variations that may cause some medicines not to work as intended. This test combines the guidance from the FDA pharmacogenomic drug labels and supplemental publications, the Clinical Pharmacogenomic Implementation Consortium guidelines, and the Coriell Life Sciences research knowledge base with genetics assay results to provide an accurate assessment of the medication risks for this patient.

This test has been limited to those medications with known genetic implications and that may be used in the treatment of COVID-19. As such, it is not a comprehensive report of all possible medications unrelated to COVID-19 treatment with pharmacogenomic associations.

Results:

<div><div></div><div>AVOID THE FOLLOWING MEDICATIONS IF POSSIBLE: Contraindicated; predicted to be ineffective or unsafe based on patient's genetics.</div></div>			
Clopidogrel	Eliglustat	Ondansetron	Tropisetron
<div><div></div><div>CONSIDER ALTERNATIVE MEDICATIONS IF POSSIBLE: These should be used with caution or modification to standard dosing. See later pages for details.</div></div>			
Amitriptyline	Diazepam	Nortriptyline	Ticagrelor
Buprenorphine	Doxepin	Paroxetine	Tramadol
Citalopram	Escitalopram	Pimozide	Trazodone
Clomipramine	Flecainide	Propafenone	Venlafaxine
Clonidine	Fluoxetine	Protriptyline	Vortioxetine
Desipramine	Haloperidol	Sertraline	
Deutetrabenazine	Hydrocodone	Sirolimus	
Dextromethorphan-Quinidine	Metoprolol	Thioridazine	



Cost-Effectiveness of Strategies to Personalize the Selection of P2Y₁₂ Inhibitors in Patients with Acute Coronary Syndrome

Kibum Kim¹ • Daniel R. Touchette^{2,3} • Larisa H. Cavallari⁴ • Amer K. Ardati⁵ • Robert J. DiDomenico^{2,6} 

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Clinical Utility of Pharmacogenetic Testing and a Clinical Decision Support Tool to Enhance the Identification of Drug Therapy Problems Through Medication Therapy Management in Polypharmacy Patients

Kibum Kim, PhD; Jonathan W. Magness, PharmD; Ryan Nelson, PharmD;
Valerie Baron, PharmD, BCGP; and Diana I. Brixner, RPh, PhD

ORIGINAL RESEARCH ARTICLES

Comparative Effectiveness of Oral Antiplatelet Agents in Patients with Acute Coronary Syndrome

Kibum Kim,^{1,2} Todd A. Lee,^{3,4} Amer K. Ardati,⁵ Robert J. DiDomenico,^{4,6} Daniel R. Touchette,^{3,4} and Surrey M. Walton^{3,4*}

¹Pharmacotherapy Outcomes Research Center, University of Utah, Salt Lake City, Utah; ²Department of Pathology, University of Utah, Salt Lake City, Utah; ³Department of Pharmacy Systems, Outcomes and Policy, College of Pharmacy, University of Illinois at Chicago (UIC), Chicago, Illinois; ⁴Center for Pharmacoepidemiology and Pharmacoeconomic Research, UIC, Chicago, Illinois; ⁵Division of Cardiology, College of Medicine, UIC, Chicago, Illinois; ⁶Department of Pharmacy Practice, College of Pharmacy, UIC, Chicago, Illinois

ARUP Family Health clinic

Our goal is to provide services that are unmatched in quality and expertise. This allows ARUP employees (~5,000 people) and their dependents access to the most comprehensive care available from a team of providers who are solely dedicated to the overall health and wellness of the ARUP community.

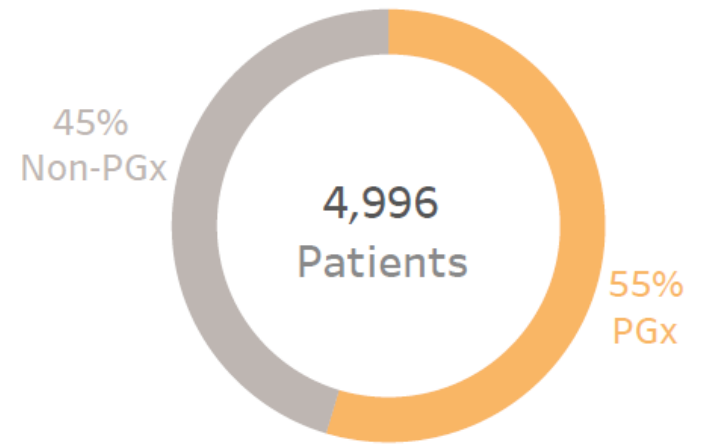
Department staff: 32 to 40

- 3 MD
- 5 PA-C
- 1 FNP
- 2 PharmD
- 4 Wellness Coaches (RD)
- 4 RN
- 13 MA (1 PRN)
- 8 support staff, phlebotomists

