

Right Drug Dose Now Act Reintroduced 3/29/24

Originally introduced by Swalwell and Emmer 2/28/22

1. National Action Plan for Adverse Drug Event Prevention – assessment and update
2. Education on Pharmacogenomics for Healthcare Professionals – as a key component of adverse event reduction
3. Improving EHR Systems to Utilize Pharmacogenomic Information – flag for appropriate testing and drug-gene interactions, gather RWE
4. GAO Study on FDA Drug-Gene Labels
5. FDA Adverse Event Reporting System Update – patient friendly submission option, automate reporting from EHRs

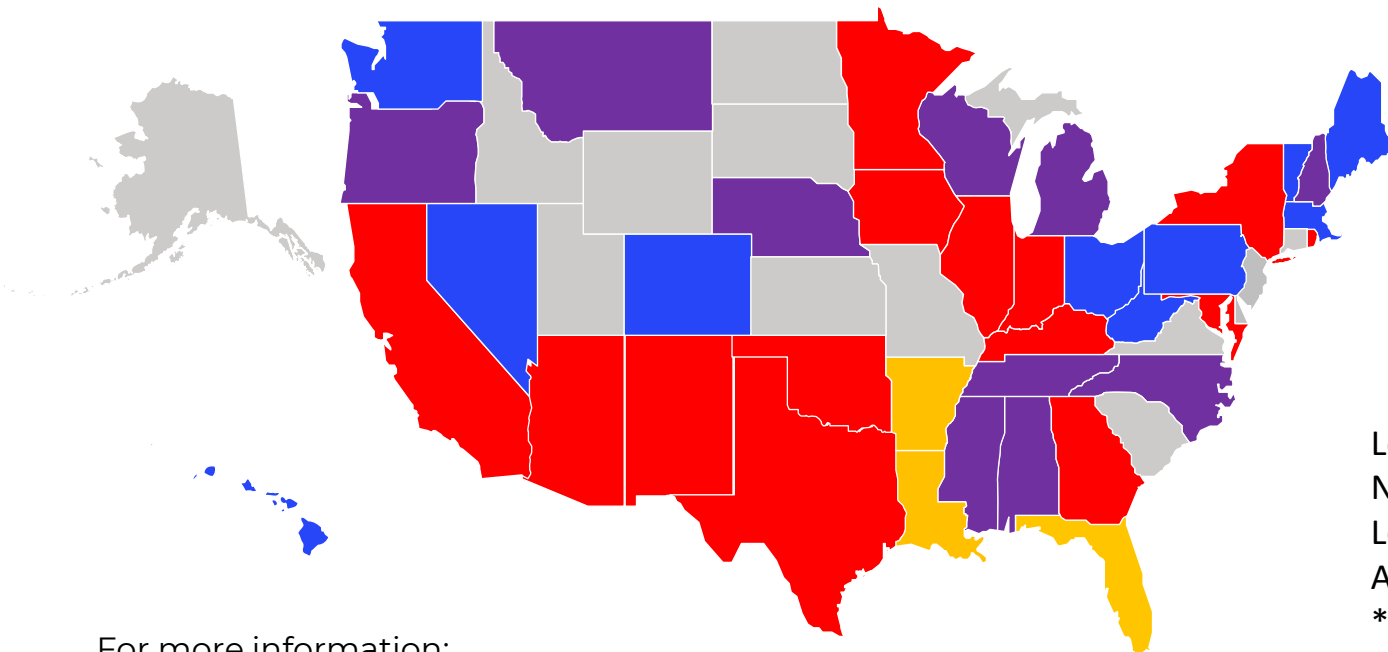
Note: Separate bill to be introduced later by Swalwell only will authorize funding

Right Drug Dose Now Act – How to help

- Sign organizational and/or individual support at <https://fourthcause.org/rightact>
- Email Kristine.Ashcraft@youscript.com if you want to volunteer to lead and/or support state efforts to:
 - Request meetings with House representatives to sign on in support of the legislation
 - Request meetings with Senators to introduce the Senate companion bill
 - Currently, the bill is in energy and commerce so targeting these members is especially important - <https://energycommerce.house.gov/representatives>
 - Talking points and sample slides will be provided

Biomarker Legislation and AB-425 (CA Medi-Cal PGx)

