



Health Equity and Pain  
Across the Life Course

*Social Determinants of Biological Pain  
Mechanisms- Insights and Implications*

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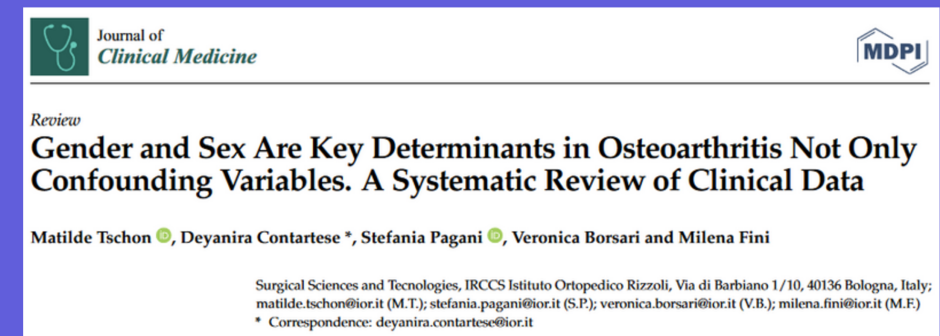
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# Objectives

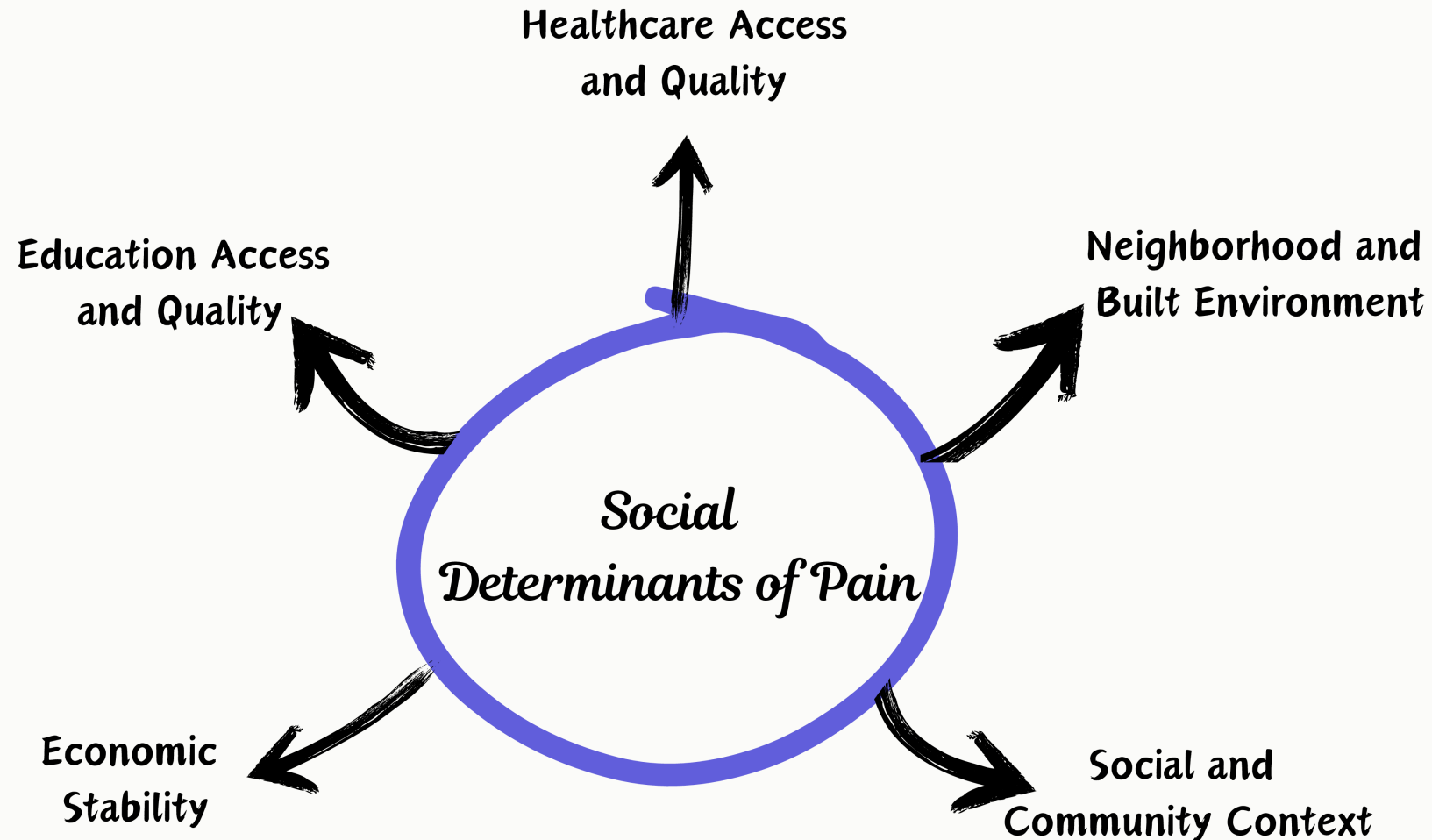
- 1** Describe social determinants of biological pain mechanisms
- 2** Identify gaps in knowledge and interventions to achieve equity in pain outcomes

# Despite significant progress in research, practice, and policy, disparities in pain management and outcomes remain a pervasive public health problem

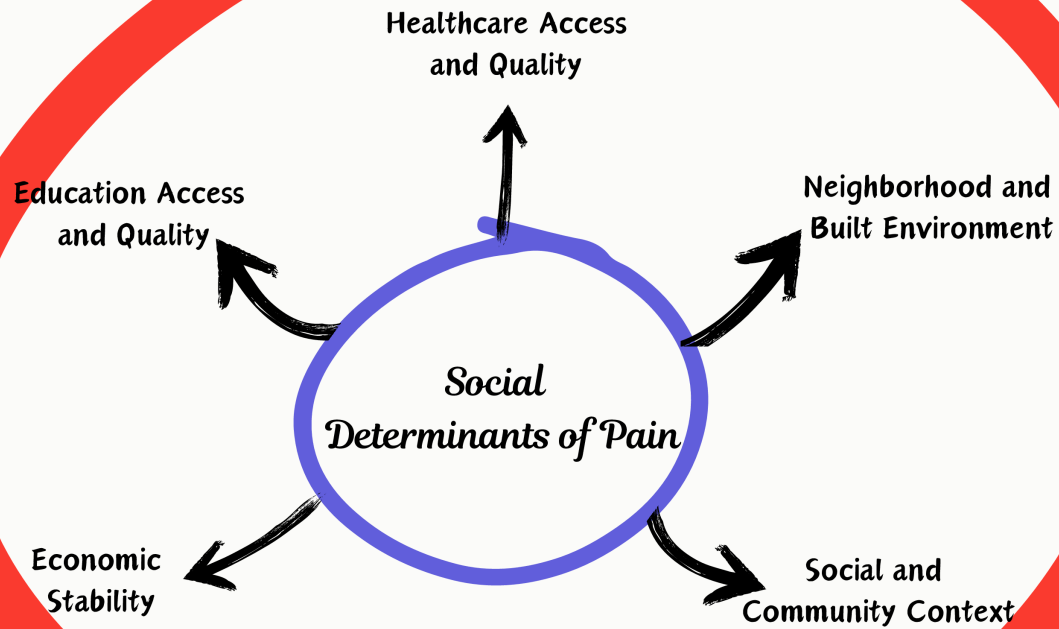
- Health disparities result from prejudices, biases, and discrimination related to several factors, including
  - Age
  - Sex
  - Race
  - Sexual orientation
  - Socioeconomic status
  - Geographic location
  - Immigration status