Pharmacogenetics Panels

Most Common PGx

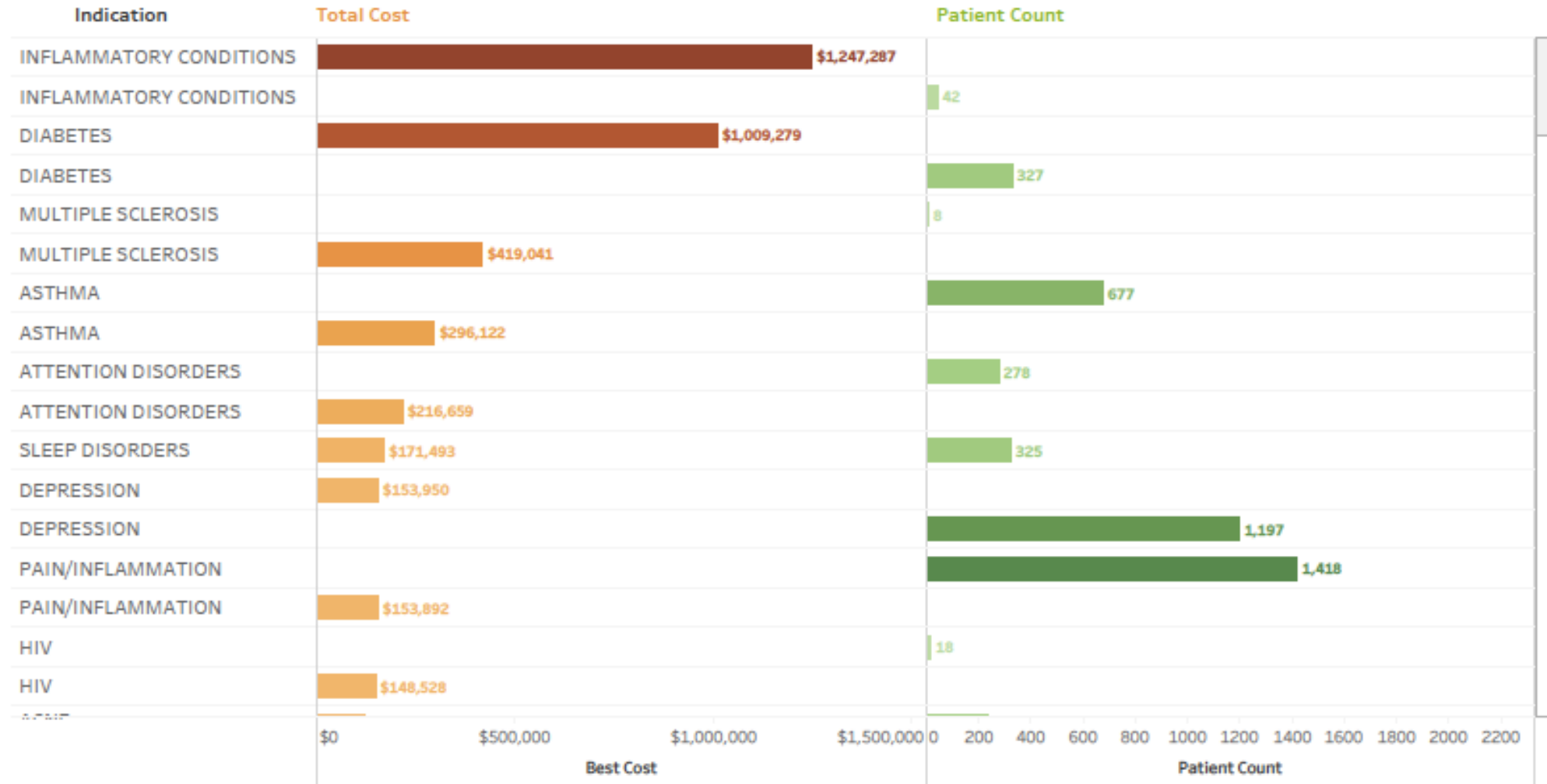
Overall Patients on PGx



% of Patients

% of Patients

Claim Analysis



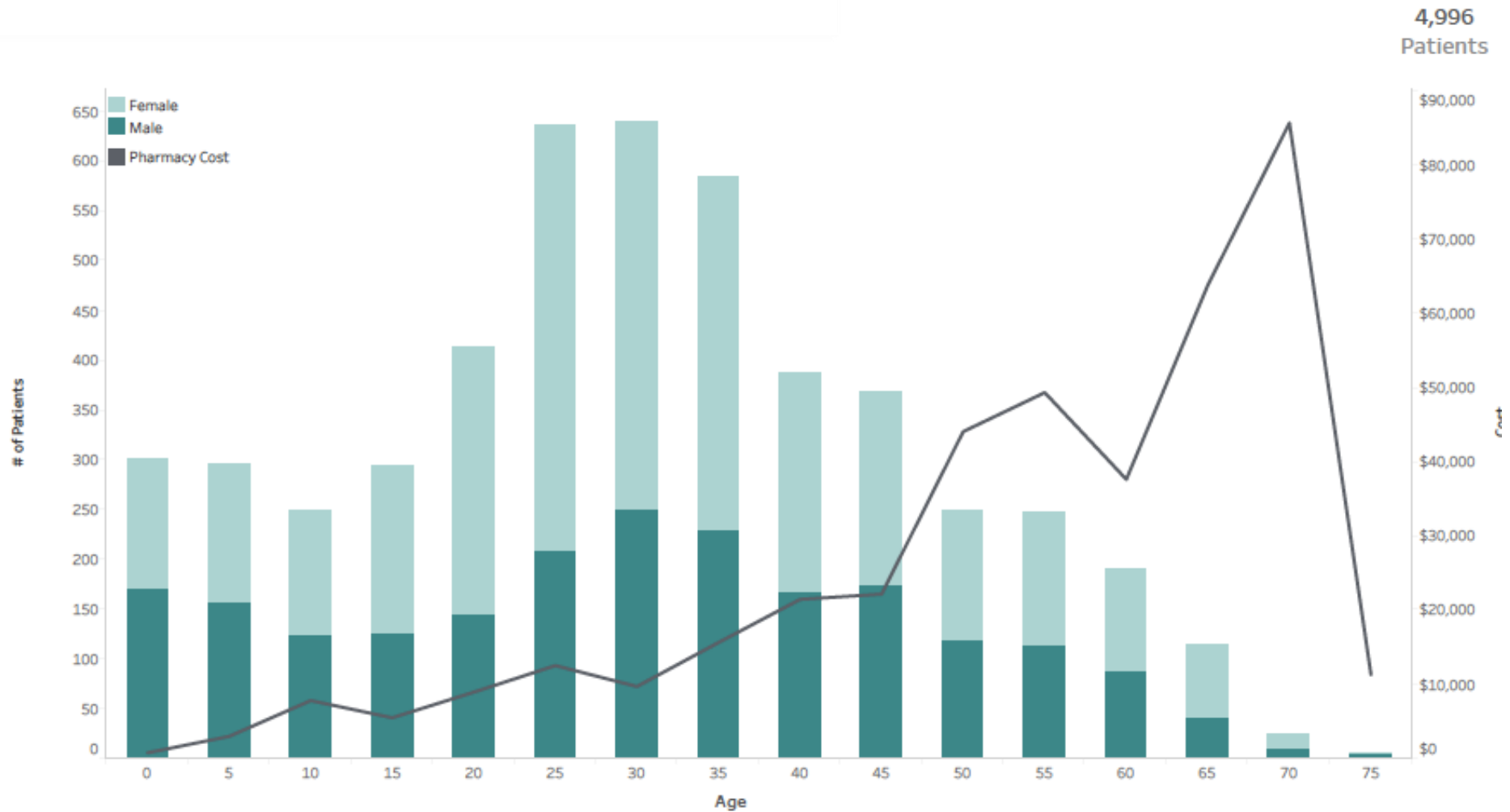
Hover over bars for specific drug information.

