GEOGRAPHIC DISPARITIES: How Location Affects Brain Health

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US Department of Veterans Affairs
BRAIN HEALTH IS NOT DISTRIBUTED EQUALLY
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English Longitudinal Study of Ageing
• 68% increase dementia incidence in those with lowest wealth independent of education and other factors

Chinese Longitudinal Healthy Longevity Survey
• Poverty associated with 34% increase in incident cognitive impairment

Cadar et al, JAMA Psychiatry, 2018; Chen et al, 2019
Brain health is not distributed equally, lowest among Asian-Americans, and intermediate among Latinos, Pacific Islanders, and whites. These inequalities in dementia incidence were observed among women and men and across all ages. Adjustment for comorbidities and health care utilization did not substantially explain differences in dementia incidence. Estimated cumulative incidence of dementia over 25 years was high for all groups. This study provides the most comprehensive view of racial/ethnic inequalities in dementia risk to date.

Prior evidence on racial/ethnic disparities in dementia incidence has relied heavily on comparisons of dementia rates across studies. Because dementia rates are extremely sensitive to diagnostic criteria adopted in each study and geographic patterns may also cause differences across studies, it has been difficult to establish the magnitude of racial/ethnic inequalities in dementia incidence. The results of the present study substantiate findings from prior studies with dementia incidence estimates for African-Americans, Mexican Americans, and Japanese Americans. Most research on disparities in dementia incidence has focused on African-Americans and whites. These studies suggest dementia risk is up to twice as high among African-Americans compared with whites. African-Americans experienced the highest dementia rates of the racial/ethnic groups included in this study and had approximately 40% higher dementia risk compared with whites, which is more modest than the estimated disparity in some prior studies.

Among Latinos, prior studies suggest dementia risk differs between Latino subgroups, with elevated risk among Caribbean Latinos in New York City but not among Mexican Americans in California compared with whites. Evidence from Hispanic/Latino Community Health Study/Study of Latinos (HCHS/SOL) provides additional evidence that dementia risk likely varies markedly across Latino

Table 2

<table>
<thead>
<tr>
<th>Race/ethnicity</th>
<th>Events</th>
<th>Person-years</th>
<th>Age-adjusted incidence rate per 1000 person-years (95% CI)</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Model 1</td>
<td>Model 2</td>
</tr>
<tr>
<td>African-American</td>
<td>4942</td>
<td>157,118</td>
<td>26.60 (25.83–27.37)</td>
<td>1.73 (1.66–1.81)</td>
</tr>
<tr>
<td>American Indian and Alaska Native</td>
<td>1224</td>
<td>41,182</td>
<td>22.18 (20.85–23.52)</td>
<td>1.43 (1.34–1.52)</td>
</tr>
<tr>
<td>Latino</td>
<td>4371</td>
<td>195,686</td>
<td>19.59 (18.97–20.20)</td>
<td>1.29 (1.24–1.35)</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>61</td>
<td>3246</td>
<td>19.63 (14.51–24.75)</td>
<td>1.26 (0.98–1.63)</td>
</tr>
<tr>
<td>White</td>
<td>45,110</td>
<td>1,750,252</td>
<td>19.35 (19.16–19.54)</td>
<td>1.25 (1.21–1.30)</td>
</tr>
<tr>
<td>Asian-American</td>
<td>3847</td>
<td>224,120</td>
<td>15.24 (14.73–15.74)</td>
<td>1.00 (ref)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; ref, reference.

NOTE. Age-adjusted dementia incidence rates use 2000 US Census as standard. Hazard ratios for dementia are from Cox proportional hazards models. Model 1: adjusted for age (as timescale) and sex; model 2: model 1 health care utilization (/C21 health care visit per year); and model 3: model 2 depression, diabetes, hypertension, stroke, and cardiovascular disease.

