

# EXPOSOME as a Stressor in the Study of Resilience

Clinician-Scientists Transdisciplinary Aging Research (Clin-STAR)  
Annual Meeting, November 2022

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# FUNDING DISCLOSURES

NIH/National Institute on Aging

NIH/National Institute on Minority Health  
and Health Disparities

Alzheimer's Association



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# EXPOSOME

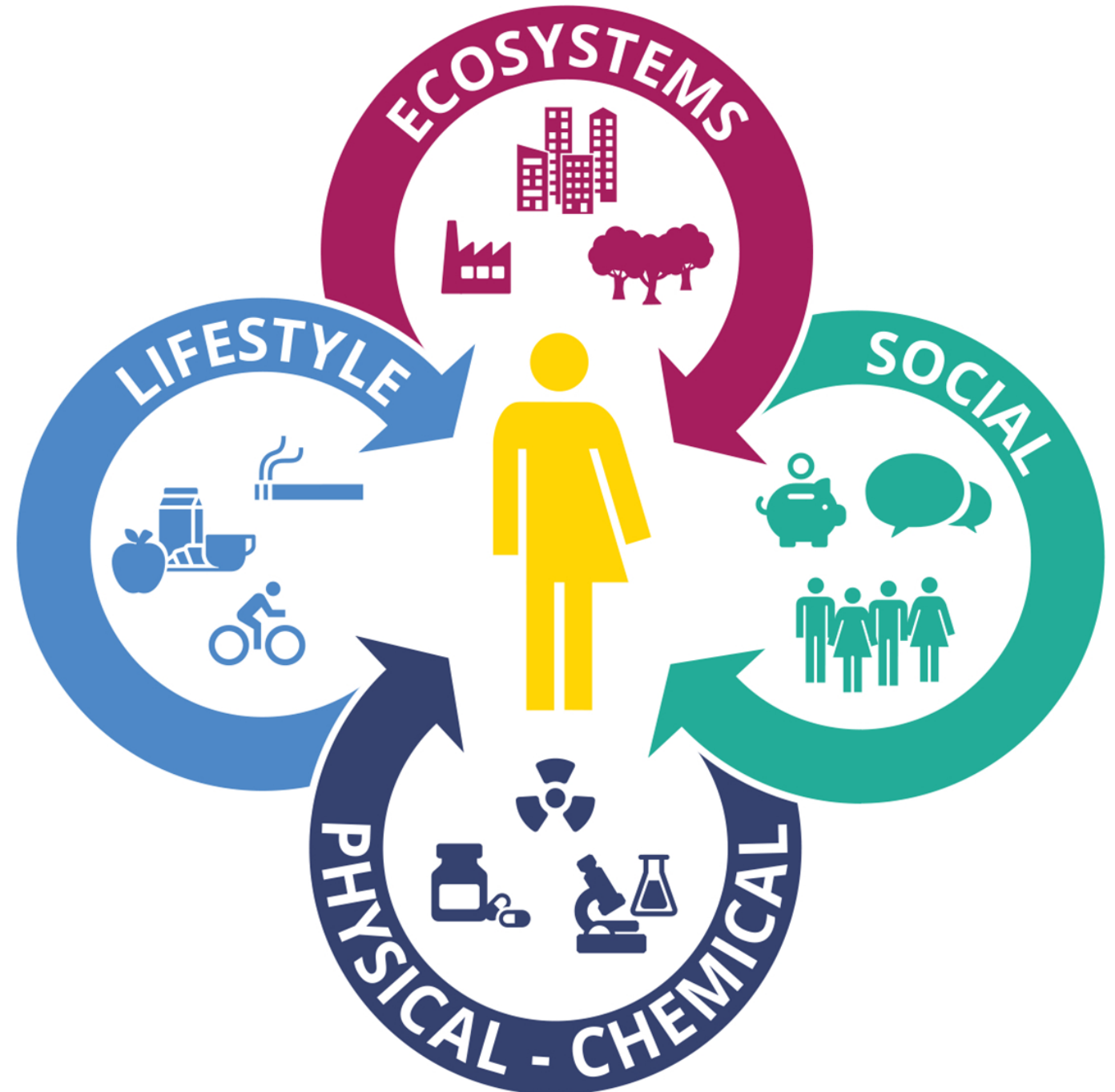
The measure of all the exposures of an individual in a lifetime and how those exposures relate to health\*

\*The National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC).  
<https://www.cdc.gov/niosh/topics/exposome/default.html#:~:text=The%20exposome%20can%20be%20defined,from%20environmental%20and%20occupational%20sources..> Accessed 4/20/2021



