

# From 'Precision Medicine' to 'Inclusion Medicine'

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# The aspiration of “Precision Medicine”

*Every patient is unique, and the evolving field of precision medicine aims to ensure the delivery of the **right treatment to the right patient at the right time.***

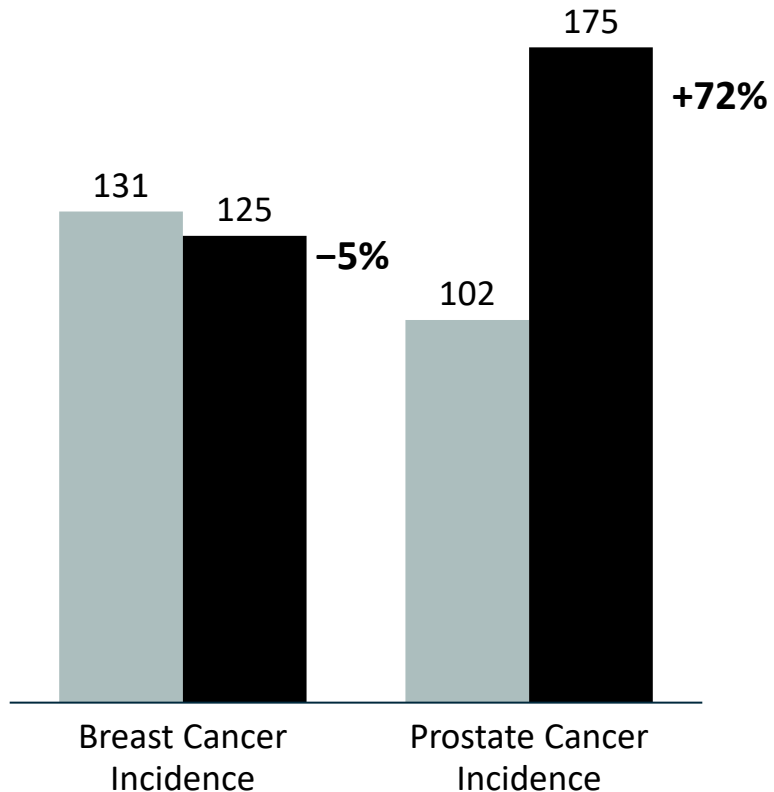
—NASEM, 2016

# Inequity in Cancer Care

## Examples

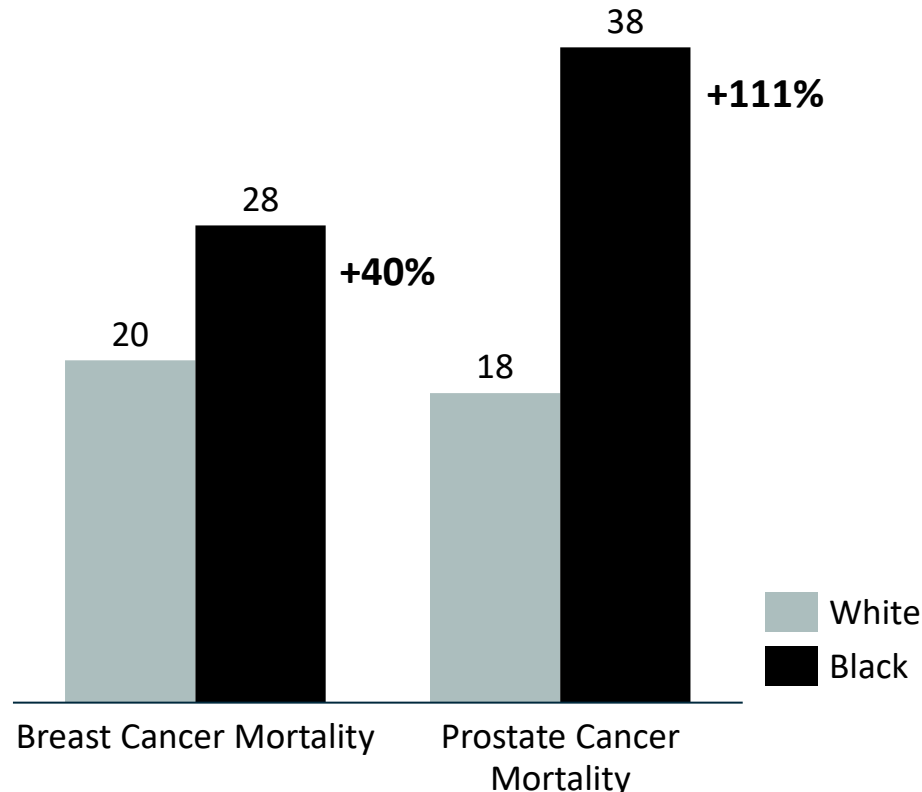
### Incidence

SEER 2013–2017: US cancer incidence rates per 100,000 (age-adjusted)



### Mortality

SEER 2013–2017: US cancer mortality rates per 100,000 (age-adjusted)



