



Otis W. Brawley, MD, MACP, FASCO, FACE

Chief Medical and Scientific Officer  
American Cancer Society

Professor of Hematology, Medical Oncology,  
Medicine, and Epidemiology  
Emory University

# Genomic Medicine in the 21<sup>st</sup> Century and A Brief History of Health Disparities

From the perspective of a Cancer Doc

# HOW WE DO HARM

A DOCTOR BREAKS RANKS  
ABOUT BEING SICK  
IN AMERICA



OTIS WEBB BRAWLEY, M.D.  
with Paul Goldberg



# Disclosures

- Employment:
  - American Cancer Society
  - Emory University
- Consulting
  - Turner Broadcasting (CNN)
  - National Institutes of Health
  - Centers for Disease Control
  - Department of Defense



## My Task

- Importance of equitable access to genetic/genomic services
- Define “disparities in health”
- Discuss fears and concerns
- Outline some areas for further study



# Genetics

The study of heredity, or how the characteristics of living things are transmitted from one generation to the next.

[Genomics and World Health: Report of the Advisory Committee on Health research, Geneva, WHO \(2002\)](#)



# Genomics

The study of genes and their functions, and related techniques.

[WHA 57.13: Genomics and World Health, Fifty Seventh World Health Assembly Resolution; 22 May 2004](#)



## Genetics vs Genomics

The **main difference** is that genetics scrutinizes the functioning and composition of the single gene whereas genomics addresses all genes and their inter relationships in order to identify their combined influence on the growth and development of the organism.





## Genetics/Genomics

- Risk of Disease
  - BRCA mutations - Breast Cancer
  - HBB mutations - Sickle Cell Trait/Anemia
  - CFTR mutations - Cystic Fibrosis
- Defining type of disease and response to treatment