Fig. 2. Dementia incidence rates per 1000 person-years by age and race-ethnicity, 2000–2013.
WHAT DRIVES DISPARITIES IN ALZHEIMER’S DISEASE?
Whenever Possible, Research Should Align Towards Action

Treatments, Interventions and Policy
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

**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*

INDIVIDUAL LEVEL
SOCIAL DETERMINANTS OF HEALTH
CONTEXTUAL LEVEL
SOCIAL DETERMINANTS OF HEALTH
IMPORTANCE OF NEIGHBORHOOD
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*
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.*
METRICS OF NEIGHBORHOOD DISADVANTAGE

• **Quantifiable**
  - Uses measures of social determinants of health in a discrete geographic area (typically 500-1500 persons)

• **Robust**
  - Metrics available in many countries
  - Privacy-compliant

• **Actionable in the ‘Real World’**
  - Actionable at community, research and policy levels
  - Guide outreach through mapping
  - Can be used for: resource targeting, program eligibility, and statistical adjustment

* Jarman et al, BMJ 1983
AREA DEPRIVATION INDEX (ADI)

- Originally created by Health Resources and Services Administration in 1990s and employed at the county level

- Education, employment, housing-quality and poverty

- Required updates for modern use and geo-alignment with European policy indices

- UW team updated to more recent and relevant data sources and refined down to census block-group level (i.e. “neighborhood” ~ 1,500 persons) to more precisely measure exposure. NIH funding to validate across US Milwaukee County
CHARACTERISTICS OF HIGHLY DISADVANTAGED NEIGHBORHOODS IN US

• More often in **urban core** and **rural** areas

• Older adults residing in US neighborhoods identify as*:

*Kind et al, Annals of Internal Medicine, 2014
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 Zuelsdorf, 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
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.
NEIGHBORHOOD DISADVANTAGE AND AD 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
- Neuropathologic features drawn from National Alzheimer's Coordinating Center and autopsy reports

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

Powell et al, JAMA-Open, 2020
Association of Neighborhood-Level Disadvantage With Alzheimer Disease Neuropathology

W. Ryan Powell, PhD; William R. Buckingham, PhD; Jamie L. Larson, PhD; Leigia 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)
Residential History: Geospatial targeting of exposure data across the life-course

- Public-data based construction (archival, genealogical and historical methods)
- 73% of all person years discoverable in pilot study (n=213)
RESIDING IN A HIGHLY DISADVANTAGED NEIGHBORHOOD IS LINKED TO:

- Epigenetic age acceleration as measured by methylation-based markers of aging (Lawrence et al, JAMA-Open, 2020)
- Higher risk of post-operative delirium (Arias et al, JAGS, 2020)
- Later dementia diagnosis and less comprehensive diagnostic evaluation (Tsoy et al, JAMA-Neurology, 2021)
- Greater challenges navigating dementia care and supports (Gilmore-Bykovskyi et al, “A Better Way” Opportunities to strengthen supports for people with dementia in the greater Detroit area, 2020*; others)
- Many other factors

Pathways to Brain Health

Cholesterol Control

*Durfey et al, HSR, 2019*
• Persons residing in the most disadvantaged neighborhoods are often poorly represented in research

• Neighborhood disadvantage should be collected as a standard demographic characteristic in all research protocols

• Research on best practices for recruitment and retention of individuals residing in disadvantaged neighborhoods is needed

*Grill et al, JPAD 2021; Powell et al, JAMA-Open, 2020; Berman et al, JAMA-Cardiology, 2021; others
All ADI groups were observed to have similar willingness to participate in research studies.
Open Science is the movement to make scientific research and its dissemination 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*
THE NEIGHBORHOOD ATLAS
www.neighborhoodatlas.medicine.wisc.edu

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

*Kind NEJM 2018
THE NEIGHBORHOOD ATLAS
www.neighborhoodatlas.medicine.wisc.edu

*Kind NEJM 2018
REAL WORLD ACTION

- Maryland Health Services and Cost Review Commission
- Multiple US Health Systems: Resource and Service Allocation
- COVID Treatment and Vaccine Allocations
- Many Others

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. Information in this


*Kind NEJM 2018
THE NEIGHBORHOODS STUDY  
(R01AG070883; PI KIND, MPI BENDLIN)

- Novel collaborative multi-site initiative to 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
- Funded by the National Institute on Aging
CONCLUSIONS

• Whenever possible research search should be aligned towards action and real-world intervention

• Social determinants of health, including neighborhood disadvantage, drive many health disparities and often reflect a society’s legacy of structural inequity

• Neighborhood disadvantage should be collected as a standard demographic characteristic in all research protocols

• Open science, data democratization should be embraced as a step towards real world change
Neighborhood Atlas is free and open to all!

Many ADI-like metrics exist for other countries

*Kind NEJM 2018*
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