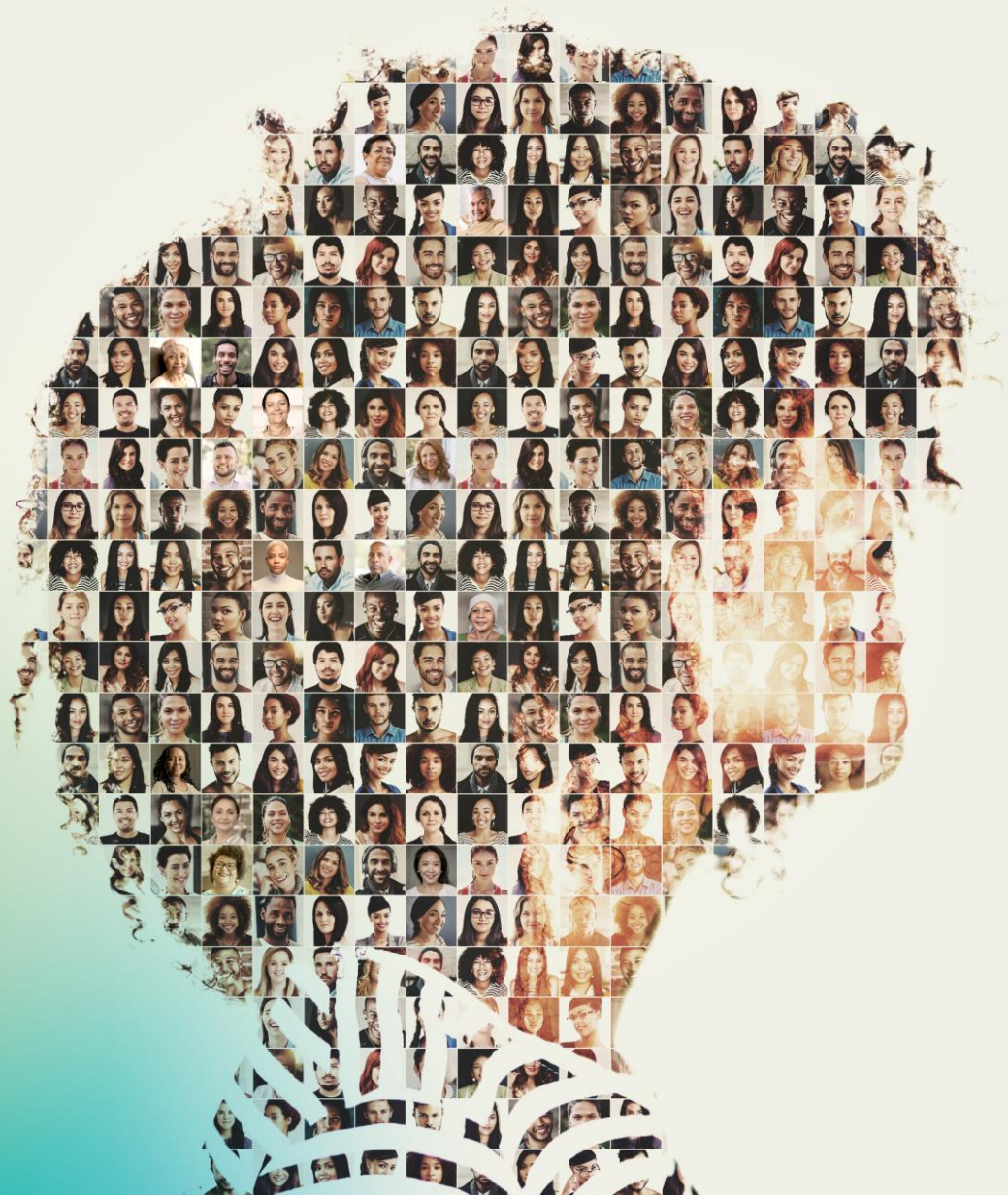


03.10.2021

AN ACCREDITED CONTINUING EDUCATION SERIES WITH THE EXPERTS

Addressing Disparities in Cancer Care and Incorporating Precision Medicine for Minority Populations

Endorsed by: W. Montague Cobb NMA Health Institute

This activity is jointly provided by the University of Nebraska Medical Center and Bio Ascend

University of Nebraska Medical Center

Bio Ascend™

Breast Cancer Disparities: Triple Negative Breast Cancer

Moderator & Course Director

Edith Mitchell, MD, MACP, FCPP, FRCP

Clinical Professor of Medicine and Medical Oncology
Department of Medical Oncology
Director, Center to Eliminate Cancer Disparities
Associate Director, Diversity Affairs
Sidney Kimmel Cancer Center at Jefferson
116th President National Medical Association

Presenter

Lisa Newman, MD, MPH, FACS, FASCO, FSSO

Weill Cornell Medicine/New York Presbyterian Hospital Network
Director, Interdisciplinary Breast Oncology Program

International Center for the Study of Breast Cancer Subtypes

Medical Director and Founder, International Center for the Study of Breast Cancer Subtypes
Adjunct Professor, M.D. Anderson Cancer Center
2nd Vice President, American College of Surgeons
Komen Scholar

This activity is jointly provided by the University of Nebraska Medical Center and Bio Ascend

University of Nebraska Medical Center

Bio Ascend™

This activity is supported by independent educational grants from

Amgen, Astellas, GlaxoSmithKline, Merck & Co., Inc., Sanofi Genzyme, and Seagen Inc.

This activity is jointly provided by

Endorsed by:

Continuing Education

JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, this activity has been planned and implemented by University of Nebraska Medical Center and Bio Ascend. University of Nebraska Medical Center is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

The University of Nebraska Medical Center, Center for Continuing Education designates this live activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

University of Nebraska Medical Center

Bio Ascend™

Disclosure

As a jointly accredited provider, the University of Nebraska Medical Center (UNMC) ensures accuracy, balance, objectivity, independence, and scientific rigor in its educational activities and is committed to protecting learners from promotion, marketing, and commercial bias. All faculty, planners, and others in a position to control continuing education content participating in an accredited continuing education activity are required to disclose all financial relationships with ineligible companies. Ineligible companies are organizations whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients. The accredited provider is responsible for mitigating all relevant financial relationships in accredited continuing education. Disclosure of these commitments and/or relationships is included in these activity materials so that participants may formulate their own judgments in interpreting its content and evaluating its recommendations.

This activity may include presentations in which faculty may discuss off-label and/or investigational use of pharmaceuticals or instruments not yet FDA-approved. Participants should note that the use of products outside currently FDA-approved labeling should be considered experimental and are advised to consult current prescribing information for FDA-approved indications. All materials are included with the permission of the faculty. The opinions expressed are those of the faculty and are not to be construed as those of UNMC or Bio Ascend.

Faculty Disclosures

Edith Mitchell, MD
Consultant: AstraZeneca, Bristol Myers Squibb, Genentech, Merck & Co., Inc., Pfizer Inc., Taiho Oncology, Inc.
Clinical Research: Amgen, Genentech

Lisa Newman, MD, MPH, FACS, FASCO, FSSO
No relevant financial disclosures

Planning Committee
The following planning committee members have nothing to disclose:
UNMC: Brenda Ram, CMP, CHCP
Bio Ascend: Chloe Dunnam; Lucja Grajkowska, PhD; Kraig Steubing

Learning Objectives

- Review racial difference in the outcomes in patients with cancer, including patients with both hematologic and solid tumors
- Evaluate sociodemographic, physician, and hospital factors that can help identify potentially modifiable patient and health care system factors that may underlie persistent racial disparities in receipt and quality of therapy
- Develop efforts to improve access to care, enhance diversity in the healthcare workforce, navigate minority cancer patients through the healthcare system, and enhance adherence to cancer-specific best practice

This activity is jointly provided by the University of Nebraska Medical Center and Bio Ascend

Lisa A. Newman, MD, MPH, FACS, FASCO, FSSO

Breast Cancer Disparities: High-Risk/Triple Negative Breast Cancer and African Ancestry

This activity is jointly provided by the University of Nebraska Medical Center and Bio Ascend

Breast Cancer Burden of African Americans

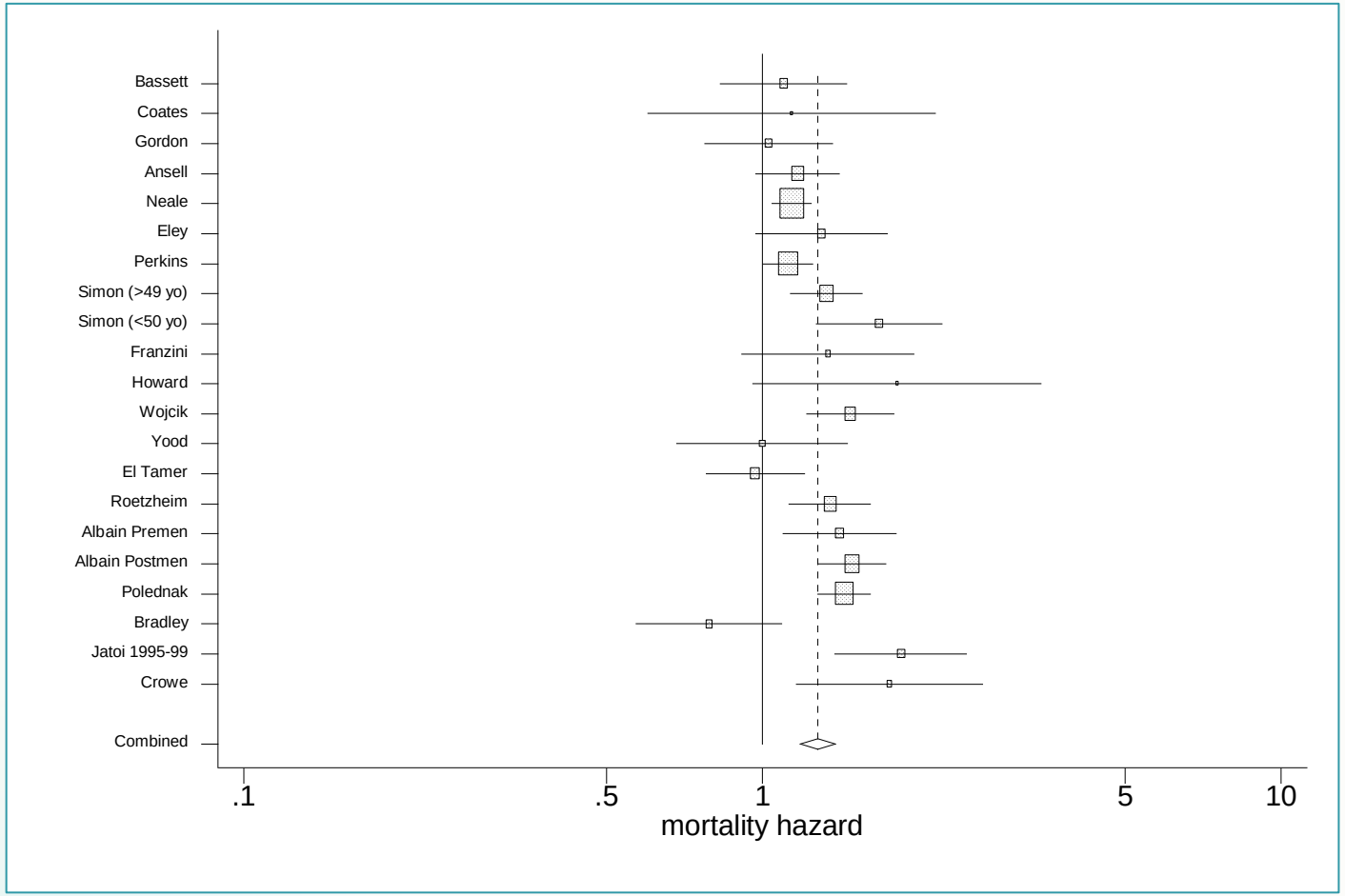
- **Higher mortality**
- **Advantage stage distribution**
- Younger age distribution
- Increased risk of adverse tumor features
- Higher incidence of male breast cancer