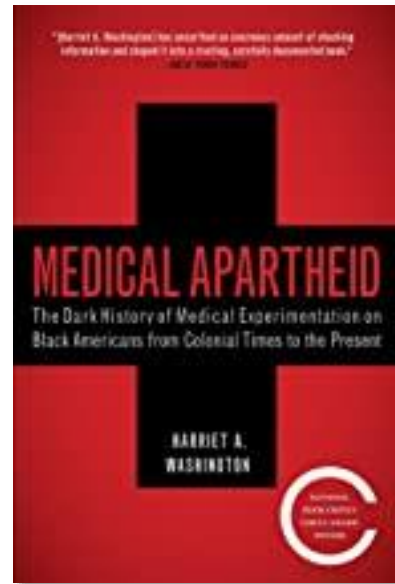
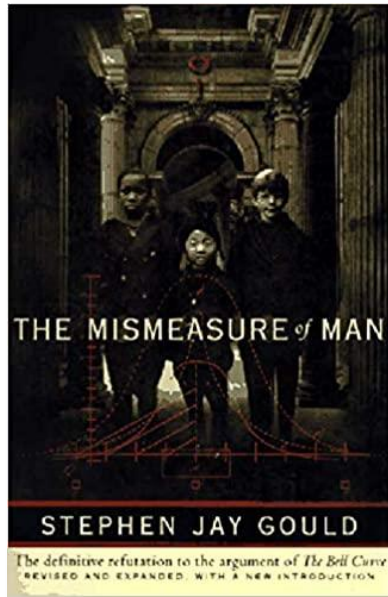
### Types of Disparity (non-mutually exclusive)

- Education
- Gender
- Geography
- Income
- Insurance plan
- Race & ethnicity
- Setting (rural/urban)
- Sexual orientation
- ...

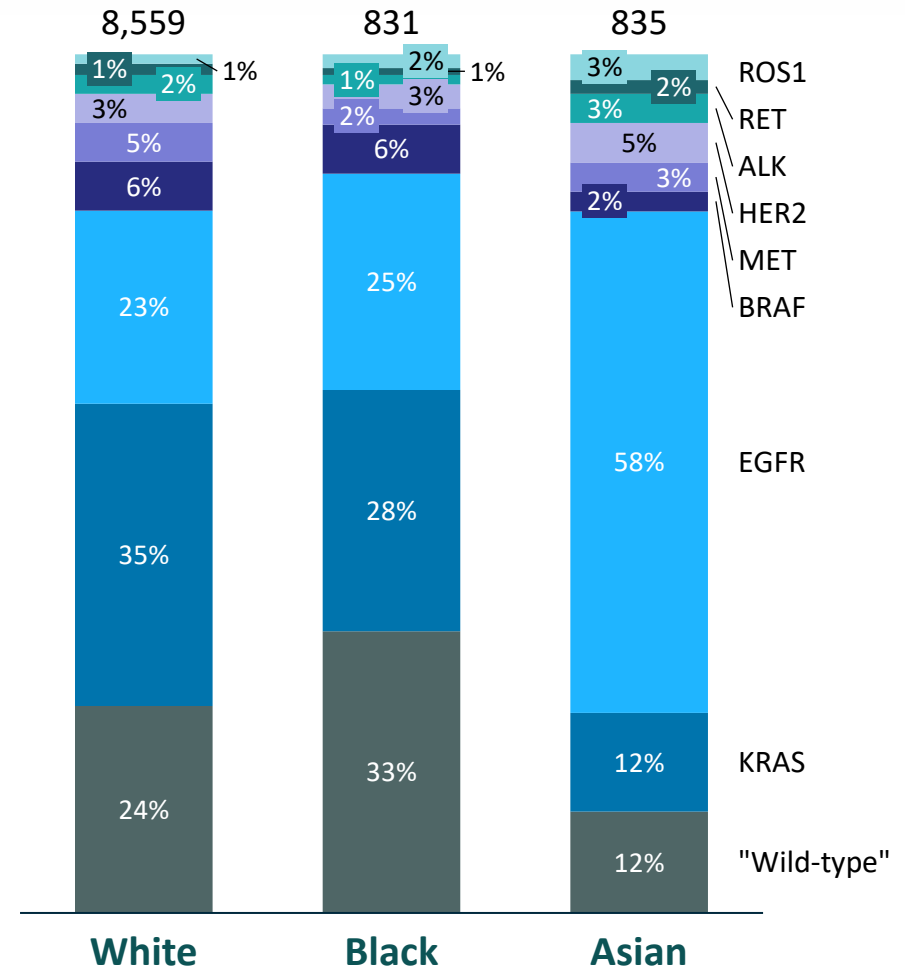
Sources: Clarion analysis; Nazha 2019 ASCO Educational Book 39:3; Guerrero 2018 Sci Rep 8:13978; SEER; Chen & Wong 9/19/2018 ProPublica; ACS; ASCO; AACR: [www.CancerDisparitiesProgressReport.org](http://www.CancerDisparitiesProgressReport.org)

