AmerisourceBergen

# Kristine Ashcraft, BS, MBA

Kristine Ashcraft, BS, MBA is a molecular biologist by training and is the former CEO and founder of YouScript, recently acquired by Invitae. She has worked in pharmacogenomics since 2000 and was recently named one of the 25 leading voices in precision medicine. Kristine has authored multiple publications on the clinical and economic benefits of pharmacogenomic testing including one lauded as one of the most influential publications at an American Medical Informatics Association meeting. She serves on the Steering Committee of  STRIPE, the FDA collaborative community for pharmacogenomics. She has been interviewed by numerous media outlets including the New York Times, the Wall Street Journal, and NBC Nightly News and has spoken at SXSW, American Society of Human Genetics, and numerous precision medicine conferences. She is committed to being a catalyst in the adoption of precision medicine.

INVITAE

# Addressing Health Equity by Improving Access to Testing

09 | 17 | 22

# Disclosures

- Ownership interest / shareholder: Invitae Corporation
- Salary: Invitae Corporation
- Presentation Compensation: International Oncology Network (“ION”)
- Neither ION nor any pharmaceutical company has influenced the content of this presentation nor has ION independently verified the presentation for accuracy.

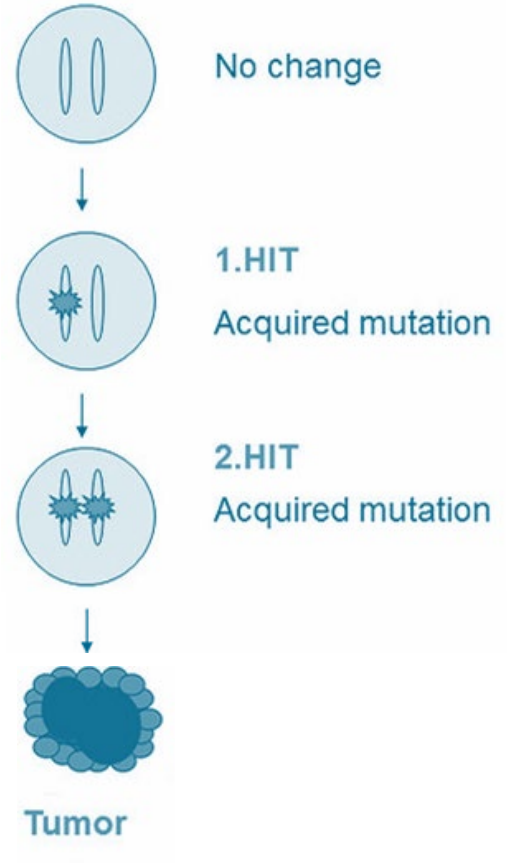
INVITAE

# All Cancers Are Due to Genetic Variants

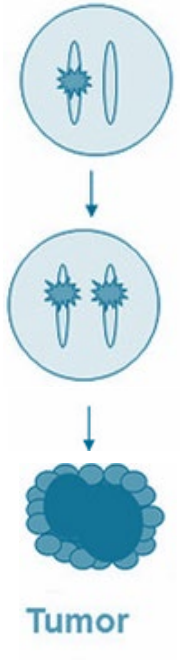
**Somatic variant**: a change in DNA that occurs after conception and is not present in the egg or sperm. Thus, it cannot be passed down to offspring.

Somatic variants acquired in key genes over time lead to cells becoming malignant

SPORADIC CANCER




HEREDITARY CANCER




**Germline variant**: a change in DNA that is present in the egg and sperm and in every cell of the body. It can be passed down to offspring.

The presence of a germline variant means that fewer somatic variants are required for cancer to develop.

- Increased lifetime risk
- Earlier onset of disease
- Risk to family members

# Germline Genetic Testing Still Underutilized

## More Testing needed in Asian, Black and Hispanic Patients to Address VUS

- Only 25.2% of breast cancer patients and 34.3% of ovarian cancer patients had genetic testing
- Underutilization of genetic testing in ovarian cancer did not improve substantially during the 7-year interval analyzed.
- In 2017, for patients with breast cancer, VUS-only rates were substantially higher in Asian (42.4%), Black (36.6%), and Hispanic (27.7%) patients than in non-Hispanic White patients (24.5%, $P < .001$).
- Similar trends were noted for patients with ovarian cancer. VUS-only rates were substantially higher in Asian (47.8%), Black (46.0%), and Hispanic (36.8%) patients than in non-Hispanic White patients (24.6%, $P < .001$).

https://ascopubs.org/doi/abs/10.1200/JCO.20.02785

# Key Statistics Reflecting Disparities in Cancer Care

| Cancer Type (Incidence Rates) | African Americans | Whites | Rate Ratio |
|---|---|---|---|
| Multiple myeloma | 14.3 | 6.4 | **2.23** |
| Prostate, males | 172.8 | 102.0 | **1.69** |
| Stomach | 9.6 | 5.7 | **1.68** |
| Liver/Cholangio ca | 11.9 | 7.4 | **1.61** |
| Colorectal | 45.5 | 36.5 | **1.25** |
| Pancreas | 15.7 | 12.7 | **1.24** |
| Kidney/renal pelvis | 19.2 | 15.7 | **1.22** |
| Cervix uteri, females | 7.4 | 6.3 | **1.17** |
| Lung and bronchus | 57.4 | 51.0 | **1.13** |
| Breast, females | 128.2 | 132.7 | **0.97** |

| DEATH RATES with cancer types | African Americans | White | Rate Ratio |
|---|---|---|---|
| Prostate, males | 38.4 | 18.2 | **2.11** |
| Stomach | 5.3 | 2.6 | **2.04** |
| Multiple myeloma | 6.0 | 3.0 | **2.00** |
| Cervix uteri, females | 3.1 | 2.2 | **1.41** |
| Breast, females | 27.3 | 19.6 | **1.39** |
| Colorectal | 18.3 | 13.4 | **1.37** |
| Liver/Cholangio | 8.5 | 6.3 | **1.35** |
| Pancreas | 13.3 | 11.0 | **1.21** |
| Lung and bronchus | 40.2 | 39.3 | **1.02** |
| Kidney/renal pelvis | 3.4 | 3.7 | **0.92** |

Next-generation sequencing (NGS) was performed among 50.1% of white patients and 39.8% of black patients ($p < 0.0001$)

Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975-2016/, Accessed on July 31, 2022
https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.15_suppl.9005

