EXPOSOME AS A STRESSOR

October 12, 2022

Overview of the Resilience World – State of the Science
AGS/NIA R13 Bench-to-Bedside Conference Series

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

ENVIRONMENTAL

SOCIOCULTURAL

BEHAVIORAL

BIOLOGICAL

LIFE COURSE

**Hill, Perez-Stable, Anderson and Bernard, *Ethnicity and Disease*, 2015**
Conditions in the environments in which people are born, live, work, play, worship, and age that impact a wide array of health, functioning, quality-of-life outcomes and risks.*


*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.*
**NIH HEALTH DISPARITIES PRIORITY POPULATIONS**

- Hispanics/Latinos
- American Indians/Alaskan Natives
- Blacks/African Americans
- Asian Americans
- Native Hawaiians and Other Pacific Islanders
- Socioeconomically Disadvantaged Populations
- Rural Populations
- Disability Populations
- Sexual and Gender Minorities
- Others

**Intersectionality**

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**Hill, Perez-Stable, Anderson and Bernard, Ethnicity and Disease, 2015; https://www.nia.nih.gov/research/osp-framework**
1. Quantifying exposures

- Rigor, reproducibility, validity, generalizability, harmonizability
- Single time point (easier)
- Life course aligned (harder)

2. Linking exposome to biology

- Methodological considerations
- Infrastructure (technical, legal, administrative)
- Multi-disciplinary expertise

3. Reporting for a diverse array of stakeholders
1. Quantifying exposures

- Rigor, reproducibility, validity, generalizability, harmonizability
- Single time point (easier)
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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®*

- Similar metrics available in most countries

- “Microtargeting”

*Kind and Buckingham, New England Journal of Medicine, 2018
Ethical Allocation of COVID Therapies
  • Example: Pennsylvania

COVID Vaccine Resource Targeting
  • Example: Alaska

Efficiently Aligning Health System Resources to Needs
  • Example: US Centers for Medicare and Medicaid Services (CMS)
    • 2022 ACO Realizing Equity, Access, and Community Health (REACH) Model

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.

<table>
<thead>
<tr>
<th>Percentile Score from 1-100</th>
<th>25 Point Adjustment for Full or Partial Dual Eligibility</th>
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<tbody>
<tr>
<td>91st – 100th Percentile (Top Decile)</td>
<td>+$30 PBPM Adjustment</td>
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<tr>
<td>51st – 90th Percentile (Middle 4 Deciles)</td>
<td>No Adjustment</td>
</tr>
<tr>
<td>1st – 50th Percentile (Bottom 5 Deciles)</td>
<td>-$6 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]
EXAMINING THE EXPOSOME

1. Quantifying exposures
   • Rigor, reproducibility, validity, generalizability, harmonizability
   • Single time point (easier)
   • Life course aligned (harder)

2. Linking exposome to biology
   • Methodological considerations
   • Infrastructure (technical, legal, administrative)
   • Multidisciplinary expertise

3. Reporting for a diverse array of stakeholders
SOCIAL-BIOLOGICAL PHENOTYPING

- Facilitate mechanistic health disparities research
- Link exposures to biological process
- Expand the potential of existing programs in completely new ways

Exposome


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EXAMINING THE EXPOSOME

1. Quantifying exposures
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3. Reporting for a diverse array of stakeholders
- 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
- Neuropathologic features drawn from National Alzheimer's Coordinating Center and autopsy reports
Living in the most disadvantaged neighborhood decile was associated increased odds of AD neuropathology
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.
• Multi-site Protected Health Information (PHI) is required for many disparities aligned life-course exposome assessments

• Requires high-security, HIPPA compliant administrative, legal and cyber infrastructure

• Substantial undertaking
**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**
<table>
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<tr>
<th>ADRC</th>
<th>Participating Components*</th>
<th>Site PI</th>
<th>Site Co-I</th>
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<tr>
<td>University of Wisconsin</td>
<td>BB/CC</td>
<td>Amy Kind/Barb Bendlin (MPI)</td>
<td>Vikas Singh, Menggang Yu</td>
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<td>Banner Alzheimer’s Institute</td>
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<td>Eric Reiman</td>
<td>Thomas Beach, Kwei Chen</td>
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<td>Indiana University</td>
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<td>Shannon Risacher</td>
<td>Andrew Saykin, Liana Apostolova</td>
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