Rudolph Ludwig Karl Virchow

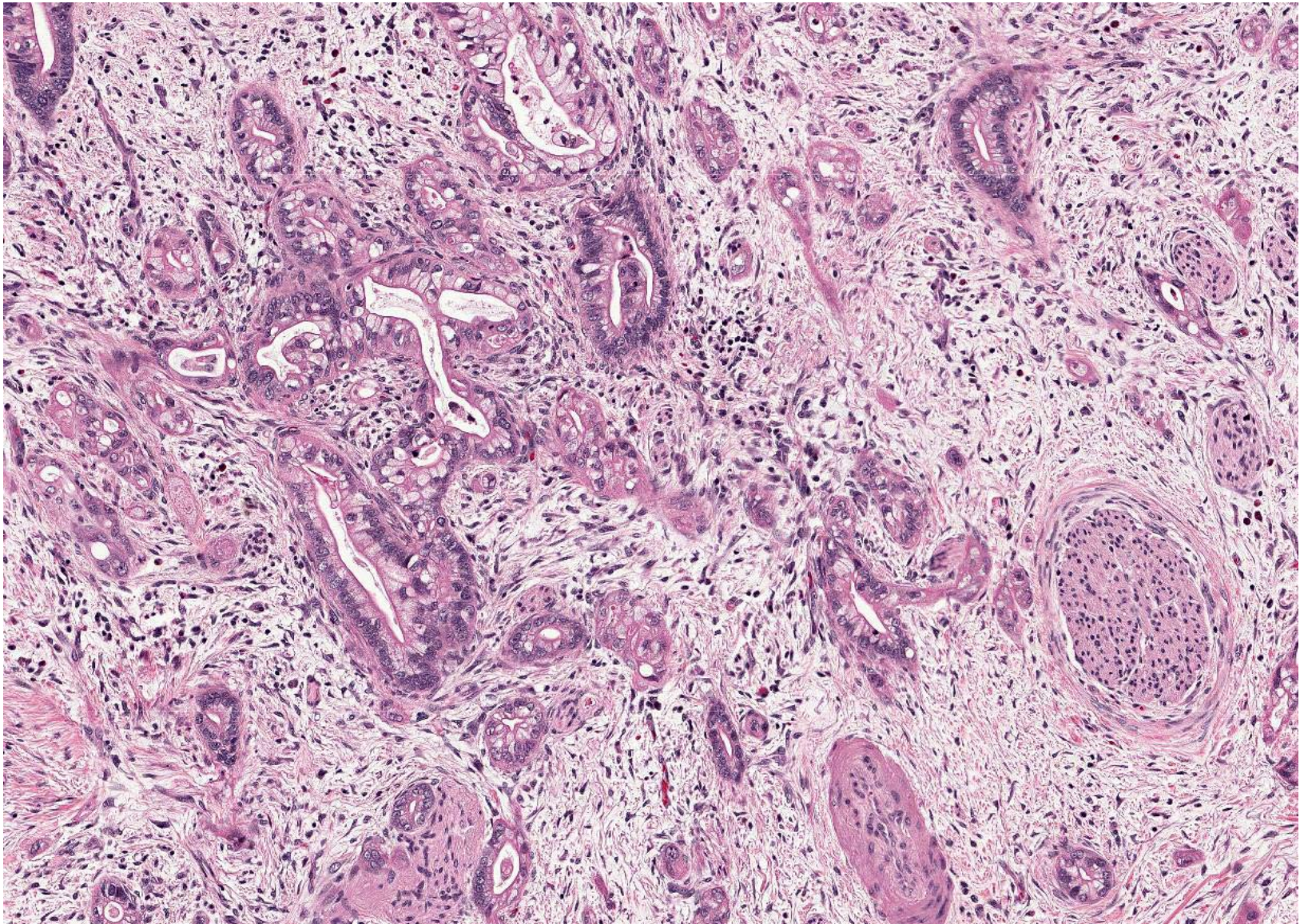
1821- 1902



## A 19<sup>th</sup> Century Definition of Cancer

- Cancer is uncontrolled cell growth, uncontrolled mitoses
- Cancerous cells spread and interfere with bodily functions.





Adenocarcinoma



A word cloud featuring various terms related to bioinformatics and genomics. The words are arranged in a roughly rectangular shape, with some terms being significantly larger than others. The colors of the words include shades of green, yellow, orange, red, and purple. The largest words are 'Bioinformatics', 'Microarrays', 'Genotyping', 'Genomics', 'Sequencing', and 'NGS'. Other prominent words include 'Variant', 'RNA', 'Methylation', 'Gene', 'DNA-seq', 'ChIP-seq', 'Transcriptomics', 'miRNA', 'Exome', 'NanoString', and 'nCounter'. Smaller words include 'CNV', 'Illumina', 'Caliper', 'allelic', 'profiling', 'samples', 'expression analysis', 'Qubit', 'PCR', 'Covaris', 'fluorescence-luminescence', 'ChIP-string', 'cBot', 'arrays', 'SNP', 'Green', 'Tecan', 'equencing', 'FFPE', 'Bioanalyzer', 'libraries', 'Tiling', 'arrays', 'TapeStation', 'DNA', 'Real-time', 'reader', and 'discrimination'.

Bioinformatics  
Microarrays  
Genotyping  
Genomics  
Sequencing  
NGS  
Variant  
RNA  
Methylation  
Gene  
DNA-seq  
ChIP-seq  
Transcriptomics  
miRNA  
Exome  
NanoString  
nCounter  
CNV  
Illumina  
Caliper  
allelic  
profiling  
samples  
expression analysis  
Qubit  
PCR  
Covaris  
fluorescence-luminescence  
ChIP-string  
cBot  
arrays  
SNP  
Green  
Tecan  
equencing  
FFPE  
Bioanalyzer  
libraries  
Tiling  
arrays  
TapeStation  
DNA  
Real-time  
reader  
discrimination



