

# Using Genetics to Improve Breast Cancer Outcomes and Reduce Health Inequities

**Olufunmilayo I Olopade, MB,BS, FACP**

Walter L. Palmer Distinguished Service Professor

Department of Medicine & Human Genetics

Associate Dean for Global Health

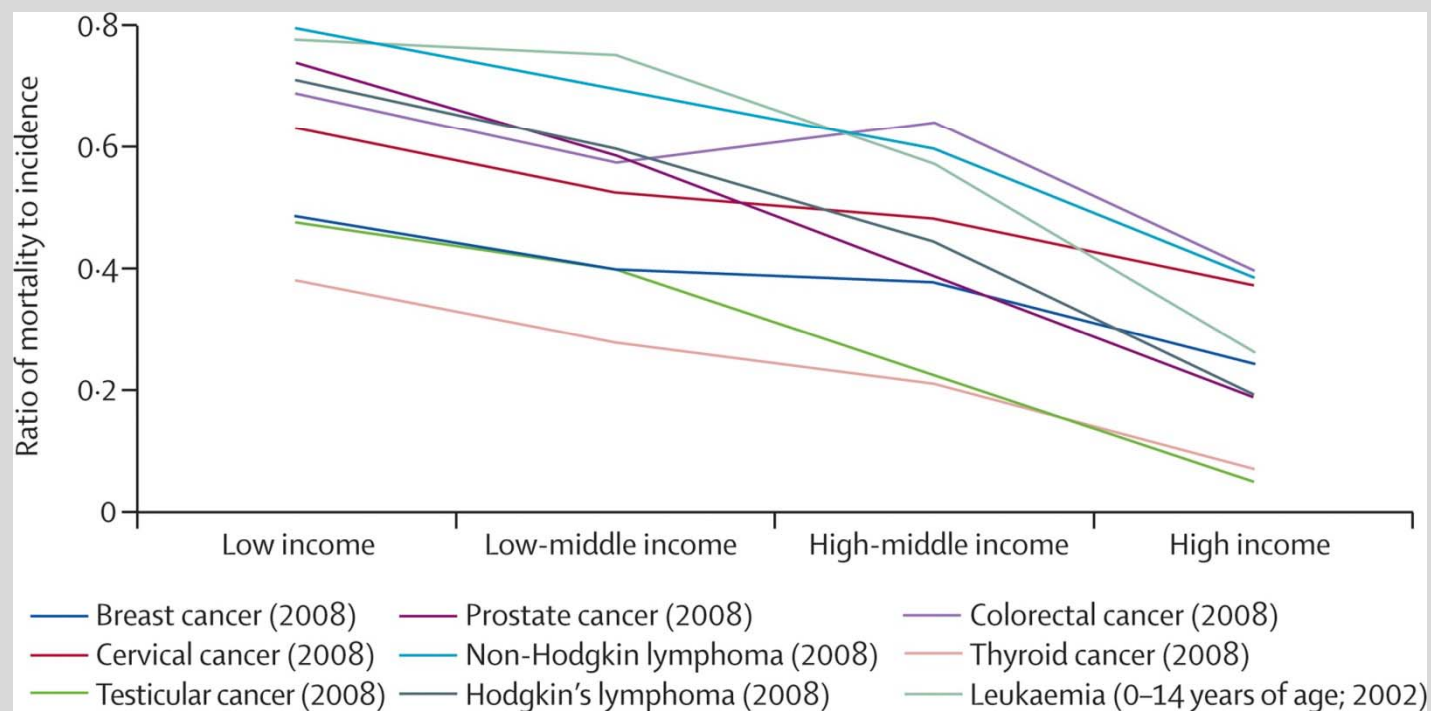
The University of Chicago

# Why reduce health inequalities?

- Inequalities are unfair
  - a consequence of unjust distribution of underlying social determinants of health (employment, education)
- Inequalities affect everyone
  - spillover effects on the whole society- spread of infectious disease, consequence of alcohol and drug misuse (crime and violence), health care cost (insurance, government)
  - Interventions to reduce social inequality will have additional benefits beyond improving health
- Inequalities are avoidable
  - health inequalities may actually be as a result of govt policies (tax, welfare benefits, health care funding). They are however amenable to 'targeted policies'
- Interventions to reduce health inequalities are affordable
  - improving access to health will reduce socioeconomic disparities in health

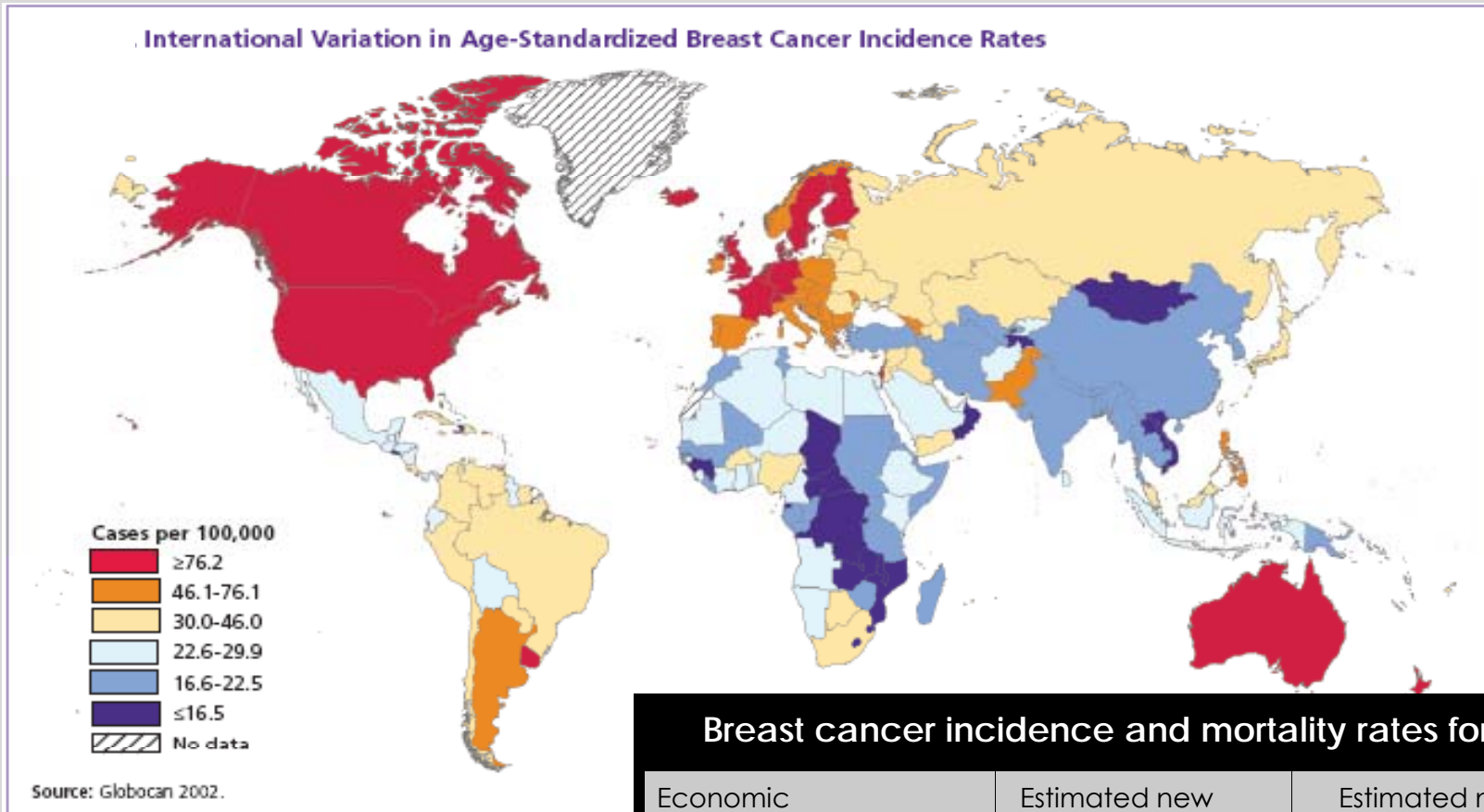
Adapted from **Why reduce health disparity**; Woodward A, et al, J Epi Comm Health, 2000 and **Benzeval M et al, Tackling inequalities in health: an agenda for action**; King's fund 1995

# Ratio of Mortality to Incidence by Cancer Type and Country Income



Estimates are based on International Agency for Research on Cancer GLOBOCAN data for 2002 and 2008 (<http://globocan.iarc.fr>)  
P. Farmer, et al, Lancet 2010

