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Overview of Biological Effectors of SDOH and Influence on Cancer Risk and Outcomes

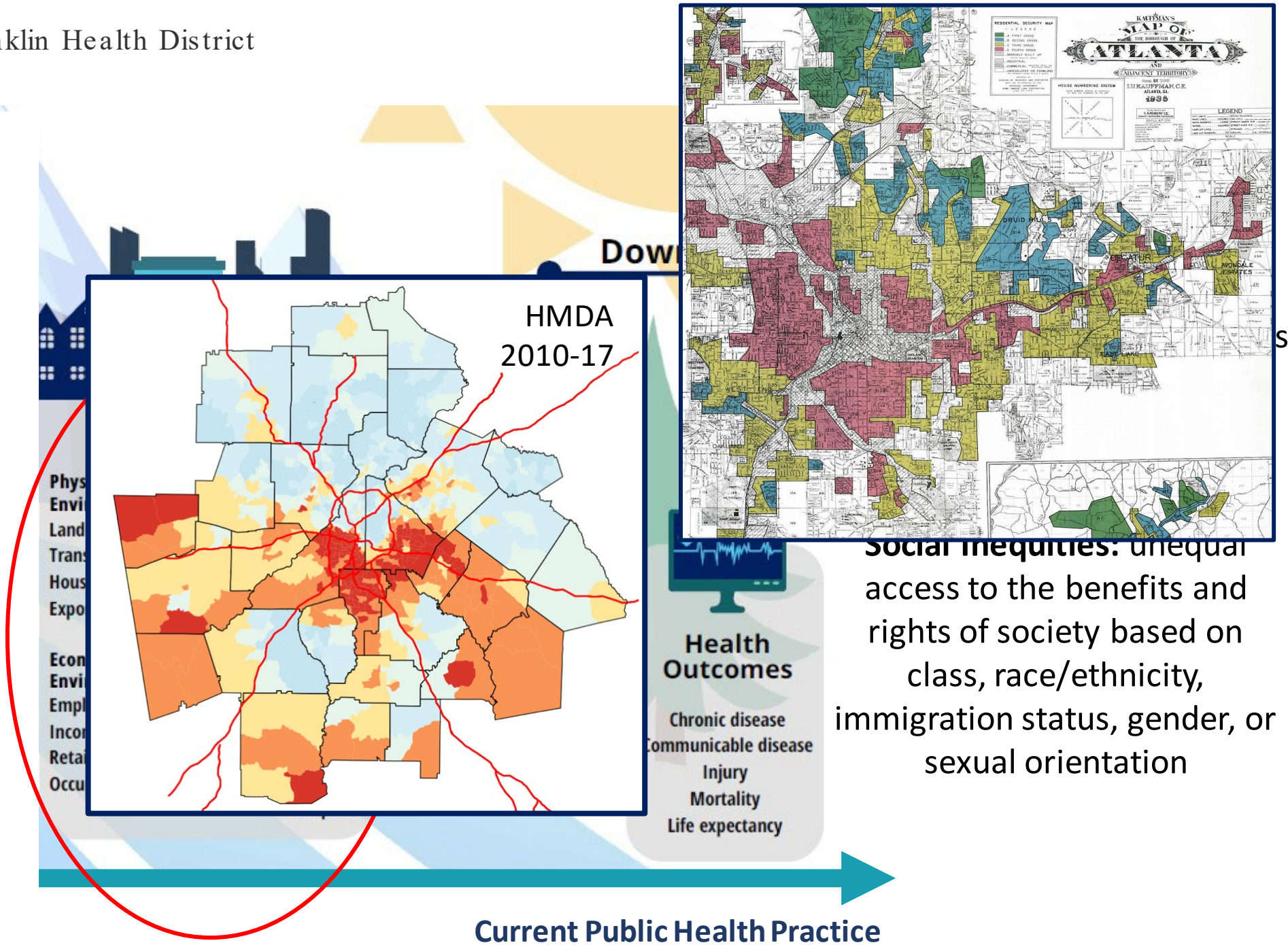
Lauren E. McCullough, PhD MSPH

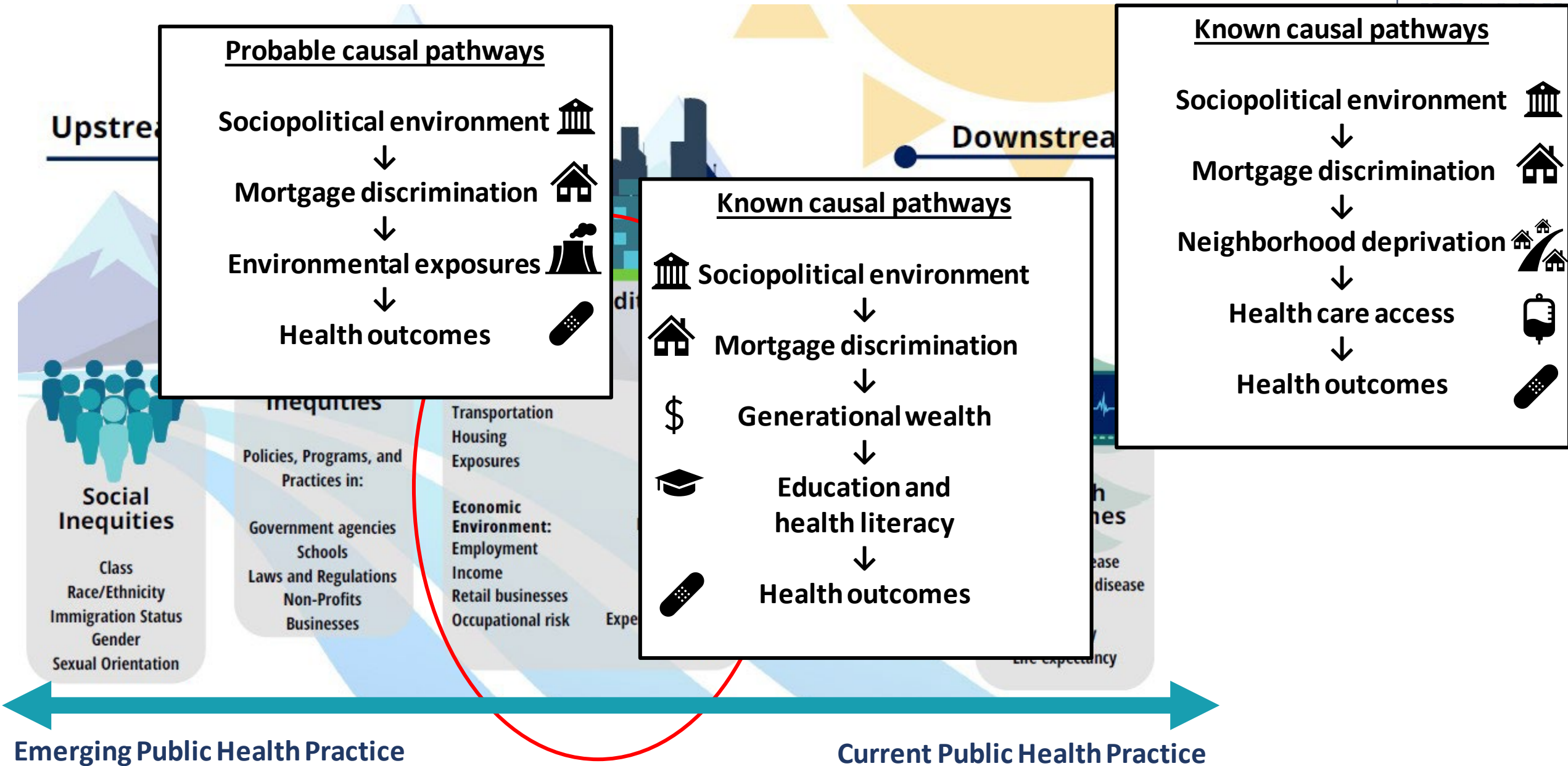
Associate Professor, Epidemiology

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Visiting Scientific Director, Population Science