- Biomarker legislation mandates commercial and Medicaid insurance coverage for evidence-based genetic testing, including pharmacogenomics (PGx) testing.
- Even after enactment, budgeting and implementation need to be monitored
 - In California both AB-425 and biomarker legislation are not in the draft budget. Due to a significant budget shortage, a recommendation has been made to delay implementation of all new bills.
 - Be prepared to proactively or reactively inform payers of these policies if coverage is denied.



| | |
|--------|--|
| Blue | Legislation introduced |
| Red | Law enacted |
| Yellow | Narrow law enacted |
| Purple | Education/ground softening for future leg |

Legislation enacted: AZ, AR*, CA, GA, IL, IN, KY, LA*, MD, MN, NM, NY, OK, RI, TX

Legislation introduced: CO, HI, MA, ME, NV, OH, PA, VT, WA, WV

Awaiting signature: FL**, IA

* Private plans only **public plans only

For more information:
<https://www.fightcancer.org/what-we-do/access-biomarker-testing>

Biomarker Updates – 5/1

- **The Iowa bill was just [signed by Gov. Reynolds](#) earlier today!** Iowa is the 16th state with biomarker testing coverage [signed into law](#) (Florida's narrowed bill is still awaiting signature).
- Massachusetts [CHIA report](#) released and is overwhelmingly positive; now that this report is finalized, the bill can move forward. We anticipate bill will be passed out of committee in next few weeks.
- Colorado – House appropriations hearing is scheduled for tomorrow, Thursday 5/2.
- Maine - The legislature adjourned without voting to fund many of the previously approved bills from this year's session. As a result, the biomarker bill is not funded and cannot be sent to the governor for consideration. The legislature may come back for a special session in May where this and other unfinished business could be taken up.
- Connecticut – We are still pushing the House to take up the bill (which passed the full Senate in April).
- Vermont – We had a great briefing today with about 30 legislators and the lieutenant governor. Lots of interest in pursuing legislation next session.

Biomarker Legislation and AB425 – How to help

- **AB425**

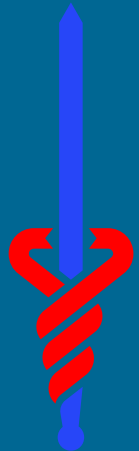
- California residents can sign a letter to Newsom at
 - <https://chnng.it/d5jY4f5KBk> - submitting 5/9
- Organizations willing to support, please email the following information to Kristine.Ashcraft@youscript.com:
 - organization name and city, state
 - submitter's name and title and signature image

- **Biomarker Legislation**

- ACS CAN has active legislation in CO, MA, NJ, OH, and PA and continuing legislative efforts in HI, ME, NV, VT, and WA. Many states have ongoing education campaigns and will transition to legislative efforts in the coming year. Please contact hilary.gee@cancer.org or cori.chandler@cancer.org if you would like to assist in state efforts.
- If you have any specific examples of qualifying tests not being covered by state-regulated plans or Medicaid in any states that have already implemented a coverage law (AZ, AR, GA, IL, KY, LA, MD (commercial effective, Medicaid 7/1/2025), NM, OK, RI and TX), please send them to hilary.gee@cancer.org by May 10th.



Laying the groundwork



Efforts to educate on the issue and build momentum towards bill introduction makes for a more successful campaign:

- Build strong, diverse coalition, including non-oncology stakeholders
- Collect patient stories
- Educate lawmakers/volunteers

Continuing these strategies after bill introduction:

- Keep coalition engaged, informed and involved in work
- Utilize patient stories
- Meeting with lawmakers to secure support
- Coalition advocacy events with volunteers
- Engage media

