

# Allostatic Load and Breast Cancer: Tracing Social Determinant of Health Pathways

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The James

## **Disclosures**

No financial disclosures

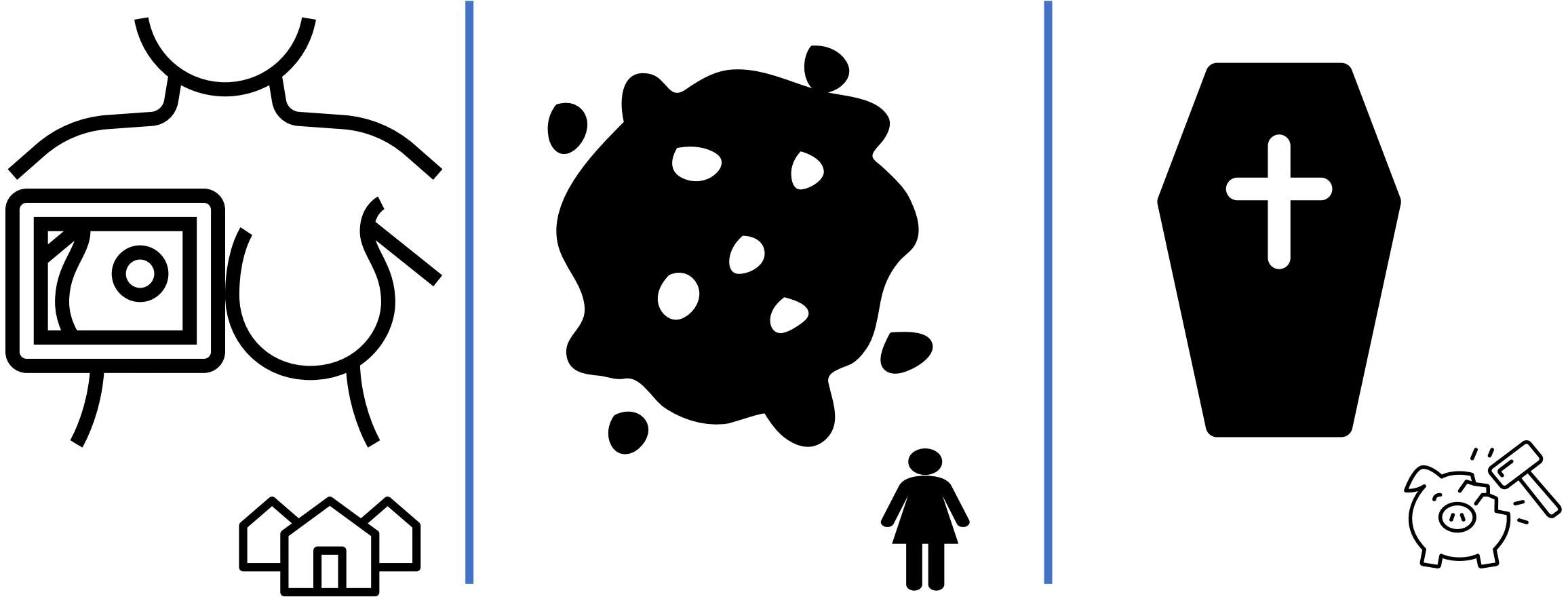
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# Socioenvironmental Factors and Breast Cancer

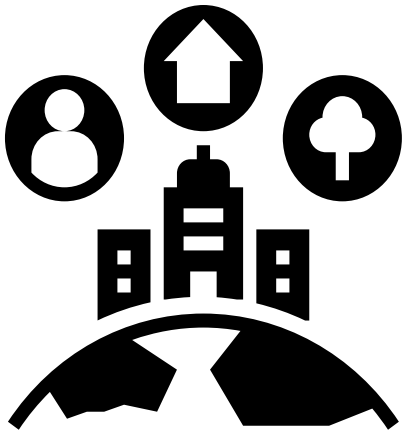


**What is the mechanistic  
pathway from  
socioenvironmental  
exposures to cancer  
initiation, progression and  
metastasis?**



