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

**Levels of Analyses**

**Environmental**
- Geographical and Political Factors
  - Structural Bias
  - Immigration
  - Criminalization
  - Residential Segregation
  - Urban/Rural
  - Toxins/Exposures

**Sociocultural**
- Cultural Factors
  - Values
  - Prejudice
  - Noms
  - Traditions
  - Religion
  - Collective Responses

**Behavioral**
- Coping Factors
  - Active Coping
  - Problem Solving
  - Stress Management
  - Cognitive Reframing
  - Emotional Regulation

**Biological**
- Physiological Indicators
  - Co-Morbidities
  - Cardiovascular
  - Sympathetic Nervous System
  - HPA Axis
  - Inflammation

**Genetic Stability**
- Telomeres
- Epigenetic Alteration
- Loss of Proteostasis

**Socioeconomic Factors**
- Education
- Income
- Wealth
- Occupation
- Limited English

**Social Factors**
- Institutional Racism
- Family Stress
- Financial Stress
- Occupational Stress
- Residential Stress
- Social Mobility
- Social Network

**Psychosocial Risk/Resilience**
- Social Support
- Discrimination
- Pessimism
- Optimism
- Control

**Health Care**
- Access
- Insurance
- Quality
- Literacy
- Numeracy

**Psychological Factors**
- Self Concepts
- Stigma
- Bias
- Loneliness
- Stereotypes

**Health Behaviors**
- Smoking
- Anger/Violence
- Alcohol/Drug
- Nutrition
- Physical Activity

**Cellular Function and Communication**
- Deregulated Nutrient Sensing
- Mitochondrial Dysfunction
- Cellular Senescence
- Cellular Stress Response
- Stem Cell Exhaustion
- Intercellular Communication

**Lifecourse Perspective**

**Hill, Perez-Stable, Anderson and Bernard, Ethnicity and Disease, 2015**
NIA HEALTH DISPARITIES FRAMEWORK

ENVIRONMENTAL

SOCIOCULTURAL

BEHAVIORAL

BIOLOGICAL

LIFE COURSE

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

*Ludwig et al, New England Journal of Medicine, 2011; Ludwig et al, Science; Many others
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

*Kind and Buckingham, *New England Journal of Medicine*, 2018
HIGHLY DISADVANTAGED NEIGHBORHOODS IN US

• More often in urban core and rural areas

*Kind et al, Annals of Internal Medicine, 2014; Kind and Buckingham, New England Journal of Medicine, 2018
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
NEIGHBORHOOD DISADVANTAGE AND CHOLESTEROL CONTROL

Cholesterol Control

Least Disadvantaged

Best Cholesterol

Most Disadvantaged

Worst Cholesterol

*Durfe et al, HSR, 2019
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

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

Hunt et al, JAMA-Neurology, 2020
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

Hunt et al, JAMA-Neurology, 2020
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.
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
• 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
Living in the most disadvantaged neighborhood decile was associated with increased odds of AD neuropathology
Life-course
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.
<table>
<thead>
<tr>
<th>ADRC</th>
<th>Participating Components</th>
<th>Site PI(s)</th>
<th>Site Co-I(s)</th>
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<tbody>
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<td>University of Wisconsin</td>
<td>BB/CC</td>
<td>Amy Kind, Barbara Bendlin (MPI)</td>
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<td>Banner Alzheimer’s Institute</td>
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<td>Richard Perrin</td>
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<td>Site</td>
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<td>Amyloid PET</td>
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<td>University of California, San Francisco</td>
<td>792</td>
<td>644</td>
<td>218</td>
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<td>University of Kansas</td>
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<td>University of Kentucky</td>
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<td>0</td>
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<td>University of Michigan ADC</td>
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<td>University of Pittsburgh</td>
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<td>Wake Forest University ADC</td>
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<td>516</td>
<td>121</td>
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<td>Washington University School of Medicine</td>
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<td>0</td>
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<td>Yale University ADRC</td>
<td>240</td>
<td>105</td>
<td>105</td>
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<tr>
<td><strong>Total</strong></td>
<td>7875</td>
<td>5155</td>
<td>1910</td>
</tr>
</tbody>
</table>

UW Ns (ADRC only) at time of submission:
- Number with T1-weighted imaging: 803
- Number with amyloid PET: 216
- Number with tau PET: 129
Table 3. Sample Size, from 22 ADRCs

<table>
<thead>
<tr>
<th>Description</th>
<th>n</th>
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</thead>
<tbody>
<tr>
<td>Active participants with UDS reported to NACC</td>
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<tr>
<td>(living cohort) with T1-weighted imaging</td>
<td>5728</td>
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<tr>
<td>with amyloid PET</td>
<td>1995</td>
</tr>
<tr>
<td>with tau PET</td>
<td>958</td>
</tr>
<tr>
<td>Brain bank decedents with NACC neuropathology form</td>
<td>10469</td>
</tr>
</tbody>
</table>

*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

<table>
<thead>
<tr>
<th>Health Behaviors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol/Substance abuse</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Co-morbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Heart disease</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Abnormal cholesterol</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Traumatic brain injury</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Individual Socioeconomic Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Income</td>
</tr>
<tr>
<td>Education</td>
</tr>
<tr>
<td>Occupation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Demographic Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race/Ethnicity</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Gender</td>
</tr>
</tbody>
</table>

Source: National Alzheimer’s Coordinating Center (NACC) data-collection forms
Elements in database have been highly conserved across data form versions

1 Form A1, Subject Demographics.
2 Form A5, Subject Health History
3 Form B1, Physical
4 Form D1, Clinician Diagnosis
5 Form D2, Clinician-Assessed Medical Conditions
6 Collected in proposed survey
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 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 EXPOSONEME

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.