American Cancer Society







Probable causal pathways

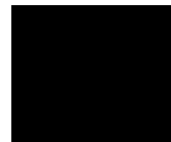
Sociopolitical environment 



Mortgage discrimination 



Environmental exposures 

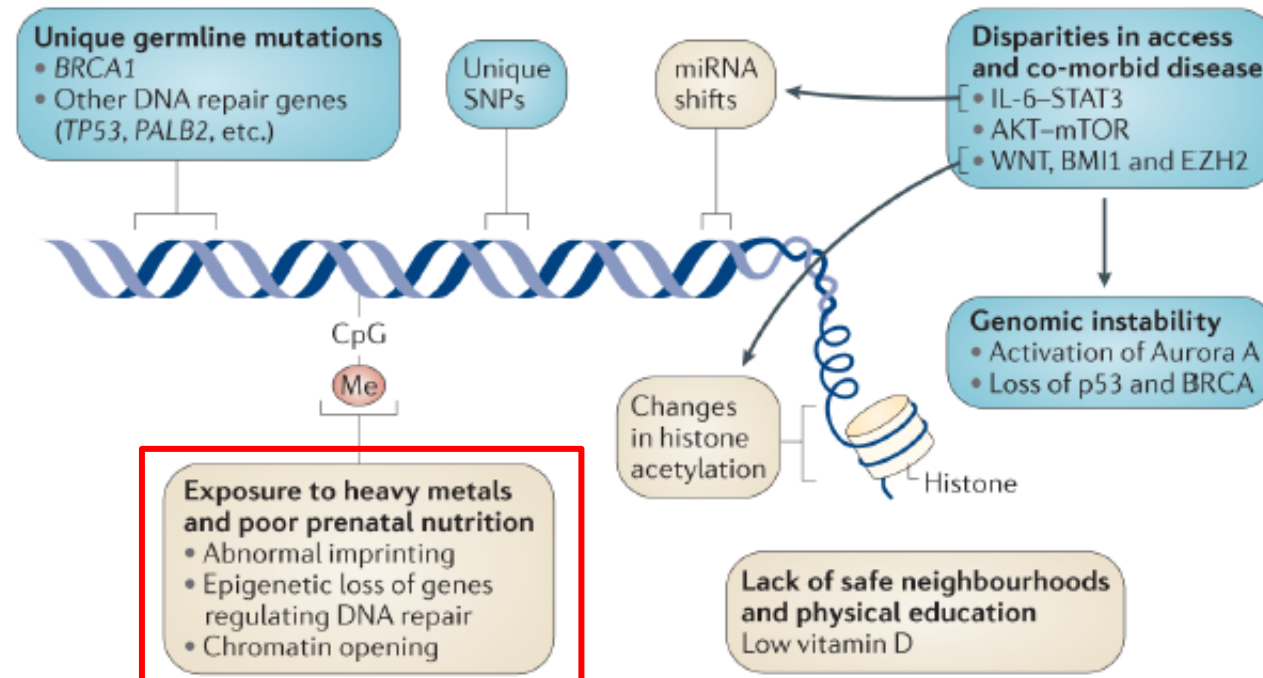


Health outcomes

> BMC Public Health. 2017 Apr 24;17(1):354. doi: 10.1186/s12889-017-4225-8.