Learn more: fightcancer.org/biomarkers

**Right drug, right dose,
right now**

Any Avoidable Adverse Drug Event is One Too Many



Michael Adams-Conroy

**Over 20 years
ago...**

Michael died from
an avoidable
drug-drug-gene
interaction

PGx enables selection of right drug and dose

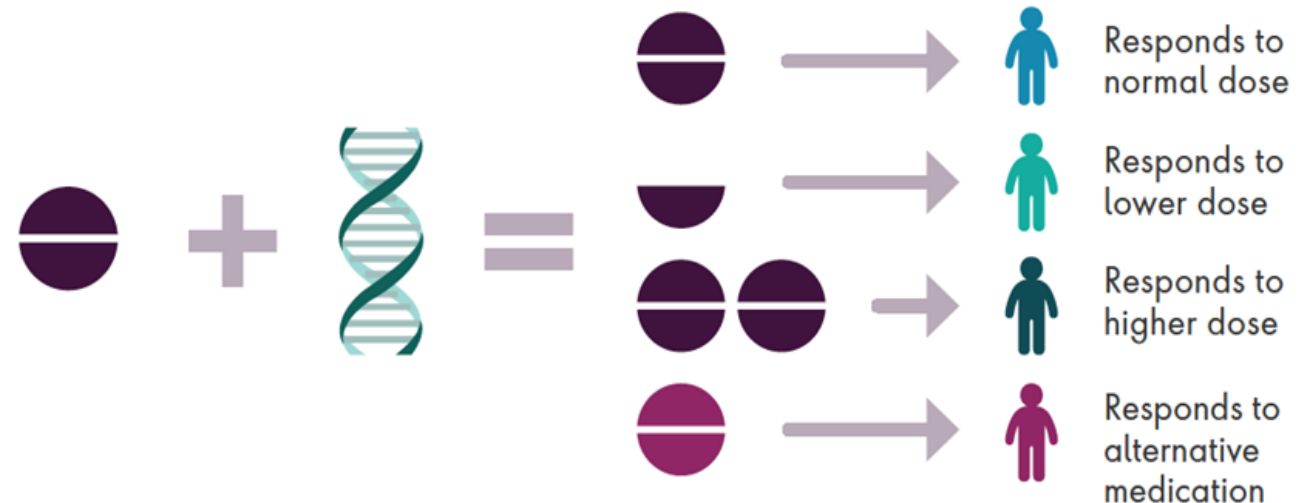
What is pharmacogenomic testing?

Pharmacogenomic testing (PGx) helps doctors determine which drugs and doses are right—and which ones to avoid—based on each patient's genetic information. It is precision medicine for medications.

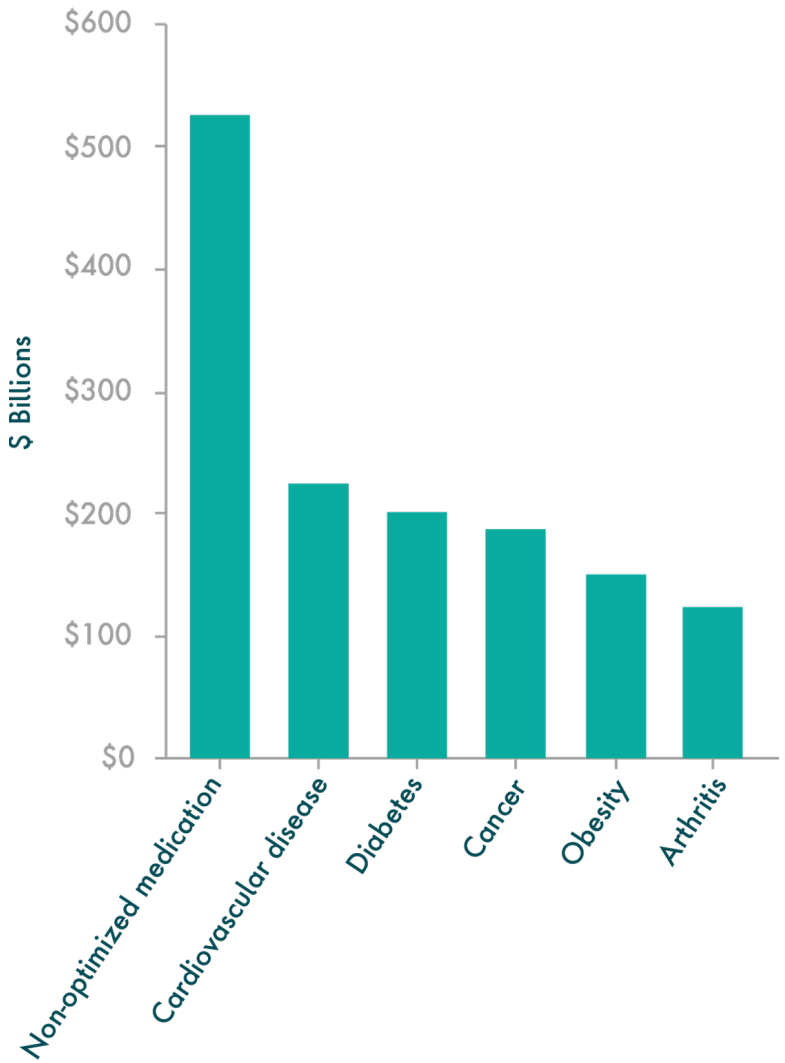
Blockbuster one-size-fits-all approach to drug development and prescribing