# Breast Cancer As a Global Problem

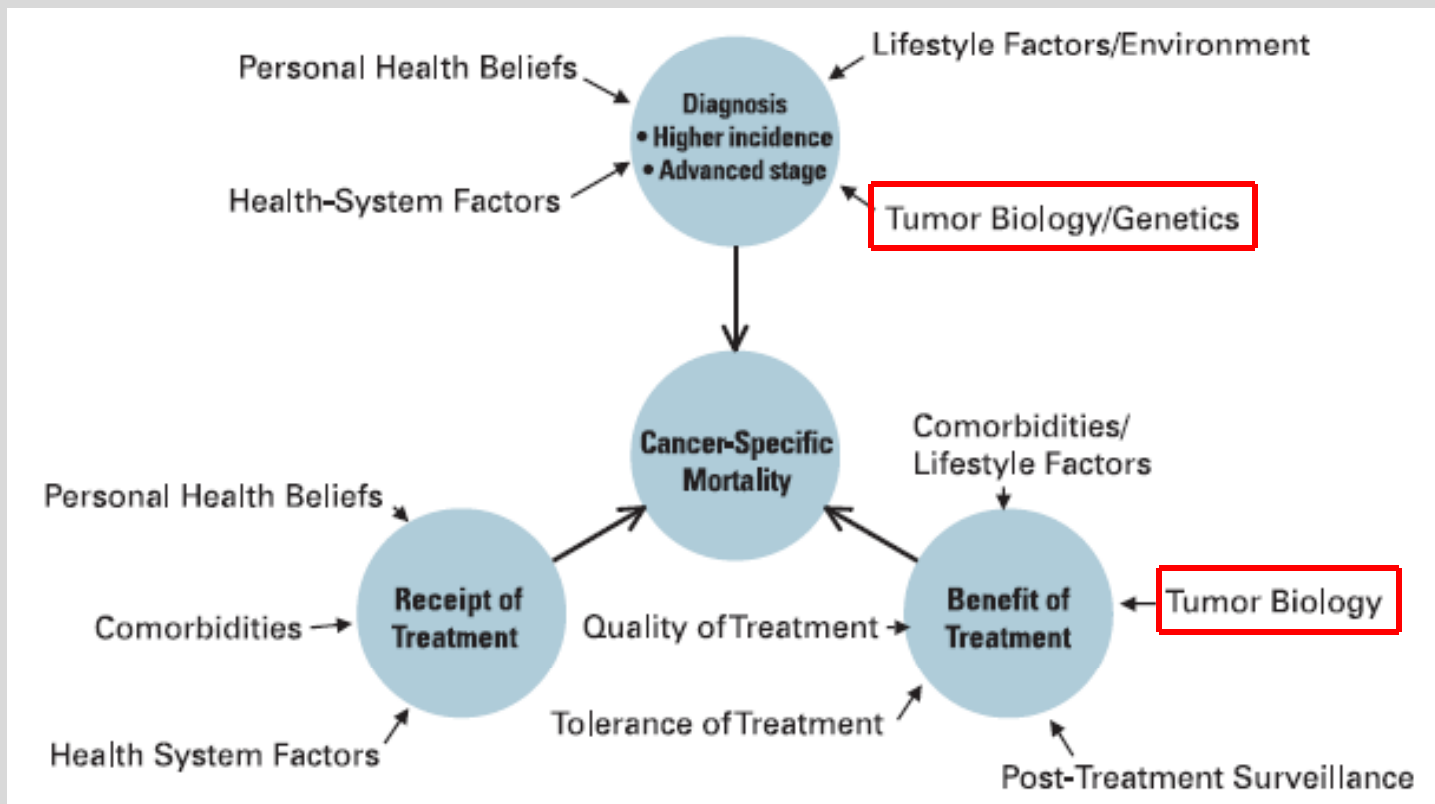


**Breast cancer incidence and mortality rates for 2007**

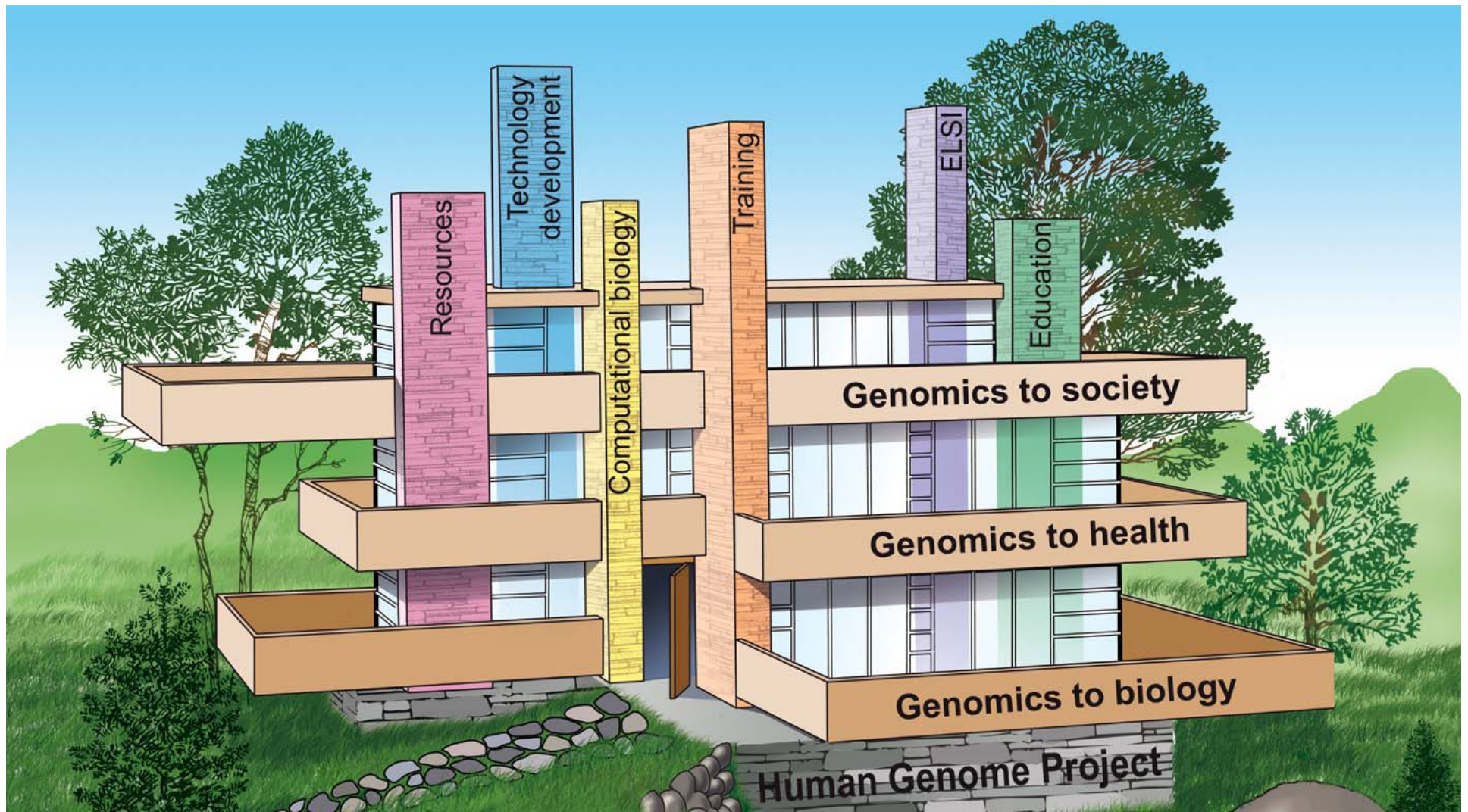
Economic development	Estimated new cases	Estimated new deaths
<b>Worldwide</b>	1,301,867	464,854
<b>High Income countries</b>	679,682	203,528
<b>Resource poor countries</b>	593,233	255,576

ACS global cancer facts and figures 2007

# Factors Contributing to Disparate Cancer Outcomes



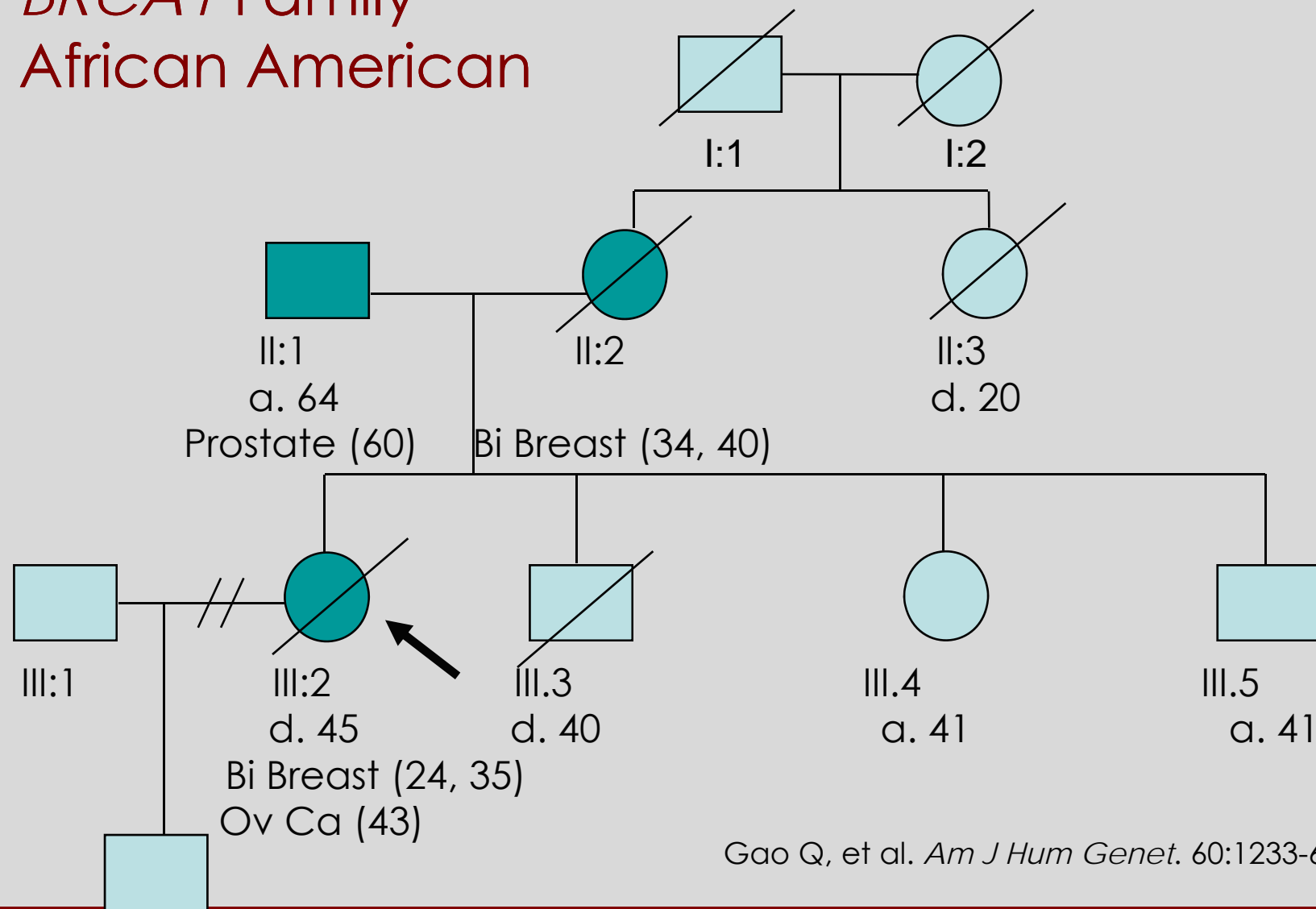
Polite BN, Dignam JJ, Olopade OI. JCO 24:2179, 2006



“Research is needed to understand the relationship between genomics and health disparities by rigorously evaluating the diverse contributions of socioeconomic status, culture, discrimination, health behaviors, diet, environmental exposures and **genetics**.”

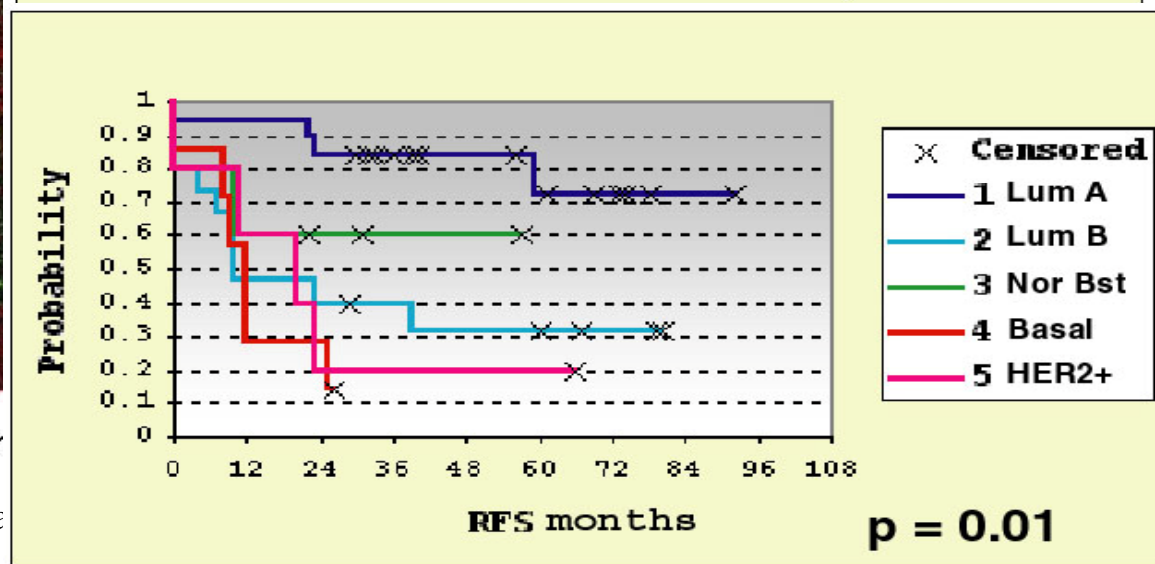
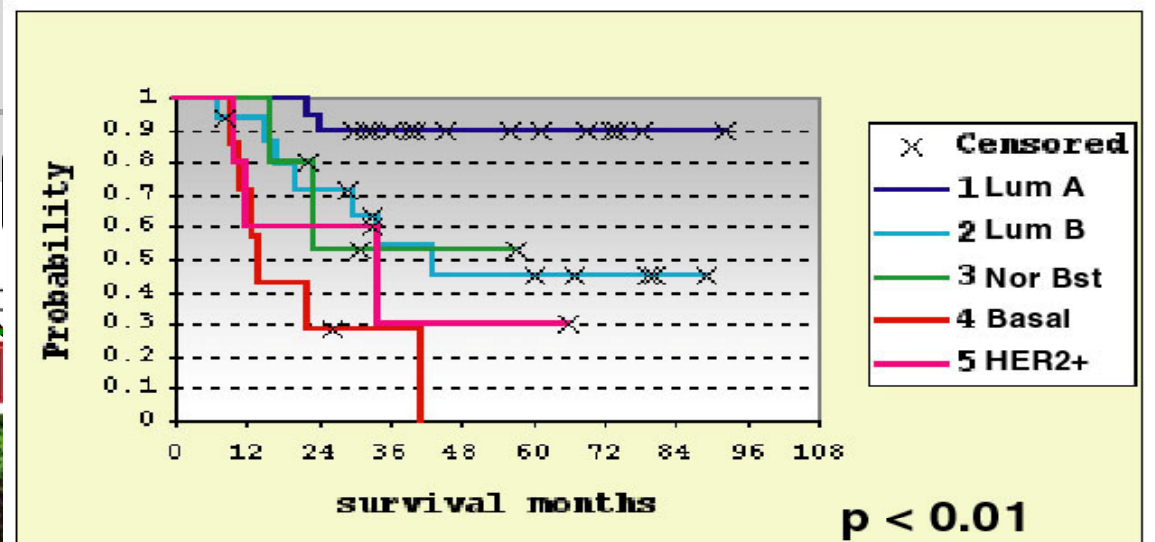
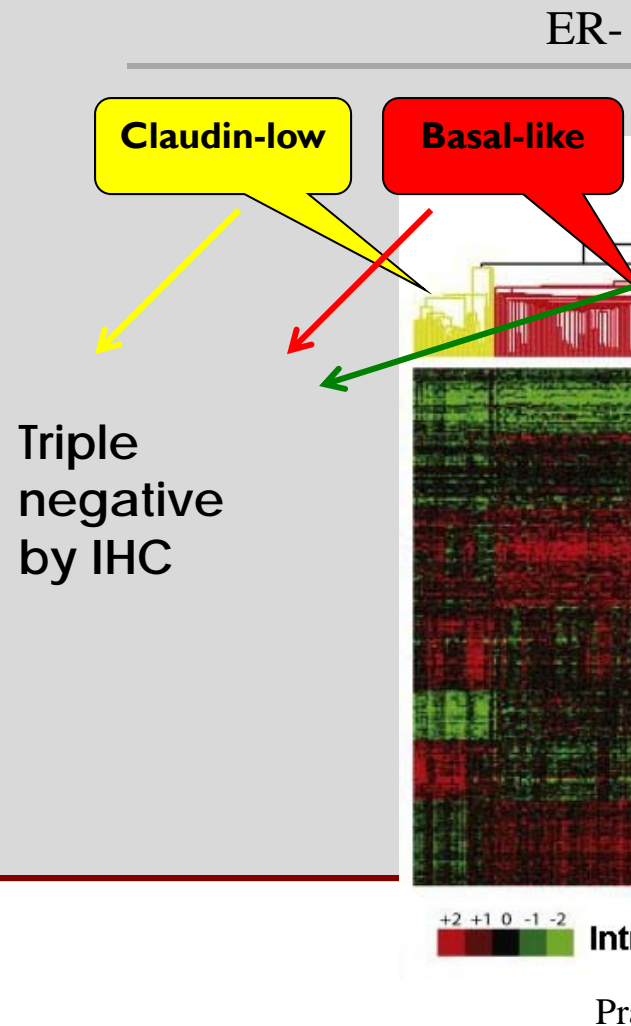
Collins et al., Nature 4/24/03