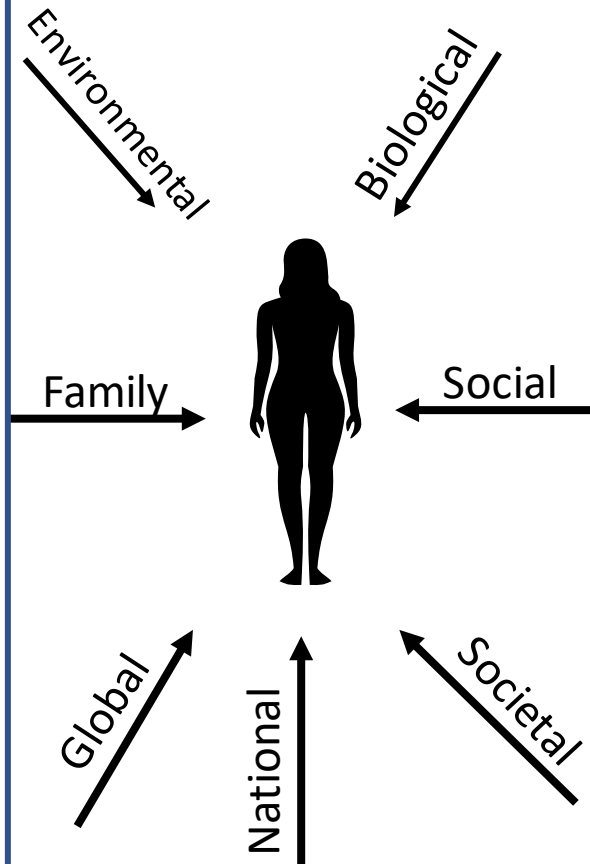
# Ecosocial Theory

## Embodiment

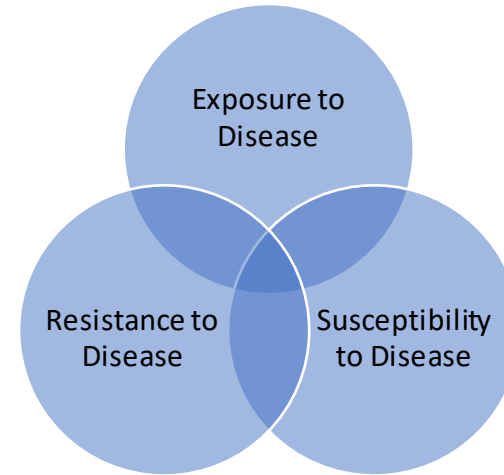


Relationship  
between the body  
and environment

## Embodiment pathways



## Cumulative Interplay between exposure, susceptibility and resistance



Disease is driven by structural  
and intermediary  
determinants of health

## Agency and Accountability



Acknowledgement of  
Structural  
determinants of health  
as major driver of  
disease distribution

# Weathering Hypothesis

“weathering is the accumulation and culmination of life experiences that are structured by historical and ongoing systemic racism and classism.”  
-Arline Geronimus PhD

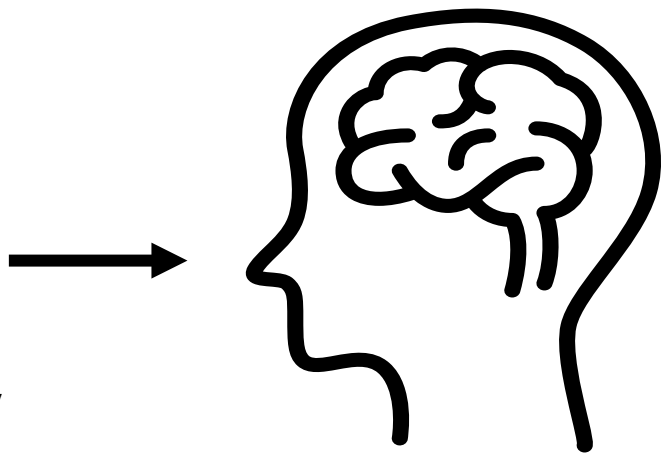
\*Example: Maternal outcomes between African Immigrants, women racialized as Black and white\*



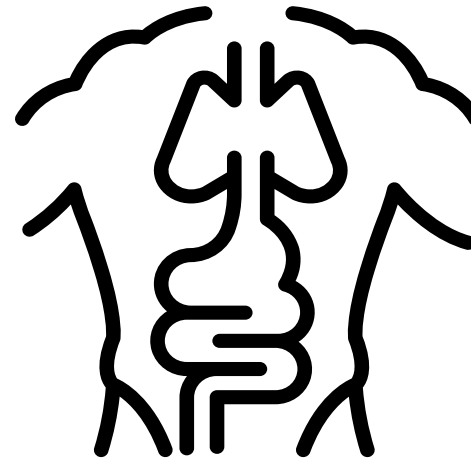
# Socioenvironmental Stressors and the Stress Pathway