# Exposome

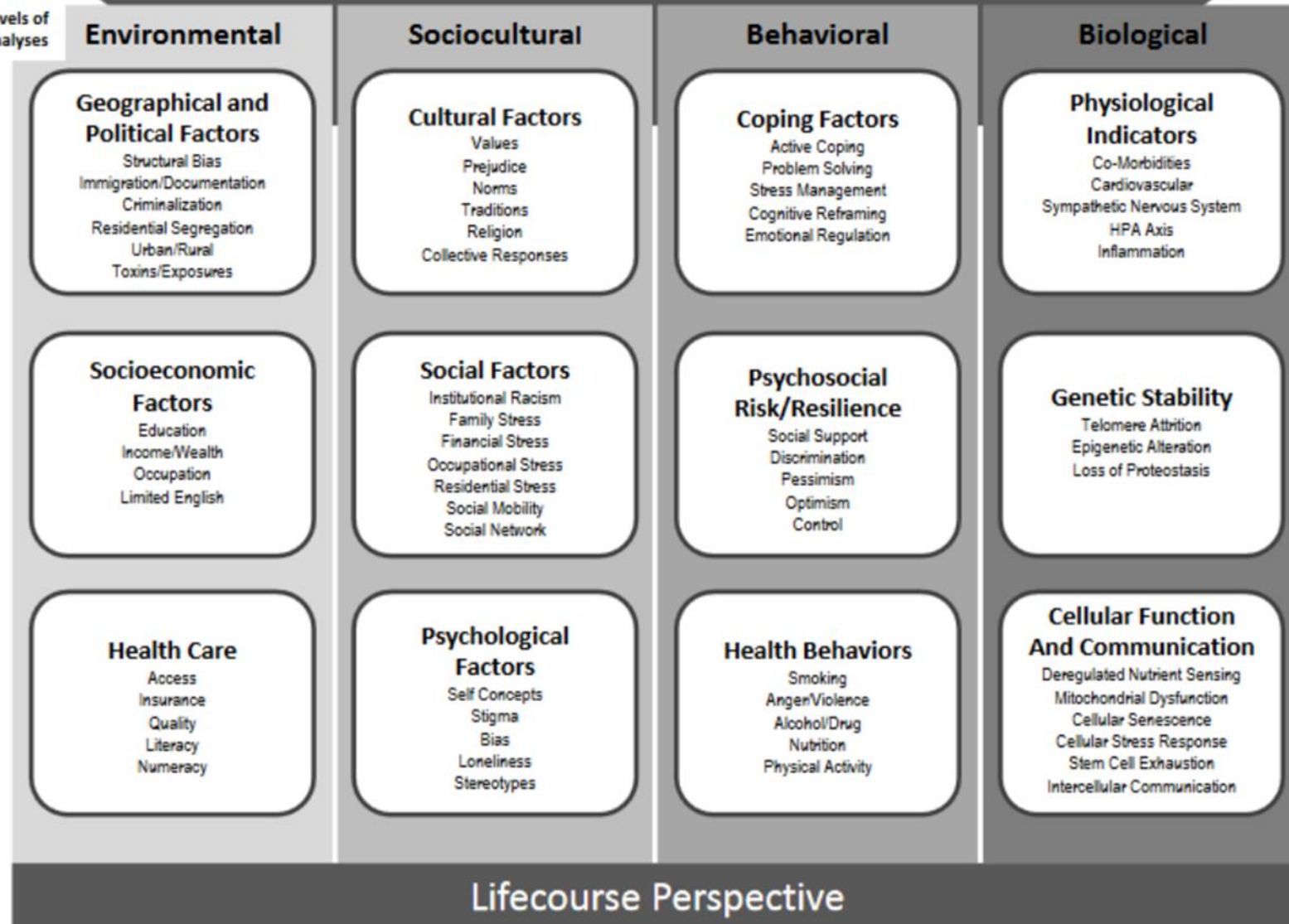
- Factors external to the biological individual
- Diverse factors ranging from microbiome to structural inequity