**A wide set of non-medical forces and systems, such as economic policies and systems, development agendas, social norms, social policies, and political systems, shape daily life and influence pain outcomes**



# How do social disparities “get under the skin” to cause pain disparities?

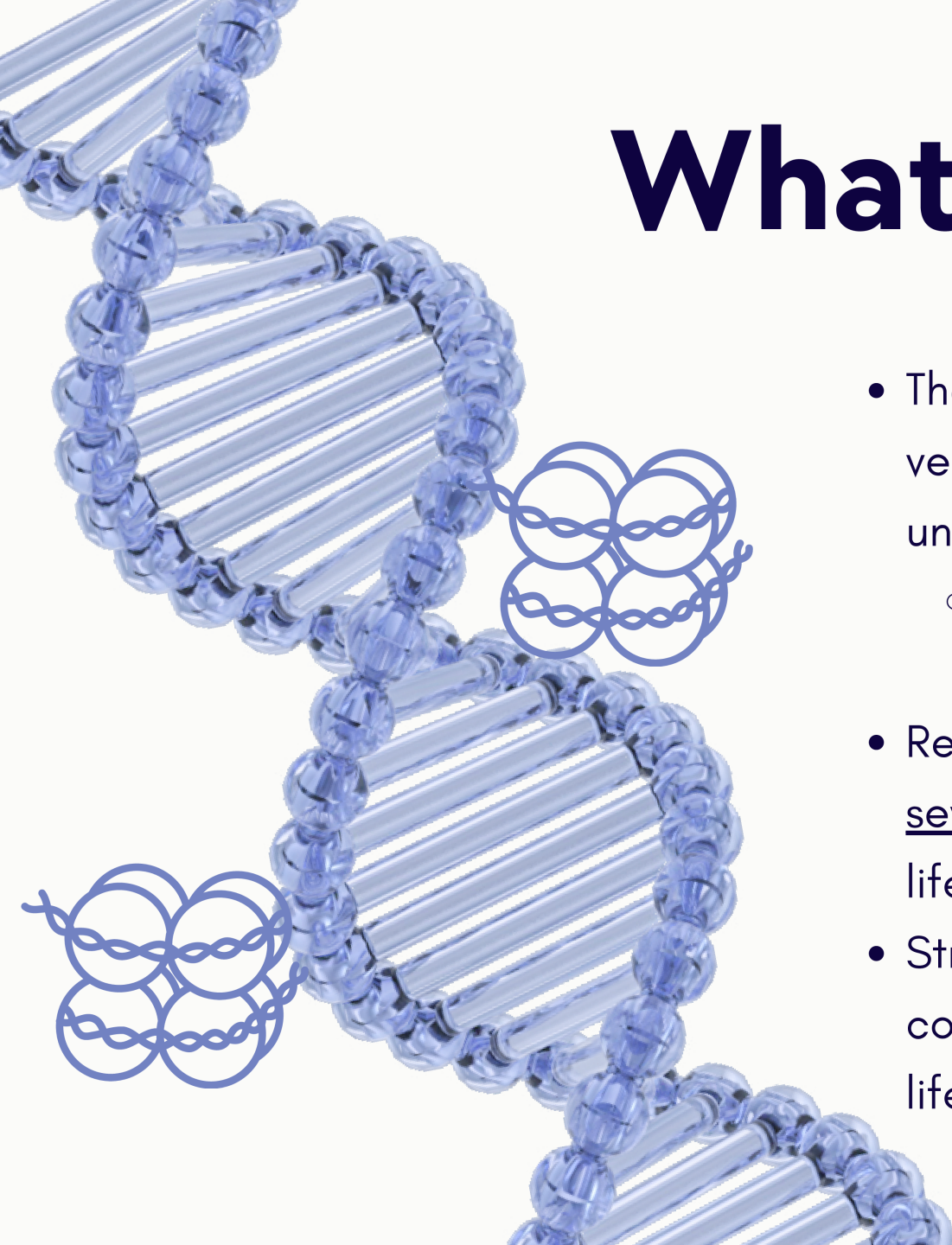


**Epigenetics**

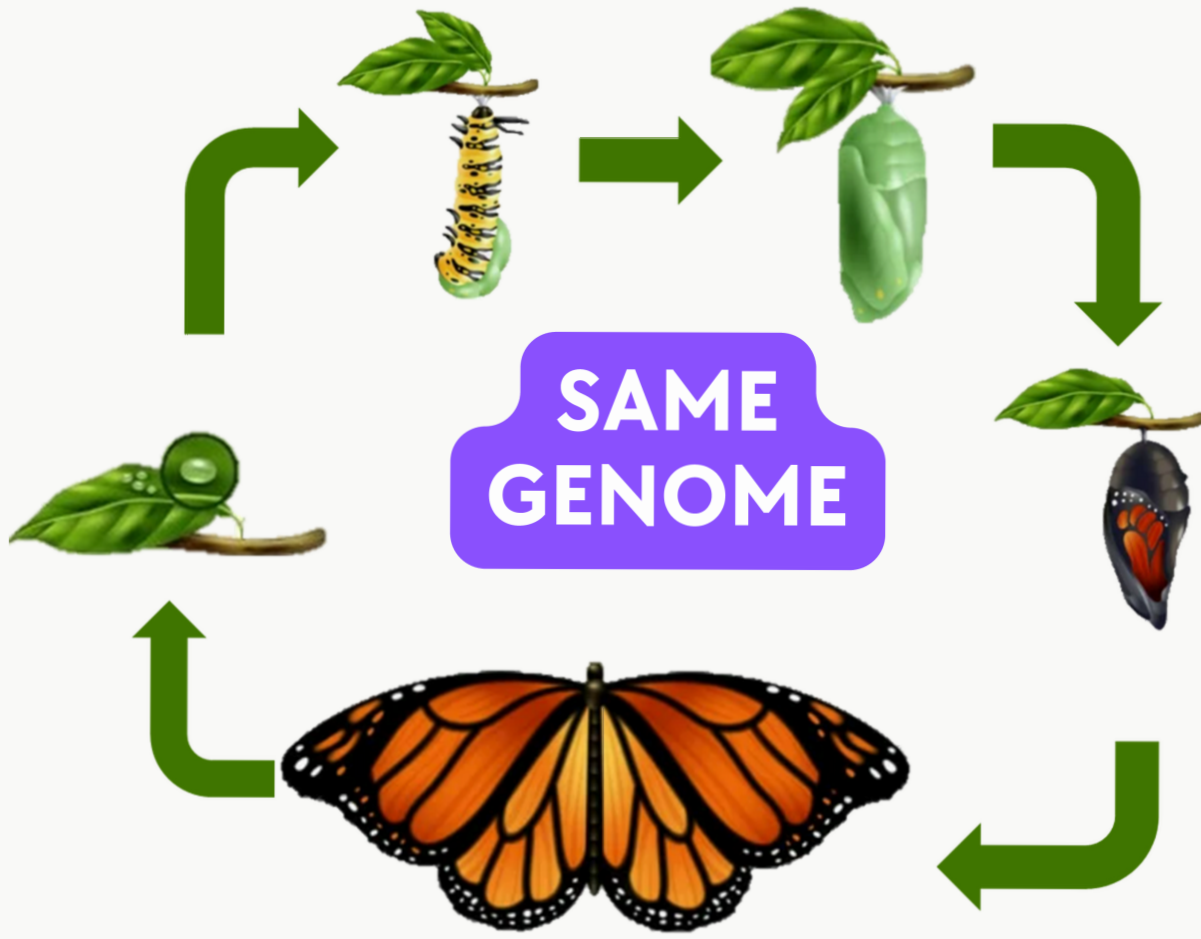


# What is Epigenetics?

- The study of heritable changes in gene expression (active versus inactive genes) that do not involve changes to the underlying DNA sequence
  - A change in phenotype without a change in genotype – which in turn affects how cells read the genes