## Socioenvironmental factors

1. Social isolation
2. Work-related stress
3. Financial instability

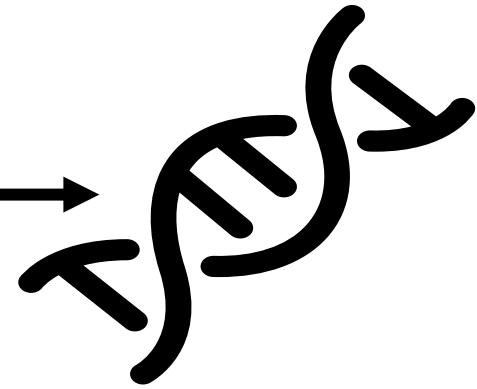


Hypothalamic-pituitary-adrenal axis + Sympathetic adrenal medullary pathway



Physiology

*(Allostatic Load)*



Molecular

*(DNA mitochondrial copy number)*

**Embodiment/Weathering**



Allostatic load: physiologic dysregulation secondary to exposure to chronic stress.

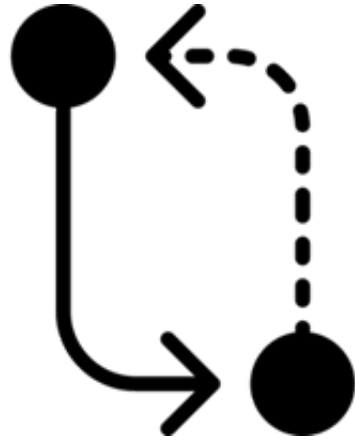
Allostasis: “maintain stability or homeostasis through change.”



## Patterns of Allostatic Load



Repeated  
events of  
various types



Failure to  
adapt to the  
same stressor



Failure to  
terminate a  
response



Inadequate  
release of stress  
hormones

# Measurements of Allostatic Load



Primary mediators  
(e.g., cortisol)



Secondary outcomes  
of primary mediators  
(e.g., systolic blood  
pressure)



Tertiary outcomes  
(e.g., hypertension)