# Sidebar: Race and Biology

*There is more genetic variability within a “race” than among “races”*

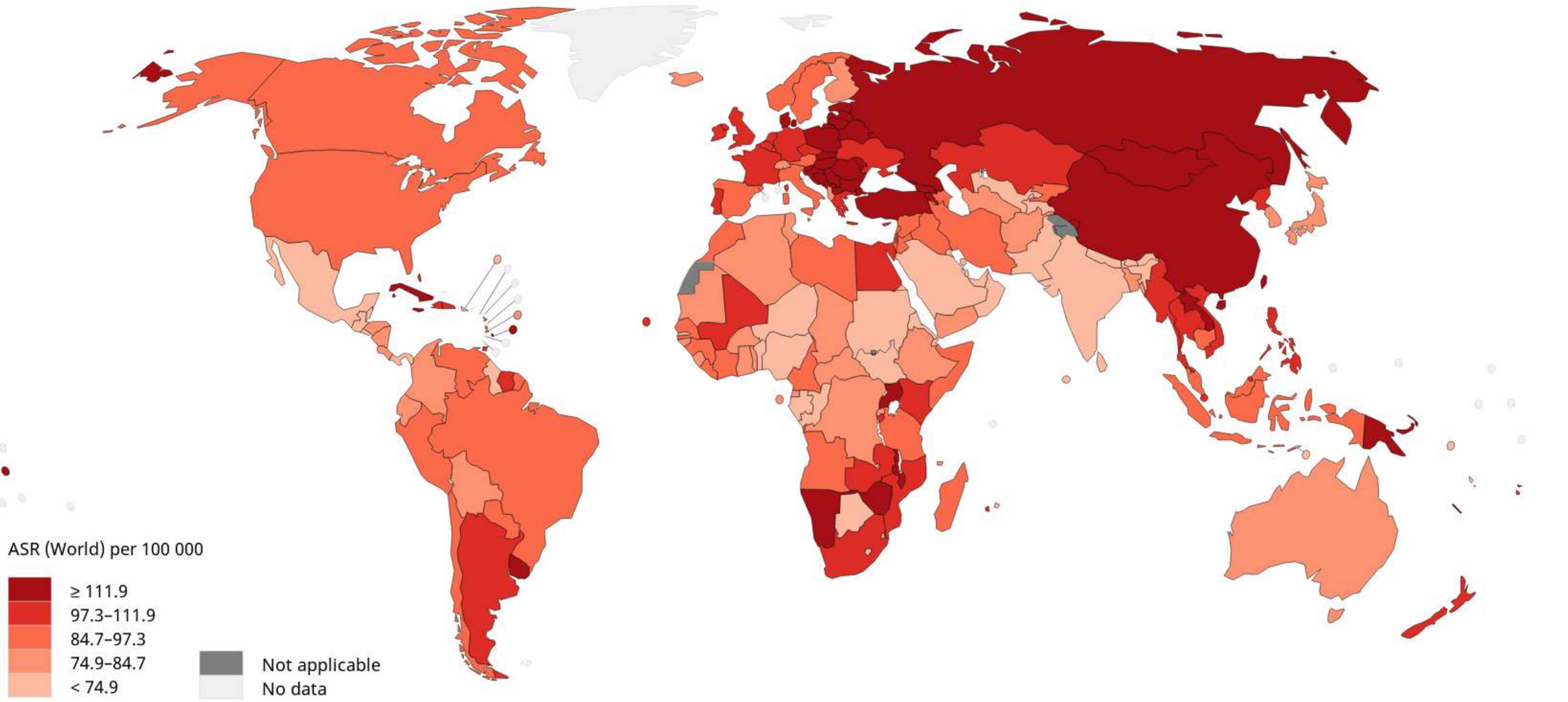


## Lung adenocarcinoma driver alterations in Project GENIE



Sources: Project GENIE v9.0 (AACR)