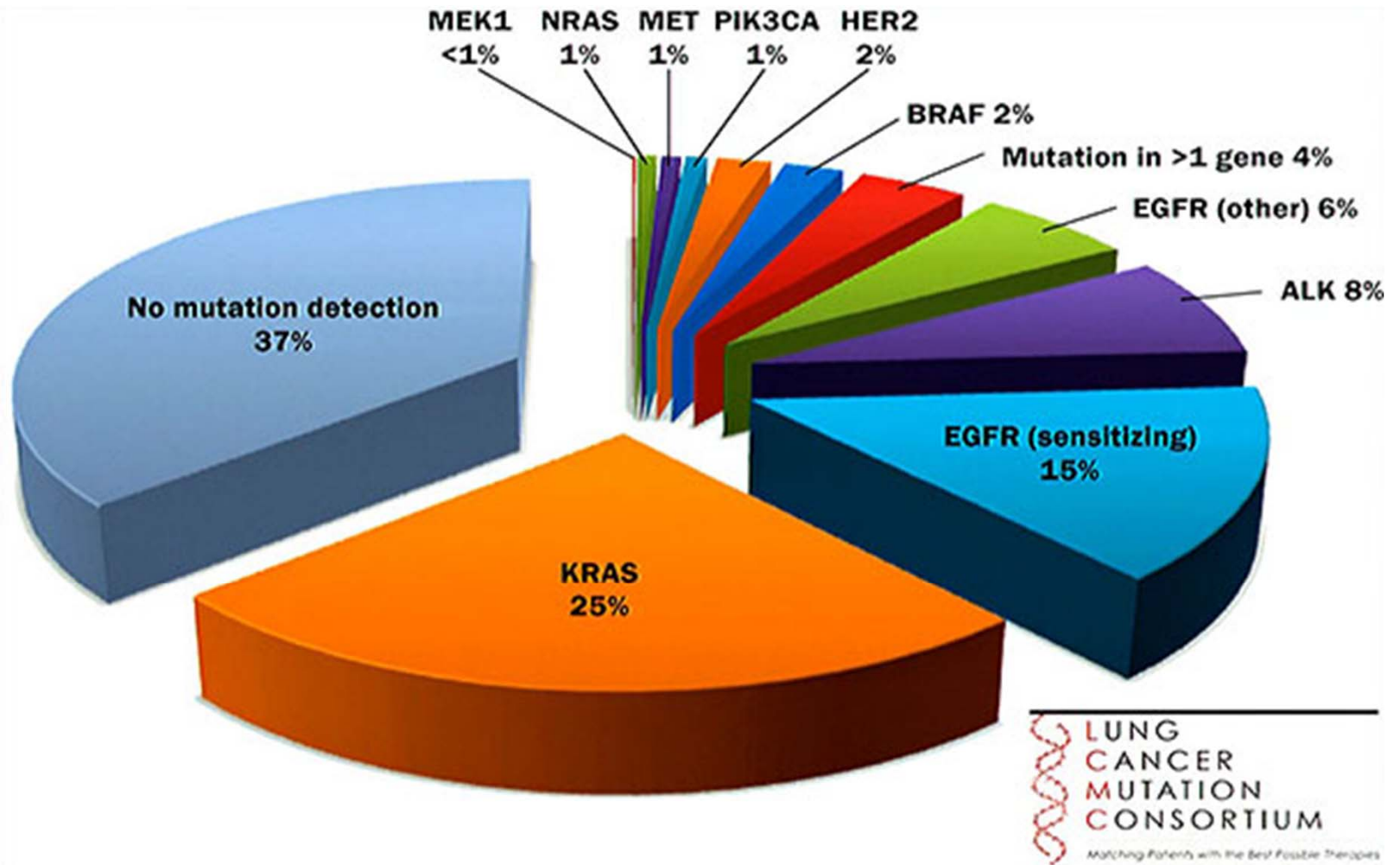
# A 21<sup>st</sup> Century Definition of Cancer

Involves histology and genomics

An understanding of the varying biologic behaviors of cancer based on histology and genomics.

Numerous molecular targets have and are being defined. Some are drugable targets.

# Non Small Cell Lung Cancer





# Oncotype Dx

for hormone receptor positive Her 2 Neu negative breast cancer

21 Gene Array Test  
Determines Therapy

Chemotherapy and  
Hormones

Hormones

Oncotype Dx can prevent 70,000 American women  
from receiving chemotherapy in 2018





# The American Healthcare System

## Inefficient!!!

- Some over consume resources  
(This can be harmful to the over-consumer)
- Some under consume resources  
(This is the cause of disparities)
- Healthcare outcomes could be better  
(People die needlessly)



# The American Healthcare System

## The True Cost of an Inefficiency

- More than 25,000 Americans die annually due to lack of healthcare
- More than 75,000 Americans die annually due to poor quality healthcare
- Thousands suffer because healthcare is not available to them

IOM 2006,  
Sathcer and Pamies 2006



## **The Most Important Question in Healthcare**

How can we provide adequate high quality care (to include preventive services) to populations that so often do not receive it?