# Allostatic Load Biomarkers

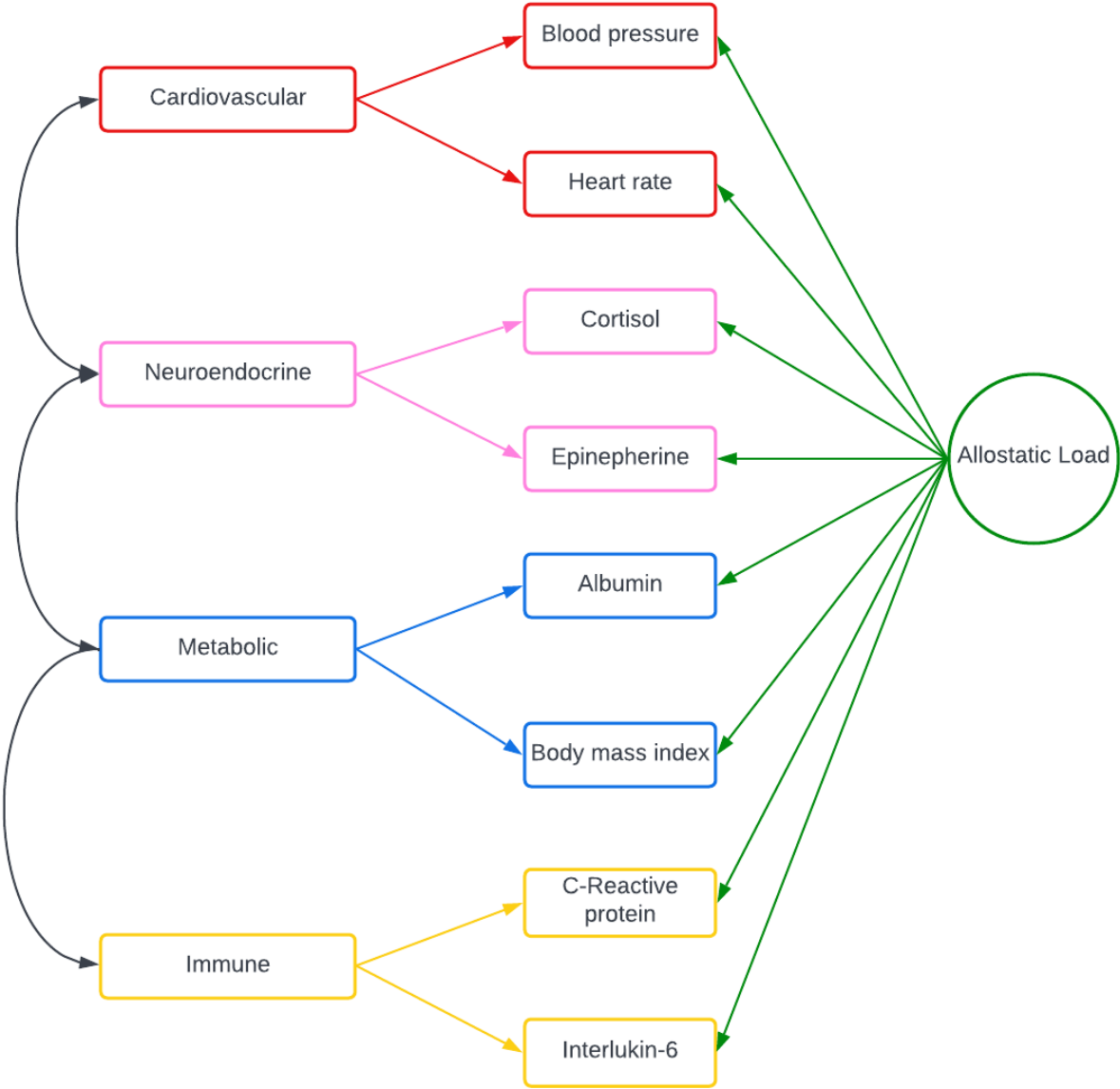
| Primary Mediators |
|-------------------|
| Cortisol          |
| DHEA              |
| Epinephrine       |
| Norepinephrine    |

| Secondary Outcomes       |                 |                    |
|--------------------------|-----------------|--------------------|
| Cardiovascular           | Metabolic       | Immune             |
| Systolic blood pressure  | A1c             | C-reactive protein |
| Diastolic blood pressure | Albumin         | WBC                |
| Heart rate               | BMI             | IL-6               |
| Cholesterol              | eGFR            | TNF-alpha          |
| HDL                      | Creatinine      |                    |
| Triglycerides            | Blood glucose   |                    |
| LDL                      | Waist-hip-ratio |                    |

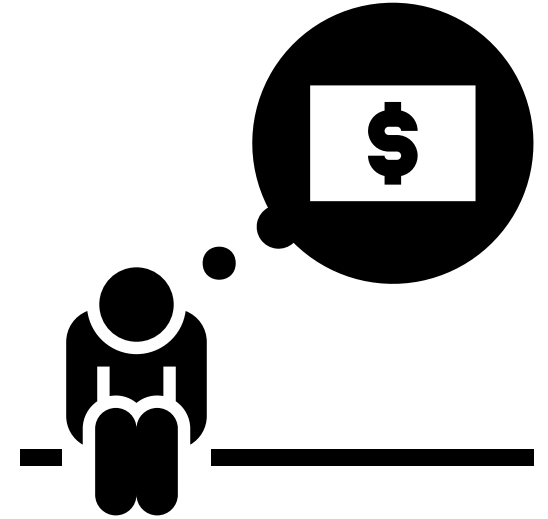
| Tertiary Outcomes |
|-------------------|
| Diabetes          |
| Hypertension      |
| Obesity           |
| Cancer            |