*Kind NEJM 2018
ADI scores from within this state are ranked from lowest to highest, then divided into deciles (1-10).
ADI scores for the entire United States are ranked from lowest to highest, then divided into percentiles (1–100).
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
• 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.

*Text taken from CMS.gov official ACO-REACH materials at https://innovation.cms.gov/innovation-models/aco-reach
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:

- **Area Deprivation Index**
  - Area-level measure of *local socioeconomic factors correlated with medical disparities and underservice*
  - Percentile Score from 1-100
  - 25 Point Adjustment for Full or Partial Dual Eligibility

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

<table>
<thead>
<tr>
<th>Percentile Range</th>
<th>Adjustment</th>
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<tr>
<td>91&lt;sup&gt;st&lt;/sup&gt; – 100&lt;sup&gt;th&lt;/sup&gt; Percentile (Top Decile)</td>
<td>+$30 PBPM Adjustment</td>
</tr>
<tr>
<td>51&lt;sup&gt;st&lt;/sup&gt; – 90&lt;sup&gt;th&lt;/sup&gt; Percentile (Middle 4 Deciles)</td>
<td>No Adjustment</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; – 50&lt;sup&gt;th&lt;/sup&gt; Percentile (Bottom 5 Deciles)</td>
<td>-$6 PBPM Adjustment</td>
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</table>

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.

*2023 ACO Realizing Equity, Access, and Community Health (REACH) Model [https://innovation.cms.gov/media/document/aco-reach-fin-meth-webinar-slides]*
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:
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.
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<td>Washington University in St. Louis</td>
<td>BB Only</td>
<td>Cyrus A. Raji</td>
<td>Richard Perrin</td>
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<td>Yale University</td>
<td>BB/CC</td>
<td>Carmen Carrión</td>
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Robert Golden, MD
Jon Audhya, PhD
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NIA Leadership, Program Officers and Staff

And many, many others . . .

Funding
NIA R01 AG070883 (Kind PI; Bendlin MPI)
NIA supplement 3 R01 AG070883-02 (PIs: Kind/Bendlin)
NIA RF1AG057784 (Kind PI; Bendlin MPI)
NIMHD R01MD010243-01 (Kind PI)
NIA F31AG062116 (PI: Hunt)
NIA P30AG062715 (Asthana PI)
NIA 1P30-AG062429-01 (Brewer PI)
NIA R01 AG077628 (Grill PI; Gillen/Kind MPI)

The NACC database is funded by NIA/NIH Grant U24 AG072122. Data are contributed by the NIA-funded ADRCs: P30 AG062429 (PI James Brewer, MD, PhD), P30 AG066468 (PI Oscar Lopez, MD), P30 AG062421 (PI Bradley Hyman, MD, PhD), P30 AG066509 (PI Thomas Grabowski, MD), P30 AG066514 (PI Mary Sano, PhD), P30 AG066530 (PI Helena Chui, MD), P30 AG066507 (PI Marilyn Albert, PhD), P30 AG066444 (PI John Morris, MD), P30 AG066518 (PI Jeffrey Kaye, MD), P30 AG066512 (PI Thomas Wisniewski, MD), P30 AG066462 (PI Scott Small, MD), P30 AG072979 (PI David Wolk, MD), P30 AG072972 (PI Charles DeCarli, MD), P30 AG072976 (PI Andrew Saykin, PsyD), P30 AG072975 (PI David Bennett, MD), P30 AG072978 (PI Neil Kowall, MD), P30 AG072977 (PI Robert Vassar, PhD), P30 AG066519 (PI Frank LaFerla, PhD), P30 AG062677 (PI Ronald Petersen, MD, PhD), P30 AG079280 (PI Eric Reiman, MD), P30 AG062422 (PI Gil Rabinovici, MD), P30 AG066511 (PI Allan Levey, MD, PhD), P30 AG072946 (PI Linda Van Eldik, PhD), P30 AG062715 (PI Sanjay Asthana, MD, FRCP), P30 AG072973 (PI Russell Swerdlow, MD), P30 AG066506 (PI Todd Golde, MD, PhD), P30 AG066508 (PI Stephen Strittmatter, MD, PhD), P30 AG066515 (PI Victor Henderson, MD, MS), P30 AG072947 (PI Suzanne Craft, PhD), P30 AG072931 (PI Henry Paulson, MD, PhD), P30 AG066546 (PI Sudha Seshadri, MD), P30 AG068024 (PI Erik Roberson, MD, PhD), P20 AG068053 (PI Justin Miller, PhD), P20 AG068077 (PI Gary Rosenberg, MD), P20 AG068082 (PI Angela Jefferson, PhD), P30 AG072958 (PI Heather Whitson, MD), P30 AG072959 (PI James Leverenz, MD).