

The Neighborhood Atlas: Linking Disparities-Aligned EXPOSOME to Brain Health through Data Democratization

February 6, 2023

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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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HEALTH IS NOT DISTRIBUTED EQUALLY



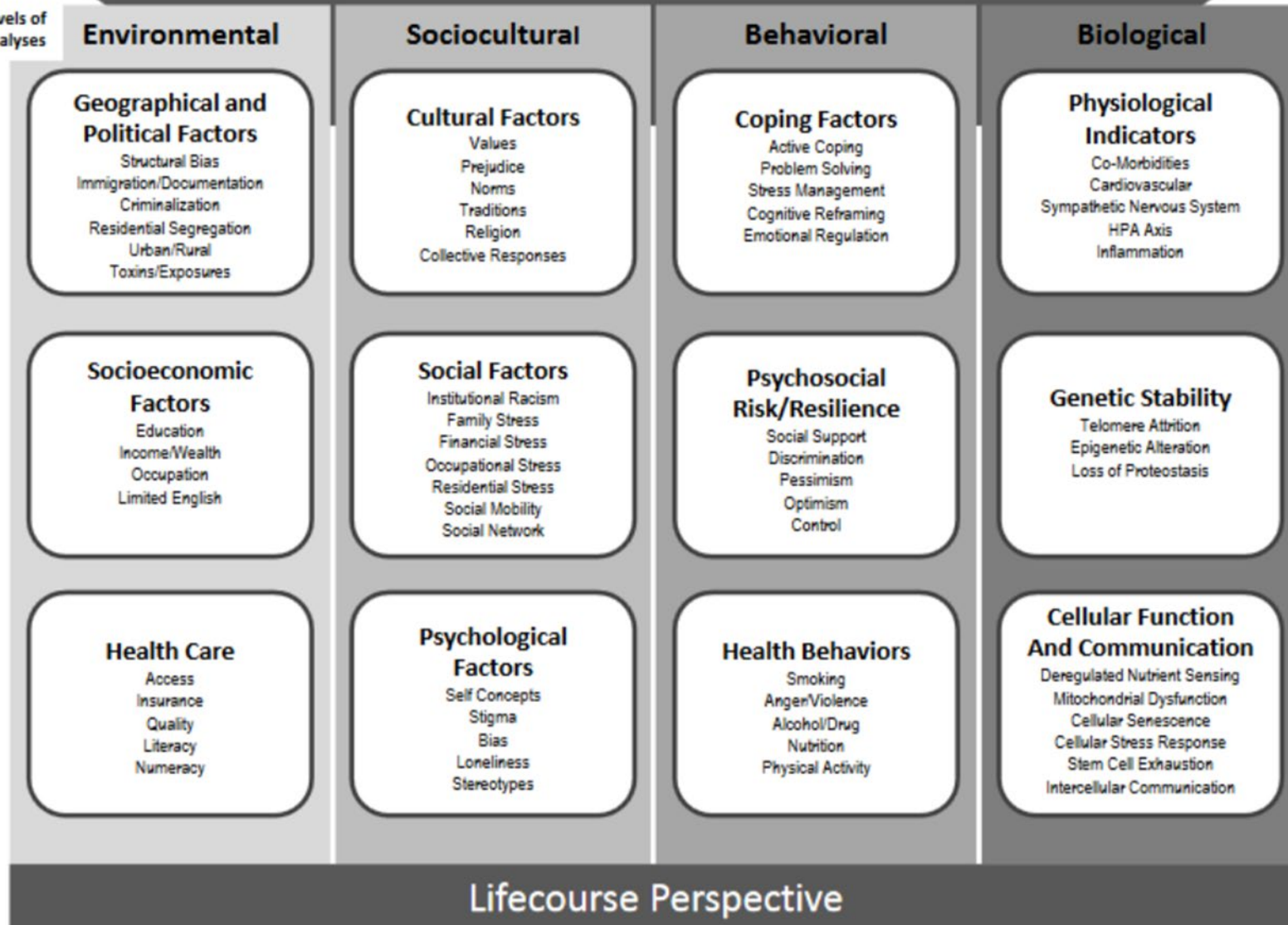
Solutions Needed



NIH MECHANISTIC 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



EXPOSOME

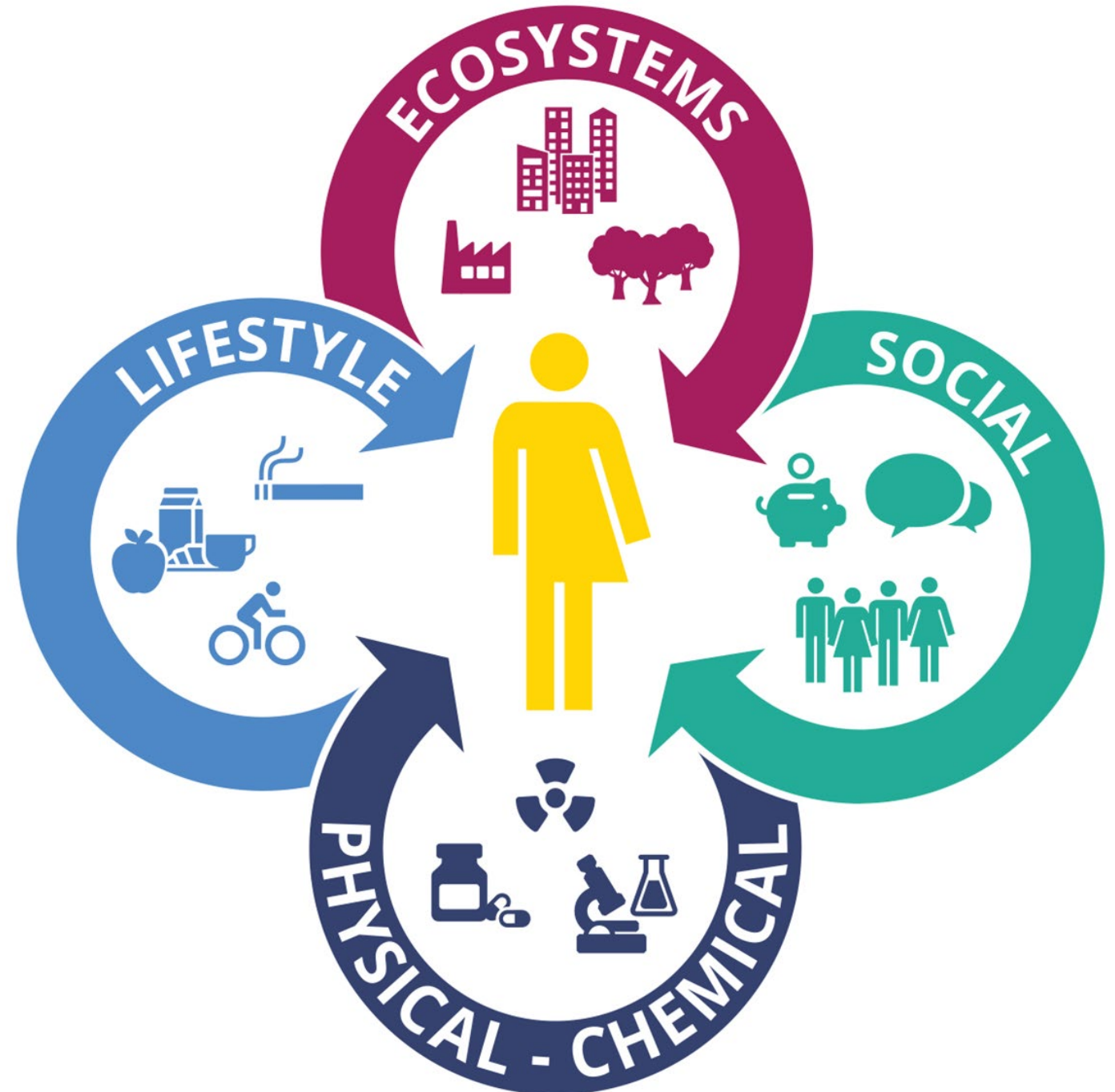
The measure of all the exposures of an individual in a lifetime and how those exposures relate to health*