Calculated with clinical cut-offs or distribution of biomarkers in sample

# Allostatic Load Conceptualization



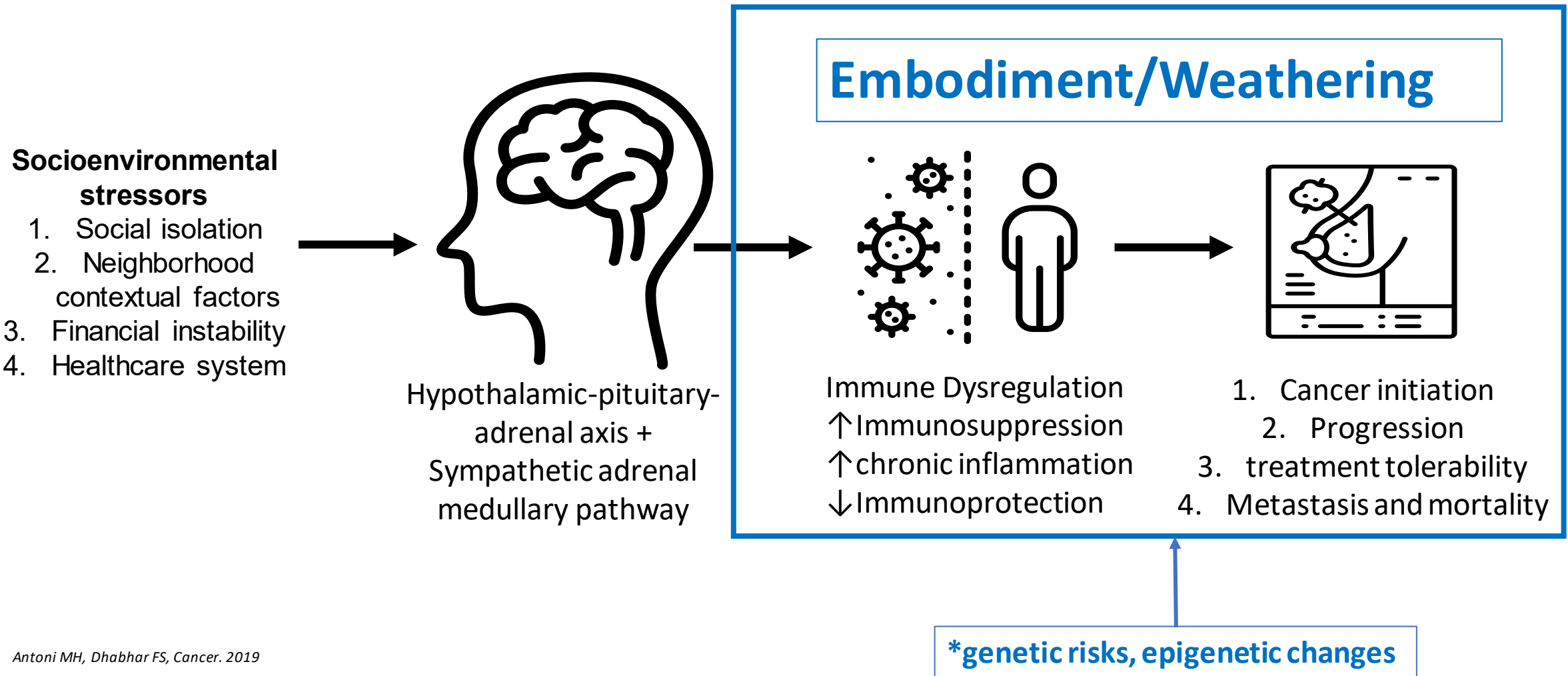
# Elevated Allostatic Load and Socioenvironmental Stressors