- **Socioeconomic Disparities**
- Tumor biology
- Genetics
- Lifestyle & Reproductive Experiences
- Environmental exposures
- Diet/Nutrition

Frequently-Asked Question in United States:

Is race a sociopolitical construct or a genetic/biologic entity?

SES-Adjusted Meta-Analysis, 2006
>13K AA & 75K WA Breast CA Pts; 19 Studies



AA Mortality Risk: 1.28 (95% CI 1.18-1.38)

Newman et al, JCO 2006

Breast Cancer Burden of African Americans Compared to White Americans

- Higher mortality
- Advantage stage distribution
- **Younger age distribution**
  - 30-40% AA <50; 20% WA < 50
- **Higher risk of adverse tumor features**
  - Two-fold higher rates TNBC in AA vs WA
- **Higher incidence of Inflammatory Breast Cancer**
- **Higher incidence of male breast cancer**

- Socioeconomic Disparities
- **Delivery of Care**
- **Tumor biology**
- **Genetics**
- **Lifestyle & Reproductive Experiences**
- **Environmental exposures**
- **Diet/Nutrition**

Disentangling SES and Inherent Racial/Ethnic Cancer Risks
Clinical Trials Data

Pooled analysis of SWOG adjuvanttherapy trials for various cancers

- Equal treatments delivered through clinical trials resulted in equal outcomes (regardless of race/ethnicity)

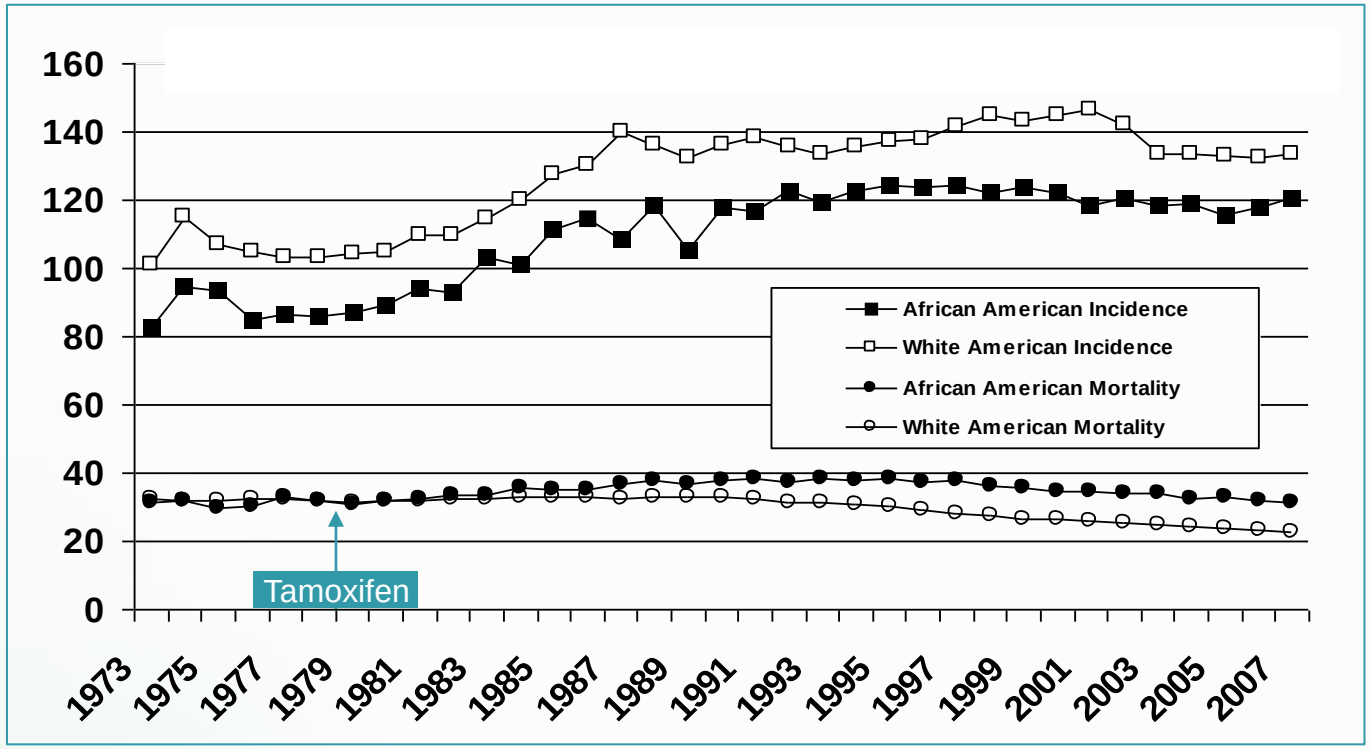
- **Exception:** African Americans with hormonally-driven cancers (e.g. breast & prostate cancers)
  - 30-40% higher recurrence and mortality hazard rates for African American breast cancer patients on SWOG adjuvant therapy trials

Albain et al, JNCI 2009

TIME.com
August 22, 2009

"Why Racial Profiling Persists in Medical Research"

SEER Program: Breast Cancer Incidence and Mortality Rates,1973-2007

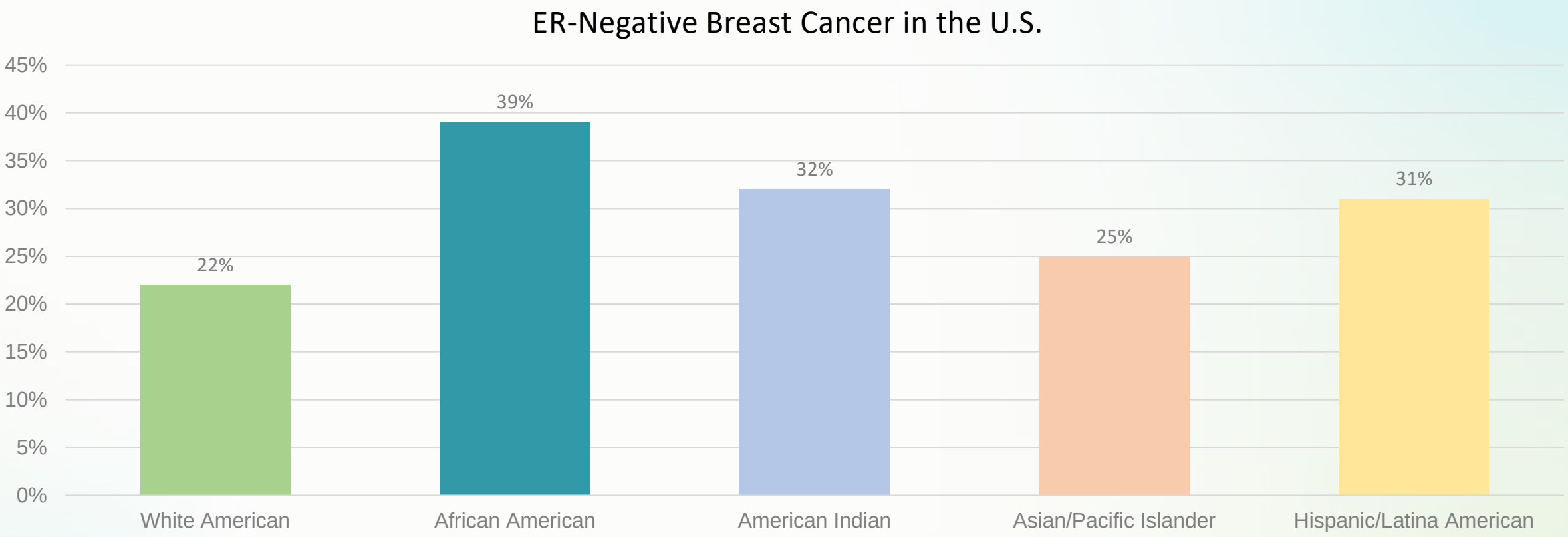


Surveillance, Epidemiology and End Results Program; Cancer.gov

"Parsing the Etiology of Breast Cancer Disparities"