# Summary of Disparities report from the AACR (American Association of Cancer Research)

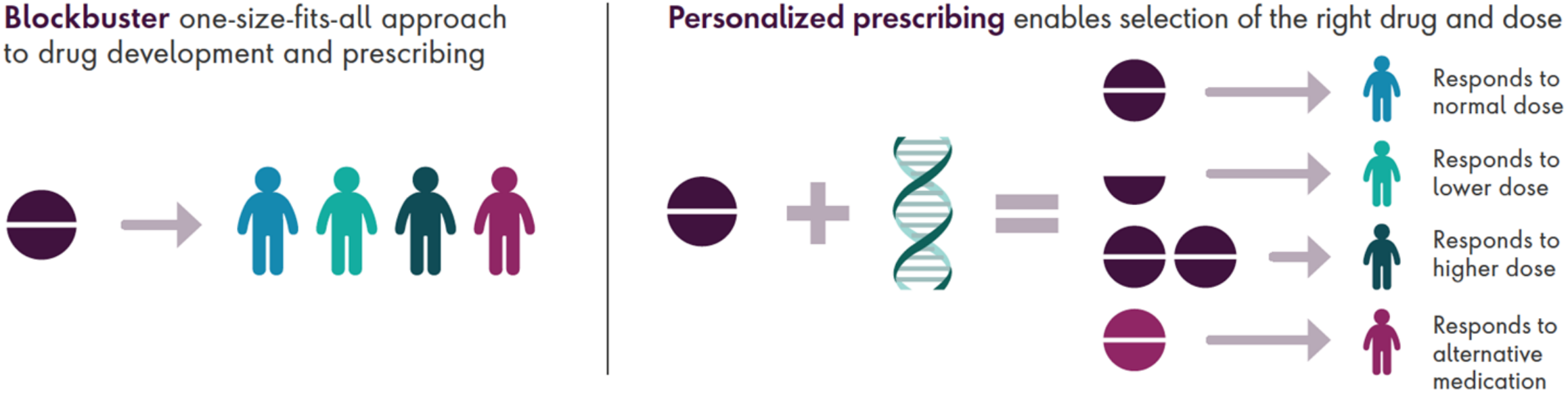
- 34% of all cancer deaths could be prevented if socioeconomic disparities are eliminated
- Eliminating healthcare disparities for racial and ethnic minorities would have saved $230 billion in direct healthcare costs and over $1 trillion in premature deaths and illnesses between 2003-6

https://cancerprogressreport.aacr.org/wp-content/uploads/sites/2/2020/09/AACR_CDPR_2020.pdf

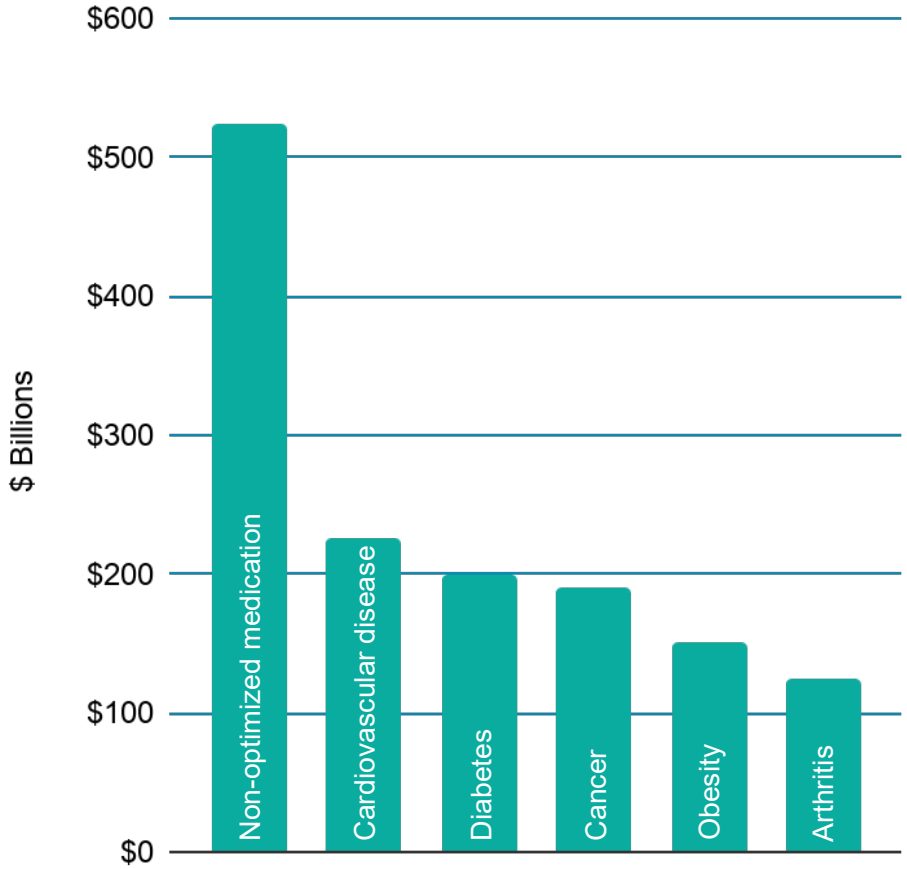
# PGx Germline Variants Also Matter

## 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.



# Non-optimized Medications Harm Patients and Increase Costs




## 99% of patients

have genetic variants that impact medication response[1]

## Every 2 minutes

a life is lost because of non-optimized medications[2]

## Exceeds disease cost

and annual cost of medications[2]

## 40 million patients

are on 5 or more meds, and the number will double by 2040[3]

[1]Chanfreau-Coffinier C, *et al. JAMA Netw Open*. 2019;2(6):e195345. doi:10.1001/jamanetworkopen.2019.5345

[2]Watanabe JH, *et al. Ann Pharmacother*. 2018;52(9):829–837.