# BRCA1 Family African American



Gao Q, et al. *Am J Hum Genet.* 60:1233-6, 1997

# Breast Cancer Is Not One Disease





# Estimated Basal-like Breast Cancer Deaths

## Descriptive Analysis of Estrogen Receptor (ER)-Negative, Progesterone Receptor (PR)-Negative, and HER2-Negative Invasive Breast Cancer, the So-called Triple-Negative Phenotype

*A Population-Based Study From the California Cancer Registry*

Katrina R. Bauer, MS CTR<sup>1</sup>  
Monica Brown, PhD<sup>2</sup>  
Rosemary D. Cress, DrPH<sup>1,3</sup>  
Carol A. Parise, PhD<sup>4</sup>  
Vincent Caggiano, MD<sup>4,5</sup>

<sup>1</sup> Public Health Institute/California Cancer Registry, Sacramento, California.

<sup>2</sup> Public Health Institute/Cancer Surveillance Program, Sacramento, California.

<sup>3</sup> Department of Health Sciences, Division of Epidemiology, UC Davis, California.

<sup>4</sup> Sutter Institute for Medical Research, Sacramento, California.

<sup>5</sup> Sutter Cancer Center/Cancer Surveillance Program, Sacramento, California.

**BACKGROUND.** Tumor markers are becoming increasingly important in breast cancer research because of their impact on prognosis, treatment, and survival, and because of their relation to breast cancer subtypes. The triple-negative phenotype is important because of its relation to the basal-like subtype of breast cancer.

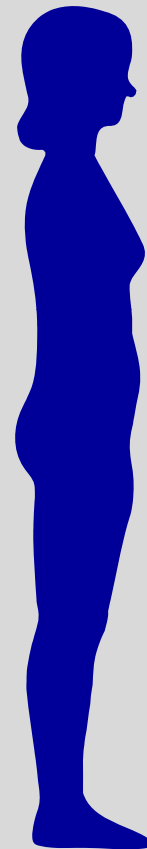
**METHODS.** Using the population-based California Cancer Registry data, we identified women diagnosed with triple-negative breast cancer between 1999 and 2003. We examined differences between triple-negative breast cancers compared with other breast cancers in relation to age, race/ethnicity, socioeconomic status (SES), stage at diagnosis, tumor grade, and relative survival.

**RESULTS.** A total of 6370 women were identified as having triple-negative breast cancer and were compared with the 44,704 women with other breast cancers. Women with triple-negative breast cancers were significantly more likely to be under age 40 (odds ratio [OR], 1.53), and non-Hispanic black (OR, 1.77) or Hispanic (OR, 1.23). Regardless of stage at diagnosis, women with triple-negative breast cancers had poorer survival than those with other breast cancers, and non-Hispanic black women with late-stage triple-negative cancer had the poorest survival, with a 5-year relative survival of only 14%.

**CONCLUSIONS.** Triple-negative breast cancers affect younger, non-Hispanic black and Hispanic women in areas of low SES. The tumors were diagnosed at later stage and were more aggressive, and these women had poorer survival regardless of stage. In addition, non-Hispanic black women with late-stage triple-negative breast cancer had the poorest survival of any comparable group. *Cancer* 2007;109:1721-8.

© 2007 American Cancer Society.

Women  
271,530



- 26% Lung (71,000)
- 9% Colon (27,000)
- 9% Breast Luminal (~27,000)
- 6% Pancreas (16,000)
- 6% Ovary (16,000)
- 5% Breast Basal-like (~13,000)
- 3% Leukemia (9,000)
- 3% Non-Hodgkin lymphoma (9000)
- 3% Uterine corpus (7000)
- 2% Brain/ONS (5000)
- 2% Liver (5000)
- 23% All other sites



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Ethnicity and Breast Cancer in the  
Women's Health Initiative: A Unifying  
Concept for Unfavorable Outcome in  
African American Women

R.T. Chlebowski et al. JNCI 2005

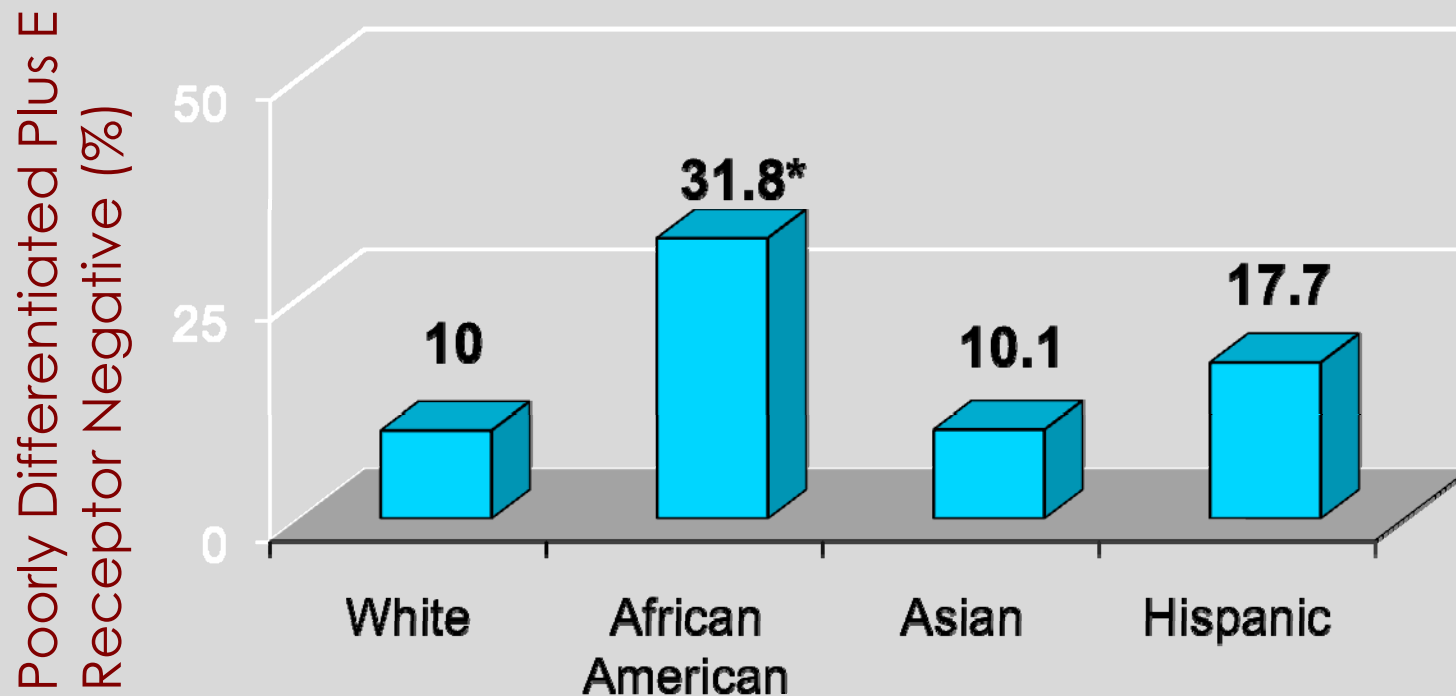
# Breast Cancer Incidence by Ethnicity/Race

Ethnicity/Race	Number	Breast Cancers
White	129,037	3,455
African American	14,170	242
Hispanic	6,388	103
Asian/Pacific Islander	4,114	88
Unknown	2,165	39
American Indian/ Native Alaskan	696	11

During 6.3 years median follow-up

R.T. Chlebowski et al. 2005

# Combined Poorly Differentiated plus ER Negative by Ethnicity/Race



\* HR 4.70, 95% CI 3.12-7.09

# Genetic Testing in an Ethnically Diverse Cohort of High-Risk Women: A Comparative Analysis of BRCA1 and BRCA2 Mutations in American Families of European and African Ancestry

Rita Nanda; L. Philip Schumm; Shelly Cummings; et al.

JAMA. 2005;294(15):1925-1933 (doi:10.1001/jama.294.15.1925)

**Table 4.** Recurrent Mutation Characteristics

Mutation	Family Race/Ethnicity*	Mean Age at Breast Cancer Diagnosis, y	No. of Breast and Ovarian Cancers in First- and Second-Degree Relatives†
185delAG (n = 9)	Ashkenazi Jewish	41	4
	Ashkenazi Jewish	40	4
	Ashkenazi Jewish	40	3
	Ashkenazi Jewish	41	1
	Ashkenazi Jewish	33	2
	Ashkenazi Jewish	51	3
	Ashkenazi Jewish	40	2
	Ashkenazi Jewish	53	1
1832del45 (n = 2)	White (German)	38	1
	African American	47	4
5296del4 (n = 2)	African American	43	2
	African American	36	1
5385insC (n = 6)	Ashkenazi Jewish	46	4
	Ashkenazi Jewish	39	2
C81G (n = 3)	Ashkenazi Jewish	47	2
	Ashkenazi Jewish	42	2
	Ashkenazi Jewish	48	3
	Ashkenazi Jewish	51	8
	White (German)	58	3
5950delCT (n = 3)	White (Polish)	50	2
	White (German)	45	4
	Ashkenazi Jewish	29	2
6174delT (n = 6)	White (German)	47	5
	White (German)	42	3
	White (German)	52	2
6174delT (n = 6)	Ashkenazi Jewish	48	3
	Ashkenazi Jewish	57	6
	Ashkenazi Jewish	65	4
	Ashkenazi Jewish	36	5
	Ashkenazi Jewish	56	3
	Ashkenazi Jewish	47	3

\*White defined as non-Hispanic, non-Jewish.  
†Count does not include proband.