# NIH HEALTH DISPARITIES FRAMEWORK

FUNDAMENTAL FACTORS: Ethnicity, Gender, Age, Race, Disability Status, Identity\*

\*\*Levels of Analyses



\*\*Hill, Perez-Stable, Anderson and Bernard, *Ethnicity and Disease*, 2015



# NIA HEALTH DISPARITIES FRAMEWORK



ENVIRONMENTAL



SOCIOCULTURAL



BEHAVIORAL

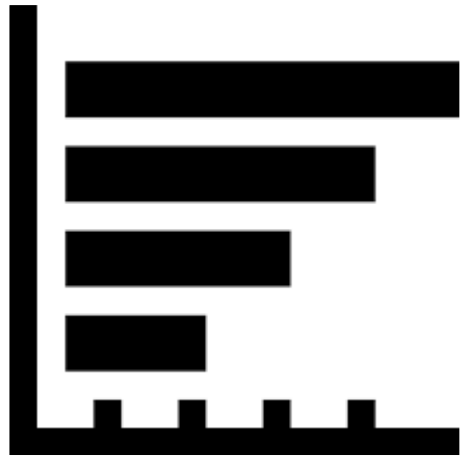


BIOLOGICAL

LIFE COURSE



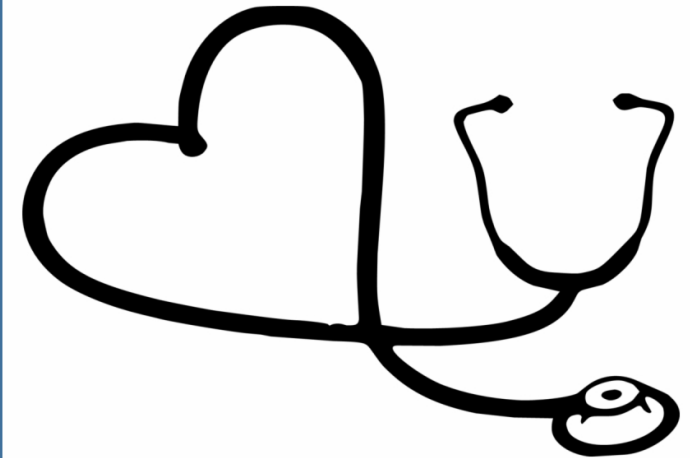
# EXAMINING THE EXPOSOME



**Quantifying  
Exposures**

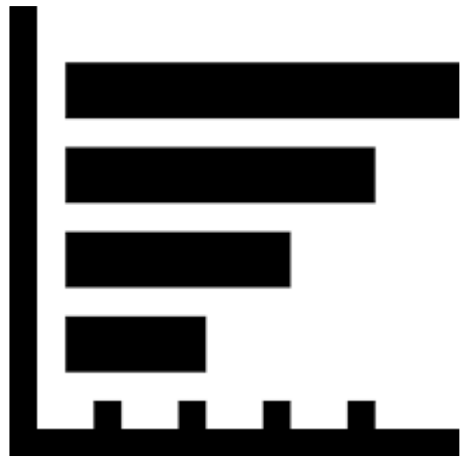


**Linking Exposome  
to Biology**



**Research to  
Action**

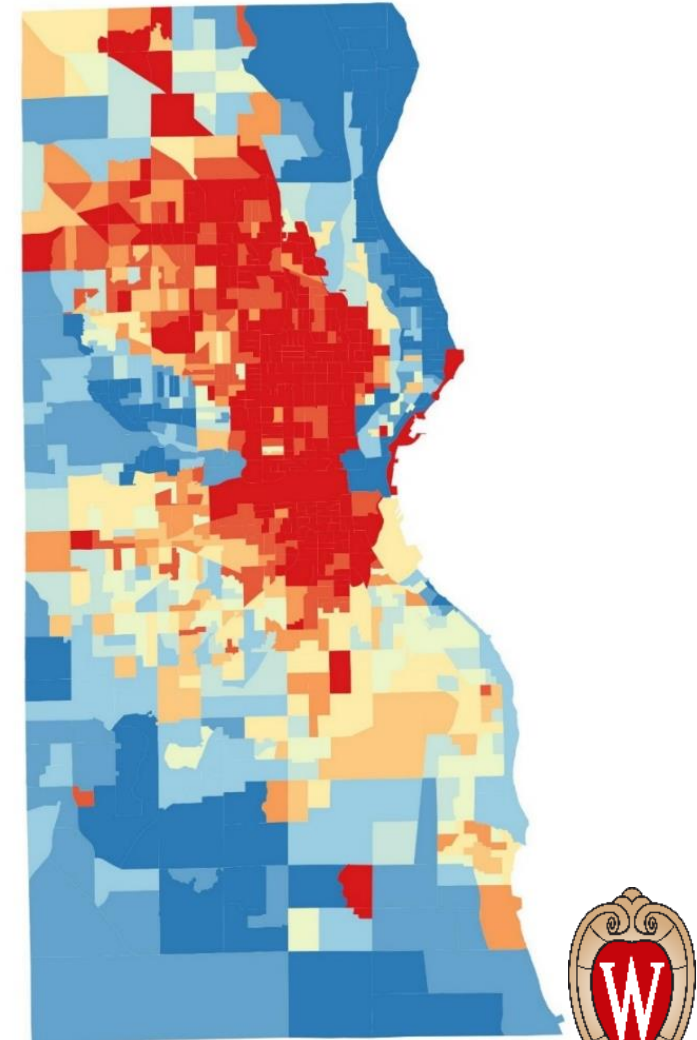