*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

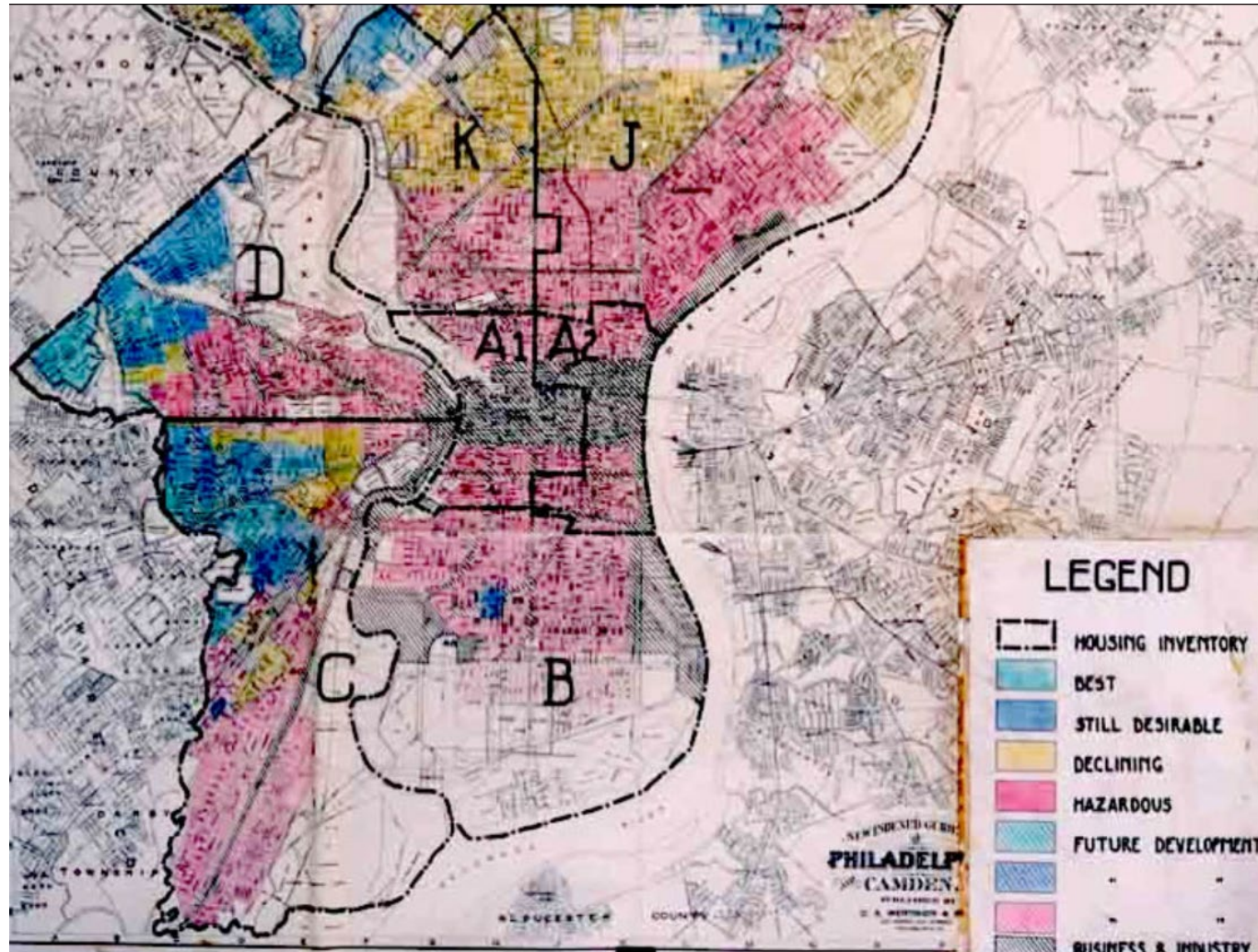


Exposome

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



STRUCTURAL INEQUITIES



*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](#).