ARUP Employee Health Clinic Project

- Based on pharmacy claims data for ~5000 patients, 83% of actionable drug-gene interactions relate to the CYPs.
- Implementing the CYP panel because drug-gene interactions are of the HIGHEST levels of evidence.
- Inviting ~400 patients to obtain PGx testing with enrolment anticipated to begin in May 2019.

Drug	% of Patients	Primary gene
Hydrocodone	9.15%	CYP2D6
Omeprazole	8.31%	CYP2C19
Ondansetron	7.55%	CYP2D6
Bupropion	6.49%	ANKK1
Sertraline	6.02%	CYP2C19
Oxycodone	6.00%	CYP2D6
Citalopram	5.06%	CYP2C19
Metformin	4.92%	ATM
Fluoxetine	4.86%	CYP2D6
Trazodone	4.14%	CYP3A4
Atorvastatin	3.98%	CYP3A4
Codeine	3.72%	CYP2D6
Escitalopram	3.30%	CYP2C19
Amphetamine	3.08%	COMT
Tramadol	2.96%	CYP2D6
Diclofenac	2.74%	CYP2C9
Clonazepam	2.16%	CYP3A4
Alprazolam	2.16%	CYP3A4
Duloxetine	2.14%	CYP2D6
Simvastatin	1.94%	SLCO1B1
Meloxicam	1.80%	CYP2C9
Quetiapine	1.70%	CYP3A4
Methylphenidate	1.60%	MTHFR
Buspirone	1.46%	CYP3A4
Tamsulosin	1.30%	CYP2D6
Amitriptyline	1.30%	CYP2D6
Venlafaxine	1.28%	CYP2D6
Propranolol	1.28%	CYP2D6
Ketoconazole	1.28%	CYP3A4
Diazepam	1.12%	CYP2C19
Metoprolol	1.04%	CYP2D6
Donepezil	0.92%	CYP2C19

Claim analysis



Claim analysis

Current MA3 Cost

28,309,168

Components of MA3 Cost

Clinic outpatient visits	0.64%
Specialty office visits	0.82%
Employee work days missed	0.95%
Laboratory services	0.09%
Urgent care visits	0.48%
Emergency room visits	2.99%
Hospital admissions	67.18%
Home health visits	25.31%
Durable medical goods	1.55%

Medication Adherence

- Limited patient engagement in treatment decisions
- Cost
- Low perceived need/efficacy
- Concern about side effects
- Forgetfulness
- Lack of social support
- Impaired cognition
- Unclear or misunderstood medication instructions
- Low health literacy
- Complex drug regimen/high pill burden

Medication Appropriateness

- Is there an indication for the drug?
- Is the medication effective for the condition?
- Is the dosage correct?
- Are the directions correct?
- Are the directions practical?
- Are there clinically significant drug-drug interactions?
- Are there clinically significant drug-disease interactions?
- Is there unnecessary duplication with other drugs?
- Is the duration of therapy acceptable?
- Is this drug the least expensive alternative compared with others of equal utility?

Medication Adversity

- Dose-related
- Non-dose-related
- Dose-related and time-related
- Time-related
- Withdrawal
- Failure of therapy

MA3

- Medication Adherence
- Medication Appropriateness
- Medication Adversity

PGx
Empowered
MTM

- ↓ Adverse drug events
- ↑ Patient satisfaction
- ↑ Overall patient health
- ↑ Quality-of-life
- ↑ Use of generic medications
- ↓ Cost of medications
- ↓ Number of outpatient visits
- ↓ Costs of outpatient visits
- ↓ Number of laboratory tests
- ↓ Emergency department visits
- ↓ Number of hospitalizations
- ↓ Costs of Hospitalization

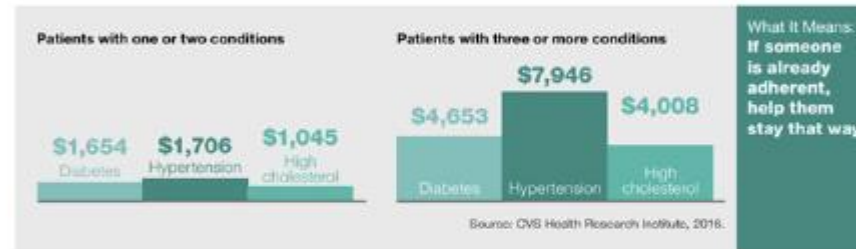
Claim analysis

Likely Indication	Patient Count	Cost of NonAdh	EPGx Savings
ANTICOAGULANT	38	\$178,975	\$46,534
ANXIETY	370	\$4,067,586	\$1,057,572
ASTHMA	677	\$3,594,450	\$934,557
CANCER	67	\$2,394,127	\$622,473
CHEMICAL DEPENDENCE	19	\$259,160	\$67,382
COPD	19	\$32,880	\$8,549
DEPRESSION	1,197	\$8,824,398	\$2,294,343
DIABETES	327	\$1,050,720	\$273,187
GI DISORDERS	144	\$1,368,685	\$355,858
HEART DISEASE	10	\$47,099	\$12,246
HIGH BLOOD CHOLESTEROL	367	\$750,177	\$195,046
HIGH BLOOD PRESS/HEART ...	807	\$1,478,505	\$384,411
HIV	18	\$215,363	\$55,994
OSTEOPOROSIS	16	\$110,960	\$28,850
PARKINSONS DISEASE	18	\$206,457	\$53,679
SEIZURES	266	\$3,729,627	\$969,703
Grand Total	2,525	\$28,309,168	\$7,360,384