- Regular and natural occurrence but can be influenced by several factors including age, diet, environmental factors, lifestyle, disease, etc.
- Stress, trauma, adversity, and socioeconomic status conditions can result in epigenetic changes, influencing lifelong health and well-being -- social epigenetics

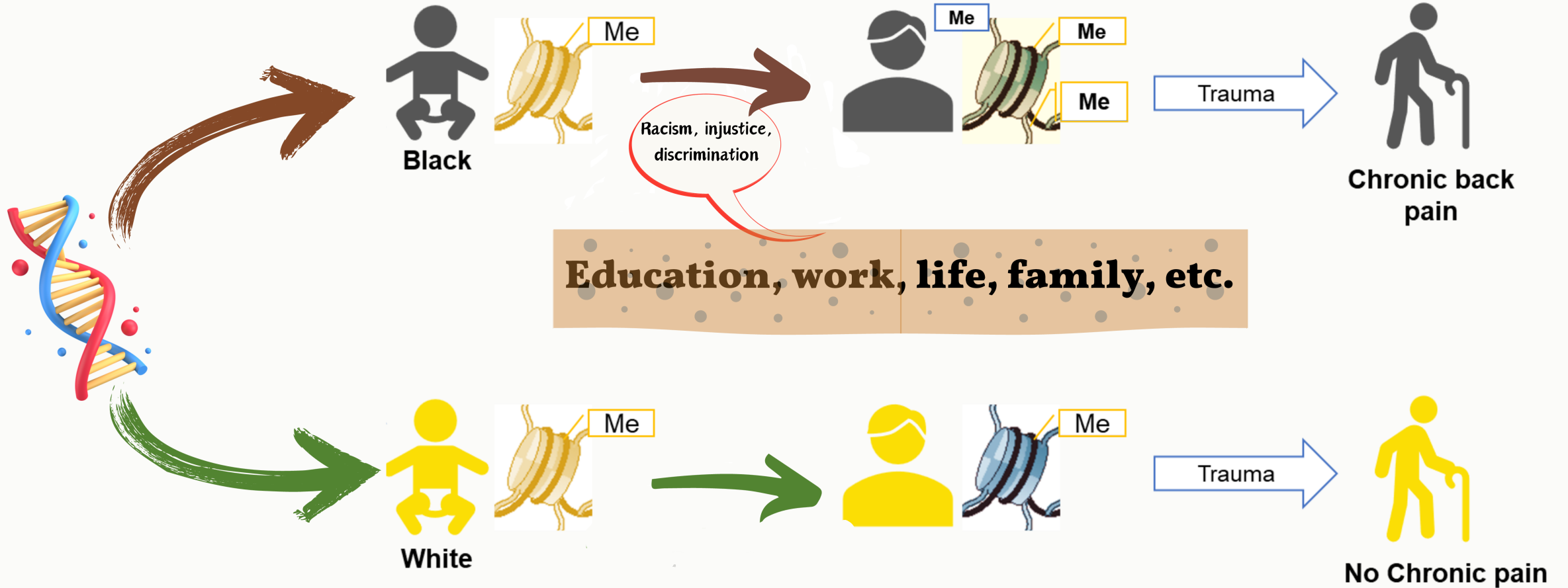


# Why the Epigenome?

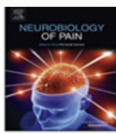


- Epigenetics explains how early experiences and environmental exposures can have lifelong and transgenerational impacts

# Could epigenetics help explain racial disparities in chronic pain?





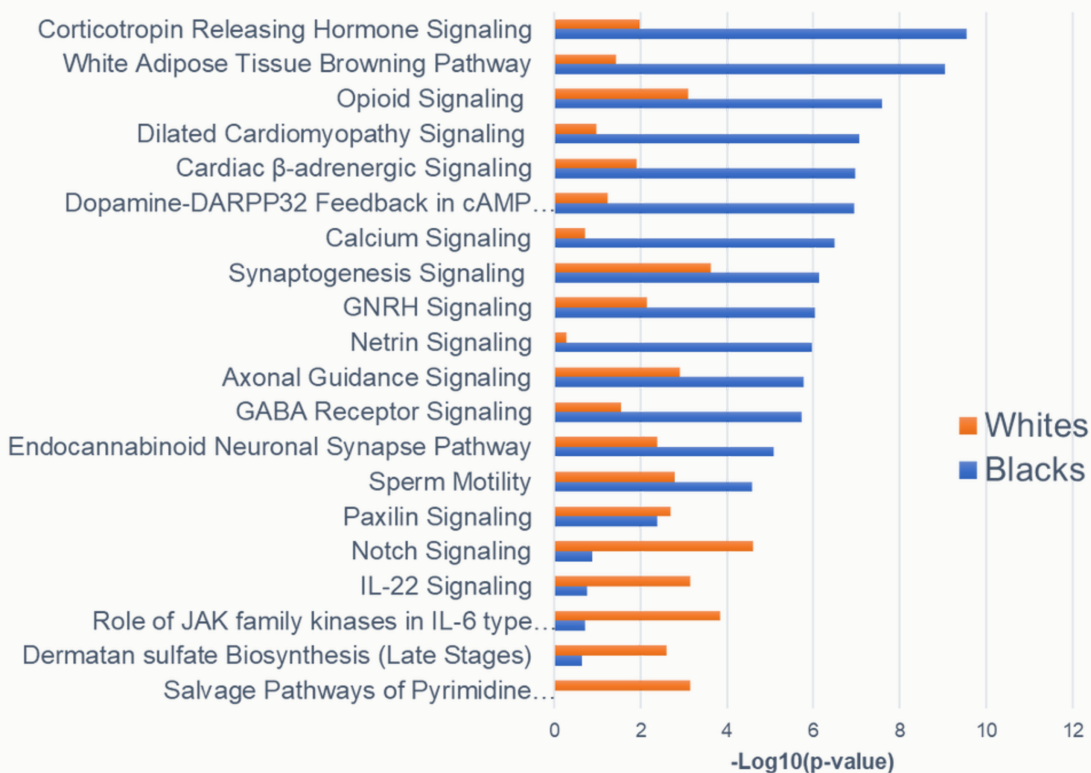


Differential DNA methylation in Black and White individuals with chronic low back pain enrich different genomic pathways