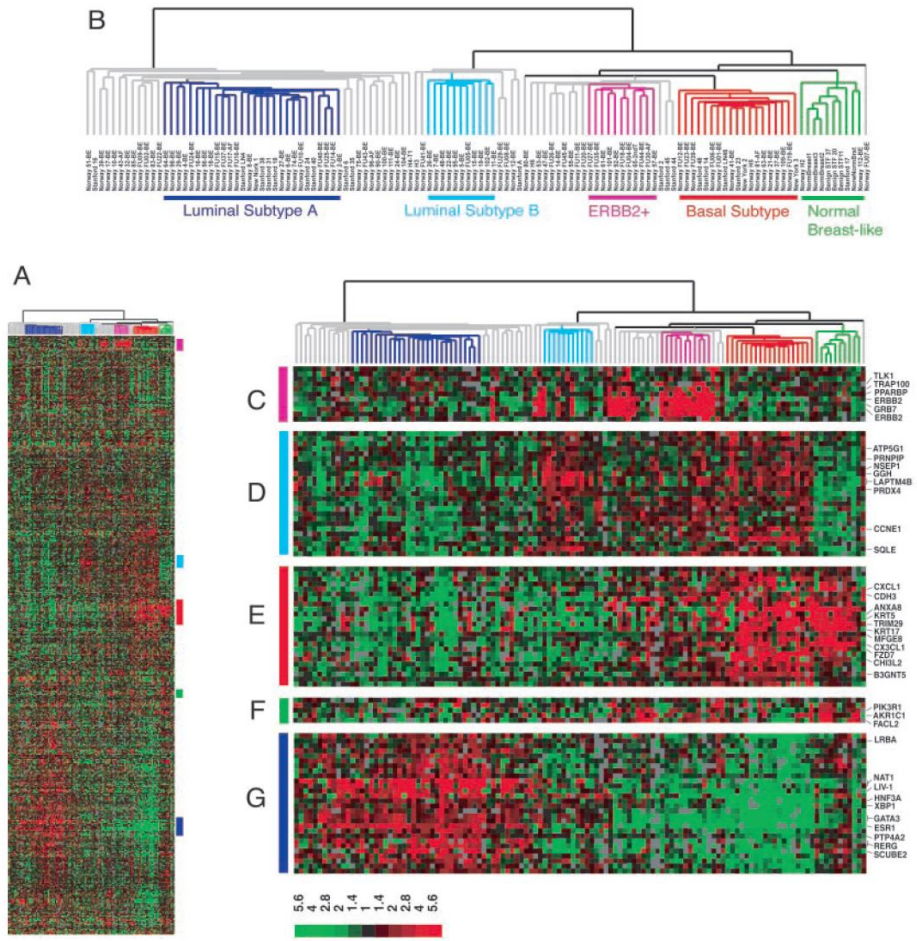
Newman, JCO 2016

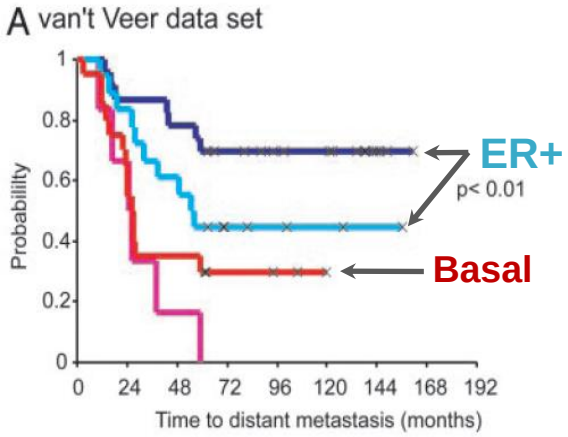
Disparities in Breast Tumor Biology: ER-Negative Breast Cancer in the U.S.

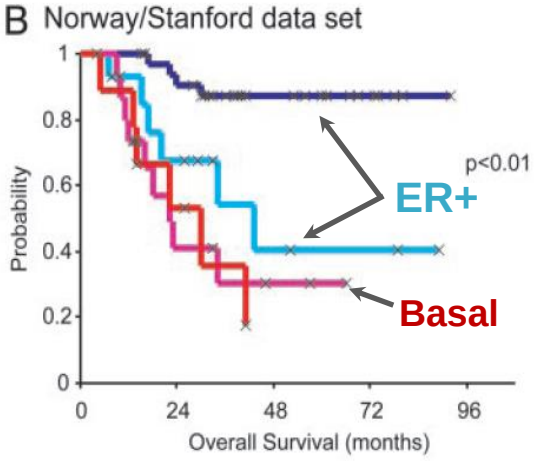


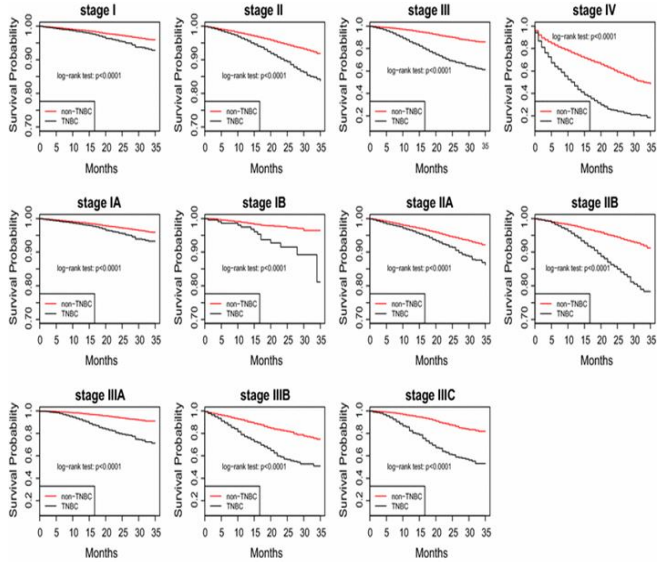
Li et al; SEER Data, 1992-98
Arch Int Med 2003

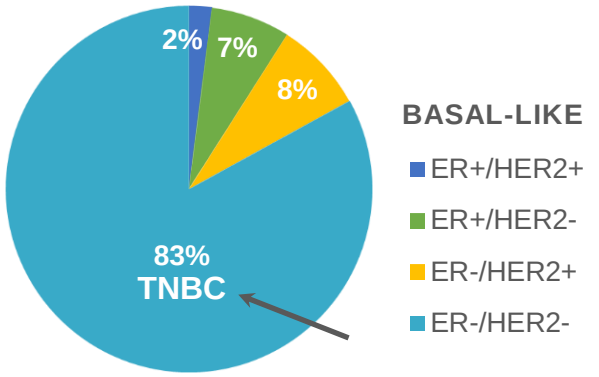
Breast Cancer Subtypes:
TNBC accounts for >80% of Basal Subtype