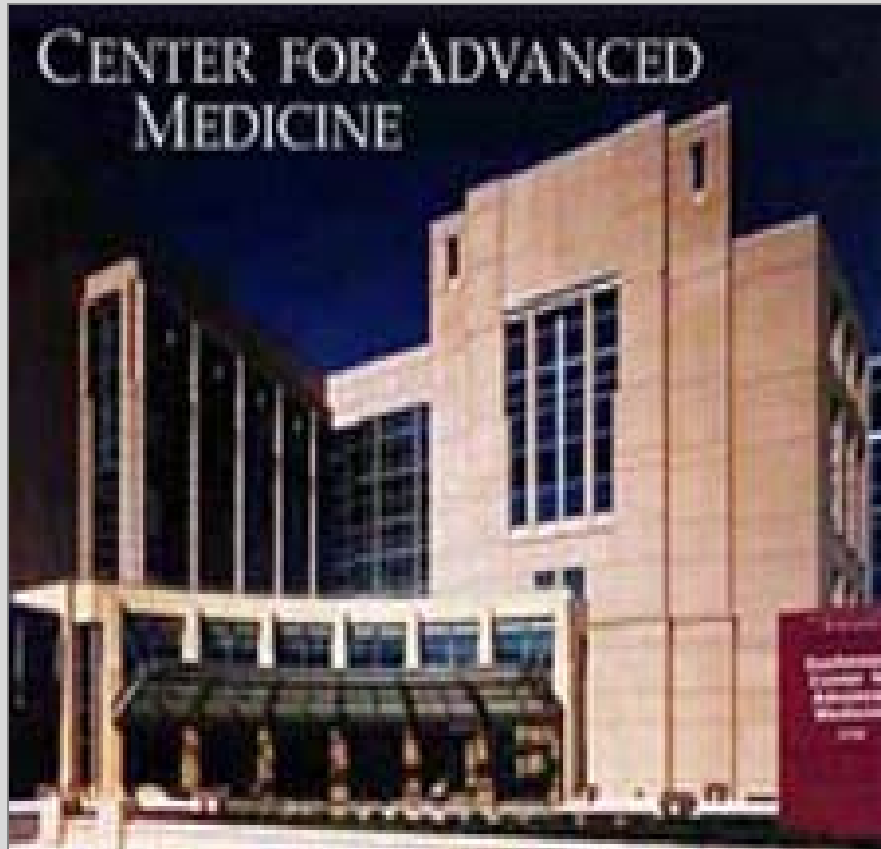
African Americans had the highest rate of unclassified variants and remained understudied

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# Chicago-Ibadan Partnership



# Nigerian Breast Cancer Study

## Genetics of Breast Cancer Case Control Study

Established in 1998

*BRCA1/2*

*Other Genes*

### Case ascertainment:

- University of Ibadan College Hospital
- All consecutive cases  $\geq 18$  years
- Refusal rate = 4%

### Control selection:

- Community-based
- Female,  $\geq 18$  years old
- Without any type of cancer

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## Prevalence of *BRCA1* and *BRCA2* Mutations in Nigerian Breast Cancer Cases (unselected)

	No. Screened	Percent with deleterious mutations+	
		<i>BRCA1</i> (%)	<i>BRCA2</i> (%)
All subjects	434	31 (7.1)	17 (3.9)
Age < 50	265	25 (9.4)	9 (3.4)
Age ≥ 50	169	6 (3.6)	8 (4.7)
Family Hx	44	7 (15.9)*	2 (4.5)

\*p<0.05

+11 were recurring mutations

Gao Q, Adebamowo CA et al. Hum Genet. 107:192-4, 2000

Adebamowo CA, Ogundiran TO et al. Ann Epidemiol. 13:455-61, 2003

Fackenthal JD, Sveen L et al. J Med Genet. 42:276-81, 2005

Zhang J, Fackenthal JD et al. Breast Cancer Res Treat;124:573-7, 2010



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# *BRCA1* Tumors Have a Distinct Phenotype






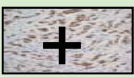











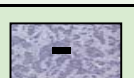




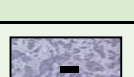


- ◆ Medullary and atypical medullary
- ◆ High mitotic rate
- ◆ Aneuploid
- ◆ High proliferation fraction
- ◆ **ER negative, PR negative**
- ◆ **No HER2 gene amplification**
- ◆ Frequent *Tp53* mutations
- ◆ **Similar to pattern described for young African American women**

Breast Cancer Linkage Consortium  
Crook T et al., Lancet, 1997  
Grushko et al. Cancer Research, 2002

# African Diaspora & Breast Cancer

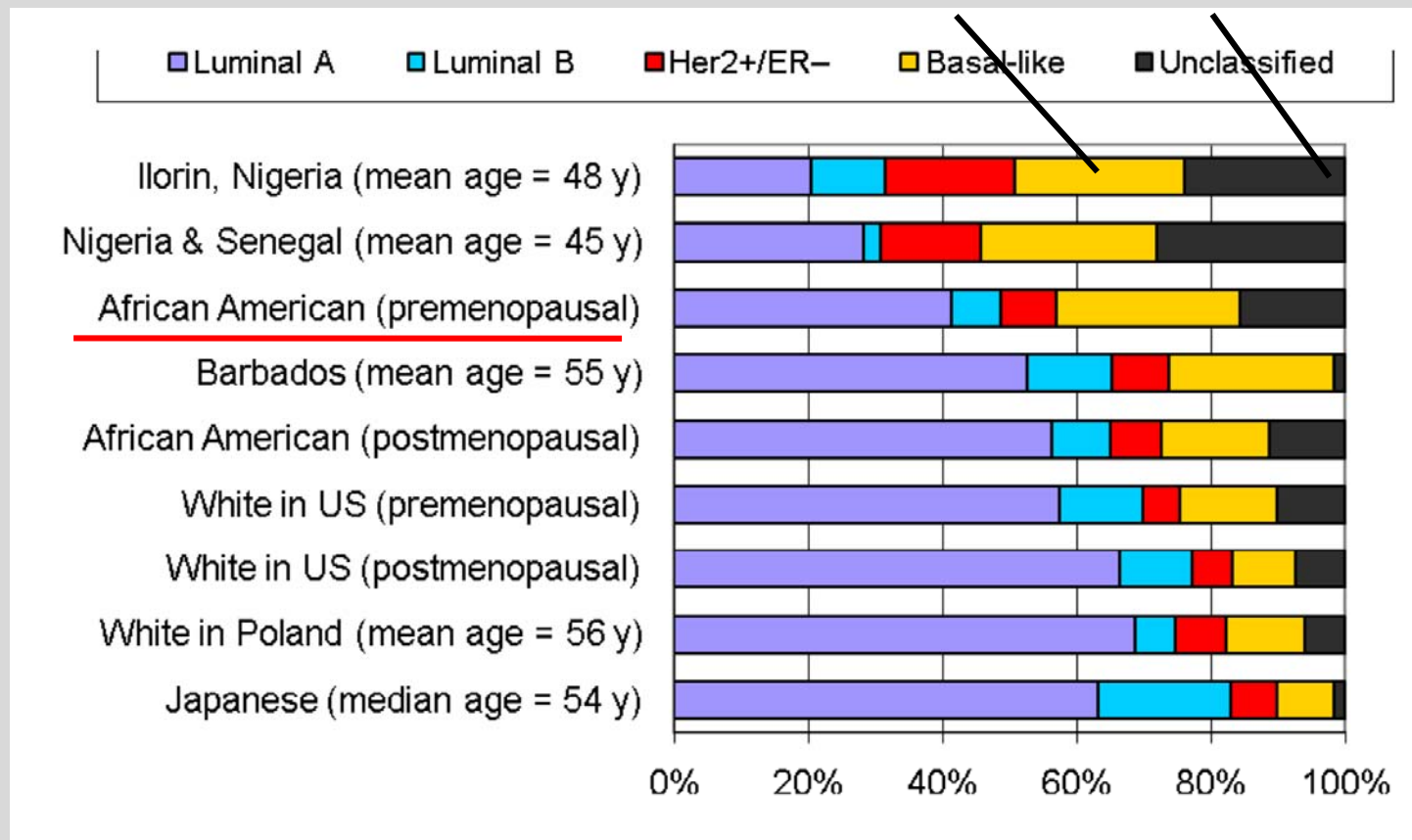


# Classification of Breast Cancers Using Immunohistochemical Profiles

Subtype	Marker				
	ER	PR	HER2	CK5/6	EGFR
Luminal A					
Luminal B					
HER2+/ER-					
Basal-like					
Unclassified					

TNBC

# Population Differences in Breast Cancer: Survey in Indigenous African Women Reveal Overrepresentation of Triple Negative Breast Cancer.



Huo D, Ikpatt OFR et al. JCO 27:4515-21, 2009

Data abstracted from Adeniji et al. 2010, Yang et al 2007

Kurebayashi et al. 2007



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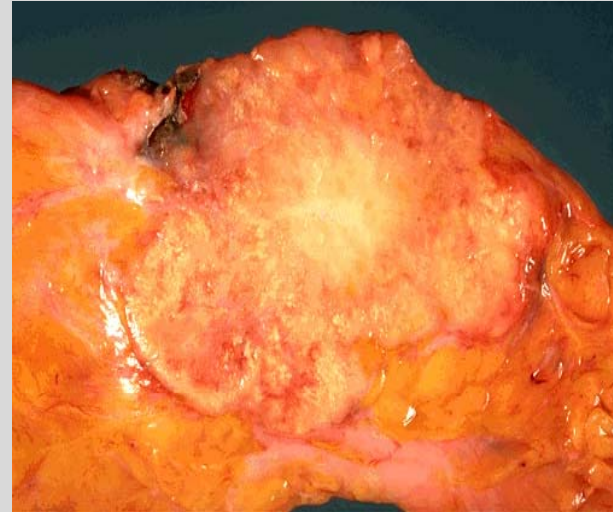
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# West African Breast Cancer Study