# EXAMINING THE EXPOSOME



Quantifying  
Exposures

# EXAMPLE: QUANTIFYING EXPOSOME USING THE AREA DEPRIVATION INDEX (ADI)\*

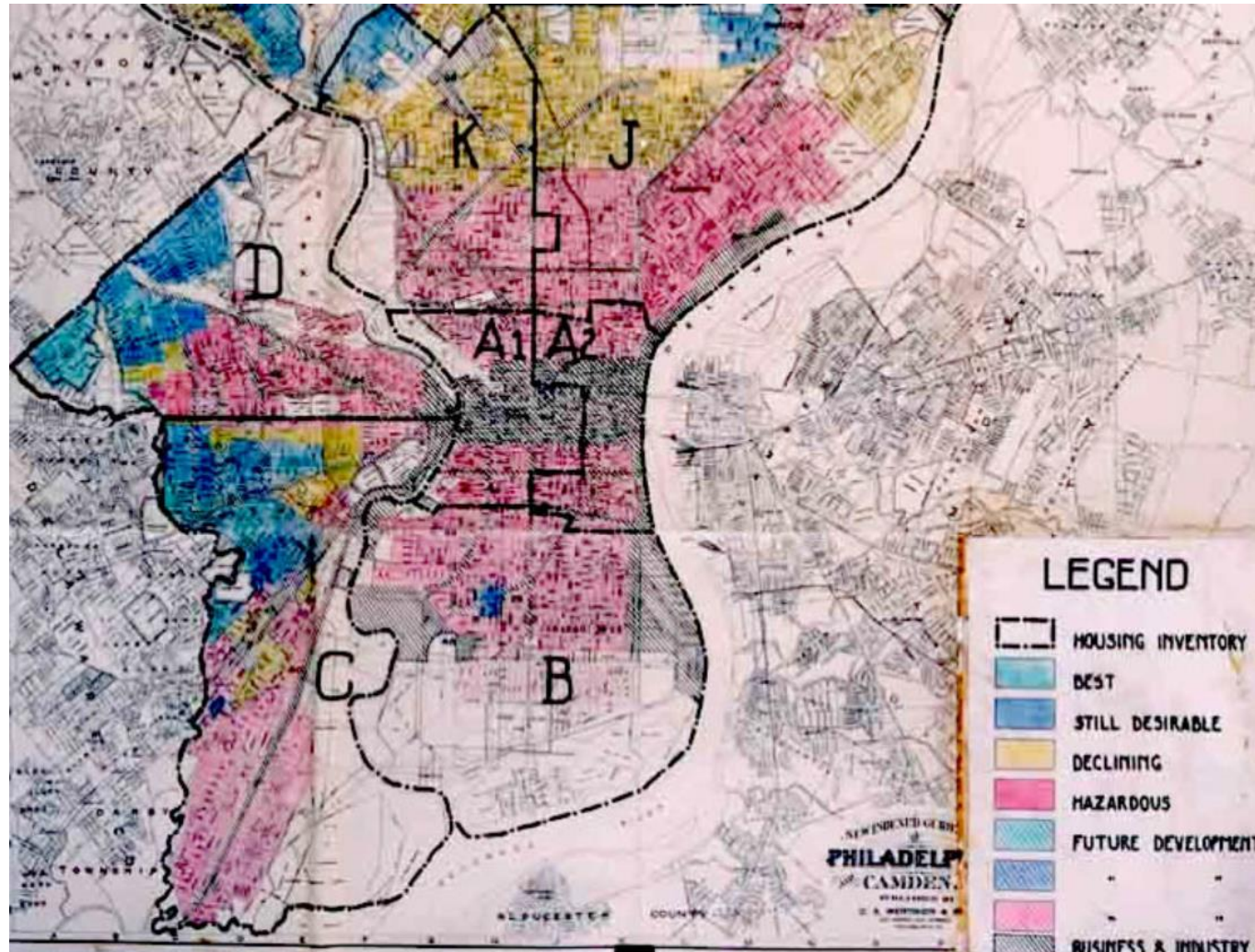
- ADI construction
  - 17 measures of social determinants of health across small, population sensitive areas
  - Ranked score
  - Time concordant
- Current ADI measures for full US available through the Neighborhood Atlas®\*
- Harmonizable metrics available internationally
- Disparities-aligned US exposome metric



Milwaukee County

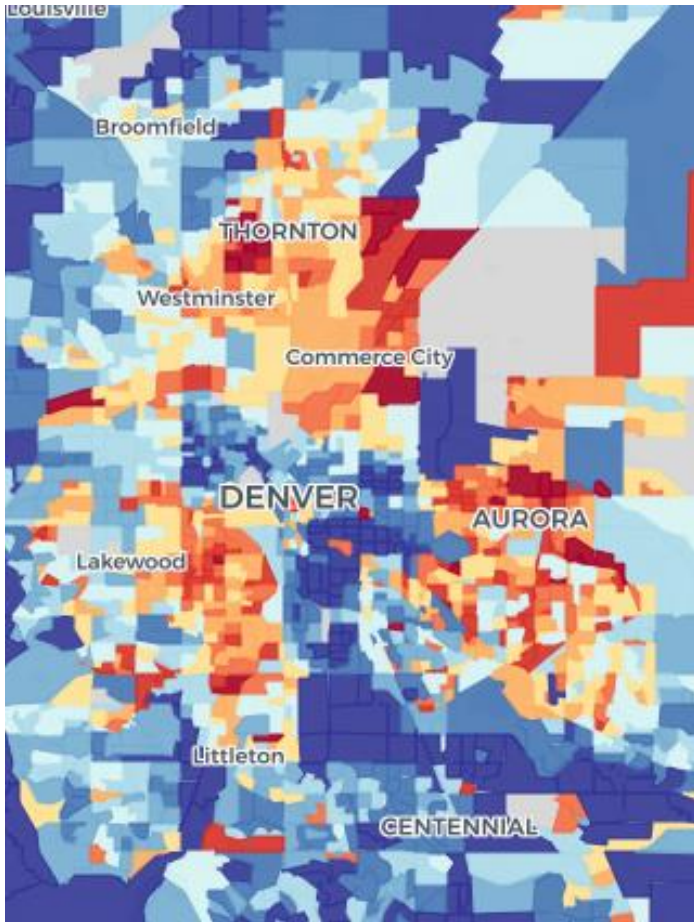
\*Kind and Buckingham, *New England Journal of Medicine*, 2018