Patients Who Became Adherent Had Lower Overall Annual Costs



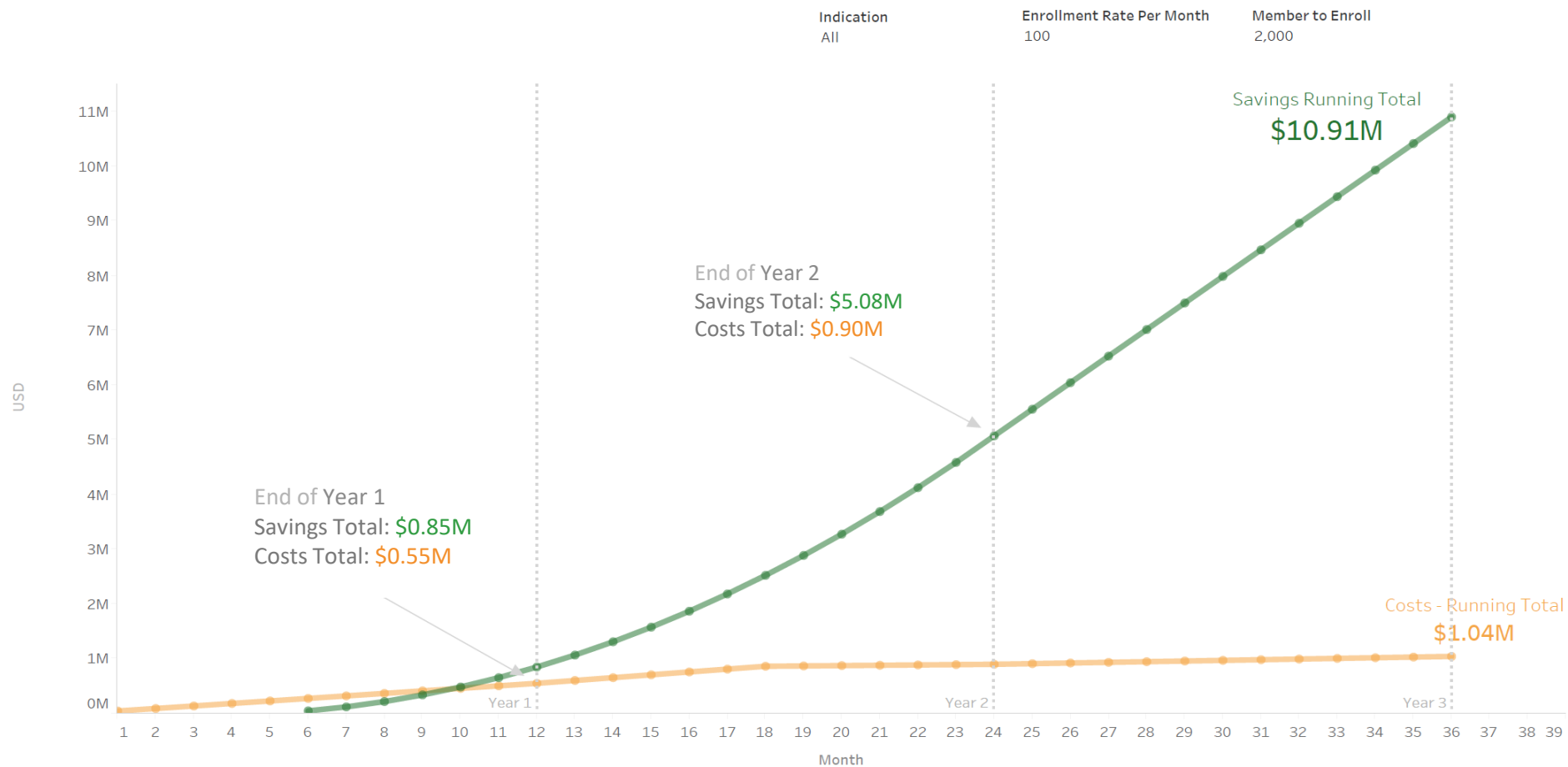
Patients Who Became Non-adherent Had Much Higher Annual Costs



Total annual savings opportunity identified using data compiled from more than 200 peer reviewed publications, greater than 200,000 clinical pharmacogenomic reports run by Coriell, and outcomes information from 5+ years of commercial implementation.



References: https://docs.google.com/document/d/11vxcOHGRQrs9Pyivb_gAN99Vu0xpjdm1QndLxi5v6sq/edit?usp=sharing



WHY WAS I CHOSEN FOR THE PHARMACOGENETICS PILOT PROGRAM?

You were chosen for this medical test due to either the number of medications you are prescribed or because of the type of medication(s) prescribed to you. This test can help you and your doctor find the right medication at the right dose.

MOST DRUGS ARE DEVELOPED AS "ONE SIZE FITS ALL."

Pharmacogenetic testing is a chance for patients to truly experience personalized precision medicine. Patients can learn which medications and doses work best for their bodies, cutting out the guess work and saving time and money.

Contact the clinic for questions or to make an appointment.



ARUP FAMILY HEALTH CLINIC
565 Komas Drive
Salt Lake City, UT 84108
Phone: (800) 584-5144
Fax: (801) 584-5206
Monday–Friday, 6 a.m.–5 p.m.
Saturday, 8 a.m.–4 p.m.
Closed Sundays and Holidays

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and its Department of Pathology*

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BD-CS-00, Rev 0, May 2019



PHARMACOGENETIC TESTING PILOT PROGRAM

HOW DO I GET THIS TEST AND WHAT CAN I EXPECT FROM IT?

THE PHARMACOGENETICS PILOT PROGRAM WORKS LIKE THIS:

1. Call the ARUP Family Health Clinic at (801) 584-5144 to make an appointment. Mention this program when you call.
2. Go to your enrollment appointment. Your blood will be drawn and you will make a follow-up appointment for your results. Bring all of your medications including over-the-counter and prescription medications, herbal supplements, eye drops, inhalers, etc. Include the names and contact information of the prescribers and/or specialists.
3. At your follow-up appointment, you will meet with a clinic pharmacist to review your results and make an action plan for changes to your medications, if needed.
4. If your preferred care provider is not at the ARUP Family Health Clinic, let clinic staff know and they will send the test results to your provider.