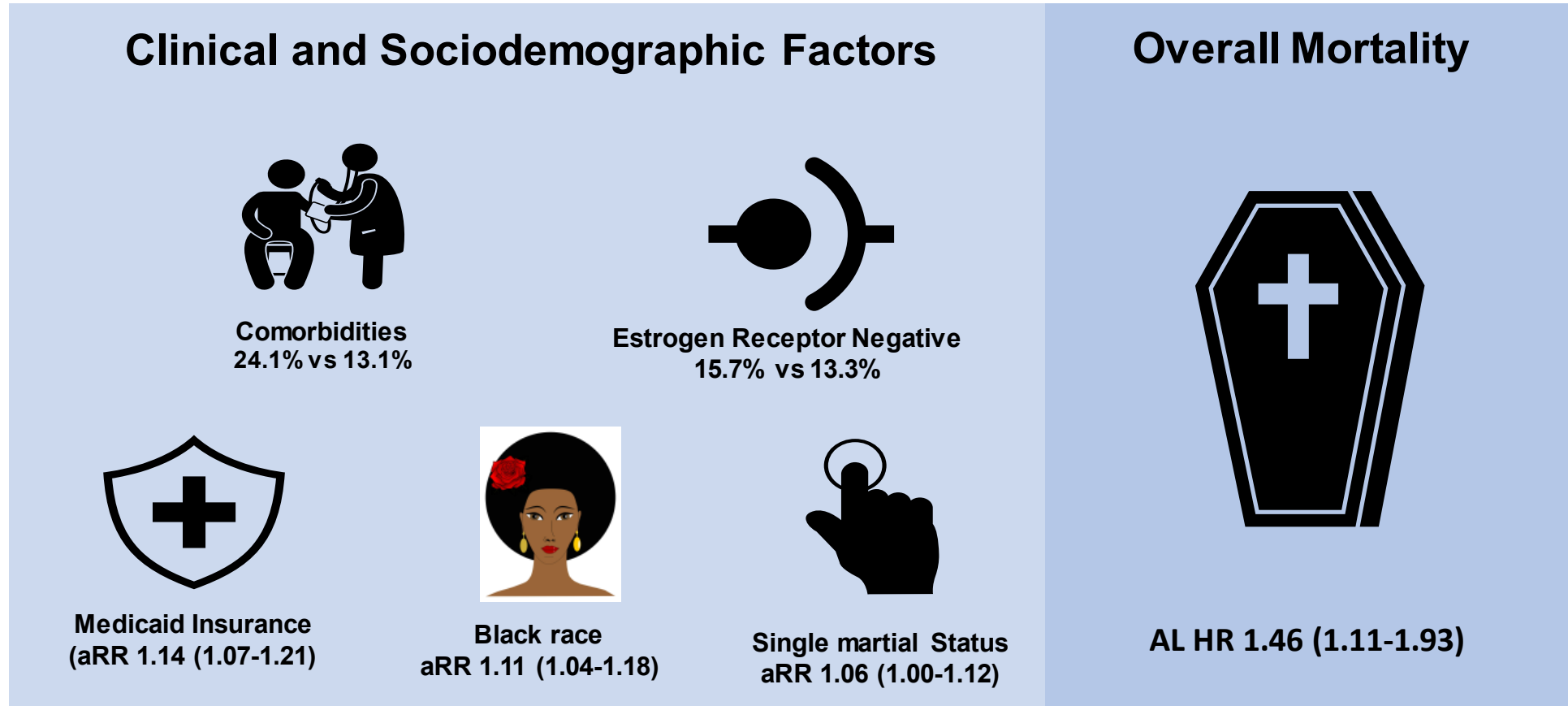


# Allostatic Load and Cancer

# Socioenvironmental Stressors and Cancer



# Association of Allostatic Load With All-Cause Mortality in Patients With Breast Cancer

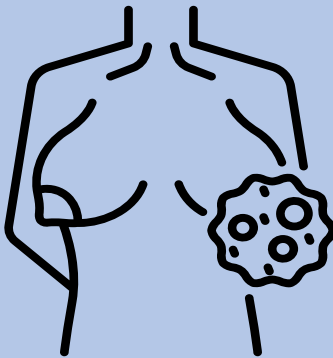


Obeng-Gyasi et al, Association of Allostatic Load With All-cause Mortality Among Patients With Breast Cancer, JAMA Network Open, May 2023

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# The Implications of Racialized Economic Segregation and Allostatic Load on Mortality in Patients with Breast Cancer