Maternal blood cadmium, lead and arsenic levels, nutrient combinations, and offspring birthweight

Yiwen Luo ^{1 2}, Lauren E McCullough ³, Jung-Ying Tzeng ^{4 5 6}, Thomas Darrah ⁷, Avner Vengosh ⁸, Rachel L Maguire ⁹, Arnab Maity ², Carmen Samuel-Hodge ¹⁰, Susan K Murphy ¹¹, Michelle A Mendez ¹⁰, Cathrine Hoyo ¹²

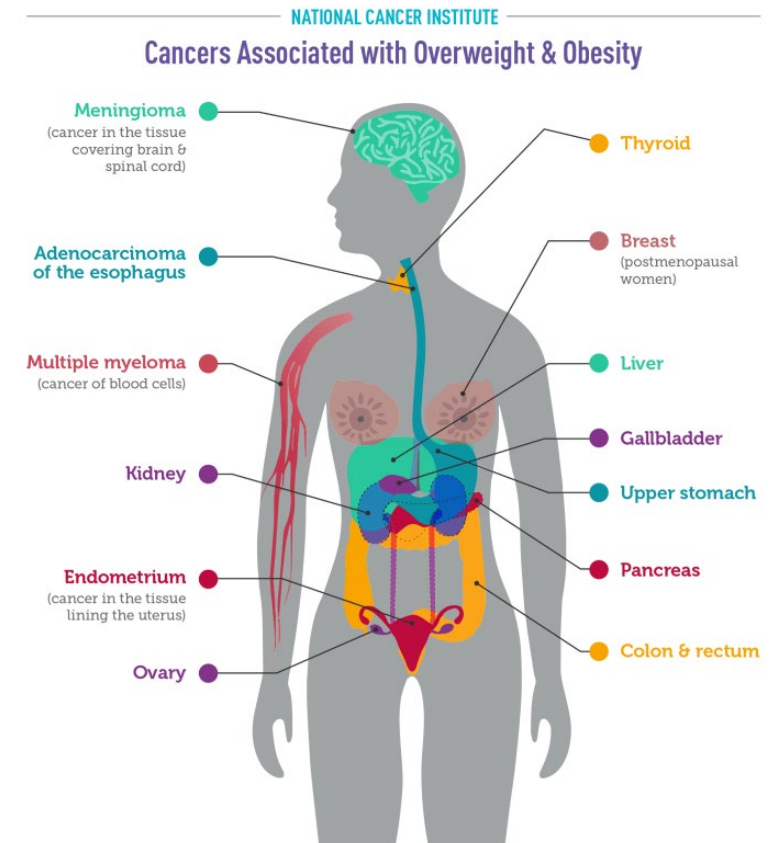
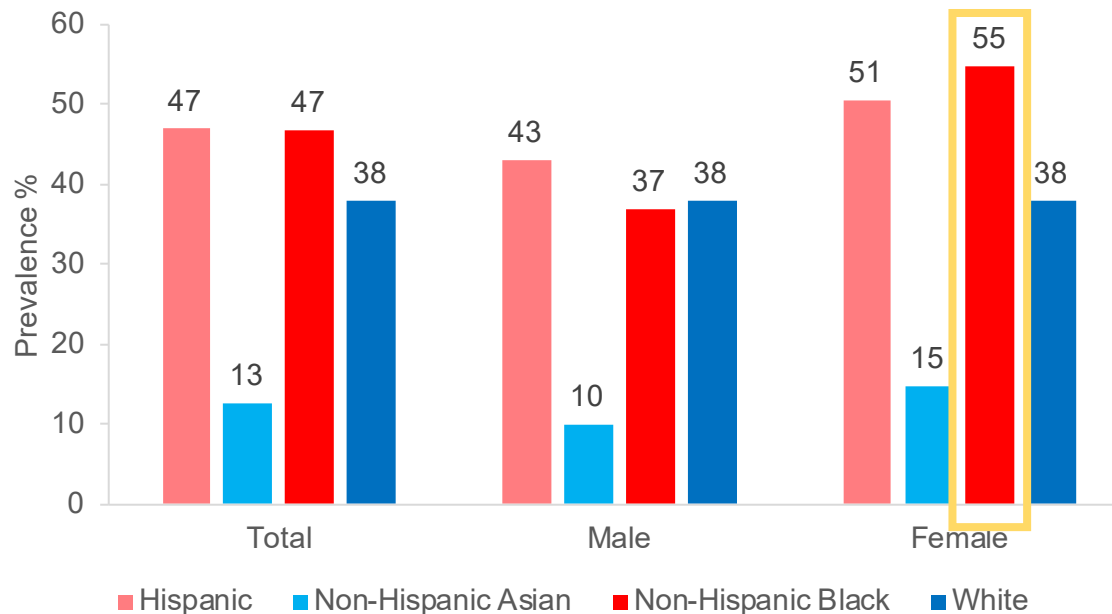