# STRUCTURAL INEQUITIES LINK TO EXPOSOME



\*The HOLC maps are part of the records of the FHLBB (RG195) at the [National Archives II Archived](#) 2016-10-11 at the [Wayback Machine](#).

# RESIDING IN A HIGH ADI NEIGHBORHOOD IS LINKED TO:



- Epigenetic age acceleration (Lawrence et al, JAMA-Open, 2020)
- Rehospitalization and Cost (multiple)
- Later diagnoses and less comprehensive diagnostic evaluation (Tsoy et al, JAMA-Neurology, 2021; multiple)
- Increased risk of post-surgical complications (Arias et al, JAGS, 2021)
- Decreased active-life expectancy (Gill et al, JAMA-IM, 2021)
- Many other factors



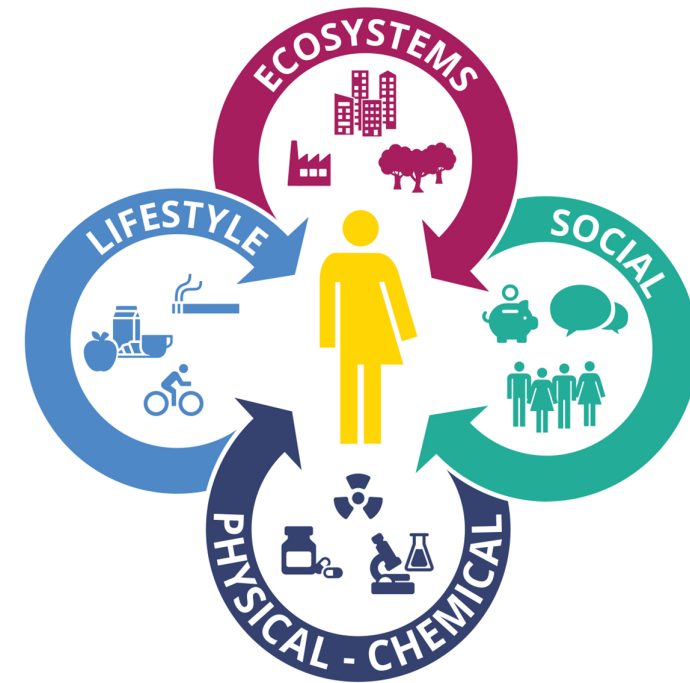
# EXAMINING THE EXPOSOME



**Linking Exposome  
to Biology**

# SOCIAL-BIOLOGICAL PHENOTYPING

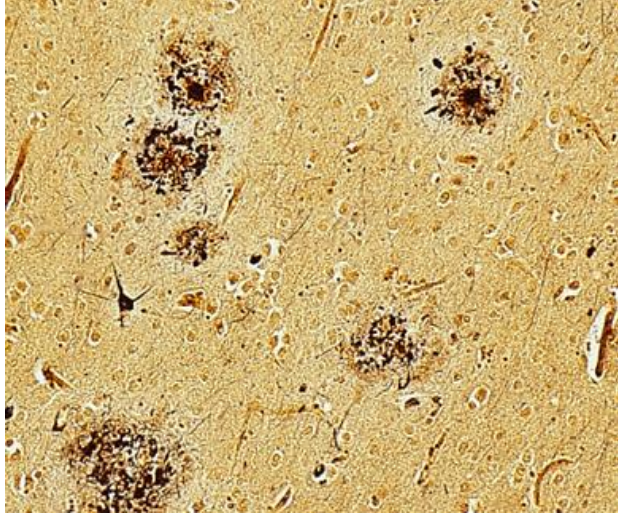
- Link exposures to biological process
- Expand the potential of existing programs in completely new ways



## Exposome

Science. 2020. 367(6476): 392–396.