## Triple Negative Breast Cancer



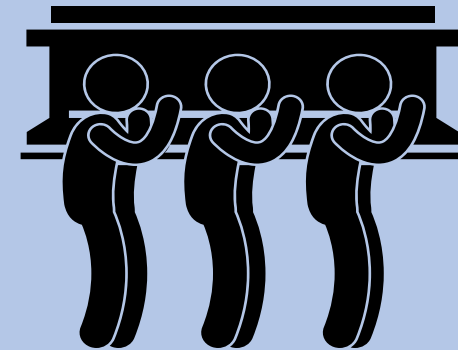
18.2% versus 11.6%,  $p < 0.001$

## High AL



OR 1.55, 95% CI 1.36–1.76

## Worse Mortality

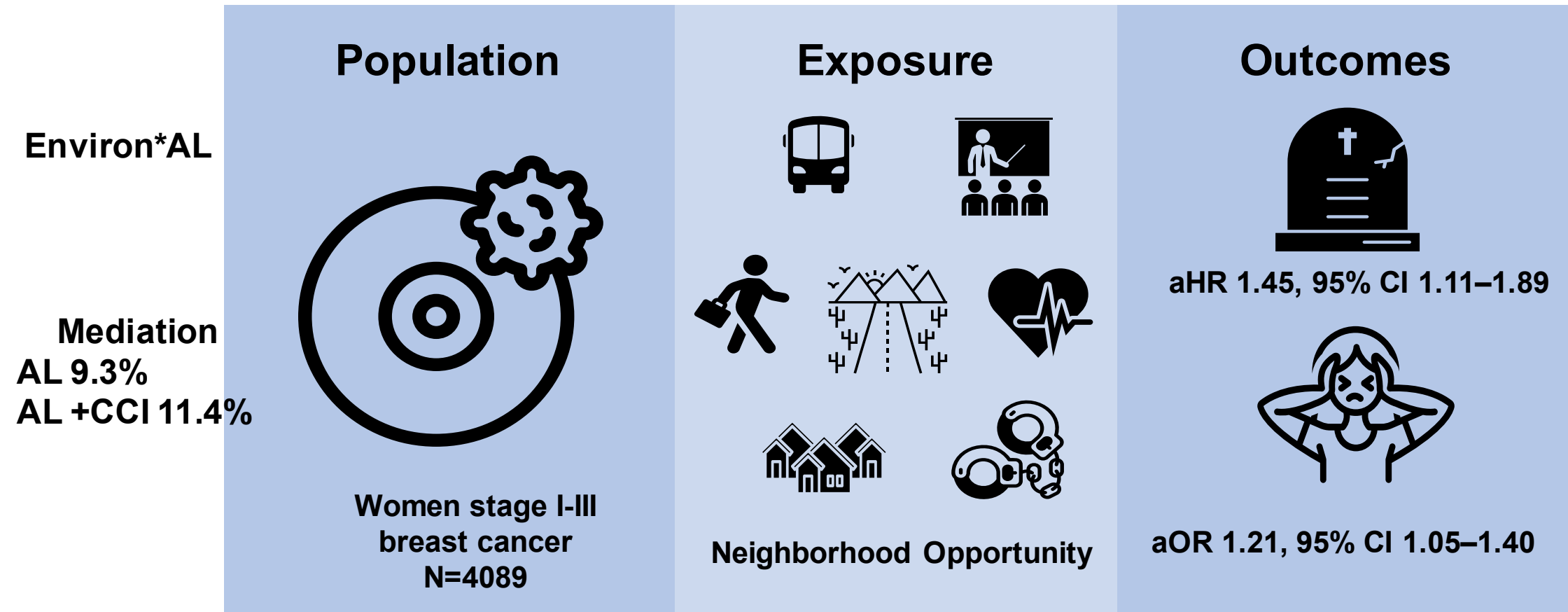


1.41, 95% CI 1.08–1.83

Chen et al, The Implications of Racialized Economic Segregation and Allostatic Load on Mortality in Patients with Breast Cancer, *Annals of Surgical Oncology*, November 2023

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# Association Between Neighborhood Opportunity, Allostatic Load, and All-Cause Mortality in Patients With Breast Cancer



Chen et al Association Between Neighborhood Opportunity, Allostatic Load, and All-Cause Mortality in Patients With Breast Cancer, Journal of Clinical Oncology, 2024

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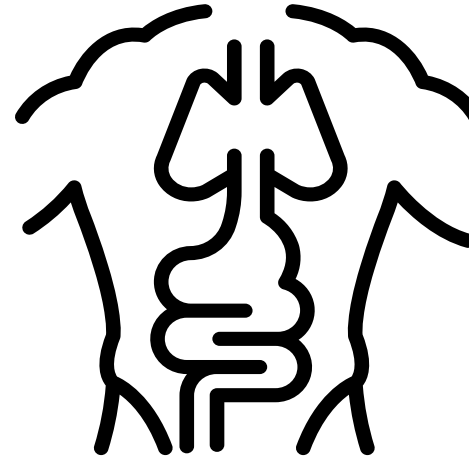
# Socioenvironmental Stressors and the Stress Pathway