MOVING TO OPPORTUNITY STUDY

**Individual
Socioeconomics**

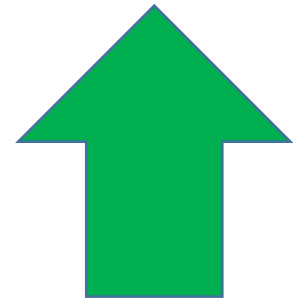


NO CHANGE

Health



IMPROVED



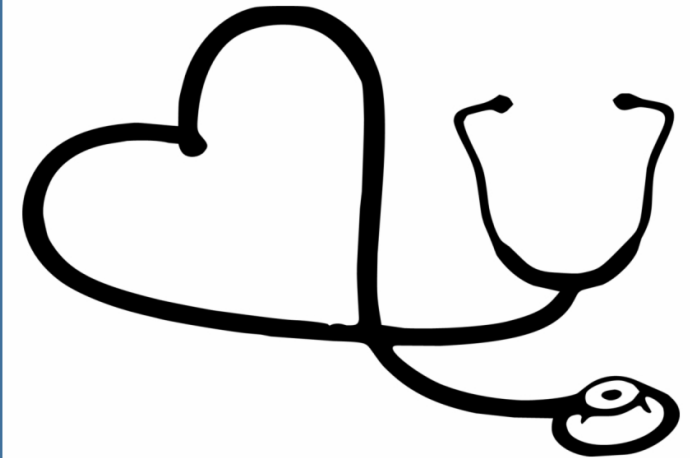
EXAMINING THE EXPOSOME



**Quantifying
Exposures**



**Linking Exposome
to Biology**



**Research to
Action**

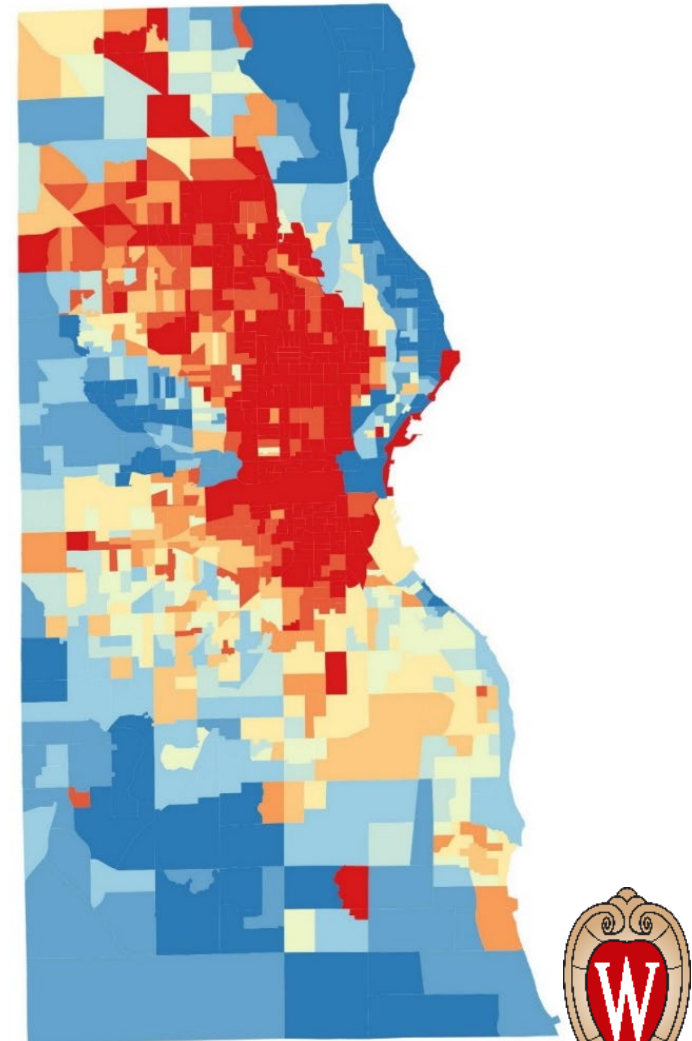
EXAMINING THE EXPOSOME



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

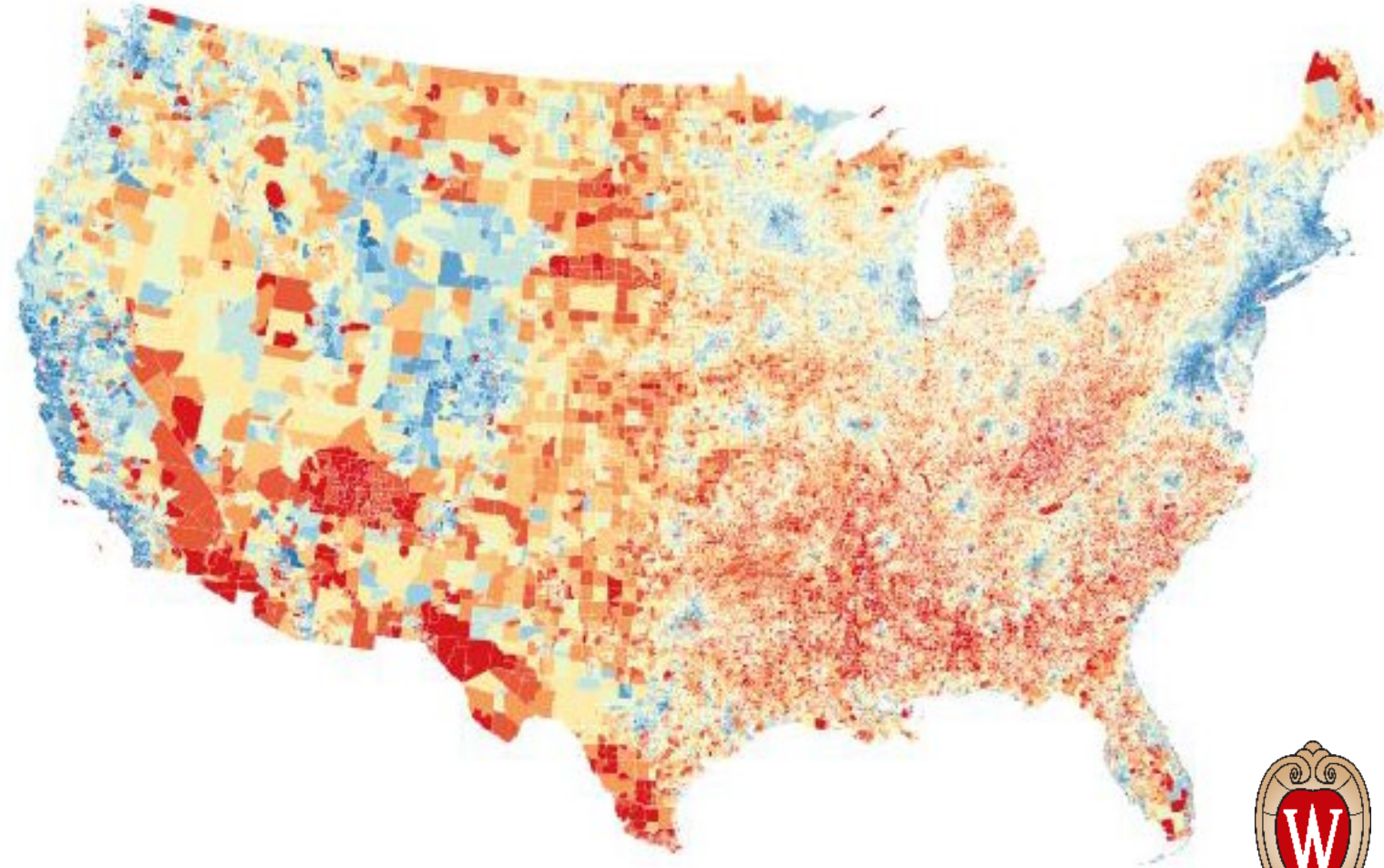


Milwaukee County

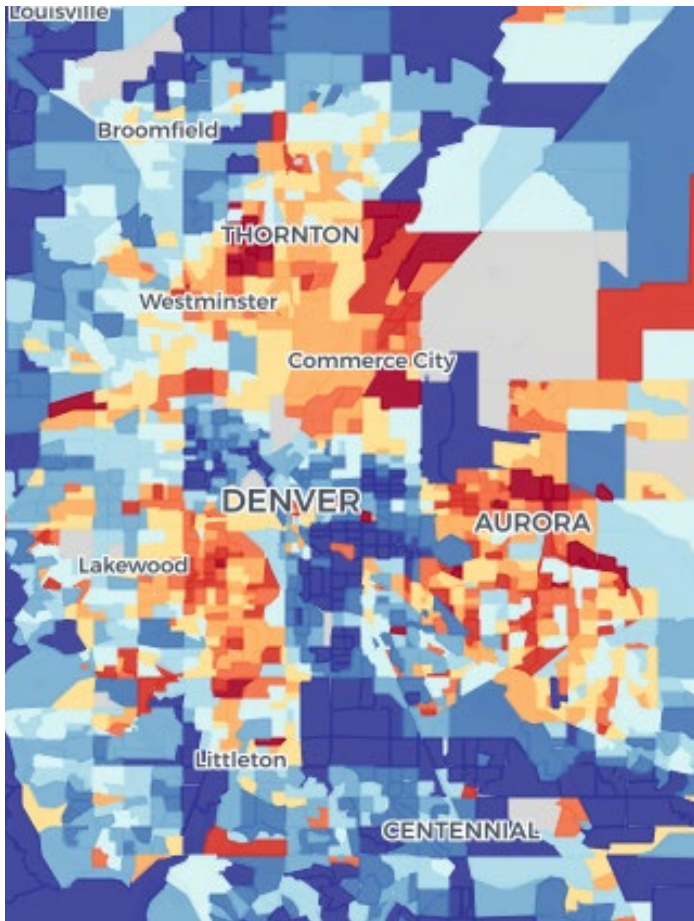
*Kind and Buckingham, *New England Journal of Medicine*, 2018

HIGHLY DISADVANTAGED NEIGHBORHOODS IN US

- More often in urban core and rural areas



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)
- Increased cardiovascular risk (Berman et al, JAMA-Cardiology, 2021; multiple)
- Decreased active-life expectancy (Gill et al, JAMA-IM, 2021)
- Many other factors





Original Investigation | Surgery

Analysis of Delayed Surgical Treatment and Oncologic Outcomes in Clinical Stage I Non-Small Cell Lung Cancer

Brendan T. Heiden, MD; Daniel B. Eaton Jr, MPH; Kathryn E. Engelhardt, MD, MS; Su-Hsin Chang, PhD, SM; Yan Yan, MD, PhD; Mayank R. Patel, MD; Daniel Kreisel, MD, PhD; Ruben G. Nava, MD; Bryan F. Meyers, MD, MPH; Benjamin D. Kozower, MD, MPH; Varun Puri, MD, MSCI

Rachel Marsh¹ a

Area Deprivation Index Predicts Readmission Risk at an Urban Teaching Hospital

and, Roe Gutman, Kristina Monteiro, William R. Buckingham,

DOI: 10.1377/hlthaff.2017.1509
HEALTH AFFAIRS 37,
NO. 7 (2018): -
© 2018 BMJ and JAMA

American Journal of
Transplantation

AST

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TRANSPLANTATION

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AMERICAN SOCIETY OF
TRANSPLANT SURGEONS

ORIGINAL ARTICLE

Neighborhood socioeconomic deprivation is associated with worse patient and graft survival following pediatric liver transplantation

Sharad I. Wadhvani, Andrew F. Beck, John Bucuvalas, Laura Gottlieb, Uma Kotagal, Jennifer C. Lai

January 2020 | <https://doi.org/10.1111/ajt.15786> | Citations: 4

June
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SPECIAL ISSUE: HEA

Neighborhood

Annals

LATEST ISSUES

PREV ARTICLE | THIS ISS

ORIGINAL RESEARCH

Safety-Net Hospitals, Under Maryland's All-

Stephen F. Jencks, MD, MPH; Alyson Schu
MSPH; Amy J.H. Kind, MD, PhD

Article, Author, and Disclosure Inform

JAMA Cardiology | Original Investigation

Association of Socioeconomic Disadvantage With Long-term Mortality After Myocardial Infarction The Mass General Brigham YOUNG-MI Registry

Adam N. Berman, MD; David W. Biery, AB; Curtis Ginder, MD; Avinainder Singh, MBBS, MMSc; Jonggyu Baek, PhD; Rishi K. Wadhwa, MD, MPP, MPhil; Wanda Y. Wu, BA; Sanjay Divakaran, MD; Ersilia M. DeFilippis, MD; Jon Hainer, BS; Christopher P. Cannon, MD; Jorge Plutzky, MD; Donna M. Polk, MD, MPH; Khurram Nasir, MD, MPH; Marcelo F. Di Carli, MD; Arlene S. Ash, PhD; Deepak L. Bhatt, MD, MPH; Ron Blankstein, MD

Original Investigation | Infectious Diseases

Racial Disparities in Incidence and Outcomes Among Patients With COVID-19

L. Silvia Muñoz-Price, MD, PhD; Ann B. Nattinger, MD, MPH; Frida Rivera, MD, PhD; Ryan Hanson, MS; Cameron G. Gmehlin, BA; Adriana Perez, MS; Siddhartha Singh, MD, MS, MBA; Blake W. Buchan, PhD; Nathan A. Ledebor, PhD; Liliana E. Pezzin, PhD, JD



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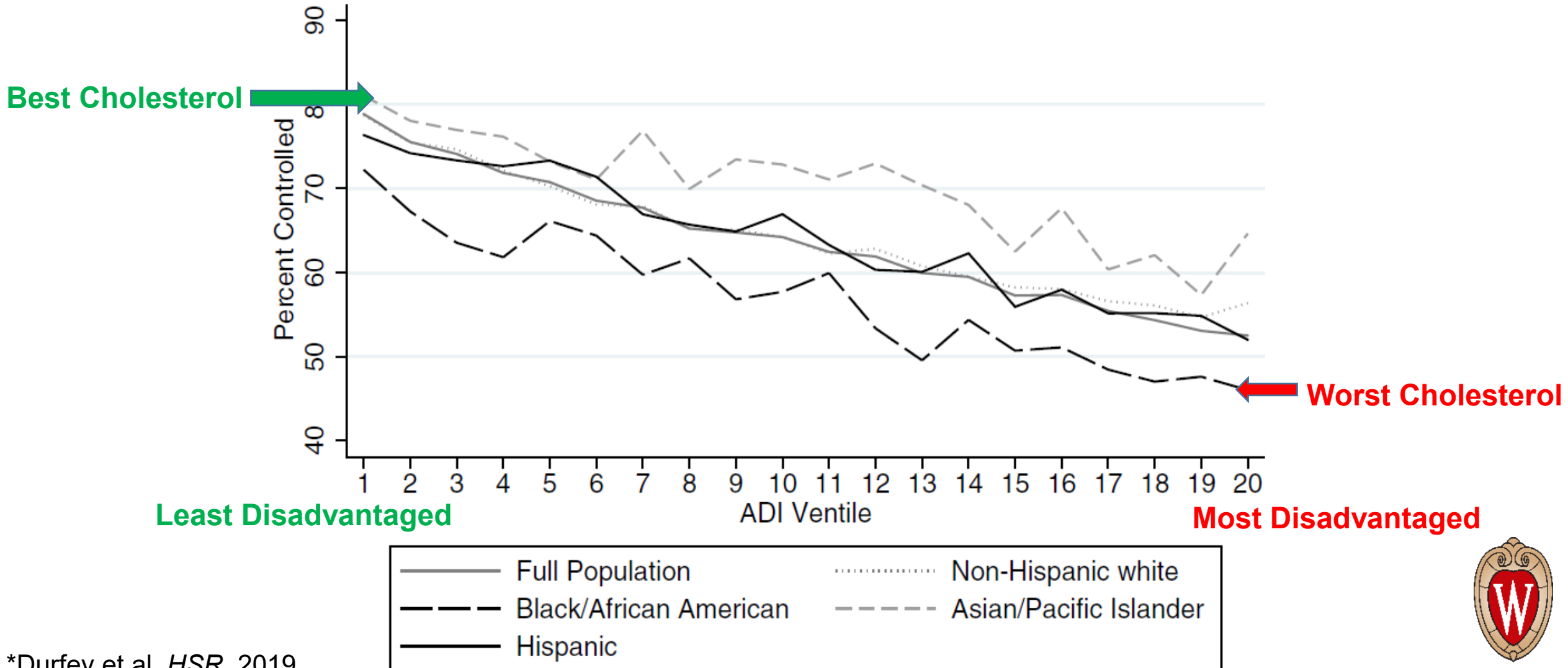


Brain connectivity and socioeconomic status at birth and externalizing symptoms at age 2 years

Bruce Ramphal^a, Diana J. Whalen^b, Jeanette K. Kenley^c, Qiongru Yu^b, Christopher D. Smyser^{c,d,e}, Cynthia E. Rogers^{b,e}, Chad M. Sylvester^b