Probable Causal Paths – Obesity example

Structural racism & discrimination → Residential segregation → Obesity → Molecular consequences → Cancer

BMI_{≥30}



Centers for Disease Control, 2017
National Center for Health Statistics



Obesity and cancer disparities (female sex)

Top sites for cancer risk disparities

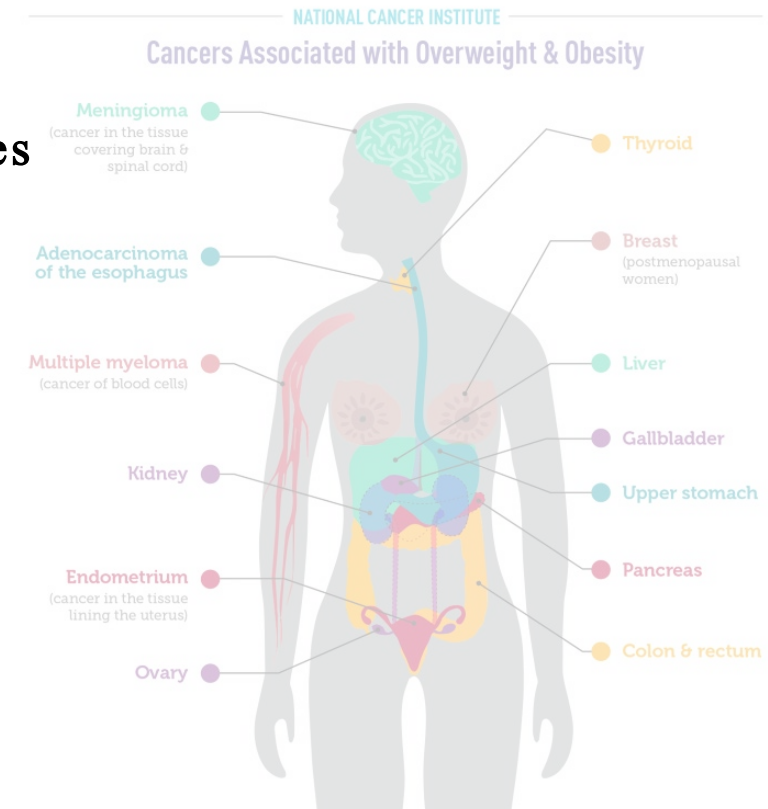
1. K. sarcoma	RR=3.60
2. Myeloma	RR=2.60
3. Stomach	RR=2.14
4. Liver	RR=1.40
5. Pancreas	RR=1.34
6. Cervical	RR=1.22
7. Colorectal	RR=1.18
8. Esophageal	RR=1.16
9. Kidney	RR=1.14
10. Endometrial	RR=1.01
All Sites	RR=0.92

