Target trial emulation for the study of social determinants in dementia research

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FUNDAMENTAL FACTORS: Ethnicity, Gender, Age, Race, Disability Status, Identity* **Levels of **Environmental** Sociocultural **Behavioral Biological** Analyses Geographical and **Physiological Cultural Factors Coping Factors Political Factors** Indicators Values Active Coping Structural Bias Co-Morbidities Prejudice Problem Solving Immigration/Documentation Cardiovascular Norms Stress Management Criminalization Sympathetic Nervous System Traditions Cognitive Reframing Residential Segregation **HPA Axis** Religion **Emotional Regulation** Urban/Rural Inflammation Collective Responses Toxins/Exposures Socioeconomic Social Factors **Psychosocial Genetic Stability** Institutional Racism **Factors** Risk/Resilience Family Stress Telomere Attrition Education Social Support Financial Stress **Epigenetic Alteration** Income/Wealth Discrimination Occupational Stress Loss of Proteostasis Occupation Pessimism Residential Stress Limited English Optimism Social Mobility Control Social Network **Cellular Function Psychological Health Care** And Communication **Health Behaviors Factors** Access Smoking Deregulated Nutrient Sensing Self Concepts Anger/Violence Mitochondrial Dysfunction Insurance Stigma Cellular Senescence Quality Alcohol/Drug Bias Cellular Stress Response Nutrition Literacy Loneliness Stem Cell Exhaustion Physical Activity Numeracy Stereotypes Intercellular Communication Lifecourse Perspective

Hill et al. Ethnicity and disease. 2015

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- Double blind assignment

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- Time points aligned by design:
 - Eligibility criteria
 - Treatment assignment (randomization)
 - Follow-up starts

Target trial emulation framework

- Estimand
- Eligibility criteria
- Treatment strategies
- Outcome definition
- Length of follow-up

Randomized trial

Observational study

- Estimand
- Eligibility criteria
- Treatment strategies
- · Outcome definition
- Length of follow-up

- Assumptions
- Statistical methods

Causal effect

Research question

What is the effect of early-life racial residencial segregation in 1940, measured by the dissimilarity index, on later-life memory decline in US population, represented by the Health and Retirement Study (HRS)?



Work led by Taylor Mobley (UCLA, Mayeda's research lab)

Section	Target trial protocol	Emulation using observational data
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Causal contrast	Intention-to-treat	Same

Estimand

$$E[Y_{1998}^{a=1}] - E[Y_{1998}^{a=0}]$$

Estimand

$$E[Y_{1998}^{a=1}] - E[Y_{1998}^{a=0}]$$

$$E[Y_{2000}^{a=1,c=0}] - [Y_{2000}^{a=0,c=0}]$$

• • • •

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• • • •

$$E[Y_{2018}^{a=1,c=0}] - E[Y_{2018}^{a=0,c=0}]$$

Identifiability assumptions

- Consistency
- Exchangeability
- Positivity
- No interference

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 - Is the dissimilarity index a good a proxy of all the racist policies that resulted in residential segregation?
 - What is a relevant intervention on the dissimilarity index, reducing under certain threshold or by certain value?

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- At best, this hypothetical intervention would be reducing the impact of all the racist policies that influenced residential segregation, determined by the frequency of these in the studied population.
- It requires deep interdisciplinary dialogue, and only with subject matter expertise we can inform how well we feel about satisfying this assumption.

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- Since there are many factors that can influence residential segregation, whatever we adjust for is not accounted into how we would intervene.
- There is a moral and ethical value in terms of what variables to adjust. "Non-allowable" sources are considered unfair and contribute to disparities (*Jackson J. Epidemiology. 2021*).

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- We can use the target trial framework even if the intervention of interest is not measured (or exists!).
- Having a better design can already prevent some sources of bias, and help us detect other sources that could be prevented (or quantified) through the analytic strategies.
- It is a dynamic process, since it requires a deep understanding of the data sources and a constant check that the causal contrasts and subsequent results are informative.

To search for all the refutable consequences of a hypothesis demands highly imaginative thinking. Imagination is needed to arrive at the hypothesis in the first place, let alone to suggest rigorous tests for it.

(Carol Buck)

Thank you, Gracias!

Mayeda Research Group

Study Contributors:

- Elizabeth Rose Mayeda
- Joan Casey
- Taylor Mobley
- Kara Rudolph
- Nick Williams
- Heather McBrien
- Milo Gordon

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Come work with us!

Dementia Epidemiology Equity and Methods Training Program

- María Corrada, UC Irvine
- Paola Gilsanz, Kaiser Permanente Northern California
- Maria Glymour, Boston University
- Elizabeth Rose Mayeda, UCLA
- Rachel Whitmer, UC Davis



Themes:

- Eliminating dementia disparities
- Methods for dementia and cognitive aging research
- Data harmonization and triangulation
- Determinants of health in the oldest-old
- Lifecourse determinants of health
- Neuroimaging