NEIGHBORHOOD DISADVANTAGE AND CHOLESTEROL CONTROL

Cholesterol Control



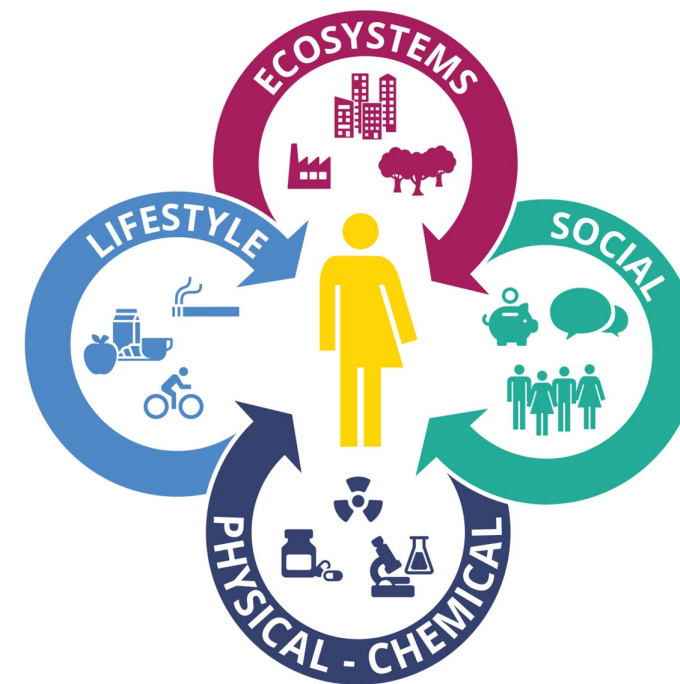
EXAMINING THE EXPOSOME



**Linking Exposome
to Biology**

SOCIAL-BIOLOGICAL PHENOTYPING

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

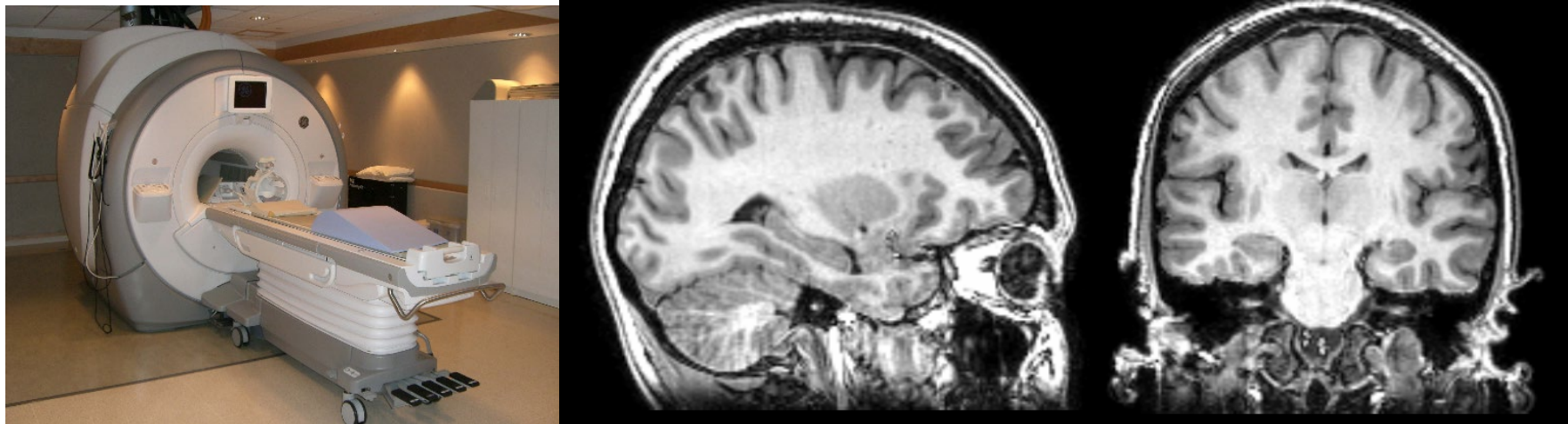


Exposome

Science. 2020. 367(6476): 392–396.

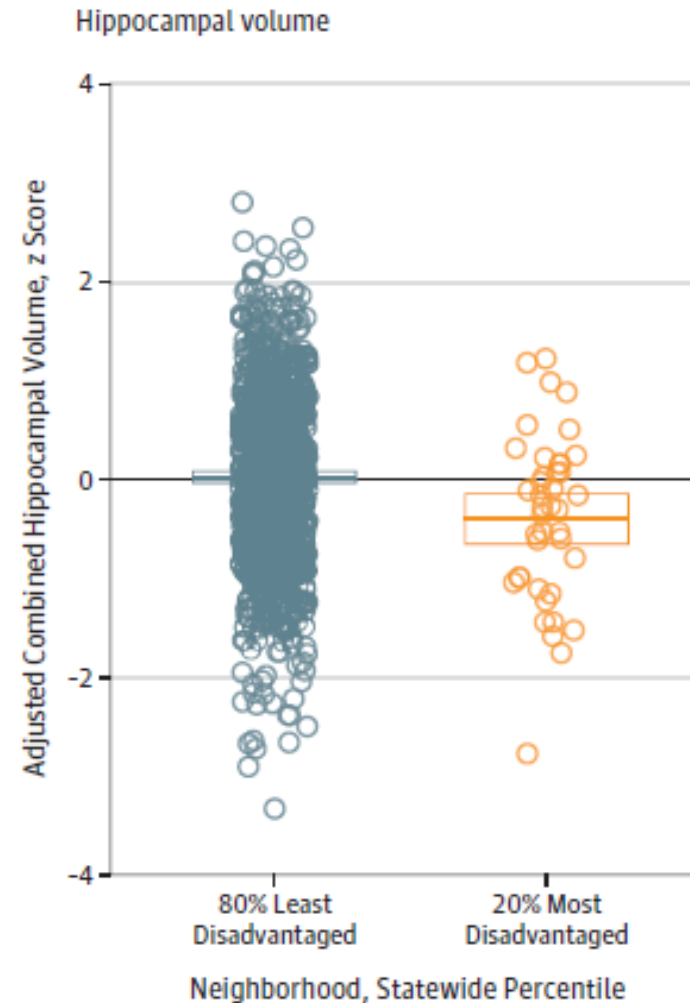
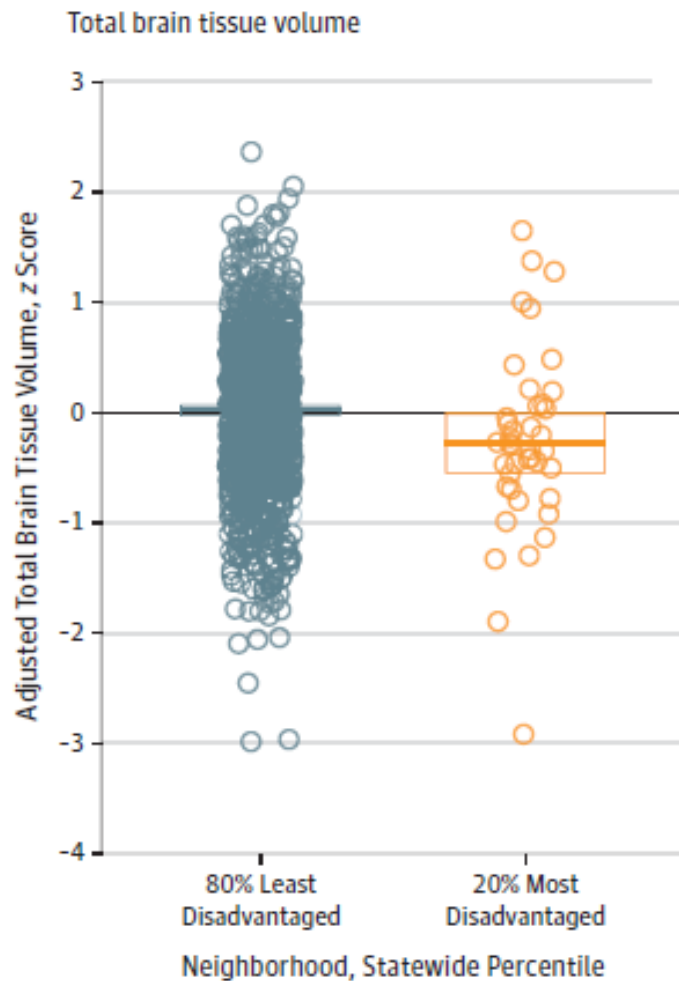
NEIGHBORHOOD DISADVANTAGE AND BRAIN STRUCTURE

- N=951 cognitively unimpaired research participants
- Residential address geocoded, linked to neighborhood disadvantage by ADI
- MRI measures of hippocampal and total brain tissue volume



Association of Neighborhood-Level Disadvantage With Cerebral and Hippocampal Volume

Jack F. V. Hunt, BA; William Buckingham, PhD; Alice J. Kim, BA; Jennifer Oh, BS; Nicholas M. Vogt, BA; Erin M. Jonaitis, MS, PhD; Tenah K. Hunt, MPH, PhD; Megan Zuelsdorff, PhD; Ryan Powell, PhD; Derek Norton, MS; Robert A. Rissman, PhD; Sanjay Asthana, MD; Ozioma C. Okonkwo, PhD; Sterling C. Johnson, PhD; Amy J. H. Kind, MD, PhD; Barbara B. Bendlin, PhD