## Socioenvironmental stressors

1. Social isolation
2. Neighborhood contextual factors
3. Financial instability
4. Healthcare system

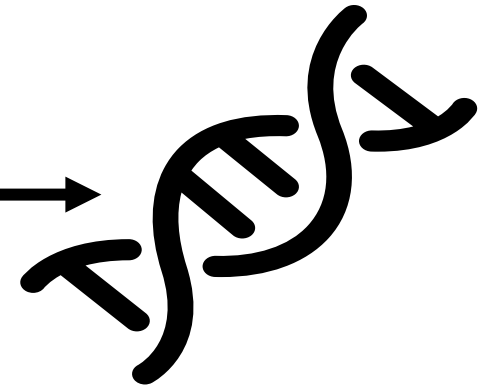


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Physiology

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**Embodiment/Weathering**



# Future Directions





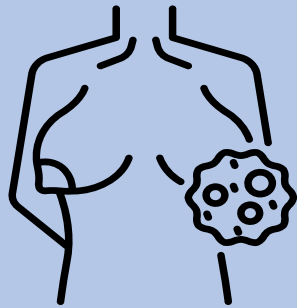
# AL in the Clinical Setting

- How should alterations in biomarkers due to treatment be managed (e.g., adrenal insufficiency secondary to systemic treatments)?
- How can allostatic load (AL) be integrated into clinical risk assessment?
- How can we treat elevated allostatic load?



# Feasibility Study of Biobehavioral Stress Reduction Intervention in Patients With Triple Negative Breast Cancer (NCT05677802)

## STUDY POPULATION



N=40  
Age 18+  
Untreated TNBC  
Stages I-III

## INTERVENTION

### Week 1

- Progressive muscle relaxation
- Responding to cancer crisis (stress, anxiety, depression)
- Physical activity log

### Week 2

- Coping (seeking disease info)

### Weeks 3-5

- problem solving (HRSN)

### Week 6-7

- assertive communication with healthcare providers

### Week 8-10

- social support

## OUTCOME

Program  
Acceptability

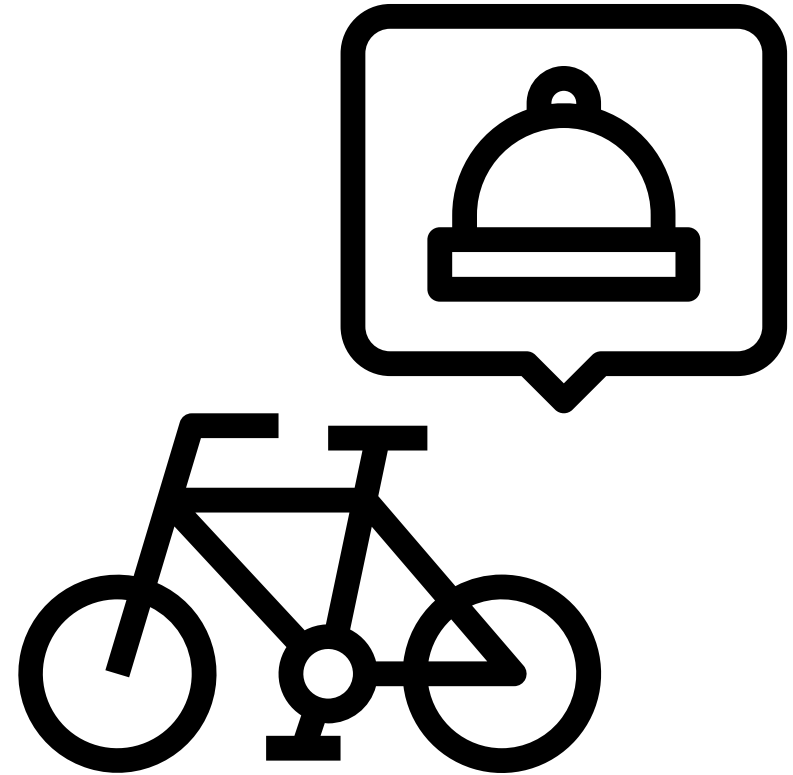
Allostatic load

Patient Reported  
Outcomes

- Self reported stress
- depressive symptoms
  - anxiety
  - QoL

# Take Away

- Ecosocial theory and weathering describe internalization of socioenvironmental factors.
- Allostatic load is a form of embodiment/weathering.
- High allostatic load is associated with poor tumor characteristics and worse mortality





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