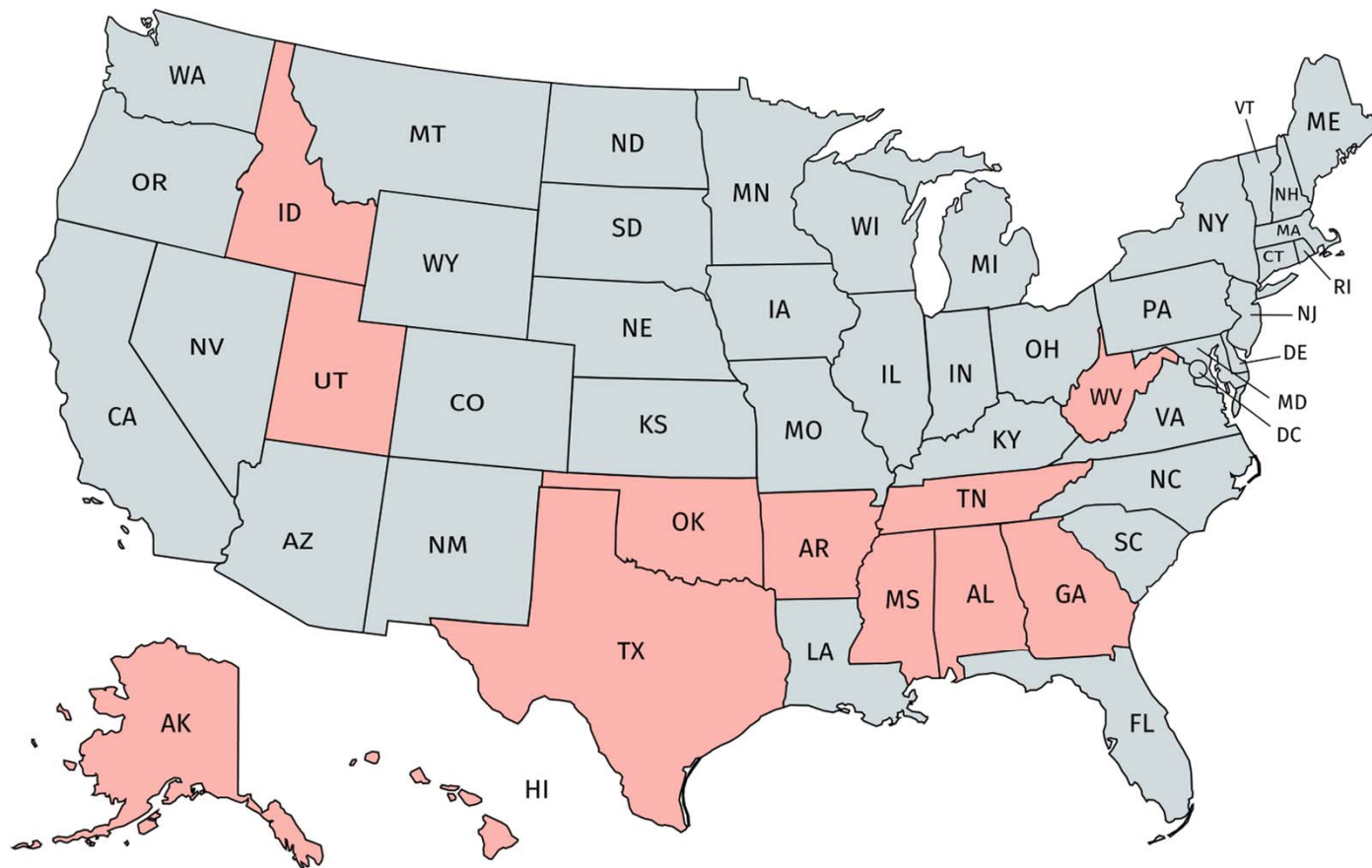
What if we applied what we already  
know about cancer?