This testing is free of charge. The results will not be billed through your health insurance and will not be available to your employer.

THINGS TO REMEMBER:

YOUR GENETIC RIGHTS ARE PROTECTED BY LAW.

The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that protects individuals from genetic discrimination in health insurance and employment.

WILL THE RESULTS OF THIS TEST AFFECT MY FUTURE ACCESS TO HEALTH CARE?

No. The only purpose of this test is to help you and your health care team determine the correct medication(s) for you, now and in the future.

WILL MY RESULTS BE SHARED WITH MY EMPLOYER?

No. The results of this medical test are part of your protected health information (PHI). The privacy of your PHI is protected by the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

WILL I NEED A FOLLOW-UP TEST?

No. This is a genetic test and the results will not change. However, this is a limited test panel that only covers a certain number of genes. You may need a different test later if you are prescribed medications that are not associated with the genes in this test panel.

WILL THIS GENETIC TEST TELL ME IF I AM LIKELY TO GET CANCER?

No, this test can only detect variants in specific genes associated with drug metabolism. This test cannot detect variants associated with hereditary disorders or cancer.

CAN I GET THE REST OF MY FAMILY TESTED?

This pilot program is only available to a limited number of invited participants right now. However, we hope to make this test available to all employees and their dependents in the future.

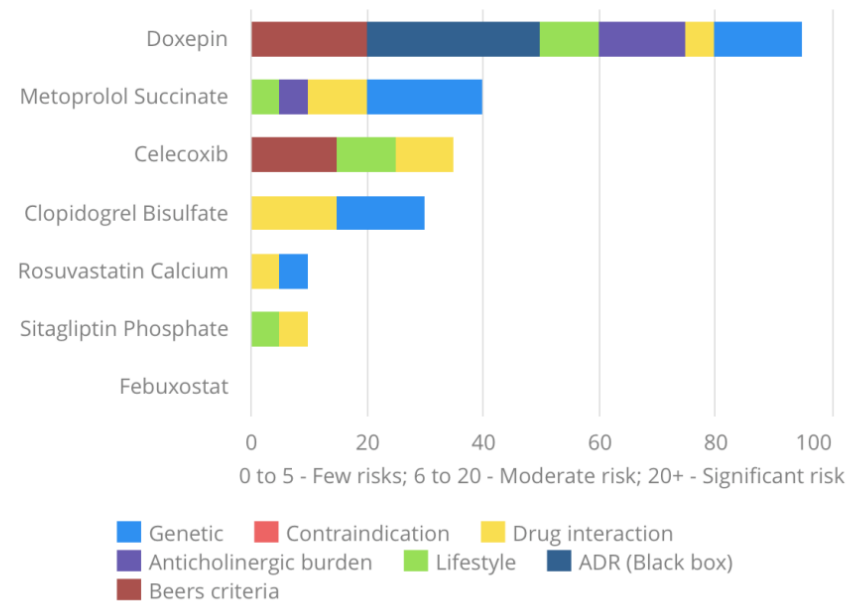
aruplab.com

Open Save Export PDF

MOST FREQUENT SIDE EFFECTS

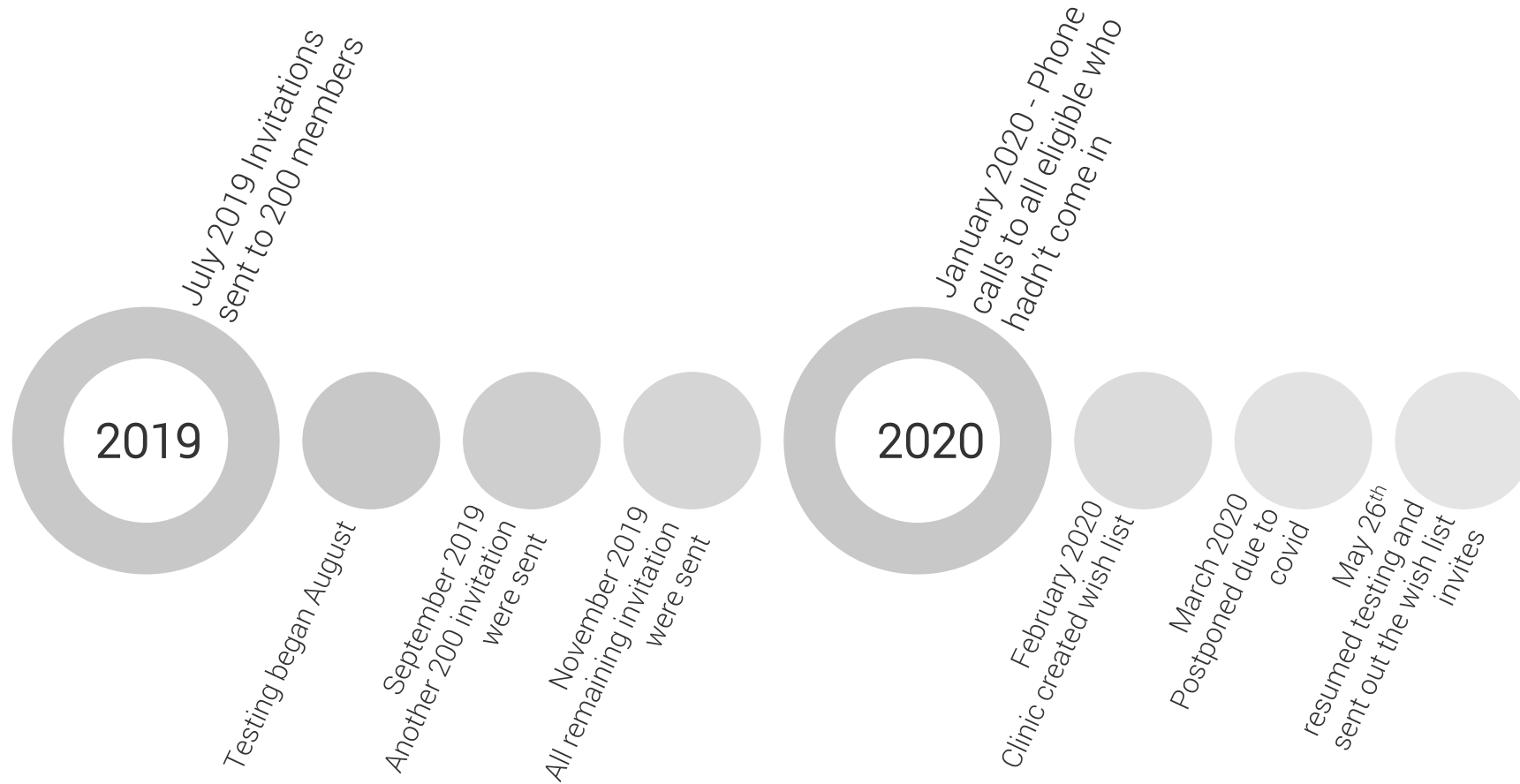
[View all side effects](#)