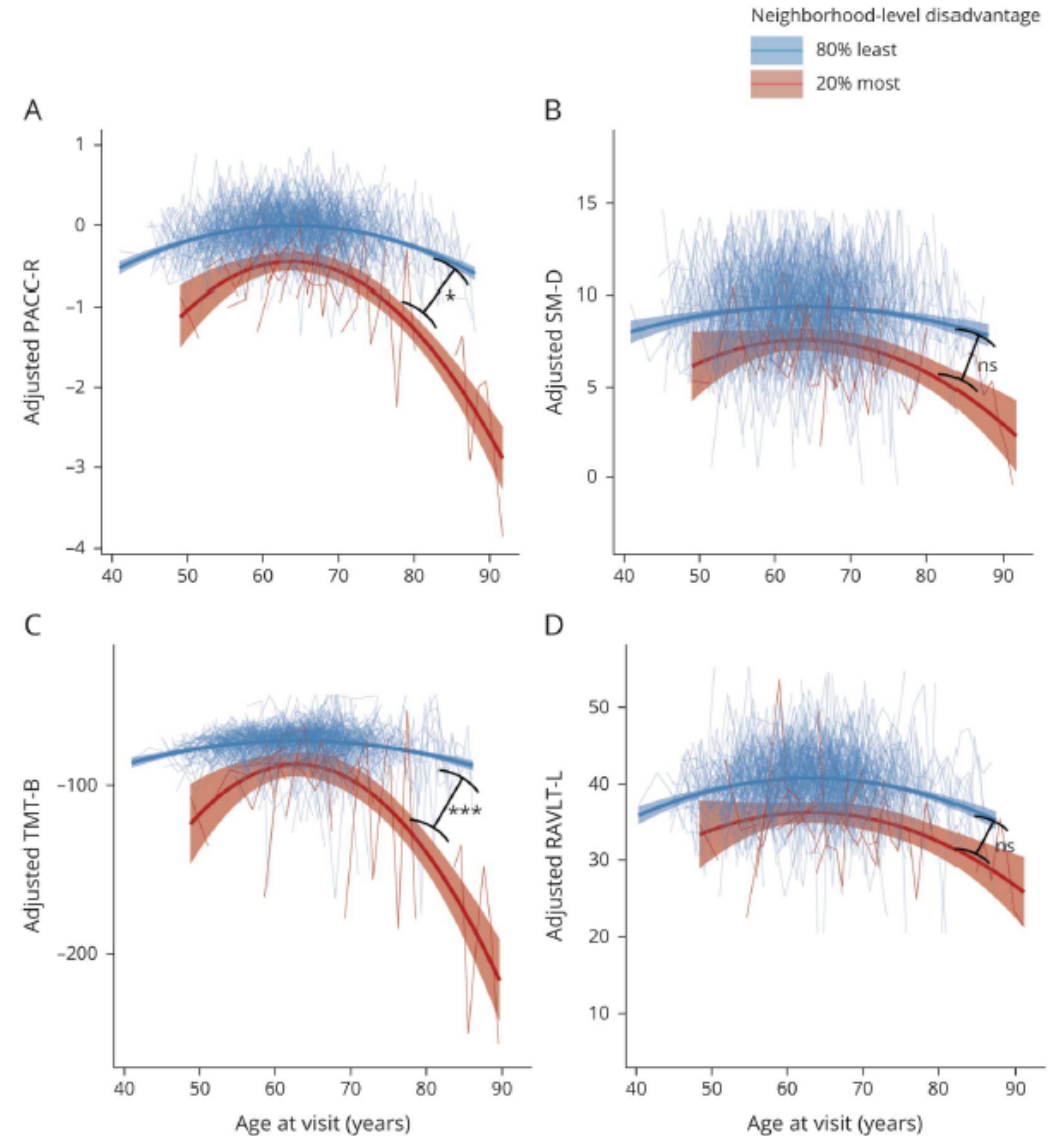
April 14, 2021 ARTICLE

Association of Neighborhood Context, Cognitive Decline, and Cortical Change in an Unimpaired Cohort

Jack F.V. Hunt, Nicholas M. Vogt, Erin M. Jonaitis, William R. Buckingham, Rebecca L. Kosciak, Megan Zuelsdorff, Lindsay R. Clark, Carey E. Gleason, Menggang Yu, Ozioma Okonkwo, Sterling C. Johnson, Sanjay Asthana, Barbara B. Bendlin, Amy J.H. Kind

First published April 14, 2021, DOI: <https://doi.org/10.1212/WNL.00000000000011918>

In this 10 year longitudinal study of cognitively unimpaired adults, living in the most highly disadvantaged neighborhoods was associated with accelerated degeneration (cortical thinning) in AD affected regions and more cognitive decline



Plots depict performance on Preclinical Alzheimer's Cognitive Composite-Revised (PACC-R) composite (A) and component subtests (B-D) on the age on the x-axis. Higher scores equate to better performance on cognitive test (Trail-Making Test, part B [TMT-B] scores are multiplied by -1 for consistency). Cognitive test scores are adjusted for sex, years of education, practice effects, and individual-level intercepts and slopes. Small lines (plot) depict individual trajectories; large lines depict estimated quadratic slopes for participants with the 80% least neighborhood-level disadvantage (blue lines, n = 582) and 20% most disadvantage (red lines, n = 19). Participants from the most highly disadvantaged neighborhoods exhibited significant decline in PACC-R and TMT-B than participants from less disadvantaged neighborhoods, but showed no difference in decline of Story Memory Delay (SM-D) or Rey Auditory Verbal Learning Test, total trials 1-5 (RAVLT-L). Unadjusted p values for age2neighborhood disadvantage interaction terms are displayed on plots for each cognitive test: ns p > 0.05, *p < 0.05, ***p < 0.001.



Associations between Amygdala-Prefrontal Functional Connectivity and Age Depend on Neighborhood Socioeconomic Status

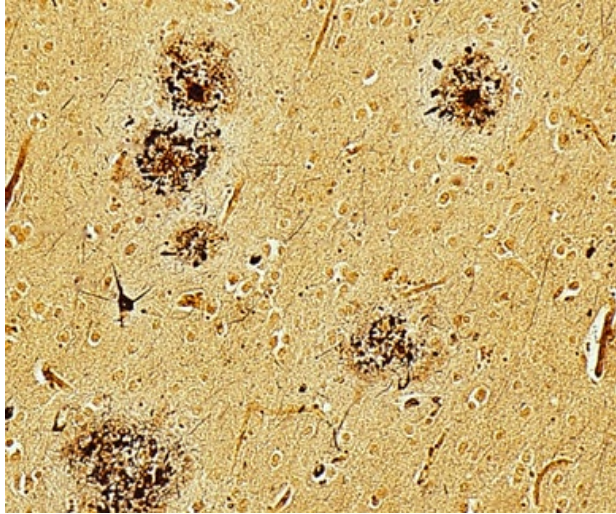
Bruce Ramphal¹, Mariah DeSerisy², David Pagliaccio¹, Elizabeth Raffanello¹, Virginia Rauh³, Gregory Tau¹, Jonathan Posner¹, Rachel Marsh¹ and Amy E. Margolis¹

¹New York State Psychiatric Institute and Department of Psychiatry, Vagelos College of Physicians and Surgeons, Columbia University, New York, NY 10032, USA, ²Department of Psychology, Fordham University, Bronx, NY 10458, USA and ³Department of Population and Family Health, Mailman School of Public Health, Columbia University, New York, NY 10032, USA

Address correspondence to Bruce Ramphal, 1051 Riverside Drive, Box 74/Room 2403, New York, NY 10032, USA. Email: bruce.ramphal@nyspi.columbia.edu.

- Cross-sectional MRI study of 127 participants aged 5–25 years NYC area
- Reduced basolateral amygdala- prefrontal cortex functional connectivity at earlier ages in participants from more disadvantaged neighborhoods by ADI, independent of individual-level SES
- Reduced connectivity in more disadvantaged youth was associated with less anxiety

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.

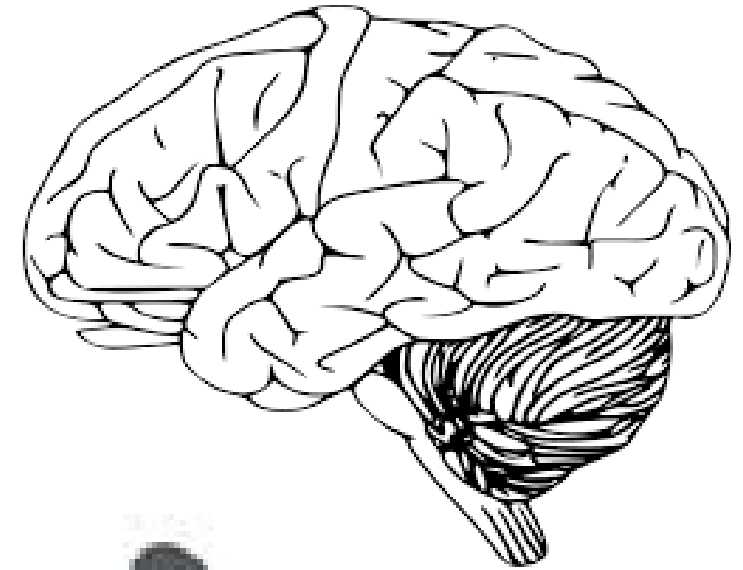
OBJECTIVE To establish the feasibility of linking neuropathology data to social determinants of health exposures using neighborhood disadvantage metrics (the validated Area Deprivation Index)

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

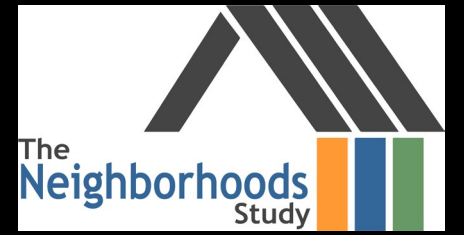




Life-course

THE NEIGHBORHOODS STUDY

(R01AG070883; PI KIND, MPI BENDLIN)



Aim 1: Determine the impact of the **cumulative dose and timing** of neighborhood disadvantage exposure (indexed by ADI), on **cognitive function and change** over time

Aim 2: on AD-specific markers indexed by neuroimaging (**amyloid and tau PET**) and the secondary outcomes of vascular burden and volumetric MRI; and

Aim 3: on **neuropathologic tissue features and diagnosis**.

Aim 4: Using existing ADRC data and newly collected survey data, define the extent to which individual race/ethnicity, age, sex, income, education, comorbidity and health-behaviors mediate these relationships.





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
Washington University in St. Louis	BB Only	Cyrus A. Raji	Richard Perrin
Yale University	BB/CC	Carmen Carrión	

Site	NACC	T1Weighted	Amyloid PET	Tau PET	Brain bank
Arizona Alzheimer's Center	328	328	214	177	390
Boston University	402	0	0	0	437
Emory University	455	250	30	10	333
Indiana University School of Medicine	480	262	119	143	436
Johns Hopkins University School of Medicine	295	215	0	0	683
Mount Sinai ADC	460	152	208	4	109
New York University	490	455	76	6	358
Oregon Health and Science University	318	81	23	9	920
Rush University Medical Center	0	0	0	0	1690
Stanford University	369	239	108	5	9
University of California, Davis	432	414	162	5	761
University of California, Irvine	319	94	40	10	153
University of California, San Diego	462	462	0	0	982
University of California, San Francisco	792	644	218	140	405
University of Kansas	341	175	76	0	47
University of Kentucky	0	0	0	0	971
University of Michigan ADC	468	268	300	300	205
University of Pittsburgh	639	495	110	31	699
Wake Forest University ADC	585	516	121	4	3
Washington University School of Medicine	0	0	0	0	296
Yale University ADRC	240	105	105	30	20
Total	7875	5155	1910	874	9907

UW Ns (ADRC only)
at time of submission:

Number with T1-weighted imaging: 803
Number with amyloid PET: 216
Number with tau PET: 129

Data sources

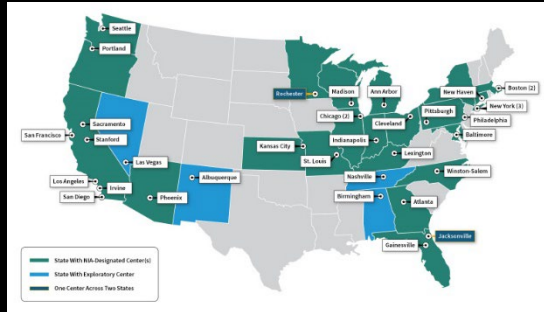


Table 3. Sample Size, from 22 ADRCs

	<i>n</i>
Active participants with UDS reported to NACC (living cohort)*	9234
with T1-weighted imaging	5728
with amyloid PET	1995
with tau PET	958
Brain bank decedents with NACC neuropathology form	10469

*UDS: Uniform data set, standardized clinical data reported by all ADRCs to the National Alzheimer's Coordinating Center (NACC).