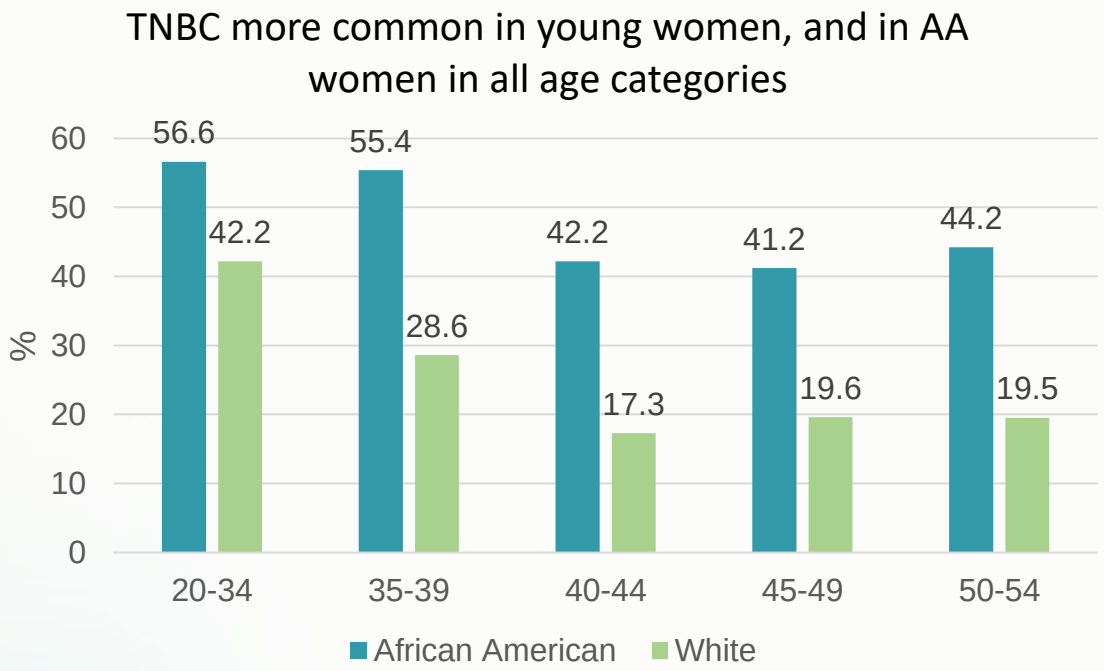


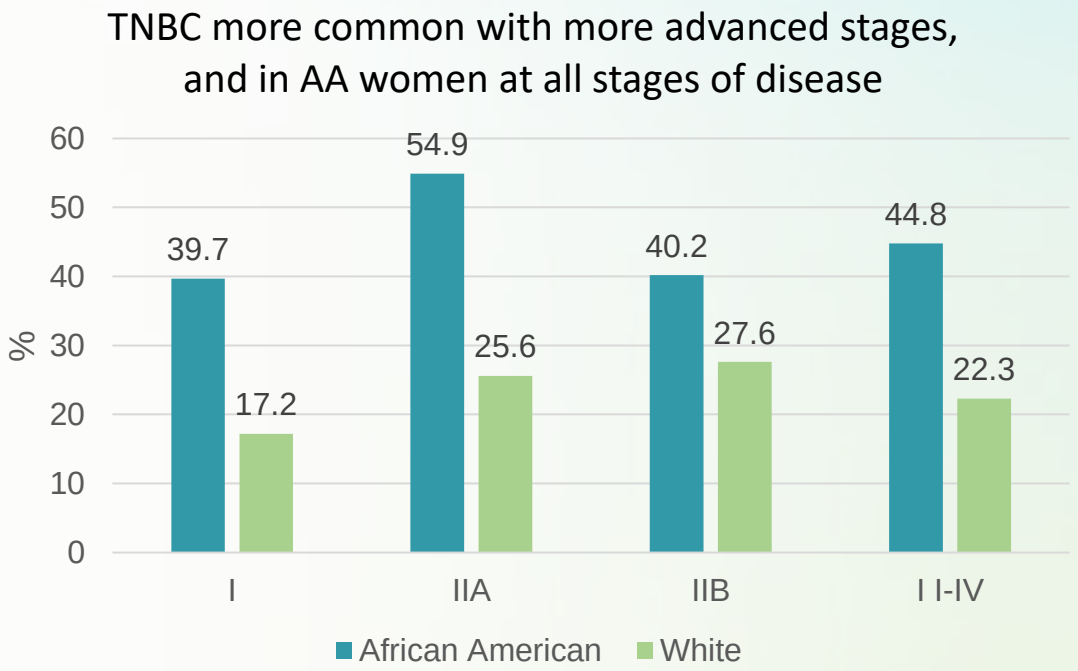






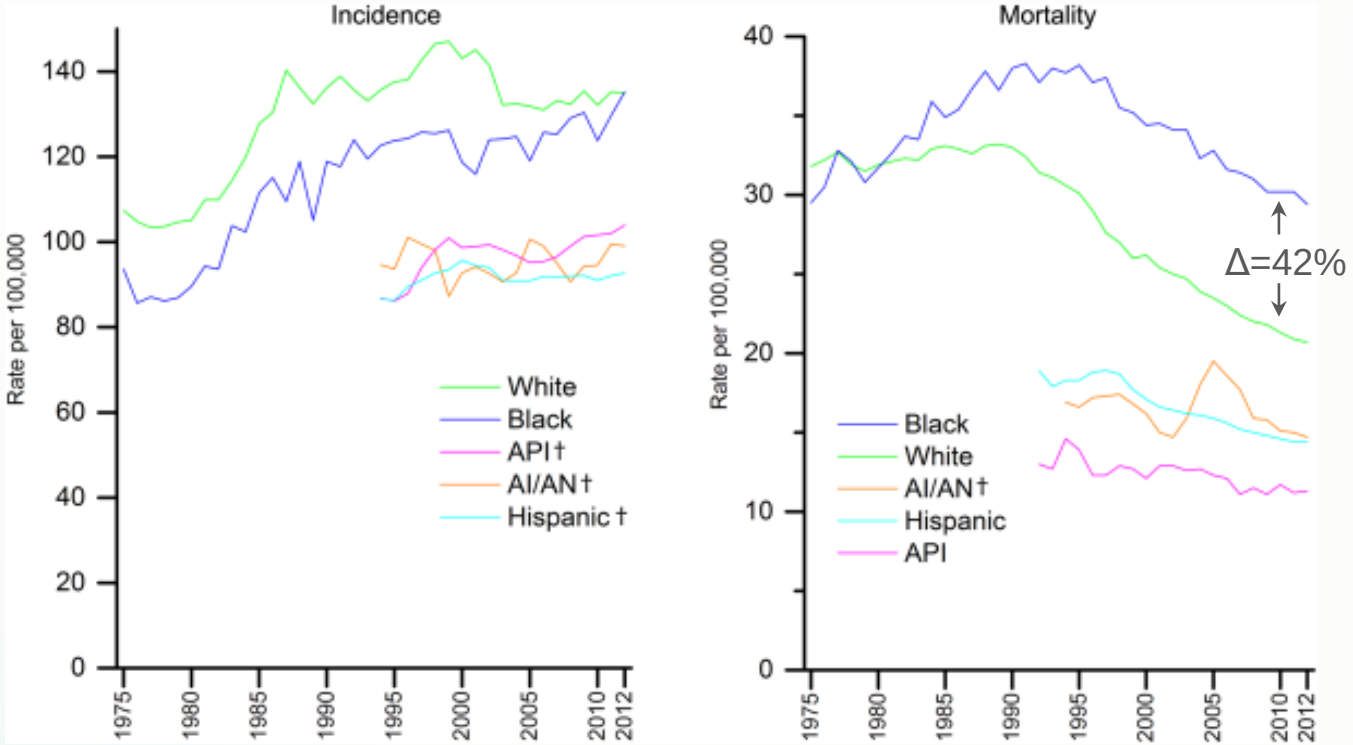
Increased Prevalence of TNBC Among AA Patients Regardless of Age or Stage at Diagnosis

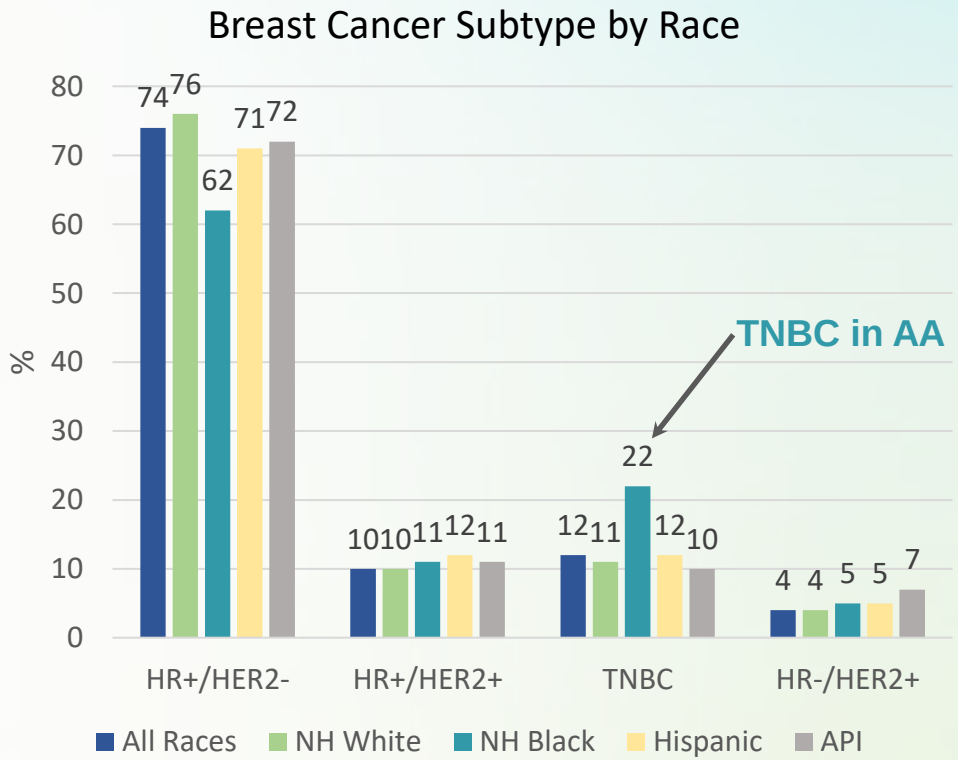




Breast Cancer Res Treat (2009) 113 : 357

TNBC more common with more advanced stages, and in AA women at all stages of disease

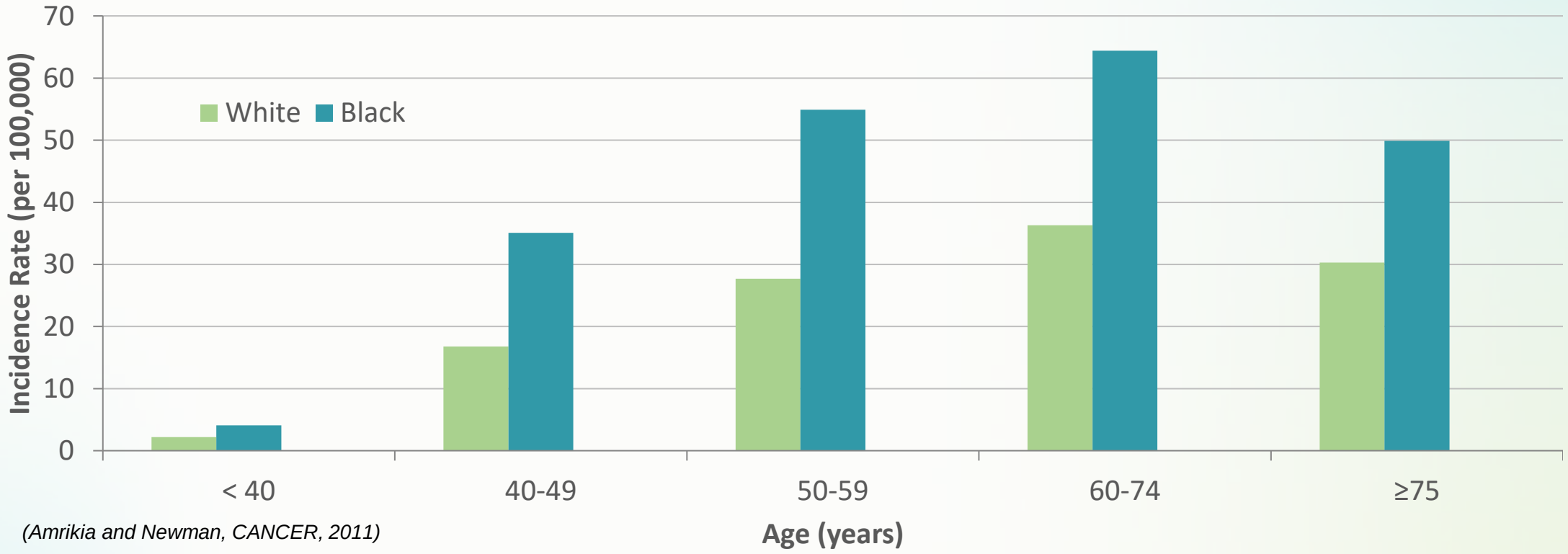




CA: A Cancer Journal for Clinicians
29 OCT 2015

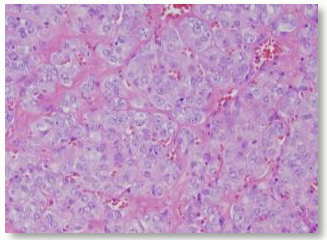
Population-Based Incidence Rates of TNBC, by Race/Ethnicity and Age: Implications for Screening Recommendations

- Delayed mammography screening may <u>worsen</u> breast CA outcome disparities between AA and WA women

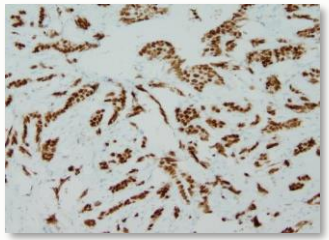


(Amrikia and Newman, CANCER, 2011)

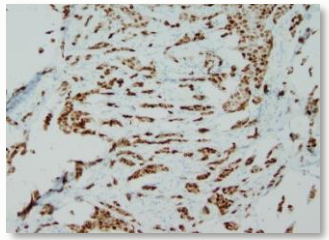
Clinical Relevance of Triple Negative Breast Cancer



