Ambient Outdoor Heat and Epigenetic Aging Acceleration

Eun Young Choi, PhD
Postdoctoral Associate

Jennifer Ailshire, PhD
Professor of Gerontology,
Sociology & Spatial Sciences

USC Leonard Davis
School of Gerontology

Disclosures

We have no commercial relationships to disclose.

Acknowledgement

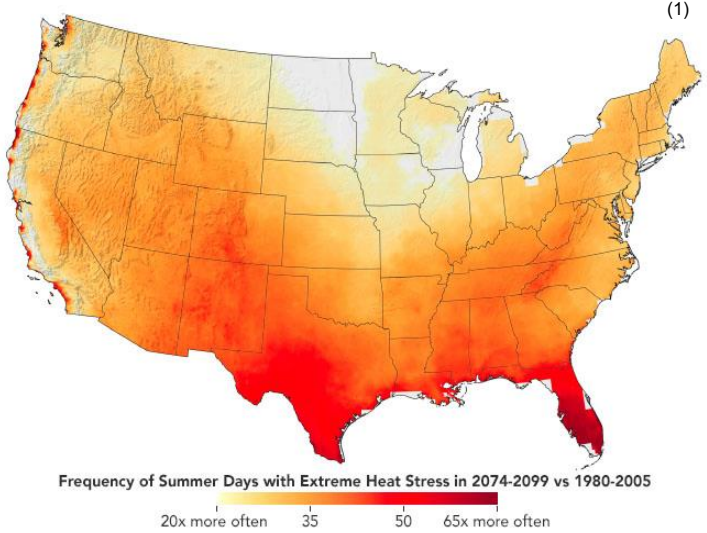
Funding: This work was supported by the Network on Life Course Health Dynamics and Disparities in 21st Century America funded by the National Institute on Aging, National Institutes of Health (R24AG045061).

Data availability: We used the publicly available, sensitive, restricted datasets from the Health and Retirement Study (HRS), which is sponsored by the National Institute on Aging, National Institutes of Health (U01AG009740) and conducted by the University of Michigan. The restricted contextual datasets linked to the HRS sample via the HRS-Contextual Data Resource include meteorological data from gridMet (https://climatologylab.org/gridmet.html) to assess heat exposure.

Extreme Heat is Increasingly Known to Adversely Affect Human Health

- Extreme heat events are projected to affect **over 100 million Americans** by 2050. Extreme heat as a **major risk** for diseases and mortality.

(1)



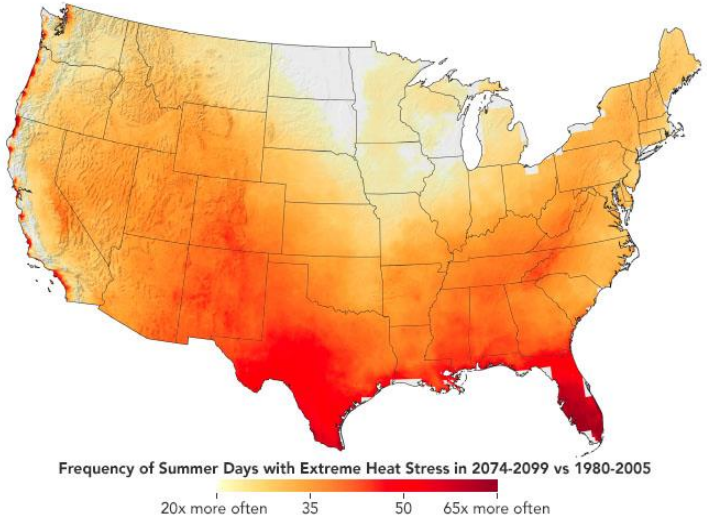
(2)(3)

- **Disease** (Cardiovascular, renal, infectious)
- **Injuries**
- **Mental & Neurological Disorders**
- **Mortality**

(1) Raymond C, et al. NASA Earth Observatory images by Joshua Stevens. Environmental Research Letters 2022;17(6):064046.
(2) Rocque RJ, Beaudoin C, Ndjaboue R, *et al* Health effects of climate change: an overview of systematic reviews *BMJ Open* 2021;**11:**e046333.
(3) Weilnhammer, Veronika, *et al.* Extreme weather events in europe and their health consequences–A systematic review. *Int. J. Hyg. Environ 2021;***233**:13688.

Biological Underpinnings Not Fully Understood

- The physiological toll exacted by extreme heat events **may not manifest immediately** as clinical conditions
- Rather, they may elicit **biological deterioration** that can serve as **precursor** of subsequent development of diseases and disabilities



Biological Aging

- Molecular changes
- Cellular changes
- Decline in system integrity

Disease (Cardiovascular, renal, infectious)