# Estimated age-standardized mortality rates (World) in 2020, all cancers, both sexes, all ages

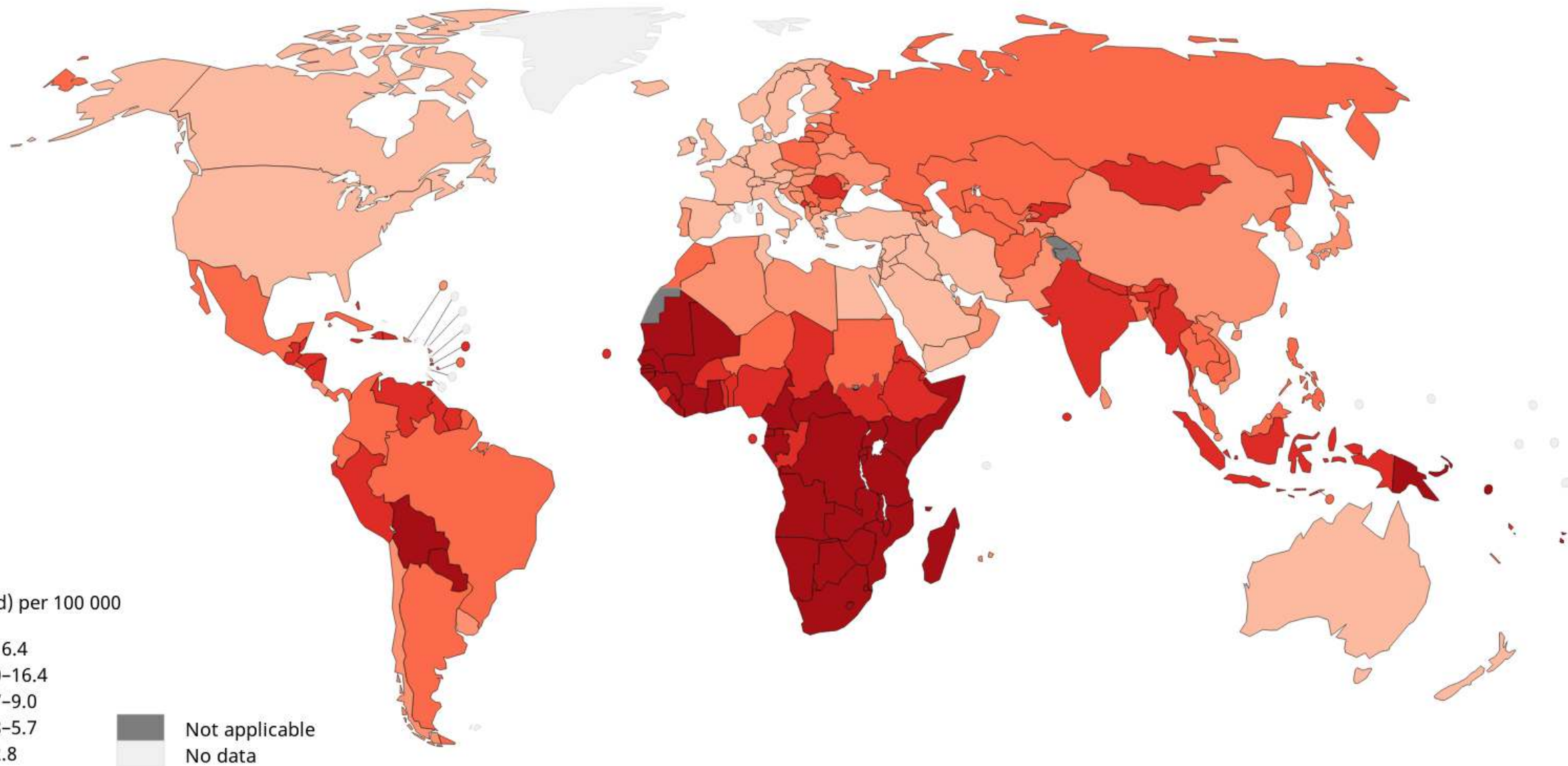


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Data source: GLOBOCAN 2020  
Graph production: IARC  
(<http://gco.iarc.fr/today>)  
World Health Organization



# Estimated age-standardized mortality rates (World) in 2020, cervix uteri, all ages

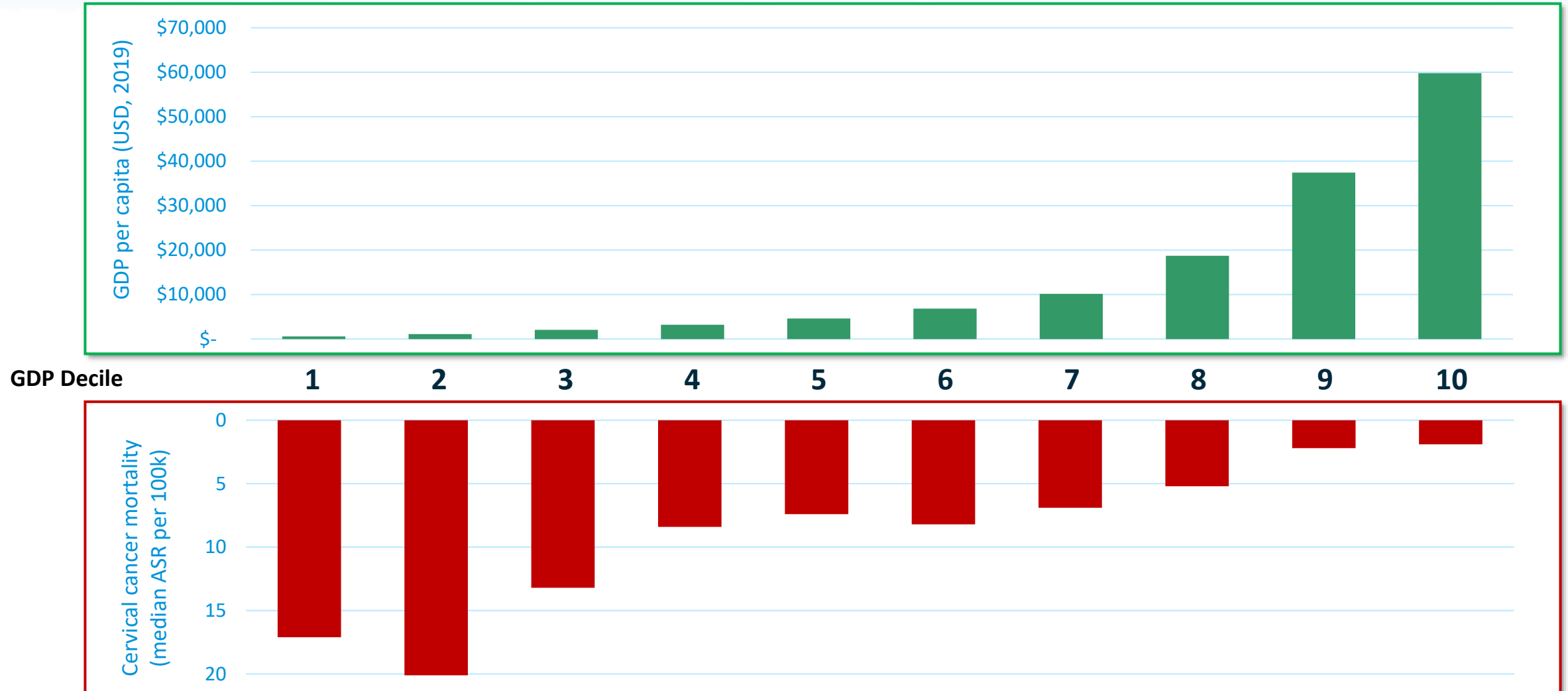


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Data source: GLOBOCAN 2020  
Graph production: IARC  
(<http://gco.iarc.fr/today>)  
World Health Organization