mean age  $43.8 \pm 11.2$  years



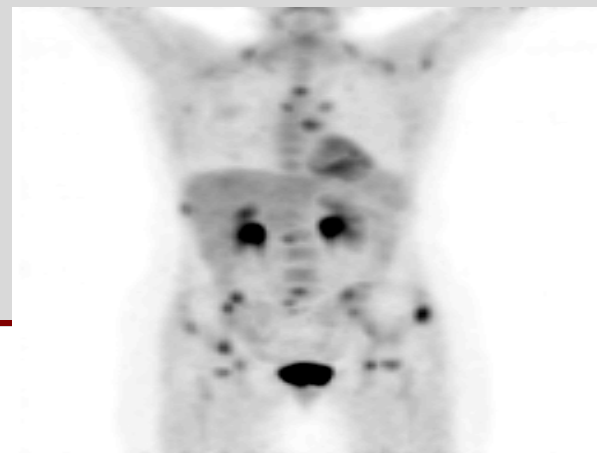
tumor size mean  $4.2 \pm 1.3$ cm



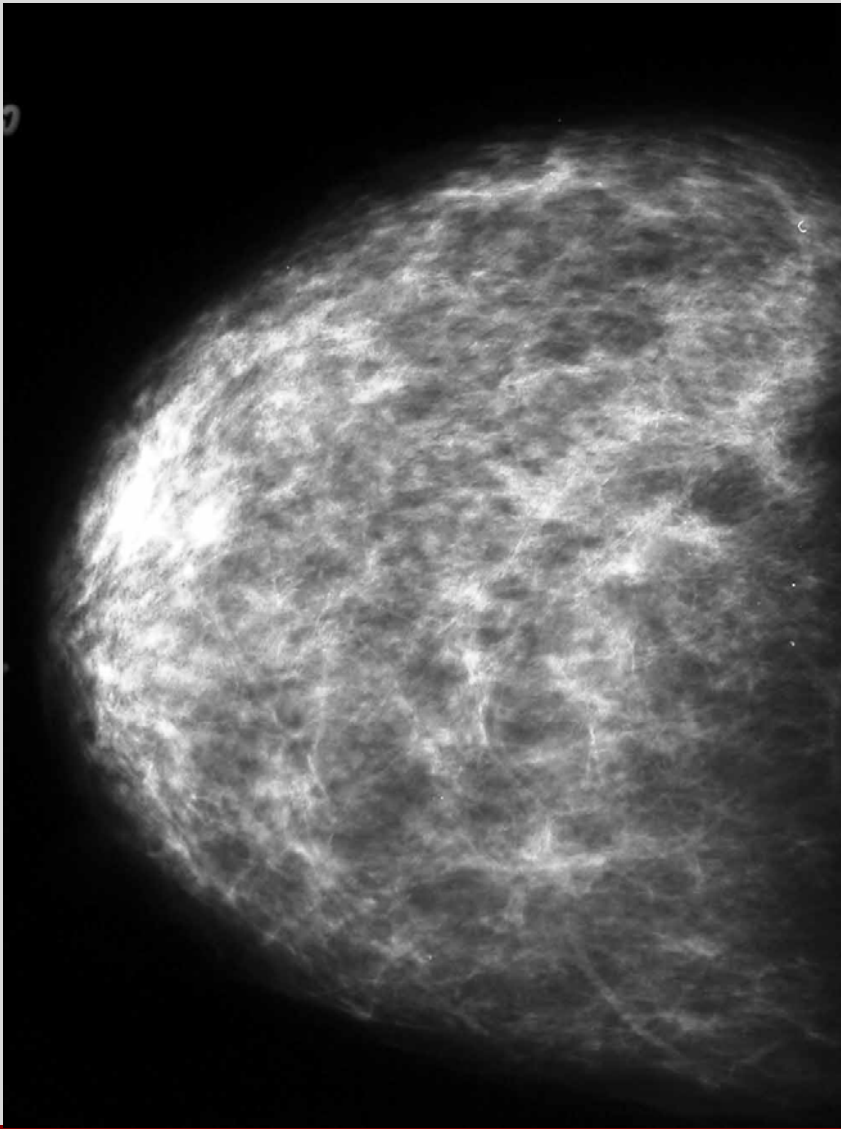
66.9% are premenopausal



73% are advanced (stages III and IV)

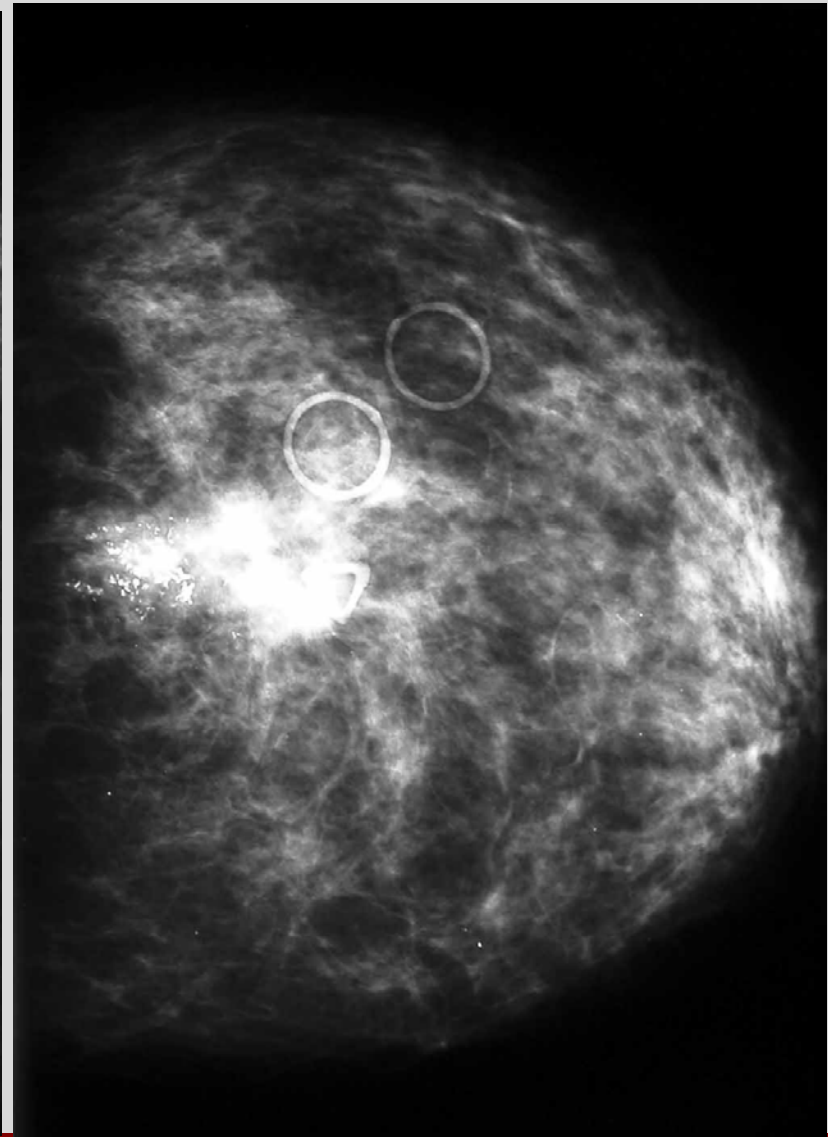


# TNBC in a 68 yr old Caucasian from Chicago



03/06/03

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i



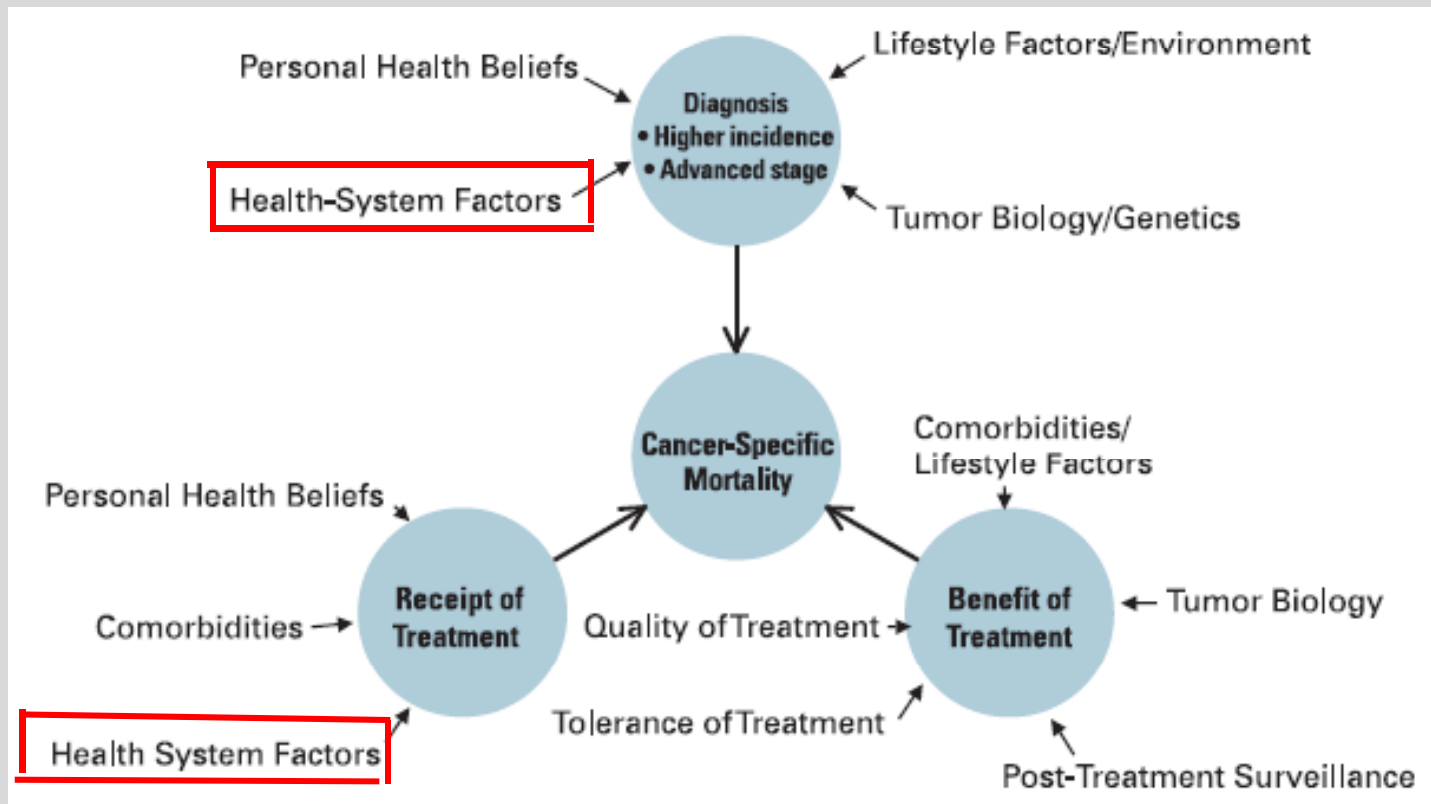
03/08/05



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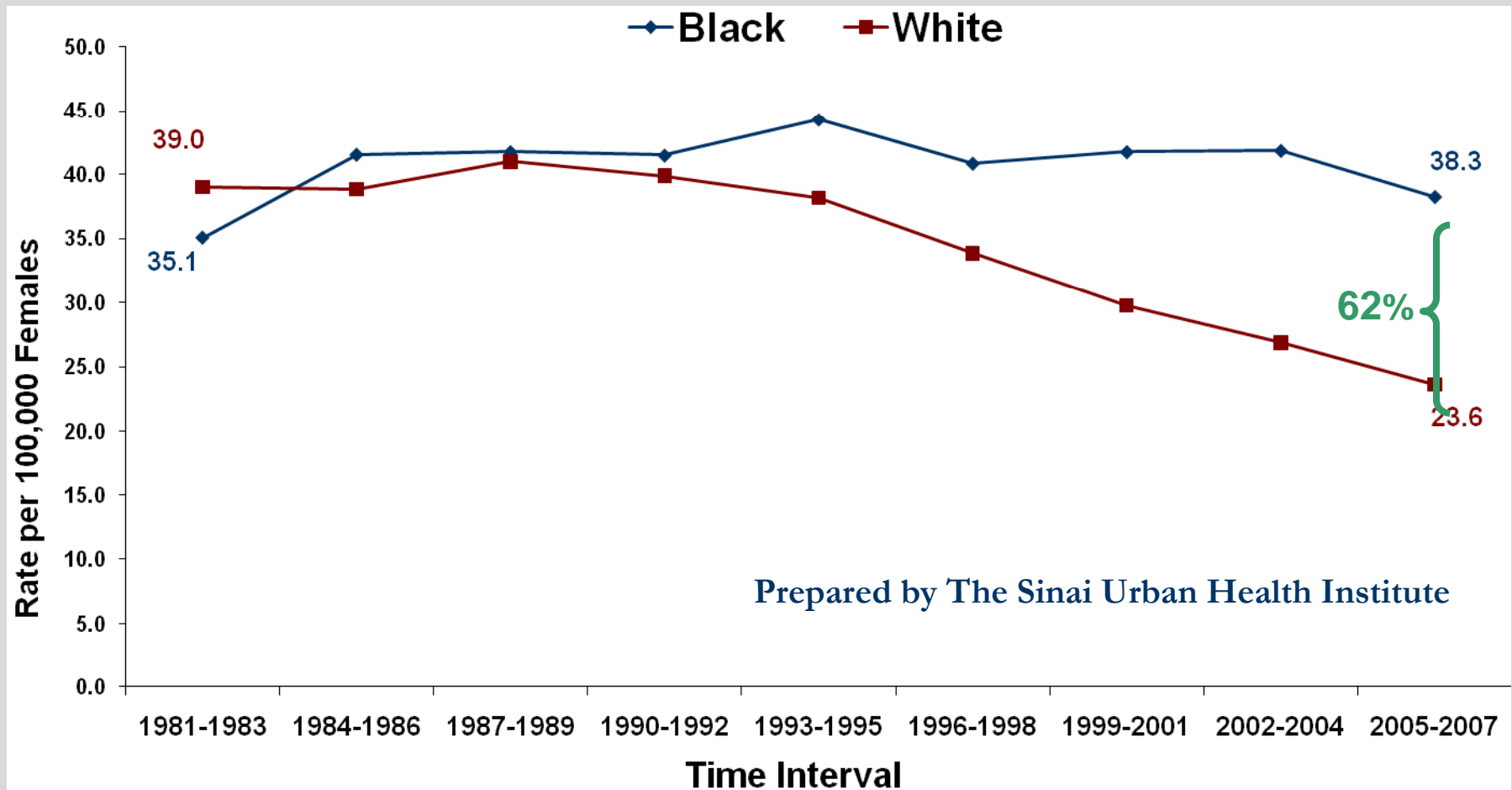
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# Factors Contributing to Disparate Cancer Outcomes