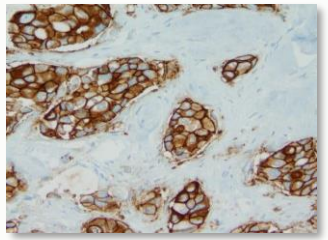
H&E



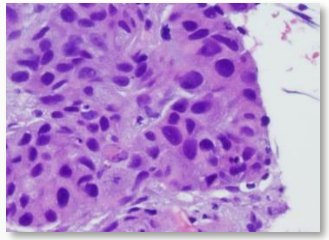
ER-Pos



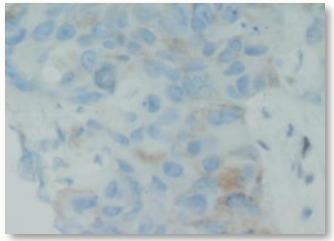
PR-Pos



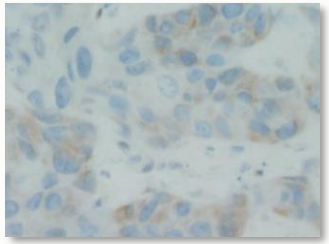
HER2/neu-Pos



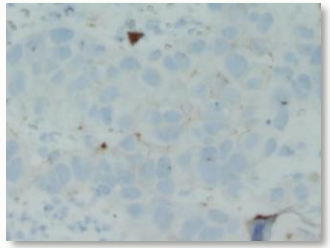
H&E



ER-Neg



PR-Neg



HER2/neu-Neg

- Inherently more aggressive pattern of breast cancer
- Fewer systemic therapy options for TNBC: no targeted therapies
- More common in African American women and in families with BRCA1 hereditary cancer susceptibility
- **More challenging to detect on mammogram**
  - more often mammographically-occult
  - may masquerade as benign lesion
- **More likely to present as an interval cancer**
- **Higher mortality rate even when detected early**

Early Stage TNBC: Detection and Outcomes

	T1a/b N0	
	CTX	No CTX
5-Yr Locoregional Recurrence-Free Survival	96.2%	96%
5-Yr Distant Mets-Free Survival	95.9%	94.5%

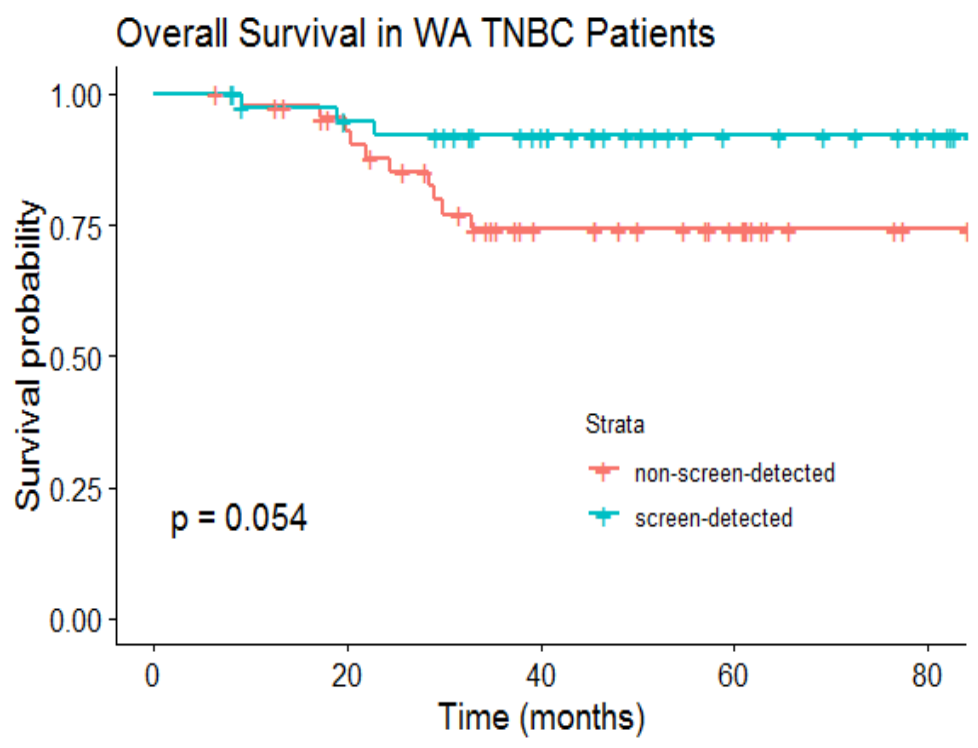
Memorial Sloan Kettering
- *Ho et al, Cancer 2012*
- 194 T1a/b N0 TNBC; 1999-2006
- 69% screen-detected

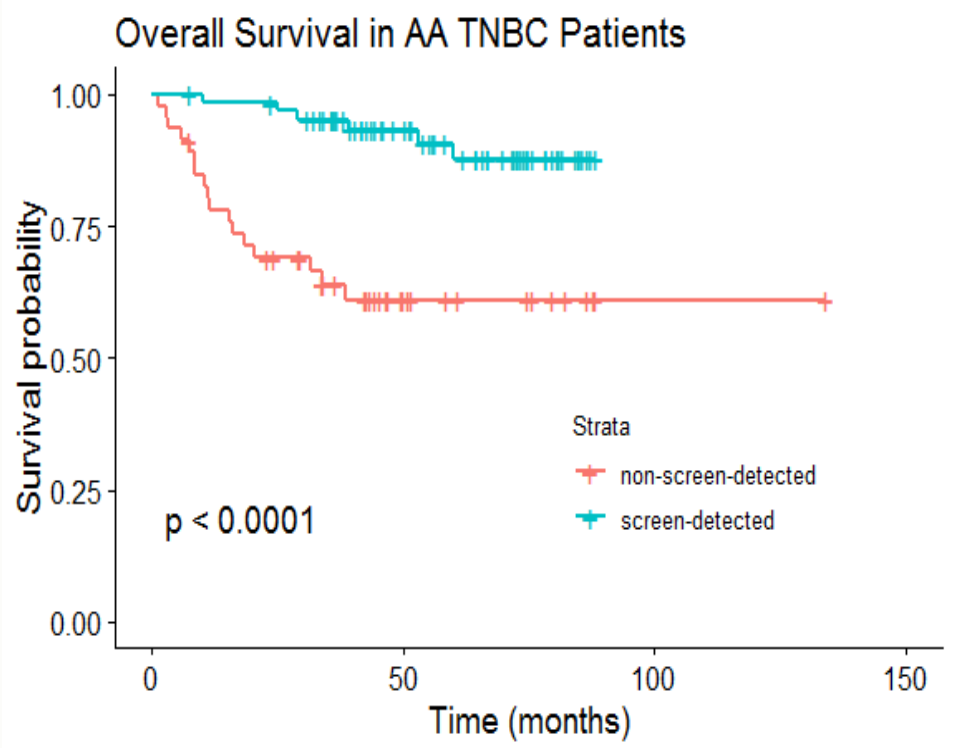
	T1a N0		T1b N0	
	CTX	No CTX	CTX	No CTX
5-Yr Overall Survival	100%	94%	96%	91%
5-Yr Distant Mets-Free Survival	100%	93%	96%	90%

National Comprehensive Cancer Network
- *Vaz-Luis et al, JCO 2014*
- 363 T1a/b N0 TNBC; 2000-09
- 75% screen-detected

TNBC Outcomes and Early Detection: Henry Ford Health System Experience 2011-15

- Mammography screen-detection strongest predictor of improved survival in TNBC patients



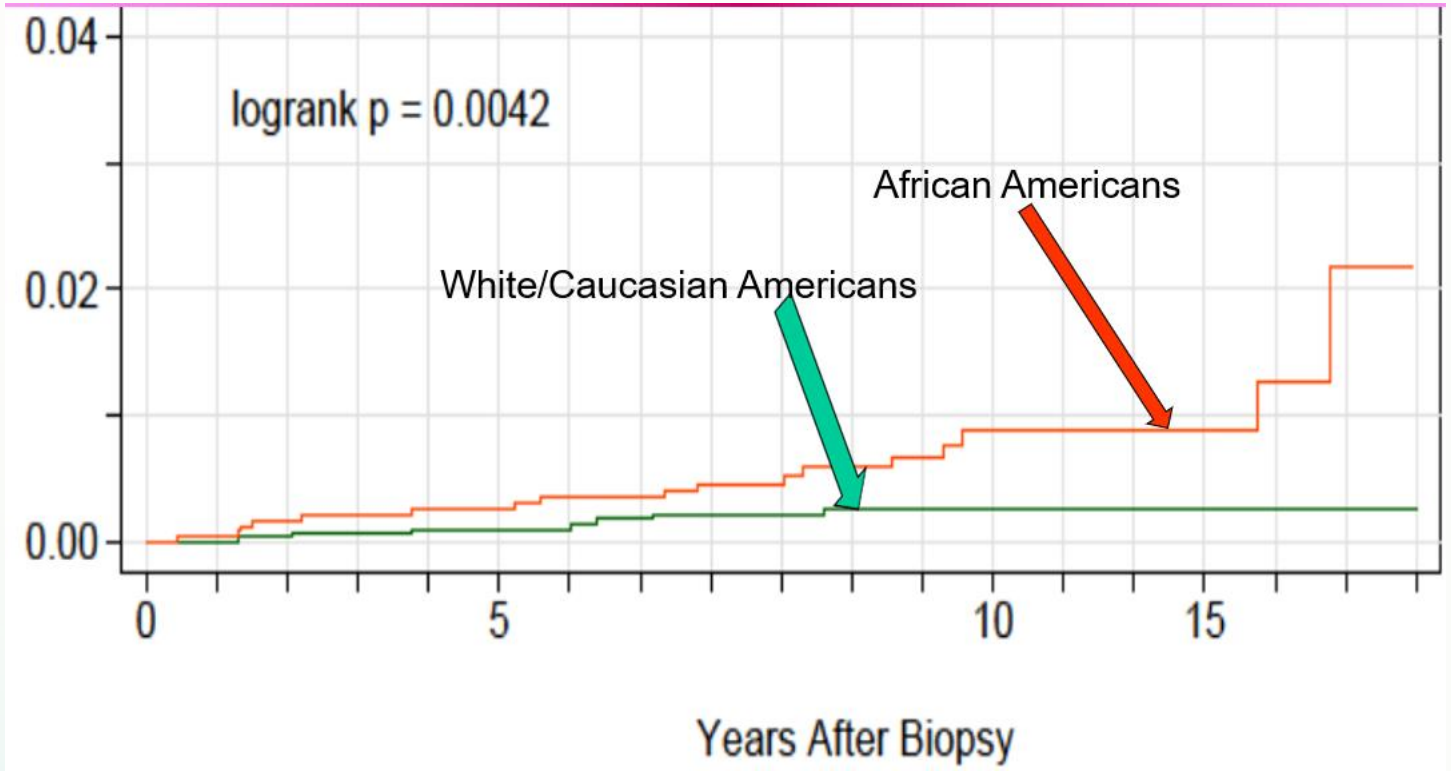


Newman et al, JAMA Surgery 2020

Current Screening Mammography Guidelines: Agreement regarding ACCESS to mammography beginning at age 40 yrs