[3]U.S. Census Bureau (2017). 2017 national population projection tables: Main series. Retrieved from https://www.census.gov/data/tables/2017/demo/popproj/2017-summary-tables.html

INVITAE

# Hispanic Patients Underrepresented in PGx

"Although the Hispanic population is continuously growing in the United States, they are underrepresented in pharmacogenetic studies."*

- Invitae internal PGx data shows - 9% Hispanic tested patients vs. 16.7% of US population
- Heart disease and cancer - two leading causes of death in Hispanics - treated with medications heavily impacted by PGx**

*https://pubmed.ncbi.nlm.nih.gov/25431893/
**https://www.cdc.gov/vitalsigns/hispanic-health/index.html

INVITAE

# Disparities in Adverse Drug Events

Death rates from adverse drug reactions are highest among black patients & rural communities**

Women have 2x more of ADEs in FDA Reporting System (FAERS)*



*FDA Adverse Event Reporting System (FAERS),https://pubmed.ncbi.nlm.nih.gov/21535369/
**https://journals.sagepub.com/doi/abs/10.1345/aph.1P592

# FDA: Drug-gene and Drug-drug Interactions Equivalent

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

INVITAE



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

# List of Drugs Impacted by Pharmacogenomics According to the FDA and Clinical Pharmacogenetics Implementation Consortium (CPIC)[1,2]

### Behavioral health

amitriptyline
aripiprazole
atomoxetine
brexpiprazole
citalopram
clomipramine
desipramine
doxepin
escitalopram
fluvoxamine
imipramine
mirtazapine
nortriptyline
paroxetine
protriptyline
risperidone
sertraline
trimipramine
venlafaxine
vortioxetine

### Transplant

tacrolimus

### Cardiology

clopidogrel
hydralazine
quinidine
simvastatin
warfarin

### Pain management

celecoxib
codeine
flurbiprofen
ibuprofen
meloxicam
methadone
oxycodone
piroxicam
tramadol

### Rheumatology

azathioprine

### Hematology/oncology

belinostat
capecitabine
eliglustat
fluorouracil
irinotecan
mercaptopurine
tamoxifen
thioguanine

### Infectious disease

abacavir
atazanavir
efavirenz
nevirapine
voriconazole

### Ear, eye, nose, throat

dextromethorphan

### Gastroenterology

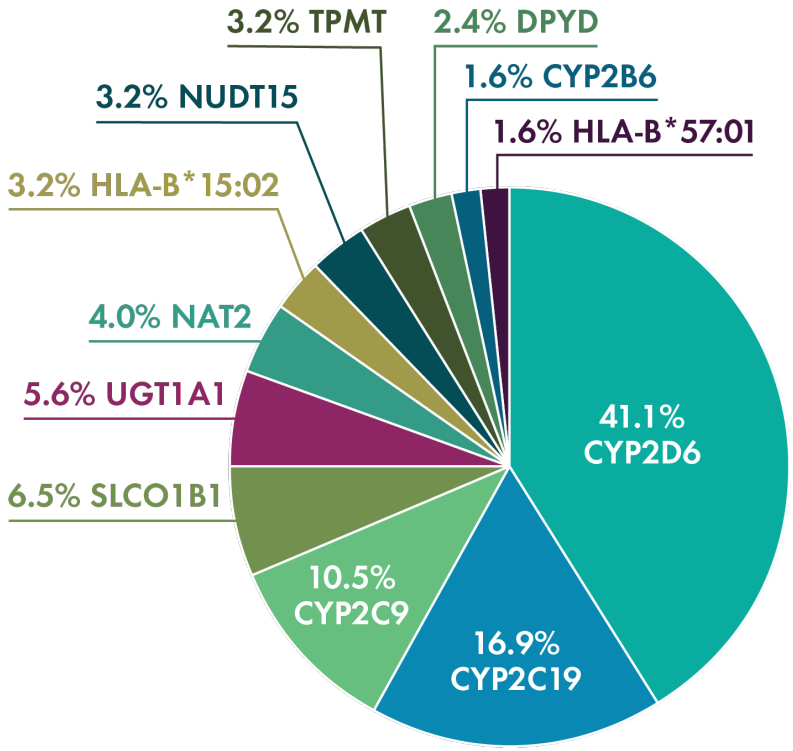
dexlansoprazole
esomeprazole
lansoprazole
omeprazole
ondansetron
pantoprazole
rabeprazole

### Neurology

phenytoin
siponimod
pimozide

**And many more…**

## 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

# Drug-gene Interactions

There are many high-evidence drug-gene interactions in oncology, including:[1,2]

| Drug name | Gene |
|---|---|
| avatrombopag | F2<br>F5 |
| belinostat | UGT1A1 |
| capecitabine | DPYD |
| eltrombopag | F5 |
| erdafitinib | CYP2C9 |
| fluorouracil | DPYD |
| fluorouracil topical | DPYD |
| gefitinib | CYP2D6 |
| irinotecan | UGT1A1 |
| mercaptopurine | NUDT15<br>TPMT |
| nilotinib | UGT1A1 |
| pazopanib | HLA-B*57:01<br>UGT1A1 |
| sacituzumab govitecan-hziy | UGT1A1 |
| tamoxifen | CYP2D6 |
| thioguanine | NUDT15<br>TPMT |

CPIC®
Clinical Pharmacogenetics Implementation Consortium

**References:** 1. CPIC: https://cpicpgx.org/genes-drugs/
2. FDA: https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

# Oncology: A Case Example

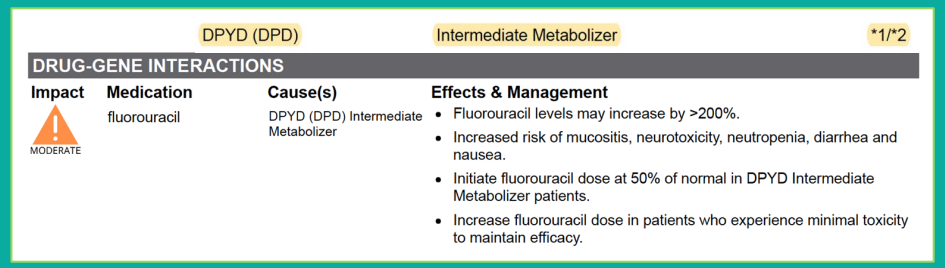
- In late 2018, Lynn was diagnosed with an early stage bowel cancer following routine screening.
- In January 2019, Lynn had a successful bowel resection surgery. Her doctors recommended chemo to knock out any residual cells.
- In March 2019, Lynn had her first ...and last dose of intravenous flourouracil (5-FU).
- Lynn died less than 4 weeks later, but NOT from her cancer.
- What happened?