Polite BN, Dignam JJ, Olopade OI. JCO 24:2179, 2006

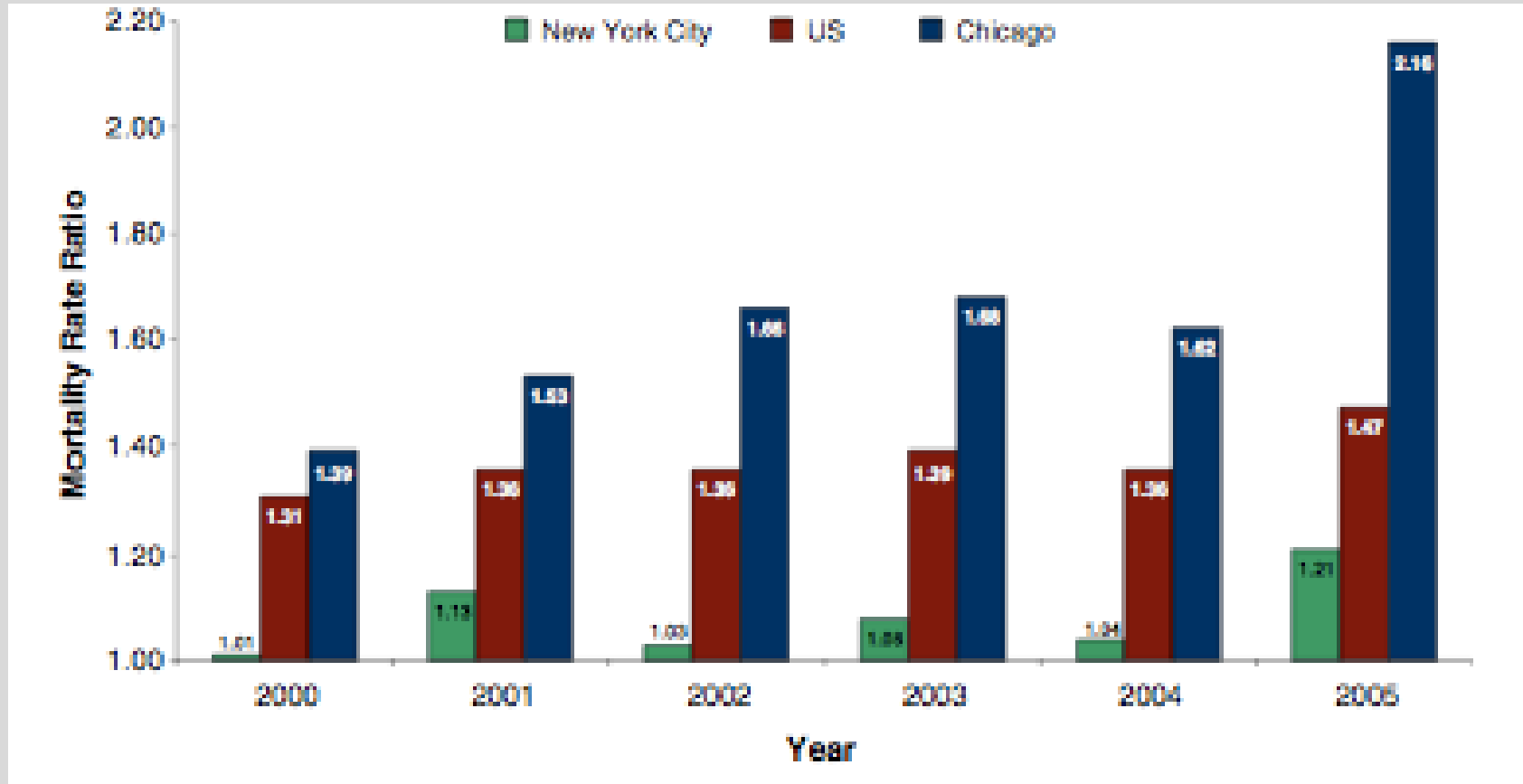
# Black and White Breast Cancer Mortality Chicago, 1981-2007



Age-Adjusted Female Breast Cancer Mortality for Chicago, Per 100,000 Population



# Breast Cancer Mortality Disparity 2000-2005

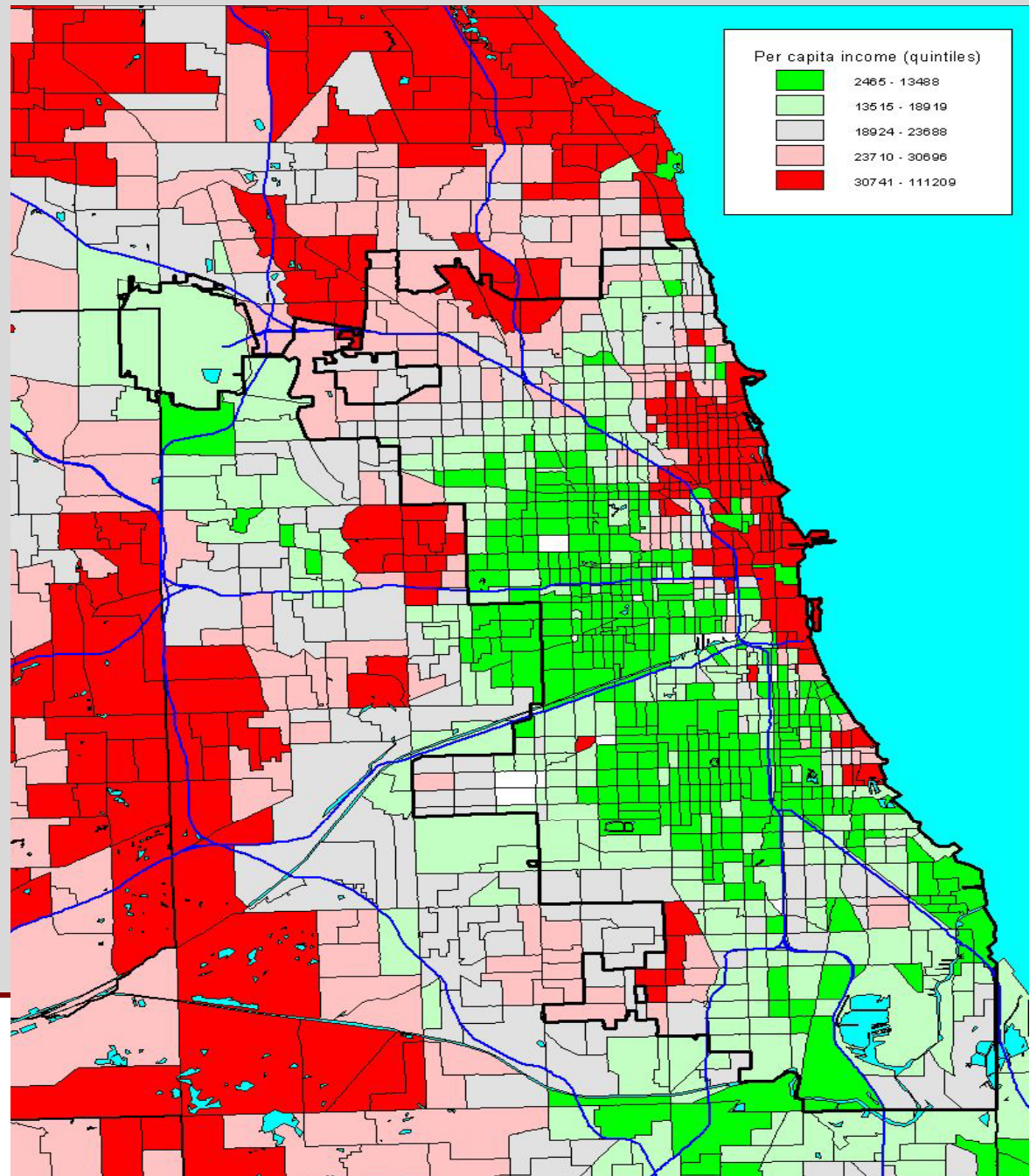
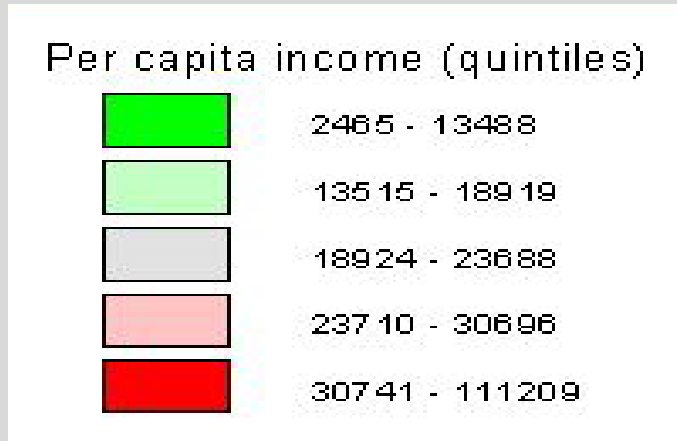


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# Per Capita Income By Census Tract, Metro Chicago, 1999