Blue text = Cancers associated with overweight obesity

Top sites for cancer mortality disparities

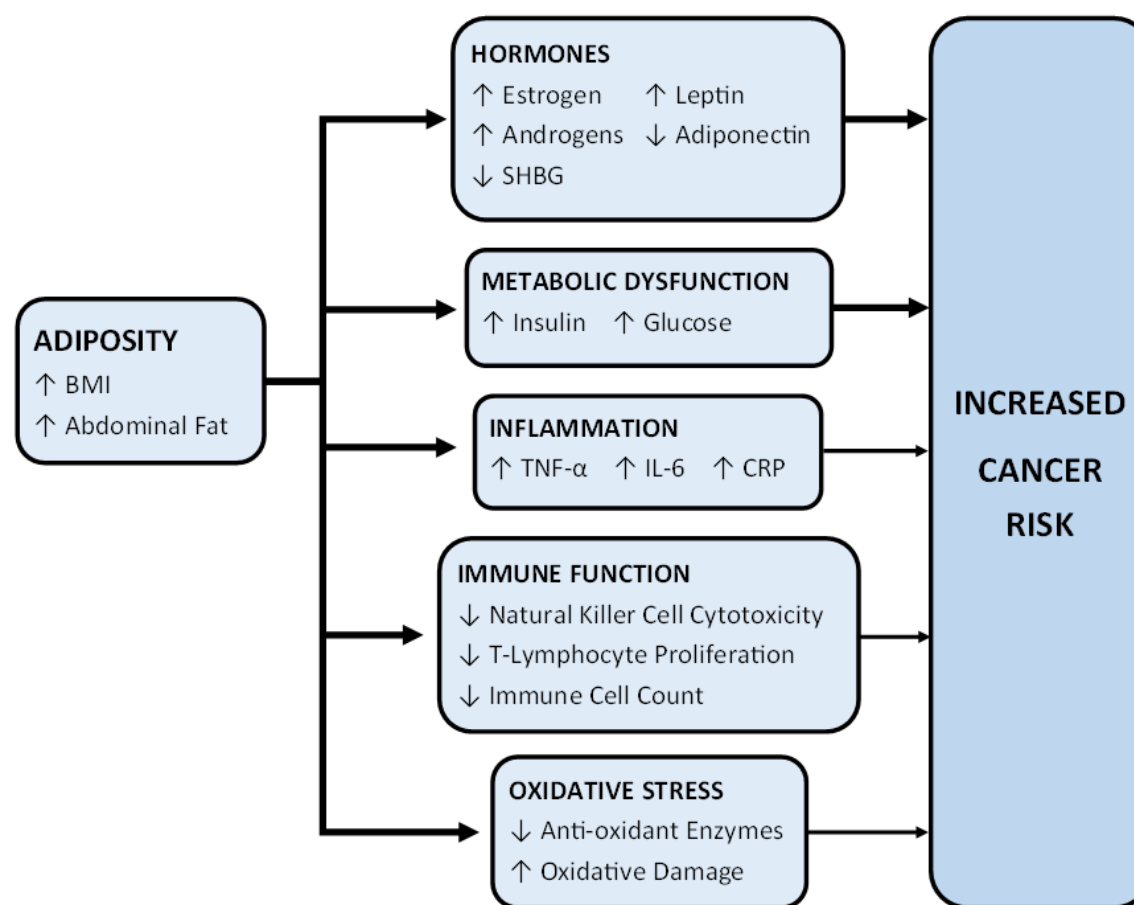
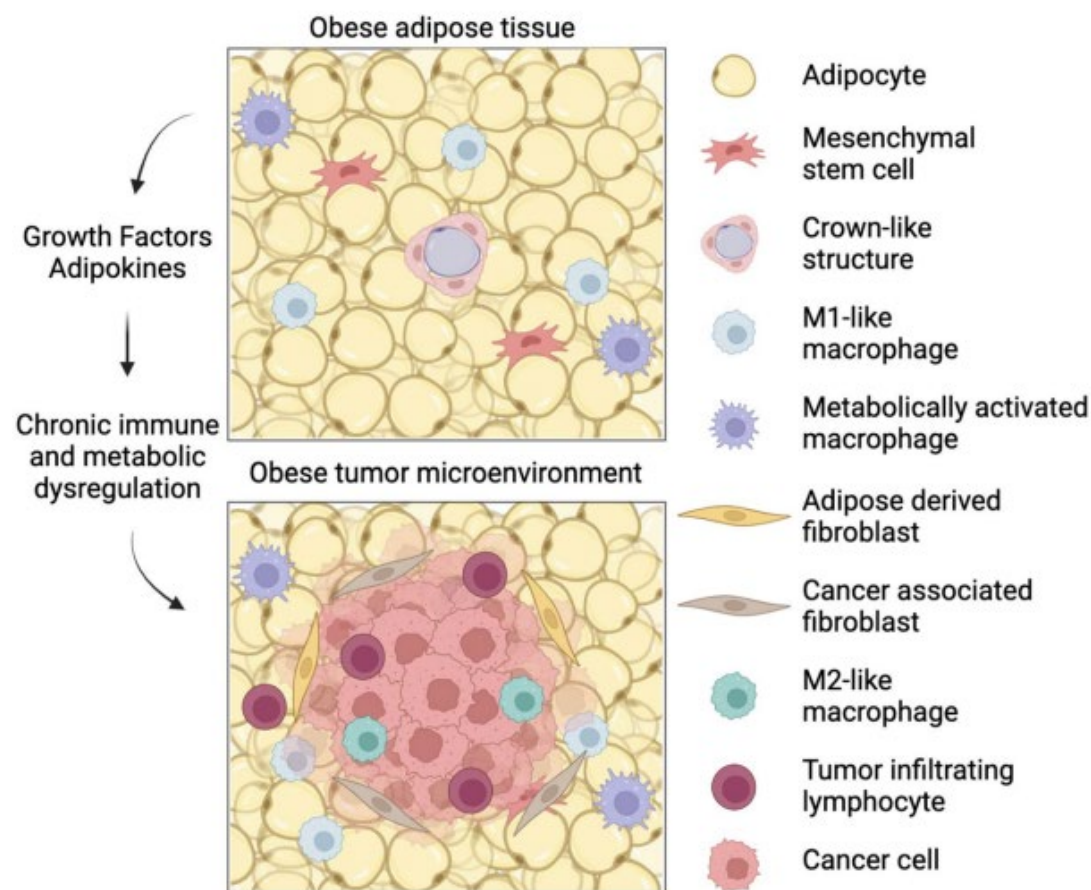
1. Stomach	RR=2.31
2. Myeloma	RR=2.24
3. Endometrial	RR=1.97
4. Cervical	RR=1.65
5. Breast	RR=1.41
6. Liver	RR=1.35
7. Colorectal	RR=1.31
8. Pancreas	RR=1.28
9. Esophageal	RR=1.04
10. Bladder	RR=1.04
All Sites	RR=1.12

Cancer Facts and Figures for African Americans 2022-2024



95% of the excess cancer deaths among Black women are due to EC, BC, CRC

Biologic mechanisms of obesity and breast cancer



The impact of obesity on the tumor microenvironment

Abstracted from Devericks EN, Carson MS, McCullough LE, Coleman MF, and Hursting SD.