## Applying Known Science (Prevention and Treatment)

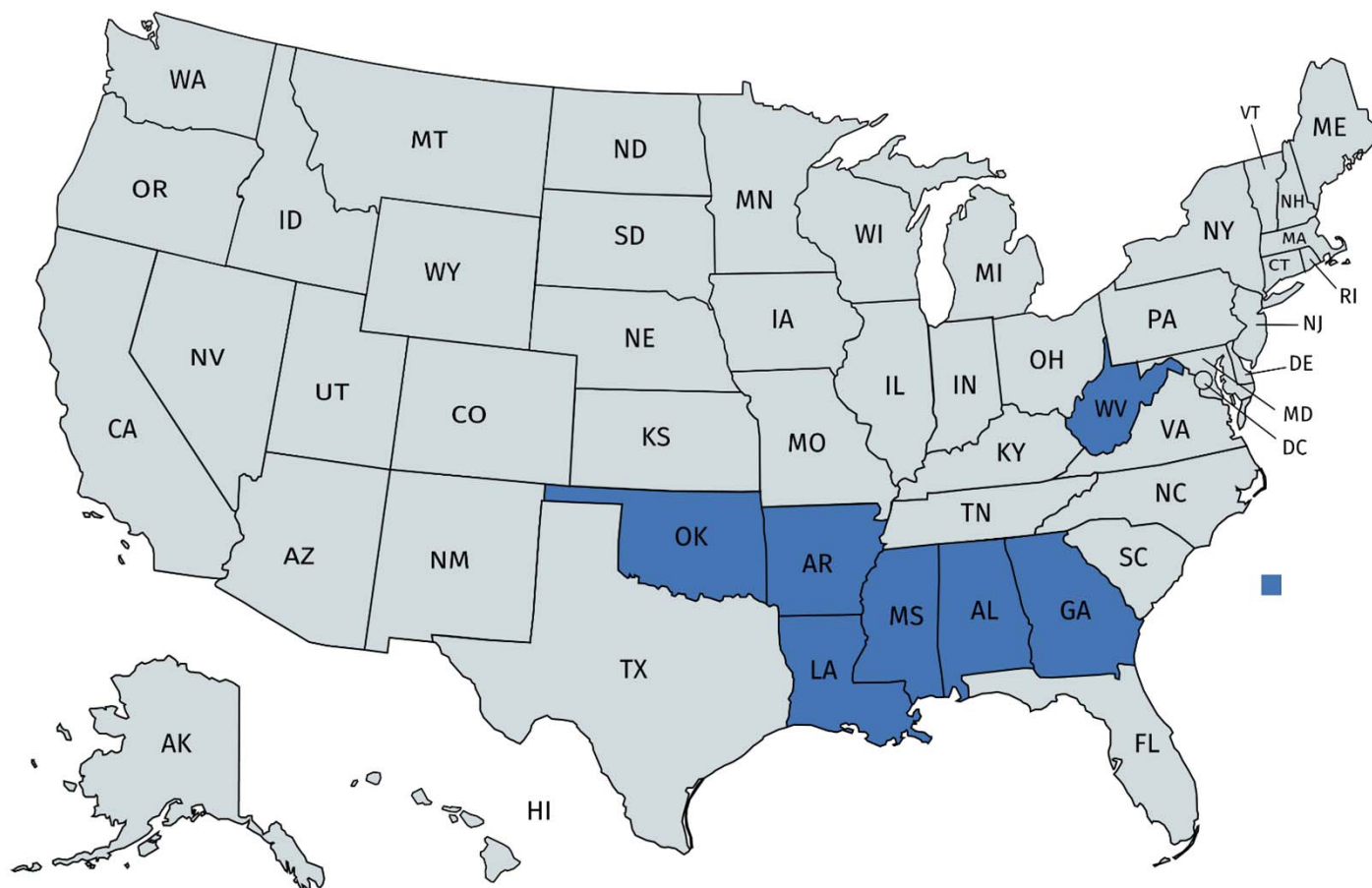
- 610,000 Americans will die of cancer this year.
- If all Americans had the cancer death rate of college educated Americans then 152,000 (25%) would not die.

There has been a 49% decline in age adjusted  
colorectal cancer death rates since 1981  
The shaded state have <30% decline





There has been a 39% decline in age adjusted  
colorectal cancer death rates since 1989  
The shaded state have <30% decline





## Access to Care

- It is not just having insurance
- It is healthy habits and access to:
  - Prevention
  - Screening
  - Diagnosis
  - Treatment



## A Brief History of A Discipline

- Minority Health
- Special Populations
- Health Disparities
- Health Equity



# Disparities in Health

Populations can be defined or categorized by:

- Gender
- Race
- Ethnicity and Culture
- Area of geographic origin
- Socioeconomic Status
- Urban vs Rural



# Minority Health

The Civil Rights Movement of the 1950's and 1960's.