# Mercy Hospital – Chicago, IL Motivational Study

Eileen Knightly, RN

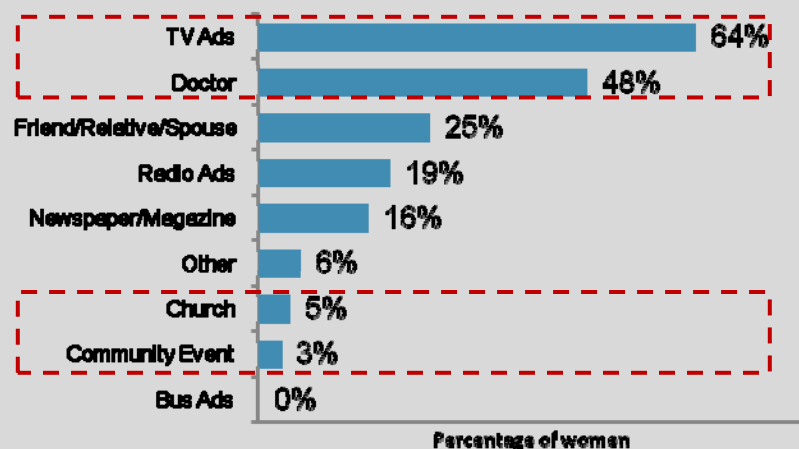
Alejandra Perez-Tamayo, MD FACS

in partnership with

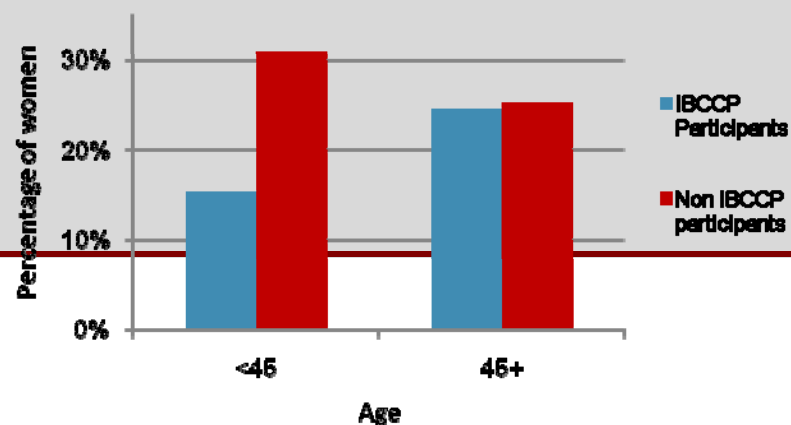
Accenture, sanofi and the University of Chicago

# An overwhelming majority of women reported advertisements and doctors as the main source of breast cancer messages.

**Top two responses of breast cancer message source**



**Women citing "Friend/Relative/Spouse" as a major source of messages**



Question 4:

Please mark the top two places where you've heard about breast cancer screenings.

Key Lessons Learned:

## TV ads

- TV ads were sources of breast cancer awareness for a majority of respondents across all age groups
- Women over 55 were significantly more likely to cite TV as a major source of information than women under 55

## Church and Community Events

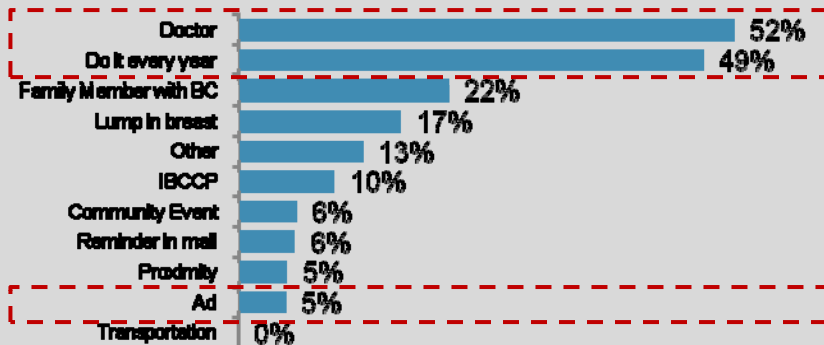
- Church and community events ranked among the bottom 3 as sources for breast cancer messages
- Limited impact comes despite the efforts of outreach organizations to focus in this area

## Friend / Relative / Spouse

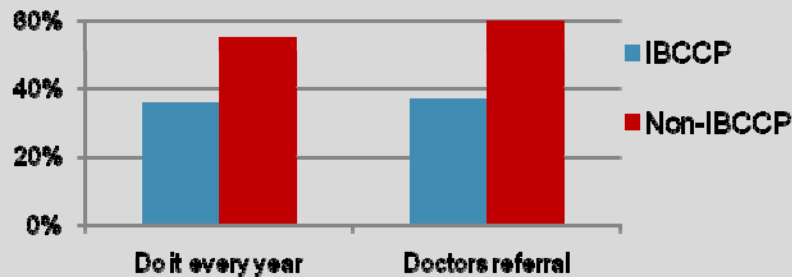
- Women under 45 participating in the IBCCP program were less likely to report a friend, relative, or spouse as a major source of breast cancer messages
- As women got older this discrepancy seemed to disappear

Doctors play a significant role in motivating women to get screened, while inconsistencies in motivators between ethnicities may provide an opportunity for improvement.

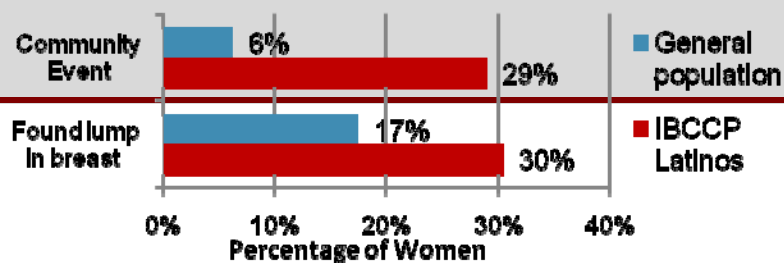
**Top two responses of motivators**



**Top two motivators**



**Motivating Factors for Women**



Question 5:

Please mark the top two most important factors that motivated you to get a mammogram.

Key Lessons Learned:

Differences between awareness and motivation

- Although television advertisements were the biggest source of awareness messages, they prompted very few women to get screened
- Doctors, however, remained an important source for both awareness and motivation

Discrepancies between IBCCP and non-IBCCP respondents

- Women participating in the IBCCP were less likely to develop yearly patterns of screening
- Women in the IBCCP were less likely to cite their doctor's referral as a motivator, likely because lack of a primary care physician

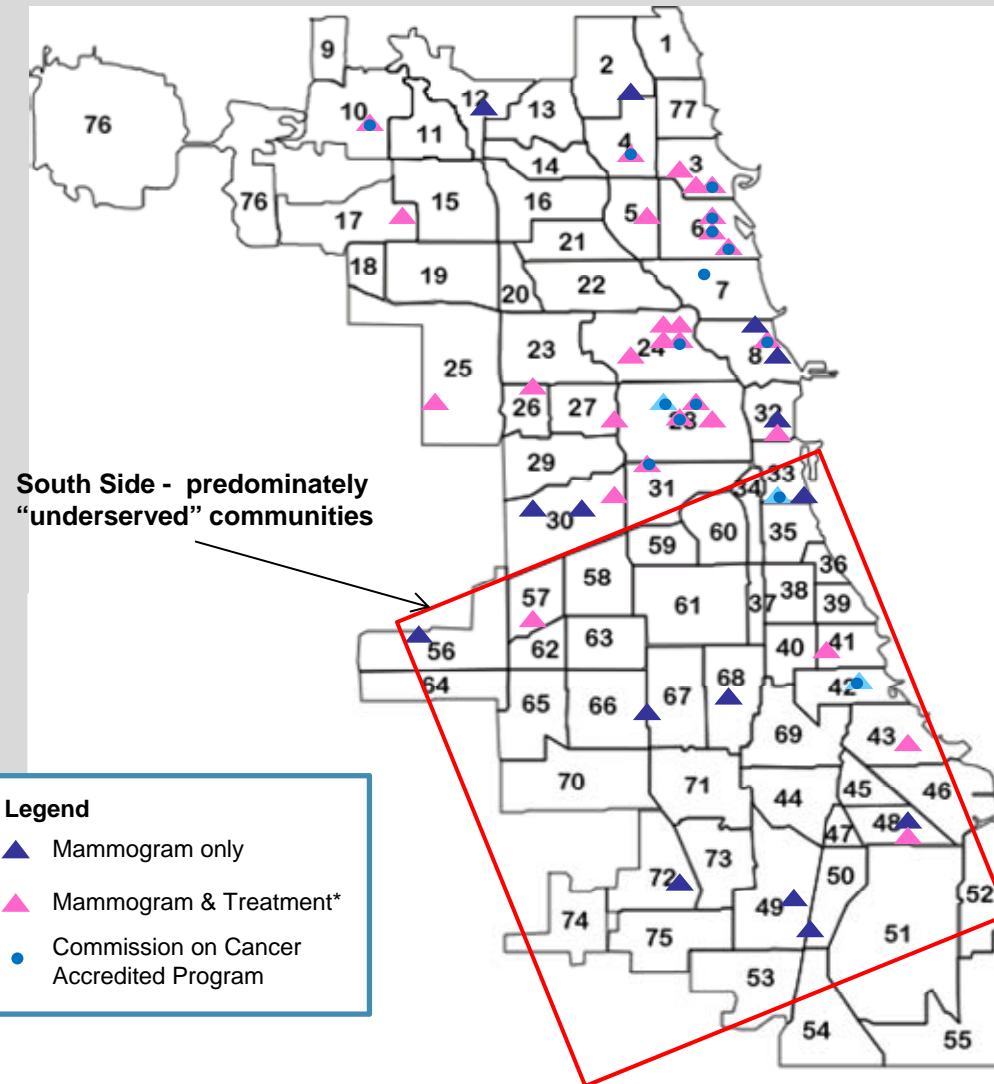
Latino differentiating behaviors

- Latino women were significantly more likely to get a mammogram as a direct result of a community event
- Nearly a third of Latino respondents were motivated to receive a mammogram because they found a lump in their breast

Importance of Financial assistance

- 30% of women involved in the IBCCP indicated that financial assistance was one of the top two motivators in getting screened

# Large healthcare disparities in breast cancer care have been identified in the underserved communities of South Side Chicago.



South Side - predominately "underserved" communities

### Legend

- ▲ Mammogram only
- ▲ Mammogram & Treatment\*
- Commission on Cancer Accredited Program

## Identified Healthcare Gaps

**Situation:** Low number of and scattered service and treatment facilities on the south side

**Result:** Low screening rates, late stage diagnoses and higher mortality rates in minority populations

(e.g. 2003 breast cancer death rate: 68% higher for black vs. white women, age of death: 19.5% for black women under 50 compared to 9.1% for white women)\*

**Situation:** Large concentration of resources in central and north Chicago

**Result:** Strain on resources available to south Chicago resulting in a backlog of patients in need of care

(e.g. only 13% of certified cancer treatment centers are in the South Side)

**Situation:** Last mammography survey of Chicago identified ~500,000 screening eligible women and only ~200,000 were screened

**Result:** 300,000 women unscreened due to improper management of resources

Source: 1. American College of Radiology, <http://www.acr.org/accreditation/AccreditedFacilitySearch.aspx>  
 2. American College of Surgeons: Commission on Cancer, [http://datalinks.facs.org/cpm/CPMAApprovedHospitals\\_Search.htm](http://datalinks.facs.org/cpm/CPMAApprovedHospitals_Search.htm)