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# Pain and stress-related genomic pathways are more significant in Blacks than Whites with chronic low back pain



## • Chronic pain and chronic stress

- Chronic pain and chronic stress are two sides of the same coin.
- Chronic stress can modify the expression of genes related to the stress response, such as the NR3C1 gene
- These modifications can influence pain sensitivity and threshold

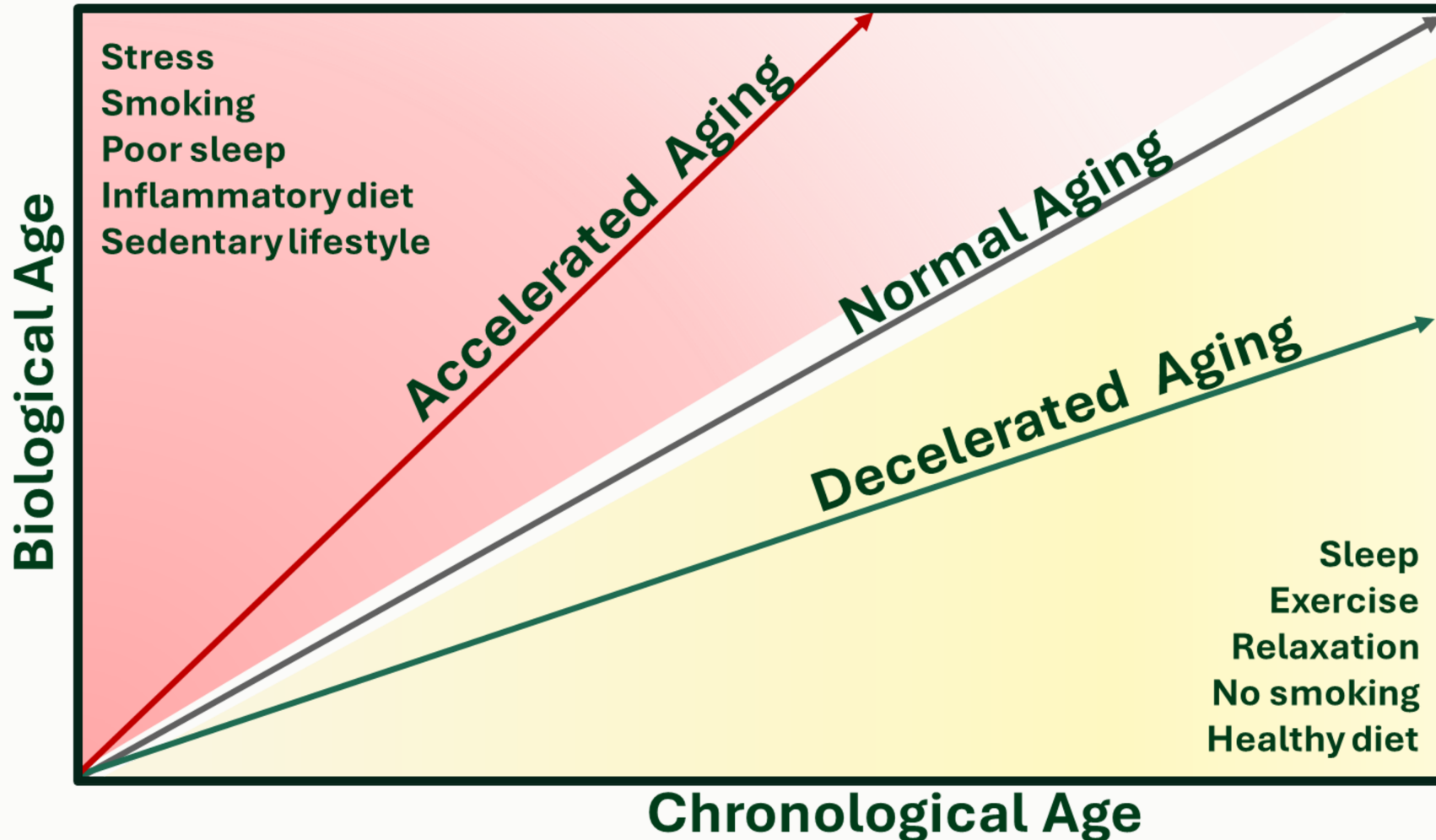
## • Neuroinflammation and chronic pain

- Epigenetic alteration of genes involved in neuroinflammatory processes can affect the development and maintenance of chronic pain
- Stress can exacerbate inflammation and pain sensitivity

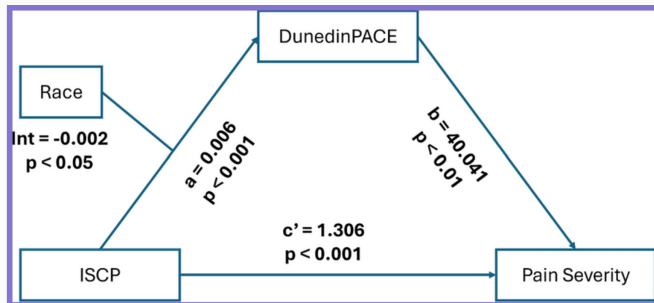
# Pathways such as the Hippo Signaling Pathways that have previously been associated with stress and stress-related disorders are enriched by differentially methylated genes between adults with low versus high internalized stigma

- Hippo signaling plays a prominent role in stress regulation
- Mechanical and oxidative stress (Mao et al. 2015)
- Epigenetically-induced upregulation of genes in the Hippo Signaling pathway has been linked to
  - learning and memory
  - increased risk of stress-related psychiatric disorders e.g., depression and PTSD (Stepan et al. 2018)
- Hippo and downstream Wnt signaling are involved in chronic pain
- Cancer pain, diabetic neuralgia, endometriosis, and low back pain (Tang et al. (2022))

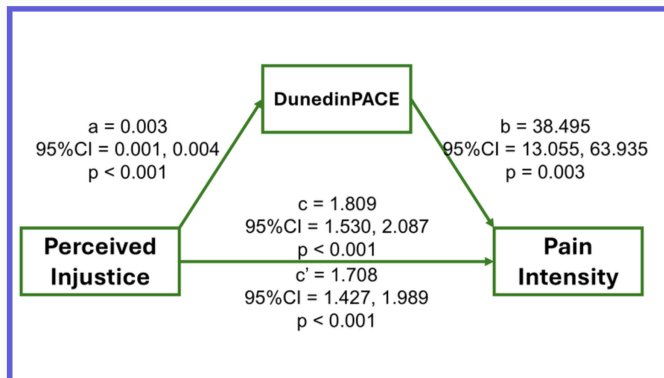
# Biological aging is a stronger predictor of chronic pain than chronological pain



# Internalized stigma and perceived injustice in the experience of chronic pain is associated with a faster pace biological aging and worse pain outcomes