MRI, Amyloid PET and Tau PET sample numbers are reflective of all available assessments across sites. Please see Neuroimaging Data section of this proposal for additional detail, including harmonization procedures.

Table 5. NACC and Survey Derived Data Elements

Health Behaviors:
Alcohol/Substance abuse ^{2,4}
Smoking ²
Co-morbidities:
Cerebrovascular disease ²
Heart disease ^{2,5}
Diabetes ^{2,5}
Hypertension ^{2,3,5}
Abnormal cholesterol ^{2,5}
Obesity ³
Traumatic brain injury ^{2,4}
Individual Socioeconomic Position
Income ⁶
Education ^{1,6}
Occupation ⁶
Demographic Factors
Race/Ethnicity ¹
Age ^{1,6}
Gender ¹

Source: National Alzheimer's Coordinating Center (NACC) data-collection forms

Elements in database have been highly conserved across data form versions

¹Form A1: Subject Demographics.

²Form A5: Subject Health History

³Form B1: Physical

⁴Form D1: Clinician Diagnosis

⁵Form D2: Clinician-Assessed Medical Conditions

⁶Collected in proposed survey

LIFE COURSE EXPOSOME CONSTRUCTION

Decedent Residential History: Geospatial targeting of exposure data across the life-course using publicly available data

- Participant addresses
- Public-data based construction (archival, genealogical and historical methods)
- 73% of all person years discoverable with considerable archival time investments

Living Cohort Residential History: Geospatial targeting of exposure data across the life-course

- Participant addresses
- Validated survey, standard approach
- Option for public data tracing

LIFE COURSE

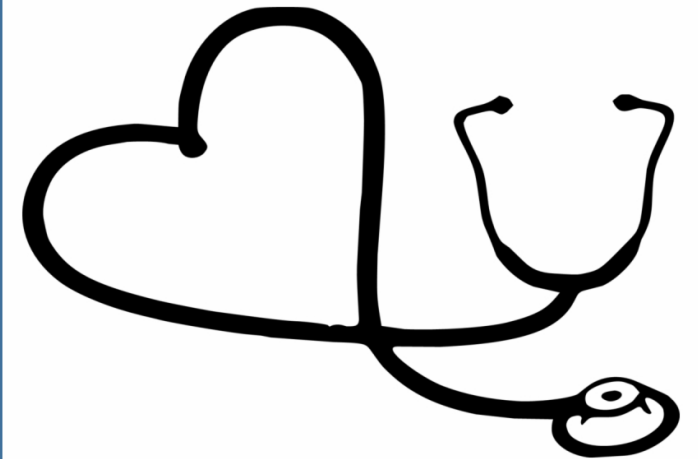


LIFE COURSE EXPOSOME CONSTRUCTION: CHALLENGES

- Technical considerations
 - Historical geocoding
 - Residential history construction on decedents
- Linking to Protected Health Information (PHI)
- Responsible and ethical sharing
- Data democratization considerations



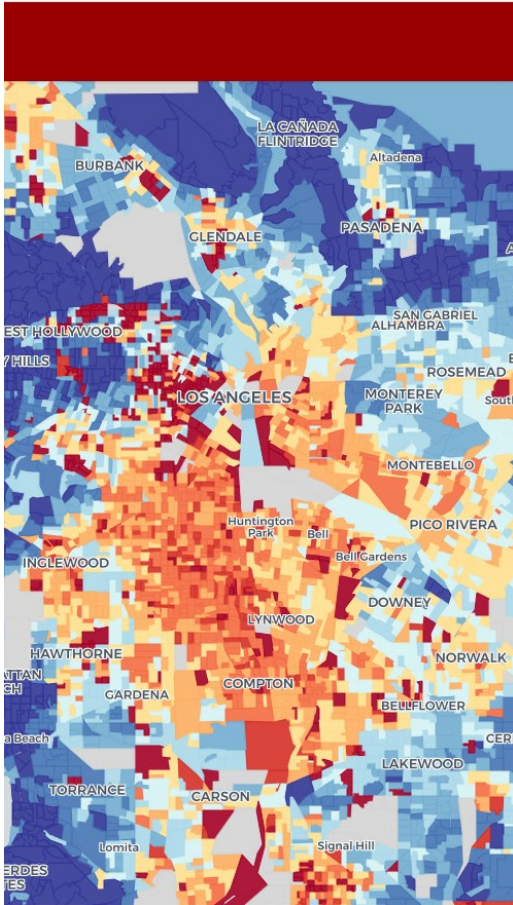
EXAMINING THE EXPOSOME



**Research to
Action**

THE NEIGHBORHOOD ATLAS

www.neighborhoodatlas.medicine.wisc.edu

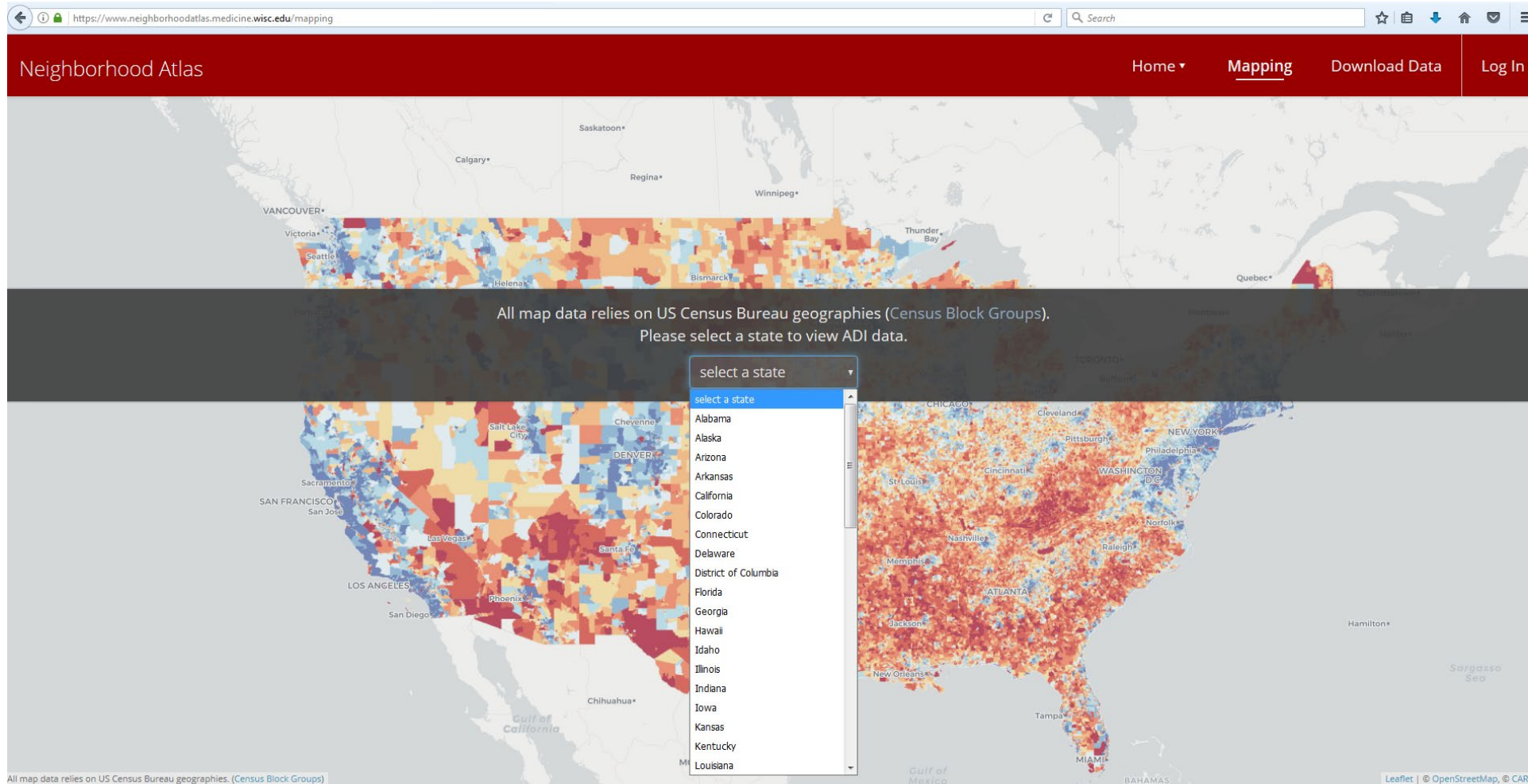


- Data democratization and open science tool for the ADI
- Customized mapping; Free, open to all
- Data downloaded tens of thousands of times by research, governmental, community, and industry groups.