**"Her last weeks were agony," Chris says. "Her entire digestive tract was burnt, as if by acid. She had constant nausea and diarrhea and couldn't process food. No one warned us this might happen. Yet as I know now, Lynn's death was avoidable."**



https://www.know-the-risk-of-5fu-chemotherapy.com/personal-stories/lynn-s-story/

# Oncology: A Case Example



DPYD (DPD) | Intermediate Metabolizer | *1/*2

**DRUG-GENE INTERACTIONS**

| Impact | Medication | Cause(s) | Effects & Management |
|---|---|---|---|
| MODERATE | fluorouracil | DPYD (DPD) Intermediate Metabolizer | • Fluorouracil levels may increase by >200%.<br>• Increased risk of mucositis, neurotoxicity, neutropenia, diarrhea and nausea.<br>• Initiate fluorouracil dose at 50% of normal in DPYD Intermediate Metabolizer patients.<br>• Increase fluorouracil dose in patients who experience minimal toxicity to maintain efficacy. |

## Outcome

- Like an estimated 5-8% of patients, Lynn produced less of a liver enzyme called dihydropyrimidine dehydrogenase or DPD, 1 in 100 to 1 in 1000 patients produce no enzyme.
- Without DPD, 5FU stays in the body and results in extensive toxicity.



Wörmann B, *et al.* Dihydropyrimidine Dehydrogenase Testing prior to Treatment with 5-Fluorouracil, Capecitabine, and Tegafur: A Consensus Paper. *Oncol Res Treat.* 2020;43:628-636.

# DPYD Testing Can Reduce Treatment-related Mortality

**Pathogenic DPYD Variants and Treatment-Related Mortality in Patients Receiving Fluoropyrimidine Chemotherapy: A Systematic Review and Meta-Analysis**

Bhavina B Sharma [# 1], Karan Rai [# 2], Heather Blunt [3], Wenyan Zhao [4], Tor D Tosteson [4 5], Gabriel A Brooks [1 5]

Affiliations + expand

PMID: 34506675 DOI: 10.1002/onco.13967 Paperpile

Free article

Carriers of pathogenic DPYD gene variants had a **25.6 times** increased risk of treatment-related death (95% CI, 12.1-53.9; p < .001).

Sharma BB, *et al.* Pathogenic DPYD Variants and Treatment-Related Mortality in Patients Receiving Fluoropyrimidine Chemotherapy: A Systematic Review and Meta-Analysis. *Oncologist.* 2021;26(12):1008-1016.

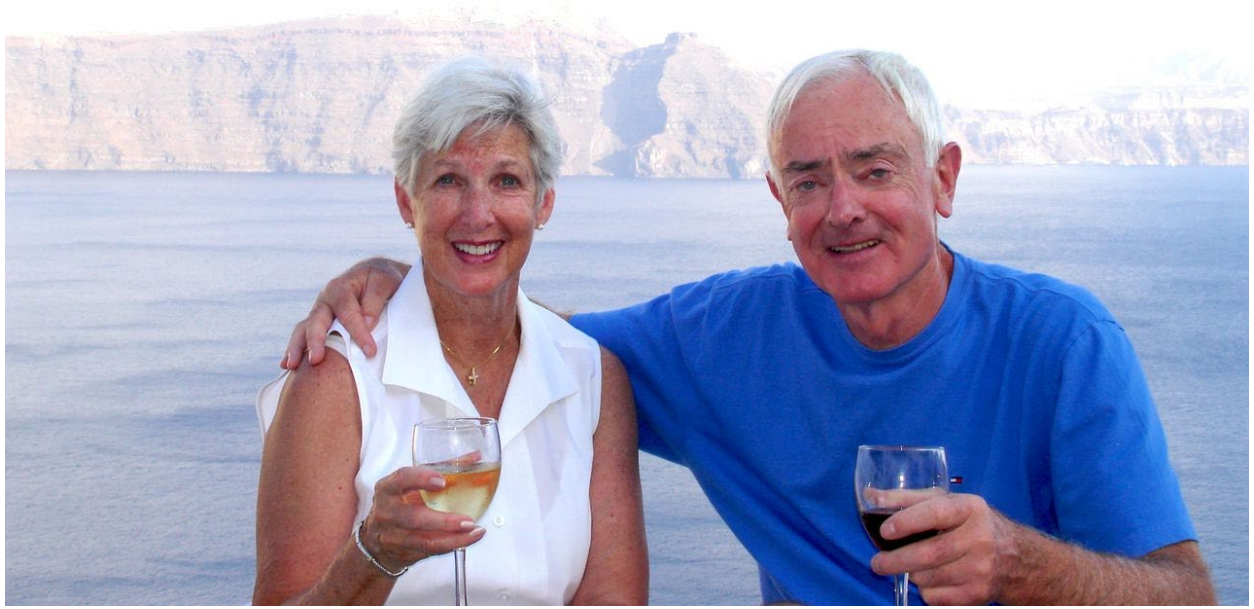
# EMA Has Recommended DPD testing for 5-FU Since 2020

EMA has recommended that patients should be tested for the lack of the enzyme dihydropyrimidine dehydrogenase (DPD) before starting cancer treatment with fluorouracil given by injection or infusion (drip) or with the related medicines, capecitabine and tegafur.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

# OHSU to Pay $1 Million, Promises Change to Settle Lawsuit from Widow of Cancer Patient

**By Fedor Zarkhin | The Oregonian/OregonLive**



David McIntyre had a fatal reaction to OHSU's chemotherapy for his cancer, his wife, left, claims in a lawsuit filed against the university.

https://www.oregonlive.com/health/2022/05/ohsu-to-pay-1-million-promises-change-to-settle-lawsuit-from-widow-of-cancer-patient.html

# Challenges and Strategies for Implementing Genomic Services in Diverse Settings

- Prioritizing integration of genomics into the EHR
- Improving clinicians' knowledge and belief about genomic medicine
- Engaging patients to participate in the genomic medicine projects

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5441047/

# Closing Disparity Gaps in PGx


- Inadequate Education
- Ability to Pay
- Geographical Barriers
- Research Inclusion
- Technology and Data Portability

Formea CM, Schultz AJ, Empey PE.Pharmacists closing health disparity gaps through pharmacogenomics.J Am Coll Clin Pharm. 2022;5(8):844-852.

# Clinic Level

## Local Level

## National Level

# What are the Ethical and Practical Implications of Pharmacogenomics?

When educated about pharmacogenomics most of a diverse group of community participants agreed:

- **physicians should inform patients of all pertinent available tests for a specific problem, including genetic testing**.
- the decision to use a particular test, including genetic tests, rests with the patient.
- insurance companies are obligated to understand the benefits offered by the tests.

American Society for Pharmacovigilance (ASP) and the Hope and Healing Center & Institute (HHCI) Community Dialogue: What are the Ethical and Practical Implications of Pharmacogenomics? Final Report November 19, 2020

Are you testing all patients who could benefit from genetic testing?