Injuries

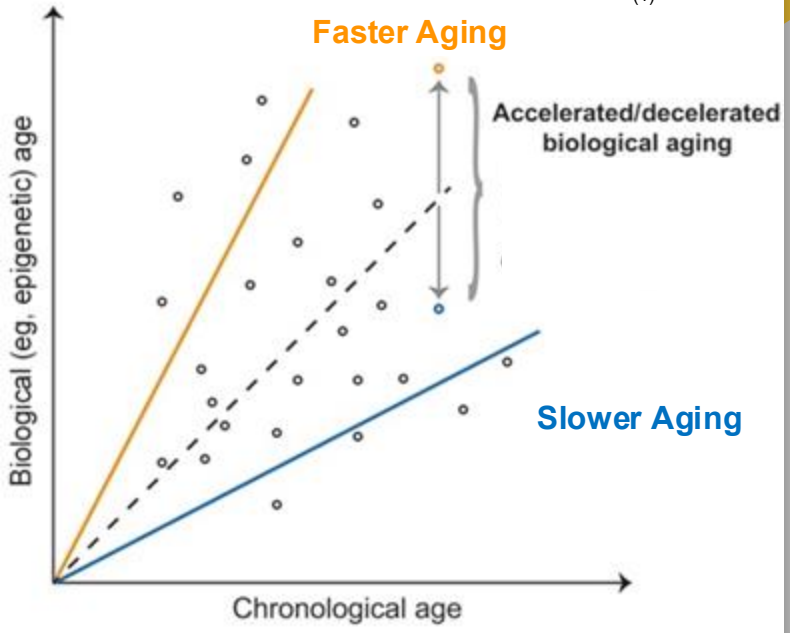
Mental & Neurological Disorders

Mortality

Epigenetic Age (Clock): Guage for Biological Aging

- Epigenetic alteration as a major **hallmark of aging**
- Markers of **age-related epigenetic changes** (i.e., DNA methylation) turned into estimates of biological age
- Accelerated epigenetic age
  - Higher epigenetic age than chronological age
  - One is **aging faster** than they should be
  - Predicts many age-related **health outcomes**
- Unique lens to **pinpoint the organism-level biological responses to heat**

(1)



(1) Zannas AS et al. Proc Natl Acad Sci U S A. 2019;116(23):11370-11379.

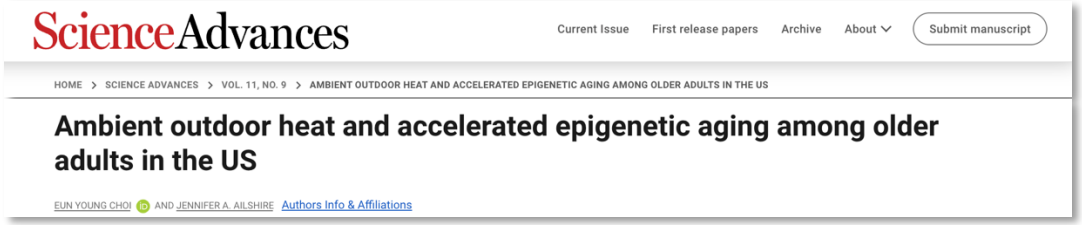
Growing Evidence Supports…

- Animal studies show that **a single episode of heat stress can lead to long-lasting DNA methylation changes**, but very little is known in humans (Murray et al., 2022)
- Cooperative Health Research in the Region of Augsburg (KORA) (Ni, 2023)
  - ~3,500 older adult observations in city of Augsburg, Germany
  - 4- and 8-week average high air temperatures are associated with increased epigenetic age acceleration measures (range: 0.24~11 years)
- Lack of population-level risk estimation using a diverse and representative sample

This study examines the association between heat exposure and epigenetic age in a representative sample of US older adults

Source: Murray KO et al. Exp Physiol. 2022;107(10):1144-1158; Ni W et al. Environ Int. 2023;178:108109.

Study Design



Sample

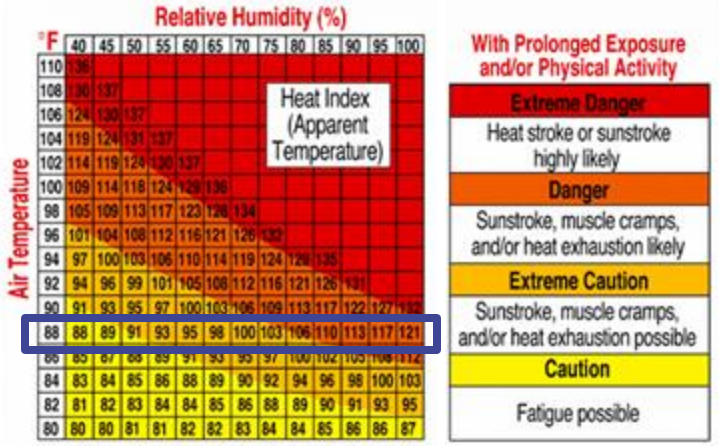
3,688 adults age 56+, 2016 Health and Retirement Study DNA Methylation (HRS DNAm) sample

Outcome: Epigenetic Age Acceleration

GrimAge: Levels of biomarkers (unit: year; 1=1 year faster)
DunedinPACE: Changes in biomarkers (unit: rate of aging per year; 1 = normal pace, 1.02 = 2% faster)