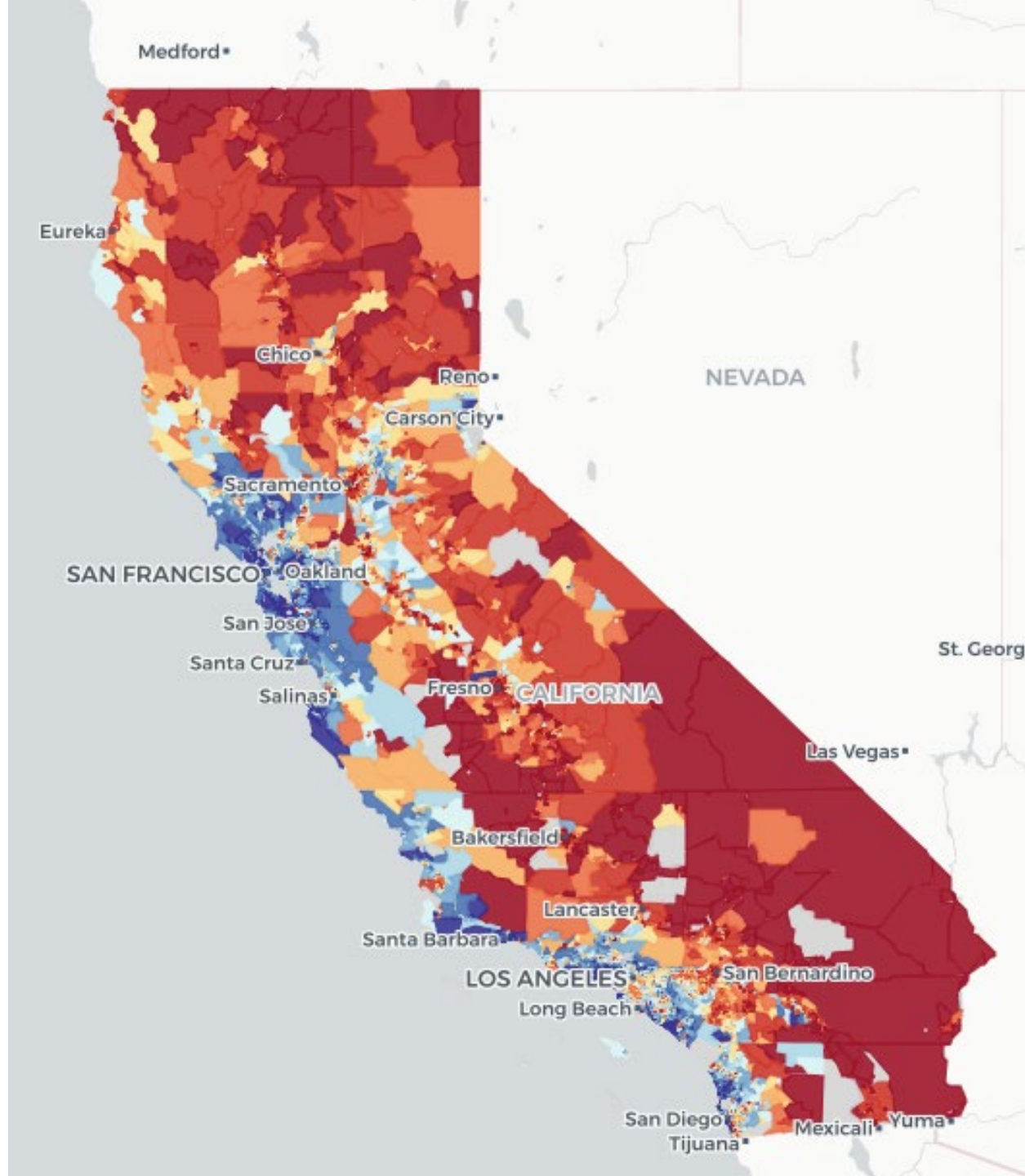
THE NEIGHBORHOOD ATLAS

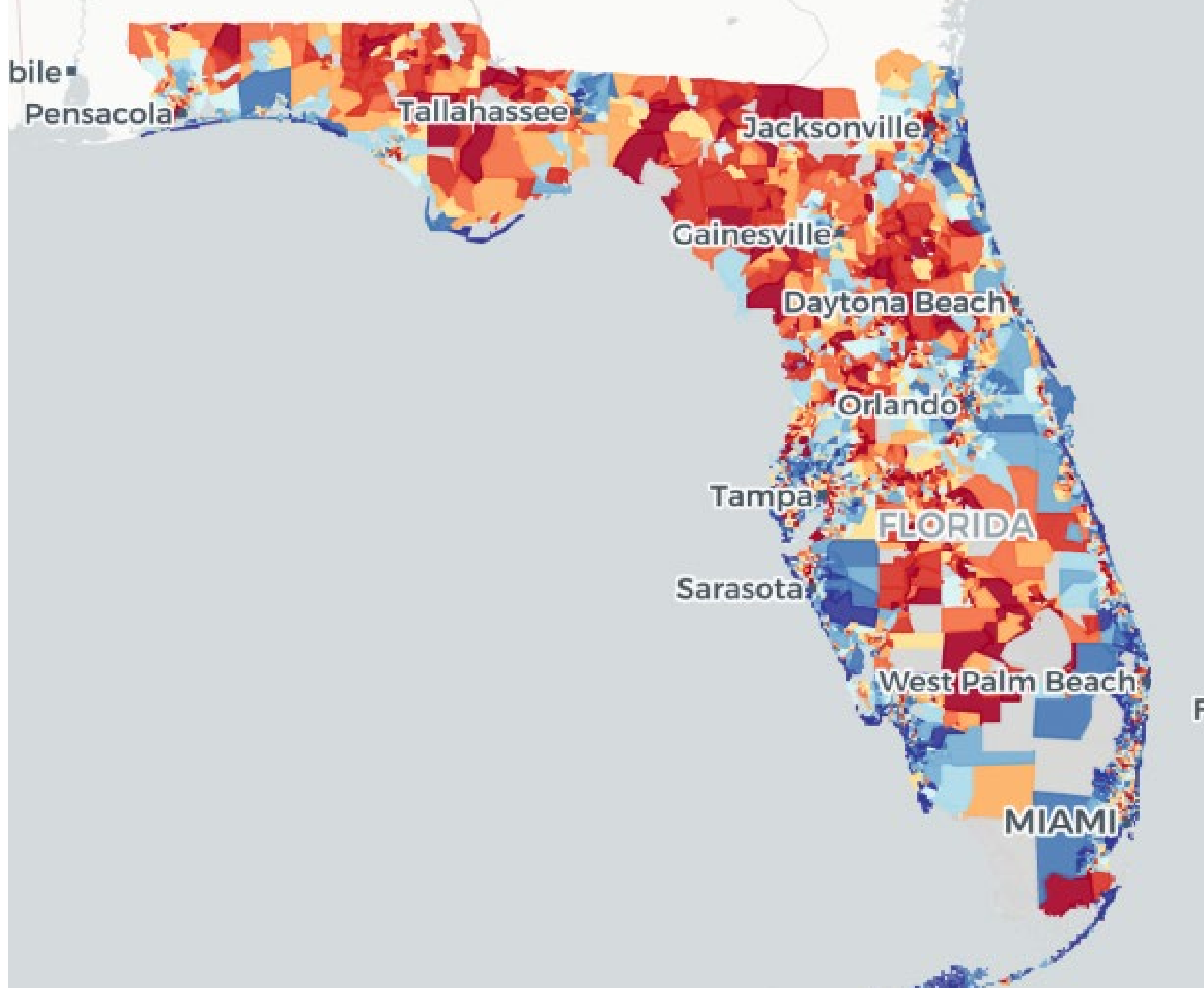
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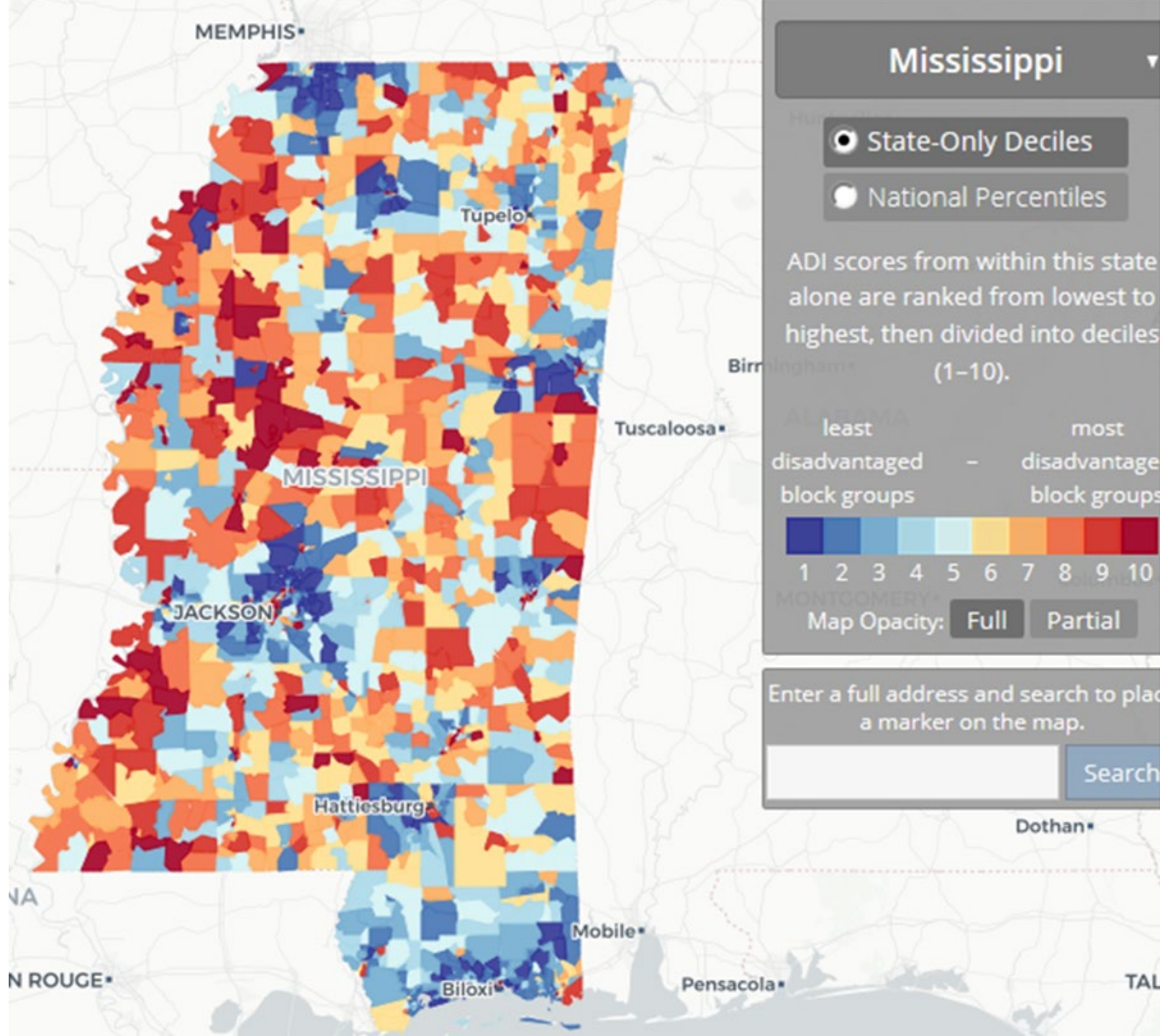