Cancer and Metastasis Reviews. 2022

Adapted from Lynch et al. 2010



Mechanisms drive the complicated obesity-breast cancer association and related disparities

Effect Estimates

Pre menopausal*	
All	0.92
ER- and PR-	1.80
Post menopausal*	
All	1.12
ER+ or PR+	1.33
Etiologic heterogeneity (compared to Luminal A)	
TNBC	1.20
Pre menopausal TNBC	1.43
Mortality	
All Cause	1.56
Breast Cancer-Specific	2.54

Obesity associated with:

- (1) **Later stage** at diagnosis
- (2) Development of **aggressive** breast cancers
- (3) **Poor treatment outcomes** (suboptimal dosing, presence of comorbidities, poor adherence)
- (4) Breast cancer-related **death**

*Sound
familiar?*

80% of Black women are overweight or obese at diagnosis

Biologic distinction vs. prevalence of risk factors



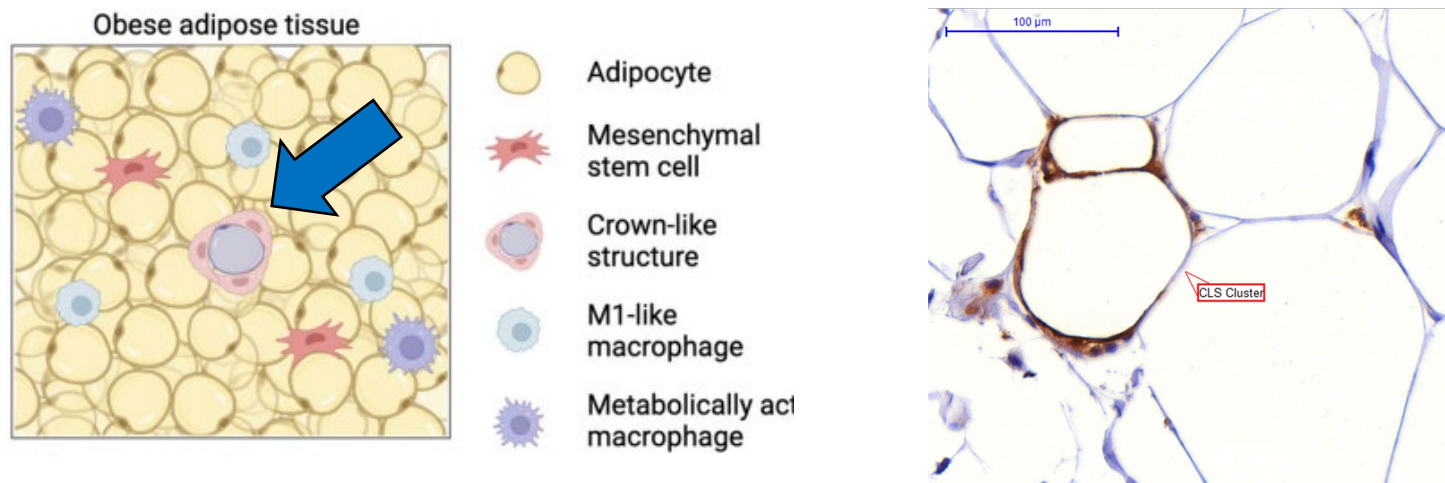
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> [Breast Cancer Res. 2020 Jun 17;22\(1\):65. doi: 10.1186/s13058-020-01308-4.](#)

Detection of crown-like structures in breast adipose tissue and clinical outcomes among African-American and White women with breast cancer

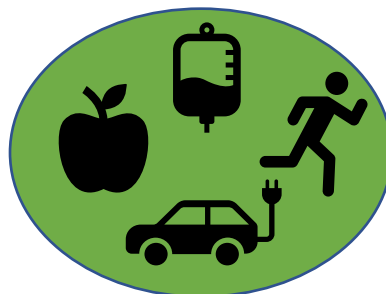
Maret L Maliniak¹, Aswathy Miriam Cheriyan^{1 2}, Mark E Sherman³, Yuan Liu^{4 5},
Keerthi Gogineni^{5 6}, Jiaqi Liu⁵, Jiabei He⁵, Uma Krishnamurti⁷, Jasmine Miller-Kleinhenz¹,
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- (1) Black women **more likely** to have CLS BUT...
- (2) Almost entirely **driven by the higher prevalence** of obesity



Direct and indirect effects on biology



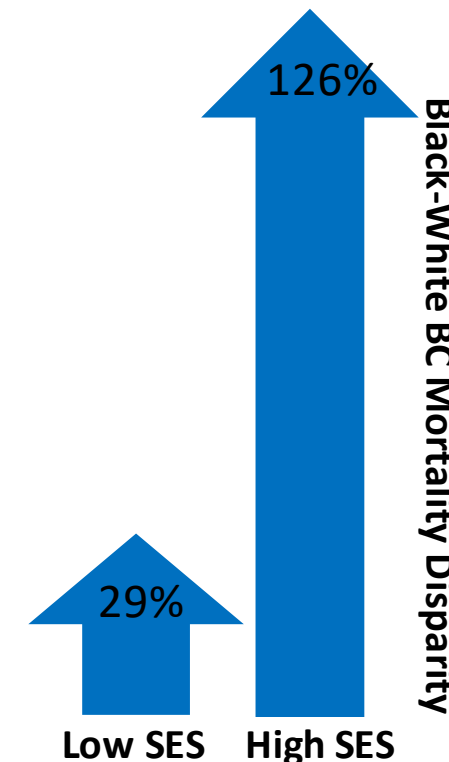
INTERVENTION

Structural racism & discrimination → Residential segregation → Obesity → Molecular consequences → Cancer