# UHI - South Side Healthcare Collaborative

**A** ACCESS Illinois Eye Institute  
3241 S. Michigan Ave.

**B** Komed Health Cntr.  
4259 S. Berkeley Ave.

**C** ACCESS Booker  
654 E. 47<sup>th</sup> St.

**D** ACCESS Booker  
654 E. 47<sup>th</sup> St.

**E** ACCESS South State  
5050 S. State. St.

**F** 5050 S. State. St.

**G** Friend Family Health Cntr.  
5843 S. Western Ave.

**H** ACCESS Ashland  
5256 S. Ashland Ave.

**I** 5256 S. Ashland Ave.

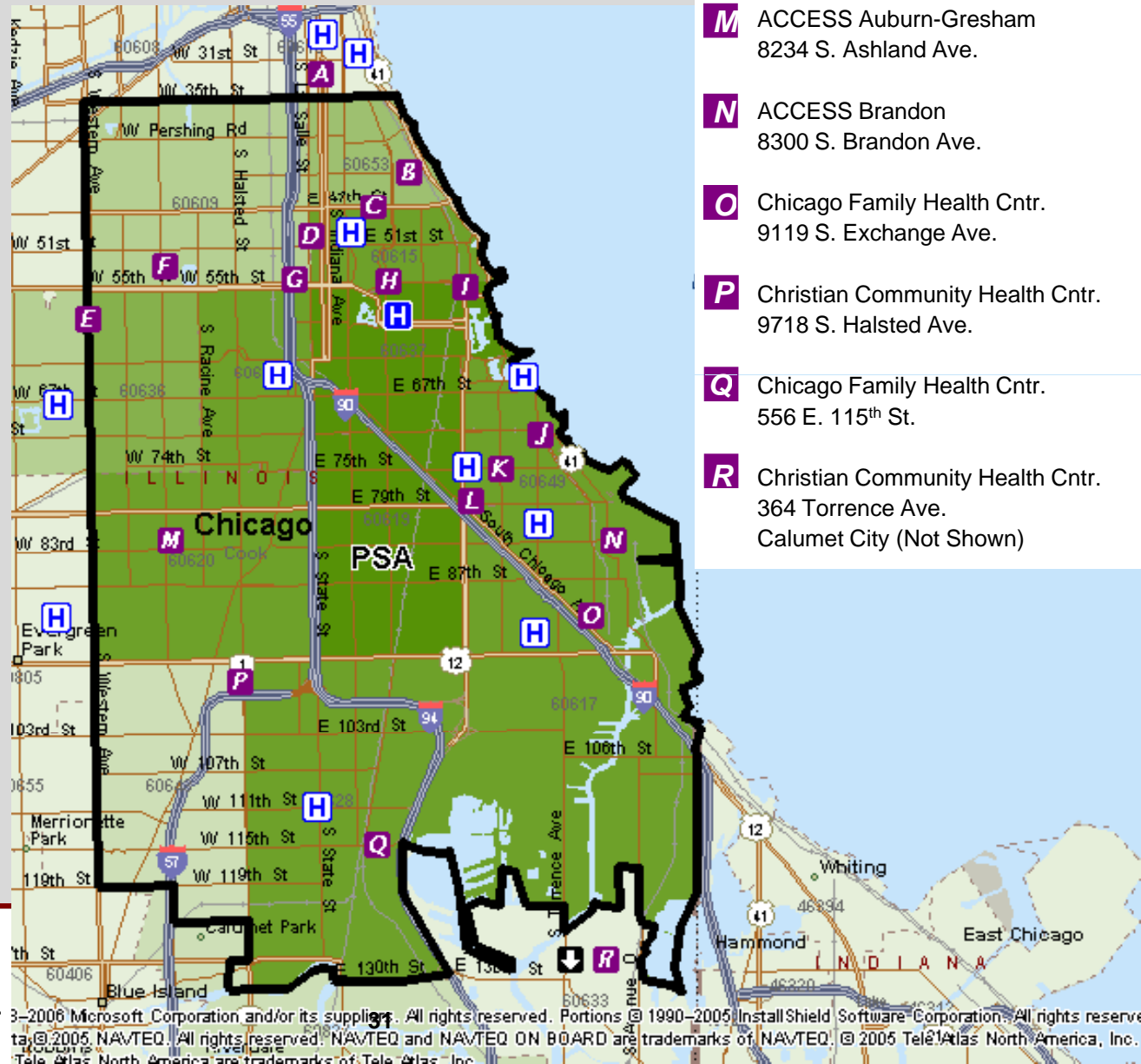
**J** ACCESS Grand Boulevard  
5401 S. Wentworth Ave.

**K** Friend Family Health Cntr.  
800 E. 55<sup>th</sup> St.

**L** 800 E. 55<sup>th</sup> St.

~~Windermere Senior Health Cntr.  
5549 S. Cornell Ave.~~

~~South Shore Senior Health Cntr.  
7101 S. Cornell Ave.~~



**M** ACCESS Auburn-Gresham  
8234 S. Ashland Ave.

**N** ACCESS Brandon  
8300 S. Brandon Ave.

**O** Chicago Family Health Cntr.  
9119 S. Exchange Ave.

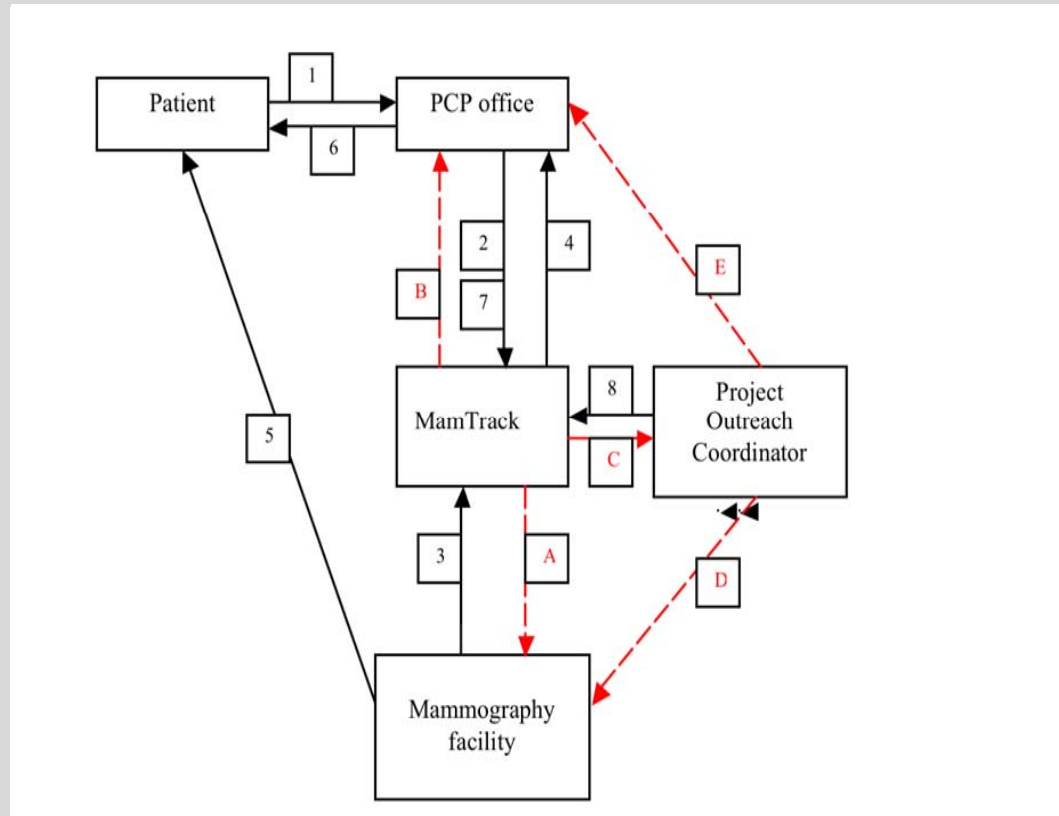
**P** Christian Community Health Cntr.  
9718 S. Halsted Ave.

**Q** Chicago Family Health Cntr.  
556 E. 115<sup>th</sup> St.

**R** Christian Community Health Cntr.  
364 Torrence Ave.  
Calumet City (Not Shown)

# MamTrack: Improving Continuity in Breast Cancer Screening

## IBCC AND MERCY Hospital Partnership



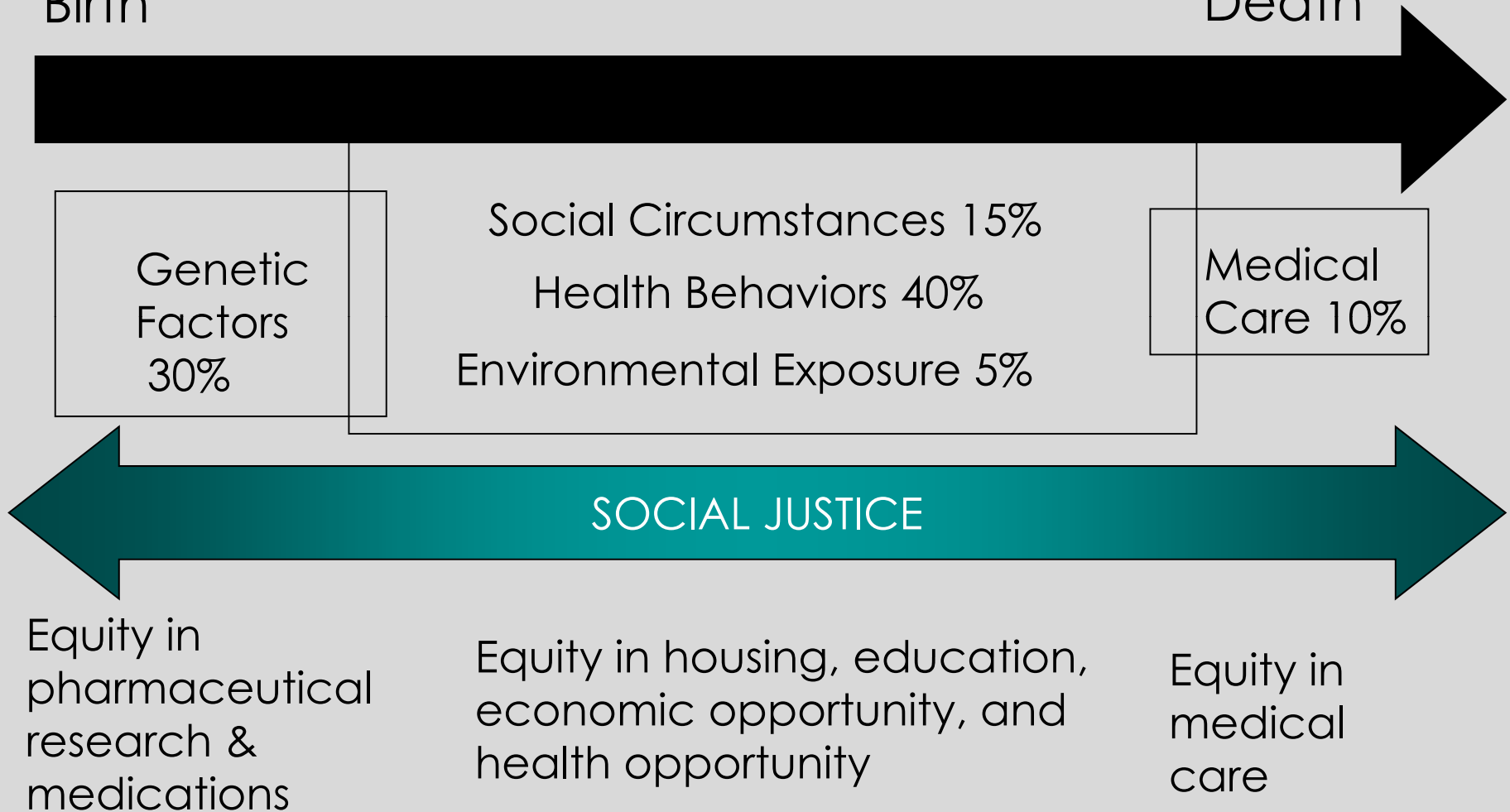
- Patient goes to primary care providers (PCP) for a mammogram referral.
- PCP registers patient into MamTrack system and submits referral (may also be able to make mammogram appointment).
- Radiology submits a mammogram report within 24 hours of mammogram appointment;
- if abnormal results, the report will be tagged as urgent. (A) 2 days after the mammogram appointment,
- MamTrack sends alerts everyday for 3 days, if the completed report is not available to the PCP.



# Reducing Breast Cancer Disparities

Birth

Death



Adapted from McGinnis et al. Health Affairs, 2002

# Genetics & Health Equity: The Next Steps

- Strengthen existing programs through research
  - GWAS of Breast Cancer
  - Whole Genome sequencing to identify novel pathways
  - Establish networks to disseminate evidence based interventions (Local and Global)
- Broaden program to include other NCDs with disparate outcomes
  - Sickle Cell Disease
  - Indoor Pollution/Asthma/COPD
  - Other Cancers
  - Clinical Pharmacology and Pharmacogenomics

# AORTIC AFRICA

*Keeping a finger on the pulse of cancer care in Africa ...”*



# Team Olopade