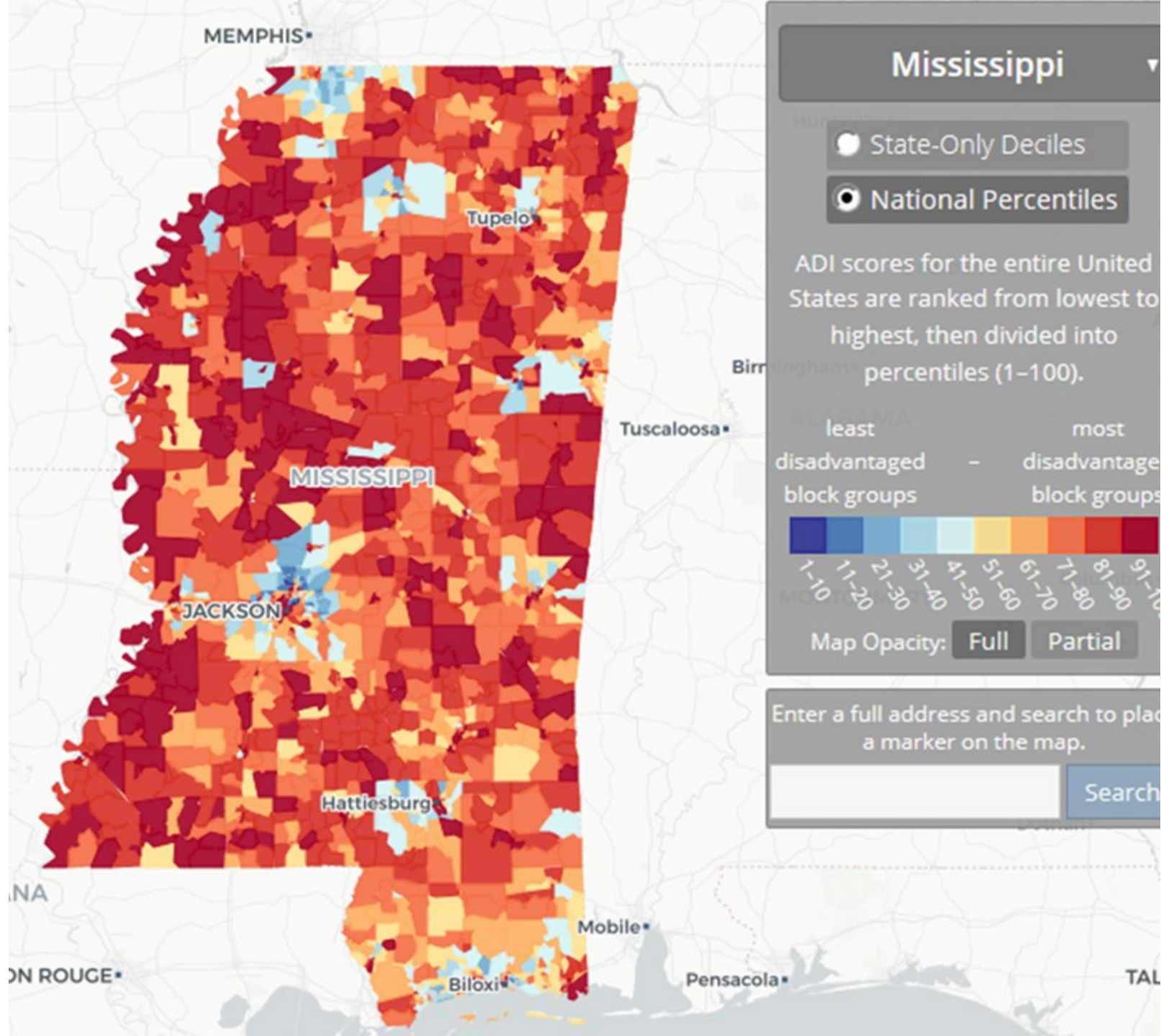
*Kind NEJM 2018

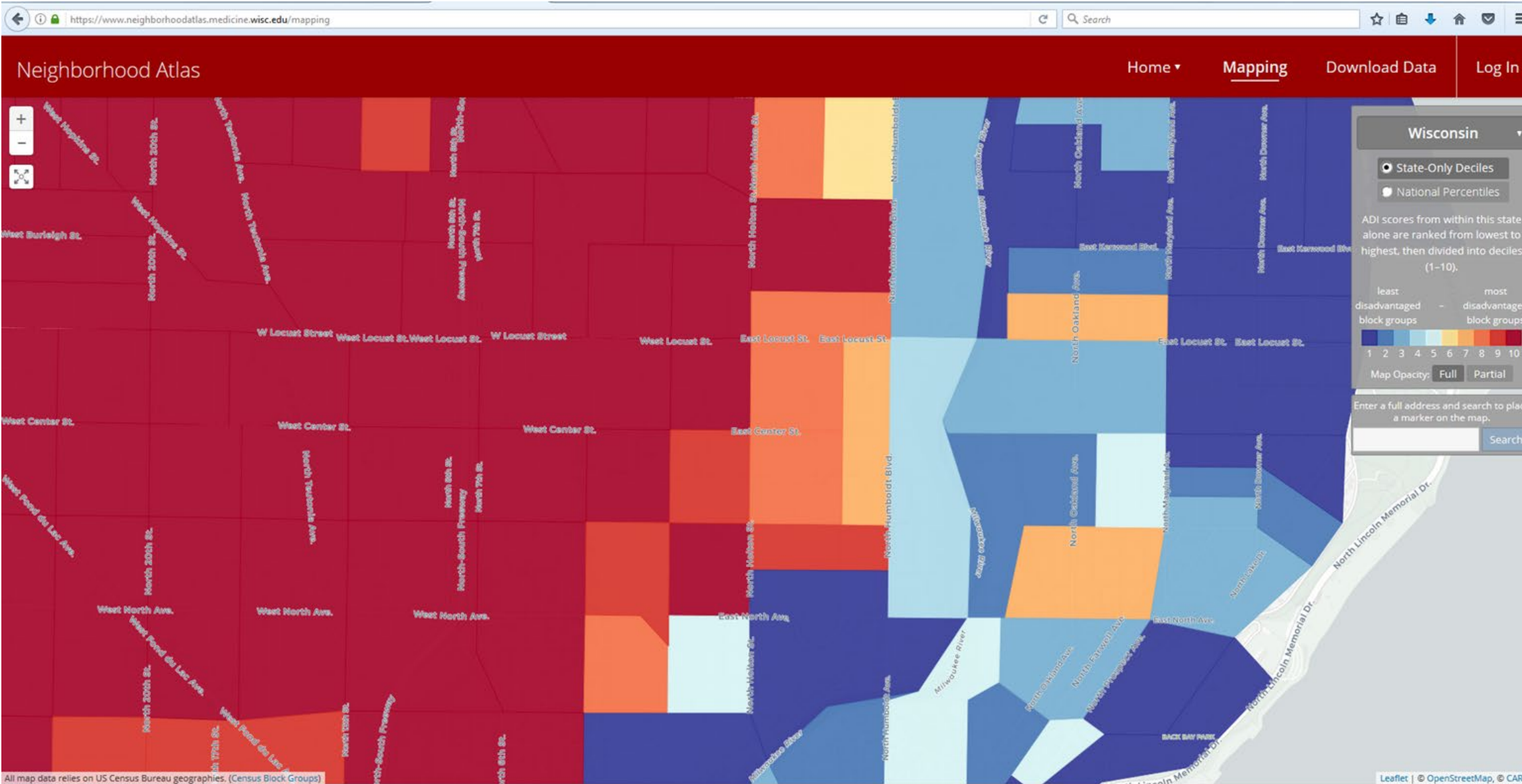












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<https://www.neighborhoodatlas.medicine.wisc.edu/>

CENTER FOR MEDICARE AND MEDICAID INNOVATION (CMMI)



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

CMS
CENTERS for MEDICARE & MEDICAID SERVICES

**DRIVE
ACCOUNTABLE CARE**



**ADVANCE
HEALTH EQUITY**



**SUPPORT
INNOVATION**



**ADDRESS
AFFORDABILITY**



**PARTNER TO
ACHIEVE SYSTEM
TRANSFORMATION**



2023 Accountable Care Organization – Realizing Equity, Access and Community Health (ACO-REACH)

- **Goal: Advance Health Equity to Bring the Benefits of Accountable Care to Underserved Communities.**
 - ACO REACH will test an innovative payment approach to better support care delivery and coordination for patients in underserved communities and will require that all model participants develop and implement a robust health equity plan to identify underserved communities and implement initiatives to measurably reduce health disparities within their beneficiary populations.



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 of¹:

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



91st – 100th Percentile
(Top Decile)

+\$30 PBPM Adjustment

51st – 90th Percentile
(Middle 4 Deciles)

No Adjustment

1st – 50th 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.

ADI USE IS WIDESPREAD, INCLUDING IN US FEDERAL POLICY

- NIH Dissemination of the ADI
- Industry Partnerships
- Professional Medical Societies
- Private Insurers
- State Medicaid Programs
- US Center for Medicare and Medicaid Services ACO-REACH Program

Examples:



TIPS TO REMEMBER

- The ADI is an extensively validated measure of the social exposome which links to a wide array of biological metrics and health outcomes.
- Individual-level social factors and exposome-level social factors are independently related to health outcomes. Both are important.
- Metrics of neighborhood disadvantage often reflect structural inequities—highly disadvantaged neighborhoods are not distributed equally.
- The Neighborhood Atlas is a freely available data democratization tool that provides customizable geographic images of block-group level ADI for anywhere within the US.





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
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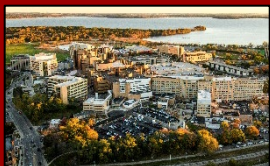
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