# Implementation Case Study: Cervical Cancer

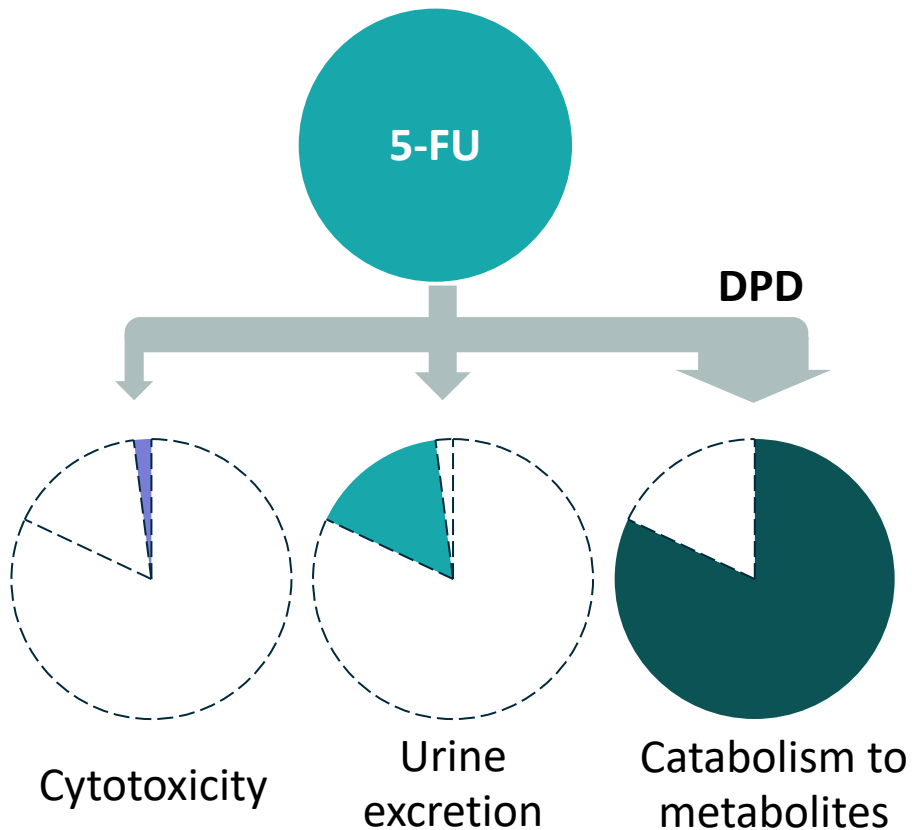
## *Cervical Cancer Mortality vs GDP in 170 Countries*



Sources: Clarion analysis; World Bank; GloboCan 2020

# Implementation Case Study: DPYD & 5-FU

*DPYD deficiency is a predictor of 5-FU toxicity but DPYD testing is not commonly done*



- *DPYD* encodes DPD, the **rate-limiting enzyme** of 5-FU catabolism
- *DPYD* deficiency raises the **risk of life-threatening toxicity** of 5-FU
- **However, DPYD genotyping is not standard practice**

NGS Test	FoundationOne	MSK-IMPACT	MI Profile
Test Developer	FMI	MSKCC	Caris Life Sci
# Genes in Panel	324	468	592
<i>DPYD</i> Included?	✘	✘	✘

Ethnicity	White	Black
Rate of <i>DPYD</i> deficiency	~1–4%	~8–12%

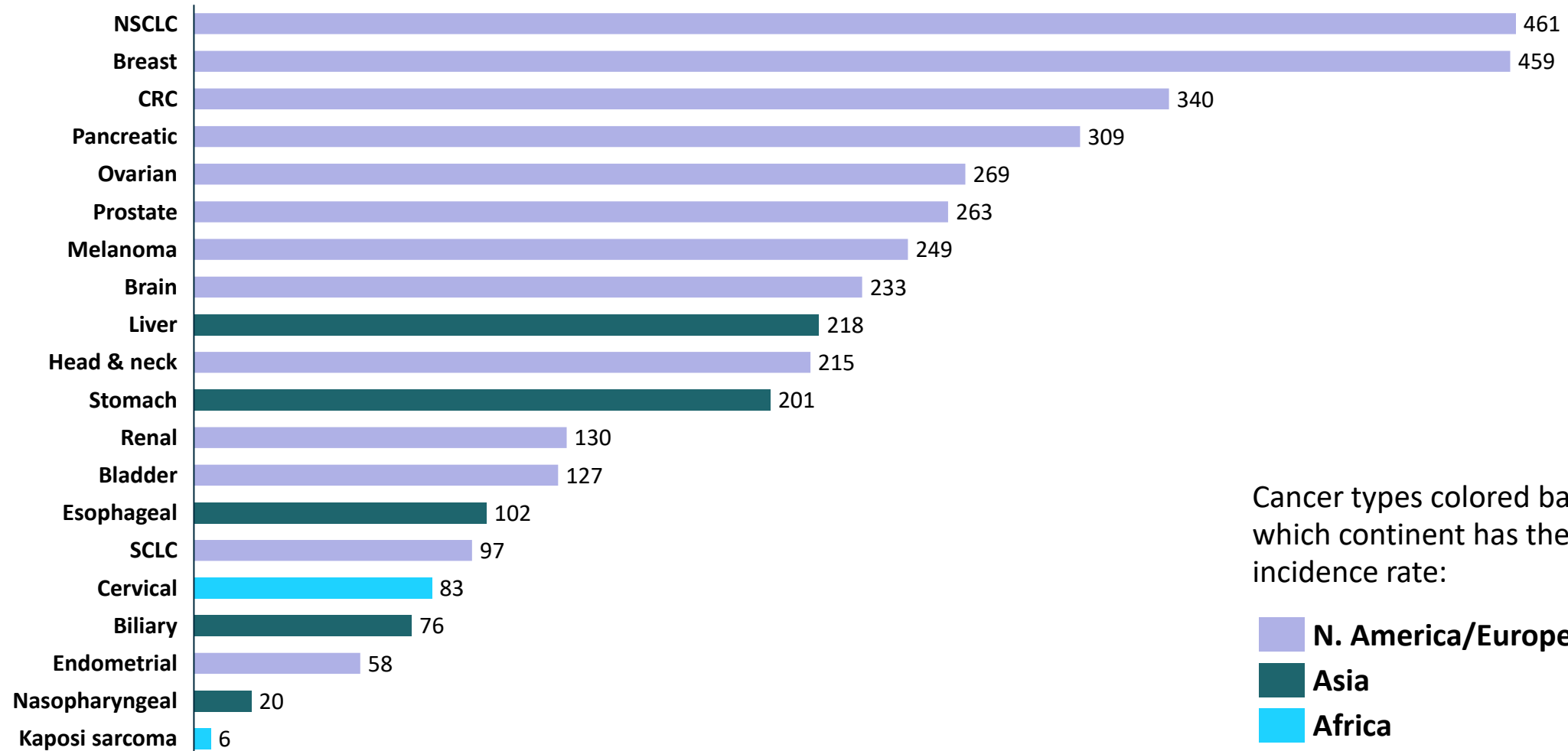
Sources: Clarion analysis; FMI; MSKCC; Caris; NCCN guidelines; Meulendijks 2015 Lancet Oncol 16:1639; Mattison 2006 Clin Cancer Res 12:5491; Mattison 2002 Pharmacogenomics 3:485