Side Effect	Drugs
gout	Febuxostat, Clopidogrel Bisulfate
headache	Rosuvastatin Ca, Celecoxib, Sitagliptin Phosphate, Clopidogrel Bisulfate
dizziness	Doxepin, Celecoxib, Rosuvastatin Calcium, Metoprolol Succinate
dyspepsia	Celecoxib, tatin Calcium, ogrel Bisulfate, iprolol Succinate
diarrhea	Celecoxib, Sitagliptin Phosphate, Clopidogrel Bisulfate



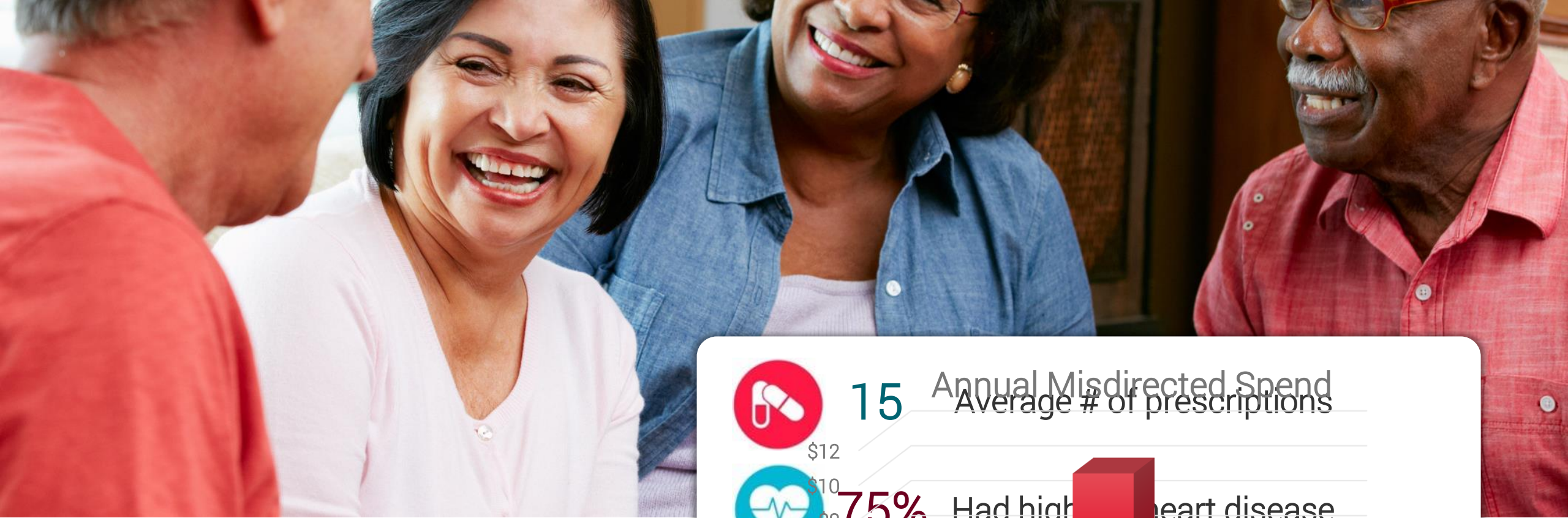
Alternative drug	Δ drug	Δ regimen	Detail	Risk chart	Est. cost/dose
<input type="checkbox"/> Maprotiline Hydrochloride Oral tablet	-60	-65	⊕		Generic: \$1.20
<input type="checkbox"/> Amitriptyline Hydrochloride Oral tablet	-35	-40	⊕		Generic: \$0.65
<input type="checkbox"/> Mirtazapine Oral disintegrating tablet	-30	-35	⊕		Brand: \$4.18 Generic: \$0.93
<input type="checkbox"/> Mirtazapine Oral tablet	-30	-35	⊕		Brand: \$5.06 Generic: \$0.46
<input type="checkbox"/> Protriptyline Hydrochloride Oral tablet	-20	-25	⊕		Brand: \$4.09 Generic: \$1.63

