EXPOSOME as a Stressor in the Study of Resilience

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

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University of Wisconsin School of Medicine and Public Health
FUNDING DISCLOSURES

NIH/National Institute on Aging

NIH/National Institute on Minority Health and Health Disparities

Alzheimer's Association
EXPOSOME

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

Exposome

- Factors external to the biological individual
- Diverse factors ranging from microbiome to structural inequity
NIH HEALTH DISPARITIES FRAMEWORK

**Levels of Analyses**

**Environmental**
- Geographical and Political Factors
  - Structural Bias
  - Immigration/Documentation
  - 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

**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

**Genetic Stability**
- Telomere Abolition
- Epigenetic Alteration
- Loss of Proteostasis

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

**Psychological Factors**
- 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**
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
*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
• Link exposures to biological process

• Expand the potential of existing programs in completely new ways
• 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

Powell et al, JAMA-Open, 2020
Living in the most disadvantaged neighborhood decile was associated with increased odds of AD neuropathology
• 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

*Woelfle et al, Nature Chemistry 2011; Boulware et al, 2020; Kind et al, 2018*
• 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
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

A health system that achieves equitable outcomes through high quality, affordable, person-centered care.
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.
- **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

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<thead>
<tr>
<th>Percentile Range</th>
<th>Adjustment</th>
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<tr>
<td>1st – 50th Percentile</td>
<td>-$6 PBPM Adjustment</td>
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<td>51st – 90th Percentile</td>
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<td>91st – 100th Percentile</td>
<td>+$30 PBPM Adjustment</td>
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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 = $
**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
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<tr>
<th>ADRC</th>
<th>Participating Components</th>
<th>Site PI(s)</th>
<th>Site Co-I(s)</th>
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<td>Amy Kind, Barbara Bendlin (MPI)</td>
<td>Vikas Singh, Menggang Yu</td>
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<td>Banner Alzheimer’s Institute</td>
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