# Product Development Case Study: Neglected Histologies

*Tumor types more common in Asia/Africa tend to have lower levels of clinical pipeline activity*

## Number of Clinical-stage Products in Selected Solid Tumors



Cancer types colored based on which continent has the highest incidence rate:

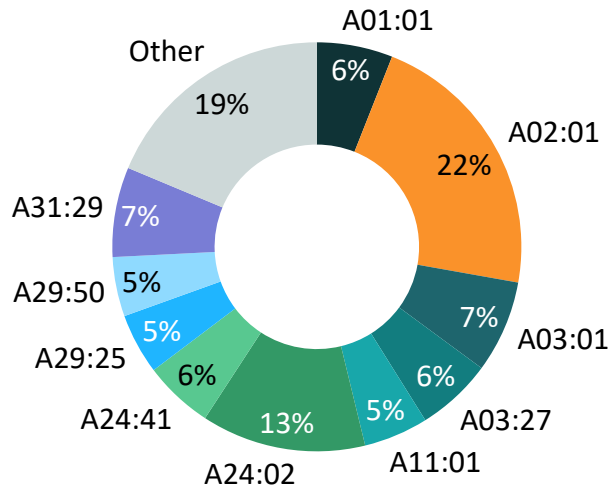


Sources: Clarion analysis; PharmaProjects (accessed 3/28/2021); GloboCan 2020

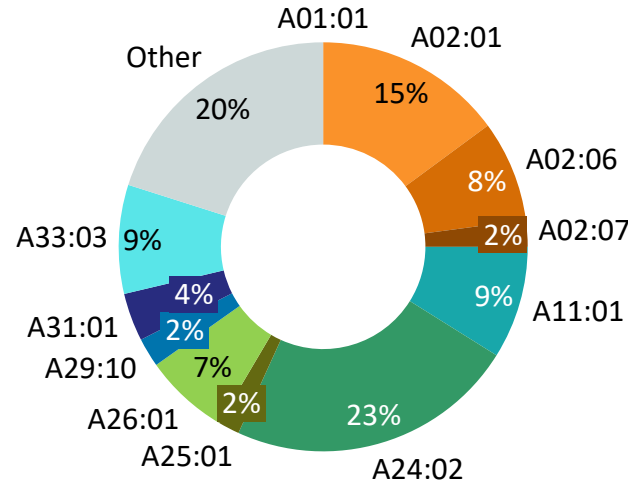
# Product Development Case Study: HLA-A2