# EXPOSOME AND NEUROPATHOLOGY



- N=453 decedents who donated their brain to Wisconsin or University California San Diego ADRC brain banks, 1993-2016
- No social factor characterization available
- Residential address at death geocoded, linked to neighborhood disadvantage by ADI



Source: www.Pixabay.com-- All images are released free of copyrights under Creative Commons CC0





Original Investigation | Public Health

## Association of Neighborhood-Level Disadvantage With Alzheimer Disease Neuropathology

W. Ryan Powell, PhD; William R. Buckingham, PhD; Jamie L. Larson, PhD; Leigha Vilen, BS; Menggang Yu, PhD; M. Shahriar Salamat, MD, PhD; Barbara B. Bendlin, PhD; Robert A. Rissman, PhD; Amy J. H. Kind, MD, PhD

### Abstract

**IMPORTANCE** Social determinants of health, such as income, education, housing quality, and employment, are associated with disparities in Alzheimer disease and health generally, yet these determinants are rarely incorporated within neuropathology research.

**OBJECTIVE** To establish the feasibility of linking neuropathology data to social determinants of health exposures using neighborhood disadvantage metrics (the validated Area Deprivation Index)

### Key Points

**Question** Can neighborhood disadvantage, a social determinant of health, be incorporated into existing brain bank data to evaluate the risk of biological outcomes, such as Alzheimer disease neuropathology?

Living in the most disadvantaged neighborhood decile was associated with increased odds of AD neuropathology