# Guideline criteria alone miss a broad swath of patients.

Two recent studies indicate that the current clinical criteria for genetic testing are restricting the detection of almost half of the variants in cancer patients.

***Annals of Surgical Oncology***

In a study of 4,196 Medicare cancer patients, Invitae found that positive results are nearly as high in patients who did not meet criteria for testing as in patients who met criteria.[1]

Positive rate for patients **in criteria**

✓ 10.5%

Positive rate for patients **out of criteria**

✕ 9.0%

***Journal of Clinical Oncology***

Invitae and TME Breast Care Network analyzed the results of 1,000 breast cancer patients and found that positive results are nearly as high in patients who did not meet criteria for testing as in patients who met criteria.[2]

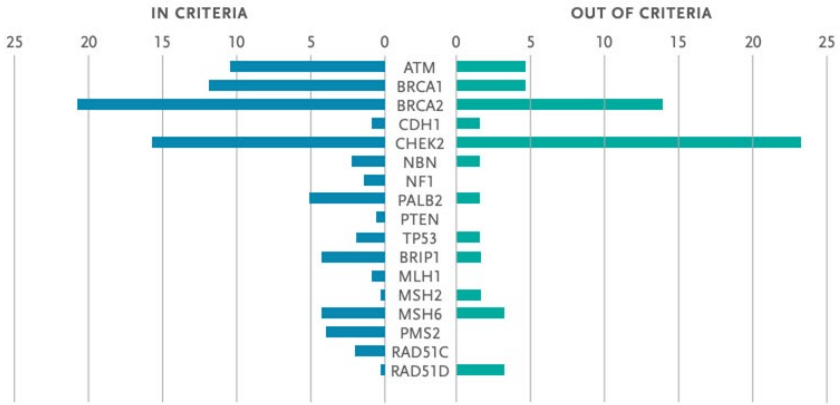
Positive rate for patients **in criteria**

✓ 9.4%

Positive rate for patients **out of criteria**

✕ 7.9%

**Clinically actionable variant count by gene (per 1,000 patients)[1]**




**Invitae recommends testing all at-risk patients, whether or not they meet criteria.**

# Lab Selection Can Impact Affordability & Access

- How many payers is the lab in-network with?
- Do they provide benefits investigations with estimated out-of-pocket?
- Do they offer affordable patient-pay options?
- Is there a patient assistance program for those with financial need and no insurance coverage?

# Is Variant Coverage Appropriate for Your Patients?

Some labs only test this variant

| *DPYD* Variant<br>HGVS<br>Other Names | Ref. SNP | Prevalence (Ethnicity) | Impact |
|---|---|---|---|
| c.1905+1G>A<br>*DPYD**2A<br>IVS14+1G>A | rs3918290 | 1.46% (European-Caucasian)[27]<br>2.7% (American-Caucasian)[40]<br>5.5% (Iranian)[38]<br>0.05% (South Asian)[45]<br>Absent (Japanese)[31–33] | CPIC: Poor metaboliser[11]<br>OR 5.42 increased toxicity in Caucasian carriers[27]<br>No increase in toxicity compared to wild type in Iranian carriers[38] |
| c.2846A>T<br>p.D949V | rs67376798 | 1.47% (European-Caucasian)[27]<br>1.8% (American-Caucasian)[62]<br>0.07% (South Asian)[45]<br>Absent (Japanese)[32,33] | CPIC: Intermediate metaboliser[11]<br>OR 8.18 increased toxicity in Caucasian carriers[27] |
| c.1236G>A<br>p.E412= | rs56038477 | 4–6% (European-Caucasian)[13,63]<br>1.4% (South Asian)[45]<br>Absent (Japanese)[32,33] | CPIC: Intermediate metaboliser[11]<br>Adj RR 1.59 in Caucasian carriers[13] |
| c.1679T>G<br>*DPYD**13<br>p.I560S | rs55886062 | 0.2% (European Caucasian)[13]<br>Absent (Japanese)[31–33] | CPIC: Poor metaboliser[11]<br>Adj RR 4.4 in Caucasian carriers[13] |
| c.577A>G<br>p.Y186C | rs115232898 | 6.4% (African-American)[36] | CPIC: Intermediate metaboliser[11]<br>Profound FP related toxicity in case studies[35,65]<br>46% lower DPD activity than wild type in carriers, ethnicity not specified[64] |



White C, Scott RJ, Paul C, Ziolkowski A, Mossman D, Ackland S. Ethnic Diversity of DPD Activity and the DPYD Gene: Review of the Literature. *Pharmgenomics Pers Med*. 2021;14:1603-1617

# Does the Lab Offer Free Family Variant Testing?

## Family Variant Testing Barriers

- Lack of knowledge of disease risk
- Cost
- Family education barriers
- Lack of access to genetic resources

**Why this matters:**

- One test result can impact an entire family
- Blood relatives have up to 50% chance of having the same variant

# Does the Lab Share Data?

- Classifications should be deposited into the ClinVar database for peer review.
- Data submissions should include evidence.
- Review commercial laboratory contributions to ClinVar.
- Clinvar is monitored and ran by the National Institute of Health (NIH)



ACMG STATEMENT | Genetics inMedicine

**Laboratory and clinical genomic data sharing is crucial to improving genetic health care: a position statement of the American College of Medical Genetics and Genomics**