*Most TCR-T therapies are restricted to HLA-A2, but HLA-A alleles are diverse*

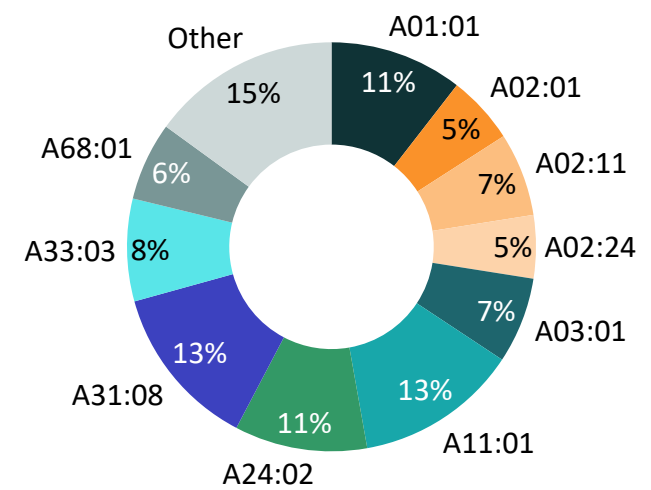
### North America



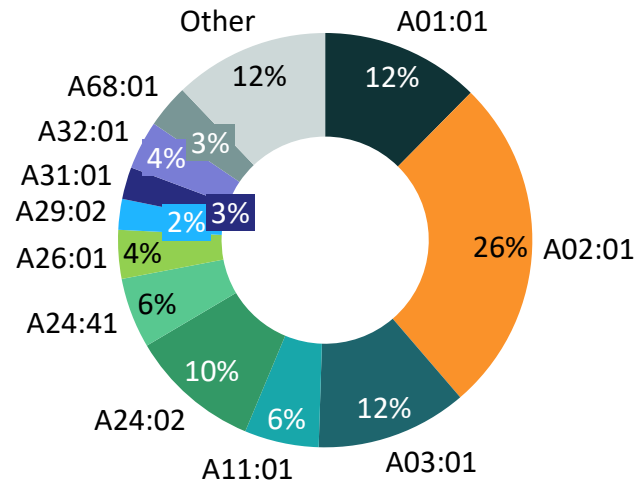
### North-East Asia



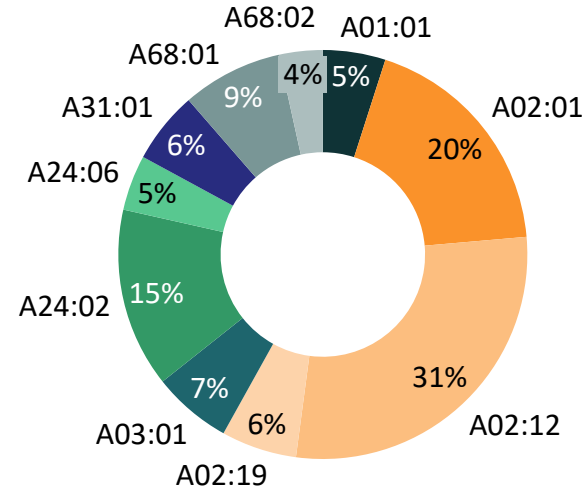
### South Asia



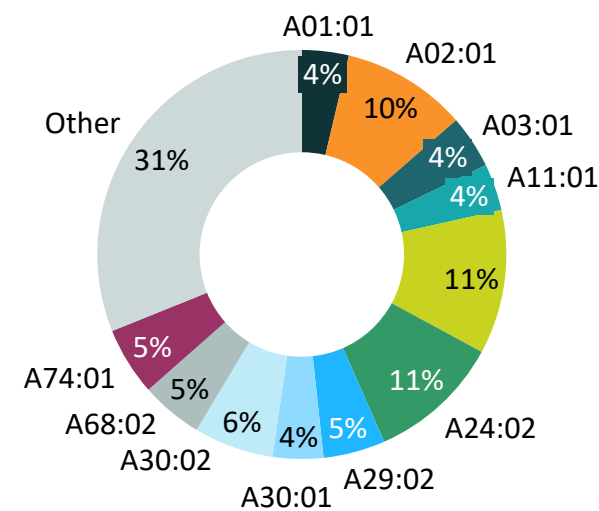
### Europe



### South & Central America



### Sub-Saharan Africa



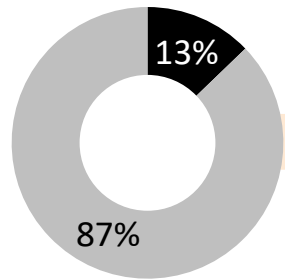
Sources: Clarion analysis; Allele Frequency Net Database

# Disparity in Representation

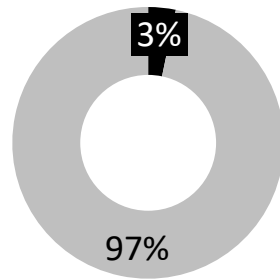
## Selected Examples

### Clinical trial representation

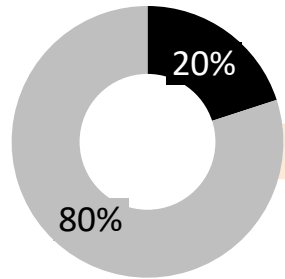
#### US population



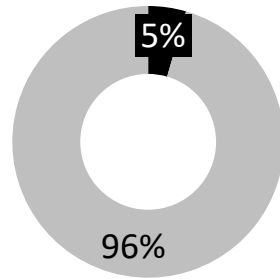
#### Onc clinical trials (in which race was reported)



