GEOGRAPHIC DISPARITIES: How Location Affects Brain Health

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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









WHAT DRIVES DISPARITIES IN ALZHEIMER'S DISEASE?





Whenever Possible, Research Should Align Towards Action

Treatments, Interventions and Policy





MECHANISTIC APPROACH

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

SOCIAL DETERMINANTS OF HEALTH

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*

*Office of Disease Prevention and Health Promotion. Healthy People 2020: Social Determinants of Health. <u>https://www.healthypeople.gov/2020/topics-objectives/topic/social-determinants-of-health</u>. Accessed 10/5/2018



INDIVIDUAL LEVEL SOCIAL DETERMINANTS OF HEALTH



CONTEXTUAL LEVEL SOCIAL DETERMINANTS OF HEALTH



IMPORTANCE OF NEIGHBORHOOD



MOVING TO OPPORTUNITY STUDY



*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

<u>Quantifiable</u>

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

• <u>Robust</u>

- 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
- <u>UW team updated</u> to more recent and relevant <u>data</u> <u>sources</u> and <u>refined</u> down <u>to census block-group level</u> (i.e. "neighborhood" ~ 1,500 persons) to more precisely measure exposure. NIH funding to validate across US



CHARACTERISTICS OF HIGHLY DISADVANTAGED NEIGHBORHOODS IN US

 More often in <u>urban core</u> and <u>rural</u> areas



RACE AND NEIGHBORHOOD DISADVANTAGE

• Older adults residing in US neighborhoods identify as*:





NEIGHBORHOOD DISADVANTAGE AND BRAIN HEALTH





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

JAMA Neurology | Original Investigation

Association of Neighborhood-Level Disadvantage With Cerebral and Hippocampal Volume

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Hunt et al, JAMA-Neurology, 2020



Figure 2 Association Between Neighborhood-Level Disadvantage and Longitudinal Cognitive Trajectories



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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. Koscik, Megan Zuelsdorff, Lindsay R. Clark, Carey E Gleason, Menggang Yu, Ozioma Okonkwo, Sterling C. Johnson Sanjay Asthana, Barbara B. Bendlin, Amy J.H. Kind

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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 disadvan lines, n = 582) and 20% most disadvantage (red lines, n = 19). Participants from the most highly disadvantaged neighborhoods exhibited significar decline in PACC-R and TMT-B than participants from less disadvantaged neighborhoods, but showed no difference in decline of Story Memory Dela (SM-D) or Rey Auditory Verbal Learning Test, total trials 1–5 (RAVLT-L). Unadjusted p values for age2:neighborhood disadvantage interaction terms are displayed on plots for each cognitive test: ns p > 0.05, *p < 0.05, ***p < 0.001.

Hunt et al, Neurology, 2021

NEIGHBORHOOD DISADVANTAGE AND AD NEUROPATHOLOGY





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- 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





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Original Investigation | Public Health Association of Neighborhood-Level Disadvantage With Alzheimer Disease Neuropathology

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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 increased odds of AD neuropathology



LIFE COURSE EXPOSOME IN BRAIN BANK DECEDENTS

<u>Residential History</u>: 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)





LIFE COURSE

© Preliminary data, Kind et al, 2020

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)
- Cognitive function (Lang et al, JAGS 2008; Al Hazzouri et al, Am J Epi, 2011; Wight et al, Am J Epi, 2006; Zuelsdorff et al, Alz Dementia 2020) and decline (Sheffield et al, Am J Epi, 2009; Hunt et al, Neurology, 2021)
- 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



*https://supportstudy.nursing.wisc.edu/wp-content/uploads/sites/906/2020/12/Detroit-Report-2020.pdf

Pathways to Brain Health



NEIGHBORHOOD DISADVANTAGE AND RESEARCH INCLUSION

- 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

NEIGHBORHOOD DISADVANTAGE AND RECRUITMENT SCIENCE



Open Science is the movement to make scientific research and its dissemination accessible to <u>all levels</u> 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.



THE NEIGHBORHOOD ATLAS

www.neighborhoodatlas.medicine.wisc.edu



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THE NEIGHBORHOOD ATLAS

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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





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

THE NEIGHBORHOOD ATLAS

www.neighborhoodatlas.medicine.wisc.edu



Neighborhood Atlas is free and open to all!

Many ADI-like metrics exist for other countries





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