American Academy of Family Physicians	• Women ages 50-74 years should undergo biennial screening mammography • **Women 40-49 yrs should make an individualized decision regarding screening mammography after considering risks and benefits**
American Cancer Society	• Initiate annual screening mammography at age 45 years • Transition to biennial screening mammography at age 55 • **Annual mammography should be available to women at age 40 years**
American Coll OB-GYN	• **Annual mammography should be offered beginning at age 40 years**
American Coll Radiology; Soc. of Breast Imaging	• **Women should have annual mammography beginning at age 40 years**
American Soc. of Breast Surgeons	• **Women should have annual mammography beginning at age 40 years** • Shared decision-making regarding annual versus biennial mammographic screening for women aged 55 and older • Biennial mammography screening for women over age 75 with life expectancy at least ten years
NCCN	• **Women should have annual mammography beginning at age 40 years**
US Preventive Services Task Force	• Women ages 50-74 should undergo biennial screening mammography • **Women 40-49 yrs should make an individualized decision regarding screening mammography after considering risks and benefits** • Insufficient evidence available to make recommendations for women age 75 years and older

Henry Ford Health System (HFHS) Benign Breast Disease Cohort

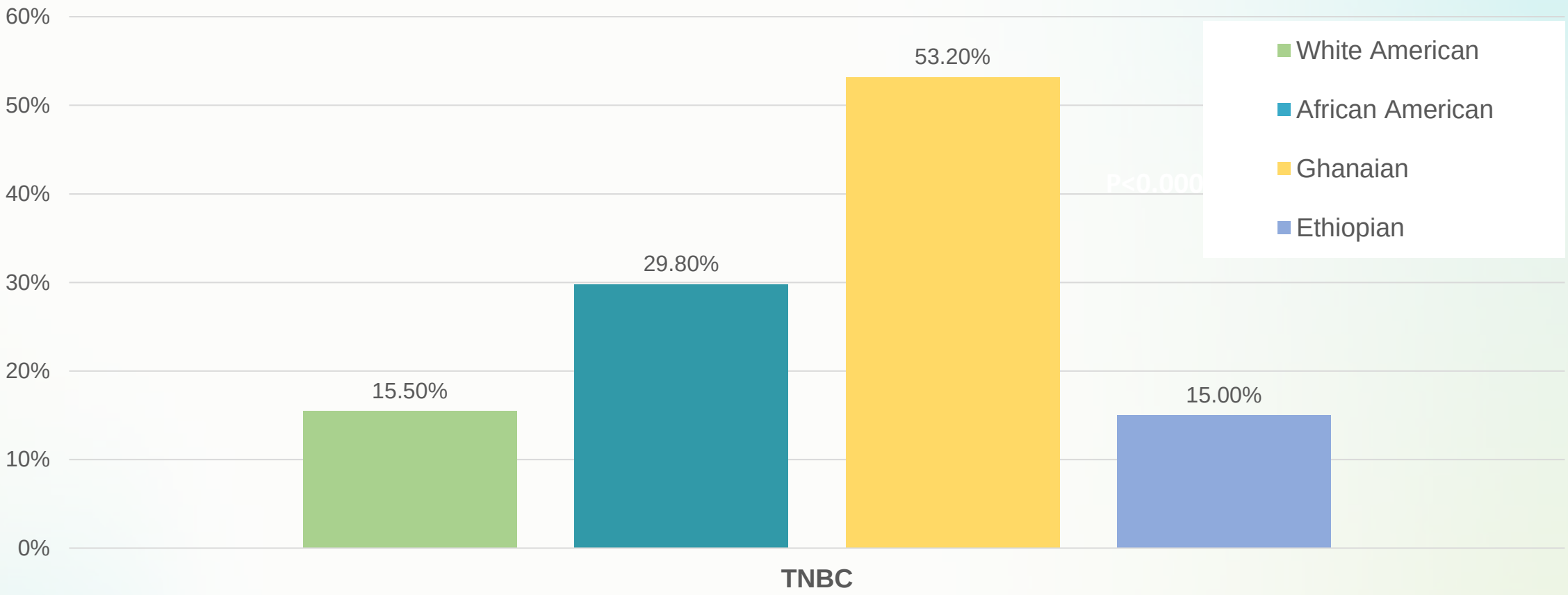


- Benign Breast Disease Cohort, 1994-2005
  - 2,588 African Americans
  - 3,566 White Americans
  - Follow-up (>10 years) and overall subsequent breast cancer detection rates (4%) as well as stage distribution similar for AA and WA pts

High-Risk Breast Cancer and African Ancestry

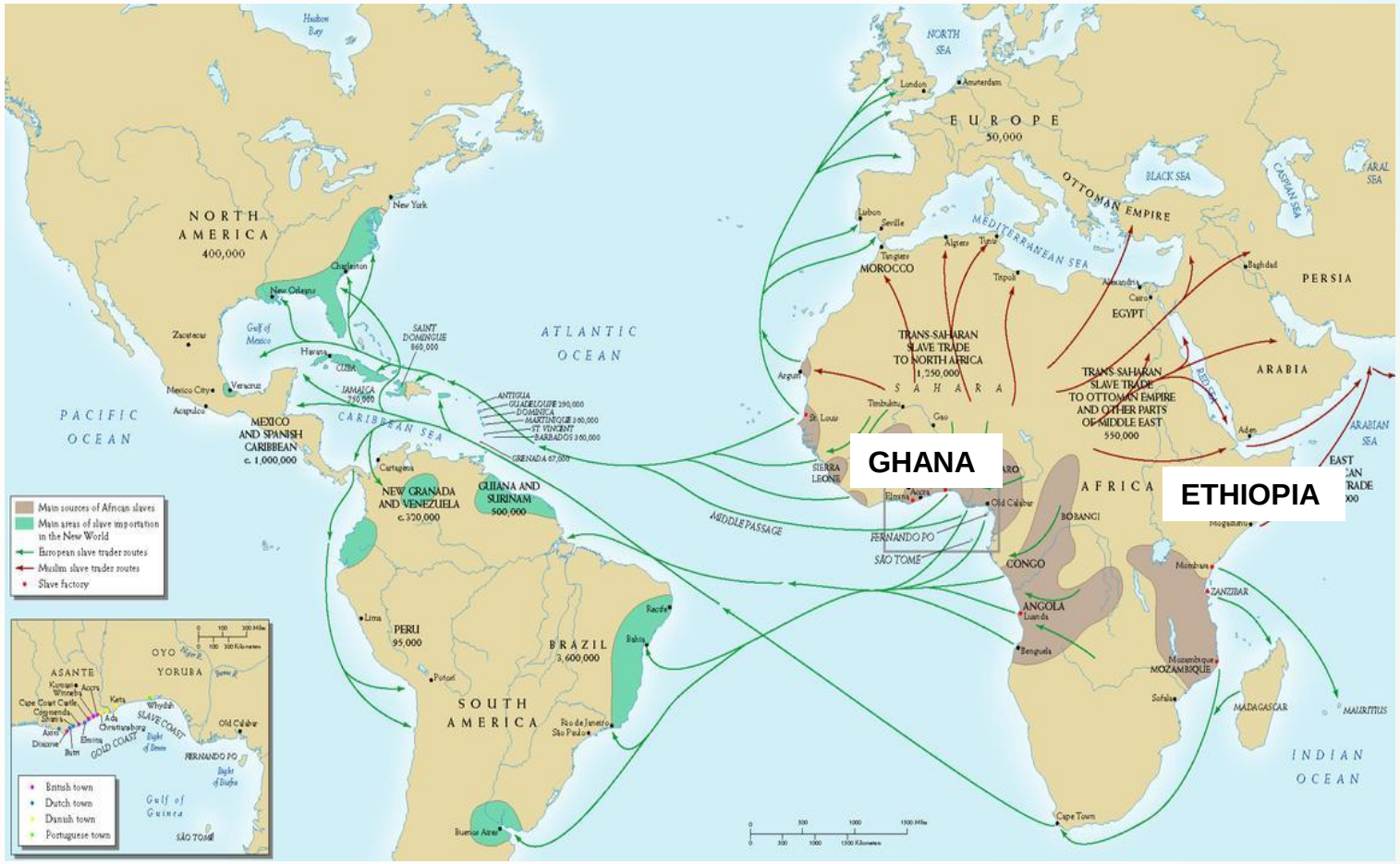
- Parallels between hereditary breast cancer and breast cancer in women with African ancestry
  - younger age distribution
  - increased prevalence of ER-neg, aneuploid tumors
  - higher risk of male breast cancer
- Is African ancestry associated with a heritable marker for high-risk breast cancer subtypes?
- Unique opportunity to gain insights regarding etiology of breast cancer disparities ***and*** the pathogenesis of triple-negative breast cancer

Breast Cancer Phenotypes in WA, AA, Ghanaians and Ethiopians



Jiagge, Newman Ann Surg Onc 2016

Biologic Plausibility: “Oncologic Anthropology”
African Diaspora/ Patterns of Forced Population Migration