| Submitter | Maximum review status | Total submissions | Submissions with interpretations | Total Genes | Last updated |
|---|---|---|---|---|---|
| Invitae | Assertion criteria | 606139 | 606136 | 14181 | Feb 08, 2022 |
| GeneDx | Assertion criteria | 309532 | 309402 | 29449 | Mar 16, 2022 |
| Illumina Laboratory Services; Illumina | Assertion criteria | 208884 | 208884 | 5749 | Dec 20, 2021 |
| Ambry Genetics | Assertion criteria | 72616 | 72616 | 1722 | Feb 03, 2022 |
| Color Health, Inc | Assertion criteria | 48462 | 48462 | 85 | Jan 07, 2022 |
| Eurofins NTD LLC (GA) | Assertion criteria | 45028 | 45028 | 2420 | Sep 19, 2018 |
| Natera, Inc. | - | 36117 | 36117 | 375 | Feb 09, 2022 |
| OMIM; Johns Hopkins University | - | 33671 | 33671 | 5612 | Mar 15, 2022 |
| CeGaT Praxis fuer Humangenetik Tuebingen | Assertion criteria | 28698 | 28698 | 7018 | Jan 24, 2022 |
| Nilou-Genome Lab | Assertion criteria | 27747 | 27747 | 2484 | Mar 06, 2022 |
| Laboratory for Molecular Medicine; Partners HealthCare Personalized Medicine | Assertion criteria | 24470 | 24396 | 1796 | Jun 10, 2021 |
| Women's Health and Genetics/Laboratory Corporation of America; LabCorp | Assertion criteria | 24211 | 24188 | 1325 | Mar 11, 2022 |
| Genetic Services Laboratory; University of Chicago | Assertion criteria | 23609 | 23609 | 1686 | Feb 18, 2022 |
| Counsyl | Assertion criteria | 20976 | 20976 | 350 | Aug 05, 2019 |
| PreventionGenetics | Assertion criteria | 18417 | 18417 | 1573 | Dec 20, 2021 |
| Cincinnati Children's Hospital Medical Center Genetics and Genomics Diagnostic Laboratory; Cincinnati Children's Hospital Medical Center | Assertion criteria | 17788 | 17788 | 19580 | Apr 27, 2020 |
| Quest Diagnostics Nichols Institute San Juan Capistrano | Assertion criteria | 17643 | 17643 | 17098 | Feb 10, 2022 |
| Athena Diagnostics Inc | Assertion criteria | 17228 | 17228 | 822 | Sep 13, 2021 |
| ARUP Laboratories, Molecular Genetics and Genomics; ARUP Laboratories | Assertion criteria | 16700 | 16700 | 1251 | Mar 09, 2022 |

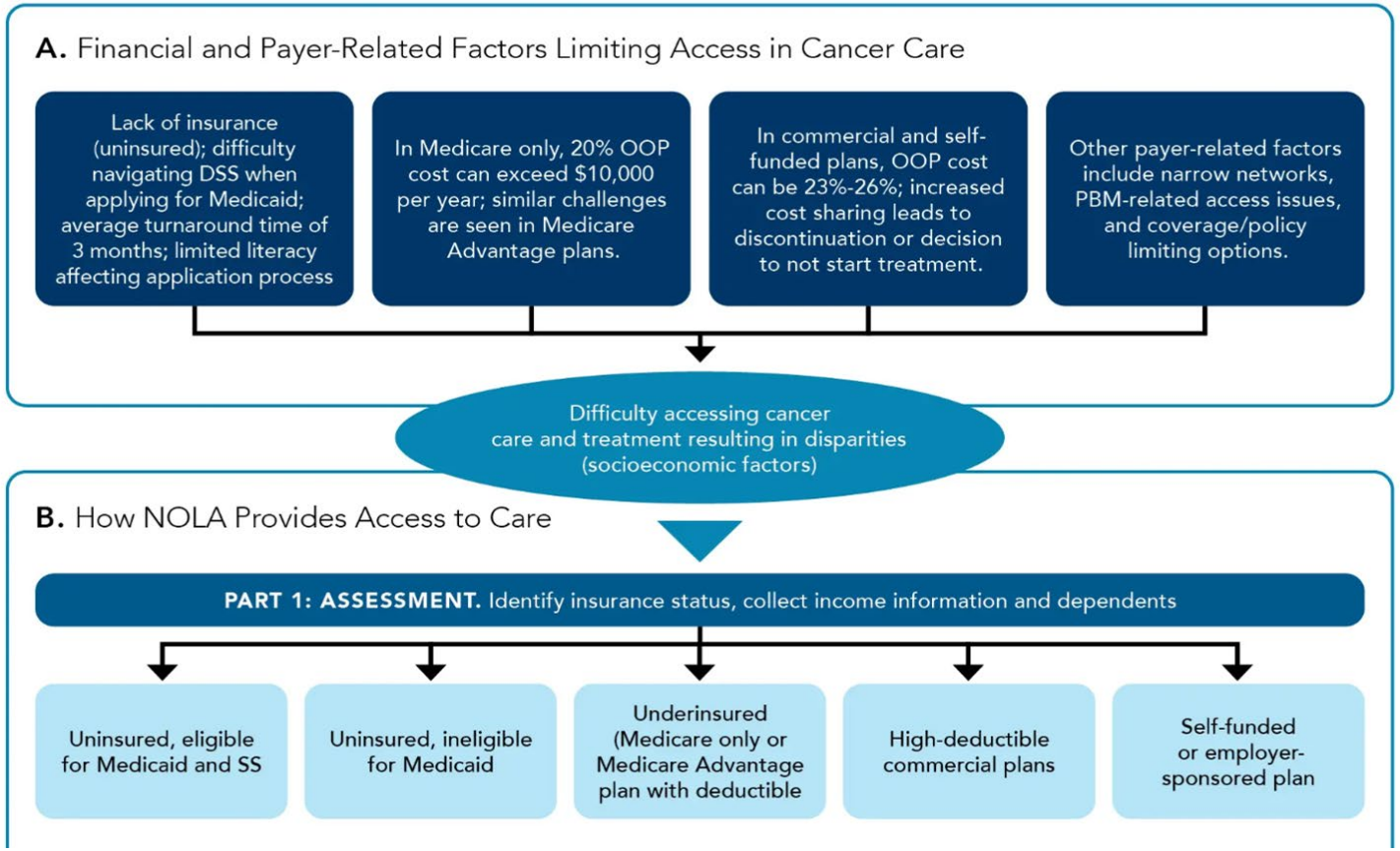
Clinic Level

Local Level

National Level

# No One Left Alone (NOLA) at Carolina Blood and Cancer Care Associates

A program to provide financial assistance and access to cancer care




https://www.ajmc.com/view/addressing-cancer-health-disparities-in-a-multilateral-collaboration-in-an-independent-community-cancer-clinic-translating-words-into-action