Social Isolation

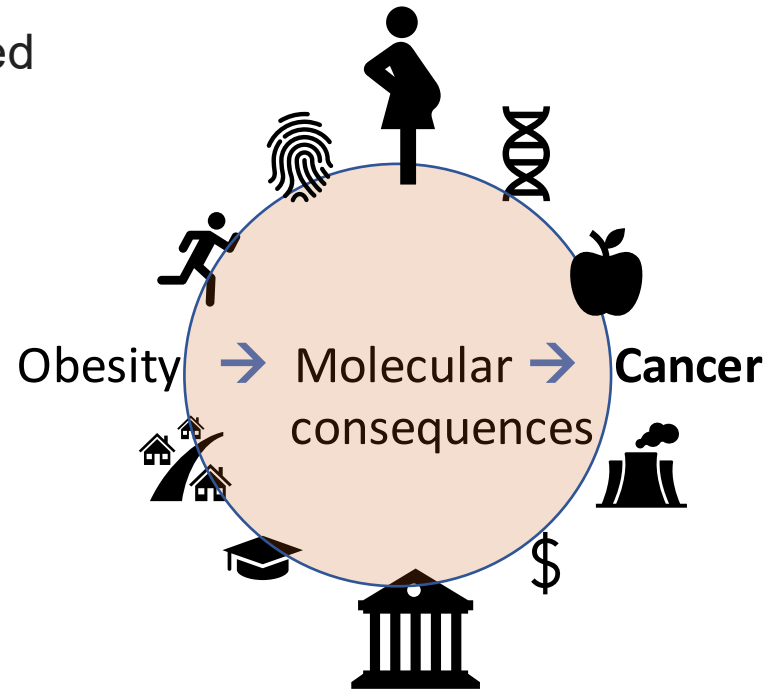
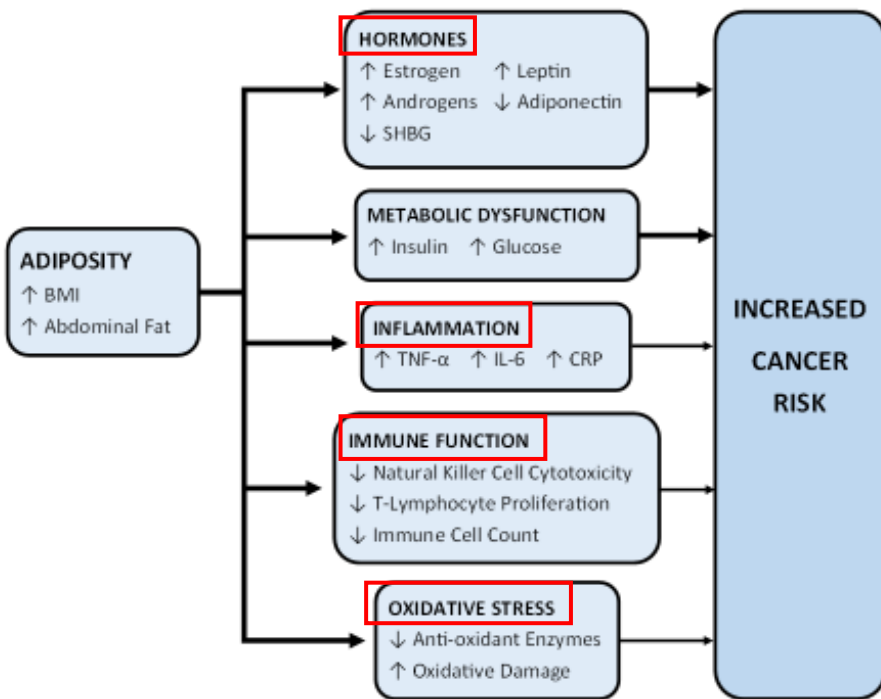
Stress → inflammation, stress induced hormones, epigenetic modifications, accelerated aging (telomere length and epigenetic age)





Direct and indirect effects on biology

Genes were **implicated in breast carcinogenesis**, including genes related to inflammation, immune function, ER activation, and stress response

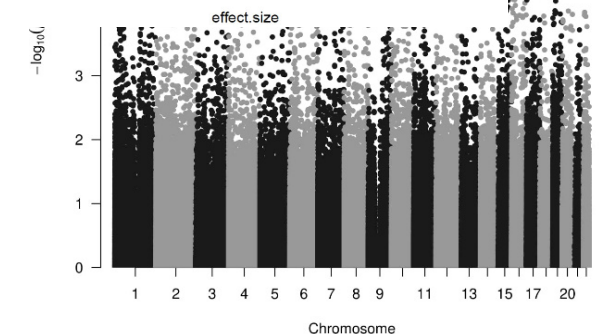
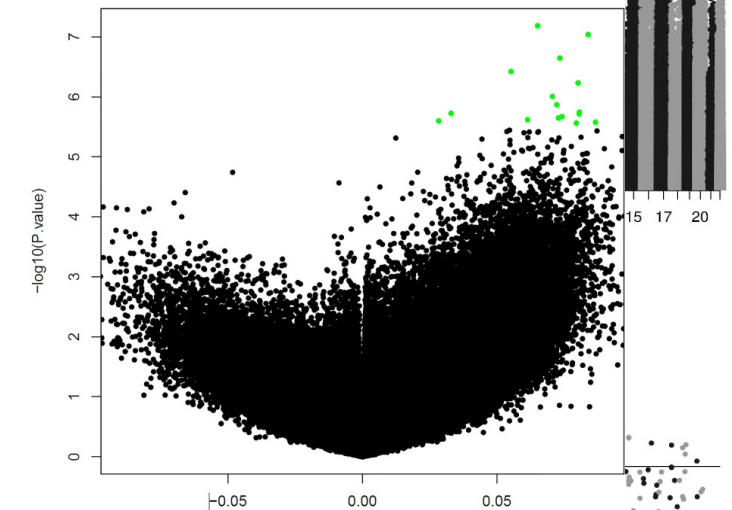