Realization that there were Black/White differences in cancer death rate and survival.

- [Fontaine SA, Henschke UK, Leffall LD Jr, Mason CH, Reinhold AW, Schneider R, White JE Med Ann Dist Columbia. 1972 May;41\(5\):293-8.](#) Comparison of the cancer deaths in the black and white U.S.A. population from 1949 to 1967.
- [Howard J, Hankey BF, Greenberg RS, Austin DF, Correa P, Chen VW, Durako S.](#) A collaborative study of differences in the survival rates of black patients and white patients with cancer. Cancer. 1992;69:2349-2360.



# Minority Health

The Civil Rights Movement of the 1950's and 1960's.

- Increasing awareness of Sickle Cell Disease as a genetic disease associated with African ancestry
- Increasing awareness of different risk in other diseases by race.
  - Hypertension
  - Certain Cancers
  - Diabetes

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# Race Medicine

An old concept!!!

Used to justify slavery

Used to justify the Tuskegee Syphilis Experiment





## Race Medicine

The concept that diseases differ amongst the races due to “genetic” differences amongst populations.

The word “genetic” has baggage!!! It is a buzzword to disenfranchised people.



## Race Medicine

The concept of biologic differences led to the thought that disparities exist because our treatments do not work in Blacks.

We have to test our treatments in Blacks!

Few said or say disparities exist because Blacks do not get the treatment!!



## The NIH Revitalization Act of 1993

“Minorities must be included in Federally sponsored clinical trials.”

“In phase III trials, there must be valid subset analysis of the differences among the races.”



## The NIH Revitalization Act of 1993

Subset analysis by race, ethnicity and gender are required of all phase III clinical studies with initial funding after 1995.

Peer review must assess each funded project for inclusion and subset analysis.

This creates some serious scientific and ethical issues.



## Scientific and Ethical Issues

- The law implies that race is a biological categorization and disparities are due to “genetic” differences among the races!!!
- The law encourages researchers to “encourage” minority participation.



# Scientific and Ethical Issues

For those who know how to design clinical trials:

- Subset analysis should be avoided as they can be very wrong!
- Subset analysis often require over-sampling. An ethical issue, putting the minorities at greater risk and violating equipoise.



# Scientific and Ethical Issues

Subset analysis should be avoided as they can be very wrong!

The case against tamoxifen in the treatment of black women with breast cancer.

The original randomized trial was before the ER Receptor assay (a genetic test) was available.

- In a world without a defined estrogen receptor and a law requiring a valid subset analysis.
  - Tamoxifen is of little use in Black Women
- In a world with an estrogen receptor
  - Tamoxifen is a good drug for Black women and women of all races with ER Positive breast cancer



## Race

Carl Linnaeus – Systema Naturae, 1735

Caucasian

Negroid

Mongoloid





## Race

Defined by US Office of Management and Budget every ten years.

- Sociopolitical and not biologic according to OMB definition
- Rejected by Anthropological community as non-scientific
- Race changes over time\*



## Population Differences in Disease Outcome

Race is not a good surrogate for genetics/genomics.

We should strive for genetic/genomic diversity in clinical studies.



## Area of Geographic Origin and Genetics

Can correlate with family/genetics/tribe

- Sickle Cell Trait – Mediterranean Basin and sub-Saharan Africa
- Cystic Fibrosis – Northern Europe
- EtOH dehydrogenase deficiency – East Asia
- The Askenazi-Jewish Mutations of BRCA (one has been traced to a woman alive about 100 to 200AD. This brings about concept of family)



## Area of Geographic Origin and Genetics

- 12% of the Thai population and a smaller portion of the Malaysian population have a genomic predisposition to a skin reaction Stevens-Johnson Syndrome when administered carbamazepine (Tegretol)
- Identifying these people can save lives by preventing use of drugs known to cause Stevens-Johnson Syndrome
- Populations profiling, is it ethical?