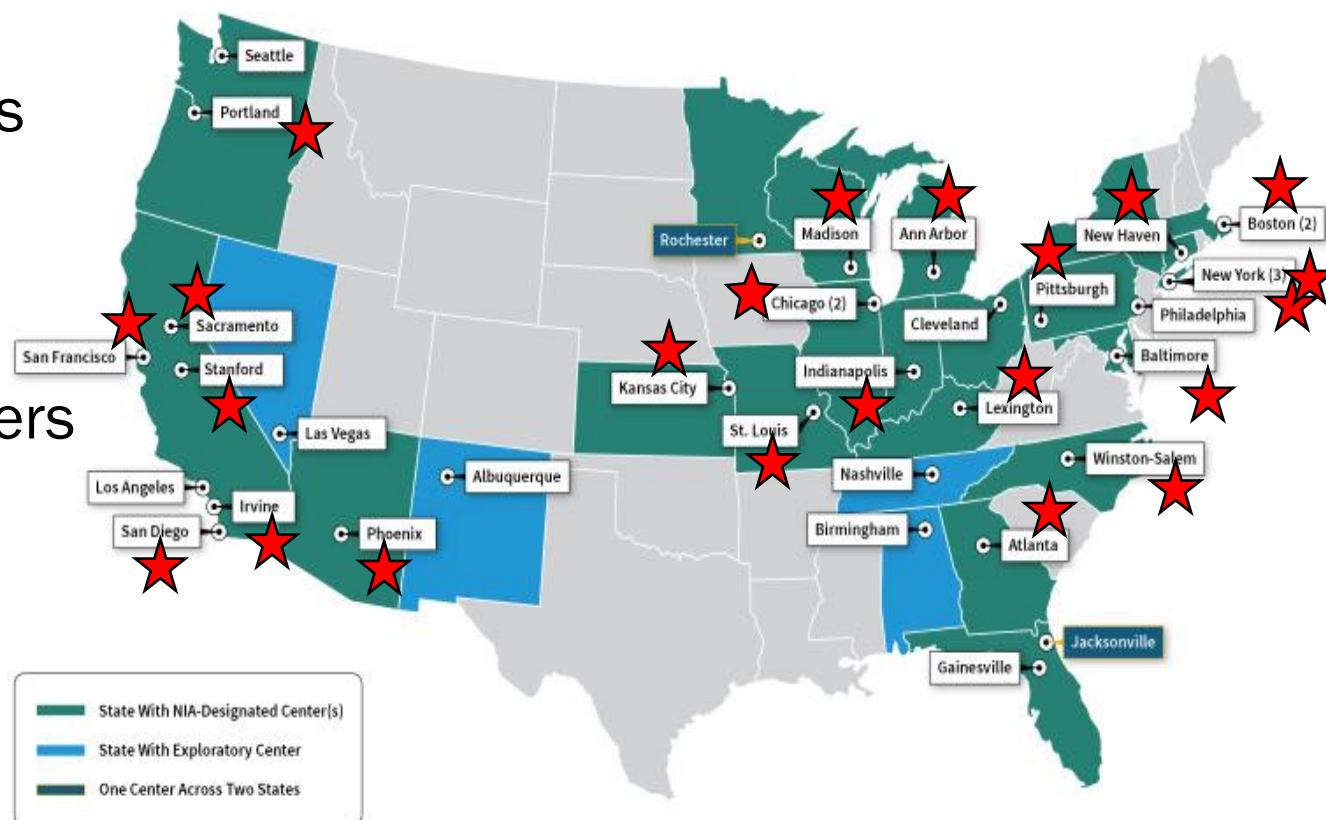


# THE NEIGHBORHOODS STUDY

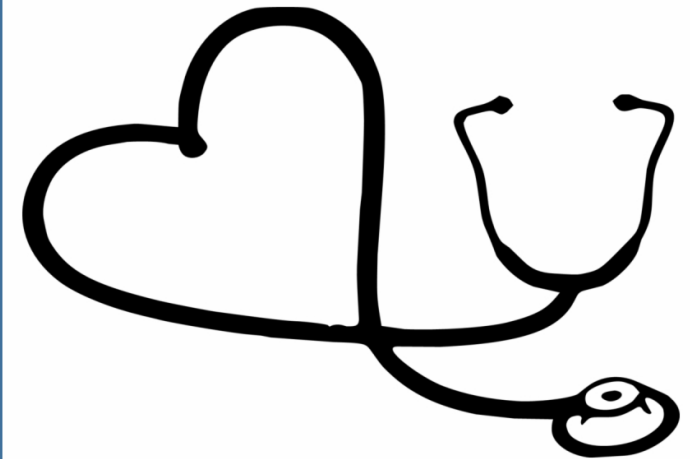
(R01AG070883; PI KIND, MPI BENDLIN)



- Examine the impact, mediators and moderators of life-course exposome on AD-specific pathologic features, vascular burden and cognitive decline
- Over 9,000 ADRC brain bank decedents
- 7,875 ADRC clinical core participants
- 22 Alzheimer's Disease Research Centers



# EXAMINING THE EXPOSOME



**Research to  
Action**

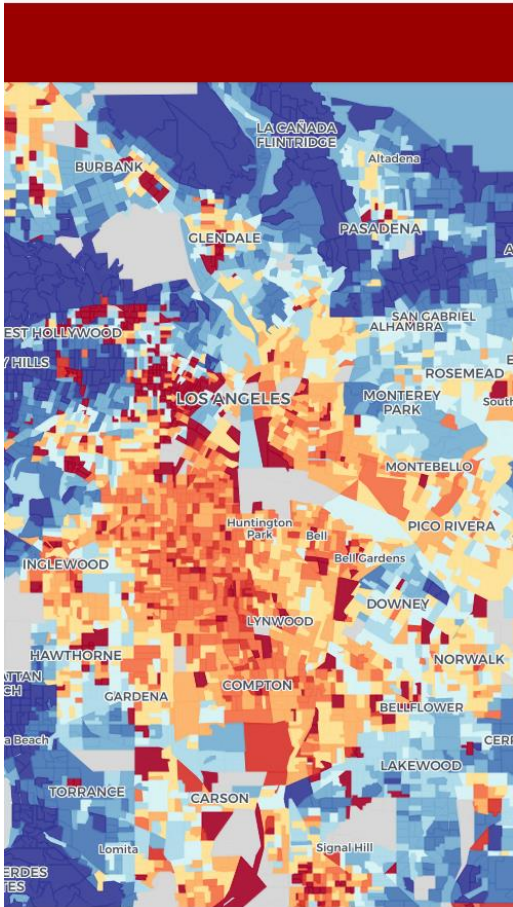
# DATA DEMOCRATIZATION IS KEY TO ACTION

Making scientific research accessible to all levels of an inquiring society, amateur or professional



# THE NEIGHBORHOOD ATLAS

[www.neighborhoodatlas.medicine.wisc.edu](http://www.neighborhoodatlas.medicine.wisc.edu)



- Data democratization and open science tool for the ADI
- Customized mapping; Free, open to all
- Data downloaded tens of thousands of times by research, governmental, community, and industry groups.



# ADI IS NOW LEVERAGED IN US HEALTH POLICY

## Ethical Allocation of COVID Therapies

- Example: Pennsylvania

## US Centers for Medicare and Medicaid Services (CMS)

- 2023 ACO Realizing Equity, Access, and Community Health (REACH) Model uses ADI to adjust payments



### Ethical Allocation Framework for Emerging Treatments of COVID-19

#### Introduction

The foundational goal of this document is to develop a broad, fair, and equitable framework for how to allocate scarce, emerging COVID-19 treatments. This document addresses remdesivir (RDV) in particular, but the ethical goals of this allocation framework should inform allocation of other scarce treatments as they become available, including monoclonal antibodies, convalescent plasma, and other emerging treatments. Information in this document (such as the clinical criteria for eligibility and dosage) that apply specifically to RDV are subject to change as more data emerges on its use and effectiveness.