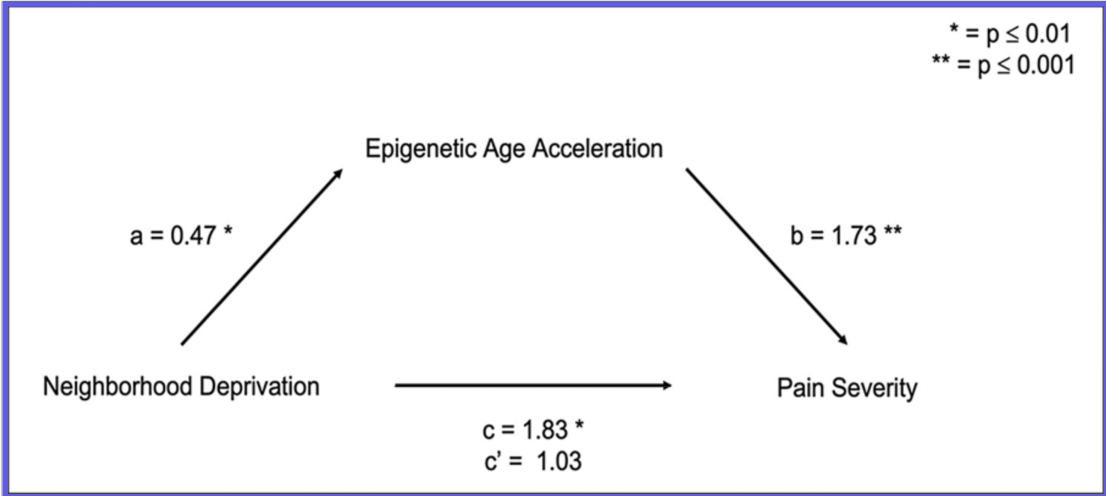
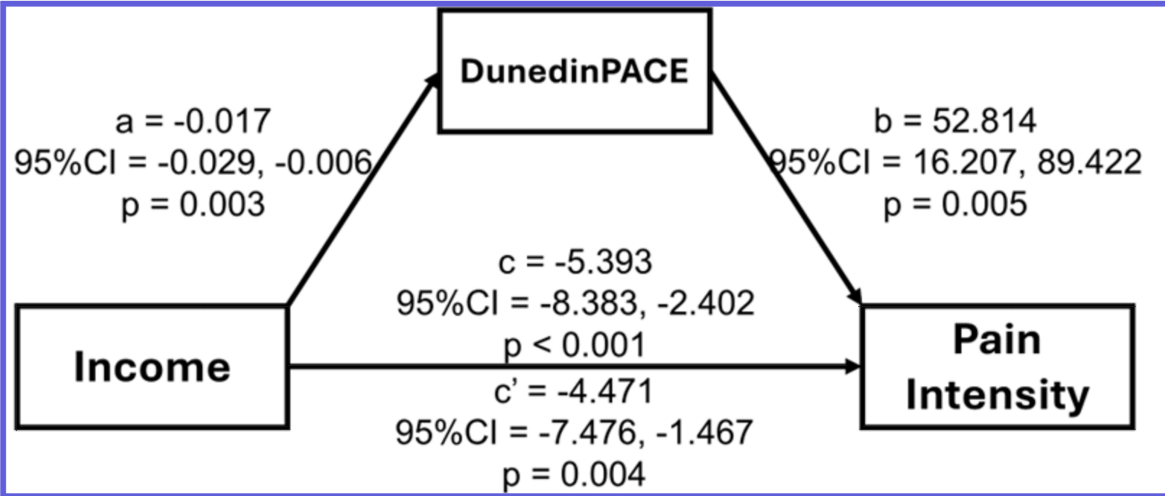


- There is significant positive relationship between DunedinPACE and internalized stigma of chronic pain ( $r = 0.34$ ,  $p < 0.001$ )
- DunedinPACE mediates the relationship between ISCP and pain severity
  - Mediation was significant for non-Hispanic Blacks but not for non-Hispanic Whites

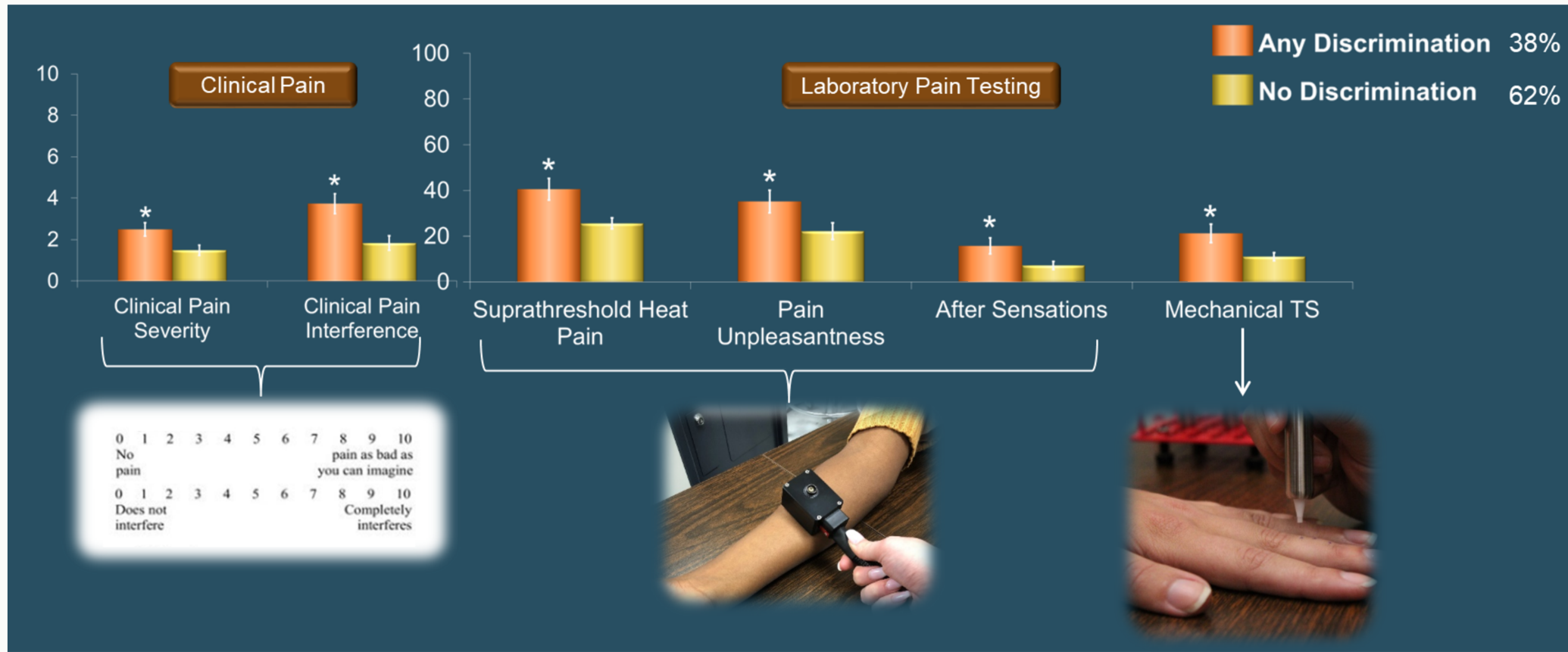


- There is a significant positive relationship between DunedinPACE and perceived injustice in the experience of chronic pain ( $r = 0.33$ ,  $p < 0.001$ )
- DunedinPACE mediates the relationship between perceived injustice and pain severity
  - Mediation significant for both non-Hispanic Blacks and non-Hispanic Whites adults