Exposure: Number of Extreme Heat Days

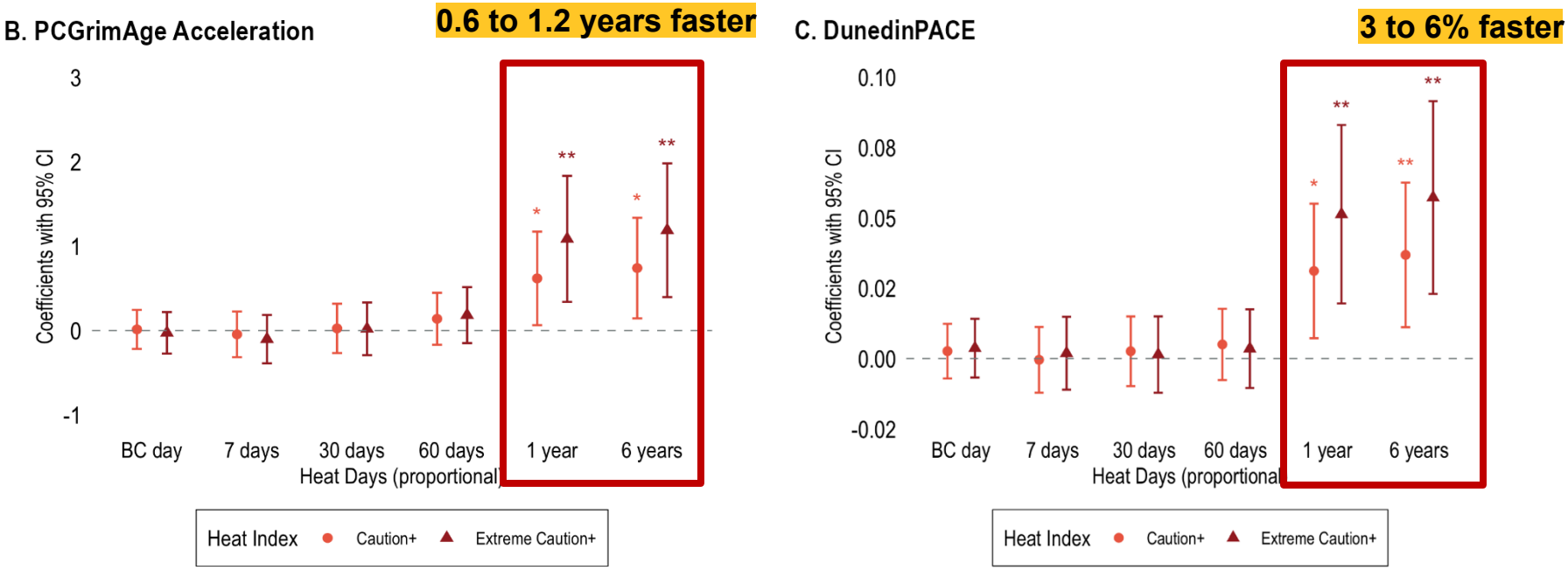
Heat? Daily Heat Index: Air temperature with an adjustment for relative humidity
Extreme? Caution+ (80°F+) & Extreme Caution+ (90°F+)
Time? Day of blood collection to prior 6 years



Courtesy of the National Weather Service

Linkage: Outdoor heat data merged with HRS DNAm sample based on their geocoded addresses at the census tract and the date of blood collection (*HRS Contextual Data Resource)

Chronic Outdoor Heat is Associated with an Increase in Epigenetic Aging Acceleration



Multilevel regression model predicting epigenetic clocks; Model adjusted for cell types, age, sex, race/ethnicity, education, household wealth, smoking status, alcohol use, obesity, physical activity, tract social vulnerability index, urbanicity, and $PM_{2.5}$ and O_3 levels; $^{**}p<.01$; $^{*}p<.05$.

Long-term Heat Exposure Does Seem to Speed Up Epigenetic Aging

- The short-term physiological effects of heat stress may last **only a few days**
- Some effects could **accumulate** over extended periods and it may be this **continuous exposure that leads to DNA methylation changes related to aging** captured by the epigenetic clocks
- **Chronic heat** may act through **psychosocial and health behavior pathways**
  - Elevated stress and anxiety due to sleep disruptions and physical discomfort
  - Altered dietary patterns (e.g., reduced appetite, dehydration-related changes)

Gaps and Opportunities for Future Research

- **Need for Longitudinal Data**
  - Current study is based on cross-sectional data, limiting understanding of **causality** and tracking **within-person changes** in epigenetic aging in response to outdoor heat
- **Specificity of Biomarkers**
  - Focus on **system-specific biological aging** could show unique pathways
- **Theoretical and Analytic Innovation for Population Heterogeneity**
  - Our outdoor heat only reflects the *potential, not direct, personal* heat exposure
  - Vulnerability to climate stressors is likely shaped by a **combination of** demographic, socioeconomic, and non-climate environmental factors.
  - How can we **conceptualize** and **model this complexity**?

Nam, Choi, & Ailshire "Unveiling Population Heterogeneity in Health Risks Posed by Environmental Hazards Using Regression-Guided Neural Network." *arXiv preprint arXiv:2409.13205* (2024).

Thank You!
Any Questions?

choieuny@usc.edu