Pilot timeline



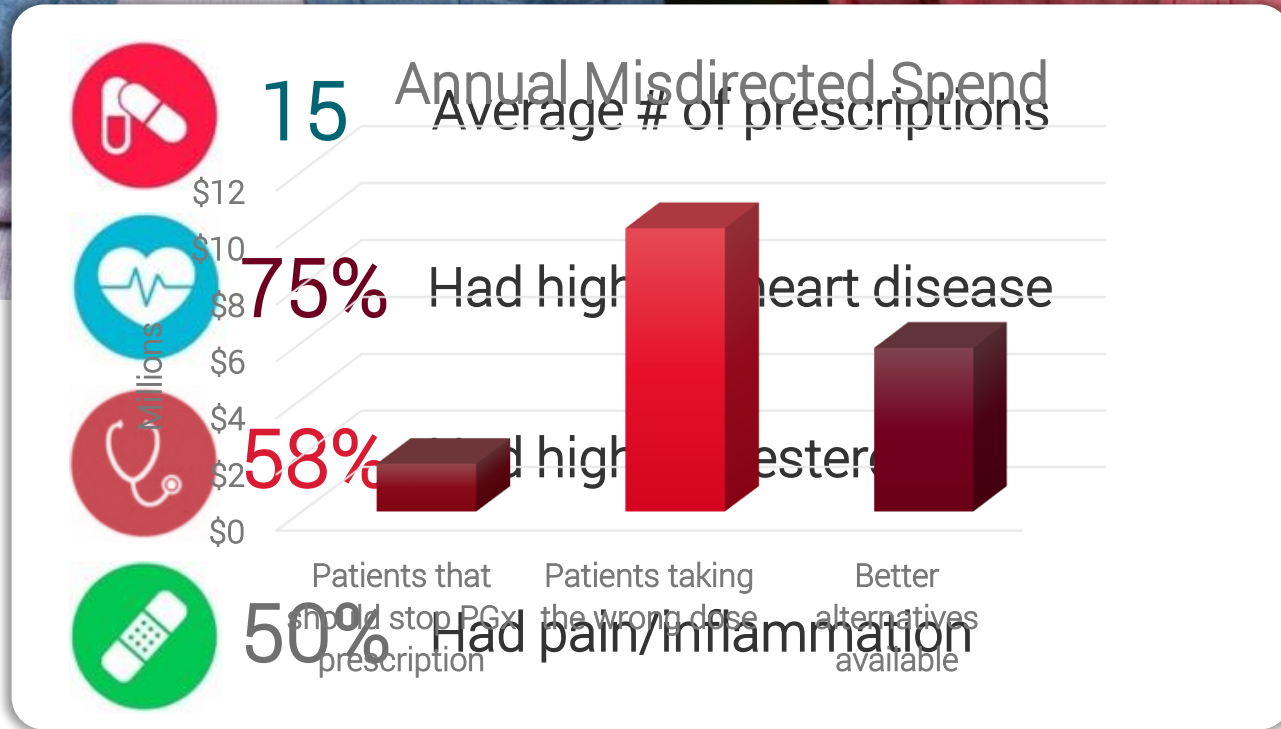
587 Initial eligible patients

7/14/20 - 372 so far, 63%

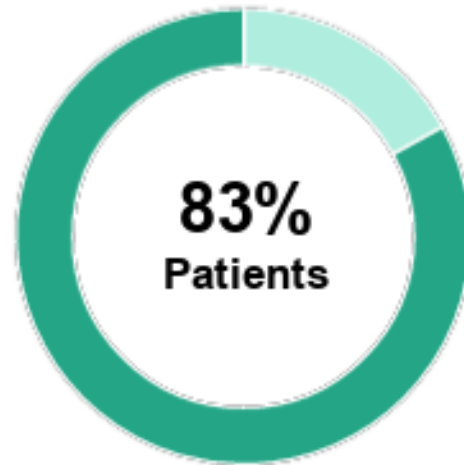


Kentucky Teachers Retirement Pension Fund Population Analytics

36,000 retirees aged 65 to 108



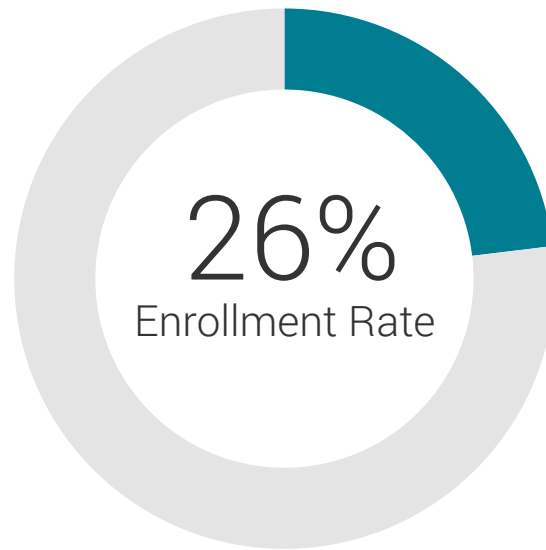
Population Analytics



% of Patients taking meds that have known PGx implications

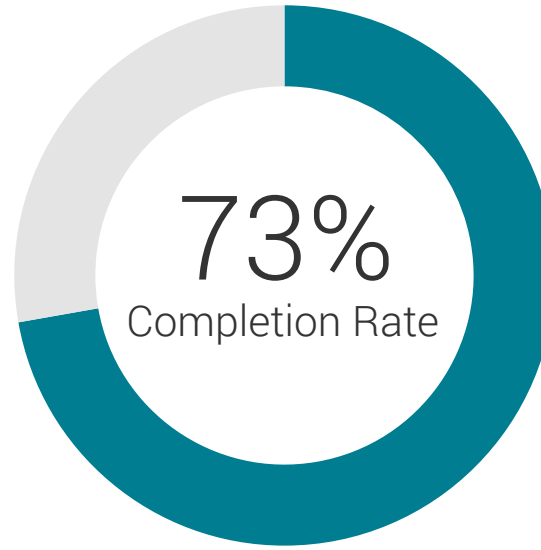
By the Numbers

36,315 Members Invited



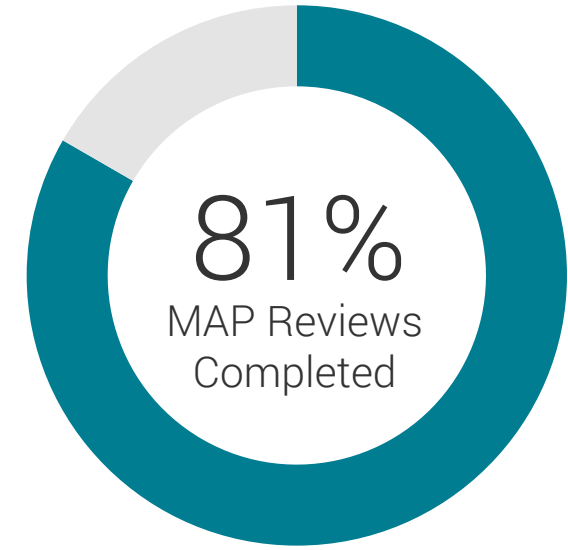
Enrollment

9,280 members



Testing

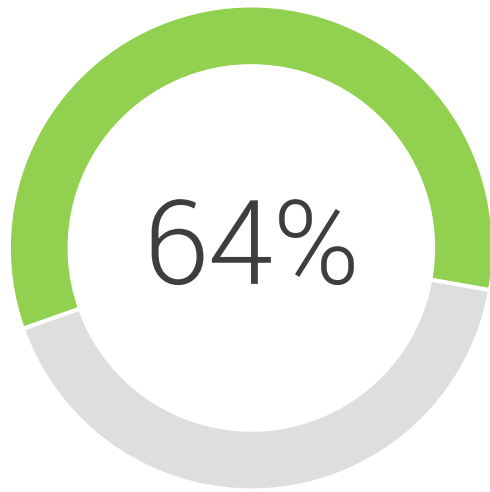
6,139 tested to date



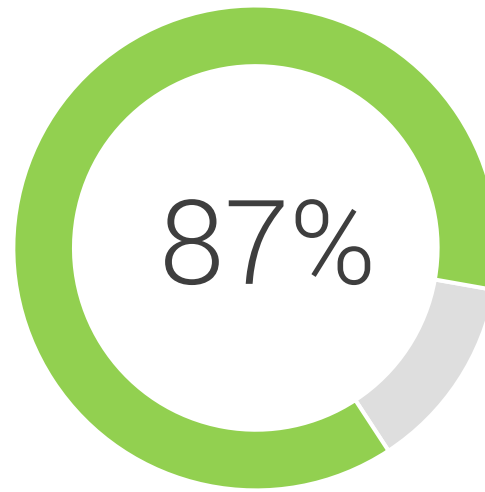
Review

5,313 MAP reviews

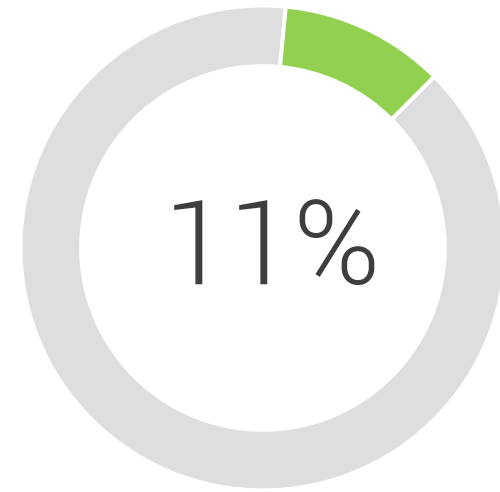
By the Numbers



**had medication
changes**