# Lower socioeconomic status is associated with a faster pace of biological aging and worse pain outcomes. Epigenetic age acceleration mediates the relationship between SES and pain outcomes

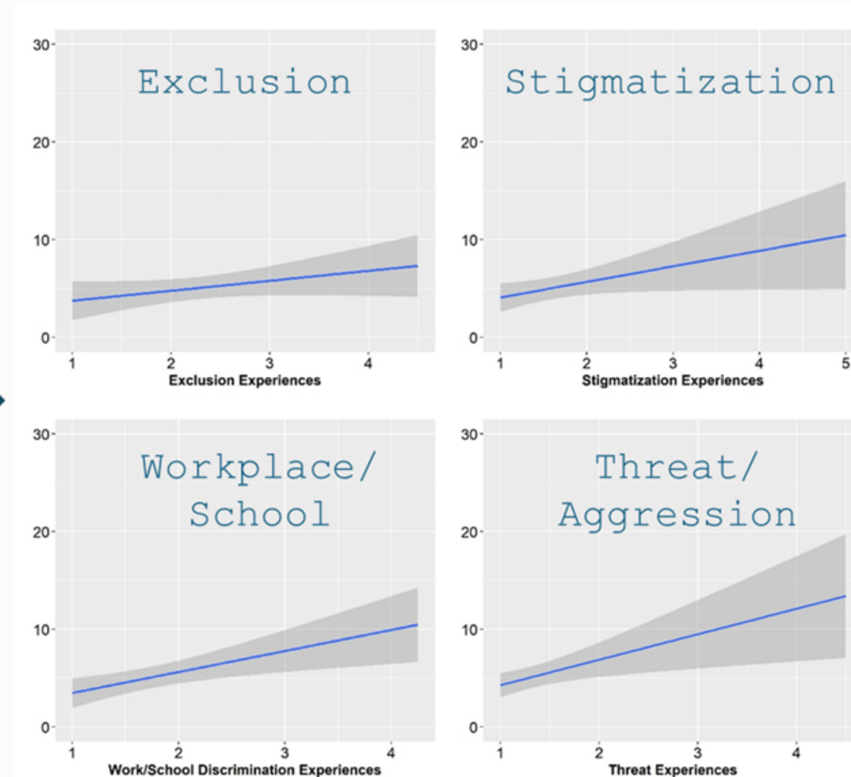
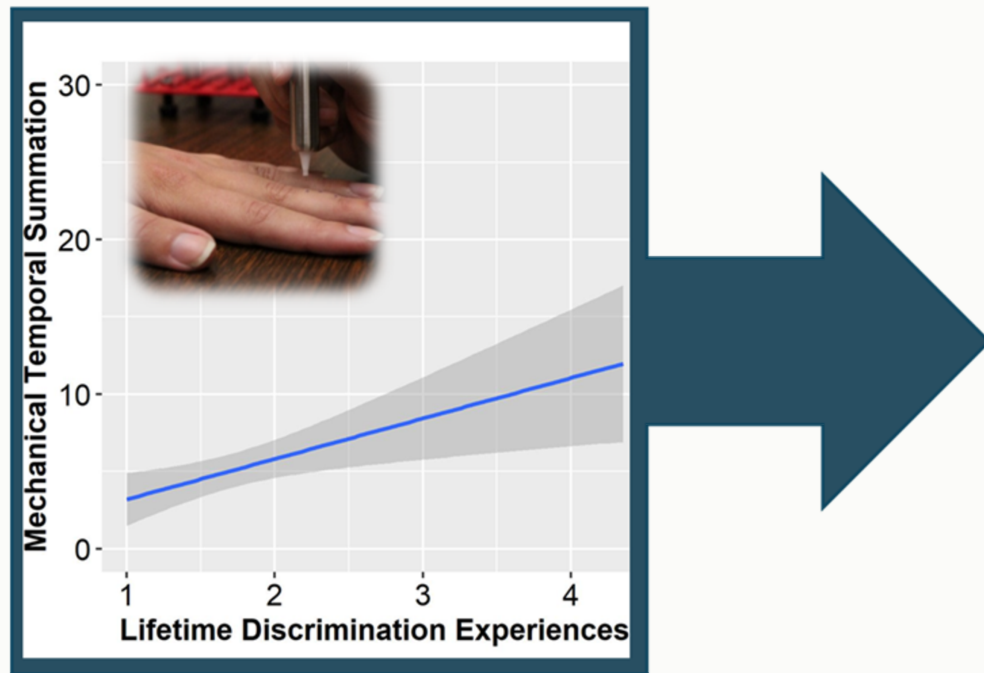


# Central sensitization among Black Americans with Sickle Cell Disease living in Maryland



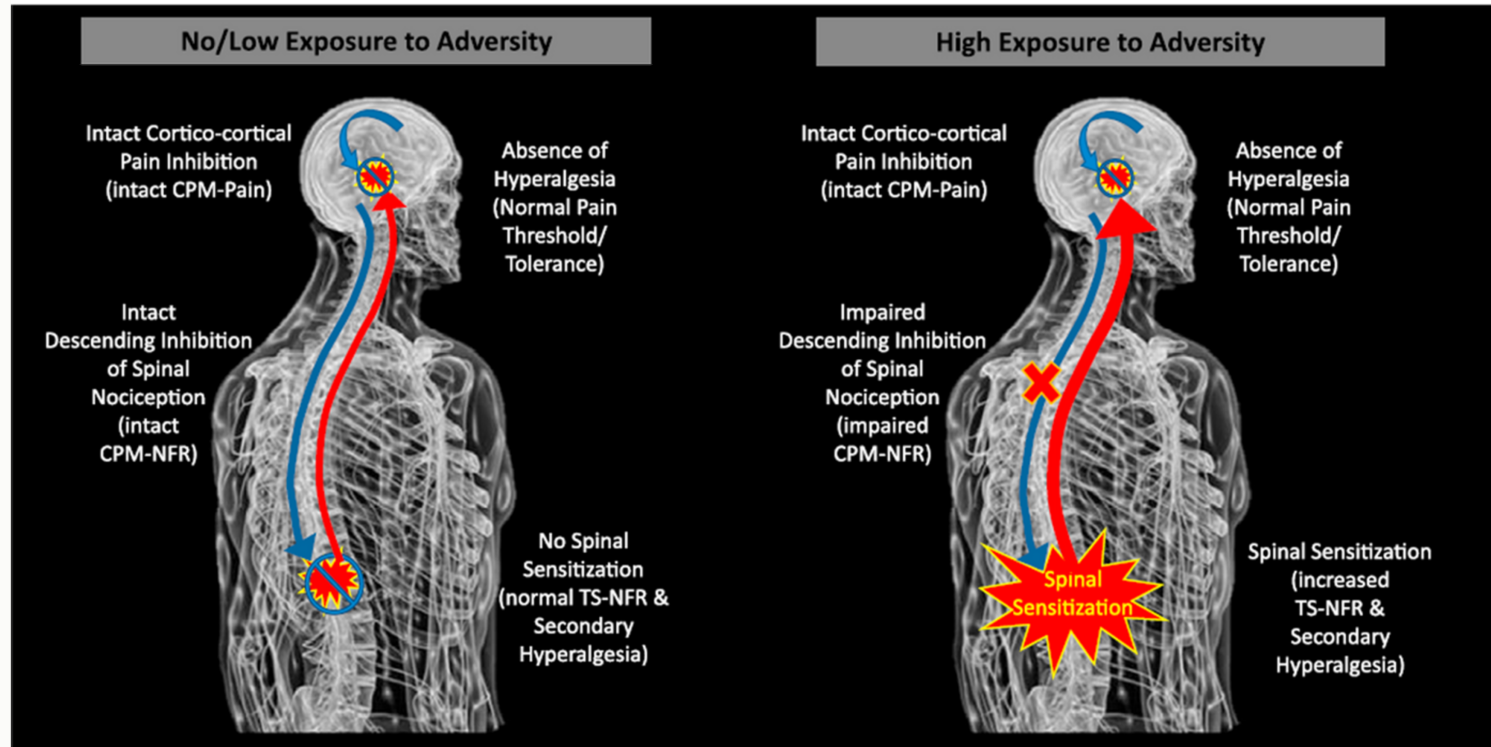
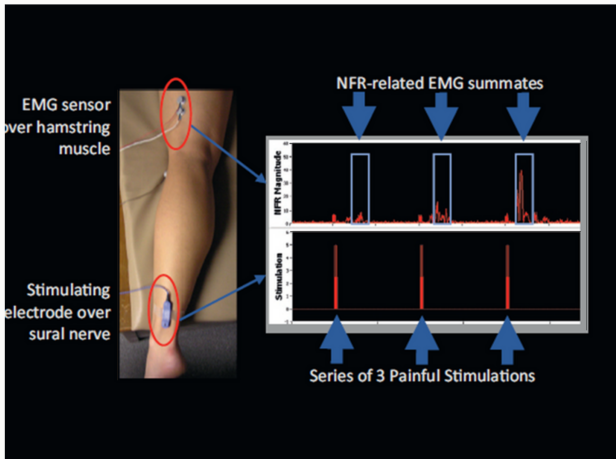
# Pre-clinical central sensitization among Hispanic/Latinx Americans living in Texas