Personalized prescribing enables selection of the right drug and dose



Non-optimized medications harm patients & increase costs









- 99% of patients** have genetic variants that impact medication response¹
- Every 2 minutes** a life is lost due to non-optimized medications²
- Exceeds disease cost** and annual cost of medications²
- 40M patients** are on 5+ medications; number anticipated to double by 2040³

1. Chanfreau-Coffinier C, et al. Projected Prevalence of Actionable Pharmacogenetic Variants and Level A Drugs Prescribed Among US Veterans Health Administration Pharmacy Users. *JAMA Netw Open*. 2019;2(6):e195345.
2. Watanabe JH, et al. Cost of Prescription Drug-Related Morbidity and Mortality. *Ann Pharmacother*. 2018;52(9):829-837.
3. Bureau USC. 2017 National Population Projections Tables: Main Series. <https://www.census.gov/data/tables/2017/demo/popproj/2017-summary-tables.html>

Genetic differences contribute to treatment failure

Percentage of population for which drug classes are ineffective, on average

| | | |
|-------------------------|-----|---|
| Cancer drugs | 75% |  |
| Alzheimer's drugs | 70% |  |
| Arthritis drugs | 50% |  |
| Diabetes drugs | 43% |  |
| Asthma drugs | 40% |  |
| Antidepressants (SSRIs) | 38% |  |

The case for personalized medicine. Accessed May 6, 2022. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/the_case_for_pm1.pdf

FDA: Drug-gene and drug-drug interactions equivalent

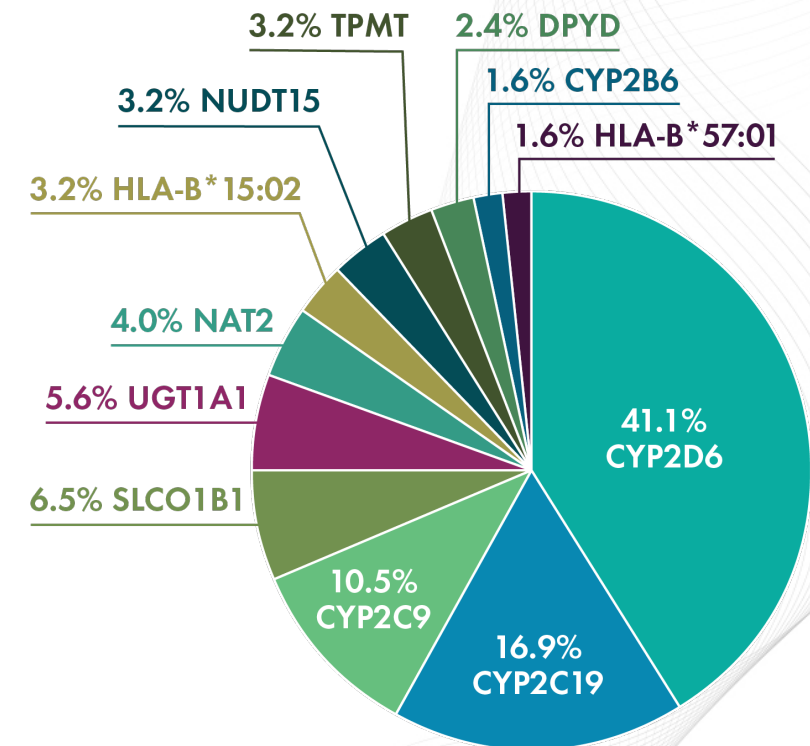
“Drug-gene interactions should be considered to be similar in scope to drug-drug interactions.”