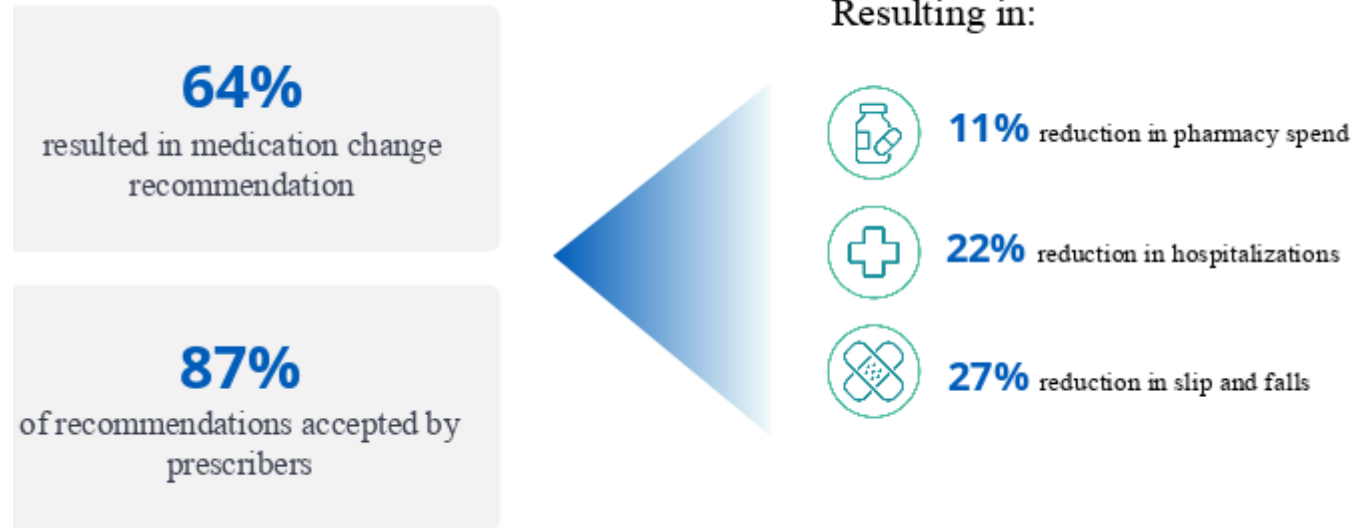
**of changes approved
by physicians**



**reduction in
prescription claims**

Source: Gary L. Harbin, CPA, Executive Secretary

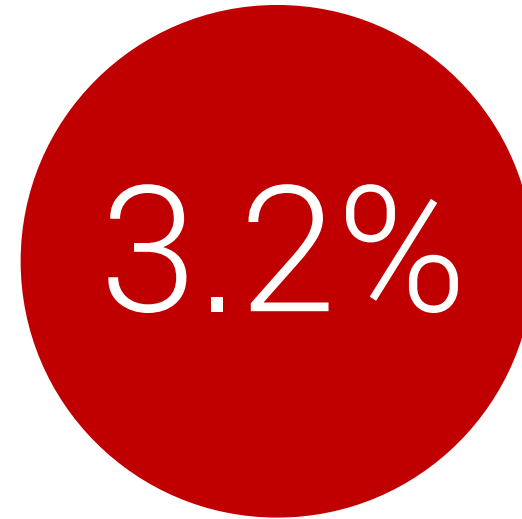
Cost Reduction



Cost Reduction



**Reduction in cost-to-plan
spending after 16 months**



Increase in control group

Learning Objectives

Describe the premise of pharmacogenetic testing and cite specific basic examples of drug-gene interactions

Explain strategies for laboratory and pharmacy to implement a pharmacogenetic panel testing to address quality and cost metrics within a health plan

Understand the potential challenges of implementing a pharmacogenetic screening program

Discuss the potential impact of pharmacogenetic testing to both patients and the health plan.