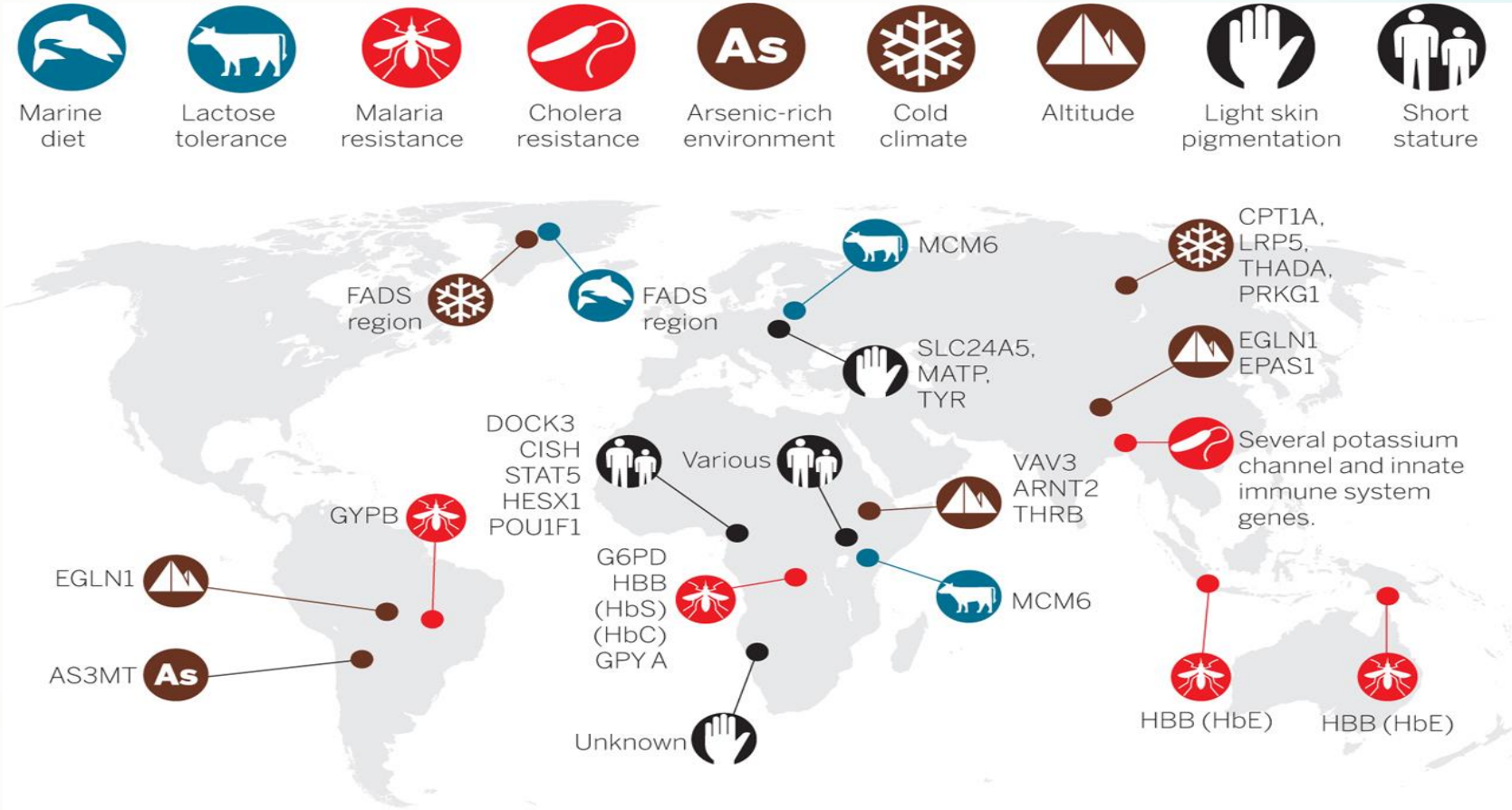
TNBC-Specific Risk Assessment (Case Series)

Melissa Davis, PhD

Scientific Director,
International Center for the Study of
Breast Cancer Subtypes

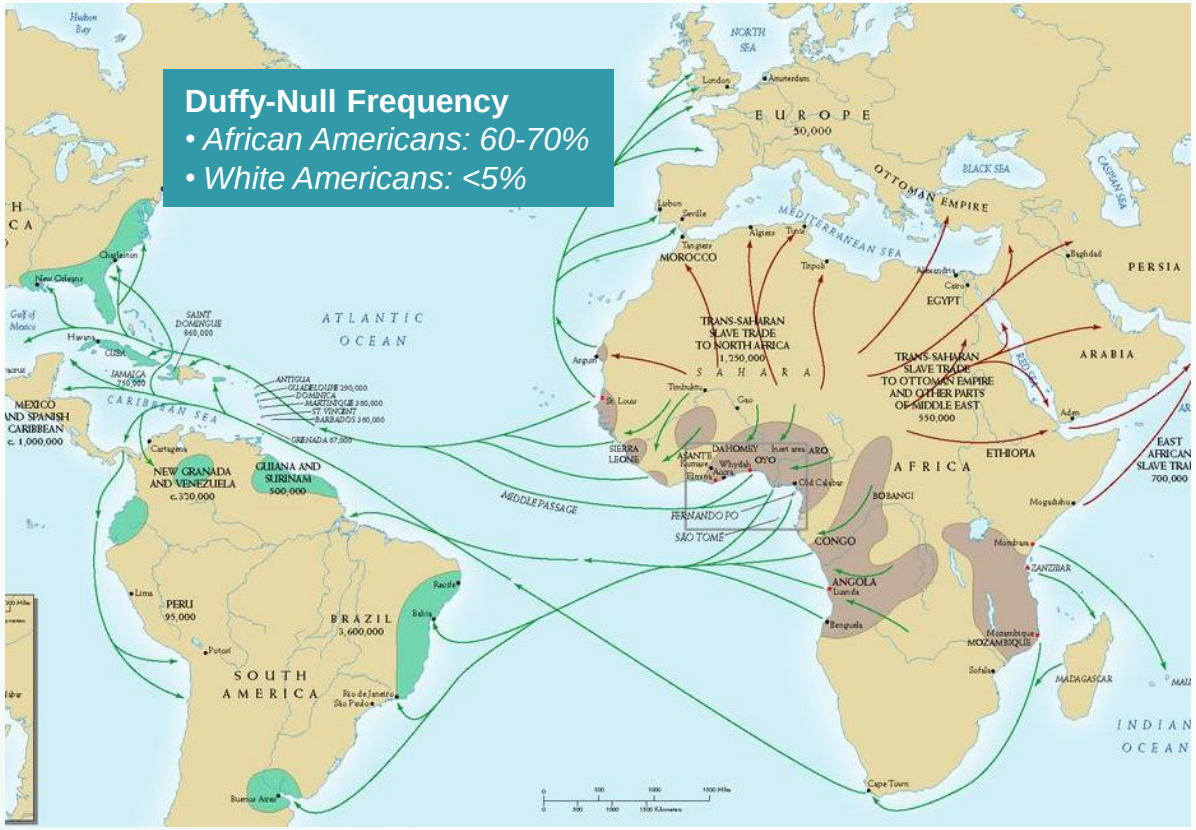
By SNP Genotypes (Dominant Model)								By SP Alleles (Dosage model)					
SNP ID	Minor Allele	OR	SE	lower 95% CI	upper 95% CI	P-value	adjusted P-value	OR2	SE2	lower 95% CI4	upper 95% CI5	P-value	adjusted P-value2
rs2814778 Duffy-null	C	7.175	0.3022	3.968	12.97	<0.0001	0.0473	3.189	0.1602	2.33	4.364	<0.0001	0.000345
rs13000023	A	0.259	0.78	0.0562	1.196	0.08353	0.03085	0.603	0.474	0.2382	1.528	0.2864	0.04996
rs2363956	G	0.274	1.127	0.0301	2.492	0.2503	0.07728	0.474	0.6857	0.1237	1.819	0.2768	0.03369
rs2981578	C	0.444	1.126	0.0489	4.037	0.4713	0.8362	0.444	1.126	0.04893	4.037	0.4713	0.8362
rs2981579	G	0.729	1.149	0.0767	6.932	0.7834	0.9271	0.964	0.6055	0.2943	3.158	0.9517	0.8631
rs3112572	A	0.84	0.8047	0.1735	4.067	0.8285	0.7438	1.193	0.6292	0.3477	4.096	0.7787	0.936
rs3745185	A	0.964	0.9019	0.1646	5.649	0.9678	0.8378	0.964	0.9019	0.1646	5.649	0.9678	0.8378
rs4245739	C	0.759	0.7908	0.161	3.574	0.7268	0.7032	0.528	0.5591	0.1765	1.579	0.2533	0.2315
rs4849887	T	1.667	0.8028	0.3456	8.038	0.5246	0.1145	1.4	0.6246	0.4114	4.761	0.5905	0.1949
rs609275	C	0.365	0.8613	0.0675	1.975	0.2421	0.5357	0.365	0.8613	0.06749	1.975	0.2421	0.5357

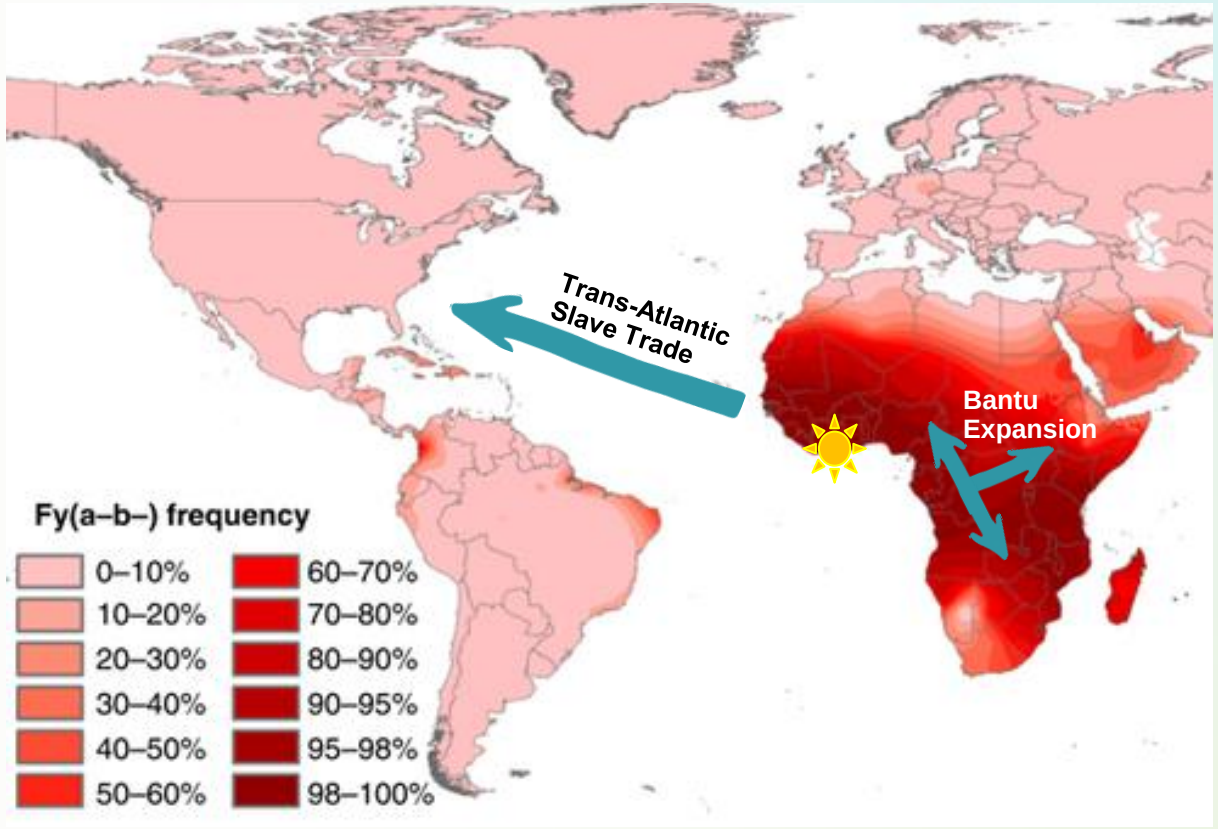
Global Distribution of Locally Adaptive Traits