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM337169.pdf>

Selected drugs impacted by pharmacogenomics according to the FDA and Clinical Pharmacogenetics Implementation Consortium (CPIC)^{1,2}

| Behavioral health | Cardiology | Hematology/oncology | Gastroenterology |
|--|---|--|---|
| amitriptyline aripiprazole atomoxetine brexpiprazole citalopram clomipramine desipramine doxepin escitalopram fluvoxamine imipramine nortriptyline paroxetine protriptyline risperidone sertraline trimipramine venlafaxine viloxazine vortioxetine | atorvastatin carvedilol clopidogrel rosuvastatin simvastatin warfarin | belinostat capecitabine eliglustat fluorouracil irinotecan mercaptopurine tamoxifen thioguanine | dexlansoprazole esomeprazole lansoprazole omeprazole ondansetron pantoprazole rabeprazole |
| Transplant | Pain management | Infectious disease | Neurology |
| azathioprine tacrolimus | celecoxib codeine flurbiprofen ibuprofen meloxicam methadone oxycodone piroxicam tramadol | abacavir atazanavir efavirenz nevirapine voriconazole | phenytoin siponimod pimozide |
| Rheumatology | Ear, eye, nose, throat | And many more... | |
| azathioprine | dextromethorphan | | |

Same set of genes affect most medications

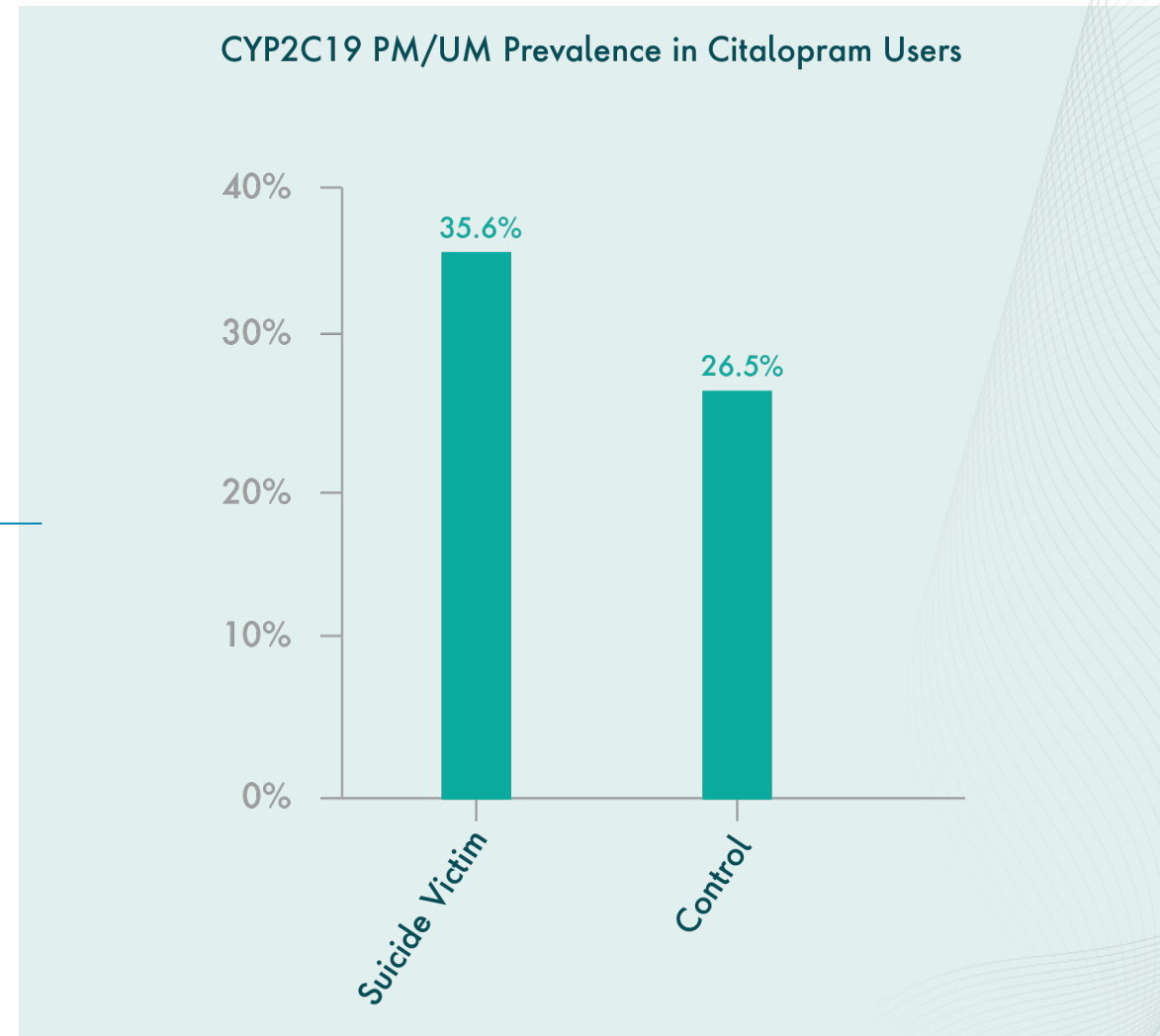


1. Genes-drugs. CPIC. June 15, 2021. Accessed April 29, 2022. <https://cpicpgx.org/genes-drugs/>

2. Center for Devices and Radiological Health. Table of pharmacogenetic associations. U.S. Food and Drug Administration. Accessed May 6, 2022. <https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations>

Pharmacogenomic impact in (es)citalopram suicides

CYP2C19 PM and UM phenotypes were found 34.3% more often in suicide victims, a 9.1% increase ($p=0.0065$)



Pain Management: PGx Variations Almost 3X Higher in Opioid Dependency Treatment

| Patient Population | Gene-Drug Interaction Rate (Causing Poor or UltraRapid Metabolism of Opioids) |
|-------------------------------|---|
| Typical U.S.* | 7.97% |
| Opioid Dependency Treatment** | 20.3% |

~12% of patients in opioid dependency programs might have a preventable addiction, if they had PGx testing before being prescribed an opioid!

*<https://www.nature.com/articles/s41398-020-01129-1#Sec20> (Specifically, https://static-content.springer.com/esm/art%3A10.1038%2Fs41398-020-01129-1/MediaObjects/41398_2020_1129_MOESM5_ESM.jpg)

** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5940523/>

Outpatient impact of PGx in four months



p=0.0002

ED¹



p=0.027

Hospitalizations¹

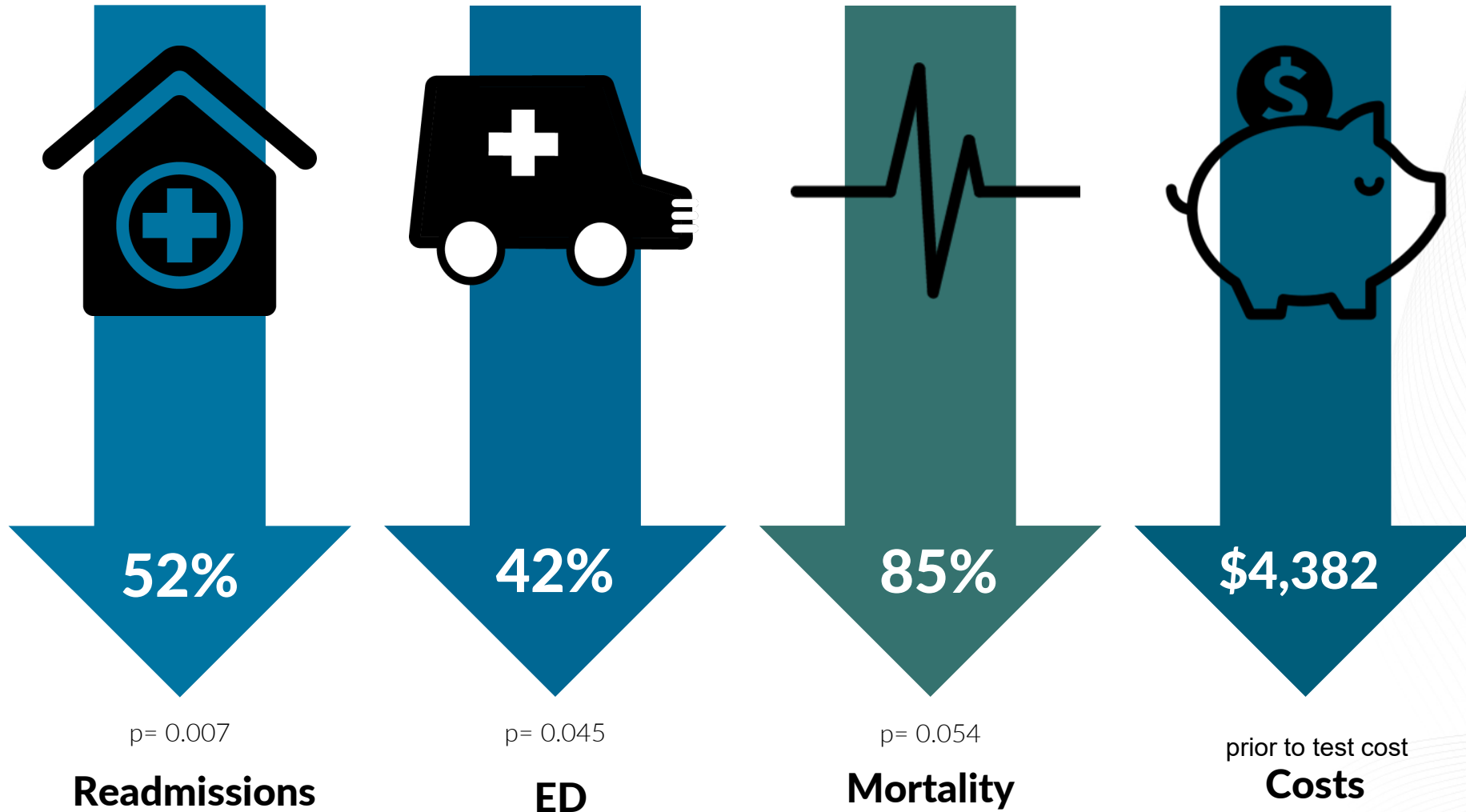


prior to test cost

Costs¹

1. Brixner D, et al. The effect of pharmacogenetic profiling with a clinical decision support tool on healthcare resource utilization and estimated costs in the elderly exposed to polypharmacy. *Journal of Medical Economics*. 2015;19(3):213-228.

Post-Hospitalization Impact of PGx in 60-days



In a recent study, PGx panel testing resulted in a 30% reduction in clinically significant adverse drug reactions in 12 weeks

- ~7000 patients in 18 hospitals, nine community health centres, and 28 community pharmacies in seven European countries
- Care settings included psychiatry, oncology, nephrology, primary care, general medicine, and cardiology
- Study also confirmed implementation is feasible in a variety of settings