- 94.2% of participants (Latinx Americans living in Texas, 2016-20) experienced racialized discrimination



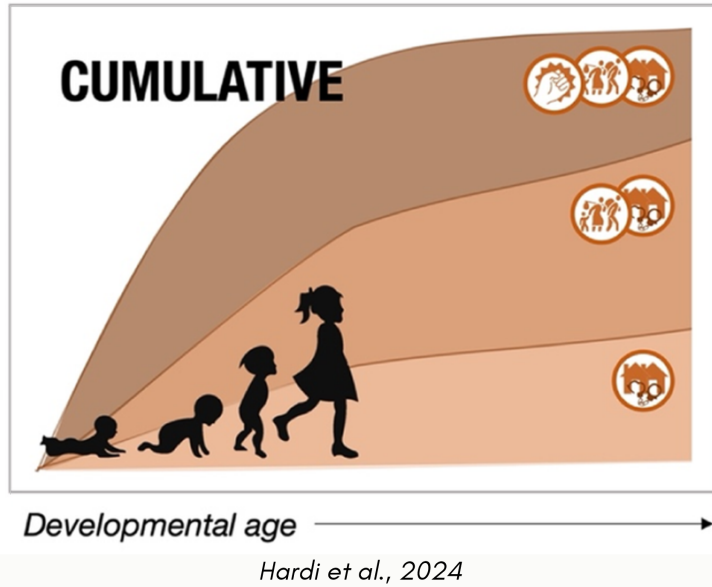
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# Pre-clinical spinal sensitization among Native Americans living in Oklahoma

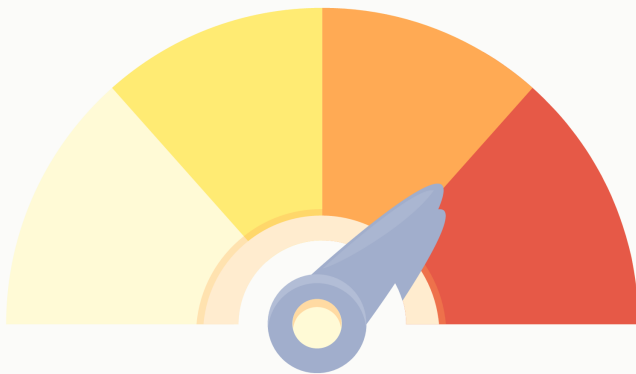
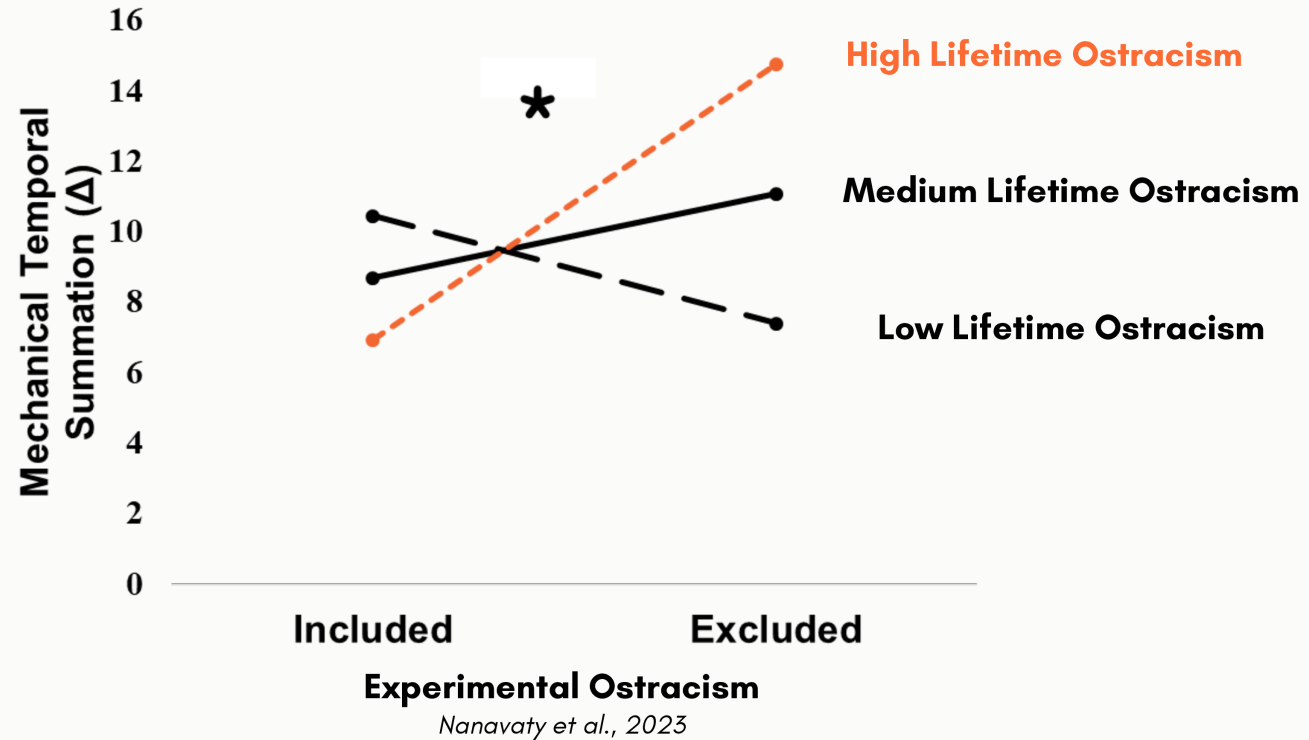


**FIG. 4** Model linking ALEs and latent sensitization. Under conditions of low ALE exposure, there is no spinal sensitization and inhibitory mechanisms are intact, so no hyperalgesia is present. However, cumulative exposure to ALEs promotes spinal sensitization (increased TS-NFR/secondary hyperalgesia, impaired inhibition of spinal nociception), but spinal sensitization does not result in hyperalgesia because pain inhibition keeps amplified spinal nociception suppressed (i.e., latent sensitization).