Tishkoff, Science 2015; 349:1282

Biologic Plausibility: “Oncologic Anthropology” and Duffy as a Candidate Gene t Explain Breast Cancer Disparities Related to African Ancestry



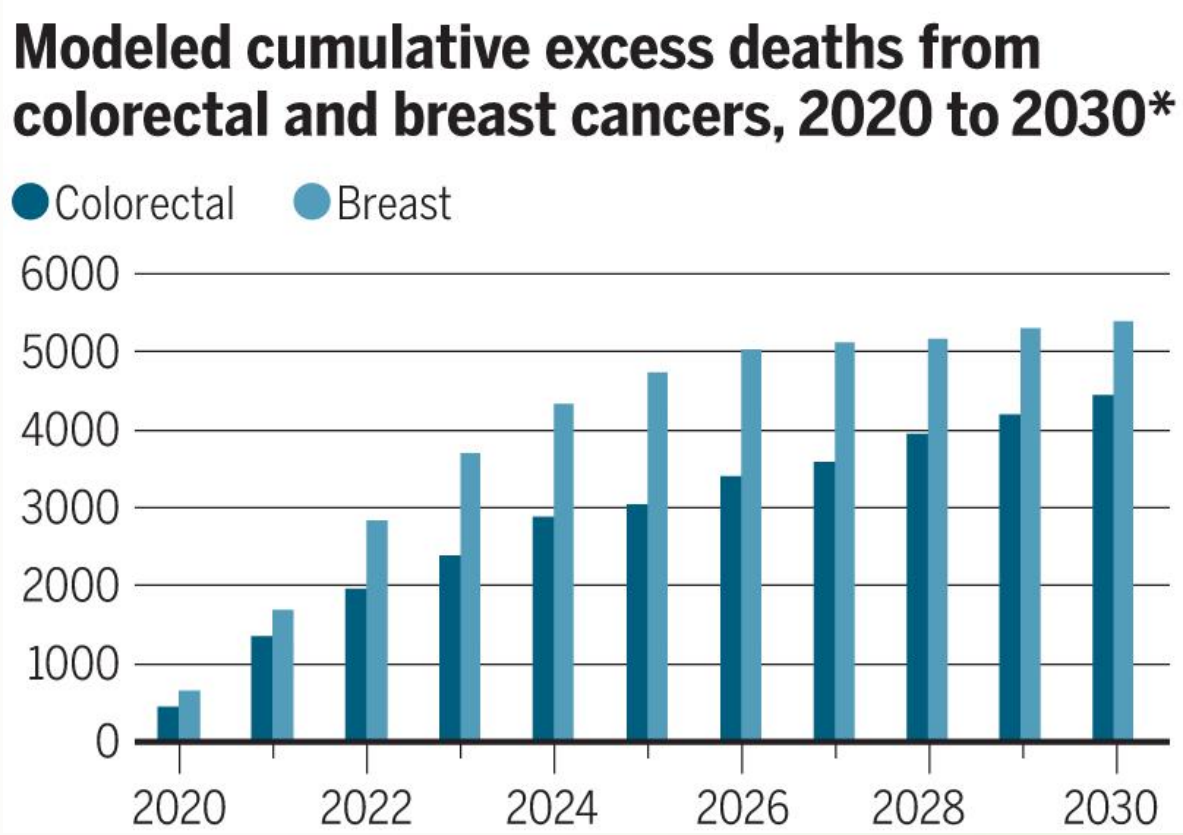


Malaria; Selection pressure for Duffy-null; African Diaspora

University of Nebraska Medical Center

Bio Ascend™

Modeled Cumulative Excess Deaths from Colorectal and Breast Cancers, 2020 to 2030*



Sharpless N; Science 2020;368:1290

Addressing and Mitigating the Impact of Covid-19 on Breast Cancer Disparities

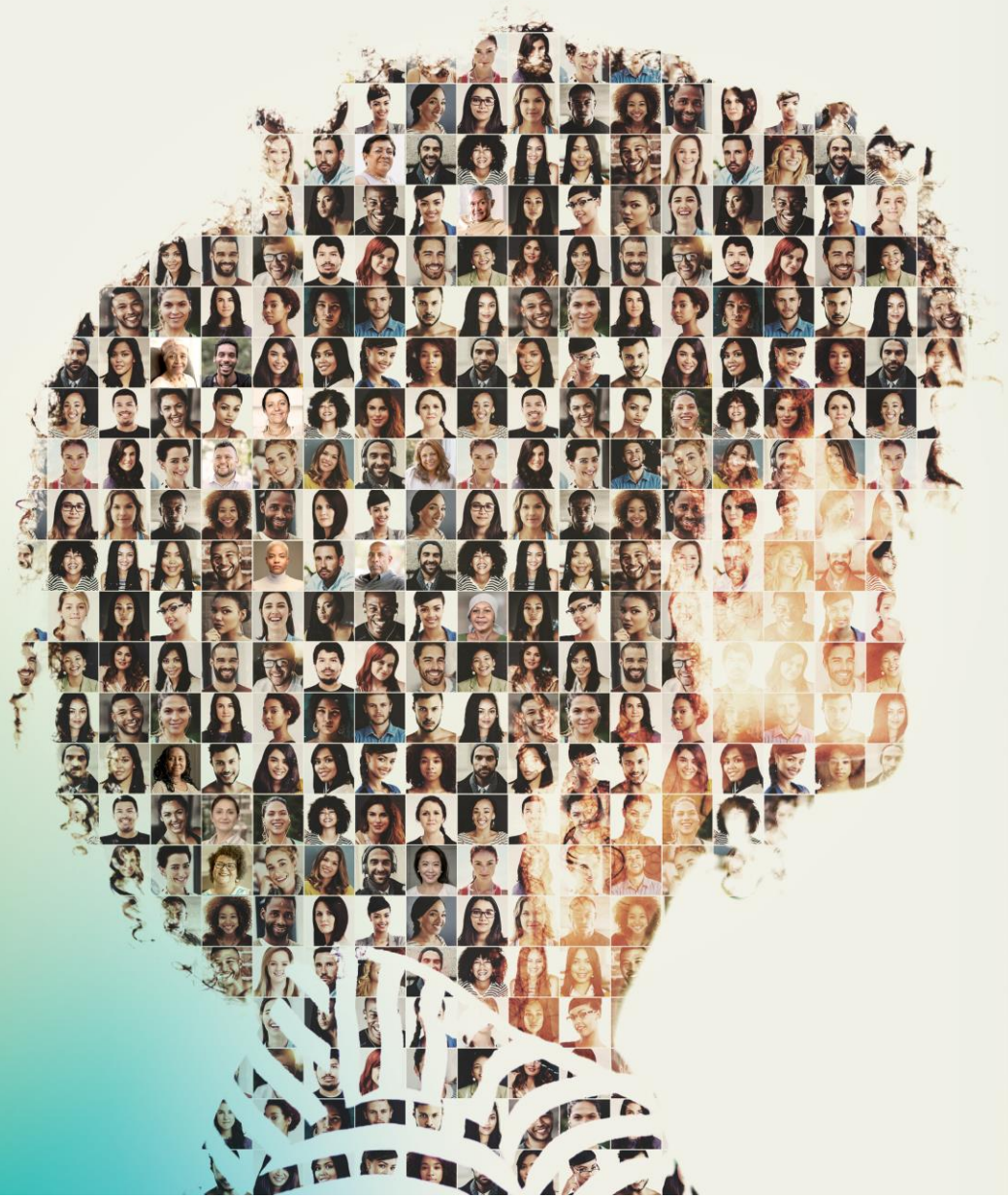
- **Disproportionate impact on health care access**
  - Covid recession unemployment 30-50% higher for AA compared to WA; loss of employment-based insurance
- **Safety-net hospitals disproportionately devastated by costs of Covid care**
  - AA rely disproportionately on safety-net hospitals for cancer care/screening
  - Safety-net hospitals serve as economic hub for many inner-city neighborhoods
- **Impact on advocacy/philanthropic fundraising efforts**
  - Many community outreach programs funded by advocacy organizations
- **Adverse impact of Covid recession on research and hospital budgets**
  - Support for disparities research and navigation services under threat
- **Increased reliance on remote technology/video visits**
  - Digital divide: no broadband/internet access in 36% AA vs 21% WA households

Thank You!

This activity is jointly provided by the University of Nebraska Medical Center and Bio Ascend

University of Nebraska Medical Center

Bio Ascend™



AN ACCREDITED CONTINUING EDUCATION SERIES WITH THE EXPERTS

Addressing Disparities in Cancer Care and Incorporating Precision Medicine for Minority Populations

This activity is jointly provided by the University of Nebraska Medical Center and Bio Ascend

University of Nebraska Medical Center

Bio Ascend™