# No One Left Alone (NOLA) at Carolina Blood and Cancer Care Associates

**PART 2: ACTION PLAN.** Take steps based on insurance eligibility category.

| | | |
|---|---|---|
| No insurance | Identify if patient qualifies for any state or federal program (ie, Medicare, Medicaid, ACA tax subsidy). Work with local county 501(c)(3). | Help complete all forms for program. Create path for facilitation. Provide legislative assistance to navigate (including legal funds). |
| Medicaid program | Verify benefits. Ensure that DSS application is processed. Reach out to congressional office. Ask if patient is LIS/dual eligible. | Verify if prescribed tests/medication(s) are approved/ indicated for diagnosis. |
| Medicare eligible (disabled) | Verify eligibility. Guide patients on how to enroll. Seek assistance for Part B premium. | Verify if patient is retiring soon; if so, and has Part A only, provide guidance for Part B and Medigap. Look at LIS/ dual eligibility. |
| Medicare: Part A/B, no Medigap | Identify if patient is dual eligible for Medicaid or Medicare secondary payer plan; if so, provide resources. | If not eligible, seek foundation assistance for Medigap payment and work with local foundations to support, if eligible. |
| Medicare: Medigap | Generally, all services are covered. Ensure benefits verification and eligibility. | Confirm Part D; if not, guide appropriately. Provide assistance for patients in Medicare Part D coverage gap, aka "donut hole." |
| Medicare Advantage plan | Go over insurance plan with patient during open enrollment to identify where they can save money (ie, changing insurance). | If changing back to Medicare, add a Part D plan and supplemental plan. If changing Advantage plan, facilitate appropriate plan. |
| Commercial and insurance exchanges | Verify prescribed medication(s) are approved/ indicated for diagnosis/place in therapy. Submit predetermination or prior authorization if necessary. | Identify if free medication is available, when necessary. Complete and submit applicable form(s). Identify patient's responsibility for prescribed medication(s). |

- Identified 700+ patients who did not have cancer screening, making arrangements to test
- Raised ~$2.3M last year for OOP cost or free drugs; created insurance fund
- Pilot already in place with a large lab with purpose to identify gaps in germline tests; paper pending
- Three large studies; reached >80% NGS testing rate
- Phase 3 soon

https://www.ajmc.com/view/addressing-cancer-health-disparities-in-a-multilateral-collaboration-in-an-independent-community-cancer-clinic-translating-words-into-action

# CA Senate Bill 1191 Medi-Cal: Pharmacogenomic Testing

Author: Senator Pat Bates

# What S.B. 1191 Does…

- Provides Medi-Cal coverage for PGx testing for patients already taking, or being prescribed, medications included within CPIC A, A/B, or B Guidelines, or the FDA Label;
- Clarifies that tests can be ordered by an enrolled Medi-Cal clinician or pharmacists pursuant to Business and Professions Code Section 4052(a)(12);
- Ensures panel tests are reimbursed based on the use of one HCPCS or CPT code per test; and
- Allows for flexibility in permissible locations for sample collection.

# American Cancer Society Biomarker Bills

# What the Biomarker Bills Do

Biomarker testing must be covered for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee's disease or condition when the test is supported by medical and scientific evidence, including, but not limited to:

1. Labeled indications for an FDA-approved or -cleared test or indicated tests for an FDA-approved drug;
2. Centers for Medicare and Medicaid Services (CMS) National Coverage Determinations and Medicare Administrative Contractor (MAC) Local Coverage Determinations; or
3. Nationally recognized clinical practice guidelines and consensus statements.

# Enacted States to Date

| State | Active Date | Note |
|---|---|---|
| Illinois | 1/1/2022 | Applies to group or individual policy of accident and health insurance or managed care plan |
| Louisiana | 1/1/2022 | Limited to advanced or metastatic stage 3 or 4 cancer |
| Arizona | 1/1/2023 | Applies to hospital service corporation or medical service corporation; health care services organization; disability insurer; group or blanket disability insurer; or administration and its contractors |
| Rhode Island | 1/1/2024 | Applies to every individual or group health insurance contract; or every individual or group hospital or medical expense insurance policy |

Introduced: CA, MN, NY, OH, WA

https://www.ilga.gov/legislation/publicacts/fulltext.asp?Name=102-0203
http://www.legis.la.gov/Legis/ViewDocument.aspx?d=1227189
https://legiscan.com/RI/text/S2201/2022
https://legiscan.com/AZ/text/HB2144/2022

# Clinic Level

# Local Level

# National Level

MOREHOUSE CARhES

*A consortium of community-based health systems (e.g. CommonSpirit, WellStar) lead by Morehouse School of Medicine giving access to precision prevention, precision medicine, and clinical trials-matching tools in the "Black Belt"*