#### US MM patients



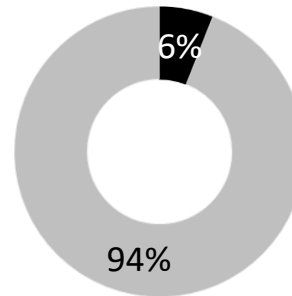
#### MM clinical trials



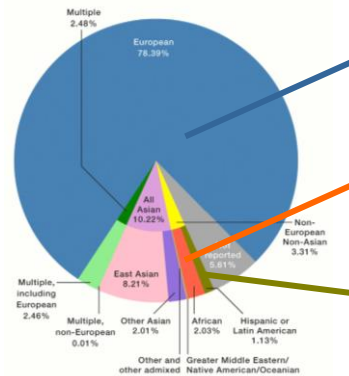
Black
  Non-black

### Genotyping

#### Project GENIE v9.0 dataset



#### Individuals in GWAS studies as of 2018



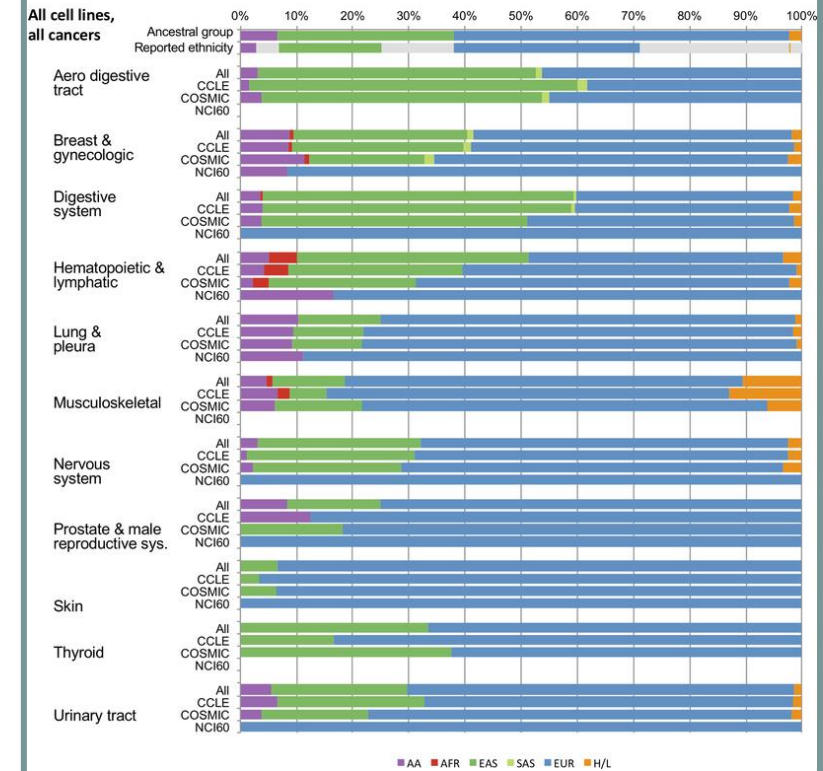
**78% European ancestry**

**2% African**

**1% Hispanic or Latin Am.**

### Preclinical models

#### Proportion of cell lines (%)



Sources: Clarion analysis; Census.gov; Nazha 2019 ASCO Educational Book 39:3; Guerrero 2018 Sci Rep 8:13978; SEER; Chen & Wong 9/19/2018 ProPublica; Project GENIE; Sirugco 2019 Cell 177:26; Dutil 2019 Cancer Res 79:1263

# Why do we fall short?

## *Underlying issues*

### Failures of Implementation

*Due to gaps in:*

Access / socioeconomics

Availability / logistics

Dissemination of best practice

Representation

### Failures of Product Development

*Due to gaps in:*

Studying biological diversity

Individualization of therapy

Model systems

Representation

# How can we make oncology innovation more inclusive?

*2 categories of solutions*

## Implementation Innovation

*More inclusively deploying the drugs/  
technology we already have*

## Product Innovation

*Generating new drugs/technology through  
more inclusive approaches*



# Implementation Innovation

## Examples

### Implementation Innovation

*More inclusively deploying the drugs/technology we already have*

#### Expanding Access



#### Generics Reforms

- Acceleration/removing delays
- Enforcing quality standards
- Ensuring supply

#### Drug Repurposing



# Product Development Innovation

## Examples

*Generating new drugs/technology through more inclusive approaches*

### Product Innovation

#### Population 'Omics'



#### Individualized Therapy

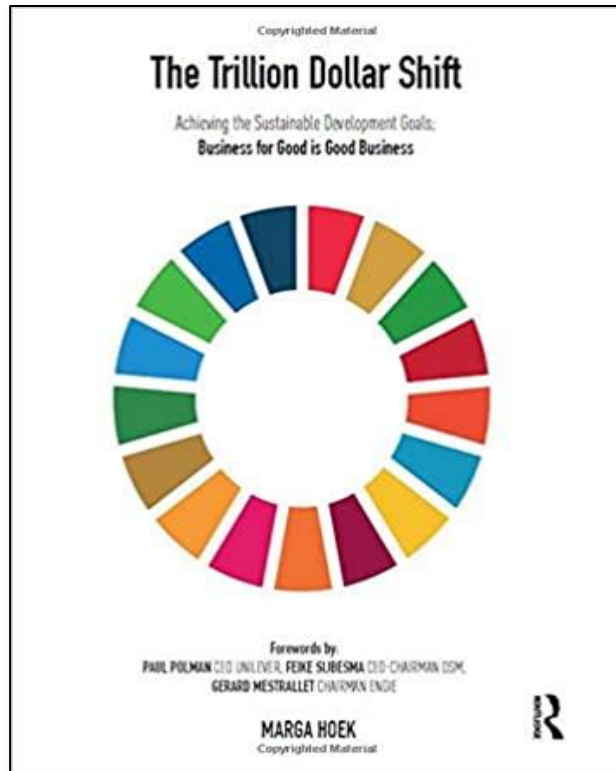
- Autologous cell therapy
- Personalized vaccines
- Avatar-guided therapy

#### Rare/Familial Cancers



Sources: Clarion analysis; AllOfUs.NIH.gov; H3Africa.org; PharmaProjects; <https://www.cancer.gov/about-nci/organization/cgh/research/irci>; <https://inheritedcancer.net/>

# Moving Away from a Zero-Sum Mindset



*Industry has a crucial role to play in bettering society*



Doing well

Doing well and  
avoiding doing  
(clear) wrong

Doing well and  
doing good

**Doing well by  
doing good**