A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study

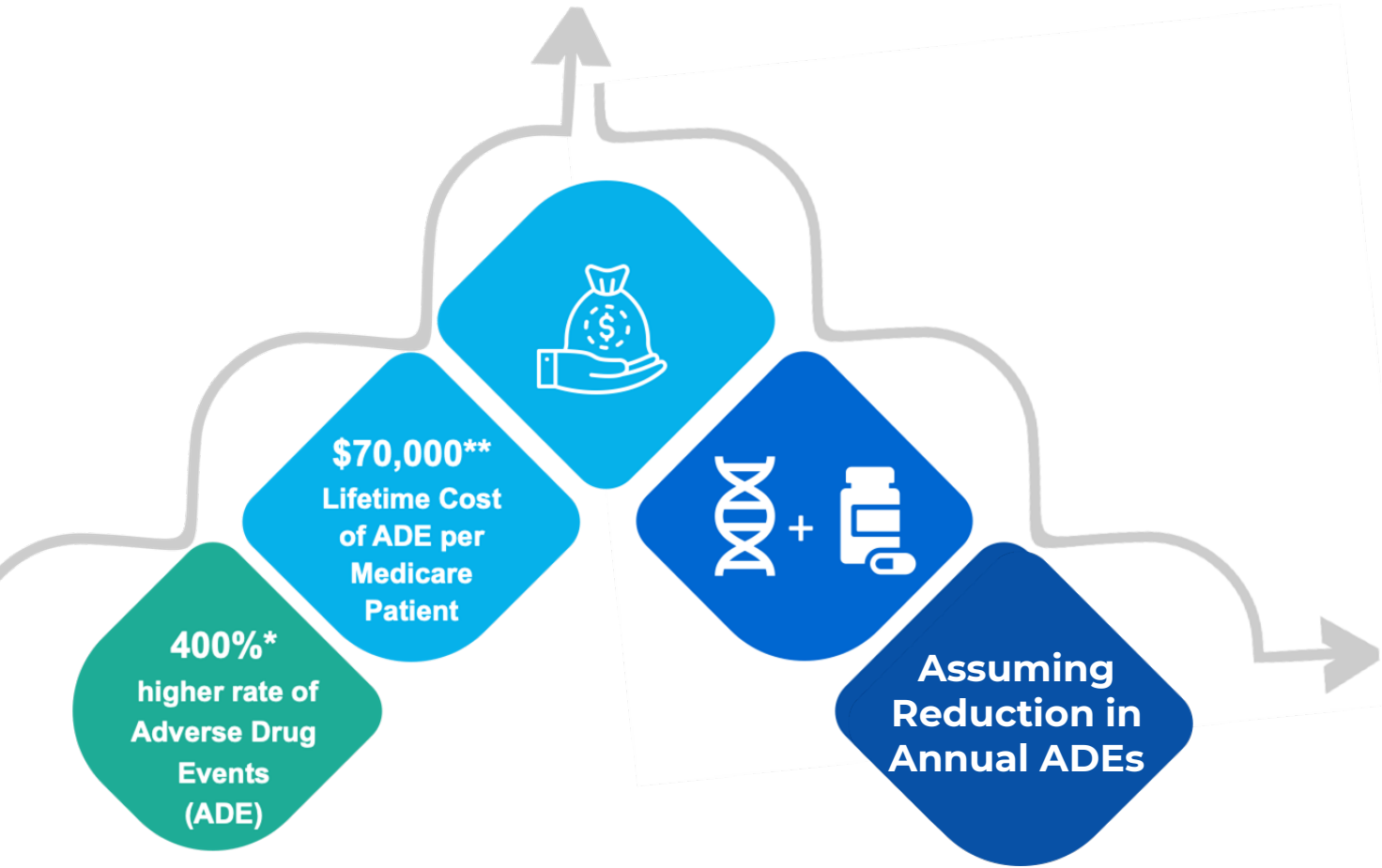
Jesse J Swen, Cathelijne H van der Wouden, Lianne EN Manson*, Heshu Abdullah-Koolmees, Kathrin Blagec, Tanja Blagus, Stefan Böhringer, Anne Cambon-Thomsen, Erika Cecchin, Ka-Chun Cheung, Vera HM Deneer, Mathilde Dupui, Magnus Ingelman-Sundberg, Siv Jonsson, Candace Joefield-Roka, Katja S Just, Mats O Karlsson, Lidija Konta, Rudolf Koopmann, Marjolein Kriek, Thorsten Lehr, Christina Mitropoulou, Emmanuelle Rial-Sebbag, Victoria Rollinson, Rossana Roncato, Matthias Samwald, Elke Schaeffeler, Maria Skokou, Matthias Schwab, Daniela Steinberger, Julia C Stingl, Roman Tremmel, Richard M Turner, Mandy H van Rhenen, Cristina L Dávila Fajardo, Vita Dolžan, George P Patrinos, Munir Pirmohamed, Gere Sunder-Plassmann, Giuseppe Toffoli, Henk-Jan Guchelaar, on behalf of the Ubiquitous Pharmacogenomics Consortium†*

Importantly, similar reductions in adverse events were seen in cancer care: For patients receiving fluorouracil, capecitabine, tegafur, or irinotecan, only grade 4 (life-threatening consequences; urgent intervention indicated) and 5 (death related to AE) were considered clinically relevant.

Swen, Jesse J., et al. *The Lancet* 401.10374 (2023): 347-356.