SYNERGISM, GREATER THAN ADDITIVE,
MORE THAN MULTIPLICATIVE, &
BEYOND QUANTIFIABLE

College Graduation



Contemporary Mortgage Discrimination



Do et al. (McCullough Sr. Author) *BCRT* (2020)

Gohar et al. (McCullough Sr. Author) *BCRT* (2022)

Miller-Kleinhenz et al. (McCullough Sr. Author) *Frontiers in Oncology* (2023)



Why it matters?

Historic Mortgage Discrimination →
Development of **late-stage** disease

	Early Stage	Late Stage	
Redlining Index	N	N	Age-adjusted OR (95% CI)
Non-Hispanic Black			
Continuous	671	155	0.92 (0.72, 1.18)
Dichotomous			
<2.5	89	25	Referent
≥2.5	582	130	0.79 (0.49, 1.28)
Non-Hispanic White			
Continuous	795	62	1.84 (1.28, 2.63)
Dichotomous			
<2.5	375	21	Referent
≥2.5	420	41	1.90 (1.10, 3.30)

OR, Odds Ratio; CI, Confidence Interval

Historic Mortgage Discrimination →
Development of **ER-** disease

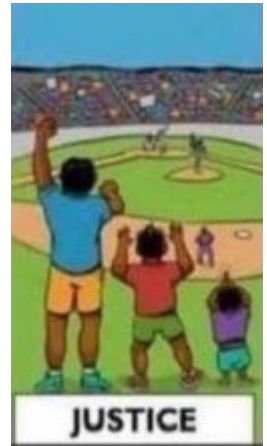
	ER+	ER-	
Redlining Index	N	N	Age-adjusted OR (95% CI)
Non-Hispanic Black			
Continuous	610	216	1.23 (0.97, 1.56)
Dichotomous			
<2.5	94	20	Referent
≥2.5	516	196	1.77 (1.06, 2.94)
Non-Hispanic White			
Continuous	765	92	0.89 (0.67, 1.18)
Dichotomous			
<2.5	352	44	Referent
≥2.5	413	48	0.88 (0.57, 1.37)

OR, Odds Ratio; CI, Confidence Interval

White Women →
Social intervention
(access)



Black Women →
Structural intervention
(justice)





Evidence to date...

Saini, G., Ogden, A., McCullough, L. E., Torres, M., Rida, P., & Aneja, R. (2019). Disadvantaged neighborhoods and racial disparity in breast cancer outcomes: the biological link. *Cancer causes & control*: CCC, 30(7), 677–686

Barnard, ME (2023). **Psychosocial stressors** and **breast cancer gene expression** in the Black Women's Health Study. *Breast cancer research and treatment*

*Jenkins, BD (2023). **Neighborhood Deprivation** and **DNA Methylation** and Expression of Cancer Genes in Breast Tumors. *JAMA network open*

*Miller-Kleinhenz, JM (2023). **Redlining**-associated methylation in breast tumors: the impact of contemporary structural racism on the **tumor epigenome**. *Frontiers in oncology*

Pichardo, MS (2023). Association of **Neighborhood Deprivation** With Prostate Cancer and **Immune Markers** in African American and European American Men. *JAMA network open*

Pichardo, CM (2023). Association of **neighborhood gentrification** with prostate cancer and **immune markers** in African American and European American men. *Cancer medicine*

*Gohar, J (2022). **Neighborhood characteristics** and **breast tumor methylation**: using epigenomics to explore cancer outcome disparities. *Breast cancer research and treatment*

Shen, J (2022). **Neighborhood disadvantage** and **biological aging** biomarkers among breast cancer patients. *Scientific reports*

Guerrero-Preston, R (2019). **JAK3 Variant, Immune Signatures, DNA Methylation, and Social Determinants** Linked to Survival Racial Disparities in Head and Neck Cancer Patients. *Cancer prevention research*

[illegible]

Acknowledgements



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Scientific Collaborators

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BRIDGE Trainees

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Community Collaborators

Jacquelyn Bryant, BRIDGE Community PI
BRIDGE Community (24 BC survivors)

Local Partners

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- Don't exploit our pain without also exploring our power
- Not passive recipients of oppression. What does it look like when communities respond to and care for one another?
- None of us were around when this house was built. But it is ours to deal with now
- Is not hatred, it is the grooves of routine and expectation, patterns of a social order that have been in place so long look natural when it isn't. Everywhere but invisible. Message – one kind of person is more deserving of freedom than another kind. Freedom to resist and fight for your human right to do so.