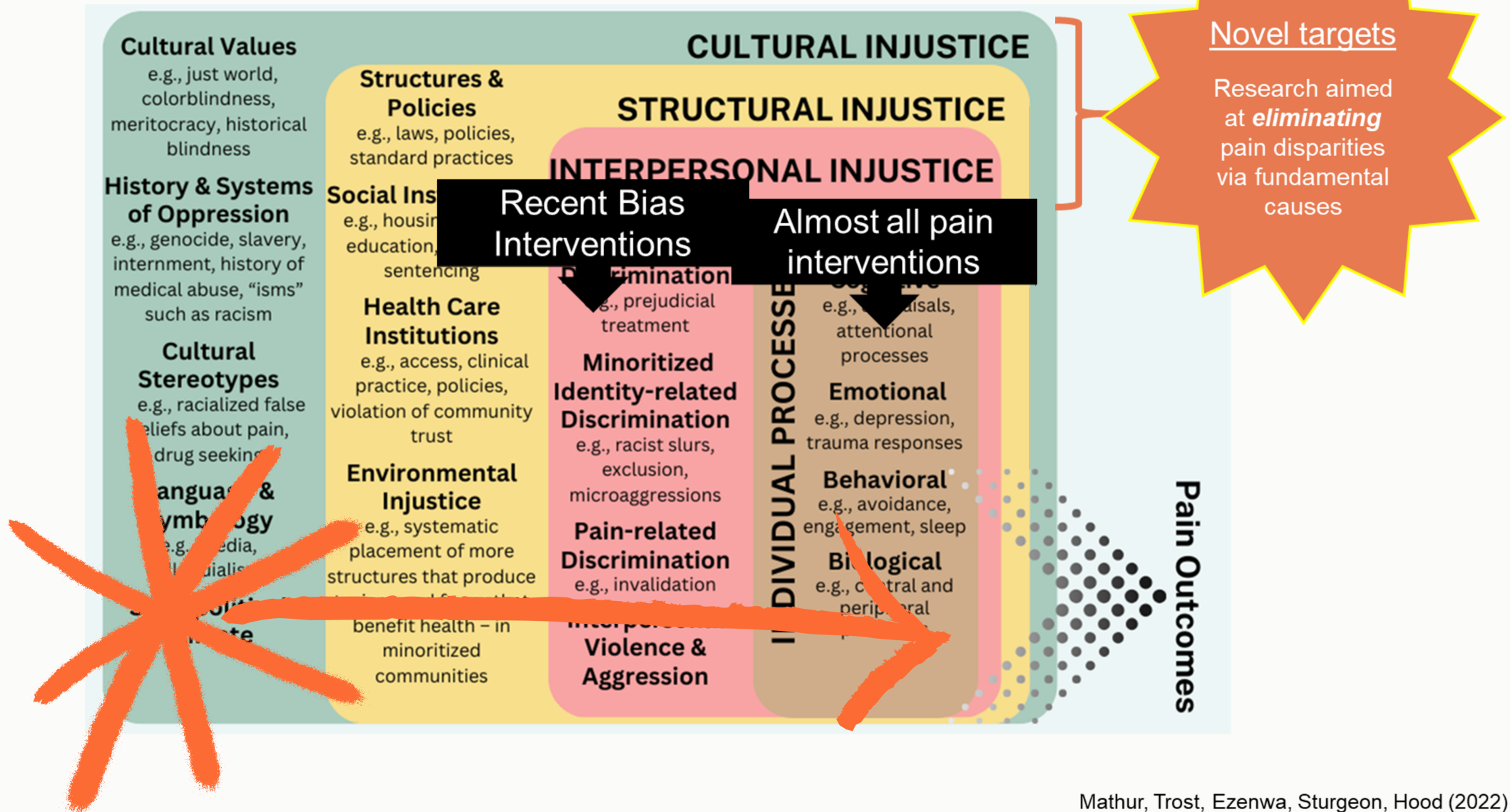


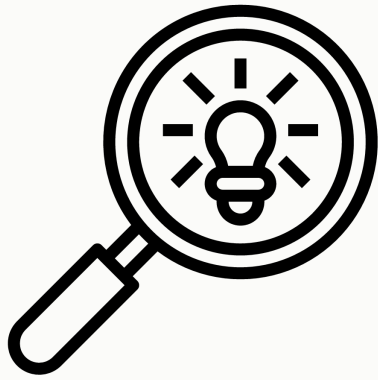


## Social-environmental conditioning: Interaction between lifetime and acute exposures



# The Injustice Model Of Pain Disparities





# Opportunities and new horizons for health equity in pain

## Deep Research

Understand risk and resilience factors among groups that disproportionately bear the burden of pain

- Longitudinal multilevel mechanistic studies among contextualized/localized specific populations
  - Appreciate diversity (geographic/historical/ sociopolitical/environmental) and intersectionality
  - Preference focus, comprehensiveness, critical approaches to identify what is missing from current paradigms
  - Integrate/center lived experience and perspective
- Within-population development
  - Valid and reliable approaches and instruments to capture major drivers of pain disparities
  - Validity and efficacy of existing interventions (one size does not fit all)
- Impact of current and historical policies/practices on pain
  - Current/expanding anti-DEI and anti-LGBTQ policies
  - Historical trauma, institutions, discriminatory policies
  - Redlining, gerrymandering, etc



# Opportunities and new horizons for health equity in pain

## Expansive Interventions

Break out of disciplinary boxes that confine pain intervention to individuals experiencing the consequences of socially determined pain, with a goal of eliminating pain injustice

1. Multi-level interventions that address the fundamental and proximal causes of pain disparities
  - Treating the cause vs the symptom
2. Novel targets for pain intervention such as environmental injustice, false cultural beliefs, housing/food insecurity, healthcare deserts, institutional/local/national policies
3. Novel intervention methods such as built environment interventions, educational campaigns, community-partnered/localized approaches

# Conclusion

- Shared environmental exposures to policies and sociocultural norms that marginalize particular segments of the population are the root causes of pain disparities
  - Social and structural forces not only impact treatment outcomes, but also mediate epigenetic and nervous system changes that sustain pain disparities across lifetimes, generations, and cultural histories
- Achieving health equity in pain management will require addressing these root causes
  - deep research to elucidate complex and interacting mechanisms & develop valid approaches
  - critical understanding of lived experiences of marginalized groups that is currently missing from the science
  - expansive, multi-level, interventions that adopt novel approaches and targets (currently missing from pain management paradigms)



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*Thank  
you!*

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