Medicare Potential Savings from PGx & Clinical Decision Support (CDS)

Medicare has covered testing since 2020, but without CDS the impact is lost over time



| Assumed % Reduction of ADEs | Estimated Annual Medicare Cost Savings |
|-----------------------------|--|
| 5% Reduction | \$9.7 Billion |
| 10% Reduction | \$23.3 Billion |
| 20% Reduction | \$50.5 Billion |

*<https://www.aafp.org/afp/2013/0301/p331.html>

**Internal calculation based on publicly available data: *Annals of Pharmacotherapy* 2018, Vol. 52(9) 829-837, U.S. Census

Key Strategies for Genomic Implementation Success



- Prioritizing EHR integration
- Improving clinicians' knowledge
- Engaging patients to participate



<https://pubmed.ncbi.nlm.nih.gov/28532511/>

Barriers to Adoption of PGx to Reduce ADEs

- Many healthcare providers lack education in pharmacogenomics (PGx)
- The public is not well informed about ADEs (adverse drug events) or PGx
- PGx-related adverse drug events are not currently tracked
- EHRs do not readily exchange, store, or alert on drug-gene and drug-drug-gene interactions



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**Michael Adams-
Conroy**

20 years later...
**We can do
better, together.**





Kristine Ashcraft
President and Founder

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Keep in touch!