# Population Science

- Genomics may :
  - Define populations at risk of disease
  - Define subsets of disease
  - Predict response to treatment
- Genomics is a scientific/objective way of defining or categorizing populations



“The ultimate goal is for medicine to become so personalized from a “fingerprint” of one’s biologic makeup, not from racial typecasting.”

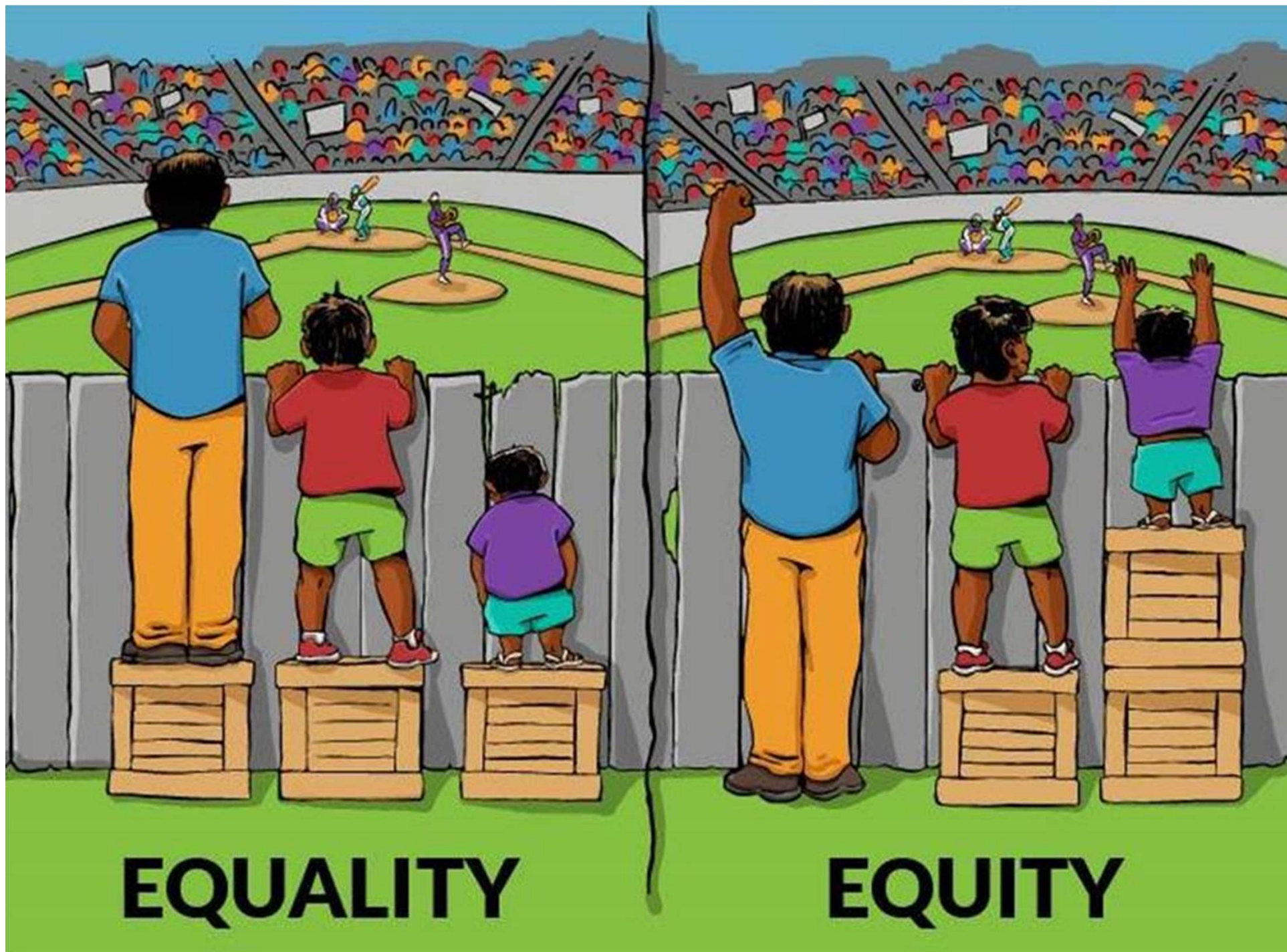
Keith Norris, MD



## **The Most Important Question in Health Disparities Research**

How can we provide adequate high quality care (to include preventive services) to populations that so often do not receive it?









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