<https://www.health.pa.gov/topics/disease/coronavirus/Pages/Guidance/Ethical-Allocation-Framework.aspx>

# CENTER FOR MEDICARE AND MEDICAID INNOVATION (CMMI)



**A HEALTH SYSTEM THAT ACHIEVES EQUITABLE OUTCOMES  
THROUGH HIGH QUALITY, AFFORDABLE, PERSON-CENTERED CARE**



**DRIVE  
ACCOUNTABLE CARE**



**ADVANCE  
HEALTH EQUITY**



**SUPPORT  
INNOVATION**



**ADDRESS  
AFFORDABILITY**



**PARTNER TO  
ACHIEVE SYSTEM  
TRANSFORMATION**



# Health Equity Benchmark Adjustment

ACO REACH includes a benchmark adjustment that increases benchmarks for ACOs serving higher proportions of underserved beneficiaries

CMS will stratify all beneficiaries aligned to ACO REACH using a composite measure of underservice that incorporates a combination of<sup>1</sup>:

## Area Deprivation Index

*Area-level measure of local socioeconomic factors correlated with medical disparities and underservice*

Percentile Score from 1-100

## Dual Medicaid Status

*Beneficiary-level measure of economic challenges affecting individuals' ability to access high quality care*

25 Point Adjustment for Full or Partial Dual Eligibility



91<sup>st</sup> – 100<sup>th</sup> Percentile  
(Top Decile)

*+\$30 PBPM Adjustment*

51<sup>st</sup> – 90<sup>th</sup> Percentile  
(Middle 4 Deciles)

*No Adjustment*

1<sup>st</sup> – 50<sup>th</sup> Percentile  
(Bottom 5 Deciles)

*-\$6 PBPM Adjustment*

1. CMS may explore other variables to include in this assessment and will notify applicants prior to the start of PY2023 if any other variables are included.

\*2022 ACO Realizing Equity, Access, and Community Health (REACH) Model  
[<https://innovation.cms.gov/media/document/aco-reach-fin-meth-webinar-slides>]

# CMS ACO-REACH RESOURCE TARGETING: SIMPLIFIED



= \$

Low ADI



= \$

High ADI



# EXPOSOME: GAPS AND OPPORTUNITIES



## **Gap: Exposome Measurement**

- Promote development and availability of rigorous, harmonizable life-course aligned exposome measures

## **Gap: Standardizing Social-Biological Phenotyping**

- Develop processes and infrastructure to promote more routine inclusion of exposome in traditional biological-focused assessments
- Increase scientific capacity to perform this work - multi-disciplinary teams

## **Gap: Health Resilience in Adverse Exposome**

- Identifying factors, interventions that promote health in adverse exposome

## **Many Other Gaps: Exposome as an Emerging Field**



## ACKNOWLEDGMENTS

ADRC	Participating Components	Site PI(s)	Site Co-I(s)
University of Wisconsin	BB/CC	Amy Kind, Barbara Bendlin (MPI)	Vikas Singh, Menggang Yu
Banner Alzheimer's Institute	BB/CC	Eric Reiman, Thomas Beach	Kewei Chen
Boston University	BB/CC	Maureen K. O'Connor	Michael Alosco
Emory University	BB/CC	Felicia Goldstein	
Indiana University	BB/CC	Shannon Risacher	Andrew Saykin, Liana Apostolova
Johns Hopkins University	BB/CC	Corinne Pettigrew	
Mount Sinai School of Medicine	BB/CC	Mary Sano	Carolyn Zhu, Judith Neugroschl
New York University	BB/CC	Thomas Wisniewski, Joshua Chodosh	Karyn Marsh
Oregon Health & Science University	BB/CC	Aimee Pierce	Randall Woltjer, Raina Croff
Rush University	BB Only	Melissa Lamar	David Bennett, Lisa Barnes
Stanford University	BB/CC	Victor Henderson	Patricia Rodriguez Espinosa
UC-Davis	BB/CC	Oanh Meyer	Rachel Whitmer, Sarah Farias
UC-Irvine	BB/CC	David Sultzer	
UC-San Diego	BB/CC	Robert Rissman	James Brewer
UC-San Francisco	BB/CC	Serggio Lanata	
University of Kansas	BB/CC	Jonathan Mahnken	Jill Morris, Rebecca Lepping
University of Kentucky	BB Only	Erin Abner	Anna Kucharska-Newton
University of Michigan	BB/CC	Henry L. Paulson	Kelly Bakulski
University of Pittsburgh	BB/CC	Jennifer Lingler	Julia Kofler, Anthony Fabio
Wake Forest University	BB/CC	Suzanne Craft, Trey Bateman	Samuel Lockhart
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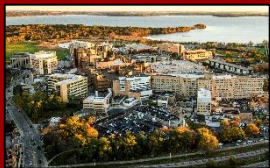
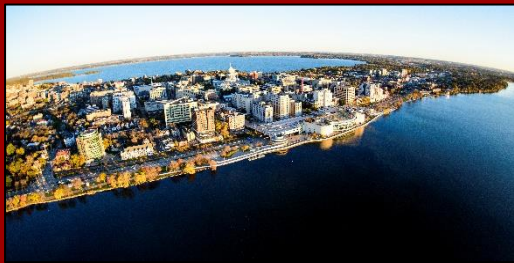
The NACC database *is funded by NIA/NIH Grant U24 AG072122. Data are contributed*

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