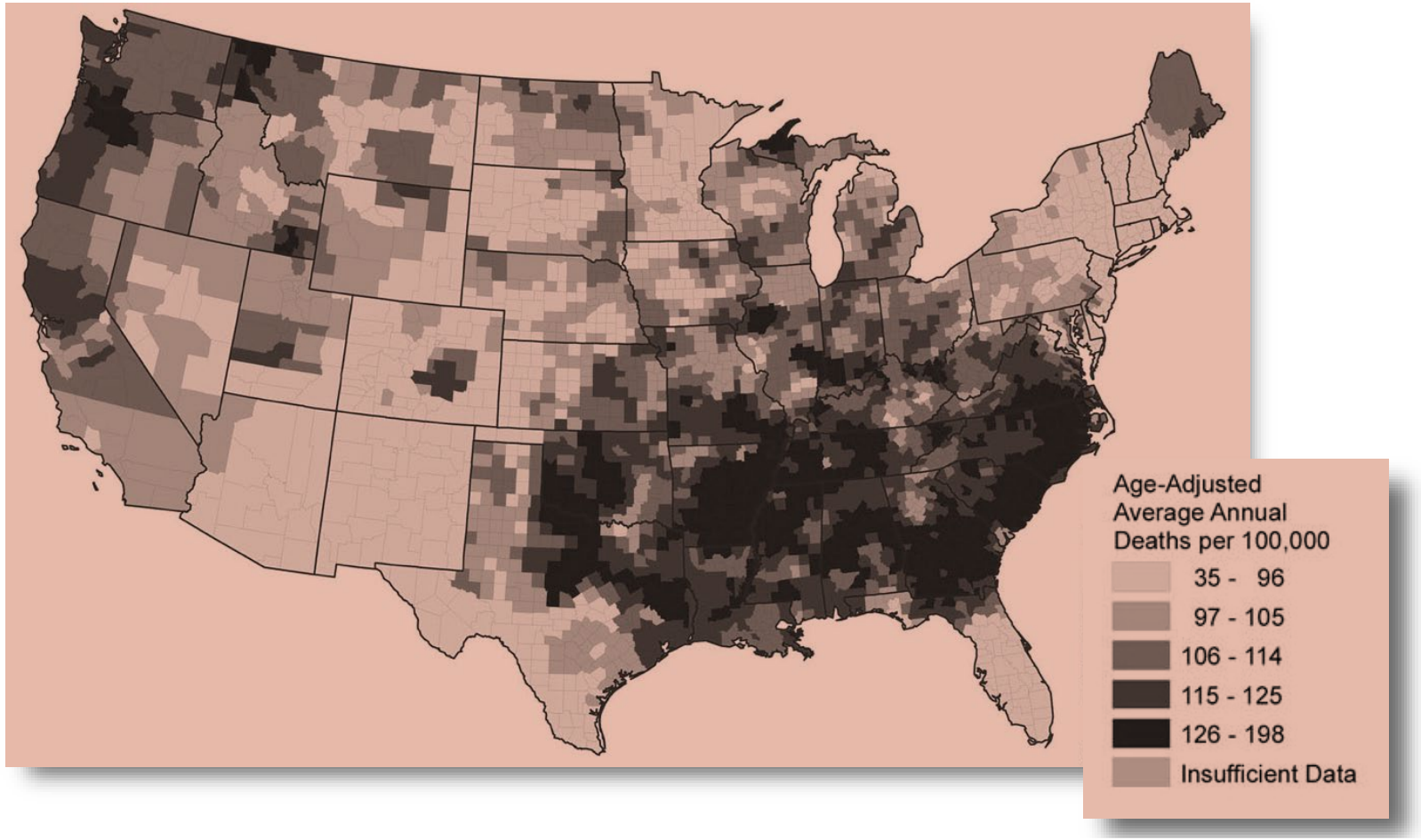
MOREHOUSE SCHOOL OF MEDICINE

CARhES

Comprehensive Approaches to Reimagine health Equity Solutions

# Why is Democratizing Precision Medicine Important to Morehouse School of Medicine?

- Provide services to underrepresented populations, at the center of a *chronic disease* belt.
- Some of the highest morbidity & mortality rates in United States.
- The incidence of COVID-19, diabetes, cancer, and stroke in GA are higher than US.
- The mortality rates of these diseases/conditions are *10 to 40% greater for* African American.




**Morehouse School of Medicine envisions leading the advancement and development of precision medicine therapies and diagnostics for African Americans to address long-standing health disparities in the BLACK BELT.**

# Ambitious Solutions Start Small, Build Momentum

**Phase 1 is broken out into education, clinical care, and research programs**

## 1 Education

*MSM owns implementation*

- MS in Genetic Counseling (Fall 2023)
- Precision Medicine Graduate Certificate program for providers
- MS/PhD in Bioinformatics & AI (Fall 2023)

## 2 Clinical Care

*Joint implementation*

- Preventatively Screen 1000 Patients/Participants w.o. Cancer Diagnosis in GI, Gynecology & PCPs
- Screen 100 ovarian cancer patients & family members (100% eligible)
- Screen 200 breast cancer patients & family members (mixed eligibility)

## 3 Research Portfolio

- *Total Cancer Care (ongoing)*
- Trulieve Medical Cannabis Oil & Chronic Pain Study (Fall 2022)

# FDA Labeling and Guidelines Can Impact Access

**NCCN Guidelines Panel**: Clinical Practice Guidelines in Oncology: Colon Cancer Version 1.2022; Clinical Practice Guidelines in Oncology: Rectal Cancer Version 1.2022; Clinical Practice Guidelines in Oncology: Anal Carcinoma Version 1.2022

Dear NCCN Panel Members,

Based on published evidence, we are writing to request review of the following proposed changes to the C
in Oncology:

**Specific changes proposed:**
*Colon Cancer Version 1.2022 Guideline*, COL-D add footnote to all regimens that contain 5-FU or capecit
targeted germline *DPYD* variant testing as a routine component of pre-treatment workup for all patients lik
capecitabine, including patients with colon cancer appropriate for resection and patients with suspected or
synchronous adenocarcinoma. Recommend dosing according to Clinical Pharmacogenetics Implementatio
guidelines for *DPYD* carriers. Key *DPYD* variants include but are not limited to (*DPYD**2A (rs3918290),
*DPYD* D949V (rs67376798), and *DPYD* HapB3 (rs56038477 or rs75017182)."

*Rectal Cancer Version 1.2022 Guideline*, REC-F add footnote to all regimens that contain 5-FU or capecit
germline *DPYD* variant testing.as a routine component of pre-treatment workup for all patients likely to re
including patients with rectal cancer appropriate for resection and patients with suspected or proven metast
Recommend dosing according to Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelin
*DPYD* variants include but are not limited to (*DPYD**2A (rs3918290), *DPYD**13 (rs55886062), *DPYD* D9
*DPYD* HapB3 (rs56038477 or rs75017182)). "

On MS-40, in the Systemic Therapy for Advanced or Metastatic Disease section add the "Severe Fluoropy
Toxicity" section from the NCCN Colon Cancer Guidelines located on MS-41-42.

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Subject: Citizen Petition Concerning the Use of Fluorouracil and Xeloda Chemotherapy Drugs

The undersigned submits this petition to request the Commissioner of Food and Drugs revise the package inserts for Fluorouracil and Xeloda (Capecitabine).

**A. Action Requested**

Revise the Drug Label inserts for Fluorouracil and Xeloda (Capecitabine) by:

1) Recommending Pre-Treatment Testing to Identify Patients with Dihydropyrimidine Dehydrogenase (DPD) Deficiency and include the recommendation in the content of the drug labels dealing with:
   a. Patient Counseling
   b. Dosage and Administration
   c. Box Warning.

2) Revising the Patient Counseling Information content to: Shift responsibility for identifying DPD deficiency from the patient to the prescribing physicians who should also discuss with patients the risk associated with DPD deficiency before the start of treatment.

3) Revising the Dosage and Administration content to: Recommend treating physicians pre-screen patients for DPD deficiency and adapt the treatment plan if partial or complete DPD deficiency is identified.

4) Adding a Box Warning that:

# H.R. 6875 The Right Drug Dose Now Act

Primary Sponsor: Representative Eric Swalwell (D-CA-15)

Original Cosponsor: Representative Tom Emmer (R-MN-6)

# The Right Drug Dose Now Act

1. Require an assessment and update of the **National Action Plan** for Adverse Drug Event Prevention;
2. Create **educational campaigns** on preventing adverse drug events, in part through the use of evidence-based PGx information.
3. Incentivize updates to **electronic health record systems** to ensure that healthcare providers are alerted to interactions between medications and genes when making prescribing decisions;
4. Enhance **reporting systems** that would assist with the tracking of PGx-associated adverse drug events; and
5. Authorize sustained **funding** for PGx implementation research and guideline development.

# Q&A

# Thank you!

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